UNIVERSITAT DE BARCELONA

Innovation on Nanoscience:

Processes and Ecosystems of Innovation with a multi-KET approach to foster Technology Transfer and Commercialization of Nanotechnologies in the Field of Healthcare

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INNOVATION ON NANOSCIENCE:

PROCESSES AND ECOSYSTEMS OF INNOVATION WITH A MULTI-KET APPROACH TO FOSTER TECHNOLOGY TRANSFER AND COMMERCIALIZATION OF NANOTECHNOLOGIES IN THE FIELD OF HEALTHCARE.

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"Ser más para servir mejor"

— San Ignacio de Loyola

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"*Cuando se viaja en pos de un objetivo, es muy importante prestar atención al Camino. El Camino es el que nos enseña la mejor forma de llegar y nos enriquece mientras lo estamos cruzando*" (Paulo Coelho, *El Peregrino de Compostela*).

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ABSTRACT

Transferring nanotechnology into marketable products and services is still considered a major challenge. In Europe, this issue has been identified as a weakness, not only for nanotechnology, but also for the other five Key Enabling Technologies (KETs), strategic for the economic growth of the region. In this regard, the current European Funding Programme Horizon 2020 is making great efforts with their action lines in order to prioritize the industrial implementation of KETs, and in this manner, address major economic and societal needs. This initiative is also fostering the cross-fertilization of KETs, since it has been determined that the sum of individual technologies increases the potential for innovation, optimizes technological development, and allows the creation of new markets. This thesis has been developed on the basis of this scenario. The aim is to analyse innovation and technology transfer challenges for the successful commercialization of nanotechnologies by emphasizing the process of cross-fertilization of KETs. The research is focused on healthcare due to the great impact that nano-scale is having on this field. For this reason, the present work has considered two approaches: from a technological perspective and from a management perspective. The analysis is comprised of a state-of-the-art and theoretical framework review, followed by a multiple case-study approach where several nano-enabled sensor-based devices are analysed at diverse levels of technological maturity. In addition, an empirical study of European nano-related innovation projects was undertaken in order to determine which projects' characteristics are influencing the creation of technological diversity; a critical element for the long-term success of an emergent technology. Finally, project leaders were interviewed in order to gain insights about the managerial strategies that are boosting the process of cross-fertilization of KETs. The outcomes of this thesis have sought to contribute to the analysis of the successful transference and commercialization of multi-KETs in the field of nanotechnologies applied to healthcare by understanding the processes and ecosystems of innovation. Accordingly, it is aimed to contribute to the reduction of the gap between research and the marketplace and to expand the knowledge of current interest regarding innovation ecosystems of emergent technologies, regional systems of innovation and strategic innovation management.

Key words: Nanotechnology, nanomedicine, Key Enabling Technologies, technology transfer, innovation management.

EXTRACTE

La transferència de productes i serveis basats en la nanotecnologia representa un gran repte. A Europa, aquest fet ha estat identificat com a punt dèbil, no només per a les nanotecnologies si no també per a les altres cinc tecnologies facilitadores transversales (KETs per les seves sigles en anglès), considerades estratègiques pel creixement econòmic de la regió. En aquest sentit, l'actual programa marc Europeu Horitzó 2020 està redirigint les seves línies d'acció per a prioritzar la implementació de les KETs i, d'aquesta manera, poder fer front a les necessitats econòmiques i socials més imperatives d'Europa. Aquesta iniciativa també pretén fomentar l'intercanvi (fertilització creuada) de les KETs, ja que s'ha establert que la suma de tecnologies individuals incrementa el potencial d'innovació, optimitza el desenvolupament de tecnologies i permet la creació de nous mercats. Sobre aquesta base es desenvolupa aquest treball d'investigació, el qual té la finalitat d'analitzar els reptes relacionats amb la innovació i la transferència tecnològica per a assolir amb èxit la comercialització de les nanotecnologies, posant de relleu el procés de fertilització creuada de les KETs en el camp de la salut. Amb aquesta finalitat, s'han considerat dues aproximacions: d'una banda una perspectiva tecnològica i, de l'altra, una perspectiva de gestió de la innovació. En aquest sentit, la tesis comprèn una revisió de l'estat de l'art i dels fonaments teòrics relacionats amb la innovació nanotecnològica, seguit d'un anàlisi d'estudi de casos de dispositius basats en sensors nano-habilitats en diferents nivells de maduresa tecnològica. Addicionalment, es desenvolupa un estudi empíric de projectes Europeus relacionats amb la innovació nanotecnològica en el camp de la salut amb l'objectiu de determinar quines característiques dels projectes estan influint en la creació de diversitat tecnològica, la qual és un element fonamental per a l'èxit a llarg termini de les tecnologies emergents. Finalment, s'inclou una entrevista a diversos directors dels projectes esmentats amb l'objectiu de conèixer les estratègies de gestió que fomenten la fertilització creuada de les KETs. Els resultats obtinguts fan aportacions per l'anàlisi i identificació dels reptes que cal afrontar per a una favorable transferència i comercialització de les nanotecnologies multi-KET en el camp de la salut mitjançant la comprensió dels processos i ecosistemes d'innovació i, d'aquesta manera, contribuir a la reducció de la separació entre el laboratori i el mercat. Finalment també es pretén ampliar el coneixement sobre temàtiques d'interès actual respecte els ecosistemes d'innovació de les tecnologies emergents, els sistemes regionals d'innovació i la gestió estratègica de la innovació tecnològica.

Descriptors: Nanotecnologia, nanomedicina, Tecnologies Facilitadores Clau, transferència de tecnologia, gestió de la innovació.

RESUMEN

La transferencia de productos y servicios basados en nanotecnología representa un gran reto. En Europa, este hecho ha sido identificado como un punto débil, no sólo para las nanotecnologías sino también para las otras cinco Tecnologías Facilitadoras Esenciales (TFE), consideradas estratégicas para el crecimiento económico de la región. En este sentido, el actual Programa Marco de la Unión Europea Horizonte 2020, está re-dirigiendo sus líneas de acción para priorizar la implementación de las TFEs, y de esta manera, poder hacer frente a las necesidades económicas y sociales más imperativas de Europa. Ésta iniciativa también pretende fomentar la fertilización cruzada de las TFEs, dado que se ha establecido que la suma de tecnologías individuales incrementa el potencial de innovación, optimiza el desarrollo de tecnologías y permite la creación de nuevos mercados. Sobre la base de este escenario se desarrolla el presente trabajo de investigación, el cual tiene la finalidad de analizar los retos relacionados con la innovación y la transferencia tecnológica para alcanzar la comercialización exitosa de las nanotecnologías, poniendo de manifiesto el proceso de la fertilización cruzada de las TFEs en el campo de la salud. Con esta finalidad, se han considerado dos aproximaciones: por un lado una perspectiva tecnológica y por el otro, una perspectiva de gestión de la innovación. En este sentido, la tesis comprende una revisión del estado del arte y los fundamentos teóricos relacionados con la innovación nanotecnológica, seguido de un análisis de estudios de caso de dispositivos basados en sensores nano-habilitados en diferentes niveles de madurez tecnológica. Adicionalmente, se desarrolla un estudio empírico de proyectos Europeos relacionados con innovación nanotecnológica en el campo de la salud con el objetivo de determinar qué características de los proyectos están influyendo en la creación de diversidad tecnológica, elemento fundamental para el éxito a largo plazo de tecnologías emergentes. Se incluye además una entrevista a diversos directores de los proyectos mencionados con el objetivo de conocer las estrategias de gestión que fomentan el proceso de fertilización cruzada de las TFEs. Los resultados obtenidos aportan al análisis e identificación de los retos a ser superados para alcanzar una transferencia favorable y comercialización de las multi-TFE en el campo de las nanotecnologías aplicadas a la salud mediante la comprensión de los procesos y los ecosistemas de innovación, y de este modo, contribuir a la reducción de la brecha entre el laboratorio y el mercado. Finalmente, también se pretende ampliar el conocimiento en temáticas de actual interés al respecto de los ecosistemas de innovación de las tecnologías emergentes, los sistemas regionales de innovación y la gestión estratégica de la innovación tecnológica.

Descriptores: Nanotecnología, nanomedicina, Tecnologías Facilitadoras Esenciales, transferencia de tecnología, gestión de la innovación.

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Acronyms

BIO	Biotechnology-based industrial processes driving competitiveness and sustainability
BN	Exploiting the cross-sector potential of nanotechnologies and advanced materials to drive competitiveness and sustainability
CAGR	Compound Annual Growth rate
CC	Clustering coefficient
CE	Capillary electrophoresis
CIP	Competitiveness and Innovation Framework Programme
CMOS	Complementary meta-oxide-semiconductor microelectronics
DEP	Dielectrophoresis
Dim1	Dimension 1 in Multiple Correspondance Analysis
Dim2	Dimension 2 in Multiple Correspondance Analysis
DNA	Deoxyribonucleic acid
EC	European Commission
EIT	European Institute of Innovation and Technology
ELISA	Enzyme-linked imunosorbent assay
EPO	European Patent Office
EU	European Union
FP	Framework Programme
GDP	Gross Domestic Product
H2020	Horizon 2020 Framework Programme
HES	Higher or Secondary Education Establishments
IA	Impedance analysis
ICT	Information and Communications Technology
IP	Intellectual Property
IPC	International Patent Classification
KET	Key Enabling Technology
LDA	Latent Dirichlet Allocation
LEIT	Leadership and Industrial Technologies
LOC	Lab-on-a-chip
MCA	Multiple Correspondence Analysis

MEMS	Micro-electrochemical systems
MS	Mass spectrometry
NG	Bridging the gap between nanotechnology research and markets
NM	Nanotechnology and advanced materials for more effective healthcare
NNI	National Nanotechnology Initiative
NSI	National Systems of Innovation
OECD	Organisation for Economic Cooperation and Development
OI	Open innovation
OTH	Other organisations
PCR	Polimerase chain reaction
PI	Principal investigator
PM	Project management
POC	Point-of-care
PPP	Purchaising Power Parity
PRC	Private for-profit entities
PUB	Public bodies
R&D	Reseach and develepment
REC	Research Organisations
RSI	Regional Systems of Innovation
SI	Sistems of Innovation
SMEs	Small and Medium size enterprises
SSI	Sectorial Systems of Innovation
STPs	Scientific and Technological Parks
TFEs	Tecnologías Facilitadoras Escenciales
TRL	Technology Readyness Level
TTO	Technology Transfer Office
UGI	University-Government-Industry association
UK	United Kingdom
US	United States of America
USPTO	US Patent and Trademark Office

Introduction

Nanotechnology is an important and very promising field of research since it plays a significant role in economic, social and regional growth. This technology has been considered the greatest impulse of technological and industrial development of the 21st century and the resource for the next industrial revolution [1]–[4]. Moreover, it is expected to be the fastest-growing industry in history [5]. Some predictions claim that nanotechnology follows a similar evolutionary pattern in industrial application as compared to biotechnology [1], [6], but with the potential to influence a broader range of industrial sectors [7], [8].

There are several facts and figures to support these assertions. In first place, nanotechnology has an intrinsic multi-disciplinary characteristic. In other words, nanotechnology is not restricted to the realm of advanced materials, extending also to manufacturing processes [9]. This characteristic allows the connection to a diversified set of industries such as communication technologies, electronics, automotive, healthcare, biotechnology, cosmetics, chemicals, and energy, among others [4], [9]–[12]. This fact results in technological superiority, increased competitiveness, and the creation of new industries and jobs [10], [13].

Healthcare is one of the fields that has been highly improved by nano-scale manipulation. In this context, the convergence of nanotechnology and biotechnology opens a challenging economic and scientific landscape leading to a huge market for nanomedicine-related products and services. Advances in nanomedicine have shown a great potential to reduce rates of morbidity and mortality, revolutionizing global health [14]–[16] and allowing the availability of innovative, cheaper and faster biomedical facilities, accurate diagnosis, less invasive procedures and more targeted drugs [17], [18].

Despite this continued growth, few scientific discoveries have impacted clinical practice compared to the significant and global progress made by genomics, proteomics, and other disciplines [19]–[21]. The complete technological and innovative lifecycle of nano-products is not realizing its full potential due to the presence of a *gap* between academia, industry and market known as the "**Valley of Death**" [4], [22]–[25]. This concept is aligned with the so-called "**European paradox"**, which suggests a contradiction between higher levels of scientific performance on one hand and the minimal contributions to industrial competitiveness and new venture entrepreneurship in Europe on the other [4], [22]–[24], [26].

Costs are often the principal barrier, especially in settings with lower levels of resources [20]. Moreover, some medical advances have not yet demonstrated the cost-effective benefits required to displace current technology or workflow [27]. However, recent findings have shown that costs or technological barriers are not the only reasons for explaining why much of the science and technology developed in research laboratories is not commercialized [28]. Therefore, it is important to consider that qualified R&D in academic and industry laboratories can not determine the success of this technology by themselves [29].

Overcoming this gap to reach commercial success and the social return of research could be a difficult process if innovation challenges are not addressed. In fact, the future of industry will rely on its ability to innovate in high-tech activities that can offer a differential added-value, rather than improving existing technologies and products [30], [31]. The European Commission (EC) has considered these premises as a concern. As a result, the current European Framework Programme Horizon 2020 (H2020) is fostering innovation through the development and industrial uptake of Key Enabling Technologies[1] (KETs), which are considered strategic for a sustainable economy. Moreover, the cross-fertilization of KETs is being emphased in this initiative in order to obtain new product properties or technological features that cannot be obtained with a single KET. Nanotechnology is part of this selected group of technologies, and since its industrial applicability is broad, its cross-fertilization with other KETs constitutes an important challenge.

Studies about the process of cross-fertilization of KETs are few [32]. Most of the approaches have focused on inter-disciplinarity [33]–[37] or partial technological convergence [38], [39]. Previous works have also analysed the cross-fertilization process by focusing on the inter-disciplinarity of research collaboration [35], [36], [40], [41], especially in the emergent field of nanotechnologies [30], [35], [42]–[44]. However, little attention has been paid to address innovation and technology transfer challenges for the successful commercialization of multi-KET outcomes.

In this regard, this work addresses the exposed challenges by focusing on the field of healthcare. Nano-enabled sensor-based devices and nano-related European innovation projects have been analysed in this work. Principal contributions have sought a better understanding of the processes and ecosystems of innovation and thus, have helped in reducing the Valley of Death gap between research and market.

The present thesis is the result of three years of research. A multi-disciplinary and international group of experts have supported the development of this work. The research was principally developed at the Bioelectronics and Nanobioengineering

[1] Group of six technologies selected by the EC on the base of their economic, innovative and competitive potential in industry [428].

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1 General objective

As mentioned above, a new paradigm is needed for research, development and innovation activities in a convergent scenario of emerging technologies. For that purpose, the general aim of this thesis is to get insights about the innovation and technology transfer challenges existent in the cross-fertilization of KETs, from fundamental research through technological commercialization, in order to achieve a successful technology transfer process of nanotechnologies. Moreover, since this thesis focuses on the application of nanotechnologies in the field of healthcare, the social return of public investment and the healthy living of end-users are highlighted.

The research focus of this work takes into account public funding. As such, it could serve to promote innovation and technology transfer in several entities such as public research centres and universities, but also start-ups or firms involved in the process of nanotechnology innovation. Accordingly, the goal of this work is to reduce the gap between basic research and the marketplace by analysing the processes and ecosystems of innovation, and as such, enhance economic and social outcomes.

2 Specific objectives

- **Objective 1**: Describe the current state-of-the-art, innovation processes, and market trends of nanotechnologies applied to healthcare.
- **Objective 2:** Identify specific applications of nanotechnologies in the field of healthcare with a multi-KET approach in order to get insights of the main

innovation and technology transfer challenges in the process of their cross-fertilization.

- **Objective 3:** Explore the ecosystems of innovation and the dynamics of the stakeholders involved in activities of technology transfer and commercialization in the field of nanotechnologies applied to healthcare after a process of cross-fertilization of KETs.
- **Objective 4:** Determine principal factors that influence and foster the development of multi-KETs in the field of nanotechnologies for health.
- **Objective 5:** Identify the profile of the stakeholders involved in the in the field of nanotechnologies applied to healthcare and their innovation management strategies.

3 Research approach

On the base of these objectives, two approaches that support innovation have been considered:

- A **technological perspective**, which is based on the analysis of nanotechnologies as a relevant KET, and the complex process of its cross-fertilization with other KETs. In addition, the creation of technological diversity is a factor analysed through this perspective, which is related to the long-term success of emerging technologies such as nanotechnology.

- A **management perspective**, which takes into account the importance of managing the innovative process of nanotechnologies, even more when this KET is being fostered to be cross-fertilized with other KETs. Thus, an adequate management of nanotechnology innovation is in this thesis, considered to be a success factor for optimizing the access to the marketplace.

4 Outline of the thesis

The thesis is divided in five chapters herein summarized:

- **Chapter 1.** This chapter offers a state-of-the-art and a theoretical framework that cover the main theoretical bases of this work. Research, trends and future perspectives of nanotechnologies focusing on healthcare are analysed, as well as principal concepts regarding the dynamics of innovation models and systems. In addition, this first chapter summarises principal facts and figures of nanotechnology innovation in Europe. This chapter aims to address **Objective 1**.

- **Chapter 2.** In this chapter, main innovation and technology transfer challenges for the successful commercialization of nano-enabled medical devices are identified at the innovation ecosystem. To this end, a multiple case study approach of nano-enabled sensor-based devices at different stages of technological maturity were selected for the analysis. Based on the results, an integrated model is suggested as a model to be further analysed in subsequent chapters. This chapter aims to address **Objectives 2 and 3**.

- **Chapter 3.** This chapter empirically analyses European H2020 nano-related innovation projects, especially those where the cross-fertilization of KETs was strongly encouraged. This study comprises two sections:

    - **Section I.** This section includes an analysis of the influence of the characteristics of the H2020 funded nanotechnology projects on the creation of technological diversity. The statistical method used for that purpose was an Ordinal Logistic Regression Model. This section of the research aims to address **Objectives 3 and 4**.

    - **Section II.** This section comprises an analysis of the innovation management strategies developed by organisations who are involved in the process of cross-fertilization of KETs. In addition, it also determines which of these management strategies are boosting higher levels of cross-fertilization of KETs. To this end, a Multiple Correspondence Analysis was used as the statistical method. This section of the research aims to address **Objective 5**.

- **Chapter 4.** This chapter exposes the general conclusions from the main results of the research. In addition, topics for further research are suggested.

- **Chapter 5.** This chapter presents the overview of the thesis in Spanish language.

5 Publications

This thesis has led to the publishing of the following (more outcomes and contributions are available at the end of this document):

- **Páez-Avilés, C**; Juanola-Feliu, E; Punter-Villagrasa, J; Del Moral Zamora, B; Homs-Corbera, A; Colomer-Farrarons, J; Miribel-Catalá, P; Samitier, J. **(2016)**. Combined Dielectrophoresis and Impedance Systems for Bacteria Analysis in Microfluidic On-Chip Platforms. ***Sensors***. *16*(1514) 1-23.
- **Páez-Avilés, C**; González-Piñero, M; Juanola-Feliu, E; Bogachan, I; Mir M; Samitier, J. **(2015)**. Innovation and Technology Transfer of Medical Devices fostered by Cross-disciplinary Communities of Practitioners. ***International Journal of Innovation Management***. *19*(6), 15400121 - 154001227.
- **Páez-Avilés, C**; Juanola-Feliu, E; Ll. Miribel-Català, P; Colomer-Farrarons, J; Samitier-Martí, J. **(2014)**. Teragnosis *in vivo*: Innovación nanomédica fomentada por la convergencia de Tecnologías Emergentes. ***Revista Médica Vozandes*** *25*, 47- 54. ISSN: 1390-1656.
- Punter-Villagrasa, J; Cid, J; **Páez-Avilés, C**; Rodríguez-Villarreal, I; Juanola-Feliu, E; Colomer-Farrarons, J; Miribel-Català, P. **(2015)**. An Instantaneous Low-Cost Point-of-Care Anemia Detection Device. ***Sensors***, *15*(2), 4564-4577.
- Juanola-Feliu, E; Miribel-Català, P; **Páez-Avilés, C;** Colomer-Farrarons, J; González-Piñero, M; Samitier, J. **(2014)**. Design of a Customized Multipurpose Nano-Enabled Implantable System for *in vivo* Theranostics. ***Sensors***, *14*(10), 19275-19306.
- **Páez-Avilés, C**; Van Rijnsoever, F; Juanola-Feliu, E; Samitier, J. Multi-disciplinarity breeds diversity: The influence of innovation project characteristics on diversity creation in nanotechnology. ***Journal of Technology Transfer***. (Under review).
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. Cross-fertilization of Key Enabling Technologies: An empirical study of nanotechnology-related projects based on innovation management strategies. ***Journal of Engineering and Technology Management***. (Under review).

CHAPTER 1

Nanotechnology and Innovation: State-of-the-art and theoretical framework

Abstract

This bibliographic section provides a broad overview of the concepts and theories on which this thesis is grounded. Nanotechnologies are viewed and analysed from the perspective of Key Enabling Technologies, which are considered strategic in innovation and competitiveness. A literature review and data base exploration recover important facts about research, development, trends, and commercialization of two fields at the nanoscale that are focused on healthcare: Nanomedicine and Nanobiotechnology. Principal applications identified include the areas of diagnosis, therapy and prevention. Subsequently, innovation models are analysed in the process of transferring and commercializing nanotechnologies with a complementary stakeholder view as the collaborative foundation. Finally, several nanotechnology innovation facts and figures are analysed within a European framework.

1.1 Nanotechnology: a Key Enabling Technology perspective

Many leading countries such as China, Japan and the United States of America (US) are currently focusing on enabling technologies, especially Biotechnology, Information and Communication Technologies (ICT) and Nanotechnology [45]. In Europe, EC has been fostering a common strategy on behalf of the development of KETs since 2009, due to their potential impact in strengthening Europe's industrial and innovation capacity [46]. In this context, the European Union (EU) is determined to address major societal challenges with a competitive industry aimed to achieve its Europe 2020 objectives.

KETs are an invention or innovation that can drive radical change in the capabilities of a user or culture; a technology supporting the development of other technologies [47]. Based on this premise**,** six KETs have been selected as the most strategically relevant based on the current research, economic analyses of market trends and their contribution to solve major societal challenges. The six KETs are Nanotechnology, Micro- and nano-electronics (including semiconductors), Photonics, Advanced materials, Industrial Biotechnology, and Advanced Manufacturing Systems. These technologies provide crucial technology bricks that enable a wide range of applications, including automotive, food, chemicals, electronics, textiles, energy, environment, pharmaceuticals, construction, aerospace and telecommunications [48] (**Table 1.1**).

KETs, as a terminology coined by the EC are "*knowledge intensive and associated technologies with high R&D intensity, rapid innovation cycles, high capital expenditure and highly skilled employment which enable process, goods and service innovation throughout the economy and are of systemic relevance*" [48](pp. 2-3). KETs are also multi-disciplinary, meaning they can cut across many areas tending towards convergence and integration. A *KET-based product* is defined as an enabling product for the development of goods and services enhancing their overall commercial and social value that is induced by constituent parts that are based on the six KETs.

Nanotechnology has been selected as one of the six KETs due to its direct and indirect capacity to address major societal problems, boost competitiveness, job generation, and a growing and wealthy economy. Nanotechnology is considered to be the manipulation of molecular-sized materials to create new products and processes. More specifically, the National Nanotechnology Initiative (NNI) defines Nanotechnology as "*the research and development at the atomic, molecular, or macromolecular levels in the sub 100 nm range (~ 1-100 nm) to create structures, devices and systems that have novel functional properties with numerous manipulation advantages*" [49](pp. 1).

This definition started having stir since the famous phrase "*There is Plenty of Room at the Bottom*" in Richard Feynman's historic 1959 lecture. However, the Professor Norio Taniguchi, in his explorations of ultra-precision machining, coined the term "nanotechnology" for the first time over a decade later. But it wasn't until 1981 that modern nanotechnology began, with the development of the Scanning Tunneling Microscope, which is able to visualize individual atoms. Nevertheless, nanotechnology is not a new technology. For instance, it has been known that nano-scale carbon particles have been used as a reinforcing additive in tires for more than a century [5] .

Table 1.1. Relevance of Key Enabling Technologies.

KET	Relevance
Nanotechnology	Development of smart nano and micro devices and systems. Radical breakthroughs in vital fields such as healthcare, energy, environment and manufacturing.
Micro- and Nanoelectronics	Essential for all goods and services which need intelligent control in sectors as diverse as automotive and transportation, aeronautics and space. Smart industrial control systems permit more efficient management of electricity generation, storage, transport and consumption through intelligent electrical grids and devices.
Photonics	A multi-disciplinary domain dealing with light, encompassing its generation, detection and management. Provides the technological basis for the economic conversion of sunlight to electricity which is important for the production of renewable energy, and a variety of electronic components and equipment such as photodiodes, LEDs and lasers.
Advanced Materials	Offer major improvements in a wide variety of different fields (e.g. in aerospace, transport, building and health care). They facilitate recycling, lowering the carbon footprint and energy demand as well as limiting the need for raw materials that are scarce in Europe.
Industrial Biotechnology	Brings cleaner and sustainable process alternatives for industrial and agri-food operations. It will for example, allow the progressive replacement of non-renewable materials currently used in various industries with renewable resources, however the scope of applications is just at the beginning.
Advanced Manufacturing Systems	Important to produce high value marketable knowledge-based goods and the related services (e.g. modern robotics). This is especially relevant in capital intensive industries with complex assembly methods such as the production and assembly of modern aircraft which involves the whole spectrum of manufacturing technologies from the simulation and programming of robotic assembly lines to reducing energy and materials consumption.

Source: [45].

Currently, nanotechnology is still at the frontier between incremental improvements and disruptive innovations [50]. Moreover, many see Nanotechnology as the technology that will underlie the next Schumpeterian wave [28]. Nanotechnology has become a global business with global applications [4]. Between 2001 and 2008, the numbers of discoveries, inventions, nanotechnology workers, R&D funding programs, and markets, have increased a 25% by year. This could be evidenced at nanotechnology related publications and patents, which are continuously expanding world-wide [51]–[53].

For more than a decade, advanced developed countries (US, Japan, and EU) have annually invested billions of dollars in nanoscale research to build the scientific foundations for nanotechnology commercialization [54]. As an example, in the US, research investment in nanotechnology since 2001 was about $12 billion. In addition, countries that lead in corporate funding include Japan, Germany, and South Korea [55]. Latin American countries are also implementing policies and programs to develop nanotechnology. However, almost all scientific research is concentrated in few countries as Brazil, Mexico, Argentina, Chile and Uruguay [56]–[59].

One of the key characteristics of Nanotechnology is that it is *convergent*, meaning that brings together different sciences and technologies into a single field [33]. Starting form this statement, many authors have described this technology as heterogeneous, multifaceted and interdisciplinary [60], combining blurred disciplines as physics, chemistry and bio/medical as subfields [4], [5]. Furthermore, it has been considered a multi-disciplinary technology since it is not restricted to the realm of advanced materials, extending also to manufacturing processes, biotechnology, pharmacy, electronics and ICT, as well as other technologies [9]. These characteristics allow the connection to a diversified set of industries as the automotive, cosmetics, chemicals, and packaging, among others. Relevant examples of nanotech impacts and possible applications in various technology realms are presented on the table below (**Table 1.2**).

Nanotechnology also holds considerable promise to generate radical new applications and foster the development of whole new sectors [6]**.** Most of the Nanotechnology research is developed mainly in universities and public research institutes [61]. Moreover, it is embedded in existing industries and research. For instance, Micro-electronics are being transformed to Nano-electronics, Biotechnologies to Nano-biotechnologies and from energy to Nano-energy [62].

Table 1.2. Nanotechnology applications in various technology realms.

Categories	Examples of materials	Examples of applications
Applications in the advanced materials realms		
One dimensional nanomaterials	Thin films and layers	Breathable and waterproof fabrics, electronic devices, vehicles.
	Engineered surfaces	Fuel cells, catalysts.
Two dimensional nanomaterials	Carbon nanotubes	Reinforced composites, antistatic packaging, sensors, nano-electronics, display devices.
	Inorganic nanotubes	Catalysis, photo-catalysis, energy storage.
	Semiconductor nanowires	High-density data storage, electronic and opto-electronic nanodevices, quantum devices.
Three dimensional nanomaterials	Nanoparticles	Sunscreens, cosmetics, textiles, aircraft paint coatings, targeted drug delivery, catalysts, water remediation, car bumpers and tires.
	Nanocrystalline materials	Magnetic resonance imaging (MRI), motors, micro-sensors, orthopedic implants, artificial heart valves.
	Fullerenes	Ball bearings to lubricate surfaces, drug delivery vehicles, electronic circuits.
	Dendrimers	Nanoscale carrier molecules in drug delivery, environmental clean-up, coatings, inks.
	Quantum dots	Solar cells, composites, fluorescent biological labels.
Applications in the biotechnology and Pharmacy realm		
Bio-mimetic structures	Catenanes and rotaxanes	Disease diagnosis, drug delivery, molecular imaging.
	Nanocrystalline silver	Wound dressing.
Array technologies	DNA chip	Gene and protein analysis.
	Lab-on-a-chip	Sensing and supporting disease diagnosis.
Self-assembly	DNA-based structure (artificial crystals)	Hybrid nano-machines.
Drug delivery	Functionalized nanoparticle	Drug therapies, gene therapies, cystic fibrosis and immune deficiencies.
Applications in the electronics and IT realm		
Information storage	Low dielectrics and higher-conductivity interconnects (wiring)	DRAM for digital camera, personal computer, video camera etc.
	Semiconductor nanowires	Hard disk drive for PC, DVD player, CD player.
Optoelectronics	Photonic crystals	Displays, optical sensing, optical computing.
	Optical devices (nanowires)	Point-of-care health screening, constant monitoring of diabetes or critical care.
Sensors	Nanocrystalline materials with increasing selectivity	Monitoring the quality of drinking water, state and performance of products and materials, detecting and tracking pollutants, checking food for edibility.

Source: [9].

1.1.1 Nanotechnologies in healthcare

Nanotechnology is having a significant impact in various fields such as electronics, energy, aerospace, and textiles, but perhaps none as significant as healthcare [2]. The application of Nanotechnology in medicine provides a great opportunity to improve the quality of medical care, combining the increased knowledge of modern medicine with the ability to manipulate materials at the nano-scale for more precise and accurate diagnosis and therapy [15]. Nowadays, the emerging sector of applied nanotechnology is basically addressed to the biomedicine: Nanobiotechnology and Nanomedicine.

The cross-fertilization between Nanotechnology and Biotechnology is leading to the Nanobiotechnology as a new and distinct research field. This opens a challenging economic and scientific scenario leading to a huge market for nanomedicine-related products and services [6]. ***Nanobiotechnology*** describes the inter-disciplinary area of research and development that involves nanoscale design based on biologic systems, at the interface between organised nanostructures and biomolecules [4]. Nanobiotechnology is attempting to borrow the cellular know-how from biology for the development of new materials in a number of interdisciplinary fields. This convergence of two existing but distant worlds, engineering and molecular biology leads to a new class of multifunctional devices and systems for biological and chemical analysis with better sensitivity, specificity and a higher rate of recognition [63]. Some of the healthcare based Nanotechnological and Biotechnological application areas include food security, cosmetic, diagnosis, treatment, genomics and proteomics [16], [64].

In the last decade, patent and publication landscape reveal emerging technological trends in Nanobiotechnology. Four areas emerge as active hubs of Nanobiotechnology convergence: nanostructures; drug delivery and biomedical applications; bio-imaging; and carbon nanotubes and biosensors [65]. Targeted drug delivery is the major Nanobiotechnological application, with the most highly anticipated potential outcomes, and with dozens of passively targeted nanobiotechnology products already clinically approved [66].

On the other hand, ***Nanomedicine*** encompasses a broad range of different approaches: from medicine to chemistry, physics, engineering, and biology [67]. Research findings suggest that these technologies will have a promising impact on health sciences specifically in three main areas: diagnostics, therapeutics and regenerative medicine [68]. Nanomedicine aims to identify several diseases at earlier stages and perform targeted drug delivery. This allows a reduction of toxicity and side effects of therapeutic drugs by releasing and activating them at the required site [15]. The interdisciplinary approach of this relative new technology offers a more efficient and personalized way to diagnose and treat a large number

of important diseases, such as cancer, diabetes, neurodegenerative diseases such as Alzheimer's and Parkinson's, as well as psychiatric disorders, infectious diseases, cardiovascular and autoimmune diseases [14], [69]. In **Table 1.3**, some applications where Nanotechnology has already a tangible and substantial impact in the treatment, diagnosis or imaging is presented. As a consequence, companies and their related products have also begun to emerge in the last several years [70].

Table 1.3. Applications of nanotechnology in some of the major diseases.

Challenges	Therapeutics	Diagnostics / Imaging	Regenerative Medicine
Cardio Vascular Diseases	Implantable devices (nano surface modification).	Nanoparticles for theranostic approaches.	Intelligent bioactive materials.
	Targeted drug delivery into plaques.		Stem cell mobilization and homing at site of injury.
Neuro Degenerative Diseases	Semi invasive nanodevices for drug delivery (for Parkinson).	Image guided implantation of advanced neuro-stimulators.	Site specific delivery of neuro active molecules.
	Nano-formulations.		Intelligent biomaterials.
Diabetes	Insulin measurement and delivery by nano enabled devices.	Encapsulation and monitoring of labelled islet transplants. Whole body imaging of fat distribution with nanoparticles. Implanted non-invasive continuous glucose monitoring.	Functionalization of 2D and 3D materials for time and spatial release of biochemical factors for artificial pancreas.
Cancer	New nano formulations for targeting agents to tumours.	Nanoparticle tracers and contrast agents for diagnosis.	Functionalized nanoparticles for targeted in vivo activation of hematopoietic stem cell production
	Nanoparticles for thermal therapy.	Composite nano particles for monitoring of therapy.	
	Implantable devices for localized delivery of drugs.	Minimal invasive endoscope / catheter for diagnostics and therapy	
	New therapeutic tools with physical mode of action	Nanostructured surfaces for biosensors	
	Monitoring of therapeutic efficacy		
Inflammation	Soft nanomaterials for bone regeneration, Rheumatoid Arthritis and Crohn's disease	Imaging of nanoparticle labelled white cells	3D Nanomaterials for stem cell immobilization at site of injury
	Bacterial free nanomaterials to avoid infection by implanted materials		Novel implant materials and surfaces to prevent implant infections

Source: [71].

Table 1.4. Examples of nanoscale medicine products incorporated into commercial and FDA-approved production in 2010.

Products	Description
Nanosphere Verigene® system	The first point-of-care nano-enabled medical diagnostic tool for on-site medical diagnostics uses gold nanoparticle technology to detect nucleic acid and protein targets of interest for a wide variety of applications.
Luna nanoparticle contrast agents	Nanoscale body imaging, give enhanced clarity and safety of diagnostic magnetic resonance imaging.
Angstrom Medica NanOSS™	Nanocristalline calcium phosphate synthetic bone material use as bone replacement/reinforcement, weight-bearing bone cement, and bioactive coatings.
Dendreon Provenge®	Immuno-therapy products are made using cells from patients' own immune systems to fight prostate cancer.
Celgene Abraxane®	Nanoparticle albumin bound (nab) technology leverages albumin nanoparticles for the active and targeted delivery of chemotherapeutics to treat metastatic breast cancer.

Source: [8].

Nano-scale medicine has also made significant breakthroughs in the laboratory, advanced rapidly in clinical trials, and made inroads in applications of biocompatible materials, diagnostics, and treatments (**Table 1.4**). Over 50 cancer-targeting drugs based on nanotechnology are actually in clinical trial in the United States alone. Nanotechnology solutions are enabling companies such as Pacific Biosciences and Illumina, to offer products that are on track to meet the $1000 genome challenge [8].

The application of Nanotechnology into medicine has some advantages. For instance, it provides great opportunities to improve the quality of medical care, contain the rising health-care costs, and manipulate materials at the nanoscale for more precise and accurate diagnosis and therapy [15]. In this context, some of the advances that Nanomedicine had demonstrated are the great potential to reduce rates of morbidity and mortality. Meanwhile, public health applications of Nanomedicine such as rapid and portable diagnostics and more effective vaccinations have the potential to revolutionize global health [14].

1.1.2 Cross-fertilization of technologies: a multi-KET approach

New technologies create value through the convergence of other technologies and the alignment of different stakeholders [62]. In this regard, Nanotechnologies can converge with other fields and other enabling technologies, especially with Biotechnology, Computational Sciences, Physical Sciences, ICTs, Cognitive Sciences, and other Social Sciences [13], [62]. This scenario is expected to be the beginning of the development of transforming tools that can be shared across fields, such as new

scientific instrumentation, overarching theoretical concepts and new methods of interdisciplinary communication [13].

Diverse technological streams are important for significant inventions regarding to product development [66]. In this regard, is has been stated that the confluence of technologies, can lead to radical innovations [66], which improves existing products attributes and functionalities at reduced costs [72]. The current terminology used to describe the convergence of technologies is ***cross-fertilization,*** which is defined as a new combination of previously distinct technologies [66]. According to the innovation system literature, cross-fertilization means a "recombinant innovation", which refers when two or more different technologies recombine among them to create a new improved technology [73]–[75].

In this respect, cross-fertilizations of KETs can offer greater possibilities to foster innovation and create new markets than individual KETs. Therefore, the integration of different KETs creates value beyond the sum of the individual technologies for developing innovative and competitive products, goods and services that can contribute to solve societal challenges. Accordingly, the term ***multi-KET*** has been generated to describe the sum of at least two KETs and Advanced Manufacturing Systems (high tech manufacturing environment).

Figure 1.1 describes the different routes to create a multi-KET product. The relevance of this combining process lies on the creation of new unique product properties or technology features, which could not have been obtained with a single technology. At the field of healthcare, Nanobiotechnology and Nanomedicine application areas of multi-KETs are for example nano-enabled products, implantable devices, Point-of-care (POCs) and Lab-on-a-Chip (LOC) systems with a personalized and less invasive approach, which are smart oriented, and with energy harvesting solutions.

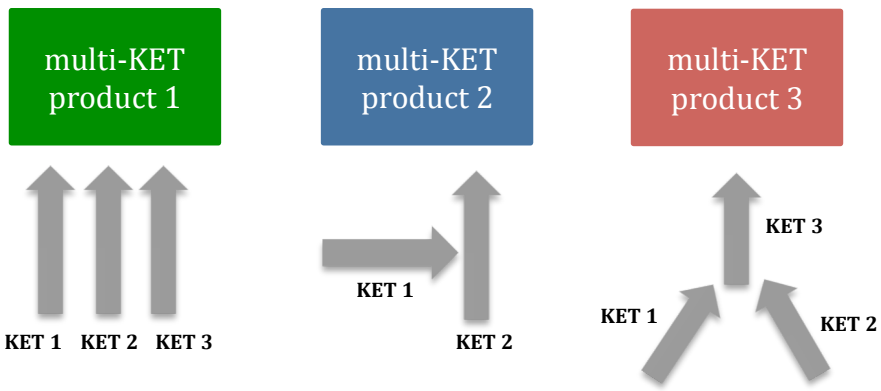

Figure 1.1. The multi-KETs product generation process (Source: [76]).

These advances are expected to be accomplished in short (2017) and medium (2020) term (**Figure 1.2**). In this regard, it has to be highlighted that personalized medicine is expected to have a major future impact. It has been estimated that to pursue personalized healthcare, biomarkers and companion diagnostics will be needed to identify patients who are likely to respond to a given therapy and particular dose of the medicine [69]. The rise of POCs testing is expected to expand access to medical services, improve health outcomes, and facilitate the sustainability of disease-control programs in low- and middle-income countries.

Additionally, these devices will enable simultaneous detection of multiple targets (multi-plexing) and will use more accurate biomarkers. Advances in engineering and test chemistry will produce devices that are smaller, simpler to operate, and potentially instrument-free, enabling reliable home-based testing or self-testing [77].

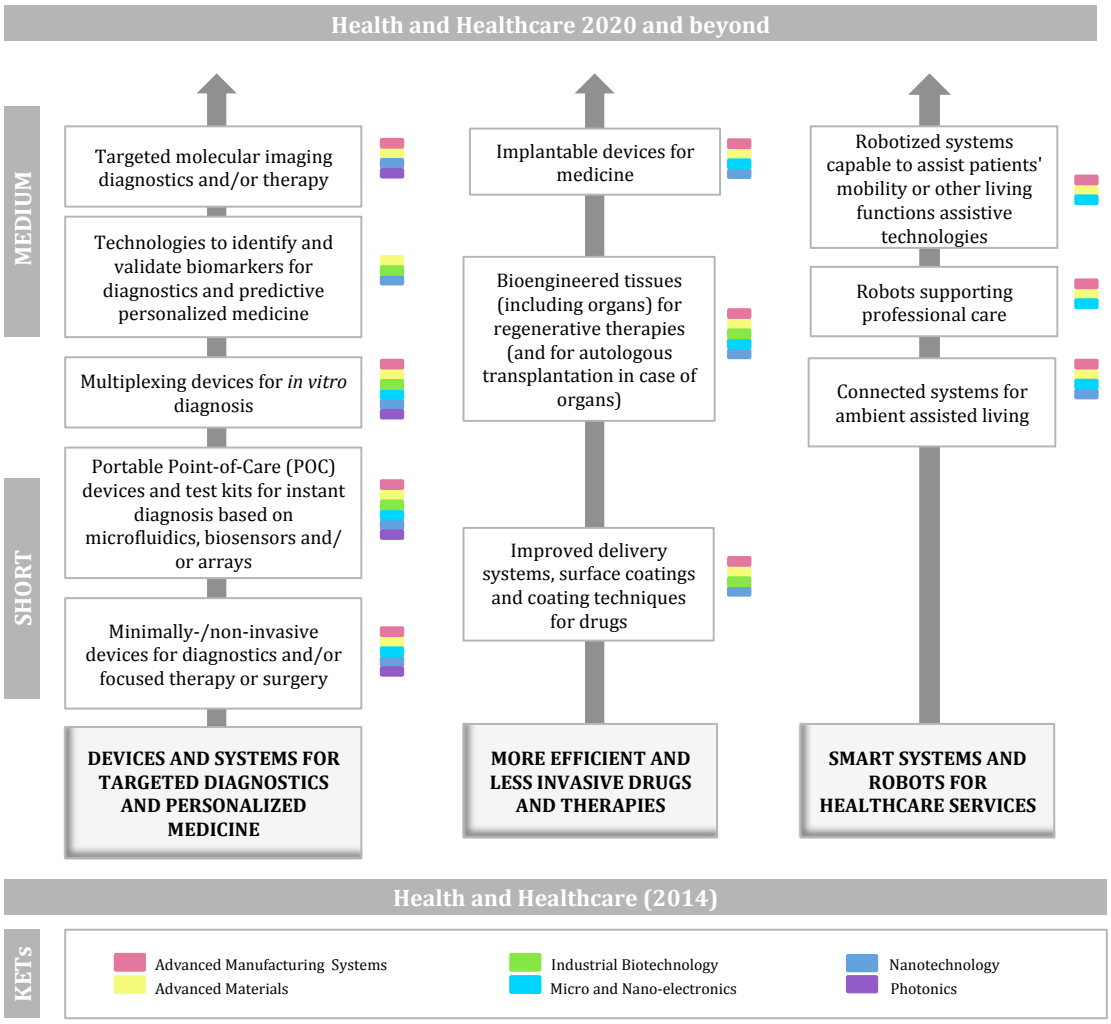

Figure 1.2. Fields for cross-cutting KETS developments in the Health and Healthcare domain (Source: [76]).

1.1.3 Future perspectives and market forecast

Nanotechnologies are expected to have a huge positive impact on economic growth and in creating new markets in a relatively short amount of time, since its applications can be used in virtually all sectors [4], [10], [50]. Indeed, it is widely predicted that this technology will drive the "next industrial revolution" [78] or that we are already living in a "nanoage" period [79]. This is why most industrialized countries and firms have invested billions of dollars in nanotechnology-related developments, where great returns are expected [10].

The expectation that Nanotechnology could be the fastest-growing industries in history [5] is leading to estimate new opportunities in the marketplace on the base of present advances [4]. For instance, there are nanotechnology-related products [11]. The emerging nanobiotechnology industry has already created more than $20 billion in revenue. For instance, the Project on Emerging Nanotechnologies has catalogued more than 1000 nanotechnology-based consumer products worldwide.

The global Nanotechnology market is projected to grow around 19% by year until 2017 and it is expected that the annual global market could achieve the US$3 trillion in 2020 (**Figure1.3**). Market trends include nanotechnology-based thin solar cells with high efficacy, nanomaterials with higher strength, robust growth in nanofibers and nanomedicine [8]**.**

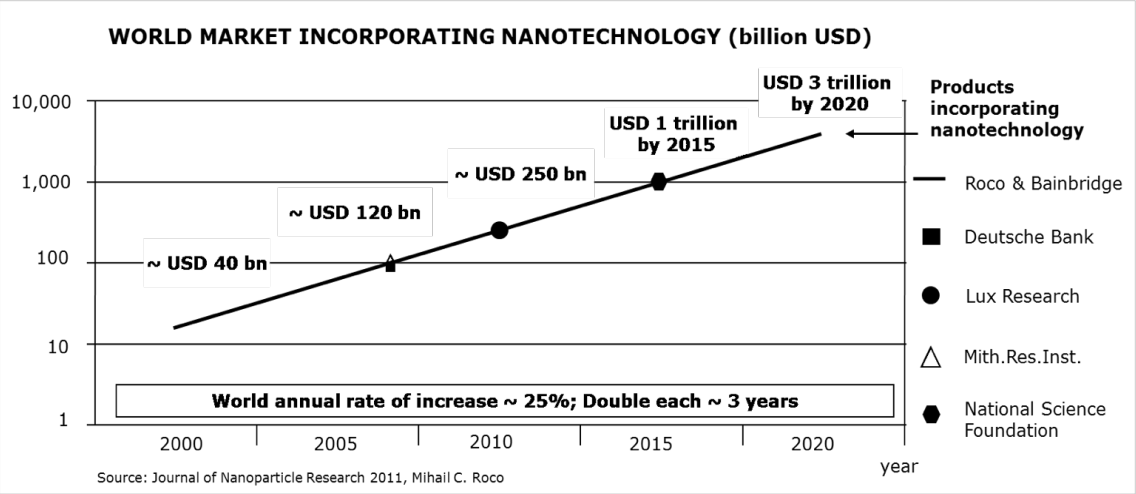

Figure 1.3. World market perspective incorporating nanotechnology (Source: [80]).

In addition, it is expected that nano R&D could accelerate innovation breakthroughs According to Roco (2007), future perspectives in nanotechnology will bring heterogeneous molecular nanosystems where each molecule has a specific structure and plays a different role. This vision is based on the statement of four generations of nanotechnologies: passive nanostructures, active nanostructures, systems of nanosystems and molecular nanosystems (**Table 1.5**) [81], [82].

toward nanosystems by design, and to lead to many additional and qualitatively new applications by 2020, guided by major societal needs (**Table 1.6**). Enhancing human longevity and improving quality of life, is a clear example of the impact of nanotechnology R&D on the present a future society [83]**.** According to Roco et al., (2011), with each new generation of nanotechnology products, there is an improved focus on economic and societal outcomes [8].

At the field of healthcare, three major projecting areas in the healthcare field are nano-diagnostics, nano-pharmaceutics and regenerative medicine [5], [66]. In 2020 the expected market size related to radical innovation based nanomedicines will be 1.000 M€ and 3.000 M€ for 2025 (**Table 1.7**) [68]. In this regard, nanomedicine is considered a long-term play in the market [4].

Table 1.5. Timeline for the beginning of industrial prototyping and nanotechnology commercialization: four generations of nano-products.

1st: Passive nanostructures	
2000	**a. Dispersed and contact nanostructures** (e.g. aerosols, colloids)
	b. Products incorporating nanostructures (e.g. coatings, nanoparticle, reinforced composites, nanostructured metals, polymers, ceramics)
2st: Active nanostructures	
2005	**a. Bio-active, health effects** (e.g. targeted drugs, bio-devices)
	b. Physic-chemical active (e.g. 3D transistors, amplifiers, actuators, adaptive structures)
3st: Active nanostructures	
2010	(e.g. Guided assembling; 3D networking and new hierarchical architectures, robotics)
4st: Active nanostructures	
2015 - 2020	(e.g. Molecular devices by design, atomic design, emerging functions)

Source: Adapted from [84].

Table 1.6. Main nano-biosystems and nanomedicine achievements since 2000 and goals to 2020.

Achievements/discoveries since 2000	Fundamental goals and barriers to overcome by 2020
Development of diagnostic methods that are sensitive down to picomole and attomole levels (for multiple analytes to be assessed simultaneously by lab-on-a-chip approaches)	Point-of-care (POC) medical diagnostics: increased sensitivity, selectivity, and multiplexing capabilities at low cost to enable point-of-care diagnosis and treatment, allowing clinicians to track and treat disease. Nanodiagnostic tools will become the backbone of clinical medicine by 2020, making the transition from remote labs to hospitals and then eventually to homes.
Is invented the first nanotherapeutic proven to be effective for breast cancer and FDA-approved (Abraxane), and a multibillion dollar pharmaceutical	Nanotherapeutics: overcome many challenges such as pharmacokinetics, biodistribution, targeting, tissue penetration, etc., to support widespread adoption by industry of nanotherapeutics.
	At least 50% of all drugs used in 2020 will be enabled by nanotechnology.
More than 50 of US pharmaceutical companies have nanotechnology-based solutions for treating cancer in clinical testing	50% of drugs for pancreatic cancer and ovarian cancer will be nanotechnology-enabled.
	Clinical approval of gene therapy for treating a wide range of diseases, including many forms of cancer.
Gene therapy enabled by nanomaterials in experimental laboratories	Inexpensive gene sequencing enabled by nanotechnology.
Use of temperature-sensitive polymer fibers to coat cell culture dishes for the purposes of cell sheet engineering and demonstrating that the technology can be used for repair of a damaged myocardium, cornea, or esophageal lining	Use nano-architectures and synthetic pro-morphogens for tissue engineering, including stem cell therapy, construction of new organs (heart or bladder), and spinal cord regeneration.
	Widespread use by 2020 of nano-enabled tissue constructs for repair of cardiac damage (in heart attack victims).
Controlled development of molecules to promote tissue repair and generation in situ	Stem cells: use nanobiology and nanomedicine to aid in understanding and control of stem cell differentiation and the transition of stem cell to widespread medicinal application.
	Multifunctional nanoparticle delivery systems that can be used for drug and siRNA delivery, as well as a combination of both.
	Widespread use by 2020 of nanotechnology-enabled stem cell-based therapies for spinal cord regeneration.
Achievement of nanoscale control in synthetic biology	Use synthetic biology in regenerative medicine, biotechnology, pharmaceuticals, and energy applications Economic impact; translation of many bionanomaterials to the medical arena, with the market size for these nanomedicine advances growing to $200 billion by 2020, by varying estimates, and in the process dramatically lowering health care costs.

Source: [8].

Table 1.7. Expected market size in nanomedicine in millions of euros.

Diagnostics		**2015**	**2020**	**2025**
In vivo imaging	Clinical Imager	-	50	700
	Tumour Therapy Delivery System	1	20	100
	SPIO/USPIO	10	100	1000
	Nano structures as carriers plus drug release	-	10	100
In vitro diagnostics	Hospital	200	700	1500
	Physician office	-	1000	1500
	Home	-	-	1500
Drug Delivery				
Nanopharmaceuticals	Non-invasive delivery of protein nanomedicines	0	10.000-+5.000	20.000-+10.000
	Non-invasive delivery of DNA based nanomedicines	0	5.000-+2.000	10.000-+5.000
	Non-invasive delivery of "Non-Lipinski molecule"	0	2.000-+2.000	4.000-+2.000
	(Enabler) Computational Tools	15	20	40
Radical Innovation nanomedicines	Radical Innovation based nanomedicines	0	1.000	3.000
	Activated Nanoparticles devices for X-ray modality	>500	>2.000	-
Targeting drugs to facilitate cell differentiation	Targeting drugs to facilitate cell differentiation	0	2.000	6.000
Nanodevices	Focused Ultrasound Therapy System	175	350	500
	Linked MRI	175	350	500
	Pressure & Thermosensitive drugs	90	350	750
	Targeted therapies in Oncology	30.000	-	-
	Anti-inflammatory diseases	0	5.000	8.000
	CNS diseases	0	0	2.000
***Regenerative* Medicine**				
Smart Biomaterials	Spine	5.000	7.000	9.000
	Biocompatible Biomaterials	35.000	43.000	52.000
	Wound Care (active dessing)	5.000	12.000	17.000
	Bone fillers	240	300	380
	Orthopedic Biomaterial	260	320	430
Cell Therapies	Non stem cell-based therapies	1.000	2.500	-
	Tissue Engineering	10.000	20.000	-
	Stem cell therapies	1.000	7.000	-
	Supporting technologies	3.500	8.000	-

Source: [68].

1.2 Innovation: Dynamics, models and systems

The word ***innovation*** comes from the Latin "innovare" [85]. According to Attridge (2007), the concept of innovation offers a considerable scope for alternative interpretations; as well it can be defined as:

i) the process of discovering something that is both new and potentially useful;
ii) the process of discovering something new and developing it into a scaleable product or service; and
iii) a cyclical economic process, whereby innovators discover, develop and commercialize new products or services and gain sufficient returns on their investments to re-invest in continued R&D [86].

Adding a simplified definition, Tidd and Bessant (2014) offers another perspective of innovation. These authors defines it as "*the process of creating value from ideas*" [85] (pp. 3). In this context, the term ***value*** is considered in terms of creating a product or service which others find useful and valuable.

Innovation can be described therefore as a complex and diversified activity with the aim to improve products, process, or organisational structures boosting for success on the marketplace [87], [88]. Giving an in-deep look to all this perspectives, a common factor can be seen: innovation is considered a ***process*** and not an event. The importance of making this distinction is the way this process is being managed in order to arrive successfully to the purpose of innovation [85] (pp. 5).

According to Pavitt (2005) ***innovation processes*** are wide and can differ in many respects according to the economic sector, field of knowledge, type of innovation, historical period and country concerned. It implies "*the exploration and exploitation of opportunities for new or improved products, processes or services, based either on an advance in technical practice ("know-how"), or a change in market demand, or a combination of the two*…." [89] (pp. 88). As such, it can be divided in three overlapping process: i) the production of scientific and technological knowledge, ii) the translation of knowledge into working artifacts and iii) responding to and influencing market demand.

Successful innovation fostered by organisations dates back to 1980s, when enterprises, small firm start-ups and organisational spin-offs increased understanding the innovative role of entrepreneurs, intrapreneurs and social entrepreneurs. In 1990s, the source of innovation was focused on multidisciplinary approaches, multi-functional teams and collaborative networks as a source of innovation. Currently in the 2000s, there is an increase of new organisational practices for innovation as crowdsourcing or outsourcing related with an open

community, and open-sharing or free-revealing information on product and toolkits to online user communities [90].

In the same line, ***technological innovation*** has been referred as engineering or science intensive innovations [91]. In this context, a technology innovation contributes nearly half of the nation's productivity, economic growth and standard of living. With this perspective, innovation can be defined as "*a process through which the nation creates and transforms new knowledge and technologies into useful products, services and processes for national and global markets, leading to both value creation for stakeholders and higher standards of living*" [92](pp. 2).

According to Swamidass (2014), technological innovation seven phases: i) conceiving an idea, ii) developing products, iii) develop a business model and plan, iv) to find investment capital, v) create a functioning start-up, vi) grow in financial maturity, and vii) continue to innovate (**Figure 1.4**). This perspective highlights the vital and irreplaceable role of the human capital: engineers and scientist in the two first phases and the cash flow, a common element in all the phases.

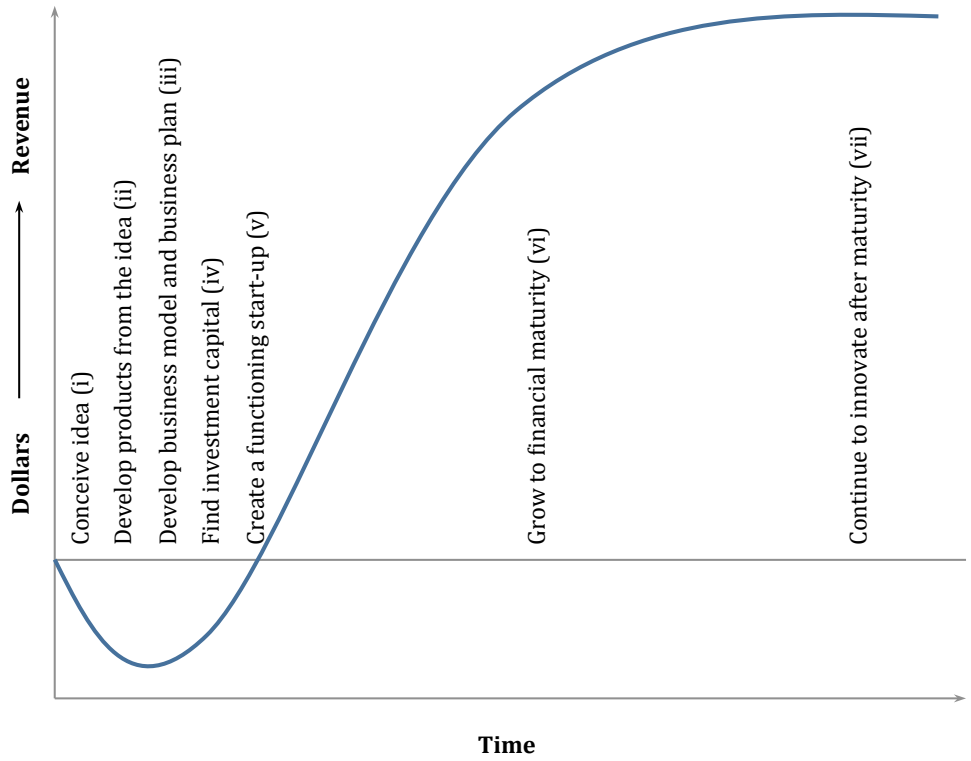

Figure 1.4. The seven phases of technological innovation (Source: adapted from [93]).

Innovation theory has been a topic of interest of firms, professionals, academics and economic development personnel [28], since it is considered an important activity at an individual firm level, groups of firms, for researchers and cross-national collaboration between them [94]. Not only firms have interest in innovation and its advantages at a competitive level, but also this practice has been expanded in other institutional spheres such as universities [94].

Furthermore, innovation has a clear and direct impact on economic growth [95], [96]; this could be the reason why innovation also has gained significance from policy perspectives concerned on knowing how to maintain strong economic growth in an era that is increasingly being defined by the globalization of competition, as well as major fiscal and demographic challenges [97]. Thus, this could be the reason why many governments in developed countries are making strong efforts to promote innovation [86].

1.2.1 Evolution of innovation models

An ***innovation model*** can be defined as a construct or framework to represent the dynamic of the innovation process in order to understand the activities, attributes or the contributions from the different players involved. Innovation models have not been always the same; they have changed over the years (**Table 1.8**). Early models considered innovation as a linear sequence of functional activities [86], [97], [98], which starts from i) basic research, ii) applied research, iii) experimental development, iv) initial production and v) diffusion [98]. During the first 20 years following the Second World War, there was an economic growth of advanced market economies as a result of a rapid industrial expansion and the emergence of new industries based largely on new technological opportunities. This first generation, or the *Technology-Push* concept of innovation assumed that more R&D generates more successful new products [99].

Towards the second half of the 1960s, while manufacturing output continued to grow, and a general prosperity perception remained high, levels of industrial concentration increased with more importance were being placed on static scale economies. Innovation process began to change with a marked shift towards emphasizing demand side factors, as for example the market place. This resulted in the emergence of the second generation or *Market-Pull* model of innovation in which the market was the source of ideas for directing R&D, which had a merely reactive role in the process [86], [99].

The third generation began at the early 1970s and middle of 1980s, a decade of severe resource constraint. Thus, it became increasingly necessary to understand the basis of successful innovation in order to reduce the incidence of wasteful

failures. This was the origin of the *Coupling Model,* which states that the successful innovation process could be modelled on the basis of a portfolio of wide-ranging and systematic studies covering many sectors and countries. *Technology-Push* and *Market-Pull* models of innovation were extreme and atypical examples of a more general process of interaction between, on the one hand, technological capabilities and, on the other, market needs. However, innovation was not considered a linear path anymore [94].

Figure 1.5 exposes a more recent conception of a nanotechnology innovation pathway that considers technology-push and market pull. The model is based on the design of nanoparticles and nanostructures, considered the building blocks of product design. In this model, understanding process improves optimal manufacturing process design. Following, product design needs to be conceived to understand the value chain and customer needs. Then understanding the value chain, it the particle design can be tested again [100].

Subsequently, in a fourth generation period, a crucial feature was the recognition in the West that the remarkable competitive performance of Japanese companies in world markets was based on considerably more than the combination of technological imitation, relationships with primary suppliers and efficient, quality-oriented production procedures. In the fifth-generation innovation process, strategy trends established during the 1980s continue, with some intensifying in importance.

Table 1.8. Progress in conceptualizing innovation models.

Generation	Period	Key Features
First	1950s - Mid 1960s	The linear models: linear progression from scientific discovery, through technological development in firms, to the marketplace. Technology push.
Second	Mid 1960 - Early 1970s	Market Pull: processes change with a marked shift towards emphasizing demand side factors.
Third	Early 1970s - Mid 1980s	Interaction between different elements and feedback loops between them. The coupling model.
Fourth	Early 1980s - Early 1990s	The parallel lines model, integration within the firm, upstream with key suppliers and downstream with demanding and active customers, emphasis on linkages and alliances.
Fifth	1990s - 2000s	Systems integration and extensive networking, flexible and customized response, continuous innovation.
Sixth?	Post - 2000	Efficient R&D with a global marketing research (Market globalization). Open Innovation and social entrepreneurship.

Source: Adapted from [74].

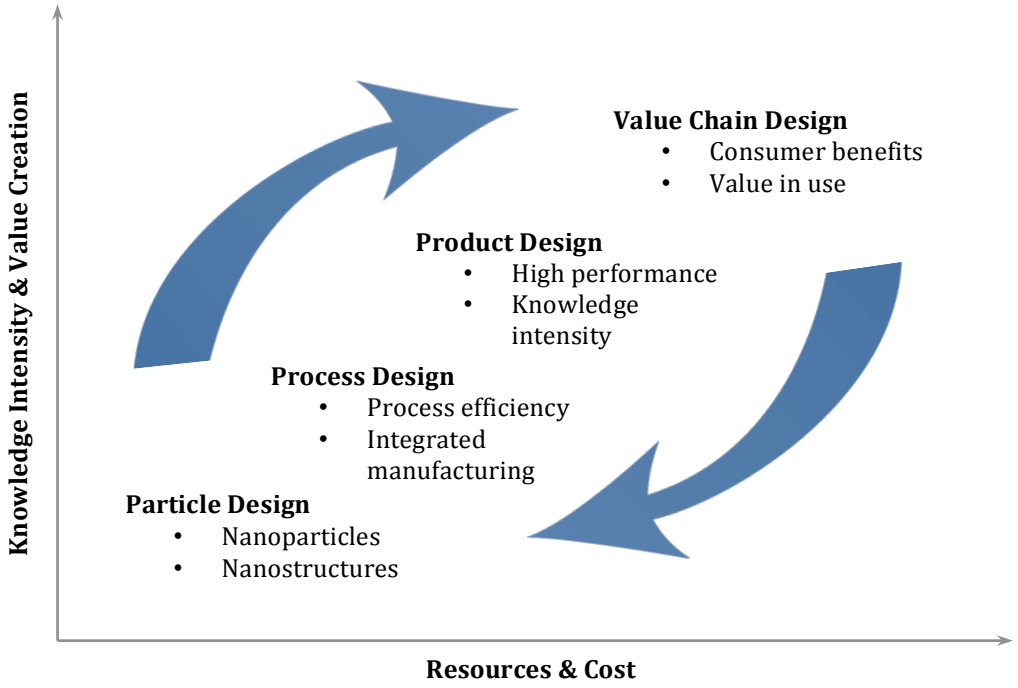

Figure 1.5. Nanotechnology innovation roadmap based on technology-push and market-pull (Source: adapted from [100]).

Leading companies remain committed to technological accumulation, strategic networking continues, speed to market remains of importance, firms are striving towards increasingly better integrated product and manufacturing strategies, greater flexibility and adaptability are being sought; and product strategies are more strongly emphasizing quality and performance features. In addition, growing concern over the degradation of the physical environment, which is resulting in intensifying regulatory activity, is once again placing regulatory issues firmly on the corporate strategy agenda [99].

As shown before, innovation is a process of endless transition [94]. This can be also evidenced by the indicators of innovation measurement that have evolved from R&D expenditures (1950s-60s), patents/publications and quality change (1970s-80s) indexing and benchmarking (1990s) to networks, clusters, and management techniques (>2000) [92]. Is in this context that we are probably facing the sixth-generation model based on marketing research with high significance in open translation of technology including open-source innovation and social entrepreneurship. However, these alternative innovation models are still "marginal" [101].

At the industrial level, Joseph Schumpeter, an outstanding economist and political scientist, brought up two new patterns of innovation and he classified as ***radical*** or

incremental. The first one shapes big changes, while the second one fills in the process of change continuously. At a firm level, Nelson and Winter (1982) and Kamien and Schwartz (1982) introduced the labels Schumpeter as *Schumpeter Mark I* and *Schumpeter Mark II* to characterize synthetically the theoretical models of innovative activities proposed by Schumpeter.

The first label is also known as "creative destruction" pattern where innovations are introduced by firms that did not innovate before, which is called "widening". Schumpeter Mark I industries are characterized by turbulent environments with relatively low entry barriers where innovations are mostly generated and developed by new "entrepreneurial" firms. Accordingly, technological competition among firms in Schumpeter Mark I industries assumes the form of "creative destruction" with successful innovating entrants replacing the incumbents. Vice versa, Schumpeter Mark II industries are characterized by stable environments with relatively high entry barriers in which innovations are generated and developed by large established firms. In Schumpeter Mark II industries technological competition is related to a creative accumulation pattern where innovations are introduced by firms that innovated before: it is called 'deepening' [102], [103].

In 1934 in the "The Theory of Economic Development", Schumpeter proposed a list of various types of innovations:

- Introduction of a new product or a quantitative change in an existing product;
- New process of innovation to an industry;
- The opening of a new market;
- Development of new sources of supply for raw materials or other inputs;
- Changes in industrial organisations [88].

On the other hand, in 1982, Freeman proposed a classification system based upon degrees of innovation*: revolutionary* and *radical* or *incremental*. Many have drawn on this typology to describe pharmaceutical innovations. The term "revolutionary" innovations can be used to describe major conceptual advances such as the identification of microbes and classes of anti-infection agents (Microbiological Revolution of late 19th & early 20th century). Alternatively, the distinction between radical and incremental innovations offers a convenient approach to making more subtle distinctions. For example, a new understanding of a disease mechanism and a new mode of action, which interferes with the disease process at a molecular levels can be described by the term radical innovation. Within this envelope, however, alternative molecules developed with different attributes, which offer value in treating particular disease variants or patient segments, can be referred to by the term "incremental" innovation [86].

A radical innovation could be considered the first product in a new class to market, while all those following are labelled incremental innovations. Alternatively, the term radical might be used to describe the class as a whole, reflecting the collective effort of the range of players involved in the process, and all the products would be referred to as "incremental" alternatives. The term radical is thus reserved for the process, while the term "incremental" is used for individual products. The majority of the innovation models used are based on assembled products or service products [28]. However, early models of the innovation process are not suitable enough to capture the complexity of innovation in the life sciences sector. In particular, narrow classifications which describe innovations as radical or incremental are not particularly useful when considered in the context of the complex patterns of interrelated innovations observed in practice [86].

Another perspective of innovation models is based on the term ***Open Innovation (OI)***, defined by Henry Chesbrough (2003) as "*a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as the firms look to advance their technology*" [104] (pp. xxiv). It is also defined to be a process of innovating with partners with whom risks and rewards are being shared [104], [105]. This model stresses the importance of new business models, other than traditional company-held intellectual property protection, for knowledge and for being connected to global and multiple diverse knowledge sources [106].

The OI model involves two way flow of intellectual property and human capital between firms and the transfer of intellectual property and people from universities and research labs to large and small companies [105]. Additionally, this model eliminates the need for vertical R&D organisations spanning the whole spectrum of discovery and research, eliminating costly infrastructure duplications and saving significant funds [107]. In this context it could be said that organisations involved in this model are Universities, Scientific Parks, Research Labs, startups, SMEs and large firms. In particular, Scientific and Technological Parks (STPs) are natural candidates to become multi-way connectors for OI. It has been mainly started in the high-tech sector, but there is a new trend for the low-tech sector to exploit the potentials of opening up their innovation process [108]. In this context, this model has also gained importance in the nanotechnologies industries [109]

More recently, new innovation models approximations are emerging. For instance, Clausen et al., (2013) defined a new taxonomy of innovation based on four modes ''open exploration'', ''closed exploration'', ''open exploitation'' and ''closed exploitation''. This type of classifications combines in a new way two well-known theory streams: closed/open innovation and exploration/exploitation [110].

1.2.2 Systems of innovation

The ***System of Innovation*** (SI) concept was originated in the 1980s in Europe and in the US in parallel [111]. It is referred to all the organisations, institutions and their interactions, that contribute in one way or another to innovation [112], [113]. It provides a consistent conceptual framework for integrating key science, technology and innovation institutions into economic development [114], therefore, the SI approach has been considered adequate to analyse technology evolution [61]. Furthermore, understanding SI can lead policy makers to propose strategies aimed to enhance innovative performance and competitiveness, but also to identify bottlenecks that can hinder technology development and diffusion [115].

SI stresses the importance of the knowledge flow in innovation process and it can be applied at different levels: national, regional, sectorial and technological [115]–[118]. Economic development was associated with a National Systems of Innovation (NSI) approach pioneered by Christopher Freeman (1995, 2002), Bengt-Ake Lundvall (1992) and Richard Nelson (1993) [114]. The NSI has been defined as "*elements that interact in shaping innovation processes as well as elements that link innovation to economic performance*" [111] (pp. 99). In this context, firms are considered very important in an NSI since they strongly influence both the direction and the vigour of their own innovative activities [97].

Most innovation policies are national in scope, however, their results are most often being produced at some regional levels [112]. In each country, innovation is concentrated in a few regional centres, therefore, and according to Braczyk et al., (1998), Howells (1999) and Cooke (2001), the SI can also be examined considering a regional perspective. These authors refer to the concept of Regional Systems of Innovation (RSI). RSIs are not simply agglomerations of private innovative firms, but they also include other organisations and institutions, the nature of which varies from one industry or technology to another [117], [119], [120]. Successful cases in the US (e.g. Silicon Valley) as well as in EU (e.g. Baden-Württemberg) have originated that governments launched many programs with the aim of supporting regional innovation policies [121].

NSI and SSI display different capabilities on the basis of their various institutional and social arrangements [114]. In this context, it is important to have indicators to compare and benchmark innovation performance at a regional level. Such evidence is vital to inform policy priorities and to monitor trends [25]. Design and development of new nano products and systems will have significant social and economic impacts [11] in nearly all sectors in a relatively short amount of time [4], [10]. For this purpose, there is a need of a well-established innovation strategy and measurement tools into the NSI. At the present, this is well recognized by most

governments who believe that innovation is a key driver for economic development and a fundamental source of competiveness in the global marketplace [22].

On the other hand, the Sectorial Systems of Innovation (SSI) approach emerges from the work of Malerba (2002). This approach asserts that different industries may have different competitive, interactive and organisational boundaries that are not necessarily national [112], [118]. A SSI is therefore a set of products and the set of agents carrying out market and non-market interactions for the creation, production and sale of those products most of the sector case studies focus on a single dimension [118]. It is based on knowledge, technologies, inputs and an existing, emergent and potential demand. The agents composing the SSI are organisations and individuals, consumers, entrepreneurs, scientists, producers and input suppliers, and non-firm organisations, as universities, financial institutions, government agencies, trade-unions, or technical associations, including sub-units of larger organisations, for example R&D or production departments, and groups of organisations (industry associations) [118]. Its performance can be evaluated and improved, as can be the specific components of each system (innovation policies, research universities, public laboratories, and others) [112].

The shift in nanotechnology from research to commercialization, although occurring in a period of globalization and internationally networked science, is influenced at least in part by the NSI of the countries in which the R&D activity is embedded. Countries that have invested in or otherwise supported a high share of enterprises early in the timeline of nanotechnology R&D are more likely to see higher levels of commercial activity in the later period [106].

1.2.2.1 Networks and multi-stakeholder ecosystems

In order to stimulate and create innovation, the interaction and connectivity of multiple actors is required [122]. The last relevant stream within the strategic management of technology literature based on these interaction and connectivity factors is the ***network theory*** [36], [121], [123]–[128]. Successful new product innovations typically come from firms, which take advantage of the different technological and market ideas available in broad networks. Bliemel and Maine (2008) argued that new technology-based firms are most successful when they are moderately embedded in networks, with a mix of strong (efficiency) and weak (exploratory) ties [129].

Table 1.9. Typology in innovation networks.

Type of innovation network	Primary purpose/target
New product or process development consortium	Sharing knowledge and perspectives to create and market new product or process concepts.
Sectorial forum	Shared concern to adopt and develop innovative best practices.
New technology development consortiums	Sharing and learning around newly emerging technologies.
Emerging standards	Exploring and establishing standards around innovative technologies.
Supply chain learning	Developing and sharing innovative good practice and possibly shared product development across a value chain.
Clusters	Regional grouping of companies to exploit innovation synergies.
Topic network	Mix of firms companies to gain traction on key new technology.

Source: Adapted from [86] *and* [97].

Networks have emergent properties. In this context, having the right connections becomes as important as the actual generation and ownership of knowledge [130]. There is growing evidence that networking is a beneficial mode of operation in innovation in any area [131], [132]. When knowledge is emerging in two or more distinct fields simultaneously, teams need to be organised to allow for deep collaboration, essentially tacit knowledge exchange [30], [66]. **Table 1.9** provides a summary of the many types of innovation networks and the ways they are used.

Coordination efficiency facilitates the process of mutual transfer of knowledge and competences, improving learning and consequently producing positive effects on innovation [133]. Even though, the impact of many network characteristics on knowledge creation and innovation production remains unclear due to the inconsistency of the conclusions from various research studies [127].

Innovation networks are currently being referred as ***innovation ecosystems*** since James Moore in 1993 have introduced this term in business management. This concept is related to the network theory and comes from an analogy of the biological ecosystems, which considers all living organisms and its physical environments in a determined area, functioning together as a unit [134]. In this context, an innovation ecosystem can be defined by taking into account elements like industry and socioeconomic systems, therefore it consists of basically government, company, and people [135].

Innovation ecosystems are complex relationships that are formed between organisations or entities whose functional goal is to enable technology and innovation [136]. Therefore, the core concept of an innovation ecosystem is that the set of organisations and factors immersed in this complex relation is what will determine a successful innovation. In this context, it is desired that all elements can

co-exist in a balanced way so that knowledge and technology can be transferred (**Figure 1.6**)[137].

Due to the drastically reduction in coordination costs, innovation ecosystems have become an essential element in the strategies of firms from a wide range of industries. Therefore, for firms, being involved in an innovation ecosystem are more willing to create value than being alone [136].

In the same line of thinking of Testar (2012), Roco et al., (2011) affirms that an innovation ecosystem will be further developed for applications of nanotechnology, including support for multidisciplinary participation, multiple sectors of application, entrepreneurial training, multi-stakeholder-focused research, regional hubs, private-public partnerships, gap funding, and legal and tax incentives [8]. In this regard, a Nano-biomedical research innovation network can be observed as exposed in **Figure 1.7**. The graph shows a balanced innovation ecosystem where nanotechnology gains an increased relevance because of the cross-fertilization of the different scientific domains: physics, biology, chemistry, and engineering [30].

As the main characteristic of a nano-enabled biomedical is its multidisciplinary, fostering the integration of knowledge from different dimensions is essential [28], [30]. In this context, the cooperation of public research institutions and the private sector that produces and diffuses nano-knowledge plays an important role in this innovation ecosystem [30], [138].

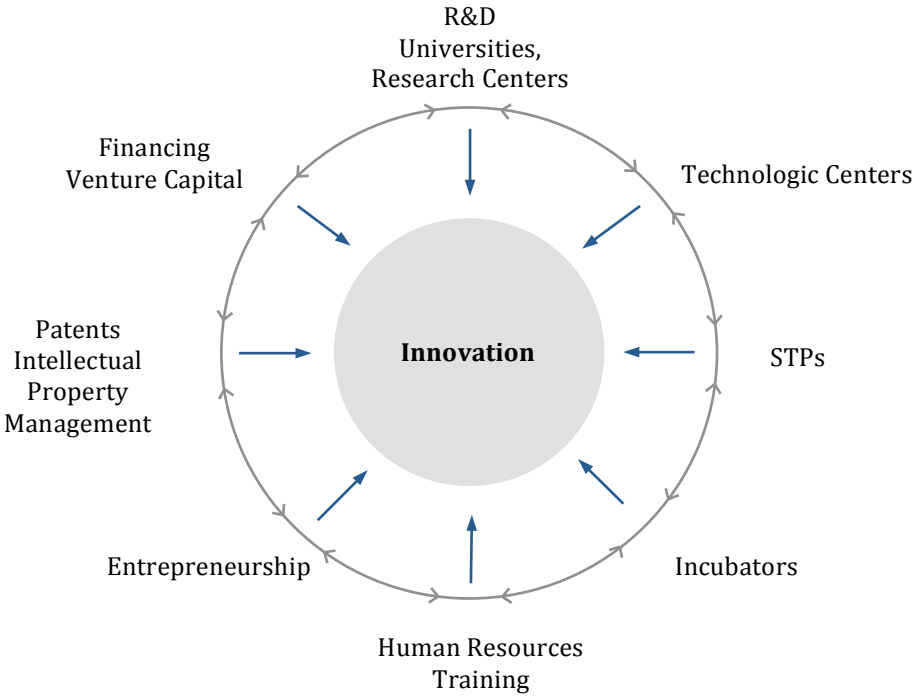

Figure 1.6. Innovation ecosystem (Source: [137]).

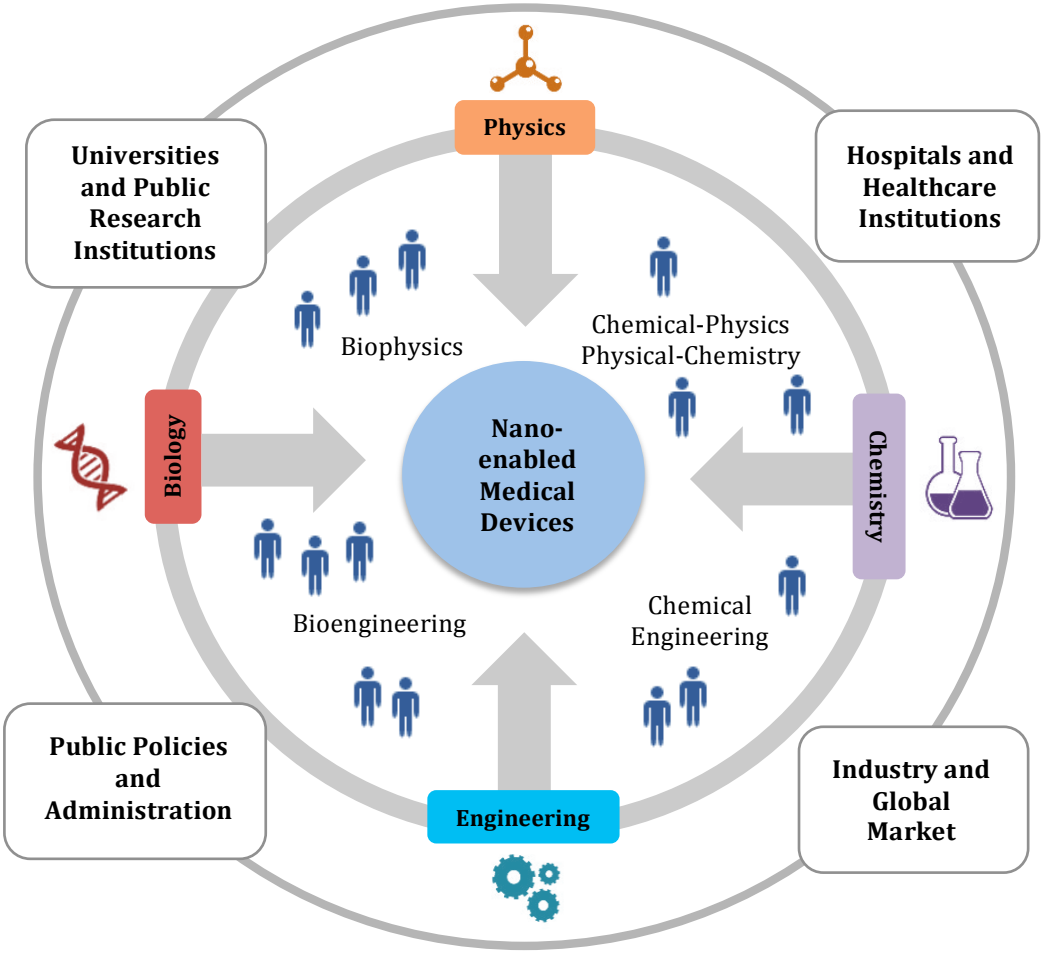

Figure 1.7. Nano-enabled biomedical devices within an innovation ecosystem (Source: inspired in [30]).

1.2.2.2 From the Triple-Helix to the Five-Helix model

In the line with the network theory, the technology policy and SI literature rose the prominence of the ***Triple-Helix model*** during the second half of the 1990s [139]. This model was initially derived from an analysis of the renewal of the Boston economy, through a university-industry-government collaboration for firm-formation from academic research in the 1930s [140]. The Triple-Helix model suggest that three sectors or helices: university-government-industry (UGI), communicate and continuously interact with one another and can occasionally, and partially, take on each other's role [141], [142]. This model provide a great insight into the complex dynamics and collaboration between the corporate world, the public sector, universities and research organisations [87], [122]. These dynamics

influence the creation and the diffusion of knowledge, the production of value added with its attendant market dynamics, and finally, regulation [122].

According with Etzkowitz and M. Klofsten (2005), some considerations of this model can be highlighted:

- This model has a prominent role for the university in innovation, on a par with industry and government in a knowledge-based society.
- There is a movement toward collaborative relationships among the three major institutional spheres in which innovation policy is increasingly an outcome of interaction rather than a prescription from government.
- In addition to fulfilling their traditional functions, each institutional sphere also "takes the role of the other" [94].

The model has highly emphasized a third role of universities, which is an "entrepreneurial" role. This entrepreneurial perspective considers that university could directly interact with society, beyond teaching and educating. The university third role include creating new high-technology firms, consulting for local industry, delivering advice to politicians and policymakers and informing general public debates and shaping the national spatial distribution of social opportunities and services [94], [142], [143]. For this reason, the emergence of a Triple-Helix of innovation, with the university as a key player, is the great transformation of the late 20th and early 21st century [141]. Consequently, this interaction among the UGI is view as the source of innovation and development in the current knowledge-based societies [94], [141].

The Triple-Helix model was the starting point of a SI theory. Nevertheless, there has been an evolutionary process in this model. The seminal Triple-Helix model stablished a nation state encompassing academia and industry and directing the relations between them (**Figure 1.8a**). A second policy model consists of separate institutional spheres with strong borders dividing them and highly circumscribed relations among the spheres (**Figure 1.8b**). Finally, the third Triple-Helix is generating a knowledge infrastructure in terms of overlapping institutional spheres, with each taking the role of the other and with hybrid organisations emerging at the interfaces (**Figure 1.8c**) [142]. Although this model has been demonstrated to promote Nanotechnology development [144], recently there has emerged a new concept at the innovation models literature: the ***Five-Helix model*** (**Figure 1.8d**) [30].

The Five-Helix concept includes the same three engines of the Triple-Helix Model University-Hospital-Administration plus Hospitals and Citizens, enhanced by Scientific and Technological STPs Parks, which are the motors of the model. It was coined and implemented by numerous authors in relative recent publications [30],

[145]–[148] and has demonstrated to be suitable for the healthcare system, including life sciences as Medicine, Biotechnology and the Nanotechnologies. Particularly in medicine there is a pressing need to ensure close cooperation between University– Hospital–Industry–Administration while specific tools and procedures are developed for use by clinicians [30], therefore the Five-Helix model could be considered an engine for economic growth and social benefits.

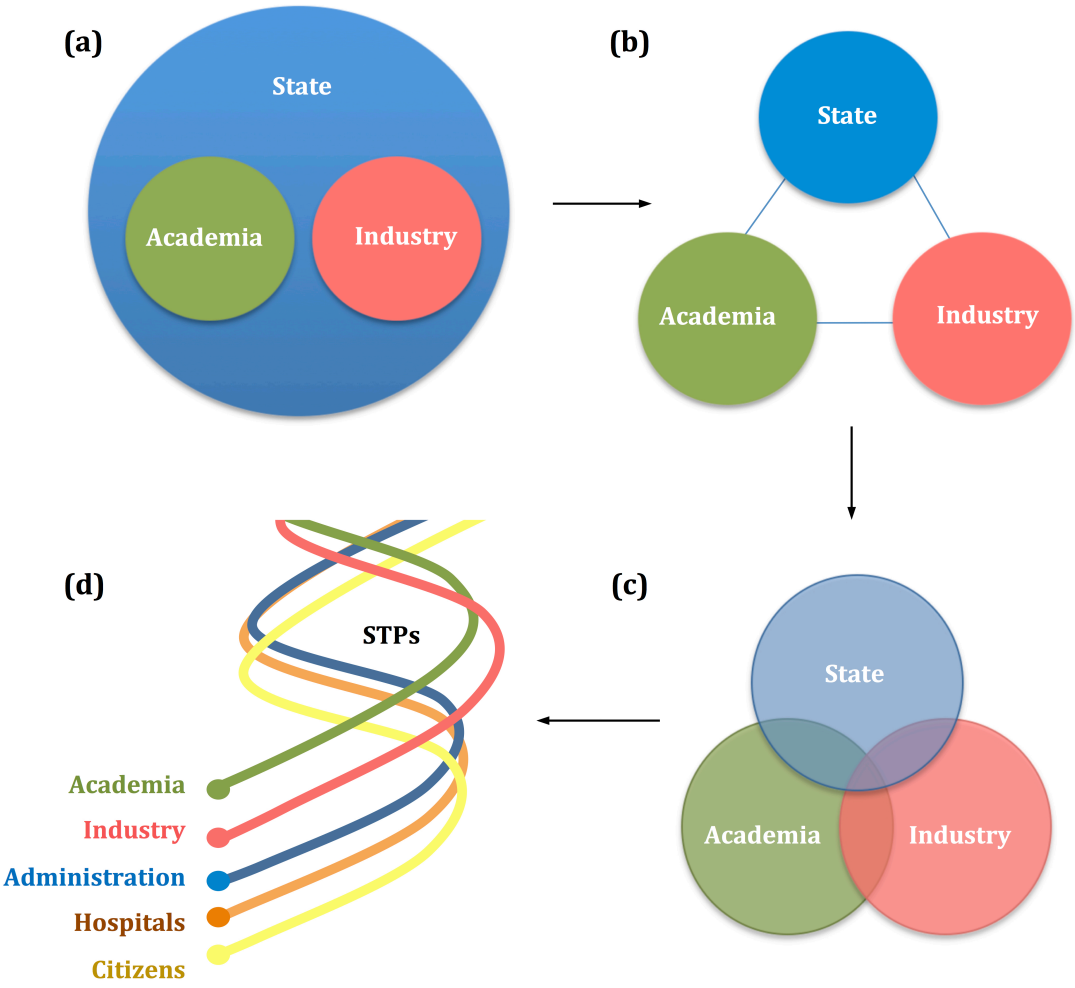

Figure 1.8. Evolution of innovation systems. (a) first Triple-Helix; (b) second Triple-Helix; (c) third Triple-Helix; (d) Five-Helix model (Source: Adapted from [142] and [30]).

1.3 Nanotechnology innovation in Europe: Facts and figures

Innovation is a complex and multidimensional activity that cannot be measured with a single indicator [87], [92]. Indeed, there isn't any single adequate measurement to capture innovation multiplicity of features [92]. Nowadays, national measurements of innovation are based on industrial economy and can be obtained by measuring intermediate *outputs* such as (publications, patents, workforce size or experience and innovative products), and *inputs* (such as R&D expenditures, education expenditures, capital investment)[92].

Patents and publications are two accepted quantitative indicators for measuring innovation [96], [149]. Patents are a measure of technological performance [53], [127] and publications of scientific performance or research production [53]. Innovation-related indicators also include the number of start-ups [150] or the number of companies generated [149], [151]. With these indicators the recent and actual development of emerging technologies can be illustrated and future potentials can be anticipated. In this section some of these output and input indicators are exposed for having an approximation of the facts and figures of nanotechnology innovation in Europe.

1.3.1 Nano-related patents

The common approach in the literature is to focus on tangible outcomes such as patenting and licensing of research results [6]. Patents are the most commonly used indicator of the results from applied research. Patents are aimed to protect inventions from imitation by third parties and therefore to obtain the exclusive right of economic exploitation for a certain period of time [53]. Number of patents registered in each region and ineach year reflect the ability of transferring scientific results into technological applications [50]. Patents are also an approximation of the knowledge production [152], invention [153], technological novelty [103] and creativity [11], as well as an indicator of past investments [154], applied research and technological development [155], [156].

According to the US Patent and Trademark Office (USPTO), the world's largest and important patent office, nano-related patents are those whose subject of matter has at least one physical dimension of approximately 1-100 nanometres, and which involve a special property, function or effect that is uniquely attributable to the nano-scale physical size [121]. On the other hand, the ISO/TS 18110[2] (First Edition

[2] International Organisation for Standardization. Nanotechnologies. Vocabularies for science and innovation indicators. Provides the necessary definitions that specify the bounds of key innovation indicators as they relate to nanotechnology, in order to facilitate and unify the global assessment of nanotechnology activities in different areas.

2015-08-15) considers that nano-related patents are those that include at least one claim related to nanotechnology. It can also apply for patents that are classified with an International Patent Classification (IPC) code related to nanotechnology, such as B82. Relevant nano-related patents (and also publications), can be found by using the prefix "nano*". However, even many patents include nano-related terms in the patent disclosure, only a limited number of patents actually claim a nanotechnology invention [121].

From 1996 to 2001, the European Patent Office (EPO) revealed 5.000 patent applications. For that range of time, 36% were from fifteen EU countries. From these, Germany, France, the UK were the leaders [157]. In a global comparison from 2000-2010, it has been identified that major contributors in nano-related patent applications were the US, Japan, Europe, Korea, and China. Involved institutions in this report were distributed as follows: Academia (12%), Research Institutions (18%), and Companies (70%) [52].

From 2006 to 2015, nano-related granted patents in EPO were approximately 9.615. In these period of time, an incremental growth can be evidenced in published patent applications, and nanotechnology granted patents as well [158]. Recent data in the EPO database shows that the US, Germany, France and Japan are the leading countries on nano-related granted patents since ten years ago (**Figure 1.9**). In this same list, European leading countries are Switzerland, UK, Netherlands, Italy, Sweden and Spain [159].

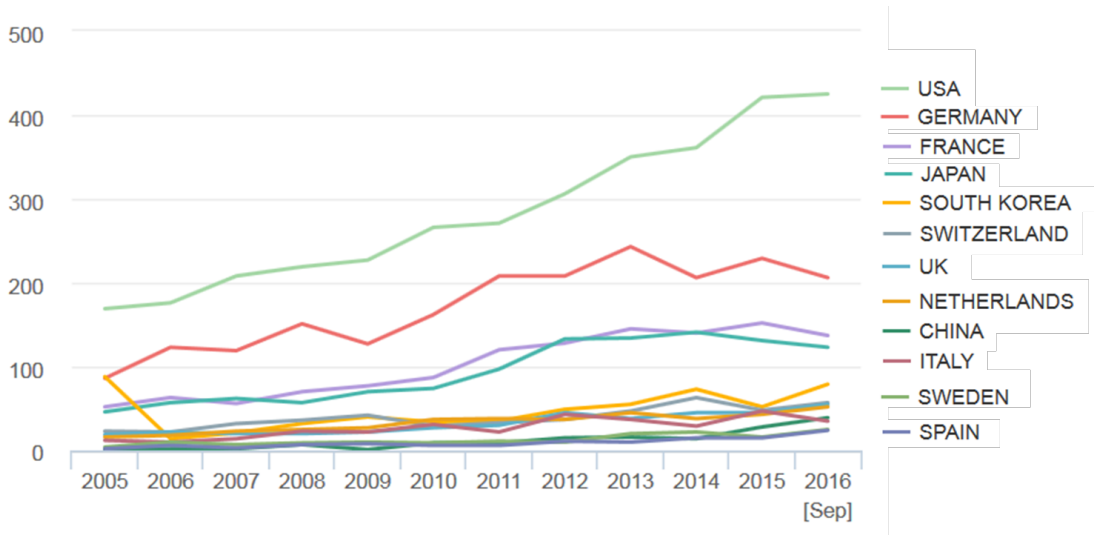

Figure 1.9. Number of nano-related granted patents in EPO from 2005-2016. (Source: [159]).

Concerning a regional contribution of nano-related patents at the EPO in comparison with other KETs, the EC has identified that for the year 2011 (which is the last year available), countries with more nano-related patents are Germany, France, the UK, and Spain (**Figure 1.10a**). **Figure 1.10** also shows that for all KETs, the patenting pattern is almost the same in EU countries. For instance, Germany, France and UK are the leading countries in Micro and Nano-electronics (**Figure 1.10b**), Photonics (**Figure 1.10c**), Advanced Materials (**Figure 1.10d**), Industrial Biotechnology (**Figure 1.10e**) and Advance Manufacturing Systems (**Figure 1.10f**). These patents are based on data provided by the Organisation for Economic Co-operation and Development (OECD) and were assigned by considering the address of the inventor [160].

In the same figure, it can also be viewed that KETs with major patents in the region are Advanced Manufacturing Systems, Advanced Materials and Micro and Nano-electronics.

1.3.2 Nano-related publications

As previously commented, publications are important output indicators in applied research, in which organisations show their current state of research and dissemination of results [53]. As well as patents, there is also a worldwide increment of nano-related publications [161]. The relative growth in number of ''nano-title-papers'' in various bibliographic databases have grown exponentially in lasts years [30]. Nano-related publications have grown from almost 40.000 in 1998 to 100.000 in 2009 [52].

Hullmand and Meyers (2003) reported that countries in the EU with major nano-related publications between 1991 and 1999 were Germany, France, IK, Italy, Switzerland, Spain and The Netherlands [53]. These results are similar for the same range of years from the ones obtained by Heinze (2004). This author revealed that one third of the global publications were attributed to fifteen EU member states [157]. In the same line, Miyazaki and Islam (2007) performed a cross-country comparison of scientific nano-related publications from 1990 to 2004. They have shown a vertiginous growth curve starting from 1994. The share of publications during this period was distributed between the US (27%) and the EU (26%) as global leaders. After them were Japan (15%) and Great China (11%) [9]. Leading the list of European countries for were Germany, France, UK, Italy and Spain. These authors also exposed that universities account a large share of the research in nanotechnologies, representing 70.45% of nanotech-related research worldwide public research institutes account for 22.22%, and the private sector a limited role with 7.33% of articles globally [9].

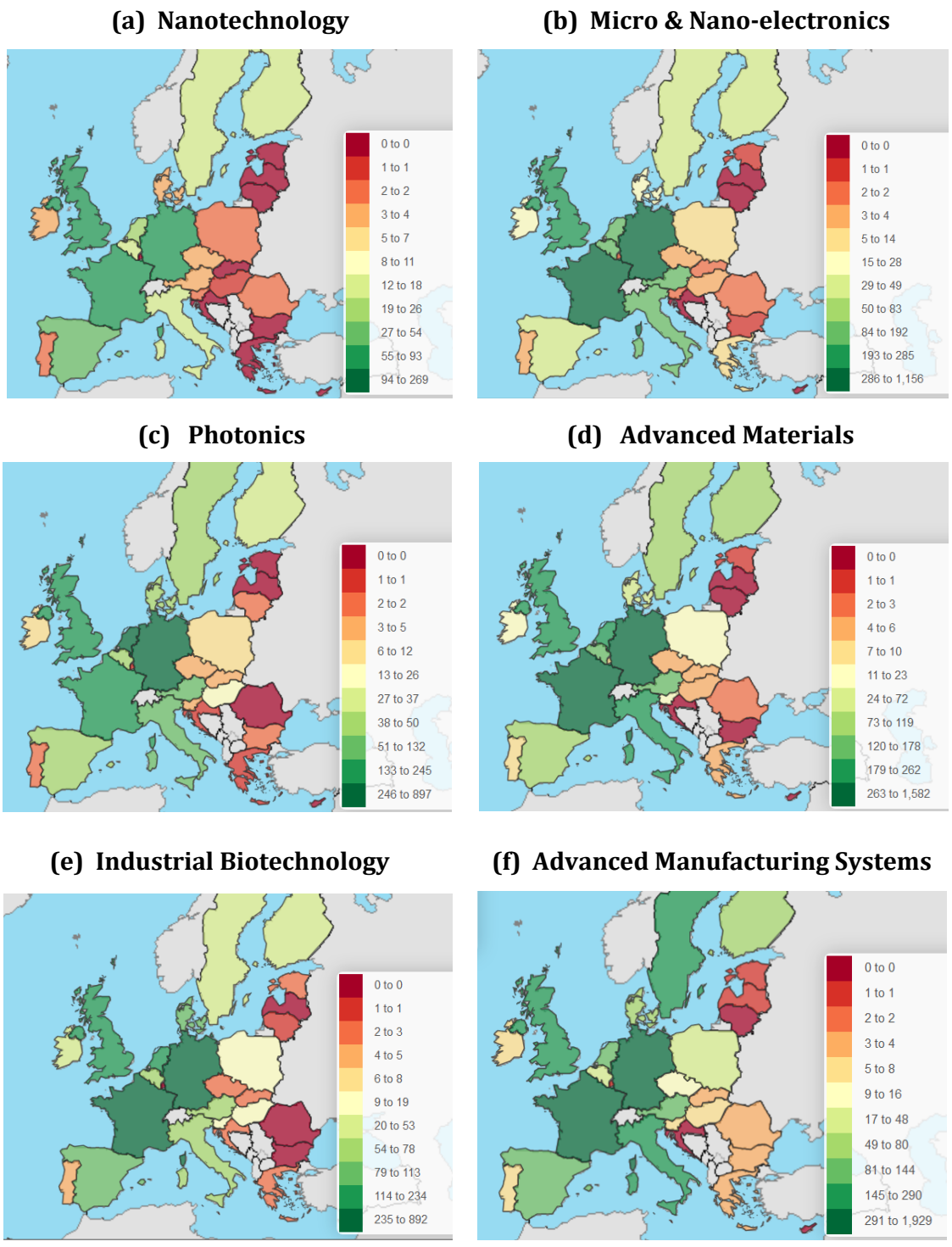

Figure 1.10. Regional distribution of KET patents in European countries for the year 2011. (a) Nanotechnology; (b) Micro & Nano-electronics; (c) Photonics; (d) Advanced Materials; (e) (Industrial Biotechnology; and (f) Advanced Manufacturing Systems (Source: [160]. Last updated 03-08-2016).

The Asia Nano Forum Report (2014) revealed that China, the US, South Korea, India, Germany, Japan, France, the Islamic Republic of Iran, England and Spain were the top 10 countries in Nanoscience and Nanotechnology publications in 2012 [51]. More recently, it was evidenced that ISI[3] indexed nano-related articles world-wide between 2006 and 2015 were approximately 910.236 [158]. The country with major publications of this type is China with a vertiginous growth curve, following by the US (**Figure 1.11**). European leading countries are Germany, France, UK and Spain [159].

Latest data regarding Health, Medicine and NanoBio sectors in an European sectorial publication analysis, showed that Germany remains to be the principal European leader, following by France, UK, Italy and Spain (**Figure 1.12**) [52].

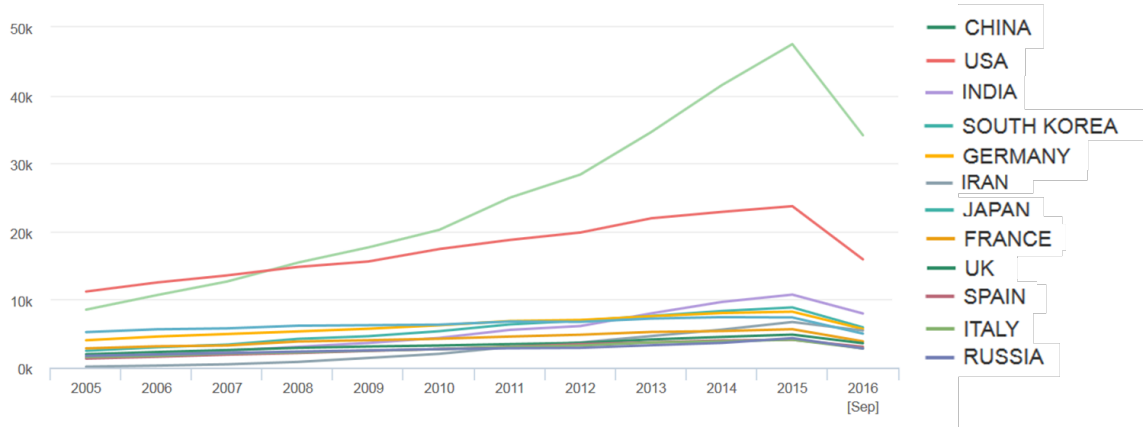

Figure 1.11. Number of ISI indexed nano-related publications in 2005-2016 (Source: [159]).

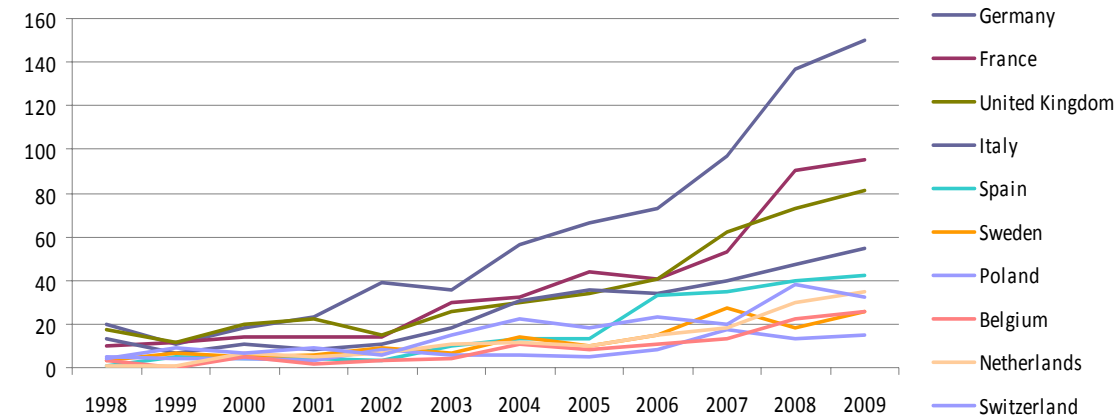

Figure 1.12. Number of publications per year (1998-2009) for Health, Medicine and NanoBio sectors (Source: [52]).

[3] Institute of Scientific Information

The world-wide growth curve in nano-related publications has also been evident at Nanomedicine and Nanobiotechnology topics (**Figure 1.13**). A quick search with the query term "Nanomedicine" at the GoPubmed[4] database resulted in 14.415 documents world-wide (**Figure 1.13a**). In this thematic, the first European country to appear is Spain, which is in the 3rd position after the US, and China (**Figure 1.14a**). On the other hand, the same search with the query term "Nanobiotechnology" resulted in 2.890 documents (**Figure 1.13b**). In this category, the first European country to show up is Germany, which is in the 5th place, after the US, India, China and Iran (**Figure 1.14b**).

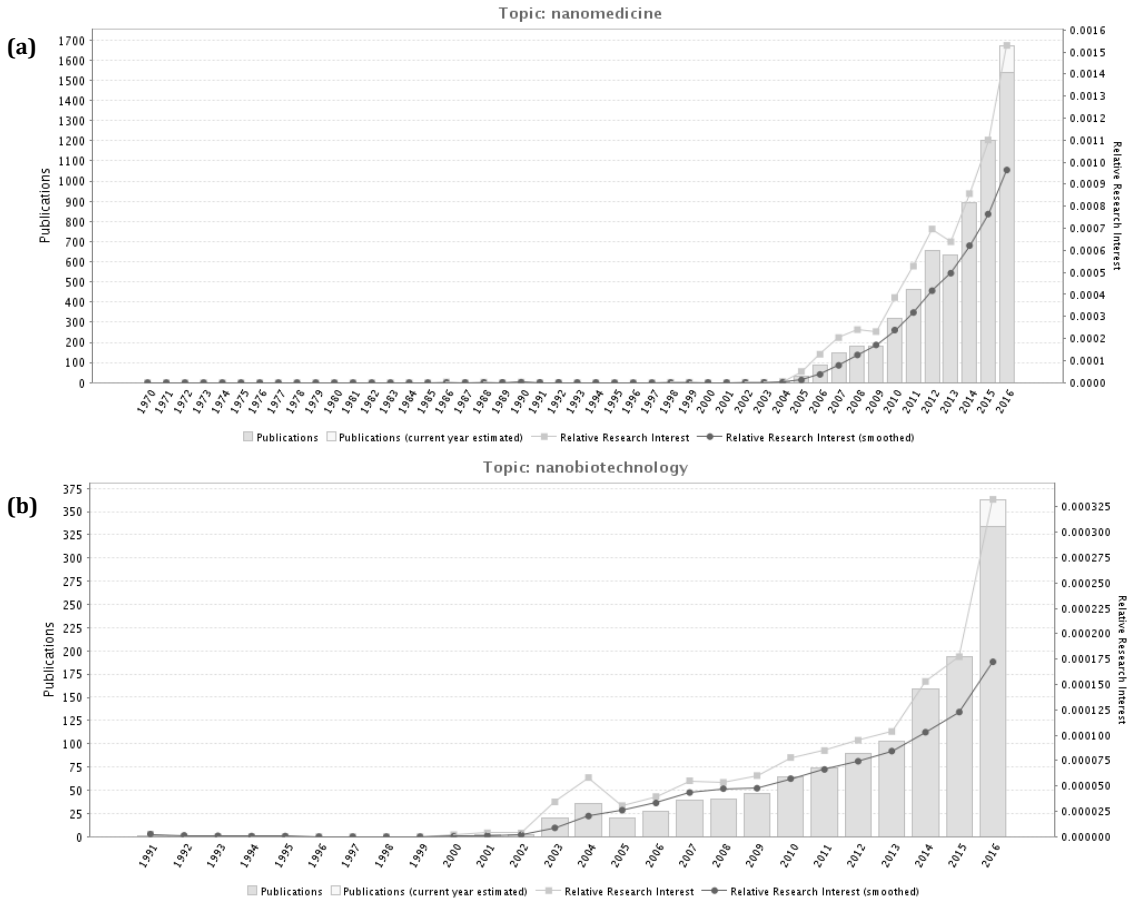

Figure 1.13. GoPubmed world-wide publications per year. (a) Nanomedicine related publications; (b) Nanobiotechnology related publications. (Source: http://www.gopubmed.com, Search date: October 2016).

[4] www.gopubmed.com/web/gopubmed

(a) Nanomedicine

Top Countries	Publications
United States	2,209
China	1,407
Spain	457
Italy	358
Germany	336
India	325
South Korea	305
United Kingdom	291
Japan	239
France	238
Australia	227
Taiwan	212
Canada	212
Brazil	143
Iran	127
Saudi Arabia	120
Netherlands	118
Singapore	112
Switzerland	105
Denmark	102

(b) Nanobiotechnology

Top Countries	Publications
United States	358
India	144
China	131
Iran	112
Germany	87
Japan	69
United Kingdom	64
Spain	61
Italy	59
South Korea	58
Australia	52
Brazil	51
Austria	51
Canada	46
Sweden	38
France	38
Russia	29
Switzerland	28
Taiwan	22
Poland	19

Figure 1.14. GoPubmed worldwide statistics. (a) Nanomedicine related publications; (b) Nanobiotechnology related publications. (Source: http://www.gopubmed.com, Search date: October 2016).

1.3.3 Nano-related industry

The creation of companies is another important indicator for the development and economic significance of a new technology. New companies are typically start-ups which are created as the result of a patent on a new technology which they can exploit themselves or license to other companies (more capable in terms of production or distribution) [50]. By analysing the number and state of companies, technological strengths and weaknesses of a country can be inferred. Analysts like Porter (1990) have shown that business firms are strongly influenced in their choice of technological strategies by the conditions existing in their home countries [97]. Therefore the number of research-based start-ups could be an indicator of excellence in a field and in a region [162].

Nanotechnology is currently entrenched in the mainstream of industry, and many companies have shown their confidence in its future by committing substantial resources to its development. Industry has gained confidence that nanotechnology will bring competitive advantages to both traditional and emerging fields, and significant growth is noted in small businesses, large companies, and venture capital firms [29]. In this context, all Fortune 500 companies involved in Advanced Materials, Electronics, Chemicals and Pharmaceuticals have shown involvement of nanotechnology in the last couple of years [13].

According to the OECD, nanotechnology firms are the ones that use nanotechnology to produce goods or services and/or perform nanotechnology related R&D. In a world-wide comparison from 2015, the US is by far, the country with the majority of nanotechnology firms according to this description (**Figure 1.15**). Following the US are Germany and France as the leading European countries. Subsequently, the Asian country with major nanotechnology firms is Korea [163].

In the same graph it can be viewed that dedicated Nanotechnology firms (defined by the OECD as firms that devote at least 75% of their production of goods and services, or R&D, to nanotechnology) are more in number in Germany, Korea, France and the US [163].

The combined industry of Nanobiotechnologies has also growth in these last years, especially in North America (**Figure 1.16**). In Europe, leading countries with major number of firms are Germany, UK and France, which are leaders in nano-related patents and publications, as have been seen in previous sections.

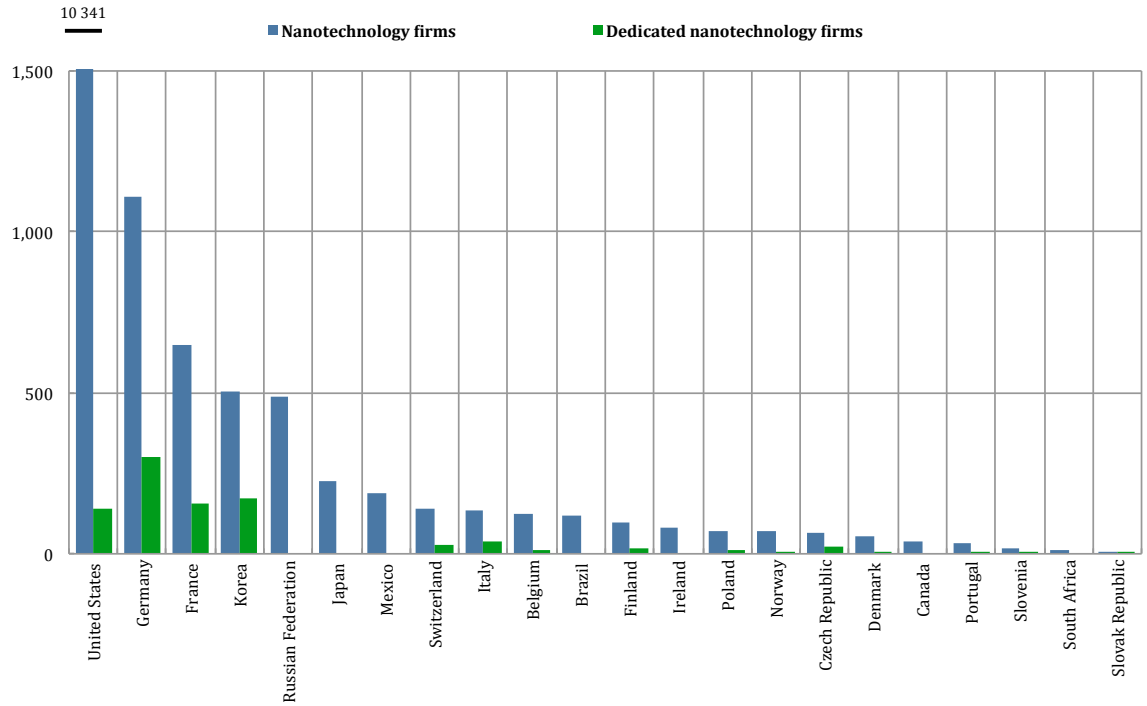

Figure 1.15. Number of firms active in nanotechnology, 2013 or latest available year. (Source: [163]).

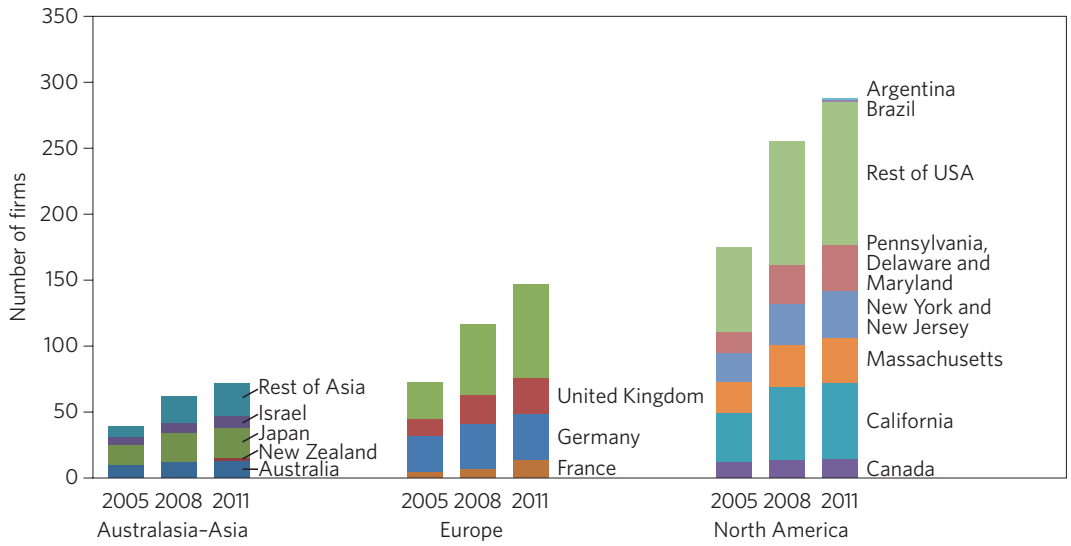

Figure 1.16. Emergence and evolution of the global nanobiotechnology industry (Source: [18]).

1.3.4 Expenditures and investments

Industrial innovation is sustained by research investments. In this regard, several strongest regions like the US, EU, and Asia are highly investing in R&D&i. Some of these indicators can be evidenced in **Table 1.10**, where it can be viewed that European countries have a good performance. Despite this fact, over the past years, the Europe's share of global R&D spending has continuously declined, compared with the increased investment of the US and the Asian countries [164].

Nanotechnology R&D activities have continuously internationally expand in recent years [106]. Key OECD Nanotechnology indicators shows that the US and Korea were the countries with major Nanotechnology R&D expenditures in the business sector in 2013 (**Figure 1.17**). Countries like Germany, Japan, France, the Russian Federation, Italy and Belgium are placed by far of these two leading countries [163].

On the other hand, government funding is a key factor and a strong support in the development of innovation infrastructures and in the subsequent local and regional innovation system as a whole [165]. In the EU, Nanoscience and Nanotechnology related strategies have been present from more than twenty years. The firsts approximations where done in 2004, where Nanotechnologies were considered strategic as was evidenced at the communication "Towards a European Strategy for Nanotechnology", followed by the communication "Nanosciences and

Nanotechnologies: An Action Plan for Europe 2005-2009" in 2005. [166]. Later on, Nanotechnologies were present in the EU's Framework Programmes (FP) for research and technological development. Specifically, the FP6 and FP7 are the ones that stressed the need of nanotechnology applications in Europe.

Even there has been a great progress in addressing Nanotechnology in legislations, environmentally and consumer associated risks are considered still insufficiently addressed. Risk assessment regulations, with regard to the application of nanomaterials are mainly distributed in two regulations in Europe: The first one is the so-called Registration, Evaluation and Authorisation of Chemicals (REACH/(EC) No 1907/2006) and Classification, Labelling and Packaging (CLP/(EC) No 1272/2008) [167].

Table 1.10. Economic, R&D and nanotechnology innovation indicators of top 5 countries.

Indicator		Country	Quantity	Position
Funding and Investment	R&D expenditure (% of GDP)*	Finland	3.55	1st
		Sweden	3.41	2nd
		Germany	2.92	3rd
		Austria	2.84	4th
		Slovenia	2.8	5th
Human Capital	Researchers in R&D (per million people)**	Denmark	7.27	1st
		Finland	7.19	2nd
		Sweden	6.47	3rd
		South Korea	6.46	4th
		Norway	5.58	5th
Science	National priority in Nanoscience generation***	Germany	0.89	1st
		France	0.87	2nd
		Spain	0.82	3rd
		Portugal	0.80	4th
		Finland	0.79	5th
	Share of international collaboration in nanoscience generation (percent)****	Sweden	74.61	1st
		Belgium	74.44	2nd
		Switzerland	70.39	3rd
		UK	70.36	4th
		Denmark	69.50	5th

** (2012); ** (2013) Researchers in R&D are professionals engaged in the conception or creation of new knowledge, products, processes, methods, or systems and in the management of the projects concerned. Postgraduate PhD students engaged in R&D are included; *** (2014) Ratio of share of nano-articles in European countries; **** (2015) Share of joint nano-articles between one country and other countries in Europe. Source:* [159].

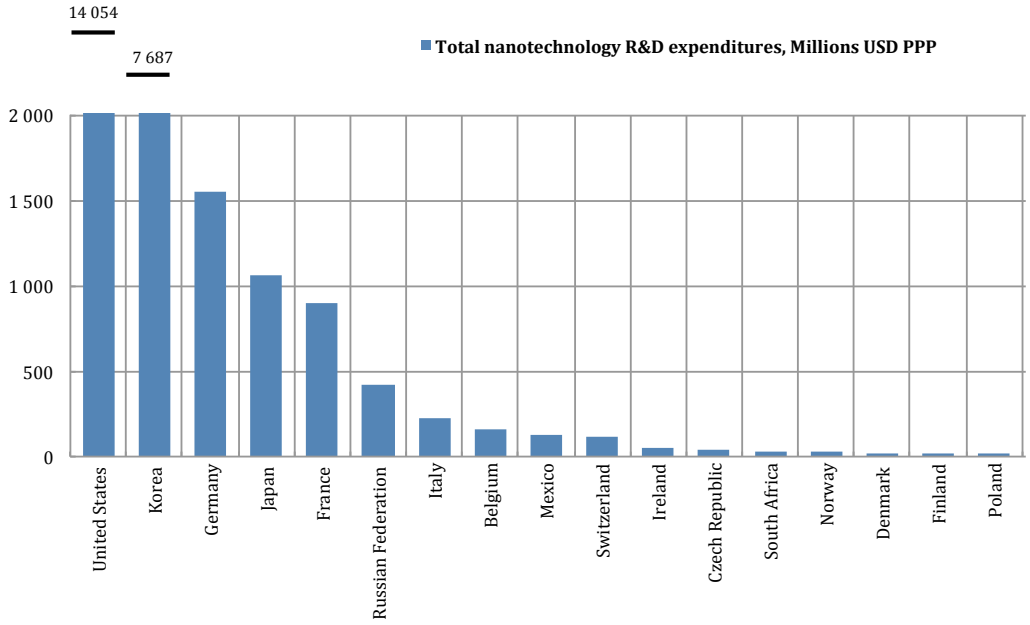

Figure 1.17. Total nanotechnology R&D expenditures in millions USD PPP[5] (Source: [163]).

1.3.4.1 Investment policies into a KETs scenario: Horizon 2020

The major economic support and investment for science research in Europe are the FPs initiatives. These funding activities are aimed to stimulate research partnerships between the productive, the academic, and the governmental sectors. FP initiatives have started in 1984 under the name of FP1 and at the beginning of 2014, the EC has launched the eighth FP under the name of Horizon 2020. Before this last initiative, the EC has invested around €80 billion, investment which has progressively increasing over the initiatives (**Figure A1 in Appendix A**) [168], [169].

FPs are organised in priority areas such as ICTs, energy, industrial technologies, life sciences, environment, transportation, and a number of additional activities. Health-related research budget have increased from 12.6% of the total in FP3 to 17.6% in FP5 [169]. Since then, the proportion has decreased to 14.0% in FP6 and to 12.0% in FP7 [168], [170]. However, this related research is still represent a very small percentage of the overall European public funds invested every year [170]. As well

[5] Purchaising Power Parity. The purchasing power of a currency refers to the quantity of the currency needed to purchase a given unit of a good, or common basket of goods and services. Purchasing power is clearly determined by the relative cost of living and inflation rates in different countries. Purchasing power *parity* means equalizing the purchasing power of two currencies by taking into account these cost of living and inflation differences.

as the budget, priority areas have been progressed through the FPs. With the economic structural change, the main thematic focus has shifted over the time from energy and industrial technologies to the application of ICTs and life sciences [171].

From FP4, the scope of activities has also been successively expanded to cover training, networking, demonstration, and preparatory activities (**Figure 1.18**) [171]. In H2020, all innovative projects are aimed to include activities related to project management (PM), quality assurance (QMS), dissemination including standardization (Dissem), and risk management strategy (Risk), this last one aimed to minimize harms to the users and the environment. Additionally, the current initiative makes reference to nine Technology Readiness Levels (TRLs), in order to measure the technological maturity in participant projects.

H2020 aims to cover all research and innovation funding currently provided through the FPs, the Competitiveness and Innovation Framework Programme (CIP) and the European Institute of Innovation and Technology (EIT), providing a simplification of existing innovation funding's [153], [172]. It is focused on turning scientific breakthroughs into innovative products and services [45]. It has scheduled over 80 billion € for research funding emphasized on three fundamental and mutually reinforced pillars: 24.598 million € intended for ***Scientific Excellence***, 31.748 million € for ***Societal Challenges*** and 17.938 million € for ***Industrial Leadership***. This last one aims to support SMEs in the industrial development and application of KETs [25]. From the total budget, 17.6% will be invested into Leadership in Enabling and Industrial Technologies, 3.5% to Future and Emerging Technologies and 0.8% to Innovative Small and Medium size enterprises (SMEs).

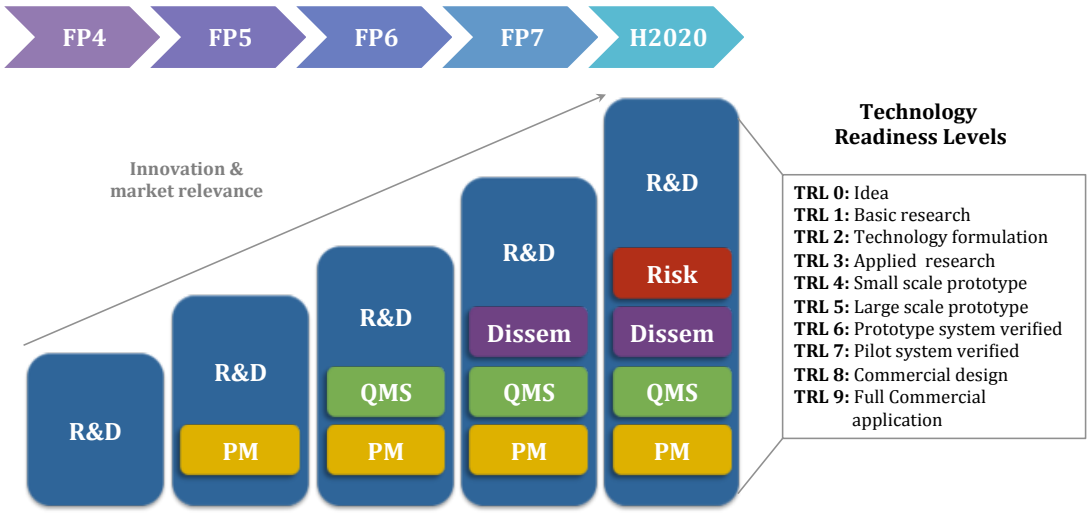

Figure 1.18. Evolution of strategies along European Funding Programmes (Source: adapted from [173]).

Although the budget seems to be extremely high, it's only one-third of what China is planning to invest in R&D [172].

Data shows that strong participation of SMEs is the particularity of H2020 compared to past initiatives. This seems to be strategic since 99% of all European business are SMEs and only about 22% of SMEs participating in EU research programs are strategic innovators [174]. In this context, the first call in the H2020 SME instrument category, which carries out a feasibility study to verify the viability of the proposed disruptive concept or innovation, has currently 155 beneficiaries.

1.4 Conclusions of Chapter 1

This first chapter introduces the state-of-the-art of nanotechnologies in the field of healthcare focusing on innovation dynamics and theories, key issues that constitute the theoretical framework of the present thesis. The chapter provides a better understanding of the current state and future perspectives for the improvement of technology transfer and commercialization in this new industrial and economic scenario.

Nanotechnology has experienced an exponential growth in the last few decades. Nowadays, it is considered the engine of the next industrial revolution due to its wide applicability in areas such as the environment, health, materials, energy, and education, among others. In particular, healthcare nanotechnologies applied in the nanobiotechnologies and nanomedicines are especially expected to improve quality of life, but also to expand the frontiers of medicine.

Diagnostics, therapeutics and regenerative medicine are the three main identified areas where nanobiotechnology and nanomedicine are having a promising impact. For instance, nanoparticles for drug delivery, nano-architectures and nanostructures for tissue engineering, bio-nanomaterials for regenerative medicine and synthetic biology are the applications where major growth is expected. Advances in POC devices are also noteworthy, since it is expected that they will have increased sensitivity, selectivity, and multiplexing capabilities, consequently creating the possibility of making the transition from remote labs to hospitals and then eventually to homes. As such, the immediate consequence will be an improved quality of life, reduced levels of morbidity, less invasive procedures and a dramatic reduction in the cost of these devices.

Besides nanotechnology R&D, an important emphasis should be placed on fostering their innovation, technology transference and commercialization, leading to a

societal return focused on enhancing safety, public participation and user accessibility. In this regard, European funding programmes have evolved over the years in order to promote industrial competitiveness through technological innovation. The best example is the current H2020 program, which stresses the importance of the participation of SMEs. The path for this objective is the promotion of cross-fertilized KETs, leading to sustainable products and processes, which is a differential added value to foster innovation. Moreover, new managerial strategies supported by the cross-fertilization of KETs could be needed in this new scenario, rather than improving existing technologies.

In this context, in this chapter it has been proposed that we move forward to an innovative new innovation ecosystem such as the Five-Helix model, where universities, hospitals, companies, administrations and citizens cooperate together, propelled by STPs. In this context, there is a need to establish new methods of cooperation: universities and companies must cooperate in entrepreneurship and in attracting talent to work together to analyse the market demand, which is one of the fundamentals of the H2020 objectives. Therefore, an innovative ecosystem improvement will be needed for the application of nanotechnology. Some of the challenges in this regard include a more multidisciplinary participation, entrepreneurial training, multi-stakeholder-focused research, regional hubs, and private-public partnerships.

CHAPTER 2

Innovation and technology transfer challenges: Insights from nano-enabled sensor-based devices

Abstract

Cross-fertilization of KETs enables for the development of new and improved devices. A nano-enabled device is an example of an outcome of this process. In the healthcare field, these devices are developed with the aim of improving the performance of a wide range of diagnostic tools. Furthermore, their evolution and wide applicability is gaining importance. However, in addition to the technological barriers that these devices need to overcome, there are some other challenges for the successful transference and commercialization of the technology. In this chapter, these challenges are being addressed by focusing on the innovative ecosystem in which they are being developed. To that end, four case studies of nano-enabled sensor-based devices at different levels of technological maturity are analysed. These devices have been developed in an academic scenario. Diverse challenges have been identified and are highlighted in this work. From the insights obtained, an integrated model is proposed for adequate technology transfer and successful commercialization of devices such as the nano-enabled sensor-based devices analysed

2.1 Introduction

As exposed in **Chapter 1**, technological cross-fertilization is the result of different technical backgrounds or industry sectors with high economic and social impact [175], [176]. Nano-enabled sensor-based devices are examples of an innovation built on this cross-fertilization process and represent the "fortuitous" result of years of interdisciplinary and complementary research in different fields of science [177]. Advances on these devices have been remarkable [178] and their applicability promise a great impact on healthcare [179]. In the future, several areas of integrated nanosensors and nanomaterials will be beneficial to tissue regeneration, cardiovascular ischemias, degenerative diseases, genetic engineering, guided surgery and transplants (**Table A1 in Appendix B**) [83].

Nevertheless, the successful commercialization of these early-stage nanotechnology-based devices is still facing several challenges. A few of the bottle-necks include large-scale production, high production costs, the public's general reluctance to new technology lacking safety guidelines and a well-established micro-scale industry [180]. According to Fadel et al., (2016), translating nanosensors should consider manufacturability and a focus on data quality to ensure the accuracy, stability, repeatability, and reproducibility of the sensor. All of these elements must be seamlessly integrated early in the product development cycle [181].

Innovation and technology transfer are also important challenges for the successful commercialization of these devices. However, few of these have been examined, especially for medical devices [30], [43]. Therefore, managing and commercializing emerging technological innovations is challenging [182]. Most of the investigations into medical devices have paid close attention to their research, design and deployment, but few are being studied with these challenges in mind. As a result, most of the scientific breakthroughs produced in academia fail to become a marketable product [23], [183]. In this context, the development of cross-fertilized devices should not only be assessed from a scientific perspective, but also take into account the wider picture [184].

In the last ten years, there has been growing literature referencing the commercialization of innovations that are developed in an academic R&D environment by considering the "entrepreneurial" role of the university [140], [185]–[189]. This role stresses the relevance of universities, and other publicly financed research institutions, as creators and providers of marketable knowledge [143] beyond their educational capabilities [141]. Therefore, the core of the university's function is currently based on the creation, acquisition, diffusion and deployment of knowledge [30].

There is also another realm in the literature that stresses that innovation success is not the function of a single organisation. In this regard, the collaboration of, and feedback from diverse stakeholders through a communitarian perspective is required [190]. For instance, the fifth Nanotechnology Signature Initiative (NSI) from the U.S. National Nanotechnology Initiative (NNI), entitled "*Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment* " is boosting the development of nanosensors by enabling the participation of Federal Agencies, seed communities and public-private partnerships [181].

It has been argued that one way to ensure success in an inter-organisation interaction, is to examine the way scientific knowledge flows between the principal agents, such as engineers, managers or researchers [30]. In this context, this chapter aims to analyse the collaborative challenges in order to innovate and transfer the technology for its successful commercialization. To that end, several nano-enabled sensor-based devices that are being developed in a public-funded academic ecosystem are going to be analysed. The selected cases meet the characteristic of a medical device based on the cross-fertilization of different KETs and are at different stages of technological maturity. Main developers have been interviewed and a cross-case analysis has been done. By gaining insights into these challenges, it is expected it will offer a better understanding of the gap between research and the market place.

2.2 Literature Review

2.2.1 Nanosensor-based devices

A ***nanosensor*** is defined as a sensor that uses a nano-scale phenomenon for its operation or is fabricated by nanotechnological methods [191]. It is generally conceived as a nanometre size-scale measurement system, comprising a probe with a sensitive biological recognition element or bio-receptor, and a transducer in between [178]. A nanosensor can be labelled as such if the size, the sensitivity of the sensor and the spatial interaction distance between the sensor and the object is not greater than 100 nm [178], [191]. Some of the current sensors are based on various advanced materials such as quantum-dots, infrared photodetectors, nanoprobes (nanosensors for biomolecules), carbon nanotube-based optical and electromechanical force sensors, transducers of biopotentials, multi-analyte biosensors, among others [192].

Nanosensors are principally applied for monitoring physical and chemical phenomena in places difficult to reach, detecting biochemicals in cellular organelles,

and measuring nanoscopic particles in industry and the environment [178]. In the field of healthcare, nanosensors play a central role in the development of early detection diagnostics and therapeutics [179]. In this regard, nanosensors are very sensitive due to the different physical properties at the nano-scale compared to the micro-scale, allowing greater perspectives for human body monitoring. It is envisaged that future applications could be stationed in tissues, bones or blood throughout the body in order to monitor different physical parameters [193].

Doubtless, cross-fertilization of technologies fosters the progress of all kind of sensors, from wearable devices, through implantable devices and more recently, to advanced flexible self-powered and self-healing sensors (**Figure 2.1**). The drivers of this evolution are principally two: i) the advances in proteomics and genomics that have led to the identification of a great number of biomarkers, and ii) the increasing request for highly efficient diagnostic tests [178]. These technological improvements are able to facilitate the early detection of emergency conditions and diseases in patients at risk comprising physical, physiological, psychological, cognitive, and behavioural processes, and reaching them even in inaccessible environments and in a reduced response time [194]–[196].

Lab-on-chip (LOC) devices can be used as a platform with high potential for the application of nanosensors [197]. LOCs are technology involving a miniaturised biochip as an analytical device and an instrumentation associated with sensors and fluidics [198]. They have evolved also as the result of the cross-fertilization of technologies from conventional diagnostic and chip-in-a-lab technologies (**Figure 2.2**) [20], [27]. The first modern microfluidic devices were made by micro-machining two decades ago. Their size was typically from a few square millimetres to centimetres, and they required additional supporting instrumentation. With the advent of modern technology, electronics and light emitting diodes, these devices are getting smaller and enabling single-molecule manipulation [27], [199].

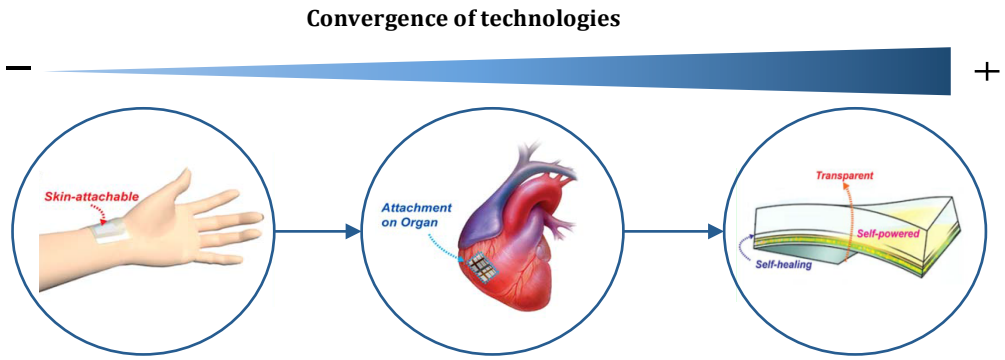

Figure 2.1. Evolution and convergence of technologies in sensor-based devices.

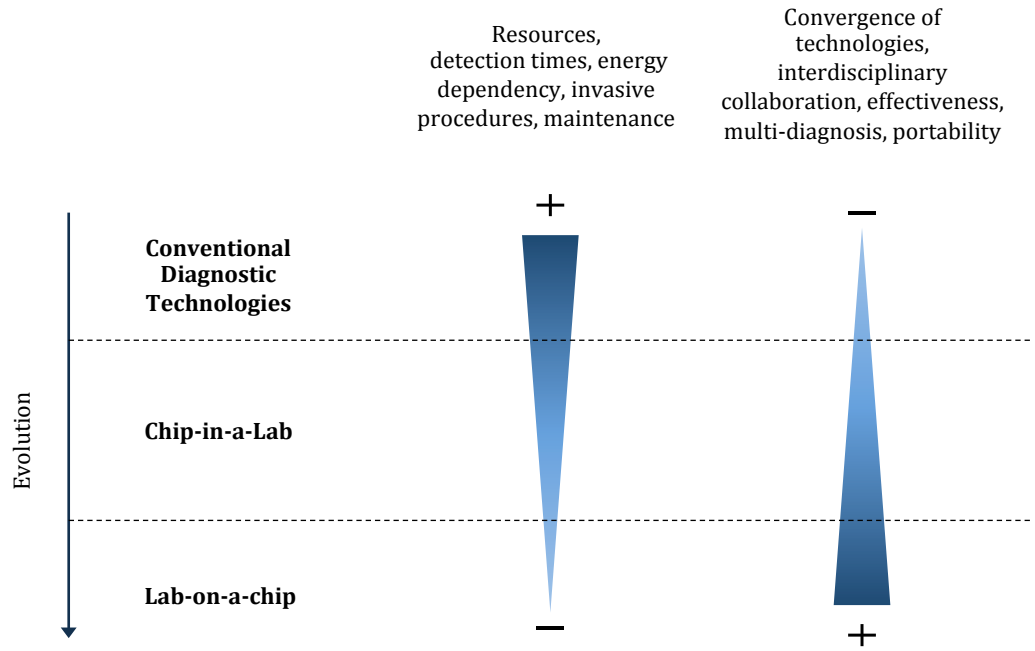

Figure 2.2. Schematic evolution and characteristics of diagnostic devices.

The development of highly sensitive sensors at the nano-scale, and its combination with nano-microfluidics solutions based on micro-channels, micro-mixers and micro-valves, are increasing the interest in the development of the LOC concept as a portable and low-cost solution [197], [200]. This technology promotes a shift away from traditional diagnostic tests in the clinical laboratory setting to near-patient situations, improving timely diagnostic information so as to make informed decisions regarding diagnosis and treatment [19]. Moreover, the principle benefits are their portability, energy harvesting, fast results and capacity for non-invasive procedures [201], [202].

The medical sensors global market is growing as the result of this evolution. It is expected to reach 15.5 USD billion in 2019, growing at a Compound Annual Growth rate (CAGR) of 6.3% from 2013 to 2019 [203]. Currently, 85% of the total market is represented by disposable biosensors specially for blood glucose [178]. Findings suggest that market growth for biosensors and biochips is virtually exploding. There are markets for biosensing technologies in the Asia-Pacific region, which show CAGR of 11% (2008–2018). CAGR of 10.7% occur in the highly developed market of the US. In fact, this market is projected to reach $8.5 billion in US in 2018 [204].

2.2.2 The need of a collaborative innovation ecosystem

Cross-fertilization between technologies requires that different stakeholders and policy makers effectively address the development of cross-fertilized products, goods or services into a collaborative ecosystem [76]. This collaborative and technological complex process needs a greater multi-disciplinary effort due to the higher number of technological elements that need to be integrated [76]. Particularly, the field of LOCs has now developed into a truly multi-disciplinary field, requiring contributions from fields spanning from biology, chemistry, physics, and material science, as well as skills of microfabrication and engineering [205].

Multi-disciplinary work encourages diverse partnership enabling a commercial advantage [206]. Multi-disciplinary collaboration therefore constitutes an important technology transfer challenge and is one of the key factors to achieving commercial success in creating and developing medical devices [207], [208]. This has been evidenced in previous literature, which has focused mostly on the importance of university-based technology transfer organisations promoting industry-science links [139], the multi- and inter-disciplinary collaboration and partnerships between universities, research institutes and industry [37], [209], as well as the collaborative relationship between medical doctors and engineers [207].

In addition, it has been stated that socio-technical relations such as strategic alliances and other forms of networking can boost the transition of new technologies [176]. For instance, the transfer of knowledge and technology from research and science communities to commercial stakeholders is a function of research centres, academia, institutions, governmental bodies and industries [172], which also need cooperation and commercialization agreements in order to facilitate shortest times-to-market [107]. In this context, Powell (1998) argued that a wide range of inter-organisational linkages is critical to knowledge diffusion, learning and technology development [210].

In the academic R&D process, collaboration is also an important element to foster innovation [122] and the effective transfer of knowledge [172] within the shortest times-to-market [107]. The interaction therefore involves multiple actors [122], [211], including research centres, institutions, governmental bodies and industries [172]. As a consequence, a number of knowledge and technology transfer policies have been designed to encourage firms to collaborate with research centres and universities through financial support and competitive funds linked to the presence of research partners [189], [212] or by encouraging the entrepreneurial orientation of universities and researchers [213]. Hence, there is a growing interest in understanding the scientific “communities” as core elements of the Innovation 3.0, which is based on a collaborative learning resulting in performance and innovation enhancement [138], [214]–[216].

These communitarian approach plays an important role in the innovation process, but also in knowledge management and the whole knowledge management lifecycle [217]. Therefore, the integration of knowledge has become a key element for the implementation of technological innovations which involve the mutual adaptation of the technological system being implemented, and the organisational context within which they are being introduced [218].

2.2.3 A roadmap for technology transfer and commercialization

The evolution of sensor-based devices is highly complex and extensive knowledge is required [219]. Since knowledge is considered an embedded value in high-tech products [220], its creation and diffusion have become important activities, not only for commercialization success but for economic impact [216]. Therefore, transferring knowledge requires the efficient application, creation, location, capturing and refining of knowledge, as well as to learn and best-practice sharing [216].

Accordingly, a systematic metric-based process that assesses the efficient transfer of technological knowledge has emerged in recent years, which is called the Technology Readiness Level (TRL) [221]. This classification is a knowledge-based standard for evaluating the maturity level of a particular technology, with the aim to have a major approach to the market. It is an internationally recognized and industrially applied concept for describing the progress of a technology in the industrialization process of transformation from ideas to the market [164].

The concept was developed by the NASA in the 1980s and was initially used by some US agencies and many of the world's major companies [222]. Nowadays, this measurement scale is being used to categorize new and emerging technological innovations [223], especially in Europe [224]. In this context, the H2020 programme is fostering the utilization of the TRL scale in participant projects, envisaging closeness to the market place. This awareness to market assessment is an added strategy compared with previous FPs, as previously exposed in **Section 1.3.4.1** and **Figure 1.18.**

According to the OECD, 4 levels must be distinguished (**Table 2.1**). The Basic Research level (TRL 0-3) starts with idea generation. In this level, basic principles are observed and therefore, practical applications are formulated. The second level is the Development level (TRL 3-5), where scientific research is translated into applied research and development. Following is the Demonstration level (TRL 6-7), where prototyped systems are demonstrated in relevant and operational environments. Finally, the Pre-Commercial Development level (TRL 8-9) where the

completed systems are tested, demonstrated and proved through successful mission operations [225].

Notwithstanding, this concept has some limitations that need to be taken into consideration. One limitation is that TRLs only focus on product development, rather than manufacturability, commercialization and organisational changes. Another limitation is that this concept needs to be adapted to the specific use purpose of the organisations according to the different operational needs. This means that the specificity of the TRLs can vary in different organisations [224].

Despite these limitations, the TRL terminology is a useful roadmap for identifying factors that could delay or prevent certain medical devices from its transference to the clinical use. The medical device regulations dictate that only devices with certain level of maturity can progress to commercialization, therefore TRLs could provide a realistic assessment of the chances for translation to clinically useful devices [222].

2.3 Case studies of nano-enabled sensor-based devices with a multi-KET approach

2.3.1 Methodology and case selection

In order to gain insights about the dynamic process of innovation and the challenges in the development of nano-enabled medical devices, *multiple case studies* have been conducted. Case studies are defined as a research strategy involving an empirical investigation of a particular contemporary phenomenon in a real life context and by using multiple sources of evidence [226]. This methodology is considered to be the most suitable when the aim is to build a rich, deep understanding of new and complex phenomena to construct a theory that can be tested in further research [226]–[229].

Four case studies at different levels of technological maturity (TRL) were selected (**Figure 2.3**). This allowed performing a cross-case analysis, which is a well-accepted method used to synthesize evidence from multiple cases [230]. This method facilitates the demonstration of differences and ascertains patterns in a comparison approach.

Table 2.1. Technology readiness level categorization.

Phase	TRL	Definition	Description
Basic Research	TRL0	Idea generation	Proposal of an unproved idea or concept
	TRL1	Basic principles observed and reported	Scientific research begins to be translated into applied research and development (R&D). Examples might include paper studies of a technology's basic properties.
	TRL2	Technology concept/formulation	Invention begins. Once basic principles are observed, practical applications can be invented.
Applied R&D	TRL3	Analytical and experimental critical function and/or characteristic proof of concept.	Active R&D is initiated. This includes analytical studies and laboratory studies to physically validate the analytical predictions of separate elements of the technology.
	TRL4	Component and/or breadboard validation in a laboratory environment.	Basic technological components are integrated to establish that they will work together.
	TRL5	Component and/or breadboard validation in a relevant environment.	Fidelity of breadboard technology increases significantly. The basic technological components are integrated with reasonably realistic supporting elements so they can be tested in a simulated environment.
Demonstration	TRL6	System/subsystem model or prototype demonstration in a relevant environment.	Representative model or prototype system, which is well beyond that of TRL 5, is tested in a relevant environment.
	TRL7	System prototype demonstration in an operational environment.	Prototype near or at planned operational system. Represents a major step up from TRL 6 by requiring demonstration of an actual system prototype in an operational environment.
Pre-Commercial Development	TRL8	Actual system completed and qualified through test and demonstration.	Technology has been proven to work in its final form and under expected conditions.
	TRL9	Actual system proven through successful mission operations.	Actual application of the technology in its final form and under mission conditions, such as those encountered in operational test and evaluation (OT&E).

Source: Adapted from [221].

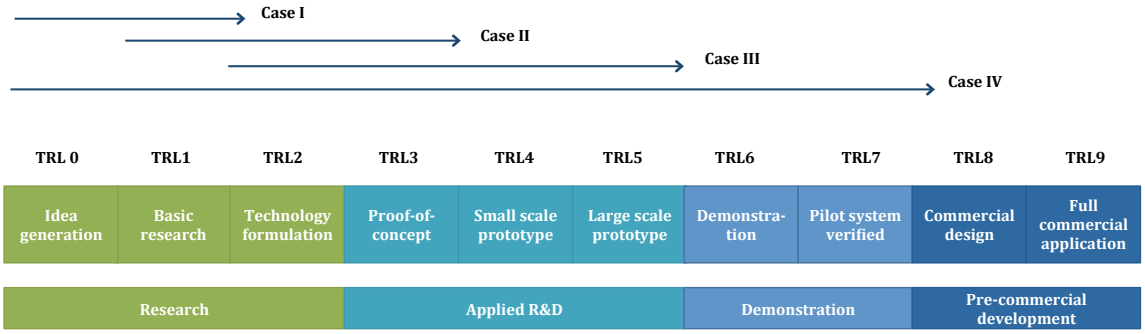

Figure 2.3. Research design of the selected case studies.

The cross-case analysis was complemented by a narrative synthesis approach. This method refers to the application of a narrative summary of the findings of the case studies that relies on the use of words and text to summarize and explain the findings obtained [231], [232].

The case selection sought to meet the following criteria: i) a device that incorporates or is envisaged to incorporate nanotechnology in its design, development or manufacture, ii) a device that combine KETs, iii) a device with healthcare applications, and iv) a device developed at a public-funded R&D environment. From the four selected cases, there is one that does not use nanotechnology, but it could be envisaged as a nano-tool in the future.

For all cases, information was obtained through primary data (interviews) and complemented by secondary data (publications, press releases, annual reports, web sites). The purpose of this strategy is to enrich the data collection process and to strengthen the reliability of the research, known as a triangulated process [230]. Main interview findings have been transcribed and presented as part of the narrative analysis approach [232].

2.3.2 Description of the cases

2.3.2.1 Case I: Nano-enabled implantable multi-sensor system for in-vivo theranostics

The first case is a biomedical multisensory system for *in-vivo* theranostics. This device is capable of monitoring human bodily functions and transmitting the resultant data for a clinical patient's control. Patients at risk, the chronically ill or elderly people can be monitored outside of and beyond visiting the hospital or at the surgery. Thus, the significant advantage is being able to monitor patients during

their routine daily activities, as traditional clinical monitoring would be replaced by continuous and remote monitoring [233].

The integration of rapid advances in areas such as microelectronics, microfluidics, micro-sensors and biocompatible materials entails the availability of implantable bio-devices for continuous monitoring or event detectors that carry out faster and cheaper clinical tasks than when these are done by standard methods. The possibility of controlling how a therapy is working, detecting symptoms, and knowing how the disease is progressing, will improve the personalized medical care known as theranostics [234], [235].

Theranostic techniques integrate therapy and diagnosis in the same device, covering a wide range of applications as health interventions with drugs (pharmacogenomics), nutrition (nutrigenomics) and vaccines (vaccinomics), as well as diagnostics for human diseases. A theranostic device has one or more specific molecular recognition markers for cells on the surface thereof, wherein the recognition markers are selected from the group consisting of peptides, proteins, antibodies, antigens, aptamers, molecular imprinted polymers and polynucleotides [236].

This is an envisaged concept conceived to be an on-chip configurable array of biosensors implanted under the human skin in the future. This configuration will take place before the implantation thanks to a standard programmable bio-nano-chip approach [237]. The key point in this new conception is that, instead of defining a particular architecture of the implantable device for each sensor, the new approach introduces the design and use of a general architecture that will require minor modifications for the final customized implantable device that could be suitable for a set of specific applications [233].

Converged KETs in this device include: Advanced Materials, Biotechnology, Nanotechnology, Advanced Manufacturing Technologies and Micro & Nano-electronics (**Figure 2.4, Case I**). A complementary metal-oxide semiconductor microelectronics (CMOS), micro-electromechanical systems (MEMS) and microfluidics will be combined to implement the programmed implantable, and easily adapted for the specific needs of the patient. This modular standard LOC approach may adapt the sensors in a quick, efficient and reliable way. The design presents two different approaches: defining a true/false alarm system based on either amperometrics or impedance into a grid of nano-biosensors that could permit the monitoring of several diseases by *in-vivo* analysis of the corresponding biomarkers. The system will implement algorithms for the control of drug delivery as well as the suitable reservoirs and pumps. The objective is to deliver drugs in a better way, more focalized in the local area or target of interest, rather than through traditional oral medication.

2.3.2.2 Case II: Nano-gap biosensor for enhanced label-free DNA hybridization detection

The second case study is a conductance-based biosensor platform with improved nano-gaps that allows label-free DNA hybridization detection through the enhancement of long range DNA transport. Nano-gaps are fabricated with two gold electrodes with a separation distance of 50 nm suitable for low conductivity measurements with the potential for mass-scale production and inherent cost-reductions. The nano-gap walls are covalently modified with short, antisymmetric thiolated DNA probes, terminated by 19 bases complementary. This device has a high specificity for the discrimination of base-pair mismatching and can be applicable for multiplexed detection well-suited for POC diagnostics and wide-scale DNA analysis [238].

Over the past two decades, many technological advances have been developed for DNA sensing [239]. DNA arrays are devices able to screen large selections of genes at the same time, with a short response time. They are relevant for the detection of infectious agents, food safety investigations, environmental monitoring, diagnosis of genetic diseases, genetic predispositions and personalized medicine. These arrays represent an alternative to microarray technologies based on fluorescent labels and optical detection [177].

Materials at the nano-scale are radically improving the current state-of-the-art of electrochemical DNA analysis. DNA-based electrochemical sensing combine nucleic acid layers with electrochemical transducers to form a biosensor. The electro-activity properties of the DNA discovered in early 60s allowed the possibility of a reliable transduction system for hybridization detection without redox markers [177]. The advantages of this technique include simple, accurate and inexpensive platforms [239]. By scaling down the device size in order to fit that of the molecules enhances the efficiency of the coupling between the biomolecules and the probes used for their detection [177]. This reduces costs, sample amount, time and human resources [238].

This device is the result of the convergence of five KETs: Advanced Materials, Biotechnology, Nanotechnology, Advanced Manufacturing Technologies and Micro & Nanoelectronics (**Figure 2.4, Case II**). It was financially supported by the OLIGOCODES project funded by the Spanish Ministry of Science and Innovation (MICINN) in the framework of the VI National R&D&i Plan with the participation of the Nanobioengineering Laboratory, Institute for Bioengineering of Catalonia (IBEC), University of Barcelona, and the Biomedical Research Networking centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN).

2.3.2.3 Case III: Combined dielectrophoresis and impedance system for bacteria analysis.

The third case is a flow microfluidic chip capable of injecting, trapping, cleaning and continuously separating and concentrating bacteria by means of dielectrophoresis (DEP) and impedance analysis (IA). Bacteria-related diseases caused by contaminated food or water ingestion result in considerable morbidity and mortality representing a significant public health threat in developed and developing countries [240], [241]. Therefore, diagnostic devices are extremely important for implementing an effective response to the prevention of bacteria related diseases [242], [243], water treatment [244], and public health [245], preventing millions of deaths caused by the lack of these facilities [246].

Bacterial detection can be made through numerous methods traditionally performed in the laboratory and using commercial equipment [247]. Conventional detection methods include performing various media-based metabolic tests; the use of magnetic beads coated with pathogen-specific antibodies or enzyme-linked immunosorbents, and oligonucleotide arrays for amplifying hybridized DNA fragments of bacteria. Other approaches include centrifugation or filtration [243], mass spectrometry (MS), capillary electrophoresis (CE), the enzyme-linked immunosorbent assay (ELISA)[248], microarrays and Polymerase Chain Reaction (PCR) [21], [249], among others. These diagnostic tools are elaborate and expensive in terms of equipment and time, typically requiring several days to obtain results [250].

Currently, some biosensors are capable to combine DEP and IA in a microfluidic chip. These chips are devices usually composed of a customized electronic module and a LOC where the sample is pre-concentrated through the DEP generation, and concentration is measured through IA monitoring. The device in this case is based on this approach but with an innovation regarding the variation of the conductivity of the media.

The device includes three KETs: Micro & nano-electronics, Advanced Materials and Advanced Manufacturing Systems (**Figure 2.4, Case III**). This work was financially supported by the THERAEDGE Project (FP7-ICT-2007-216027), funded by the "Information and Communication Technologies" programme under the 7th Research Framework Programme of the European Union.

2.3.2.4 Case IV: Electrochemical array for gastric ischemia detection and in-vivo monitoring.

The fourth case is an innovative device that shapes and sizes a sensor array prototype. It was designed for the detection and real-time monitoring of ischemia inside the stomach by means of endoscopic tools. Ischemia is a hypo-perfusion of the blood through an organ or tissue caused by a pathologic constriction or obstruction of its blood vessels, or an absence of blood circulation. It can occur in any part of the body, but is especially relevant in the brain, heart, bowel and stomach [251], [252]. Its detection is difficult in organs such as the stomach, since the low pH in the gastric juice makes it challenging to fabricate stable and functional all-solid-state pH sensors [253], [254].

A prolonged ischemic condition causes severe tissue damage and failure of organs, therefore, real time detection methods on the organ tissue are needed [253]. There are few commercial products available in the market. These products are tissue oxymeters and are based on optical readouts. Unfortunately, the remarkable developments in medical and surgical aspects cannot help to improve the diagnostics of this disease [255].

The electrochemical sensor device of this case uses an electrode insulated with a commercial bio-compatible resin and is hence resistant to the stomach pH. The surgeon teleoperates the surgery by controlling robot arms remotely by the incorporation of joystick remote controllers and 3D vision in a bi-manual laparoscopic surgery to the endoluminal surgical by integration of advanced micro-nano-bio technologies and electronics. Therefore this device includes three KETs: Micro & nano-electronics, Advanced Materials and Advanced Manufacturing Systems (**Figure 2.4, Case IV**). This approach is, in addition, four times less expensive than commercial equipment, easy to mass-produce, of small size (portable) and applicable to endoscopic systems.

This innovative ischemia sensor was financially supported by the ARAKNES project under the 7th FP of the EU and by the FET programme within the 7th FP for research of the EC. It had the multiple and complementary participation and collaboration of key stakeholders involved in biomedical research and innovation: the Department of Electronics at the University of Barcelona, the Institute for Bioengineering of Catalonia (IBEC), the Clinic Hospital, the UB Scientific Park and the Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN). Therefore there is an involvement of university, scientific parks, research institutions, hospitals and the public sector [138].

2.4 Cross-case analysis: Identifying challenges

In this section, some characteristics of the innovation ecosystem and the challenges of transferring the devices into the market place are analysed and discussed. Some of the questions of the interview were related with the multi-disciplinary and collaborative features of the nano-based innovation ecosystem, the relationship among the stakeholders in terms of their formality or informality and technology transfer and commercialization challenges. **Table 2.2** resumes the principle thematic areas and outcomes of the responses obtained.

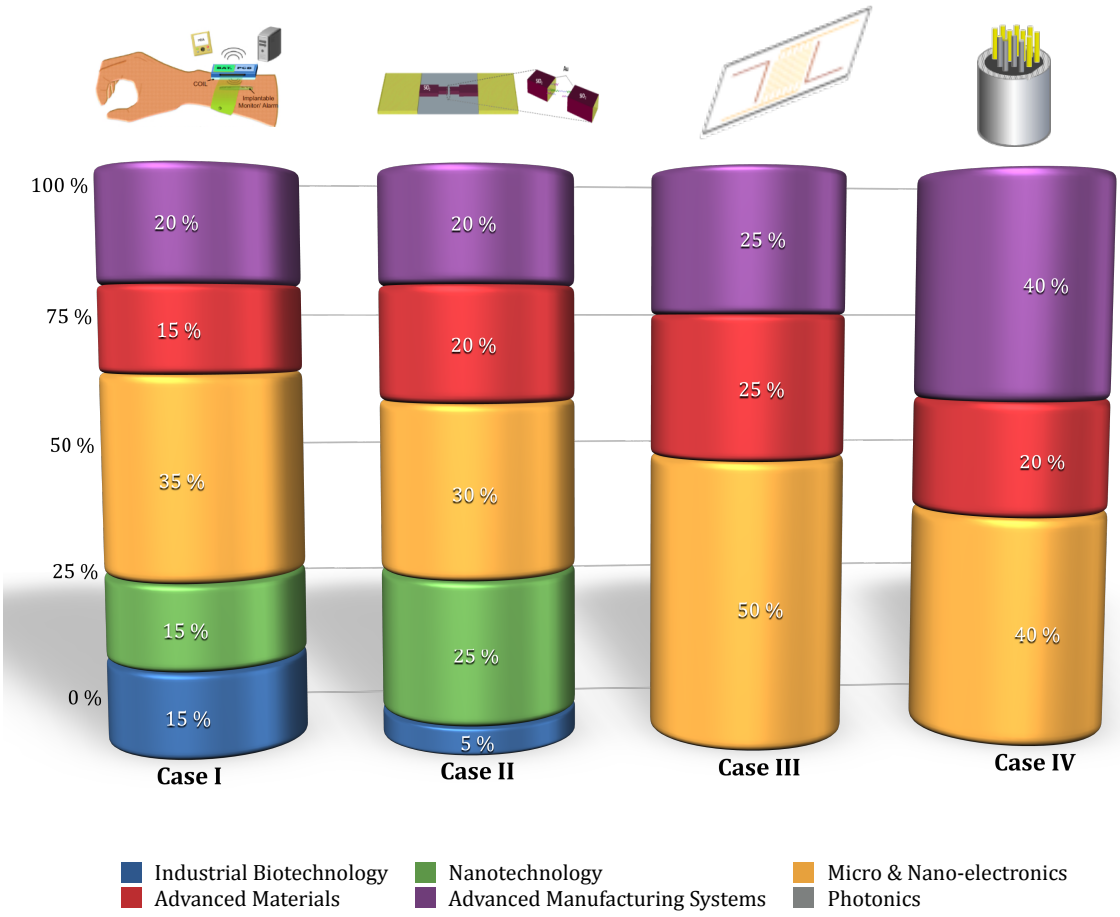

Figure 2.4. KETs distribution of the selected case studies.

Table 2.2. Interviewed thematic areas and their answers per case study.

	Case I	Case II	Case III	Case IV
Multi-disciplinarity	The team consisted on engineers, biochemistries, physics and informatics with strong knowledge in electronics and microfluidics.	Physics, biochemistries, and engineers that made the modelling.	Biologist specialized in cell culture, engineers and technician specialized in developing microfluidics and electrochemistry.	Surgeons, vets, engineers (robotics, chemical, electronics) and scientists together for the integration of bio-robotic, microsystems and sensor technologies.
Purpose	To accomplish a goal.	To develop member's capabilities.	To develop member's capabilities.	To develop member's capabilities.
Duration of relationships	Lasted as long as the reason to connect existed.	Lasted until the end of the project	Lasted as long as the reason to connect existed.	Lasted until the end of the project
External facilities	Scientific and technique services form the STP. Not from the TTO of the University.	The technical services from the STP were used.	It was not necessary.	Contact with the TTO from the university.
IP strategy	Industrial protection was considered.	Patenting was considered but the patent application was rejected.	Any.	Patenting.
Transfer barriers	Implantable normative, existence of substitutive and alternative technologies, reliability of the device and financing.	Technology was very expensive and complicated. It had low detection limits.	Lack of time and money. The technology is very complicated and more people focused only in this type of project were needed.	Intellectual protection, which was considered too expensive.
Market research	Technological surveillance was a very important activity during the project.	Technological surveillance but not costumer and market needs.	Technological surveillance.	Competitor and risk analysis; customer and market needs were taken into account.
Time-to-market	5-10 years.	3 years.	More than 4 years.	2 years.

2.4.1 A collaborative innovation ecosystem

The first characteristic found in the four cases was a collaborative innovation ecosystem. This ecosystem was characterized by the participation of multi-disciplinary agents. Thus, scientist from different backgrounds participated in the development of the device at different phases of technology maturity. In this context, it can be said that a shared goal was viewed from different perspectives, facilitating creative ideas and the optimization of problem solving:

> […] *it was a great experience working with people from different disciplines, because you can evidence how different people from different backgrounds can see the problem so differently and they can have completely different solutions. In this multidisciplinary project, the contribution of each institution was unique and the project could not successfully finish without their help* (Interviewed from Case IV).

Consequently, a multi-disciplinary working environment allowed for the exchange of different points of view from people with different backgrounds (medicine, electronics, mechatronics, chemistry, physics, and biology), thus achieving a completely different approach to facing problems. This also helped to break fixed routines and prevent narrow thinking in a pre-determined way depending on academic or social background. Although there were deep interdisciplinary collaborations from different groups, researchers needed to understand the necessities of the industry and the achievements in basic research. Besides, interdisciplinary-formed personnel were also essential, so they could understand the diverse sciences, diverse needs and speak the same technical language. In other words, they could be a "translator" between different languages such as physics, chemistry, biology, electronics, software etc.:

> […] *we made collaborations with universities, research institutes, hospitals and companies. Each institution has different priorities, interests and expectations from the project. It is necessary to observe and realize the priorities of each partner for having a good collaboration* (Interviewed from Case IV).

A second factor found at the ecosystem was an intra-collaboration. This type of collaboration allows the involvement of multiple agents or organisations. Cases II and IV expanded their collaboration through other organisations rather than only from academia. In Case II, the university (UB) developed the electronic part of the device; the microfluidic part was facilitated by the first research centre (IBEC) and the samples were supplied by the second research centre (IREC). In Case IV, they collaborated with a hospital (Barcelona Clinic Hospital), where engineers were in close contact with physicians, and with a firm (NOVINEON), which was the partner

that did the *ex-vivo* and *in-vivo* experiments. This intra-collaboration factor was highlighted in Case I, which stayed at the early stages of the process:

> […] *the representation and know-how from different stakeholders is important to solve the necessities. The participation of all is fundamental. This was one of the reasons why we stayed at early stages of development* (Interviewed from Case I).

For *in-vivo* applications, numerous permissions were needed, as well as animal or human experiments. This process takes years and the costs of these experiments are extremely high. Thus, it is nearly impossible for a university or small company to invest in it. In this context, an intra-organised process which could allow economic support between the different stakeholders is required. This asseveration is also supported by the fact that researchers, on their own, face organisational difficulties. For instance, it was found in Case III that structural disposition of the communities is a special barrier, particularly for small groups of scientists that are responsible, not only for teaching activities, but also administrative duties:

> […] *interest and time organisation from the researchers is also required. But they have many other responsibilities and this let you less time for research* (Interviewed from Case III).

Another characteristic found at the innovation ecosystem was the degree of formality. According to Wenger and Snyder (2000), organisational collaborations can be differentiated with respect to their collective purpose and relationships among their members and these characteristics lead to define the degree of formality or informality in relationships. Based on these author's defined characteristics [256], it can be said that Cases II, III and IV tend to have informal interactions, since they have considered that the principle purpose for developing a nanosensor-based device is to develop the member's capabilities. This "member-focused" approach has been considered as the basement of a communitarian strategy [138], [214]. In contrast, it can be seen that Case I considered accomplishing a goal as the main purpose of developing the project. This purpose is related to formal interactions such as a project teams.

The duration of the relationship is another characteristic that defines the formality of relationships. In this regard, Case I and III showed an informal tendency, meanwhile Case II and IV showed a more formal interaction. Since these findings are the opposite regarding the purpose of developing the device from cases II and IV, it has been assumed that there is not a marked formal or informal tendency.

2.4.2 Innovation model and intellectual property strategies

As stated in **Chapter 1**, there are several innovation models used by organisations for innovating their technology. Fundamentally, two approaches can be distinguished, closed and open innovation. In contrast to closed innovation, an open innovation model combines internal and external ideas into architectures and systems whose requirements are defined by a business model. This business model utilizes both external and internal ideas to create value, while defining internal mechanisms to claim some portion of that value [104], [257]. In an open innovation model, organisations principally tend to collaborate and share their knowledge with other organisations, as well as use external facilities.

An open innovation strategy has been found in cases I, II and IV. Especially, in Case IV there was collaboration with different organisations, namely, firms, universities and research institutions. On the contrary, Case III considered it not necessary to use external facilities from the Technology Transfer Offices (TTO) or the scientific and technique services from the STPs. Even this is not a good measure to determine the degree of openness or closeness in their business models, the search for external help and share of information tend to be aligned with an open innovation approach.

The intellectual property (IP) strategy was also considered as part of the innovation model and this can be a challenging and limiting factor for the development of a cross-fertilized device. For instance, patenting is an IP strategy where costs are very high. In this context, a profitability analysis is an important step to take into consideration because it gives information about the cost-effectiveness of the project. This consideration was found in Case II from the beginning of the technological maturity of the device:

> […] *the strategy was to patent the technology, but the final argument was that the device cannot be patented because it was not original enough and marketable due to the vast alternatives in the market* (Interviewed from case II).

Patenting was found to be the IP strategy in Cases II and Case IV. On the other side, Case III had not considered any IP strategy. In Case I, industrial protection was considered as an alternative to patenting. In this case the open innovation model was considered.

2.4.3 Technology transfer and commercialization

It has been found that Case I, Case II and Case III failed in transferring their technology to the market. Technological barriers were considered the principle

technology transfer challenges for all four cases. Two perspectives in this regard were found: i) the existence of alternatives in the market, and ii) the reliability of the technology. For instance, simpler and cheaper alternative technologies already established in the market were considered as a limiting factor to positioning a more complicated and expensive technology. Therefore, alternative technologies could explain the slowdown in the development of proof-of-concepts:

> […] *alternative technologies already integrated in the market place for the same type of necessity are cheaper and more efficient* (Interviewed from Case I).

> […] *genosensors already exist and competing with their performances is not easy* (Interviewed from Case II).

In addition to these barriers, time, financing and the viability of the device were all reasons for the difficulty of translating the device to the market in all the cases. These results are in accordance with the literature that states that technology transfer depends on both, technical bottlenecks and cost considerations [258]:

> […] *the high technology that involves the development of these devices implicates a lot of time and money…. This device has a lot of potentiality, but the resources and time effort are overwhelming*. (Interviewed from Case III).

It has been also stated at the literature that technological barriers from nano-scale building blocks vary significantly depending on the application [259]. In addition, the size makes it amenable to a higher degree of failures due to: i) manufacturing defects, ii) transient faults resulting from reduced noise tolerance because of the reduced voltage or current levels and iii) aging faults because of molecular and other kinds of techniques for creating nano-devices [260].

On the other hand, higher manufacturing costs were perceived as an important technology transfer challenge in all four cases. It is recognized that managing costs is a difficult duty. Until the product is actually on the market, cost estimations are likely to be inaccurate [261]. Rather, it is recommended that the device be cost-effective, meaning that the acceptable cost of a POC test depends on the expected clinical benefit [19].

Technological surveillance and market needs analysis were also found as relevant challenges in the commercialization of these devices. According to Maine et al., (2014), "technology-market-matching" is a managerial strategy that must be present when there is convergence of technologies in order to generate innovation and ensure market success [66]. Technological surveillance is also important to manage and make decisions [262].

In this study, technological surveillance was considered and implemented in all cases. However, Case I, Case II and Case III failed in identifying costumer and market needs. This could be an explanation for the failure of translation to market for these three cases since addressing market needs is an important factor for innovation success and the commercialization stage [263]. Moreover, the process of standardization and validation are required to gain market acceptance, which leads to further investment for technology transfer and demonstration purposes [178]. This is suggested at the design, operation, and workflow of clinics in order to ensure that testing is accessible and results are used in real time [77].

It was found that market research was considered in Case IV. Agents in this case included competitor and risk analysis, and research regarding costumer needs. The literature states that continuous contact and feedback during the development of the device from the end user is beneficial because it can determine the path of the research. Thus, it will increase the success rate and optimize the time of the overall process in terms of bureaucracy, reducing therefore the expected time-to-market [263]–[265].

2.5 Summarizing findings: A suggested innovation model for a successful technology transfer and commercialization

Identified technology transfer and commercialization challenges from the four analysed case studies could be considered in order to suggest an adequate innovation model for the development of cross-fertilized nano-based devices. In this regard, a model is suggested to overcome the gap between research and market. Based on the findings aforementioned, a preliminary atttempt could emphasize a multi-disciplinary ecosystem. This could be conceived as a communitarian approach, meaning that actors from different communities could be joined together in a new and integrative community (**Figure 2.5**) from the very beginning of the development value cycle.

The resulting flow of knowledge from other communities of different backgrounds influence the level of innovation and the cross-fertilization of ideas [266]. Different professions intersected allow innovation and creativity, therefore novelty comes from fusing elements which were not connected before. They manage and generate conflicts as a result of the cross-cutting alliances [267]**.** In this line, Wenger (1999) refers to this integrative activity as "*constellations of practice*", referring to multiple interlinked communties which can be overlapping or nested in some way [268]**.**

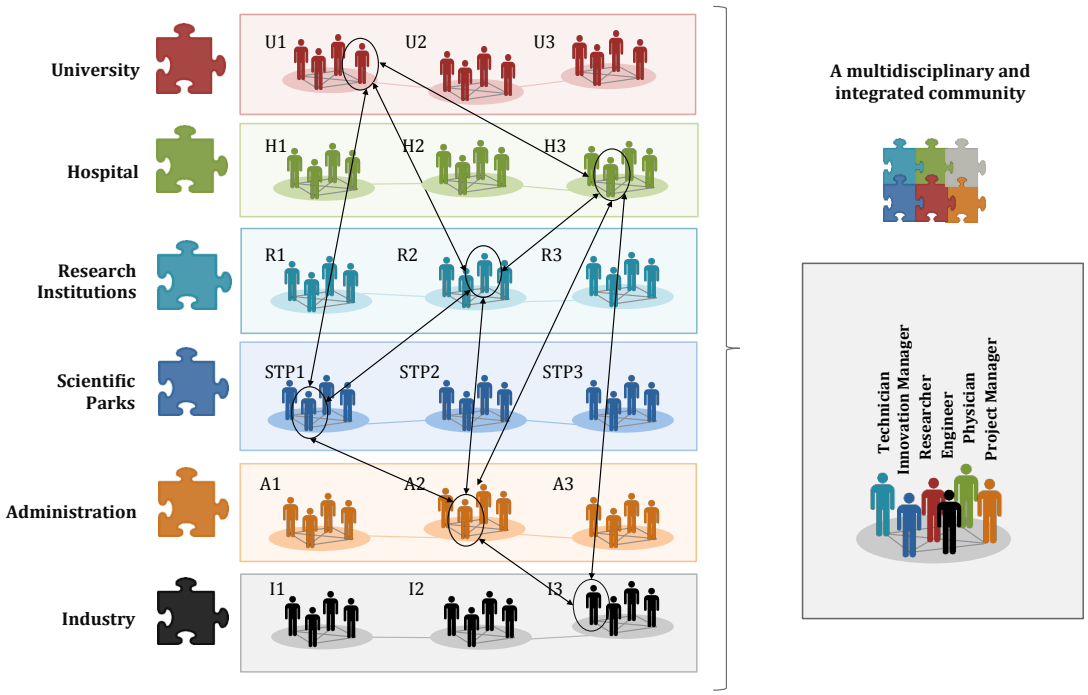

Figure 2.5. Scheme of the suggested structure of the community for developing cross-fertilized nanosensor-based devices.

Moreover, it has been argued that an intra-organisational collaboration expands beyond the traditional structural spatial networking, or knowledge boundaries [268]–[271]. Sharing knowledge to external agents allows the participation of multiple communities at once and this particular organisation is considered an effective way to handle unstructured problems [270]. According to Adler and Heckacher (2006), a communitarian-based organisation generates and shares knowledge as a primary benefit. In fact, in modern industry, a wide range of competences and knowledge bases are needed, meaning that this cannot be reached through the usual "teamwork" [272].

In this regard, the complete overview provided here of the value chain of research and technology transfer processes highlights the importance of a common framework in which multi-disciplinary agents meet together [30]. Case IV showed that the value is generated when the different communities are integrated from the first step of the value chain. In this context the proposed model for developing nanosensor-based devices is built on transfer of technology through an integrated process from research to market. The aimed result of this process is the generation of new ideas or knowledge for product development and time optimization. In **Figure 2.6**, the suggested model is represented as a puzzle or a mosaic, where different organisations or pieces of the puzzle could develop an integrative innovation community.

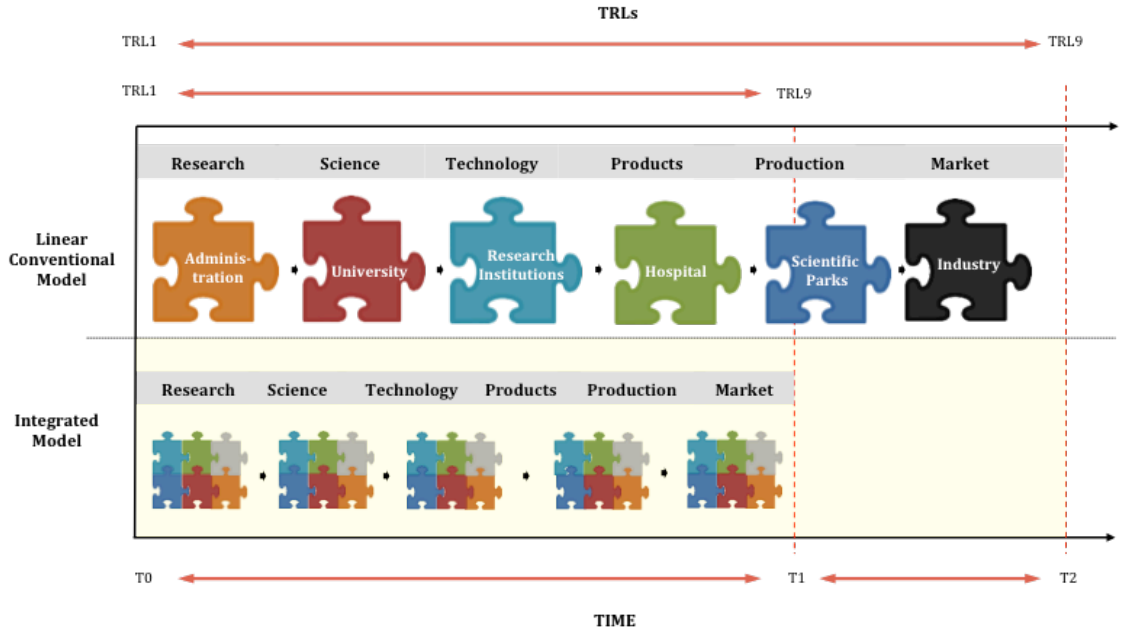

Figure 2.6. Time comparison scheme of the conventional model and the integrated suggested model of a cross-disciplinary innovation community approach among the value cycle.

It has to be said though, that this suggested model would also require overcoming other challenges. For instance, challenges originated because of the diversity of backgrounds and expertise of members. Depending on the organisation they come from, different activities should be agreed and coordinated. Each community, their activities and their technology transfer challenges are depicted in **Table 2.3**.

Finally, the overall suggested model envisages that the gap between academia and market could be reduced with the participation of multi-disciplinary collaborative communities, facilitating technology transfer from the academic to the commercial sector. To this end, the active involvement of the different communities from the beginning of the process and continuing the social interaction up to the point of the commercialization of the nanosensor-based device is required. As a consequence, higher TRLs can also be achieved in less time than in a conventional model.

Table 2.3. Characteristics, main activities and actions from the different communities.

Organisations	Characteristics	Main activities	Actions
University	Principal members are academics, PhD candidates and Master's students. They are more involved in the first stages of product development.	Basic research.	They need to be informed about the characteristics of the disease and patient needs.
STPs	Technicians with expertise and knowledge in the machines owned by the scientific park.	Fabrication process and experimentation.	Technical language and terminology need to be clearly transmitted to other communities.
Hospital	Formed by surgeons, nurses or physicians with experience in clinical trials.	Guidance at the experimental *in-vivo* stage of the research.	Medical terminology and language need to be transmitted and understood by other communities.
Research Institution	Members include researchers and technicians with skills in protocols and technical procedures. They are also in charge of different projects.	Experimentation and certification.	Efficient transfer of basic research to technology development addressing the needs of all communities.
Industry	Project leaders, project and innovation managers, manufacturers, technicians.	Scale-up, manufacturing.	Understand the principal obstacles of miniaturization and scalability in pilot production and manufacturing.
Adminis-tration	Project managers with expertise in finance, management and public policies.	Auditing, monitoring and stretching the focus of the research. Launching scientific and industrial policies.	The principal objective and focus of the research must be maintained and encouraged. Flexibility in bureaucracy is also a time-challenge for this community.

2.6 Conclusions of Chapter 2

Innovation and technology transfer challenges need to be addressed for the successful commercialization of cross-fertilized products. In this chapter, these challenges have been explored with the aim of understanding the reasons for a particular technology having success or failing in getting to the market place. For this purpose, four nano-enabled sensor-based devices, at different stages of technological maturity, were considered as the element of study and as outcomes of the process of cross-fertilization of KETs. In this regard, a cross-case analysis was carried out using methodology through a triangulated process of information retrieval that included interviews with device developers.

From the data obtained, it was found that the four cases shared common characteristics. In all cases, a multi-disciplinary group of people were involved in the development of the device. This characteristic was incremental according to the level of technological maturity. This means that cases at higher TRLs had more multi-disciplinary participants. Another common characteristic was the level of formality of relationships. It has been found that there was not a marked tendency towards a formal or informal relationship on the basis of the purpose and the duration of the relationships, which are two indicators from Wenger and Snyder (2000).

Findings have also shown common challenges in the four cases. For instance, manufacturing costs, technological barriers and technology-market matching were identified as important challenges. The existence of cheaper and well-positioned alternatives in the marketplace, as well as the lack of market-oriented strategies, have been considered relevant limiting factors. Additionally, findings have shown that more KETs were cross-fertilized at lower levels of technological maturity. Emerging difficulties in these cases, due to the complexity of involving diverse KETs, resulted in a relevant challenge for technology transfer and consequently commercialization. This leads to the deduction that, in order to overcome this challenge, innovation management strategies should not be based on traditional strategies in those cases.

Despite these similarities, it has been found that an intra-organisational collaboration and market research strategies were more evident at higher levels of technological maturity. In this respect, the case that showed a relative success and time-to-market reduction was Case IV. From this case, several factors could be highlighted. Firstly, the ischemia-sensor device was developed within a multi-disciplinary participation. Secondly, an intra-organisational structure was evidenced. This could imply that no significant barriers are present for knowledge transfer across organisational boundaries. Thirdly, this case has shown a

communitarian approach among stakeholders, in which different agents from diverse backgrounds were motivated to accomplish a mutual goal by pooling their knowledge together. Finally, competitor risk analysis and customer needs considerations were taken into account in market research activities in this case. In this regard, it could be concluded that a complete overview of the value chain of research and technology transfer processes highlights the importance of a common framework for a nano-based innovative community ecosystem in which the resulting outcome could be the social return of public-funded investments.

These identified challenges were considered as the basis for introducing an innovation model in order to overcome the gap between research and the marketplace, and which could be suitable for further study in subsequent chapters. The suggested model is therefore conceived as a communitarian network that includes different communities performing together as a "mosaic" structure in a new and integrative nano-based innovation community, where flow of knowledge comes from different technological backgrounds. A strategic advantage could be obtained by considering this integration of the community from the beginning of the value chain. This model is suggested as a common framework in which multi-disciplinary teams and organisations can work together under the direction of a determined scientific leadership. As a consequence, technicians, innovation managers, researchers, engineers, physicians and project managers can offer greater value through a new entrepreneurial community.

Finally, findings from this study allow innovation managers and those responsible for technology transfer, to update their knowledge and to be aware of identifying principle challenges in order to reshape the innovation management strategies in their organisations, leading to a successful technology transfer and commercialization of nano-enabled medical devices.

CHAPTER 3

Empirical study

Abstract

In this chapter, two characteristics previously found in the innovation ecosystems from **Chapter 2** are further analysed; these are the level of multi-disciplinarity and the level of cross-fertilization of KETs. The chapter is therefore divided into two sections. In **Section I**, an empirical study of multi-disciplinarity and its influence on the creation of technological diversity is presented. Creating adequate technological diversity is fundamental to ensuring the long-term success of an emerging technology, and it usually takes place in innovation projects. To this end, EU-funded nanotechnology-related projects, where cross-fertilization of KETs was strongly encouraged, have been selected as the element of study. Other project characteristics of the projects that have a plausible influence on diversity creation were also included. Complementarily, **Section II** presents the analysis of the innovation management strategies that are boosting the cross-fertilization of KETs. These strategies were analysed by considering network theories, absorptive capacity and dynamic capabilities literature. For this purpose, project leaders from the aforementioned selected projects have been interviewed. Findings suggest that multi-disciplinarity is a highly influential factor for the creation of technological diversity and that management strategies that are boosting high levels of cross-fertilization of KETs are principally market and customer oriented strategies. Practical and methodological contributions from this study could enrich innovation literature from the point of view of technological and management approaches.

3.1 Introduction

In the previous chapter, the innovation and technology transfer challenges of nano-enabled medical devices based on the cross-fertilization of KETs were explored. Findings suggested that a multi-disciplinary and integrated community-based ecosystem could be an appropriate model to better overcome the challenges studied. In this chapter, the aim is to further analyse the proposed innovation model so that the long-term success of cross-fertilized medical outcomes could be achieved. Moreover, two characteristics found in the innovation ecosystems, the level of multi-disciplinarity and the level of cross-fertilization of KETs, are deeply analysed in this empirical study. This chapter is therefore divided in two sections.

Section I takes into account the evolutionary economics literature that states that the long-term success of an emerging technology requires the sufficient ***creation of technological diversity*** among its alternatives in the system [74], [273], [274]. Having sufficient technological diversity helps to prevent an early lock-in[6], facilitates recombinant innovation[7], increases resilience of a technology in case of unexpected circumstances, and allows market-growth [273], [275], [276]. Moreover, the heterogeneous knowledge that exists in technological diversification facilitates the possibility of new combinations and the cross-fertilization of technologies, generating greater innovative outputs [277], [278].

In **Section II** the level of cross-fertilization of KETs is considered. As observed in **Chapter 2**, the more KETs that are intended to be cross-fertilized, the more complex the process of technological transfer and commercialization is. This scenario leads us to think that the way this complex process is managed should not be based on conventional management strategies. In this regard, this section presents the analysis of the ***innovation management strategies*** that could boost the process of cross-fertilization of KETs. Previous studies revealed that innovation management strategies are influential for converging technologies [66], [279]. These strategies are also important due to the fact that they give a roadmap and a clear sense of direction from which to make decisions, taking into account the finite resources of organisations [85]. Moreover, these strategies affect productivity and teams' performance [66].

For both analyses, EU nanotechnology-related projects were selected as the element of study. Selecting funded projects was considered adequate for the reasons that are

[6] According to Arthur (1989), *technological lock-in* occurs when a single technology dominates the entire market, preventing the market entrance or success of other alternative technologies (which can be potentially superior) [457].

[7] *Recombinant innovation* is defined as the innovation generated when there is a fusion (or recombination) of two or more existing paths or technologies, accelerating the progress and transition of a technology [73].

explained as follows. Firstly, creating new technological diversity usually takes place in innovation projects in which different organisations such as firms, universities, and research institutes, collaborate among themselves [112], [280], [281]. For emerging technologies, these innovation projects are often publicly supported. Hence, funding instruments are a tool for policy makers to influence the level of technological diversity [273], [282], and thus, to secure the long-term viability of the technology. Secondly, the cross-fertilization of KETs is highly encouraged by public funding initiatives such as H2020, therefore the level of cross-fertilization and the strategies applied for in this process can be evidenced in EU-funded projects.

In the following section the process of selecting the projects is explained. In addition, principal characteristics of the system of projects and their organisations are described.

3.2 Research design

3.2.1 Sample selection

The study focussed on one hand, in nanotechnologies applied in the field of healthcare following the objectives of the thesis, and in the second, in the process of cross-fertilization of KETs. For this purpose, nanotechnology-related projects for healthcare applications were selected from the Work Programme LEIT 2014-2015 of H2020 called "*Nanotechnologies, Advanced Materials, Biotechnology and Advanced Manufacturing and Processing*", which fosters the technological cross-fertilization of nanotechnologies, advanced materials, biotechnologies and advanced manufacturing systems [283]. The projects belong to the following four types of categories:

- **Nanotechnology and advanced materials for more effective healthcare (NM)**: focuses on the potential of advanced materials and nanotechnologies to enable effective therapies and diagnosis. The major innovation challenge in this call is to achieve clinical applications from pre-clinical laboratory-scale proof-of-concepts.
- **Exploiting the cross-sector potential of nanotechnologies and advanced materials to drive competitiveness and sustainability (BN)**: this call focuses on the break-through potential of nanotechnology and advanced materials on several applications and economic sectors by boosting European industry.
- **Bridging the gap between nanotechnology research and markets (NG):** this call addresses three key nano-enabled industrial value chains

(lightweight multifunctional materials and sustainable composites, structured surfaces, and functional fluids) by taking them from the laboratory to the industrial scale.

- **Biotechnology-based industrial processes driving competitiveness and sustainability (BIO)**: this call focusses on delivering novel products that cannot be produced in the current industry on the basis of efficient biotechnological methods with less environmental impact.

The data was obtained from the Community Research and Development Information Centre (http://cordis.europa.eu/), a public repository and open access portal of the EC providing information of EU-funded research projects. **Figure 3.1** summarizes the pathway for selecting the cases.

A total of 69 projects were obtained and 222 different organisations as coordinators and participants were retrieved. Since some organisations participated in more than one project, a total of 239 observations have been considered for the descriptive analysis. The different organisations were classified into five categories according to the established categories from H2020:

- **Higher or Secondary Education Establishments (HES).** Are legal entities that are recognized as such by their national education systems. They can be public or private bodies.
- **Research Organisations (REC).** Are legal entities that are established as non-profit organisations and whose main objective is carrying out research or technological development.
- **Private for-profit entities (PRC)**. Are organisations from the private sector, including small or medium-sized enterprises and excluding Universities and Higher or Secondary Education Establishments.
- **Public bodies (PUB)**. Are any legal entity established as public body by national law or an international organisation. Research Organisations and Secondary or Higher Education Establishments are excluded.
- **OTH:** Other. Any entity not falling into one of the other four categories

3.2.2 Methodology

The information retrieved from the selected projects was initially analysed through descriptive statistics, network graphs and text mining approaches in order to have a complete overview of the element of study. Next, to analyse the creation of technological diversity in **Section I**, the Topic Modelling approach was used. This is

a novel text mining method for categorizing technological alternatives from text data. This method allows the calculation of diversity creation in a more efficient manner than in conventional qualitative approaches. The hypotheses formulated in this section were tested with an Ordinal Logistic Regression Model.

For the second section of the study, project leaders were interviewed in order to retrieve information about their innovation management strategies. The hypotheses formulated for this section were tested through a Multiple Correspondence Analysis. The methodology applied in both sections is summarized in **Figure 3.2**.

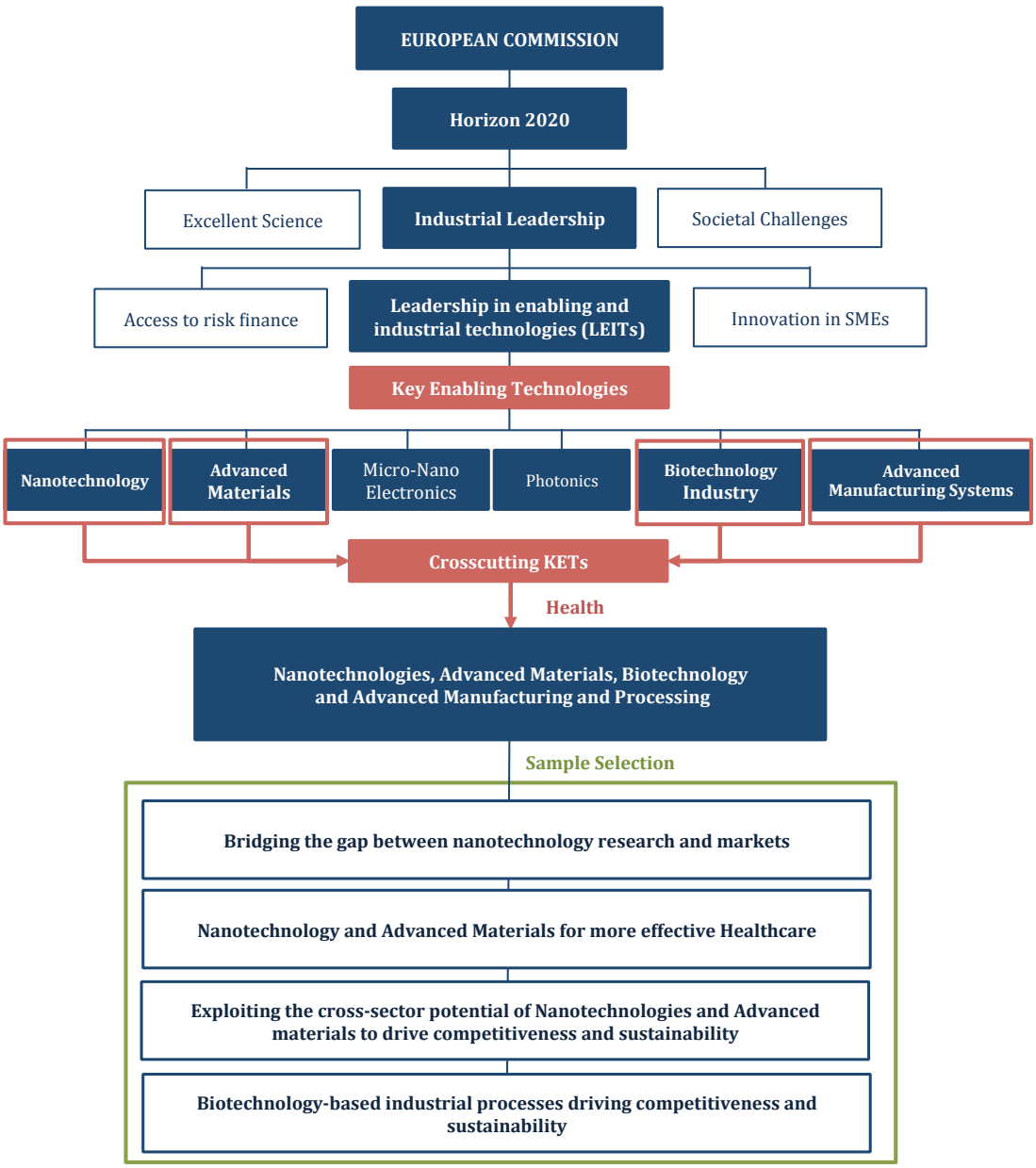

Figure 3.1. Pathway for selecting the sample: projects from the CORDIS database.

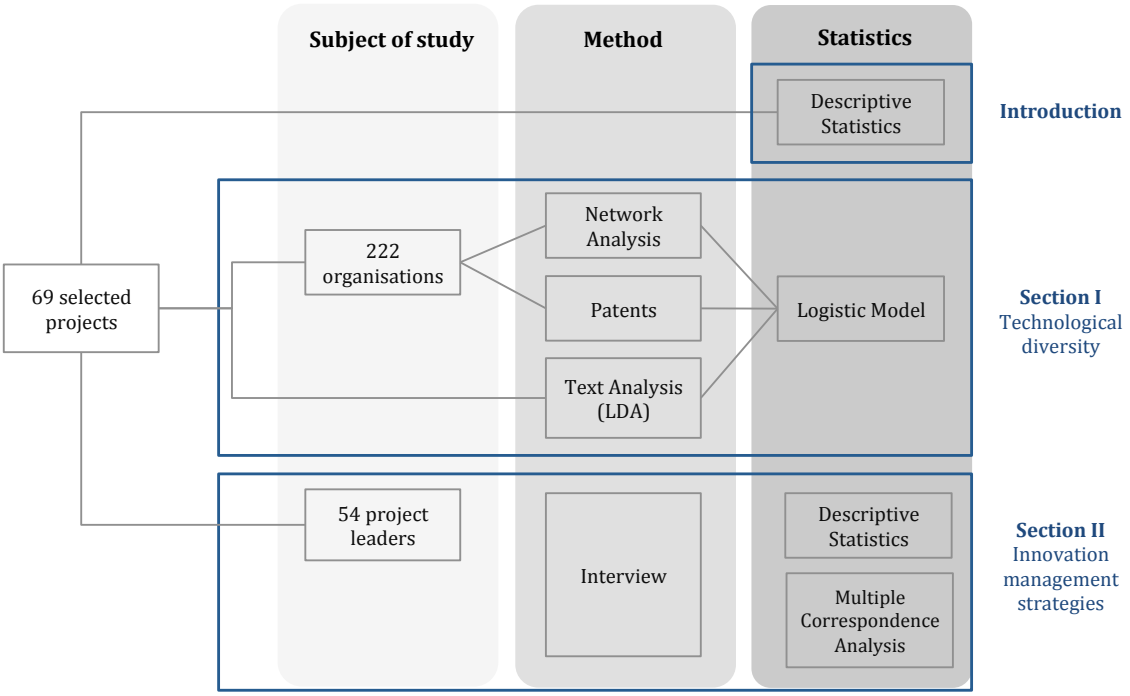

Figure 3.2. Summary of methodology used in the empirical study.

3.3 Element of study: A descriptive analysis

From the set of projects, it was found that there were 26 participant countries (**Figure 3.3**), including 23 Member State Countries of the European Union and their overseas departments, and 3 Non-Member States: the UK[8], Israel[9] and the US[10]. In this sample, the country with the greatest number of projects was Spain (with 36 projects) and the countries with fewer projects were Croatia, Estonia, Hungary, Lithuania, Poland, Slovakia and the US (with one project each one).

Figure 3.4 shows the cluster map of the total system of projects. As can be seen, countries that participate in a collaborative consortium are Spain, Germany, the Netherlands and the UK. Countries with no partnerships are Hungary, Estonia, Lithuania, and Slovakia, shown on the lower left side of the graph. On the other hand, it has been found that 22% of the projects were developed with organisations involved in a consortium, meaning that there is one coordinator and one or more

[8] On June 23rd 2016, 52% of voters decided that the UK should leave the EU. At the date of the Work Programme H2020, the UK was still considered a Member State of the EU.

[9] Associate country to the Seventh Framework Programme (FP7) that has been associated to H2020.

[10] Associated countries whose principal objective is to promote scientific and technological cooperation in Europe.

partners in the project. From the 222 total project leaders retrieved, 19 of them are coordinators working with other partners.

Regarding the category of call, it was found that from the 69 projects, 7 belong to the NM call (10%), 34 to the BN (49%), 7 to the NG (10%), and 21 to the BIO (30%) as shown in **Figure 3.5a.** The majority of participant organisations are PRC, (65%), following by HES (22%) and REC (12%). The sample also shows very little participation of PUB and OTH organisations, with 1% of participation each **Figure 3.5b**. **Figure 3.6** shows the distribution of the types of organisations according to the four different categories. A similar participation of PRCs in all calls can be seen. Except for the BN call, there is also a proportional participation of REC and HES. The BN call only shows one type of participation because it was a specific call for SMEs[11]. In addition, as can be seen in the figure that the call NM is the only call that includes public organisations (PUB).

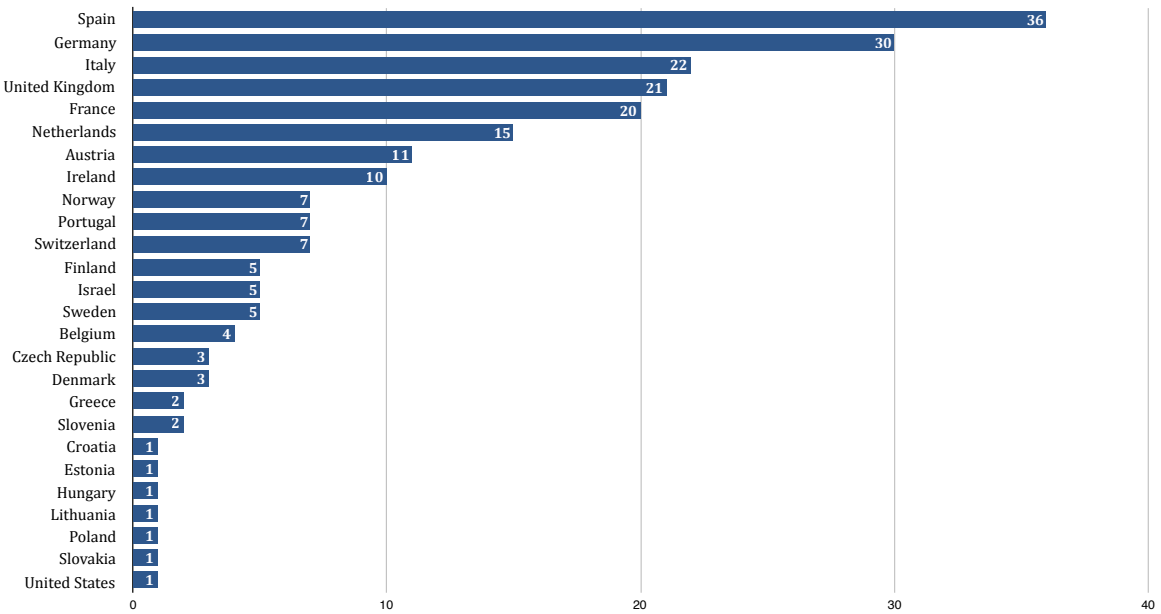

Figure 3.3. Number of projects per country.

[11] NMP 25 – 2014/2015: Accelerating the uptake of nanotechnologies, advanced materials or advanced manufacturing and processing technologies by SMEs

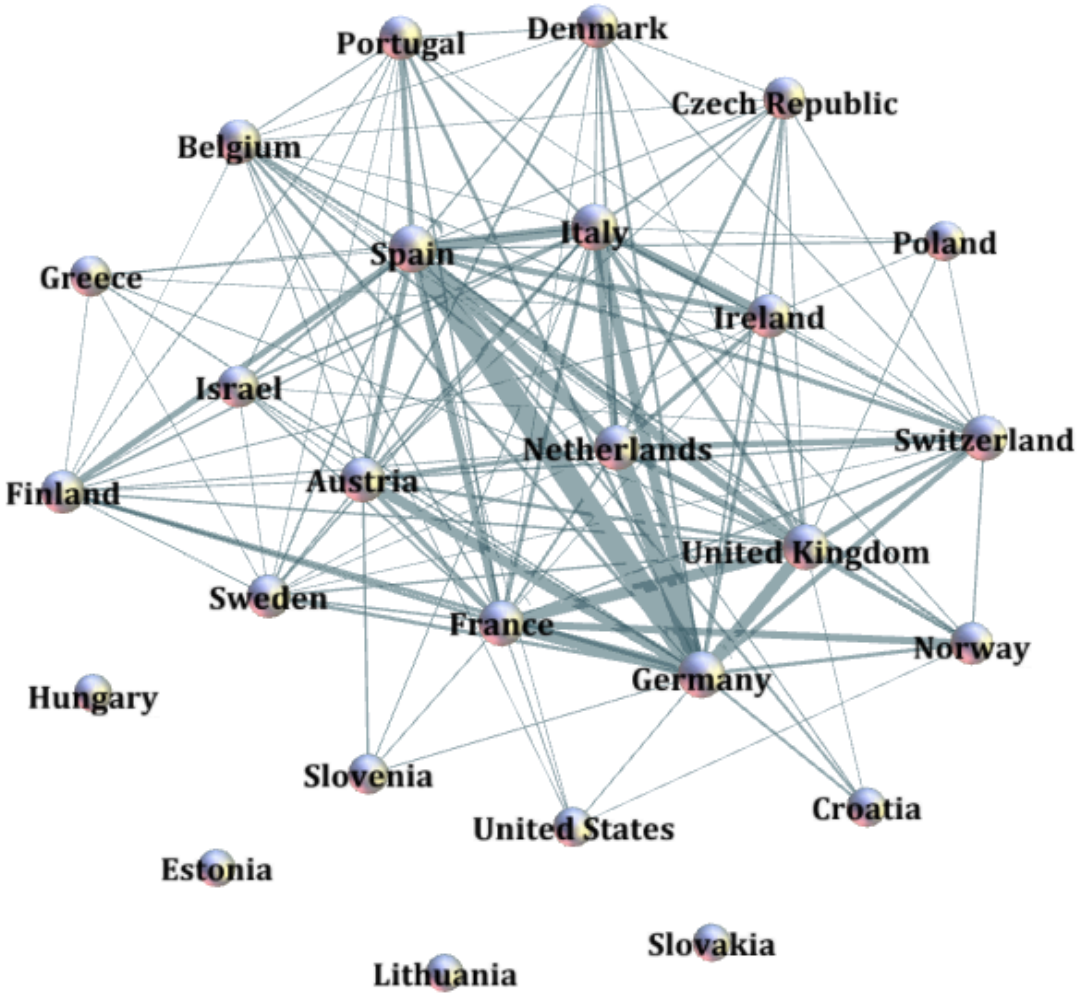

Figure 3.4. Network of countries in the system of projects. Nodes are the countries and lines (edges) are partnerships. The thickness of the line represents the number of partnerships: thicker lines represent greater numbers of projects that are shared partnerships.

Figure 3.7 shows the distribution of the different types of organisations per participant country. It can be seen that there is a homogeneous participation of PRC in most of the countries. On the other hand, France and the Netherlands are the only countries that show participation of public institutions. A similar pattern occurs with the distribution of the different calls per country. **Figure 3.8** shows that most of the countries with more than three projects each are participating in the four calls.

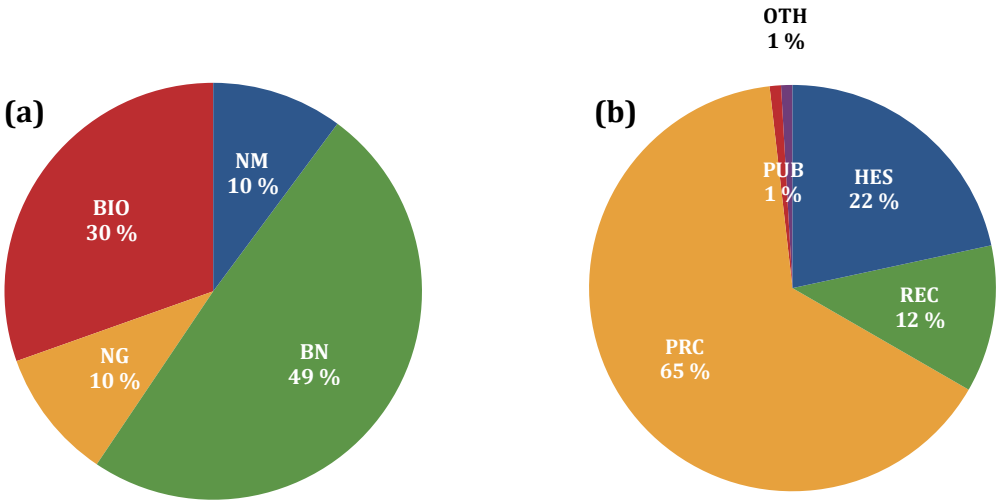

Figure 3.5. Participation percentages. (a) Per type of call and (b) Per type of organisation (For abbreviations, please refer to **Section 3.2.1**).

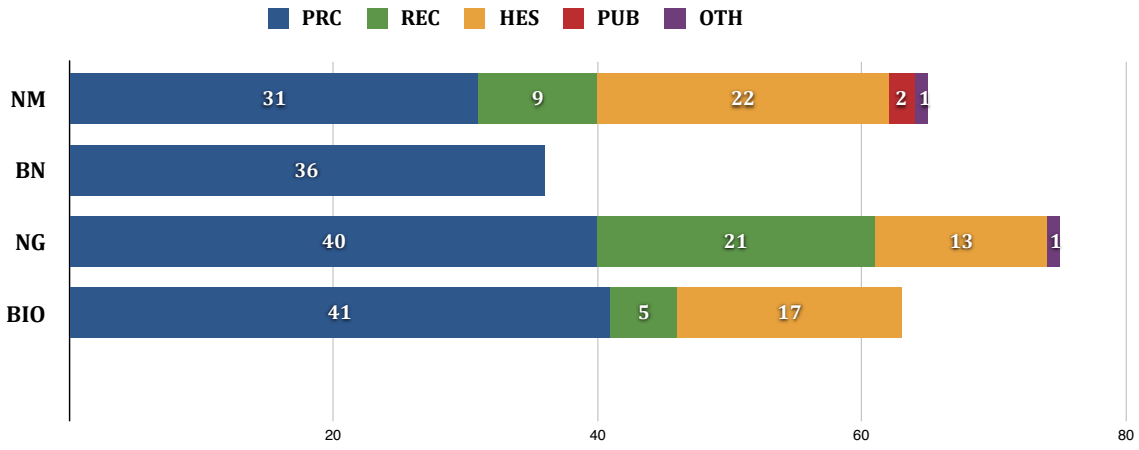

Figure 3.6. Proportion of participation of different types of organisations in each call.

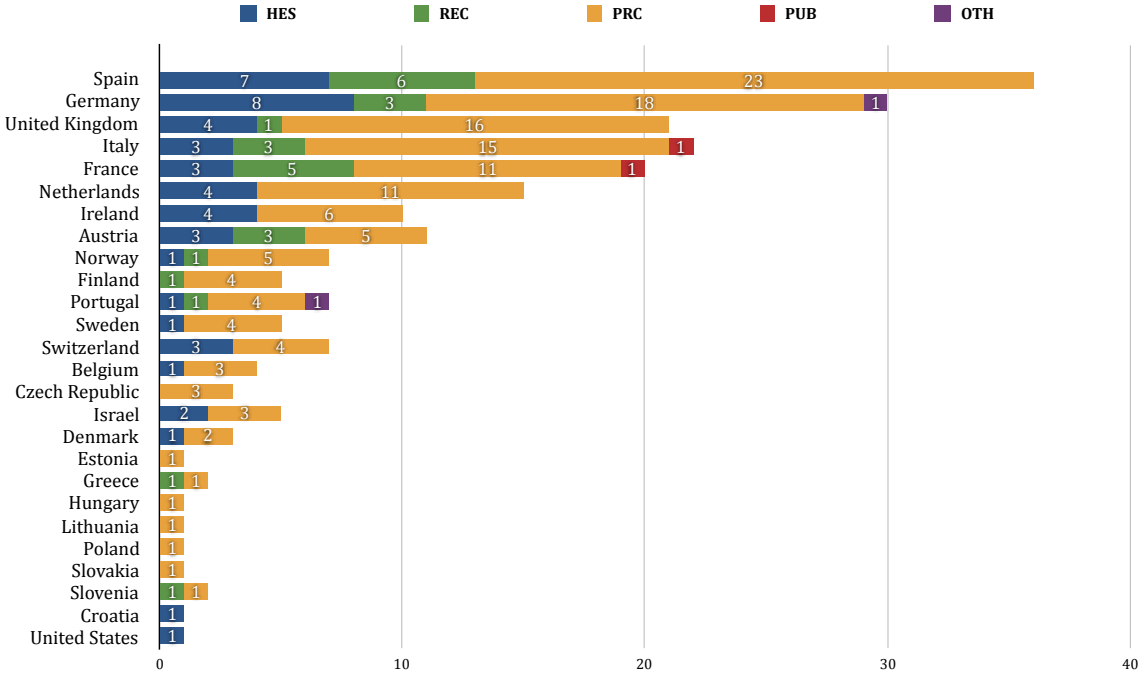

Figure 3.7. Types of organisation per country.

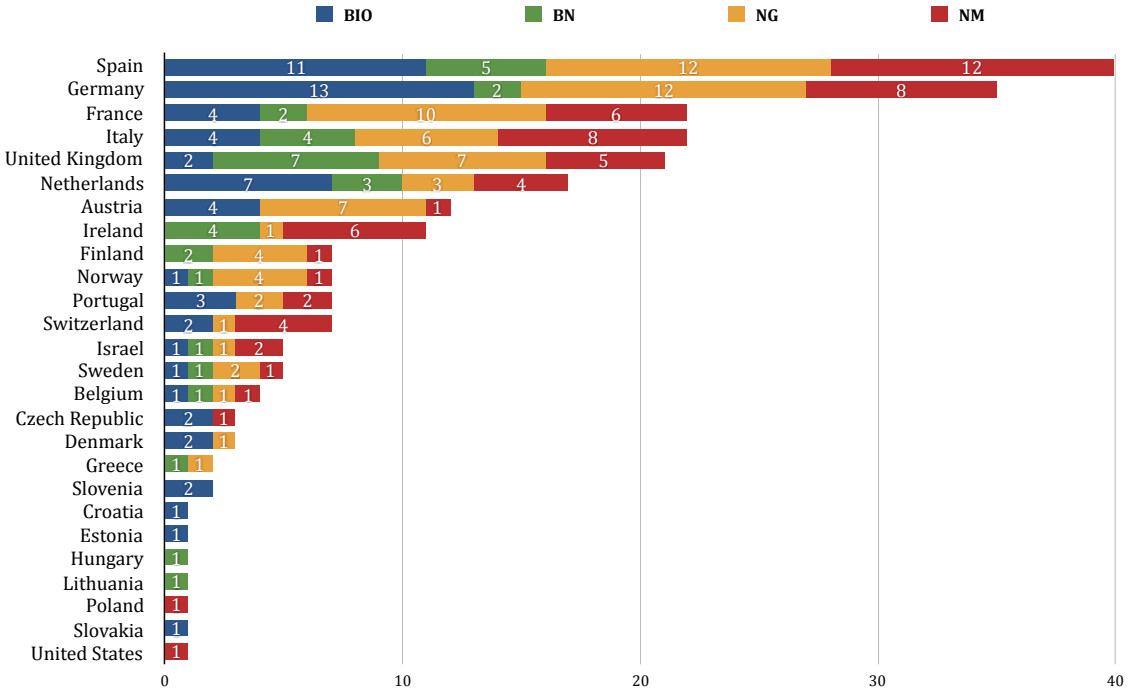

Figure 3.8. Percentage of projects per call category and country.

Complementarily, a text exploratory analysis was done in order to visualize the word trends using the *VOSviewer* software. This tool is used for constructing and visualizing bibliometric networks. The following figures show the density visualization of the content of the system of projects based on the density of words. Each point in the map has a colour that depends on the density of words at that point. The larger the number of words in the neighbourhood of a point and the higher the weights of the neighbouring words, the closer the colour of the point is to red. Conversely, the smaller the number of items in the neighbourhood of a point and the lower the weights of the neighbouring words, the closer the colour of the point is to blue. Following the two approaches of this thesis, an analysis was done for visualizing technological trends and other analysis was done for visualizing managerial trends. In this regard, two graphics were created according to these criteria. **Figure 3.9** shows the density graph for technological-related words and **Figure 3.10** shows the density graph for managerial-related words. As can be seen, technological-related words showing more density in the text are: “material”, “nanocapsule”, “enzyme”, and “vaccine”, among others. Managerial-related words with more density are “application”, “platform”, “patient”, “industry” and “company”. These findings give a general vision about what are the projects mainly focusing on and the discourses that can be found in the system of projects.

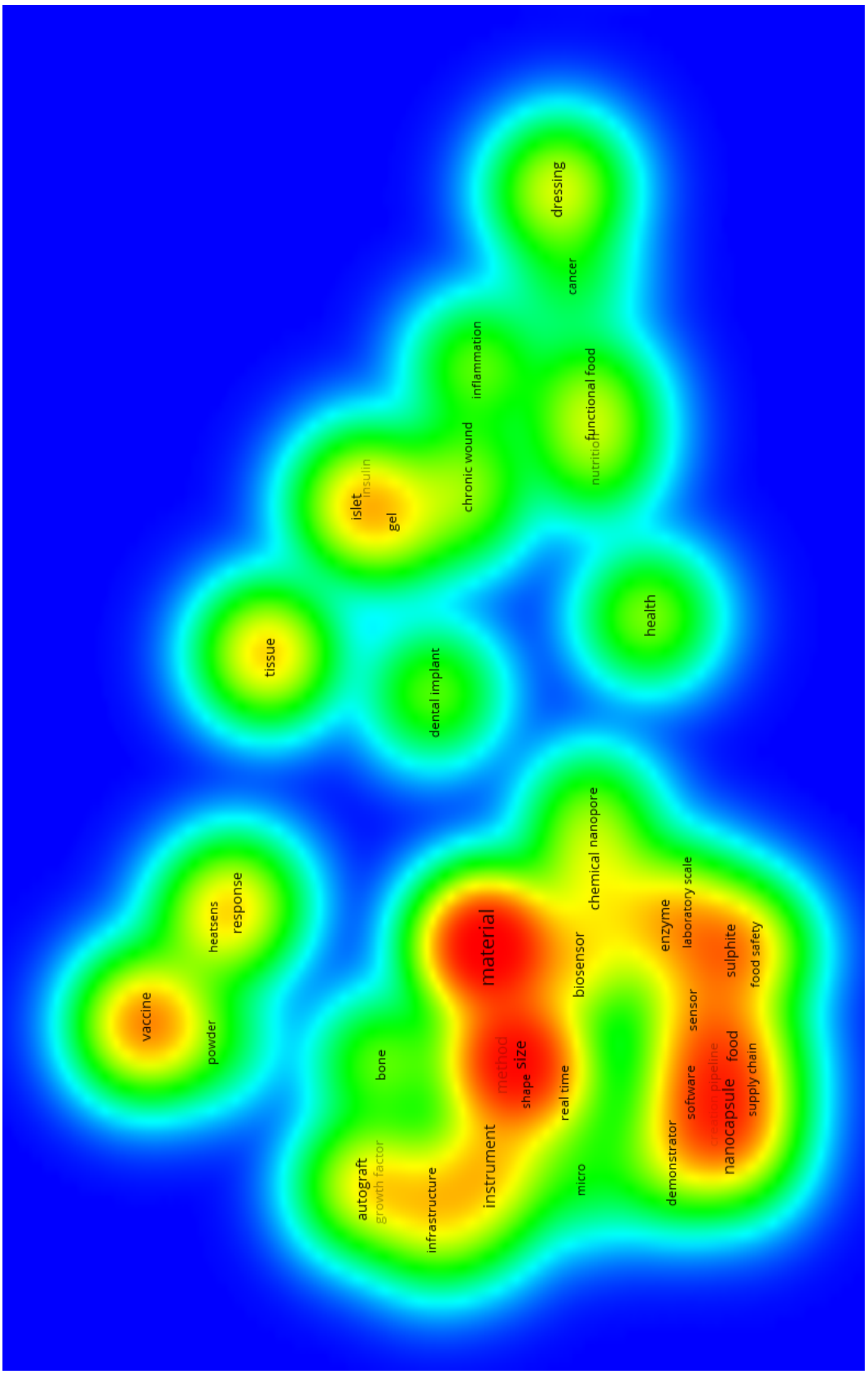

Figure 3.9. Density visualization map of *technological-related* words. Density of words are represented in red areas.

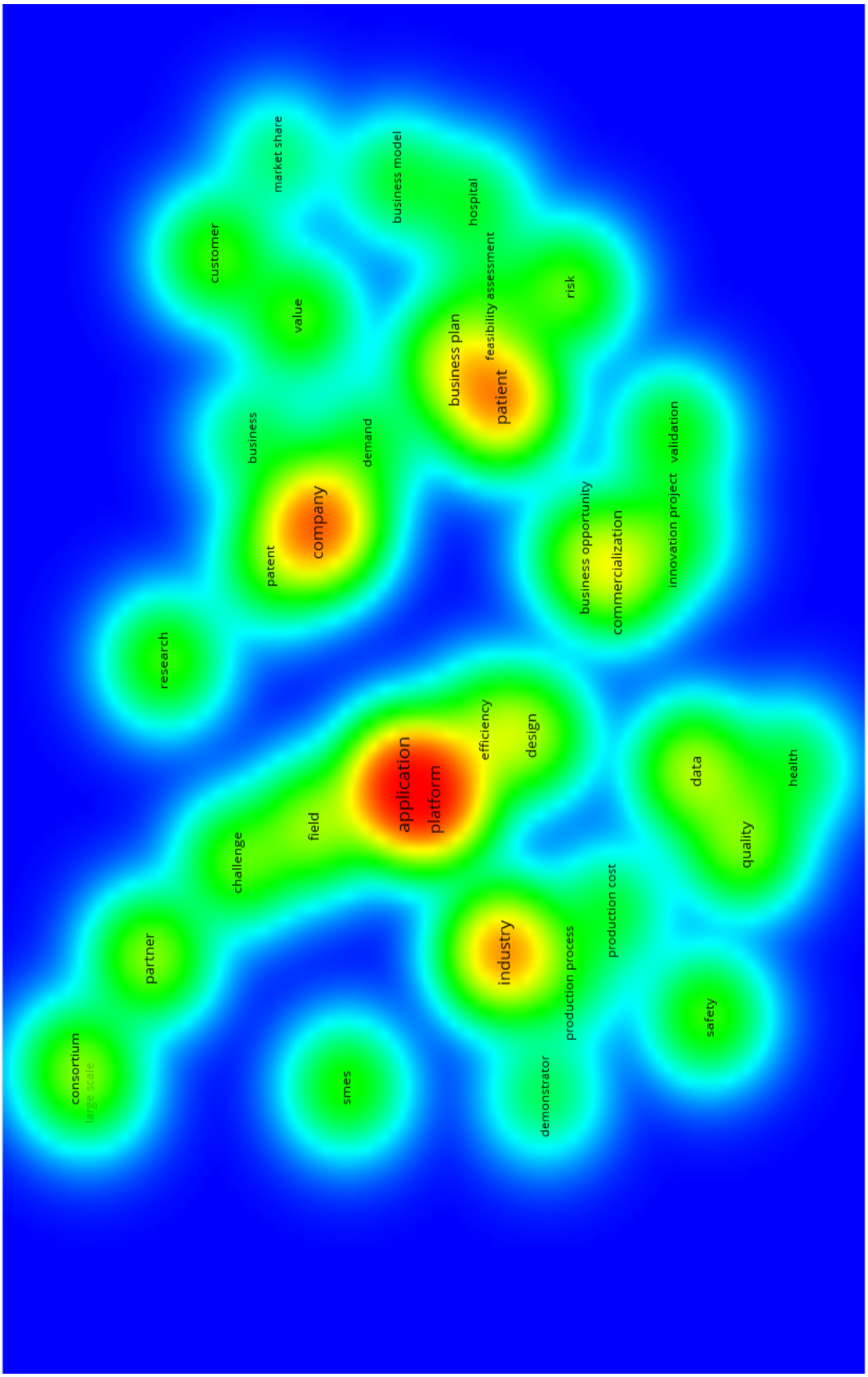

Figure 3.10. Density visualization map of *managerial-related* words. Density of words are represented in red areas.

Section I: Focusing on technology

3.4 Introduction

For an emerging technology like nanotechnology, creating sufficient technological diversity among its alternatives is important for its long-term success [74], [273], [274]. Innovation is an evolutionary process of variation and selection [284], [285]. The diversity of a technology changes as new technological alternatives are created [273], [286], [287]. If a new technological alternative represents a common technological design, diversity decreases. Technological alternatives that have a novel or less common design increase diversity [288], [289].

The creation of new technological alternatives often takes place in innovation projects in which different organisations such as firms, universities, research institutes, collaborate [112], [280], [281]. For emerging technologies, these innovation projects are often publicly supported, for example, through EU-funding. Hence, funding instruments can be used as a tool for policy makers to influence the level of technological diversity [273], [282], and thus to secure the long-term viability of the technology.

Simulations [290] and conceptual works [281] indicate that the creation and persistence of technological diversity depends on learning from their neighbourhood and network externalities. Yet, there is little empirical evidence about the characteristics of innovation projects that influence diversity. Van Rijnsoever et al., (2015) demonstrated that diversity created by an innovation project is related to the network position and organisation composition of a project. Adding to insights from innovation systems [285], Van Rijnsoever et al., (2015) argue that it is also important to consider the structure of the network to make a technology successful in the long term. In nanotechnology European founded projects, Pandza et al., (2011) found that there is a significant degree of collaborative diversity in terms of international and institutional affiliation in a research network. This should be beneficial to technological diversity creation, but they did not test this implication empirically. In this section, these current approaches are extended by studying the influence of characteristics of EU-funded nanotechnology projects on the creation of technological diversity. In addition to organisation diversity and the network of the project, novel variables that have a plausible influence on diversity creation are included. The degree of multi-disciplinarity of the project and the knowledge base of the organisations in the project can increase the chances that unique novel combinations are made, increasing technological diversity.

Further, to understand technological diversity, studying the content of the documents is needed. Scholars use pre-existing categories like patent classes or Web of Science categories to measure diversity [35], [291]. Another approach to determine diversity is to look at the network of citations of the documents [35]. Yet, these approaches are mainly applicable to patent or publication data, and not to EU-projects. Hence, to study diversity, topic modelling was applied [292] as a novel approach to categorize technological designs that are described in 69 EU-projects from 2014-2015. This method allows calculating diversity creation in an efficient manner.

The change in technological diversity caused by a project was related to the independent variables mentioned above and results have shown that the largest contribution to diversity comes from the multi-disciplinary nature of a project and the nanotechnology knowledge base of the organisations in a project. Moreover, the obtained results largely confirm the results by Van Rijnsoever et al., (2015). Policy makers can use these results to use subsidies as a tool to influence the level of diversity in a technological field.

3.5 Theoretical background and research hypotheses

3.5.1 Technological diversity

Technological diversity refers to evenness in distribution of technological alternatives [293]. These alternatives can be designs [273], [286], [294], technical characteristics [273], [286], [287] or numbers of different technological lineages represented in a technology [295].

Technological diversity is a macro-level concept, as it applies to a set of technologies. The concept is related to the micro-level concepts of radical and incremental innovation, which are commonly used to assess specific innovations or the performance of firms. Radical innovations are new technologies and are often based on the combination of different technologies [75]. As radical innovations are new, they increase technological diversity by definition. In contrast, incremental innovations can be achieved without novel information or the integration of different technologies [296], and can either decrease or increase diversity, depending on how abundant the incrementally improved technological design is among existing alternatives. Incremental innovations on rare technological designs increase diversity, while incremental innovations on common technological designs decrease diversity.

The evolutionary economics literature states that technological diversity contributes to more rapid technological change [297]. For this they give three

reasons. First, diversity mitigates the possibility of an undesirable lock-in, reducing the likelihood that superior alternatives remain undiscovered or underdeveloped [289], [298], [299]. Second, diversity increases the chances of making recombinant innovations, and hence of further developing the technology. Third, technological diversity means that there are more alternatives, which provides flexibility [300], [301]. As a consequence, diversity increases the resilience of a technology against unexpected environmental changes, which are particularly common in emerging stages [274]. These reasons influence the long-term success of an emerging technology and are important to consider when analysing the functionality of innovation systems [273]. Technological diversity can thus be used to help assess the long-term viability of a technology.

However, having too much diversity also has drawbacks [302], [303]. For instance, diversity hampers the development of standards, economies of scale, and the learning of routines to exploit the technology [304]. Among organisations, more diversity requires time, effort, and coordination [305] to resolve differences among perspectives that can emerge [306]. These advantages and disadvantages imply that there is an optimal level of diversity [74].

Despite there being no established parameters to obtain this optimal level, it is possible to analyse factors that influence the creation or otherwise of diversity [273]. Innovation subsidies can be such a factor, but this is not enough to stimulate diversity creation. In this context, it is also necessary to consider how these subsidies are distributed.

3.5.2 Networks of innovation projects

In line with innovation system thinking, Van Rijnsoever et al., (2015) argue that the concept of technological diversity creation needs to be studied at a project level, rather than at the level of the individual organisation, because new technological alternatives are the output of innovation projects and not of the organisations themselves. Organisations contribute knowledge, resources and skills required for successful innovation to these projects, and share the risks of failure [307]. In this study it is discussed how a project's degree of multi-displinarity, and the composition of the project in terms of the prior knowledge base of organisations, the number of organisations, the diversity of organisation types, geographical distance between partners and network position influence technological diversity.

3.5.3 Degree of multi-disciplinarity

The concept of discipline has been subject to much debate. For instance, it has been used with "inter", "trans" and "cross" prefixes. Schummer (2004) makes a distinction between multi and interdisciplinary: multidisciplinary refers to the involvement of many disciplines, meanwhile interdisciplinary refers to the interaction between disciplines [37]. In the context of this research, the definition from Rafols and Meyer (2010) is considered. These authors define multi-disciplinarity as the spanning of a diversity of knowledge areas, which could be disciplines, technological fields or industrial sectors [35]. Many other scholars have analysed multidisciplinary projects from the perspective of collaboration between team members [40], [308]–[310], or on the skills required to manage these types of projects [41], [311]. However, to the best of our knowledge, no research has focused on the degree of multi-disciplinarity of projects and how this contributes to technological diversity.

Yet, there are good reasons to suspect such a relation. A multidisciplinary environment favours a greater diversity of idea generation and promotes creativity [312]. Due to the juxtaposition of ideas, tools, and people from different domains [310], multi-disciplinarity within projects enhances recombinant innovation [313]–[316]. Hence, the chances that novel technological alternatives emerge increase. It is thus expect that the degree of multi-disciplinarity of a project has a positive effect on the creation of technological diversity. This leads to the first hypothesis:

Hypothesis 1*: The degree of multi-disciplinarity of a project is positively associated with the creation of technological diversity.*

3.5.4 Knowledge base

Technological diversity is associated with prior technological knowledge of inventors [302], [317]. This prior knowledge can be measured as patents and publications since they are two quantitative proxies of knowledge production [149], [152]. Previous studies showed that R&D intensity and patents increase with the degree of technological diversification of firms [318]. Prior knowledge also strengthens the absorptive capacity of organisations by increasing "*the prospect that incoming information will relate to what is already known*" [319] (pp. 131). Hence, a large knowledge base enhances the ability of an organisation to make novel combinations. Moreover, a larger prior knowledge base demonstrates that organisations have the experience and routines needed to combine knowledge [320]. This effect is even stronger if the joint knowledge base of all project partners is larger, as it further increases the chances of making novel combinations.

Hypothesis 2*: The size of the joint knowledge base of organisations within a project is positively associated with the creation of technological diversity.*

3.5.5 Number of organisations

Number of organisations refers to "*the size of the project consortium in terms of distinct actors*" [273] (pp. 1097). A common position in the literature is that larger project teams provide a larger chance of recombining different types of knowledge, expertise and ideas, and thus innovation [321], [322]. Yet, few studies explicitly address the influence of the number of organisations involved on the creation of technological diversity. In this context, evidence suggests that there is a negative association between the number of project partners and the creation of technological diversity [273]. The argument is that intense collaborations could result in conformity of norms and conventions producing less novelty [323]. Keeping this in mind the following hypothesis is proposed:

Hypothesis 3*: The number of organisations in a project has a negative association with the creation of technological diversity.*

3.5.6 Diversity of organisations

Innovation projects commonly involve different organisation types that come from different institutional spheres [324]. In this study, the organisation types previously described in **Section 3.2.1** are distinguished. Previous studies on the nanotechnology innovation networks demonstrated that networks in this field are indeed characterized by a high degree of international and institutional diversity. Pandza et al., (2011) demonstrated that usually, the inter-institutional collaboration is taking place between private industry and public research organisations [282]. Juanola et al., (2012) also showed that the development of nano-enabled biomedical devices requires the interaction between multiple organisations such as universities, public research institutions, industries, and hospitals or health care institutions [30].

The argument for involving organisations' partners from different institutional spheres is that each organisation type brings to the project unique knowledge and skills which can be recombined to form novel concepts and designs [325], creating more technological diversity [273]. Following these arguments, a positive relation between organisation's diversity and technological diversity creation is stated:

Hypothesis 4*: The diversity of organisations in a project has a positive association with the creation of technological diversity.*

3.5.7 Degree of clustering

As organisations can participate in multiple projects, a network emerges in which projects are nodes and organisations are ties between the nodes. Clustering is a property of a local network structure which refers to the likelihood that two organisations that are connected to a third organisation are also connected to one another [127], [326]. The more they are connected, the higher the degree of local clustering [327].

There is a debate about the effect of clustering on innovation. On the one hand, clustered networks are argued to be dense local neighbourhoods where organisations trust each other, shared norms emerge, information is verified or diffused [322], [328], [329] and novel combinations are being made [330]. However, too much clustering can have negative effects on innovation. Many of the ties are redundant, yet costly to maintain [331]. Also, sharing the same information sources also means that knowledge becomes more homogenous. Moreover, the shared norms can hamper creativity. The opposite of clustering is that there are *structural holes* in a network [331]. Structural holes occur when two organisations that are connected to a focal partner are not connected to each other [331], [332]. This means that the focal partner has access to two different sources of information, which allows for making novel combinations [331] that add more to technological diversity [273]. Hence, it is hypothesized:

Hypothesis 5*: The degree of clustering around a project is negatively associated with the creation of technological diversity.*

3.5.8 Geographical distance

Geographical distance between organisations in a project is another network dimension that influences knowledge diffusion [333]. Based on the theory of regional innovation systems [117], it has been shown that higher concentration of *talents* in a region helps to connect and exchange knowledge resulting in enhanced innovations [87], [334]. However, knowledge is bound to a geographical location, and the content of knowledge bases varies geographically [335], [336]. Therefore the further the distance between organisations, the more likely it is that their knowledge bases differ. This increases the possibility of making novel combinations. Van Rijnsoever et al., (2015) tested this relationship but found inconclusive evidence. A possible explanation for this is that their study only included Dutch innovation projects. There might have been too little geographical distance between partners for the knowledge bases to differ. Hence, it is hypothesized:

Hypothesis 6*: The geographical distance of organisations within projects is positively associated with the creation of technological diversity.*

3.6 Variable measurements

3.6.1 Technological diversity

Diversity is a multidimensional concept. Stirling [337] recognized variety, balance and disparity as the three dimensions of diversity. Variety represents the number of elements or categories in the system. Balance refers to the distribution of these elements and disparity to the degree these elements are distinct from each other. In this study variety and balance are used to calculate diversity. Disparity is not taken into account since there has been no satisfactory measure of these three dimensions [35], [273], [300], [338].

To analyse the creation of technological diversity, the first step was to find all the technological alternatives present in the system of projects. In the case of publications and patents this is often done by looking at citation patterns or pre-existing categories [35], [335], [339]. Yet these measures are not applicable to the selected project data, as only the abstracts were accessible. Hence, topic modelling techniques were used. Topic Models represent a set of probabilistic variable models used to evaluate the semantic structure of documents based on a hierarchical Bayesian method [292], [340] which can be used to identify topics among documents. The different technological alternatives are based on semantic clusters, which are usually identified as "topics". Therefore, topics are a set of words that represent a theme. For example, the words "nano-capsule", "delivery" and "enzyme" can be classified in one topic because these words are related to each other. The distribution of topics is the relation that links words in a vocabulary and their occurrence in documents (mixture of topics). In this study, documents are the abstracts of each project.

To obtain the distribution of topics, Latent Dirichlet Allocation (LDA) was used. This is a common type of topic model that uses discrete probabilistic techniques for information retrieval, and text and data mining [341]. LDA assumes that K number of topics have an association with a collection of documents, and estimates for each document the probability that it belongs to a topic [342]–[344].

For the LDA analysis the *lda* package of the R-program was used [345], [346]. The first step was to pre-process the documents in order to avoid possible "noise". This was done by cleaning the text corpus (e.g. remove punctuation, stop words, numbers, etc.) and stemming or merging words equivalent in meaning. For that purpose the *tm* package was used [347]. Second, an appropriate number of topics

needed to be selected for the LDA analysis. Choosing too many topics will result in the "over-clustering" of a corpus into many small, highly-similar topics, while selecting too few can produce overly broad results [348]. For the estimation of the optimal number of topics, the *LDA tunning* package were used [349]. This package estimates the optimal number of topics based on a Bayesian selection model which computes the likelihood probability distribution of a possible parameter setting by assigning all words of the corpus *w*, over a number of topics *T* expressed as P(*w*|*T*) [350], [351]. The number of topics is therefore the model that leads the highest posterior probability. **Figure 3.11** plots the posterior probability against the number of topics. The graph suggests that data are best described by a model with 33 topics.

In order to visualize the distribution of topics per project, a level plot graph was developed by using the *lattice* package in R [352]. **Figure 3.12** shows the LDA graph, where the x axis shows the projects, and the y axis the 33 topics found in the whole system of projects. The distribution of each topic in each project is defined by the intensity of colours: more intense blue colours show few topics distributed in a project (so the colour is concentrated only in one point), while light red colours show a distribution of more than one topic in a project. To confirm the validity of the result, it has been verified that the topics assigned to the documents made sense. As can be seen, most projects were clearly on just one topic. The most common topics were related to scaffolds[12], nano-biosensors, tissue regeneration, wound dressing, and drug delivery, to give just a few examples.

After estimating the most suitable number of topics and the distribution of each topic in each project, it was calculated how much a project *i* influences technological diversity in the population of *N* projects [273]. For that purpose the Shannon's entropy statistic measure was used [353]. This variable measures the randomness of a distribution or the uncertainty associated with a random variable, and takes into account variety and balance. Entropy is calculated as follows:

$$H = -\sum p_s \, \mathrm{Log}_2 \, p_s \qquad (1)$$

where H is the entropy, and p represents the proportion of projects with a specific design or topic *s.* The diversity that a project *i* creates in the system is obtained through the difference between the entropy of the population of projects (H_0) and a hypothetical population where the specific project does not exist (H_{-1}):

$$dH_i = H_0 - H_{-1} \qquad (2)$$

[12] Scaffolds are three-dimensional structures that mimic extracellular matrix, providing an adequate environment for tissue, bones and organ regeneration and also as a cell delivery platform [458], [459].

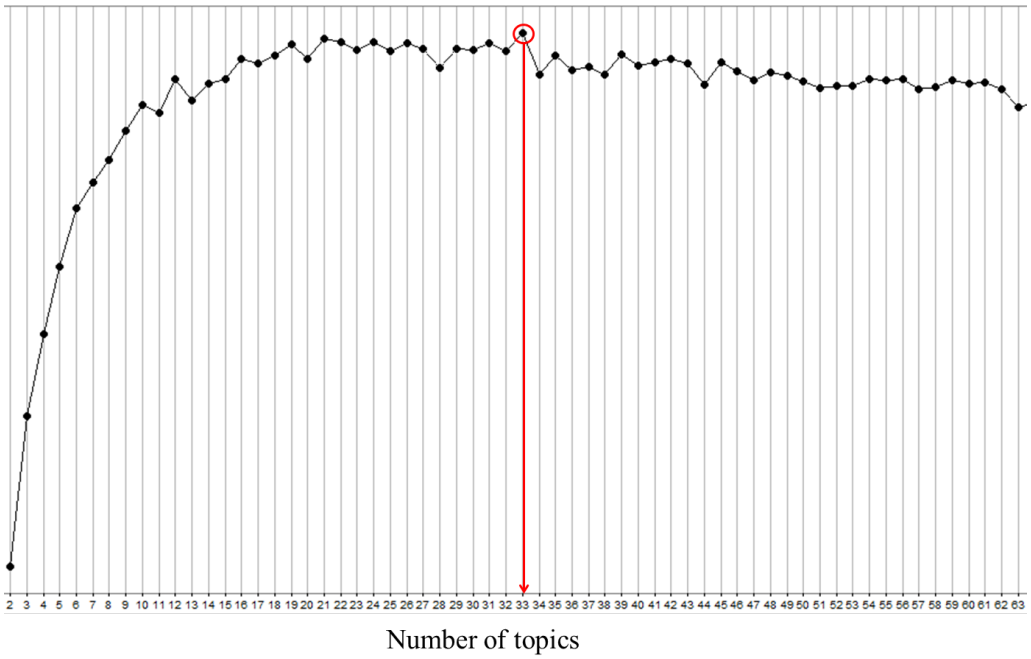

Figure 3.11. Estimation of the optimal number of topics. Maximum likelihood distribution of all words over a number of topics.

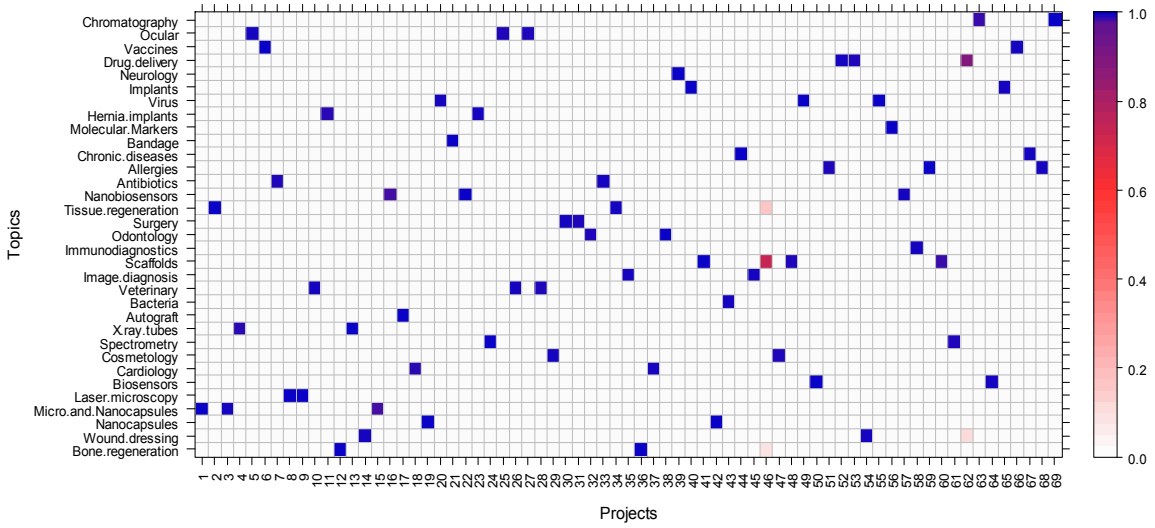

Figure 3.12. Topic distribution per project.

H_0 was obtained through Eq (1) and H_{-1} was calculated by using the following formula:

$$H_{-1} = -\left(p_{si} * Log_2\, p_{si} + \sum_{sj} p_{sj} * Log_2\, p_{sj}\right) \quad (3)$$

where p_{si} represents the proportion of projects with the same design i and p_{sj} is the proportion of any other designs. Both variables are calculated assuming that the focal project does not exist in the hypothetical population n_s. Therefore, it was needed to consider that there is one project fewer with that design in the population, represented by:

$$p_{si} = \frac{n_{sj}-1}{N-1} \quad (4)$$

$$p_{sj} = \frac{n_s}{N-1} \quad (5)$$

A positive value of *dH* indicates that diversity is created. A negative value indicates reduction of diversity in the system of projects. These calculations revealed that there were four different levels of diversity creation.

3.6.2 Degree of multi-disciplinarity

In line with suggestions by [35], [339], the degree of multi-disciplinarity by the diversity of topics were measured. Instead of looking at how often a combination of topics occurs at the system level, the diversity of topics within a project was calculated, using the probabilities from the LDA and **Eq. (1)**.

3.6.3 Knowledge base

The number of patents in a project was used as an indicator for the size of the knowledge base. Patents are a very homogeneous measure of technological novelty [103]. They reflect creativity [11] and the ability to transfer scientific results into technological applications [50]. Nano-related patents of each organisation were retrieved from the European Patent Office - Espacenet Website (EPO) from 1980 to 2015. This period of time was selected based on the fact that 1980 was the starting year of the "boom" of nanotechnology. In order to avoid the generalized nano* research query and eliminate other terms that contains the "nano" word but aren't related to nanotechnology, the standardized nano-related queries from Porter et al., (2008), Mogoutov and Kahane (2007) and Maghrebi et al., (2011) were considered [354]–[356]. These queries are detailed in **Appendix C.**

Only European patents were selected because this enlarges the chances that the knowledge captured by the patent is present in the project. It is less likely that individuals in a project will be familiar with knowledge captured by a patent that is registered only in the US. In order to select the normalized name of each assignee, the *AcclaimIP Patent Search and Analysis Software* was used in parallel, checking the standardized names of the organisations in both sources for more thoroughness. As the number of patents has a skewed distribution, its natural logarithm was used. This also makes the realistic assumption that each extra level of the variable results in a decrease in marginal returns for diversity creation.

3.6.4 Number of organisations

This variable was obtained by simply counting the number of organisations per project. This variable had a skewed distribution; therefore its natural logarithm was used. The transformation also makes the realistic assumption that each extra level of the variable results in a decrease in marginal returns for diversity creation.

3.6.5 Diversity of organisations

Based on the standard classification of organisations from H2020 at **Section 3.2.1**, the diversity in organisation types per project was calculated, using the Shannon entropy mentioned in **Eq. (1)**.

3.6.6 Degree of clustering

The degree of clustering was obtained by calculating the local clustering coefficient (CC) of a project [327]. The CC is a quantitative way to study the structure of a network [357]. It represents the probability that two random neighbours of an organisation from a project are connected. It measures the extent of interconnectivity between the neighbours [358] and is represented as:

$$CC_i = \frac{2L_i}{D_i\,(D_i - 1)} \tag{3}$$

where I is the focal project or node, D_i is the number of other neighbour projects that have an organisation in common with I, and L_i is the number of links that connect the neighbour projects D_i, if they are connected.

Van Rijnsoever et al., (2015) indicate the need to distinguish projects that are not connected to other projects (isolates) from projects that are connected, but whose

neighbours are unconnected, since both receive a value of 0. Hence, an extra dummy variable for isolates was created. The number of organisations is also correlated by definition on the clustering coefficient. This is because clustering is conditional on having at least two ties. To separate the effects of isolates and number of ties, both of them were regressed on the clustering coefficient. The residuals of this regression form an unconfounded measure for clustering, and this was used as an independent variable in the models.

3.6.7 Geographical distance

The geographical distance variable was obtained by calculating the average distance in kilometres between the organisations' coordinates (latitude/longitude) from a project and a calculated geographical centre or centroide (**Figure 3.13**). The geographical centre was retrieved by using the geosphere package [359], and the geographical distances were calculated using the *fossil* package, both from the R program [360]. This variable had a skewed distribution; therefore, its natural logarithm was used. The transformation also makes the realistic assumption that each extra level of the variable results in a decrease in marginal returns for diversity creation.

Figure 3.13. Example of the calculated geographical centre of a project.

3.7 Analysis

As there were only four levels of diversity creation, it would be inappropriate to fit a linear regression model, as this assumes that a dependent variable has continuous value. Four values are insufficient to meet this assumption. Hence, the hypotheses were tested using a cumulative (Ordinal) Logit Regression. This model is more robust against non-normal distributions or outliers than ordinary least squares regression.

The change in entropy caused by a project was the dependent variable. Independent variables were added as predictors. Moreover, the type of call was added as categorical control variable with four levels. Two projects were outliers with regards to the dependent variable and the degree of multi-disciplinarity. As this violates the assumption that there are no outliers, these two projects were removed from the final model presented below. However, it was noted that the models with and without the projects gave very similar results.

3.8 Results

Table 3.1 displays the descriptive statistics and the correlation matrix. As can be seen, the variable number of organisations is strongly correlated with the geographical distance, with a correlation of 0.72. This correlation makes sense since more organisations increase the probability of establishing large geographical distances between them.

Table 3.2 shows the results of the cumulative Logit Model. The McFadden R^2 of the model is 0.11, which is an acceptable fit. The variance inflation factors are all below 10, except for the number of partners, which was at 13. It was decided to leave this variable in, as it controls for other variables that are dependent on project size. Yet, the interpretation of the estimator of this variable needed to be done with caution.

Table 3.2 also shows that the degree of multi-disciplinarity has a strong and significant positive association with the creation of diversity. This supports the idea that a multidisciplinary environment generates greater diversity and supports **Hypothesis 1**. Regarding the knowledge base variable, it can be observed that the number of nanotechnology-related patents also has significant positive association with the creation of technological diversity, which supports **Hypothesis 2**. In this context, the effects of knowledge creation and diffusion measured by patents contribute to explaining technological diversity creation. Moreover, it demonstrates that knowledge in nanotechnology is important for the creation of new alternatives in the system and this ratifies the transversal nature of nanotechnologies.

In contrast, it was found that there is a negative association between the number of organisations on the creation of technological diversity, but this is only significant at the 10% level. Moreover, the variance inflation factor of this variable is rather high. Yet, it ratifies previous literature that argues that when there are more people involved it is more difficult to manage and more conflicts between them can emerge [273], [323]. Overall, this finding was interpreted as partial support for **Hypothesis 3**.

Table 3.1. Descriptive statistics and correlation matrix.

	Mean	Standard deviation	Technological diversity	Degree of multi-disciplinarity	Knowledge base	Number of organisations	Diversity of organisations	Degree of clustering
Technological diversity	-0.01	0.01						
Degree of multi-disciplinarity	0.09	0.03	0.29					
Knowledge base	0.78	2.71	0.11	0.12				
Number of organisations	3.43	4.49	0.08	0	0.45			
Diversity of organisations	-0.01	0.28	-0.1	0	0.41	-0.03		
Degree of clustering	0	0.16	-0.07	0.17	0.57	0.01	0.32	
Geographical distance	399.59	831.32	0.08	-0.04	0.35	0.72	0.04	-0.1

Table 3.2. Results of the cumulative Logit Model.

	Estimate Std.	Pr(>z)
Degree of multi-disciplinarity	2 .33	0.01**
Knowledge base	1.83	0.01*
Number of organisations	-2.41	0.04*
Diversity of organisations	-1.95	0.07[a]
Degree of clustering	-4.78	0.02*
Geographical distance	0.39	0.08[a]
Call 2: BN[1]	-0.55	0.4
Call 3: NG[2]	-0.62	0.63
Call 4: BIO[3]	0.62	0.61
LogLikelihood	-59.24	
No. obs.	67	
McFadden R2	0.11	

[1]BN: Exploiting the cross-sector potential of nanotechnologies and advanced materials to drive competitiveness and sustainability; [2]NG: Bridging the gap between nanotechnology research and markets; [3]BIO: Biotechnology-based industrial processes driving competitiveness and sustainability.
*[a] p < 0.1; * p < 0.05; ** p < 0.01; *** p < 0.001.*

The diversity of organisations is not significantly related to the dependent variable, which does not support **Hypothesis 4**, and cast doubts on the claims made by Van Rijnsoever et al., (2015). A possible explanation is that in the context of nanotechnology, the content of technological knowledge is independent of the type of organisations.

The variable degree of clustering is significantly and negatively associated with the creation of technological diversity, which is in line with the structural holes arguments and supports **Hypothesis 5**. Projects that bridge holes in the networks are more likely to make novel combinations, and hence increase diversity.

On the other hand, the model shows that there is a small positive effect of geographical distance within projects that is significant at the 10% level. This supports **Hypothesis 6** and corroborates the results obtained from Van Rijnsoever et al., (2015), and is line with the argument that the knowledge base is geographically bound.

Finally, it was found that some of the projects where connected between them by organisations that participated in several projects from different categories of calls. In **Figure 3.14** it can be seen that the category NM has four organisations sharing projects with the NG category and, this last one is sharing three organisations with the category BIO.

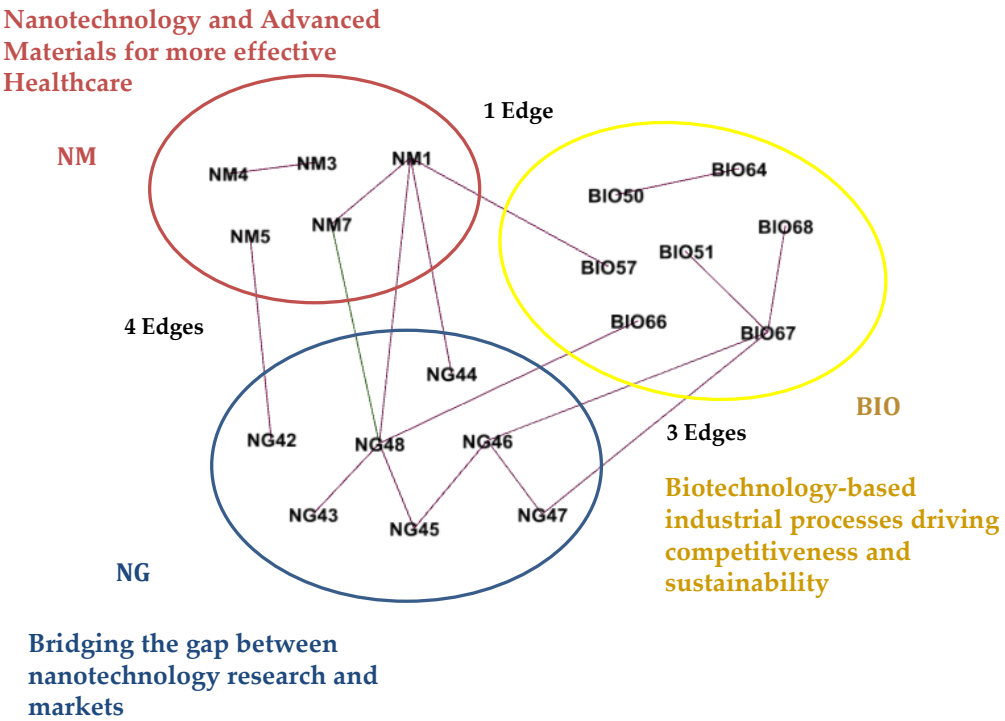

Figure 3.14. Network between project categories. Nodes are projects, edges are organisations.

The categories NM and BIO are connected only by one organisation. The category BN does not have any connection between the categories. This graph gives an idea of how is the network connected according the different category calls.

3.9 Discussion

This research suffers from a number of limitations. In the first place, the sample of projects was relatively small. European nanotechnology healthcare projects were only taken into account as this makes projects more comparable. However, it also limits the generalizability of the obtained results. It also resulted in limited levels of variation in the dependent variable, which required resorting to a more conservative cumulative Logit Model. For this reason, future research could focus on other industrial fields where nanotechnology is applied, such as environmental, energetic, textile, cosmetics, construction, communication, or other technologies that are not related to nanotechnology. Although the number of topics covered was quite broad, the European focus of the projects also implies that there were possibly missed regional initiatives or priorities that can result in different national foci for application areas. This could explain regional differences in knowledge bases.

A second limitation is related to the patent data. It is important to consider that not all innovations are patented, especially in basic science research [318] and neither patents nor publications databases always provide complete information about the names or affiliation of researchers [361]. A possible solution for future research is to take into account previous participation in funded programmes to further validate the robustness of the prior knowledge base of organisations.

3.10 Conclusions of Section I

In this Section, the creation of technological diversity was explained by using the characteristics of innovation projects. The hypotheses were tested on data from EU-funded nanotechnology projects belonging to H2020 calls that prioritize the cross-fertilization of emerging technologies, and there was applied LDA as a novel method to study the contents of the innovation projects.

The main addition to the literature is that the degree of multi-disciplinarity of a project and the size of the joint knowledge base of project partners are strongly predictive for diversity creation. In this context, the hypothesis that different disciplines and broader knowledge base increases the chances of recombinant innovations was supported.

Second, the results mostly support earlier findings by Van Rijnsoever et al., (2015), and the theoretical expectations with regards to the number of organisations in the project the clustering coefficient, and the effect of geographical distance. However, the claim that an organisational diversity adds to technological diversity creation was not completely supported. This negative finding could be the result of contextual differences between nanotechnology projects and bio-gasification projects. Innovation system research argues that building networks is important for the success of an emerging technology. These results verify the claim that it is also important to consider what the network should look like.

Finally, this study presents a methodological contribution. The LDA method allowed understanding the topics of the projects in an efficient and reliable manner. It allowed to calculate diversity and the degree of multi-disciplinarity, and can also aid future researchers with understanding the topics of innovation projects, in addition to publications or patents. In this regard, these contributions allow to further developing a theory on the creation of technological diversity, and hence to increase the possibilities of preventing technological lock-in and increase the chances of recombinant innovation as well as increasing the resilience of the technology.

The obtained results can serve as guidelines to policy makers, especially at the EU-level, for fostering the success of emerging technologies on the basis of their cross-fertilization and technology diversity creation. In order to encourage creation of technological diversity, emphasis should be placed on subsidizing: 1) projects involving or developing multiple disciplines, 2) projects with organisations that show a strong background in nanotechnology knowledge, 3) projects with partners from different geographical regions, and 4) projects with a limited number of partners that are not too closely connected with each other. The first three are already explicit or implicit criteria in H2020. Yet these projects often involve large consortia. These results suggest that it is better for diversity if these consortia are smaller. Moreover, in some instances, partners are involved in multiple projects. Finally, these results show that these cases should be handled with care, as this can decrease technological diversity.

Section II: Focusing on management

3.11 Introduction

Innovation management strategies are essential activities in a convergent scenario such as the process of cross-fertilization of KETs. A previous study focused on the convergence of Nano and Biotechnologies from Maine et al., (2014), has shown that there are three central innovation management strategies in this convergence: i) *to import ideas from broad networks*, ii) *to create environments for deep collaboration* and iii) *technology-market-matching*. The first strategy refers to the search and synthesis of concepts or ideas that could be taken up from networks with different technology streams. The second strategy involves the dynamic collaborative flow of knowledge between R&D groups. Finally, these two strategies need to be complemented by considering market needs, which is the third strategy.

This study is grounded in the three aforementioned strategies, taking into account other aspects related to network theories, absorptive capacity and dynamic capabilities' literature. The aim is to obtain an expanded vision of these three strategies and the possible influence they could have on the cross-fertilization of KETs. To that end, project leaders were interviewed in order to get insights about the level of applicability of nanotechnologies in their organisations, the level of cross-fertilization of KETs in their projects, and their innovation management strategies.

Answers were statistically treated by using Multiple Correspondence Analysis (MCA). Results showed that market-oriented projects, with organisations strongly motivated to search for ideas through broad informal networks and where their partners do not have specific technological knowledge, are factors that boosts higher levels of cross-fertilization of KETs. Another interesting finding in this study showed that organisations that have a substantial inclusion of nanotechnologies are the ones with higher levels of cross-fertilization.

3.12 Theoretical background and research hypotheses

Managing innovation is essential to increase the creation of knowledge in order to obtain or improve products, processes or services. This process is successful only when those generated outputs could overcome obstacles to being transferred to the market and fulfilling market needs. Therefore managers tend to develop strategies or actions in order to influence the productivity and impact of their scientists and product development teams. These strategies are even more indispensable in a

convergent scenario when the process gains complexity from managing different technologies. Three strategies have been identified by Maine et al., (2014) in this scenario: i) importing ideas from broad networks, ii) creating a collaborative environment and iii) technology-market matching. These strategies are analysed in this study taking into account wider perspectives and are described hereafter.

3.12.1 Importing ideas from broad networks

Taking advantage of technological and market ideas from broad networks is based on network theory, a relevant stream within the literature of strategic management [66], [104], [362]–[364]. It refers to getting concepts or ideas from networks with different technology streams [66]. In this study, this innovation management strategy is analysed from different perspectives. The first is that the process of importing ideas could be based on the knowledge flow between organisations in a network. This network could be broad in terms of two dimensions, their geographical or technological distances [128], [365]. The first one has been argued to have no significant influence on innovation projects [273], therefore, this study considers technological distances as an approximation to the broadness of the network. This dimension also considers that the process of cross-fertilization of KETs involves two or more technologies.

A second perspective is the effort organisations need to make to search for external knowledge or ideas from the network and this could be considered as an influencing strategy in the process of cross-fertilization of KETs. The third perspective is that organisations could give more or less weight to the prioritization of having access to external information from the network and this could be an important reason for belonging to a network. Based on these considerations, the following hypotheses are formulated:

3.12.1.1 Technological distance

Technological distance is a concept related to the extent that technological fields are different from each other [366], [367]. It could also be viewed as a dimension of the embeddedness of an organisation in a network that might affect the flow of knowledge and how much an organisation could learn or integrate new information from its network [128], [368], [369]. In this context, technological distance could be related to the absorptive capacity[13] of organisations since the level of novelty of the shared knowledge can vary according to this distance [370].

[13] Absorptive capacity is defined as the ability to recognize the value of new knowledge, assimilate, and apply it to commercial ends [319], [460], [461].

It has been shown that short technological distances facilitate mutual understanding and trust. Moreover, the benefits of recombining information across different techno-scientific domains increase when the distance between those domains decreases [371]. However, when the distance is too short, knowledge could be overlapped and little could be shared, reducing the level of novelty produced [128]. If the opposite occurs with too great a technological distance, communication problems could emerge [372], especially when the technological knowledge is tacit or "sticky" [373]. In this case, transferring knowledge and information could be more difficult and costly, hampering the assimilation of ideas from the network and therefore negatively affecting the absorptive capacity of organisations [374].

Combining new knowledge from different technology sources generally reflects large technological distances and this has a positive effect in novelty creation [375], [376]. Moreover, it has been shown that high-tech firms exhibited reluctance to cooperate jointly with other organisations where technologies were similar [377], [378].

Technological distance could also be associated with radical and incremental innovations. Diverse technologies have been found in radical innovations while the opposite occurs in incremental innovations [379]. In this regard, there are two positions in the literature. One says that technological distance and innovation is an inverted u-shaped relationship [128], [370], [376], [380]. The other position states that radical innovations and technological distances are more of a linear relationship [381], [382]. In the context of this study, where it is expected that cross-fertilization of KETs could give rise to radical innovations, authors are inclined to think that this process is being boosted when there are larger technological distances within the broad network. Therefore the knowledge that is imported from the network is more heterogeneous rather than homogeneous. Hence, the following hypothesis are advanced:

Hypothesis 1*. Cross-fertilization of KETs is being boosted when there are larger technological distances in the network.*

3.12.1.2 Technological effort

In a collaborative network where there is richness of technological resources, organisations are more exposed to new ideas, projects, and technologies. In this study, importing ideas from broad networks takes into account the effort of searching for those external ideas, projects, and technologies. Technological effort could be related to the amount of resources invested in R&D activities and the acquisition of technological capabilities [383], [384]. Other perspectives suggest

that technological effort is the use of technological knowledge along with further resources to create, assimilate or adapt technology [385].

Srivastava et al., (2015) state that organisations who make strong technological efforts have an increased motivation to search, evaluate and apply that external knowledge or those ideas. To this end, they need to pool the skills of specialized participants to help the overall flow of information and resources in the network [386]. However, there is a reduced technological effort when organisations are more concerned about protecting their knowledge resources, through fear of losing their control over valuable technological competencies [387]. These opposed dimensions operate and influence the level at which an organisation could benefit from the network [387], [388].

Based on the above, it is argued that when there are different technologies involved in the process of developing a product, it is difficult for an organisation to be specialised in all of them. The consequence is that organisations tend to search for that specialization in external sources, resulting in stronger technological efforts. Therefore the following is hypothesised:

Hypothesis 2*. Cross-fertilization of KETs is being boosted when organisations make stronger technological efforts to import the ideas from the network.*

3.12.1.3 Access to external information

In accordance with the Open Innovation theory, having access to external technological or knowledge resources and information from competitors could be an advantage that boosts innovation [104]. The ability to interact with their ecosystem has an impact on an organisation's performance [389]. Moreover it has been shown that an open prioritization as a strategy for importing knowledge could accelerate the commercialization end [108].

Many firms with an open innovation strategy consider external sources and networking as the means of getting access to technological sources and innovative firms [390]. The final consideration is that having access to external information could be a determinant for belonging to a broad network. Based on this, the following hypothesis is formulated:

Hypothesis 3. *Cross-fertilization of KETs is being boosted when organisations consider it important to have access to external information.*

3.12.2 Creating a collaborative environment

There is a sharp growth of R&D collaborations that began in the late 1970s [208]. Empirical findings in Europe assert that interactive learning among organisations is crucial for innovation process. Indeed, between 62% and 97% of all product innovations are achieved in collaborations between innovating firms and other organisations [386], [391], [392].

It has been demonstrated that collaboration is effective for innovation development and has an impact on the survival of the organisations [393], [394]. A collaborative environment has advantages regarding information diffusion, ideas, skills and resource sharing, access to specialized assets, and inter-organisational learning [395], [396]. But, when the relationship is poorly coordinated, collaborating with other organisations could be a drawback [386].

In this context, creating a collaborative environment is viewed from different perspectives in this study. The first perspective considers previous collaboration, arguing that this could influence the capabilities when cross-fertilizing technologies is taken into account. Second, the influence of the type of these relationships from the point of view of their level of formality is also considered.

3.12.2.1 Having previous collaborative experience

When organisations in a collaborative network are meaningful involved from the early stages of the process, common communicational skills and standard procedures are being developed in an inexpensive and rapid manner, reducing uncertainty and risk [388]. Based on these advantages, there is an increasing emergence of collaboration along the entire value chain, especially in radical innovations [368], [397].

Due to the technological complexity, its innovative character and the high capital investments when cross-fertilizing KETs, cooperation from the beginning of the process is crucial [398]. Evidence from the first case studies in the multi-KET[14] pilot lines showed the importance of long term cooperation in the generation of confidence and common goals [399].

Complex tacit knowledge could become more explicit as partners develop a wider bandwidth of communications. If the partnership gains in maturity and time, sharing information becomes more subtle [400]. In addition, when collaboration

[14] Are the sum of at least two KETs and advanced manufacturing technologies or processes (high tech manufacturing environment).

emerges from the beginning of the value chain, technology is jointly transferred from research to market in a timely manner [30], [148], [401]. The straightforward argument is that in the cross-fertilization of KETs, where knowledge is complex and technologies are different, organisations tend to collaborate from the beginning of the process, therefore:

Hypothesis 4. *Cross-fertilization of KETs is being boosted when organisations have had previous collaborations at early stages of the value chain.*

3.12.2.2 Types of collaboration network

Collaboration networks could take a number of forms according to different criteria. Powell and Grodal (2006) for example, differentiate the type of networks according to the characteristic of the authority the network has, therefore the network can be hierarchical (being monitored by a central authority), or heterarchical, where there is a strong self-organisation with diffuse authority [402].

Networks can also be classified based on the level of formality or informality. Informal relationships are characterized by a high level of trustworthiness and could significantly contribute to the innovativeness of projects [402], [403]. Individuals in this kind of network are unbounded and ungoverned organic structures [404]. On the other hand, formal social networks are prescribed by management and usually directed by strategies or missions to be accomplished [405].

The different varieties of research collaboration could also be defined by funding instruments, therefore their dimensions have significant policy and strategy implications [406]. It has been shown that public funding in the context of national or regional policy programmes assists the formation of R&D partnerships. These partnerships are formal collaborations, usually formed between industry and universities [407], [408], especially where high technology is involved [402]. Taking this into consideration, it is expected that a formal network organisational structure is more related to this funding initiative H2020, rather than informal ones. Therefore:

Hypothesis 5*: Cross-fertilization of KETs is being boosted when the type of collaborative structure tends to be formal.*

3.12.3 Technology-market matching

Matching technological solutions with market applications or recognizing the appropriate market for a technology is a type of dynamic capability[15] [409]. Dynamic capabilities are key for the success of emerging technologies as a result of the convergence of two or more technologies [410]**.** According to Hellman & Boks (2006), "*technology matches a market in terms of consumer demand, if the technology performs a task that a consumer desires*" (pp. 1). In this same line, Maine et al., (2014) asserts that there are two aspects of this strategy: the recognition of promising opportunities to exploit and prioritization through resource allocation. The first aspect could imply that the innovation process is a market-oriented process that takes into consideration unmet needs and the customer availability for a technology. The second perspective could be interpreted as a market orientation involving market research activities and customer prioritization. In this study it is argued that prioritization through resource allocation could be related to the experience of organisations in activities associated with product demonstration or pilot production and with activities that are positioned at higher levels of technological maturity, activities which are closer to the market. These three aspects are analysed as following:

3.12.3.1 Market orientation

The manner in which high technology firms match their technology to market applications has not been described in detail. This process is particularly important since most firms have to take critical market application decisions based on explicit knowledge of customer needs and market demands, which are difficult to identify [263]. It has been shown that market orientation improves organisational and product performances [265]. In nanotechnologies, the level at which an organisation is capable of identifying commercial applications could affect its success [6].

In addition, the big European paradox in R&D is that organisations and funding policies have primarily focused on science and less so on the commercial applications, failing to recognize market opportunities. The resulting scenario is difficulty in bringing products to the market [4], [264]. In this context, and in contrast to previous FPs, H2020 pays much of its attention to projects that are market-oriented and therefore closer to commercialization. Following these arguments, it is expected that the cross-fertilization of KETs is developed in market-oriented innovation projects.

[15] A dynamic capability is defined by the ability of organisations to integrate and reconfigure internal and external competences in changing environments [462].

Hypothesis 6. *Cross-fertilization of KETs is being boosted when this is a market-oriented process.*

3.12.3.2 Customer prioritization

The inability to understand user needs could be a determining factor for the success or failure of an innovated product [411]. Product development studies point out that a success factor is related to the in-depth understanding of customer requirements and demands [263], [264]. Prioritizing customers facilitates adoption and implementation of new innovations [412]. These asseverations led to consideration of the crucial role of users in the innovation process [413]. In this context, an increased number of publications have focused on user involvement or user innovation theories [414]–[418].

Nevertheless, Christensen (1997) and Hoeffer (2003) argued that focusing on customers could impede radical innovations due to the fact that customer feedback could be irrelevant [419], [420]. They stated that customers cannot express the need for a new product that doesn't exist yet. Therefore it is difficult to assimilate customers' needs during the development of radical innovations [421], especially at early phases of technology commercialisation [422]. Due to this fact, and considering the above-mentioned concerns of H2020, it is hypothesized that organisations involved in cross-fertilization of KETs could be more conscious of customers by prioritizing their needs.

Hypothesis 7. *Cross-fertilization of KETs is being boosted when customer needs are being prioritized.*

3.12.3.3 Experience in higher TRLs

Market uncertainties could be reduced by management practices [423]. Testing the value of new products and demonstration of new technologies are critical activities for commercialization [263]. In this context, the criterion for matching the technology to a market is not only concerned with the intensity of market research but also with the organisations' experience in these related activities [424]. For instance, Hellman & Boks (2006) argued that there is a relation between the experience in product-market activities and the ability to recognise market and customer demands. In addition, according to the resource-based theory, experience represents a source of competitive advantage [263].

In addition, a previous survey of European industries showed that more than 50% were explicitly involved in activities related to pilot production, and that the

majority of them have experienced participation in joint projects, especially when nanotechnology and micro & nano-electronics were involved [401].

In view of the above and considering that cross-fertilization of KETs is being fostered at higher TRLs to incentivize the scalability of products, it is expected that organisations involved in this process have already participated in previous activities in the context of pilot production and product demonstration. With this aim in mind, the following hypothesis is established:

Hypothesis 8. *Cross-fertilization of KETs is being boosted when organisations have experience in higher levels of technological maturity.*

The proposed hypothesis and sub-hypothesis are summarized in **Table 3.3.**

3.13 Methodology

3.13.1 Data collection

In order to get information about the innovation management strategies from the projects, a semi-structured interview was developed. Various kinds of question were included in the questionnaire: multiple-choice, multi-responses, Likert scale and open questions. The questionnaire was first piloted with experts from different organisations including two experts from a university (UB), one from a research institute (IBEC) and one from a hospital (Vall d'Hebron Hospital). Feedback from the pilot-test was used to refine the questions (**Appendix E**). The interview was addressed to project leaders and was developed under three formats: face-to-face, telephone and online. For this last one, a website was designed which was accessible only through formal invitation.

From the total of 222 actors, 206 actors' contact data (mail, telephone, and address) were obtained from web pages, publications or press releases. The interviews took place between May 28th and July 8th of 2016. Respondents were informed that their participation was voluntary and confidential. The average duration of the final interview was 35 minutes. A total of 60 responses were received. Interviews with partial responses and data with missing values were discarded before the analysis. Finally, 54 responses were deemed useful (**Figure 3.15 and Appendix F for responses of open questions**) with a response rate of 26.2%, which is considered an acceptable response rate for management surveys [425]–[427]. The sampling error was 1.6% at 95% confidence. From the 54 respondents, only 41 participated within a consortium, therefore, hypotheses of this study were tested over this sample size.

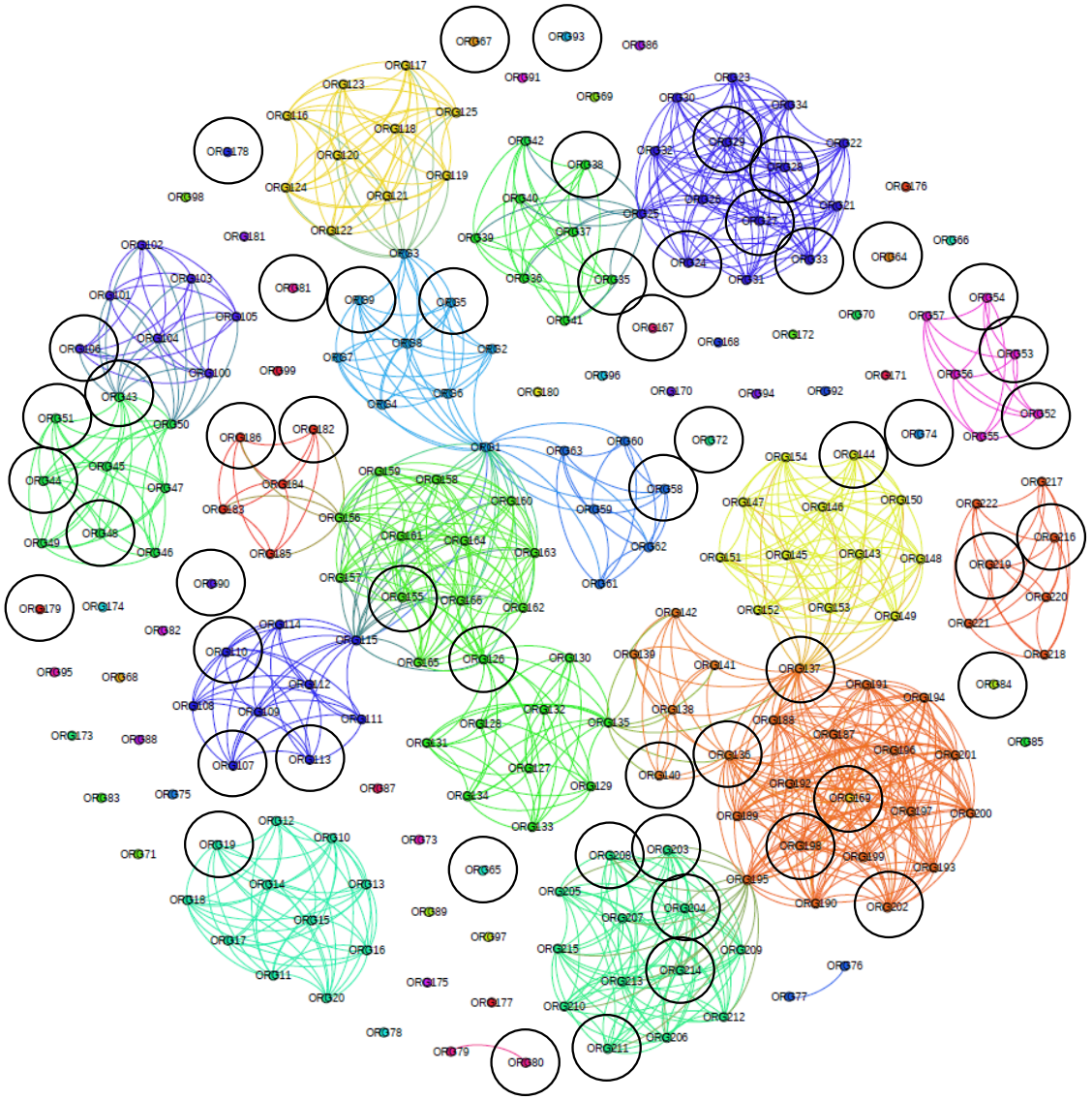

Figure 3.15. Network of the 222 organisations and their connections within projects. Black circles are the 54 interviewed organisations.

Table 3.3. Hypotheses and sub-hypotheses for each variable

Variables	Hypotheses	Sub-hypotheses
Importing ideas from broad networks		
Technological distance	Cross-fertilization of KETs is being boosted when there are larger technological distances in the network.	Actors perceive themselves as having a different technological internal knowledge compared with the technological knowledge of partners in the network.
		The process of communication, agreement or problem solving is perceived as difficult by actors.
Technological effort	Cross-fertilization of KETs is being boosted when actors make stronger technological efforts to import the ideas from the network.	Actors prioritize search for external knowledge and share internal knowledge.
		Actors assume there is an unequal benefit from the technological or knowledge resources of the participants in the network.
		Actors invest several hours in data and knowledge sharing.
Access to information	Cross-fertilization of KETs is being boosted when actors consider it important to have access to external information.	Having access to a competence is a very important reason for actors to collaborate in a project network.
		Having access to technological or knowledge resources is a very important reason for actors to collaborate in a project network.
Creating a collaborative environment		
Previous collaboration	Cross-fertilization of KETs is being boosted when actors have had previous collaborations at early stages of the value chain.	Actors have previously collaborated with the same or some of the partners in the same project
Type of collaboration	Cross-fertilization of KETs is being boosted when the type of collaborative structure tends to be formal.	The collective purpose of the project is to deliver a product rather than to develop members' capabilities, collect and pass on information or merely accomplish a goal.
		Project members are established by a group manager rather than consisting of members who select themselves, newly contracted employees or friends or business acquaintances.
		The drivers of accomplishing the project are the job requirements and common goals rather than passion, commitment and identification with the group's expertise, the project milestones, mutual needs, or economic purposes.
		The relationship with the project or team members lasts until the next reorganisation, rather than until the project has been completed, as long there is an interest in maintaining the group and as long as a reason to connect exists.
Technology-market matching		
Market orientation	Cross-fertilization of KETs is being boosted when this is a market-oriented process.	Market reasons are the principal drivers of product demonstration or pilot production for actors.
		Actors have a high intensity of market research activities.
Customer prioritization	Cross-fertilization of KETs is being boosted when customer needs are being prioritized.	Before or during the development of the project, actors have observed customer/clinical practices or developed ideas about unmet costumer needs.
		Actors consider customer viability for technology attributes when prioritizing potential markets.
Experience	Cross-fertilization of KETs is being boosted when actors have experience at higher levels of technological maturity.	Actors have participated in other activities in the context of product demonstration or pilot production.
		Actors that have participated in other activities in the context of product demonstration or pilot production have more than one year of experience.

3.13.2 Variable measurements

Questions from the interview were formulated and variables measured on the basis of several categorical indicators, which are explained in this section and summarized in **Table 3.4**.

Table 3.4. Indicators and measurement scales for each variable.

Variable	Indicator and measurement scales
Level of cross-fertilization	*Number of KETs involved in the project*
	1-6
	Level of involvement of each KET in the project
	(0) Not at all
	(1) Very little
	(2) Somewhat
	(3) To a great extent
Technological distance	*Perceived technological knowledge from their network*
	(1) Very similar
	(2) Slightly similar
	(3) Slightly dissimilar
	(4) Very dissimilar
	Process of communication, agreement or problem solving among their network
	(1) Very easy
	(2) Easy
	(3) Moderate
	(4) Somewhat difficult
	(5) Very difficult
Technological effort	*Openness in knowledge sharing*
	(0) Use and protect internal knowledge
	(1) Search for external knowledge and share internal knowledge
	Perceived benefit from the network
	(0) Equal
	(1) Unequal
	Invested time in knowledge sharing
	(0) <1 hour
	(1) 1 hour or more
Access to information	*Motive to cooperate: access to competence*
	(0) No importance
	(1) Less important
	(2) Somewhat important
	(3) Very important
	Motive to cooperate: access to technological/knowledge resources
	(0) No importance
	(1) Less important
	(2) Somewhat important
	(3) Very important
Previous collaboration	*Previous collaboration with same partners*
	(0) No, none of them
	(1) Yes, some of them
	(2) Yes, all of them

Table 3.4. (continued)

Variable	Indicator and measurement scales
Type of collaboration	*Collective purpose of the project*
	(informal) To develop members' capabilities, skills or knowledge
	(informal) To collect and pass on information
	(formal) To deliver a product
	(formal) To accomplish a goal
	Establishment of members
	(informal) Members who select themselves
	(informal) Friends or business acquaintances
	(formal) Everyone who reports to the group's manager
	(formal) Employees assigned by a senior manager
	Drivers of accomplishing the project
	(informal) Passion, commitment and identification with the group's expertise
	(informal) Mutual needs
	(formal) Job requirements and common goals
	(formal) The project`s milestones and goals
	Duration of the relationship
	(informal) As long as reason to connect exists
	(informal) As long as people have a reason to connect
	(formal) Until the next reorganisation
	(formal) Until the project has been completed
Market orientation	*Principal driver of innovation activities, product demonstration or pilot production*
	(0) Others (information of research activities, access to public subsidies, social responsibility)
	(1) Market regulation activities (e.g. industrial policy, standardization activities, market deregulation, other environmental, or social legislation)
	(2) Market reasons (e.g. competitive pressure, customer requirements, estimated market potentials, etc.)
	Intensity of market research
	(0) None
	(1) Low
	(2) Moderate
	(3) High
Customer prioritization	*Observed customer practices or unmet customer needs*
	(0) No
	(1)Yes
	Customer viability for technology attributes considered for the prioritization of potential markets for a technology invention
	(0) No
	(1) Yes
	Cooperation with customers in product demonstration or pilot production
	(0) No
	(1) Yes
Experience in higher level TRLs	*Previous experience in product demonstration and pilot production*
	(0) No
	(1) Yes
	Years of experience in product demonstration and pilot production
	(1) Up to 1 year
	(2) Around 2 to 5 years
	(3) More than 5 years

Since there are no established measures for each variable, the organisations were classified and categorized by weighting the responses at each indicator as shown in **Table 3.5.**

Table 3.5. Variables, values and weighted categories for the study.

Variable	Categories	Established values	Min. possible answer	Max. possible answer
Level of cross-fertilization	Very low	(85-105)*	1 KET/Very little	6 KETs/ To a great extent
	Low	(64-84)*		
	Moderate	(43-63)*		
	High	(22-42)*		
	Very high	(1-21)*		
Technological distance	Short technological distance	(2-4)	2	9
	Medium technological distance	(5,6)		
	Large technological distance	(7-9)		
Technological effort	Any effort	0	0	3
	Low effort	-1		
	Moderate effort	-2		
	Strong effort	-3		
Access to information	Any importance	0	0	6
	Less important	(1,2)		
	Somehow important	(3,4)		
	Very important	(5,6)		
Previous collaboration	Any of them	0	0	1
	Some of them	-1		
	All of them	-2		
Type of collaboration	Strong informal	All informal	All informal	All formal
	Informal	3 informal, 2 formal		
	Informal/Formal	2 informal, 2 formal		
	Formal	1 informal, 3 formal		
	Strong formal	All formal		
Market orientation	No market orientation	0	0	5
	Low market orientation	(1,2)		
	Moderate market orientation	-3		
	High market orientation	(4,5)		
Customer prioritization	No customer prioritization	0	0	3
	Low customer prioritization	-1		
	Moderate customer prioritization	-2		
	High customer prioritization	-3		
Experience	No experience	0	0	3
	Low experience	-1		
	Intermediate experience	-2		
	Significant experience	-3		

**Values show the deviation from the "ideal cross-fertilization" where there are 6 KETs, all of them with a "high level of involvement". An ideal cross-fertilization has a value of 108 as the result of multiplying the number of KETs by the sum of the intensity of involvement of KETs. The ranges showed the sample divided into five categories where 105 was the highest value found.*

3.13.2.1 Level of cross-fertilization

In order to see if the three management strategies are influencing the cross-fertilization of KETs, the variable *level of cross-fertilization* in innovation projects is considered in this study. The research leads to believe that higher levels of innovation could be obtained at higher levels of cross-fertilization. This consideration is based on the assumption that the sum of individual technologies increases the potential of innovation, optimizes technological development and allows for the creation of new markets [428]. Therefore the level of cross-fertilization was measured by asking the organisations about two indicators i) the number of KETs that are involved in the project and ii) its level of involvement. For the second indicator, the question offered four options: "not at all", "very little", "somewhat" and "to a great extent".

Resulting answers were first normalized as presented in **Table 3.5.** The number of KETs per project was multiplied by the sum of the intensity of involvement. Following this, the deviation of the obtained value with respect to a hypothetical "*ideal cross-fertilization*" was calculated. In this study, an ideal cross-fertilization was considered as the *highest* level of cross-fertilization, in other words, when a project involves all six KETS, all of them "to a great extent" of involvement. Therefore, the level of cross-fertilization of a project could be depicted as the difference between the highest possible value of cross-fertilization and the calculated value.

To obtain the level of cross-fertilization, the maximum values obtained in the sample were considered and the sample was divided it into five categories: i) very low, ii) low, iii) moderate, iv) high, and v) very high.

3.13.2.2 Technological distance

Several methods could be used to measure technological distance. The majority of them use patent data [368], [429]–[431]. In the context of this study, the intention was to know the managerial strategies; therefore, a "perceived" technological distance was considered in order to know the organisation's strategies when belonging to a network. Therefore, technological distance here is measured as the perceived difference between one organisations' technological knowledge compared with the technological knowledge from the partners in its network. This is the first indicator for this variable. If the perceived technological knowledge is very different, technological distances are considered to be larger, and where the opposite is the case, the distance is considered to be shorter.

For the second indicator, it was considered that technological distance could be evaluated according to the perceived difficulty in the process of communication, agreement or problem solving between the partners in the network [128], [372], [373]. Therefore, it was argued that with greater technological distances, this process could be perceived as difficult, and that with shorter distances the opposite is likely to be true.

3.13.2.3 Technological effort

The first indicator for this variable is based on the fact that stronger technological efforts could be related to sharing internal knowledge, rather than to protecting internal knowledge [387]. Technological effort could also be associated with the benefit that organisations perceive as coming from their network. It has been shown that organisations that perceived unequal benefits from their network tended to strive to obtain these benefits from the knowledge present in their network [387]. In this context, the second indicator for this variable is that according to the equal or unequal perception of benefits from the alliance network, technological effort could increase or decrease.

In addition, having stronger technological efforts could involve expending more time in sharing or assimilating technological knowledge [385]. In this regard, the argument for the third indicator is that organisations with stronger technological efforts expend more hours in data and knowledge sharing.

3.13.2.4 Access to information

This indicator is measured by considering that having access to external information could be an important reason to belong to a network. In this study, this premise is viewed from two perspectives. The first perspective is the importance that organisations could give to competitors' information and the second is the importance that organisations could give to the technical or knowledge resources from the network. The first indicator is based on the argument that having access to competitors reflects the commitment and capacity of each partner to learn and absorb the other's skills, this being an important reason to belong to a collaborative network [432], [433]. This idea is supported with the open innovation theory, by affirming that collaborating with competitors is associated with external search strategies, which are sources of innovation [434]–[436].

The second indicator is based on the fact that organisations could tend to develop networking mechanisms in order to acquire potential information or resources that could lead to new technological opportunities [437], [438]. Therefore the

importance that organisations give to external information, resources or competitors could be influencing the level of cross-fertilization.

3.13.2.5 A previous collaborative experience

Evidence from the survey on multi-KET Pilot Lines production activities in Europe (conducted in April 2013) showed that 77% of the respondents usually cooperate with other stakeholders in joint projects when planning, setting up or operating a pilot production, resulting in a strong cooperation along the value-chain [401]. Taking these previous data into account, the indicator for this variable is based on the idea that having a good collaborative experience in previous alliances, gives organisations relational capabilities that fosters the development of superior competences [439] and the effective selection of future alliance partners [440]. Therefore, having previous collaborative experience could be an influencing factor for cross-fertilization.

3.13.2.6 Types of collaboration network

To measure the type of collaboration in the network, the formality of the collaboration with respect to four parameters described by Wenger and Snyder (2000) were considered (**Table A2 in Appendix D**). These are: i) collective purpose, ii) establishment of members, iii) drivers of accomplishing the project, and iv) duration of the relationship. According to these criteria, collaboration could be formal (formal work groups or project teams) or informal (such as communities of practitioners or informal networks). Therefore, this hypothesis is measured according to the level of formality weighted on the basis of these four parameters.

3.13.2.7 Market orientation

Considering the market is fundamental for pilot production or product demonstration and a very important element in its success. In the survey on multi-KET Pilot Lines production, more than 90% of interviewed organisations answered that market reasons are one of the most important triggers of pilot production activities [401]. In this context the first indicator is related to knowing if market reasons are the principal drivers of product demonstration or pilot production for organisations.

The second indicator for this variable contemplates market research activities, considered to be important in the phase of pilot studies, when products are being pre-tested prior to release [441]. These activities enable us to understand how markets work [442] as well as the customer and their requirements [263]. In

addition, these activities are important when decisions need to be taken in terms of accessibility and acceptability of customers [443]. Therefore, in order to evaluate this variable the interviewers were asked to weight the level of intensity that market research activities have in the development of the project.

3.13.2.8 Customer prioritization

To measure the level of customer prioritization[16], two indicators were considered. Technology match requires, on the one hand, understanding specific customer demands, and on the other, that the technology's operational performance is suitable for the end customer [263]. Therefore the first indicator is to know if organisations have observed customer/clinical practices or developed ideas about unmet customer needs before or during the development of the project.

The second indicator is based on Zhao at el. (2003) and Hellman & Boks (2006). They affirm that product design requires matching product functionality to customer needs and for this, it is necessary to validate and prove technology functions, attributes and performance. The resulting scenario in this sense will be marketable products or licensable intellectual property [100], [263]. Therefore, for this indicator the aim is to know if customer viability for technology attributes is a considered factor for the prioritization of potential markets for a technology invention.

3.13.2.9 Experience in higher TRLs

Experience in higher levels of technology maturity is measured based on two indicators. The first indicator is the participation of organisations in other activities in the context of product demonstration or pilot production. The second indicator is related to the temporality of this activity, measured in years of experience. In order to match technology to customer needs, Hellman (2006) argues that experience with operation in practice is important. In accordance with this argument, knowing the previous experience in product demonstration or pilot production could be a good measure of experience in higher TRLs.

[16] Customer prioritization in this study is not related to the field of customer relationship management (CRM) where some kinds of customers are preferred by using marketing instruments [463].

3.14 Analysis

In first place a descriptive statistic was performed for the entire sample in order to get insights into the characteristics of the element of analysis. Second, the hypotheses were tested only for those organisations within collaborative projects. To that end, MCA was used. This statistical descriptive mapping method is based on scaling dimensionality reduction for nominal qualitative and multivariate data [444]. It is based on analysing the similarity of the data, which is graphically represented as points in two or three dimensional space. Observable differences can be viewed in a graph, which are percentage maps, composed of coordinate axes of a Euclidean space. This method is commonly used to analyse data from surveys [445]. For this analysis the packages *FactoMineR* [446] and *factoextra* [447] from the R software were used.

The analysis included the established variables and other qualitative supplementary variables such as the size of the organisations and the level of nanotechnology applicability in order to also explore the relationships of these characteristics to cross-fertilization.

3.15 Results

3.15.1 Descriptive statistics

3.15.1.1 Profile of the respondent

Table 3.6 shows the descriptive statistics of the profile of the respondent. Regarding the gender distribution from the 54 interviewed organisations, data obtained showed that 25.9% were women and 74.1% were men (**Figure 3.16**).

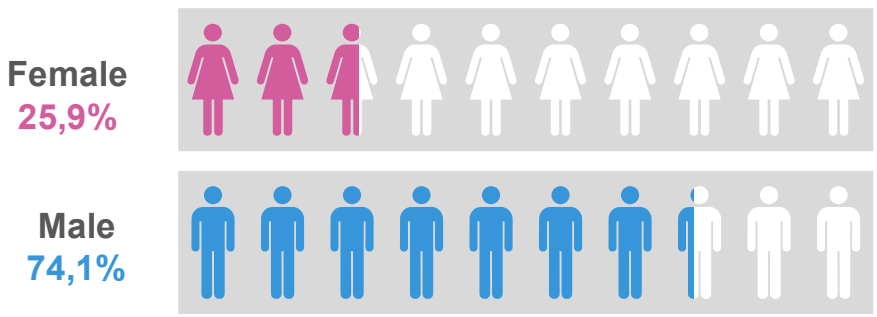

Figure 3.16. Gender distribution of respondents

Table 3.6. Profile of the respondents.

Item	Categories	N	%
Gender	Females	14	25.9
	Males	40	74.1
Age	25-34	6	11.1
	35-44	21	38.9
	45-54	17	31.5
	55-64	8	14.8
	>65	2	3.7
Highest educational degree	Engineer	3	5.6
	Graduate	2	3.7
	Master	11	20.4
	Medical Doctor	2	3.7
	Other	3	5.6
	PhD	27	50
	Post-Doc	6	11.1
Role*	Academic	5	4.3
	Student/Undergraduate	0	0
	Researcher	18	15.4
	Management	32	27.4
	Business development	18	15.4
	New product development	18	15.4
	Manufacturing and production	2	1.7
	Health and safety	3	2.6
	Documentation	7	6
	Marketing	6	5.1
	Project management	2	1.7
	Other	6	5.1
Educational background*	Engineering	13	15.5
	Chemistry	24	28.6
	Material science	6	7.1
	Physics	4	4.8
	Biology	7	8.3
	Medicine	4	4.8
	Biotechnology	17	20.2
	Environmental science	1	1.2
	Nanotechnology	3	3.6
	Social Sciences	1	1.2
	Economics and business organisation	4	4.8
Total		**54**	**100**

**More than one option was allowed*

The average age of the respondents was between 35 and 44 years (**Figure 3.17a**). 50% of the project leaders had PhD studies, 20.4% a Master, and 11.1% a Post-Doctoral degree (**Figure 3.17b**).

More than 28% of the respondents have a chemical educational background, followed by 20.2% with a biotechnology specialization. Only 3.6% of them have a nanotechnological background (**Figure 3.18**). It is interesting to note that 27.4% of the respondents have a managerial role at the organisation, while 15.4% of them are researchers and 15.4% are business developers (**Figure 3.19**).

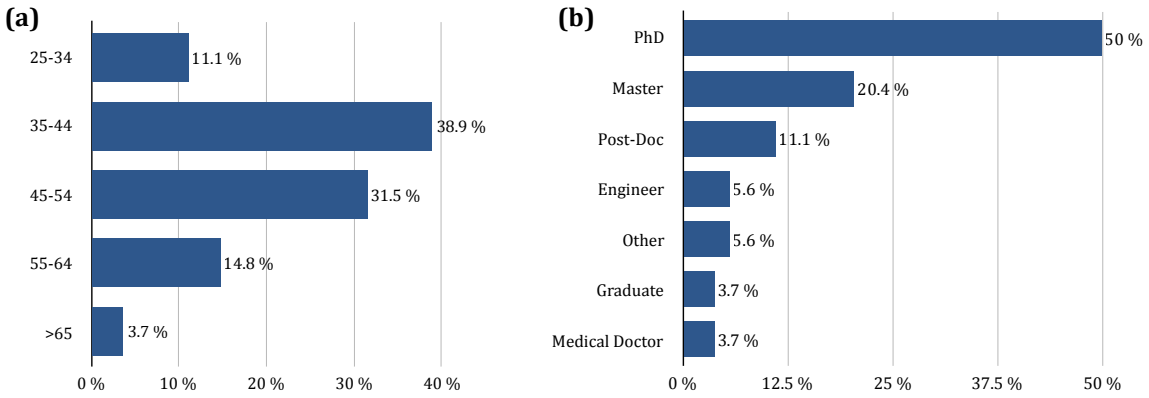

Figure 3.17. Profile of the respondent. (a) Age distribution, (b) Education degree.

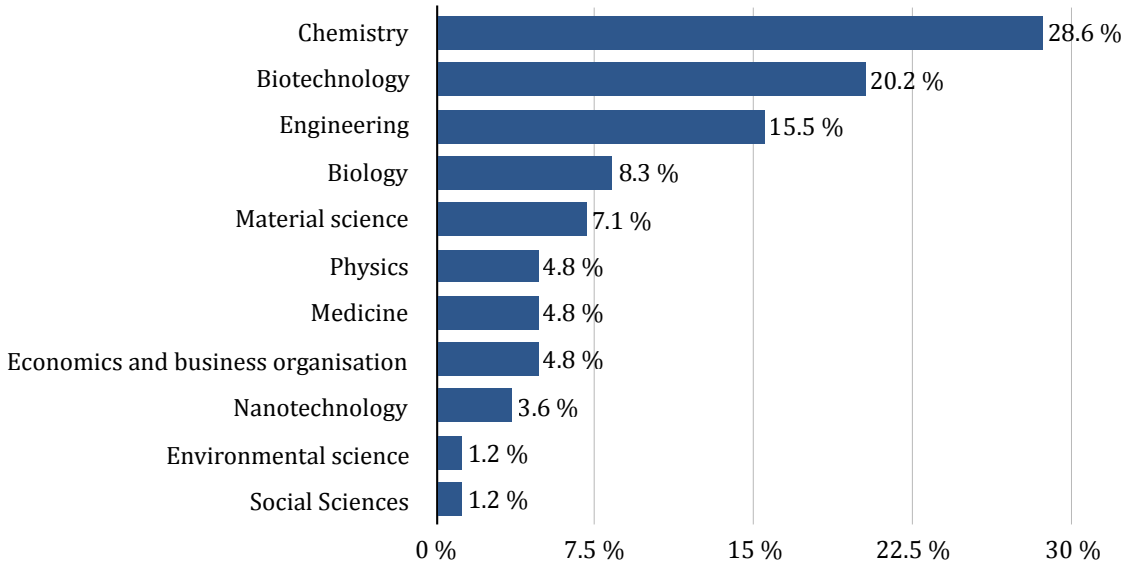

Figure 3.18. Education background.

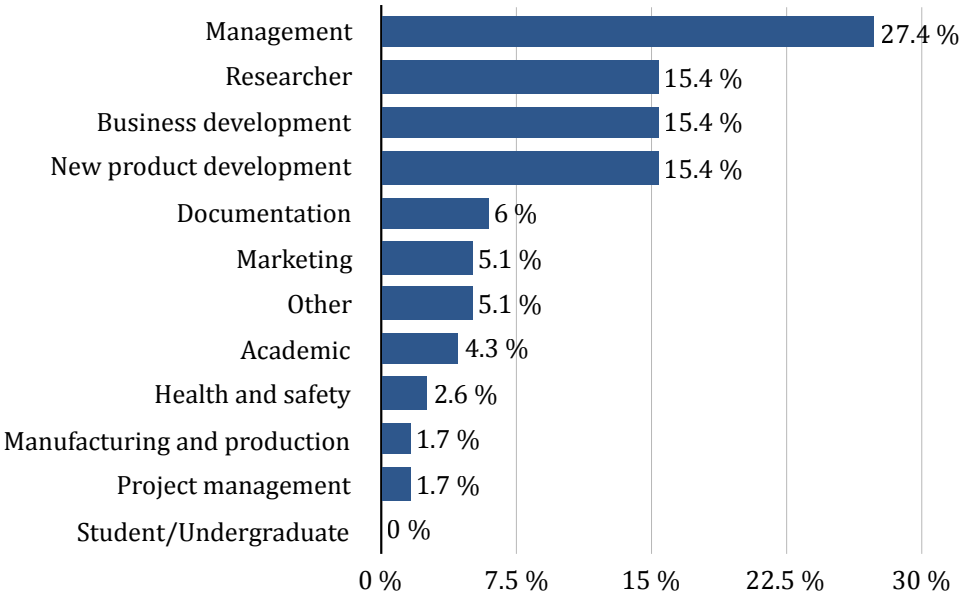

Figure 3.19. Role at the organisation.

3.15.1.2 Profile of the organisations

There were 15 countries participating in projects involving the interviewed participants. The country with most projects is Spain, followed by Italy, The Netherlands, Germany and Ireland (**Figure 3.20**).

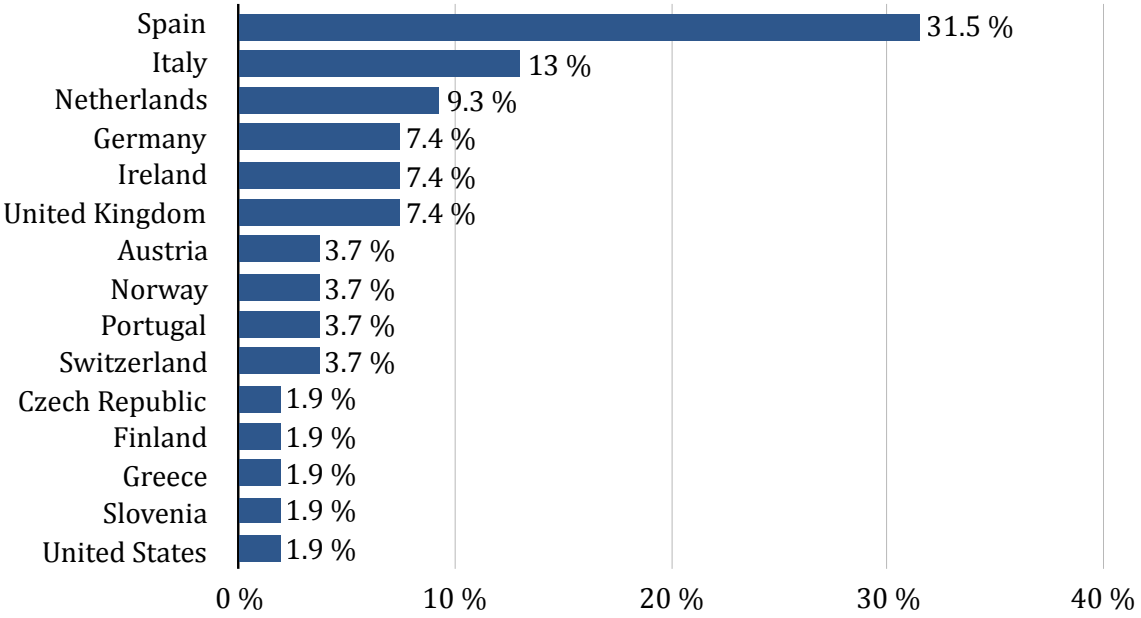

Figure 3.20. Percentage of projects per country.

Most of the interviewed organisations were PRC at 69% of the sample, followed by HES at 15% and REC at 15% (**Figure 3.21a**). 9.3% of those interviewed were project coordinators (PRCA); while 35.2% were project partners (PRC). 24.1% of those interviewed were companies participating without a consortium in H2020 (PRCB) (**Figure 3.21b**).

33% of the interviewed organisations were from small organisations (between 10 and 50 employees) followed by micro organisations (< 10 employees) at 29.6 % and large organisations (at least 250 employees) at 22%. Medium sized organisations (between 50 and 250 employees) represented a percentage of 14.8% (**Table 3.7 and Figure 3.22**).

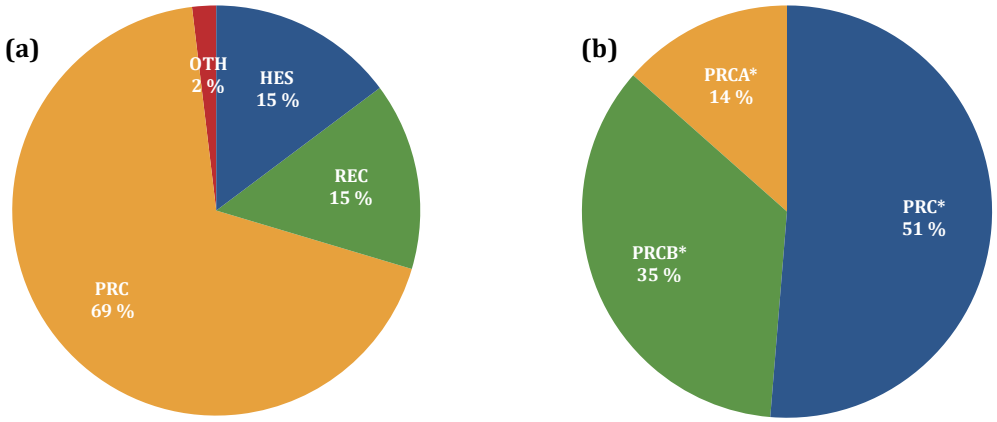

Figure 3.21. Type of project leaders interviewed. (a) All types of organisations, and (b) Private organisations. (*PRA are project coordinators, *PRC are project partners and *PRCB are for-profit entities participating without a consortium. For more abbreviations, please refer to **Section 3.2.1**).

Table 3.7. Size of organisations.

Categories	N	%
Micro	16	29.6
Small	18	33.3
Medium	8	14.8
Large	12	22.2
Total	**54**	**100**

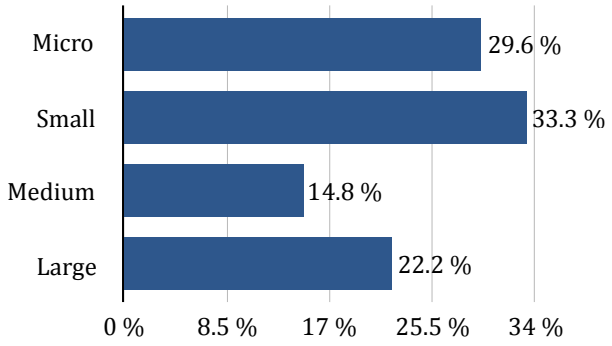

Figure 3.22. Size of organisations.

A large percentage of organisations were founded before the year 2000 (40%), while just a few of them were recently founded (**Table 3.8 and Figure 3.23**).

It is interesting to note that almost half of the interviewed organisations are located on scientific and technological parks or in an urban framework. There is also a good quantity of them which are located at universities (7.4%) or which are universities (14.8%). A lesser percentage is located either in hospitals, on private land or in business incubators (**Figure 3.24**).

Table 3.8. Year of foundation.

Categories	N	%
< 2000	22	40.7
2000-2004	9	16.7
2005-2009	11	20.4
2010-2012	8	14.8
2013	1	1.9
2014	3	5.6
Total	**54**	**100**

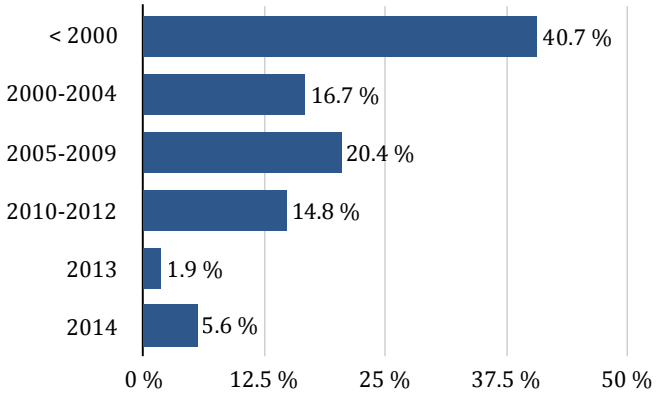

Figure 3.23. Year of foundation.

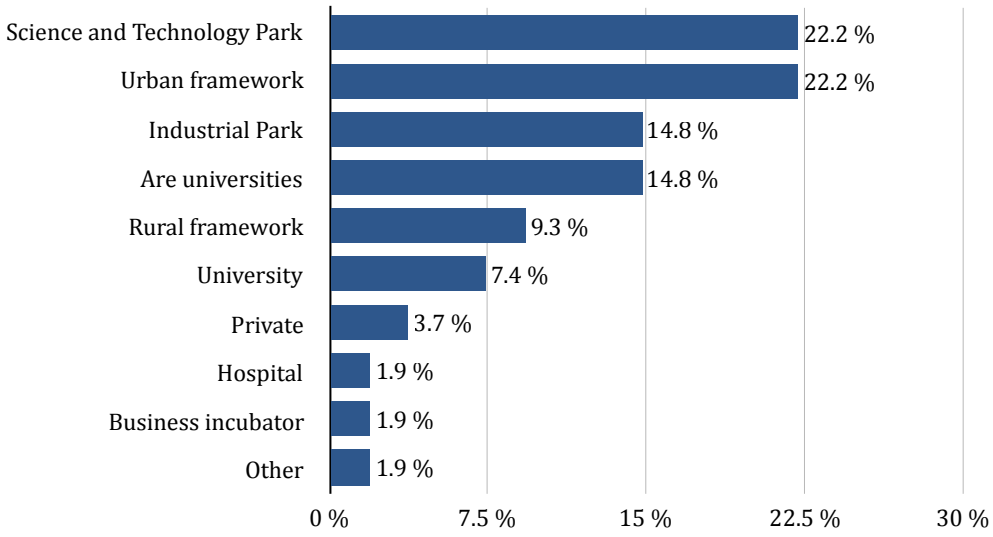

Figure 3.24. Location of interviewed organisations.

Life sciences is the most frequent area of specialization of the interviewed organisations, followed by materials, pharmaceuticals, health and chemistry (**Figure 3.25**)

The principal activity in the value chain is R&D (55%), followed by production, commercialization, service, consultancy and transfer. Only a few of the interviewed organisations (1.9%) are specialized in the entire value chain (**Table 3.9 and Figure 3.26**).

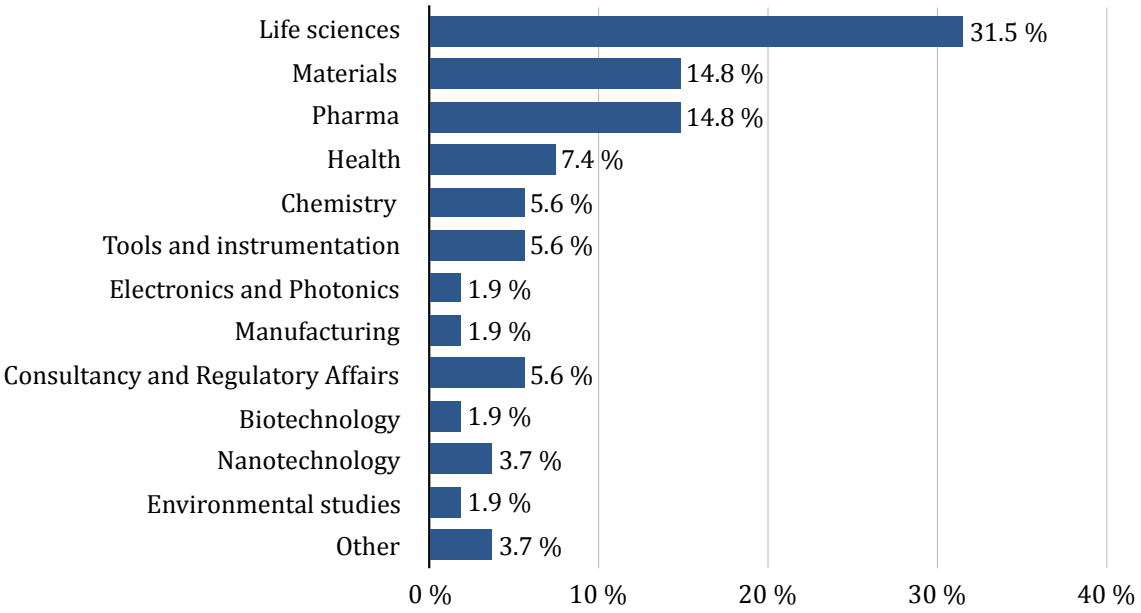

Figure 3.25. Area of specialization of interviewed organisations.

Table 3.9. Principal activity.

Categories	N	%
R+D	30	55.6
Production	11	20.4
Commercialization	3	5.6
Service	4	7.4
Consultancy	3	5.6
Transfer	1	1.9
Complete chain	1	1.9
Other	1	1.9
Total	**54**	**100**

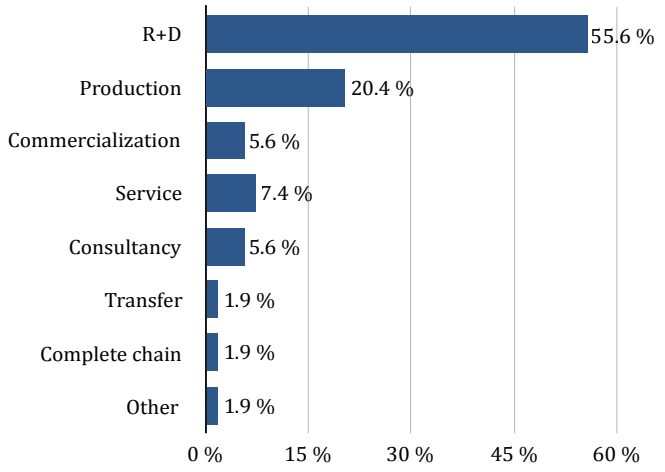

Figure 3.26. Principal activity.

Table 3.10. KETs' significant domain

	Any	Very low	Low	Moderate	High	Very high
Nanotechnology	14.8%	**22.2%**	14.8%	16.7%	9.3%	**22.2%**
Micro & Nano-electronics	**55.6%**	18.5%	7.4%	3.7%	3.7%	11.1%
Photonics	**57.4%**	9.3%	22.2%	0.0%	5.6%	5.6%
Advanced Materials	22.2%	7.4%	7.4%	16.7%	14.8%	**31.5%**
Industrial Biotechnology	18.5%	13.0%	9.3%	9.3%	11.1%	**38.9%**
Manufacturing Systems	16.7%	7.4%	9.3%	**24.1%**	20.4%	**22.2%**

When organisations were asked to rank the KETs that have a significant technology domain in their organisations, findings show that the most prevalent KETs are advanced materials (32.5%) and industrial biotechnology (38.9%) with a very high level of significance. As can be seen in **Table 3.10**, KETs rated with any significant domain are photonics (57.4%) and micro & nano-electronics (55.6%). Regarding nanotechnology, only 22% of the interviewed leaders affirm this KET as having a very high significance, while the same percentage affirmed having very low significance of this KET in their organisations.

Project leaders were also asked to rank the level of application of nanotechnology in their organisations. 33.3% of them answered that they apply nanotechnology at their organisations to a medium level and the same percentage was found for lower levels of applicability (**Table 3.11 and Figure 3.27**). Only 11.1% of them believe the application of nanotechnology is high and 16.7% that it is very high in their organisations.

Table 3.11. Level of application of Nanotechnologies.

Categories	N	%
Low (less than 30%)	18	33.3
Medium (between 30% - 60%)	18	33.3
High (between 60% - 85 %)	6	11.1
Very high (over 85% of products or process)	9	16.7
Unknown	3	5.6
Total	**54**	**100**

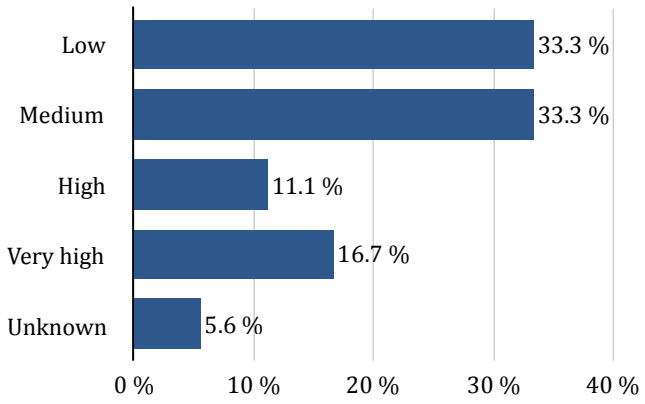

Figure 3.27. Level of application of Nanotechnologies.

Table 3.12. Previous participation in EU programmes.

Categories	N	%
Yes	42	77.8
No	12	22.2
Total	**54**	**100**

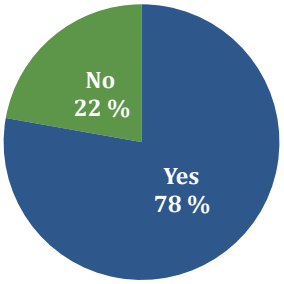

Figure 3.28. Previous participation in EU programmes.

Finally, when project leaders were asked if they have participated in other previous EU FPs, the majority of them affirmed that they had previously participated (77.8%) and 22.2% affirmed not having participated before (**Table 3.12 and Figure 3.28**).

3.15.1.3 Project information

Figure 3.29 shows the level of involvement of the different KETs for each project. It can be seen that there are few projects that involve all KETs (e.g. project 7 or project 49). In addition, the figure shows that KETs with the categories *somewhat* or *to a great extent* in relation to involvement (represented with darker colours), are advanced manufacturing systems, advanced materials, industrial biotechnology and nanotechnology.

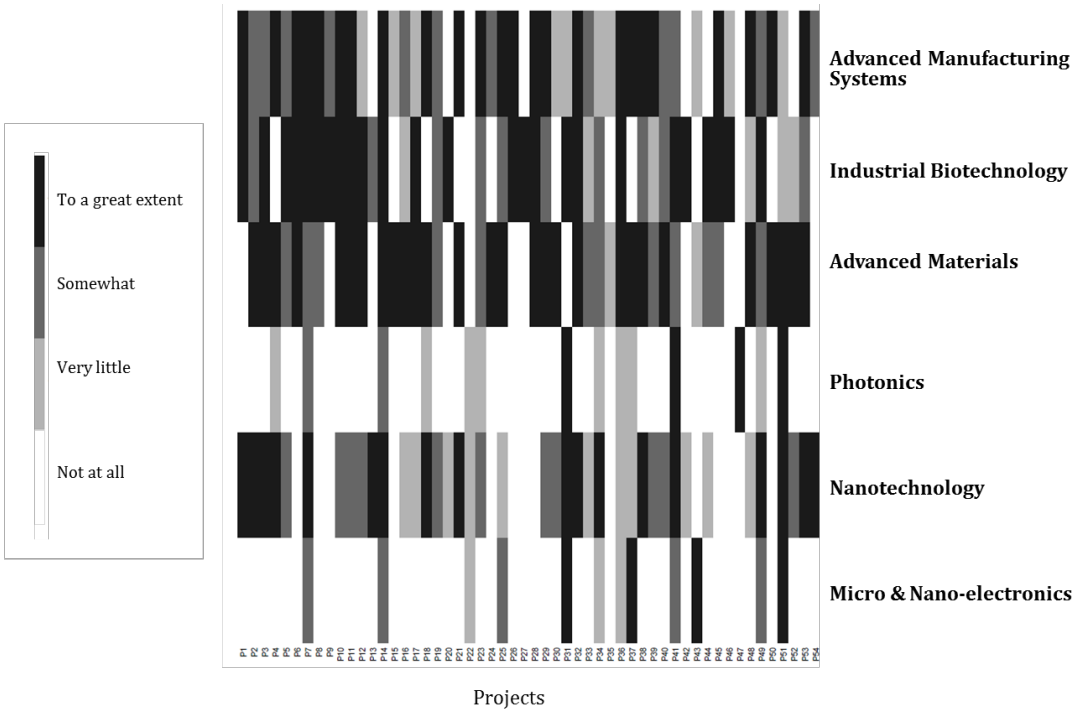

Figure 3.29. Level of involvement of each KET by project.

Photonics and micro & nano-electronics are the KETs with less involvement in projects. The authors suggest this "bar-code" of KETs as a picture of the level of involvement of the different KETs in the total system of projects.

On the other hand, the initial TRL in projects was principally TRL3 (33.3%), TRL4 (24.15) and TRL6 (18.5%). Only a few projects, 5.6%, stated that their projects began at TRL1 or TRL2 (**Table 3.13 and Figure 3.30**). TRL6 and TRL9 are the most frequent envisaged TRL in the projects with 25.9% each one (**Table 3.14 and Figure 3.31**).

Table 3.13. Initial TRL of projects.

Categories	N	%
Basic research (TRL 1)	3	5.6
Technology formulation (TRL 2)	3	5.6
Applied research (TRL 3)	18	33.3
Small scale prototype (TRL 4)	13	24.1
Large scale prototype (TRL 5)	4	7.4
Prototype system verified (TRL 6)	10	18.5
Pilot system verified (TRL 7)	3	5.6
Total	**54**	**100**

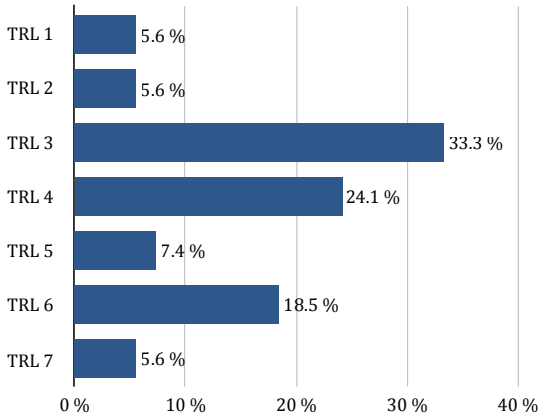

Figure 3.30. Initial TRL of projects.

Table 3.14. Envisaged final TRL of projects.

Categories	N	%
Applied research (TRL 3)	2	3.7
Small scale prototype (TRL 4)	3	5.6
Large scale prototype (TRL 5)	8	14.8
Prototype system verified (TRL 6)	14	25.9
Pilot system verified (TRL 7)	10	18.5
Commercial design (TRL 8)	3	5.6
Full commercial application (TRL 9)	14	25.9
Total	**54**	**100**

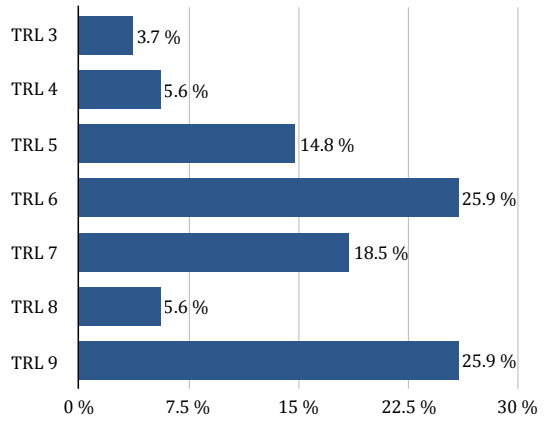

Figure 3.31. Envisaged final TRL of projects.

From the 54 organisations interviewed, 41 of them (76%) participated within a consortium in H2020, meaning that there is one organisation as project coordinator and other organisations as project partners. 13 of the organisations interviewed (24%) participated alone in H2020, and 11 of them had other types of collaboration, even if they were not explicitly included in the call. They stated that the other type of collaboration is by subcontracting or by collaborating with suppliers. The remaining 2 organisations working alone without any type of other collaboration, argued that there were three reasons for this decision: i) risk of losing knowledge that is core to their competitive advantage, ii) a higher complexity of management and iii) the risk of losing flexibility.

Project leaders participating in a consortium were asked about the motives that drive them to work in a collaborative system (**Figure 3.32 in next page**). 68.3% of them ranked having access to technological or knowledge resources as a very important reason, 61% mentioned having access to competence and 41.5% a previous positive project experience with partners. Financial risk sharing was a less important reason with 51.2% of respondents and for 14.6% this had no importance at all. Reduced market risk is also a reason with some importance for 19.5% of the organisations interviewed, and with less importance for 22% of them.

From those 41 project leaders collaborating within a consortium, 30 of them, meaning 73.1%, have previously collaborated with the same partner. The remaining 26.8% have not previously collaborated with any of their actual partners. Leaders with previous collaborations with the same partners were asked the TRL of previous collaborations. 33% of them answered that the initial collaboration was at TRL3 and 20% at TRL1 (**Table 3.15 and Figure 3.33**).

Project leaders were also asked to evaluate the process of communication or agreement with their partners or team members. The majority of them agreed that this process was very easy (22.2%), easy (38.9%) or moderate (33.3%). No project leader answered that this represents a very difficult process but a small percentage (5.6%) believe it was somewhat difficult (**Table 3.16 and Figure 3.34**).

Table 3.15. TRL at previous collaboration.

Categories	N	%
Idea generation (TRL 0)	4	13.3
Basic research (TRL 1)	6	20.0
Technology formulation (TRL 2)	5	16.7
Applied research (TRL 3)	10	33.3
Small scale prototype (TRL 4)	5	16.7
Total	**30**	**100**

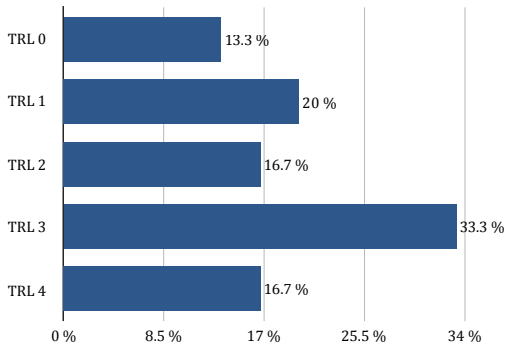

Figure 3.33. TRL at previous collaboration.

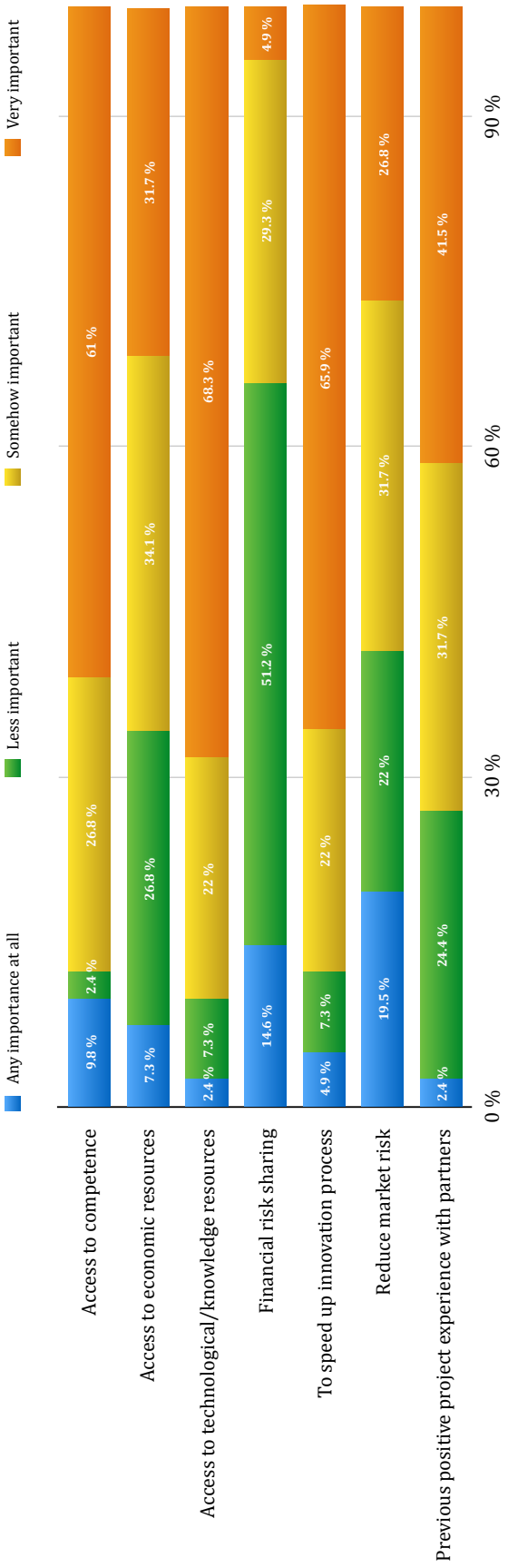

Figure 3.32. Motives to collaborate ranking.

Table 3.16. Process of communication.

Categories	N	%
Very easy	12	22.2
Easy	21	38.9
Moderate	18	33.3
Somewhat difficult	3	5.6
Very difficult	0	0
Total	**54**	**100**

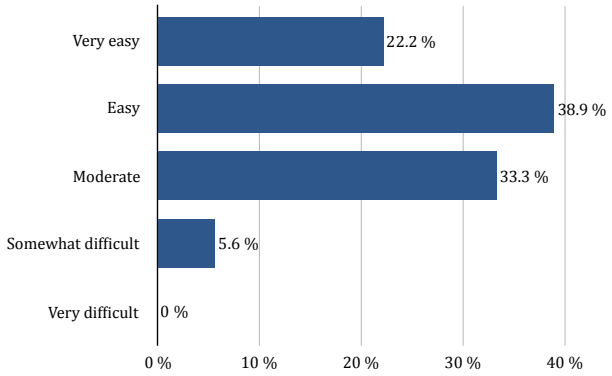

Figure 3.34. Process of communication.

From the 41 leaders participating in a consortium, 24.4% of them believed that their technological knowledge was very dissimilar compared with the technological knowledge of their partners in the consortium. 19.5% of them answered that their knowledge was very similar (**Table 3.17 and Figure 3.35**).

Table 3.17. Technological knowledge.

Categories	N	%
Very similar	8	19.5
Lightly similar	14	34.1
Lightly dissimilar	9	22.0
Very dissimilar	10	24.4
Total	**41**	**100**

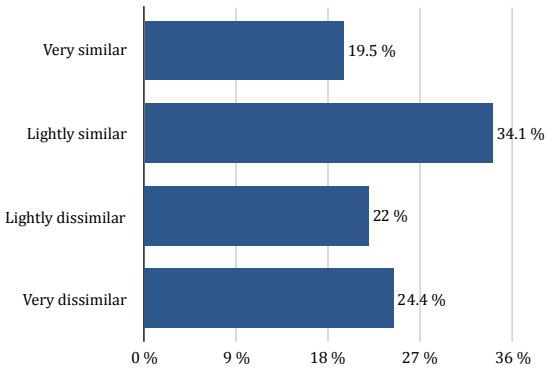

Figure 3.35. Technological knowledge.

Interviewed project leaders were also asked to choose what they considered to be the principal driver of innovation activities, product demonstration or product production at their organisations (**Figure 3.36**). A great majority answered that market reasons, such as competitive pressure, customer requirements or estimated market potentials, are the principal drivers. Other reasons such as economic ones were less often selected.

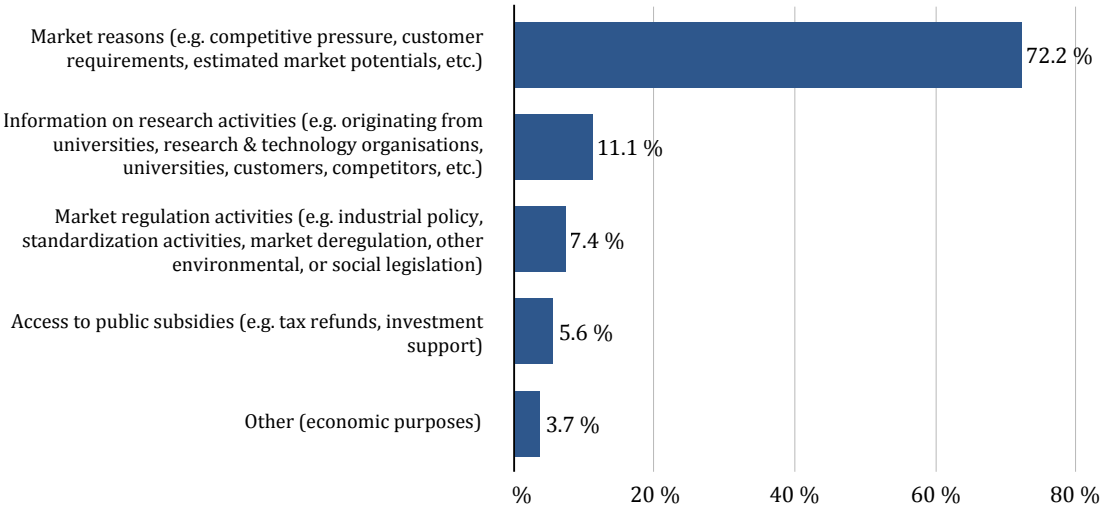

Figure 3.36. Principal drivers of innovation activities, product demonstration or pilot production activities.

61% of the interviewed leaders affirm having participated in activities related to the context of product demonstration or pilot production (**Figure 3.37**). From this percentage, 23.5% usually cooperates with other research and technology organisations and 21.2% cooperates with customers. 5.9% usually cooperates with other organisations, specifically companies or spin-offs interested in the commercialization of their products. Only a small percentage, 4.7%, usually cooperates with engineering services.

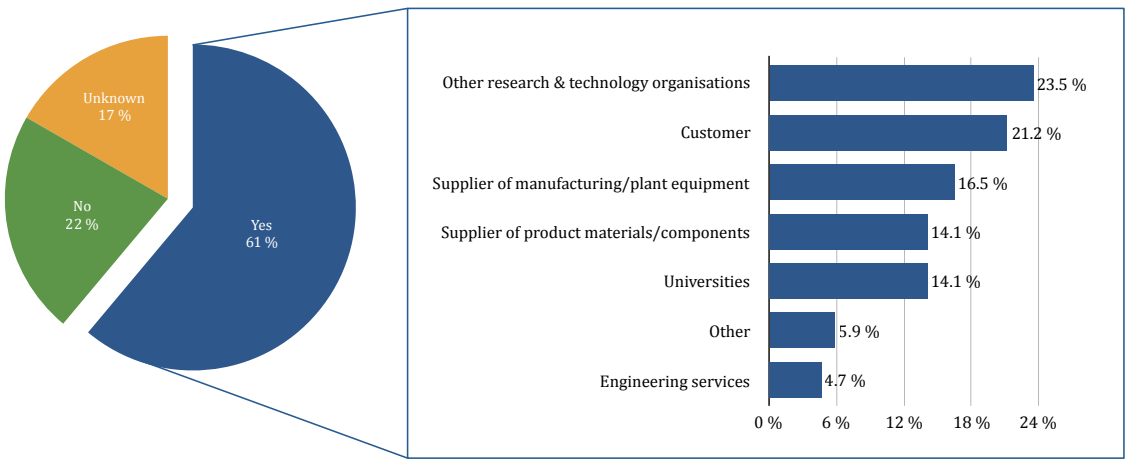

Figure 3.37. Co-operators in product demonstration or pilot production activities.

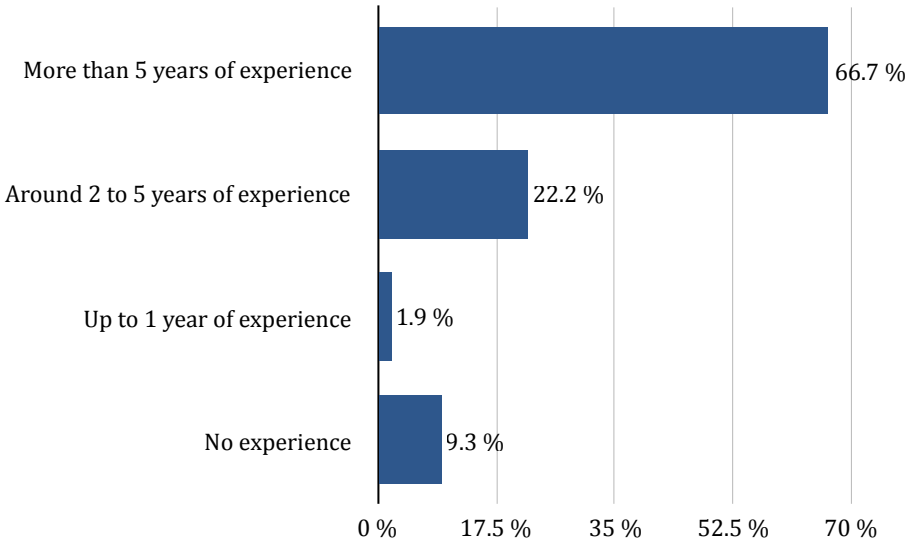

Figure 3.38. Experience in pilot production.

Project leaders were also asked about their experience with planning, setting up or operating product demonstration or pilot production activities (**Figure 3.38**).

3.15.2 Multiple Correspondence Analysis

MCA located the categories from the variables in the Euclidean space. The first two dimensions were plotted to examine the association among these categories (**Figure A2 in the Appendix D**). For instance, it can be seen that in the top-right quadrant of the plot, the associated categories are: *no importance to have access to information*, *low cross-fertilization* and *no customer prioritization*. In the same way, the plot shows an association between the categories *less importance to have access to information* and *low levels of technological effort*. These interpretations are based on considering the points that are located approximately in the same region in the space and in the direction from the origin. Distances among the points cannot be considered in MCA [448].

Table A3 in the Appendix D shows the variances, the percentage of variances retained by each dimension and the cumulative percentage of variance. The variance is the average of the distances between points and measures the dispersal of the cloud of points. It explains the relative importance of each dimension. Percentage of variances shows how much a dimension can be explained by reference to the model. The first dimension (Dim1) obtained a percentage of variance of 19.2%, and the second dimension (Dim2) obtained a percentage of

14.5%. These results mean that variables show greater dispersal in Dim1 than in Dim2. The model with two dimensions is therefore sufficient to retain 33.7% of the total cumulative variance of the data. In other words, 33.7% of the data is explained by the first two dimensions.

The contribution of each variable to the first two dimensions can be obtained by interpreting the position of each variable in the plot (**Figure A3 in the Appendix D**). Coordinates that are located at greater distance from the origin show a major contribution to the dimension (**Table A4 in the Appendix D**). In this regard, variables that give more information to Dim1 are access of information, level of cross-fertilization and technological effort, while the variables market orientation, access to information and customer prioritization are the ones that give more information to Dim2.

Figure 3.39 shows the result of the MCA in the dimensional map for each variable. As can be seen in **Figure 3.39a**, there is a well differentiated position of organisations in the plane according to the variable level of cross-fertilization. Organisations with high and very high levels of cross-fertilization are located below the x axis. Meanwhile, organisations with low and very low levels of cross-fertilization are located above it. Moderate levels of cross-fertilizations are found in both axes. When these positions are compared with the variable technological distance in **Figure 3.39b**, findings suggest that organisations with a short and medium level of technological distance between their partners are positioned in the same space as organisations with higher levels of cross-fertilization. In the same manner, organisations with large technological distances between them correspond in location to organisations with moderate, low or very low levels of cross-fertilization. This result rejects **Hypothesis 1** and suggests that high levels of cross-fertilization could be found when technological distance is short or medium.

On the other hand, it can be seen that organisations with stronger levels of technological effort (**Figure 3.39c**) correspond in location to organisations having higher levels of cross-fertilizations. This result could confirm **Hypothesis 2** and supports the fact that cross-fertilization of KETs could be boosted when organisations make stronger technological efforts.

A well-defined phenomenon occurs regarding the importance that organisations give to having access to external sources of information. In **Figure 3.39d**, organisations considering it very important to have access to external sources of information are also the ones that show higher levels of technological cross-fertilization. This well-defined position compared with the other categories of this variable supports **Hypothesis 3**.

In contrast, there is not a clear distinction in correspondence between the variable of previous collaboration (**Figure 3.39e**) and the variable of level of cross-

fertilization. Even so, it can be seen that having collaboration with some of the previous partners within a project has a closer correspondence with higher values of cross-fertilization according to the ellipses of this plane. Overall, this result is interpreted as a partial support for **Hypothesis 4**.

Regarding the variable type of collaboration (**Figure 3.39f**), it is appreciable that organisations showing informal relationships among their network correspond to the ones with higher levels of cross-fertilization. This finding does not support **Hypothesis 5** and casts doubts on the idea that public funding of projects leads to formal interactions.

For the variable market orientation, **Figure 3.39g** suggests a clear correspondence among organisations in which projects are more oriented to the market and those showing higher levels of cross-fertilizations**.** This result supports **Hypothesis 6** and confirms previous findings from the multi-KET pilot online interview where a market-oriented strategy is highly regarded [401].

Prioritization of customers (**Figure 3.39h**), however, is not well-distinguished among their categories. Nevertheless, it can be seen that organisations with moderate and high levels of customer prioritization correspond to organisations showing higher levels of cross-fertilizations, partially supporting **Hypothesis 7**. Indeed, what is quite clear is that organisations with no or low customer prioritization could have a clear correspondence to organisations with lower levels of cross-fertilization.

Finally, an interesting position in the graph shows that no previous experience in pilot production or product demonstration activities (**Figure 3.39i**) could be required for having higher levels of cross-fertilization, rejecting **Hypothesis 8**.

On the other hand, an interesting finding can be highlighted regarding the level of application of nanotechnologies by analysing the MCA for qualitative supplementary variables. As can be seen in **Figure 3.40**, interviewed leaders who said that they had a low applicability of nanotechnology on their organisations, correspond to organisations with lower levels of cross-fertilization.

Finally, if the level of cross-fertilization regarding the type of organisations is analysed, there is no evident distinction among them (**Figure 3.41**). The same occurs with the area of specialization or the initial TRL. However, there is a differentiated position regarding the final TRL of projects. As can be seen in **Figure 3.42**, organisations with higher levels of cross-fertilization correspond with projects with envisaged final TRL7 and TRL9.

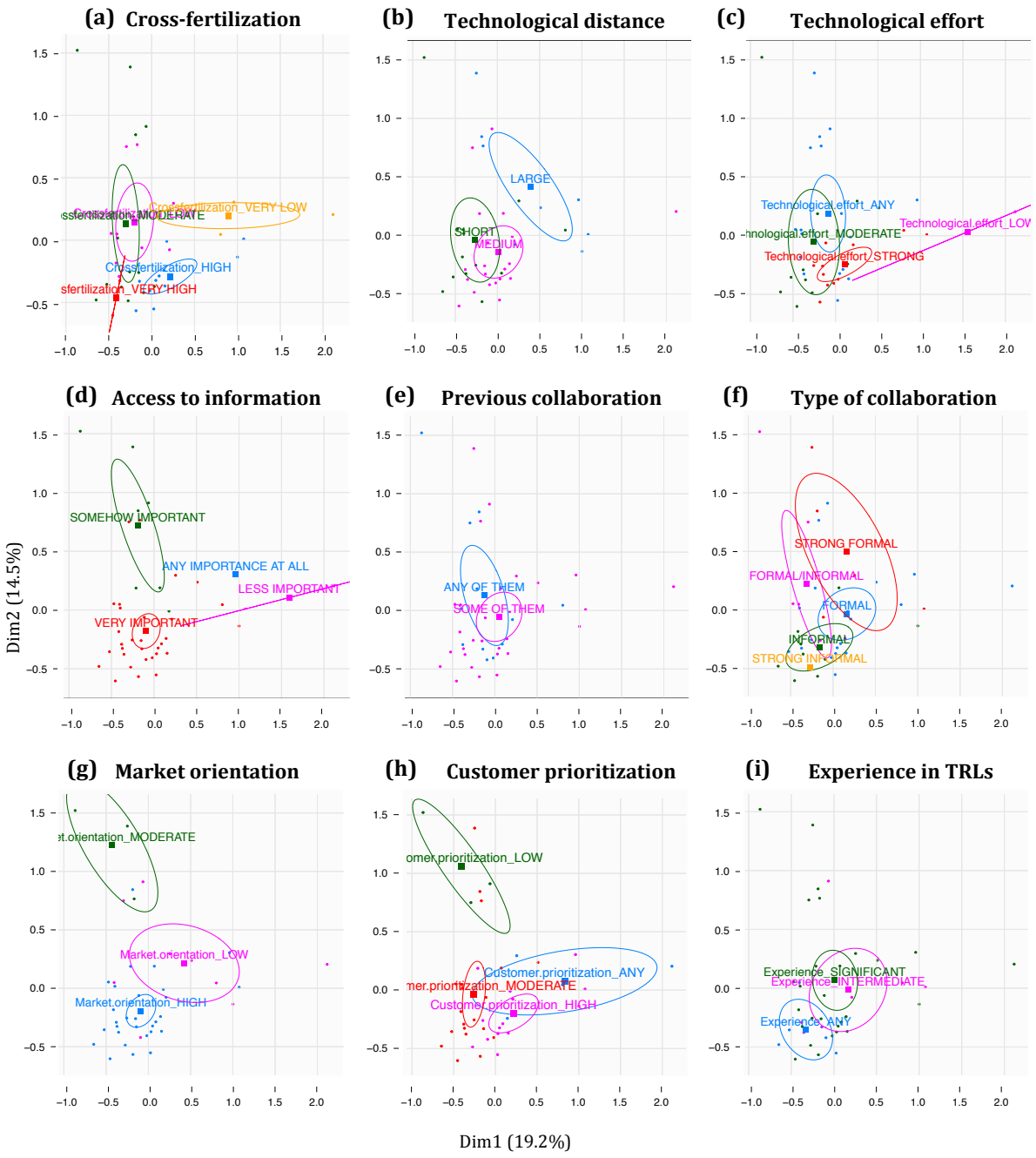

Figure 3.39. MCA for each categorical variable. Ellipses plot. Variables: (a) level of cross-fertilization, (b) technological distance, (c) technological effort, (d) access to information, (e) previous collaboration, (f) type of collaboration, (g) market orientation, (h) customer prioritization, and (i) experience in TRLs.

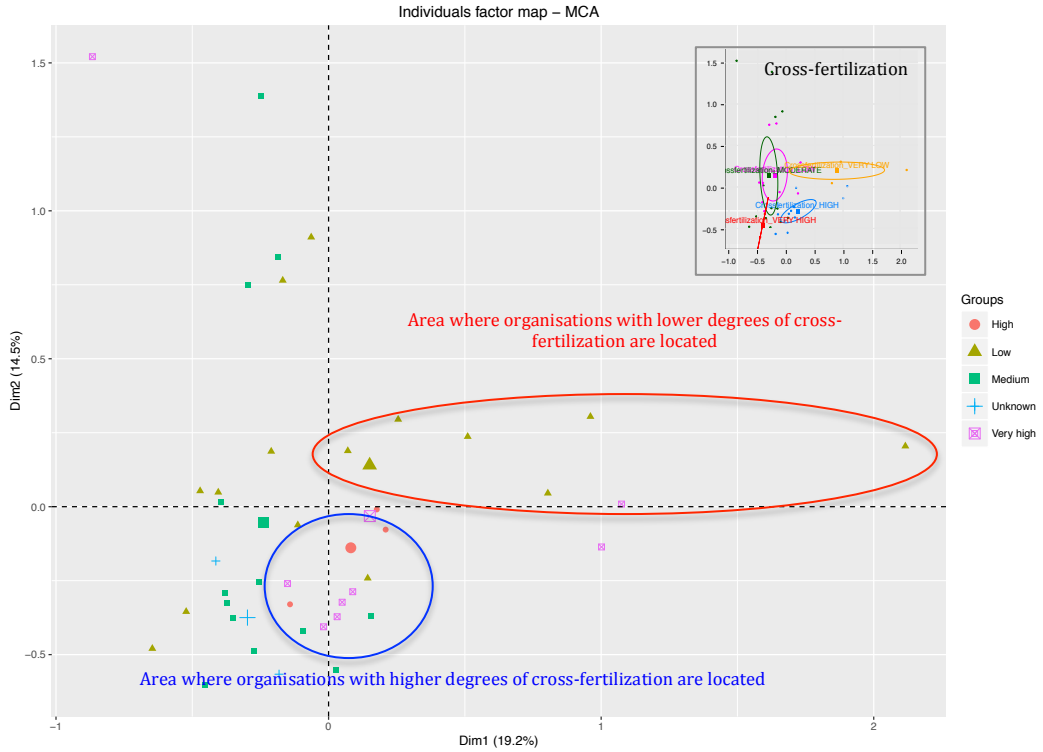

Figure 3.40. MCA for the qualitative supplementary variable "nanotechnology applicability" in the organisations.

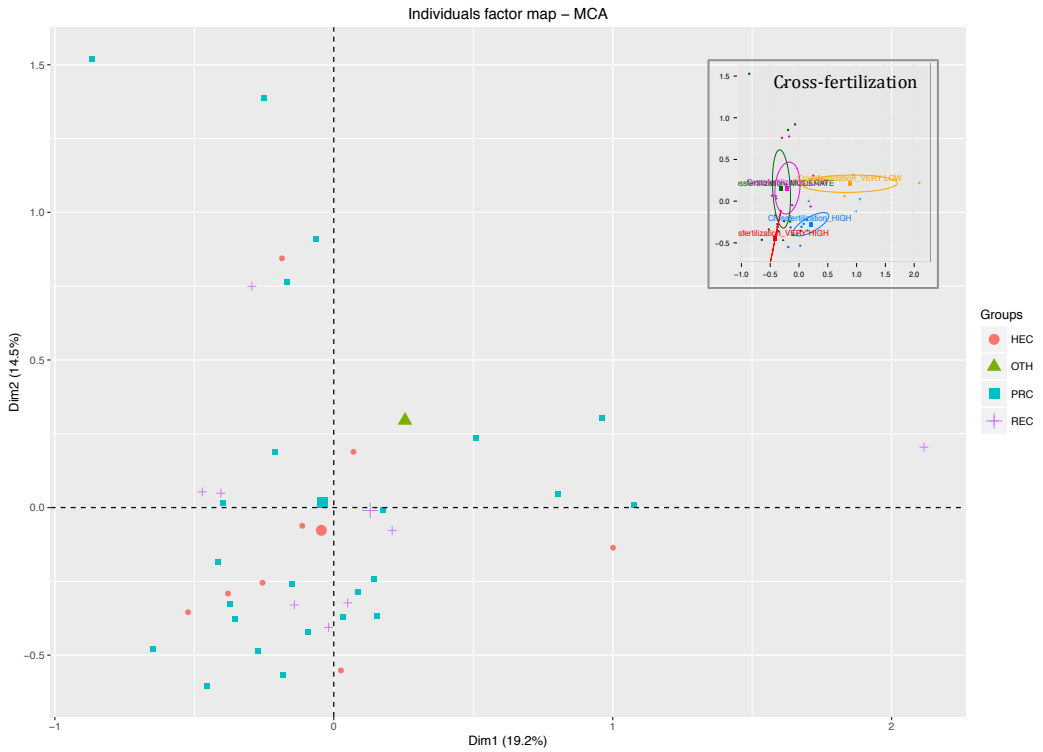

Figure 3.41. MCA for the qualitative supplementary variable "type of organisations".

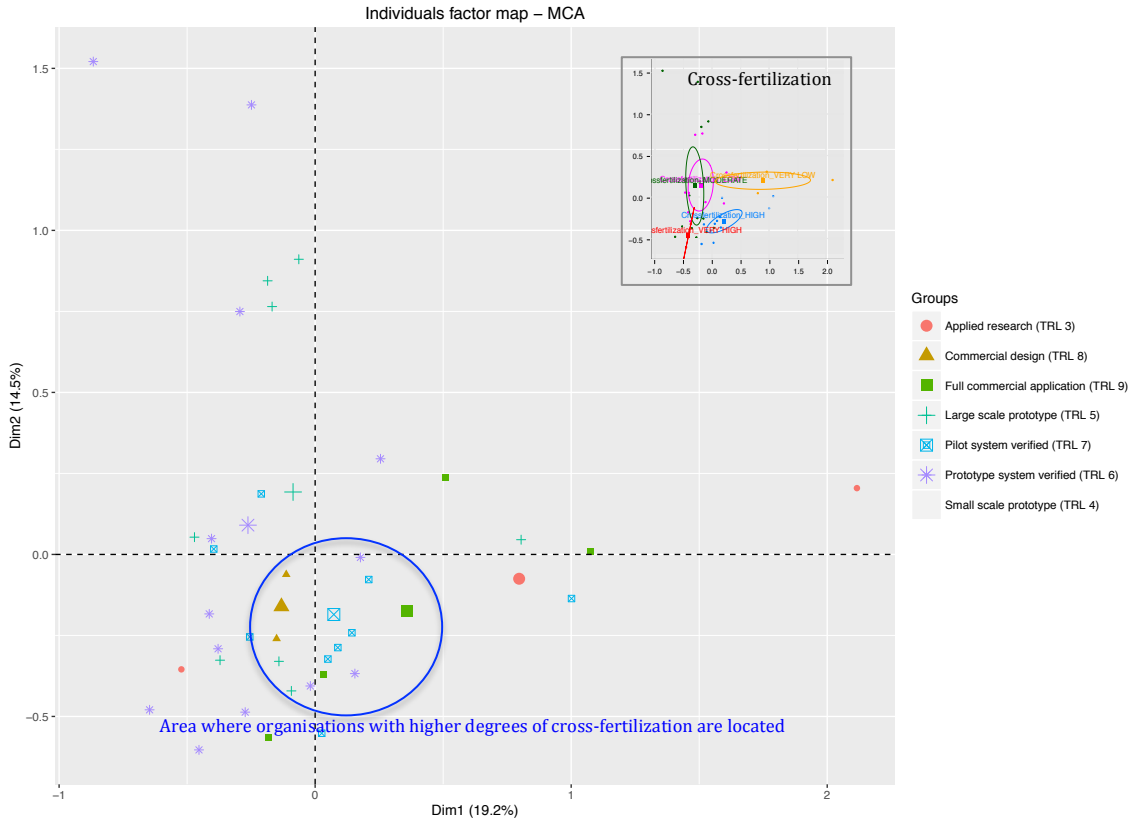

Figure 3.42. MCA for the qualitative supplementary variable "final TRL of the project".

3.16 Discussion

The results obtained in this study give rise to the belief that the cross-fertilization of KETs is a process developed through an open innovation strategy. The first evidence that suggests this consideration is the relevance that organisations leading higher cross-fertilized projects give to searching for external sources of information. In this case, project leaders have shown that they are not afraid to lose their internal know-how because they believe that obtaining external knowledge is more beneficial for their organisations and for their products. A resulting effect is that stronger efforts are made by these organisations in order to import and apply those external ideas or knowledge.

The second evidence could be related to the informal type of collaborative partnerships founded in projects with higher level of cross-fertilization. An open innovation strategy supports the fact that social structures tend to be more informal and that this informality is also associated with creating radical innovations [256]. For instance, "innovation communities" are informal networks that have been

demonstrated to better support sustainable innovation [449], especially when more than one technology is involved [131], [138].

On the other hand, the unexpected result obtained with the variable technological distance suggests that there should be a mid-point with regard to the diversity of technological knowledge in the network. Findings showed that too diverse a range of technological knowledge could hamper cross-fertilization of technologies. A plausible explanation could be related to the realm of literature that proposes that innovation performance and cognitive distance have an inverted u-shaped relationship [128], [370], [376], [380]. This relation states that knowledge must be sufficiently distant to be transferred but not so distant as to impede mutual understanding. This concept could also be related to an open strategy since mutual understanding is associated with the familiarity and trust in the network and its effect on learning by interaction.

So far, findings should be carefully interpreted. In the first place, the small sample represents a limitation in this study and could be a consequence of the low participation obtained in the interview process. Interviews are often viewed as a time consuming and sometimes a tedious procedure [230]. In this context, even when some variables show very clear tendencies, results have low variances and statistical significance. As such, the authors suggest that this study could be viewed as a starting point for further research. For instance, it could be suitable to evaluate innovation management strategies at the KIC Health initiative[17] where cross-fertilization of KETs is also an aim, and where the sample size could be larger and therefore more representative. A second limitation has to do with the generalization, since only nanotechnology and health related projects were taken into account. Future research could improve on this aspect by considering wider domains of nanotechnology applicability.

3.17 Conclusions of Section II

This study has empirically explored three innovation management strategies in the process of cross-fertilization of KETs. The first strategy is related to importing ideas from broad networks. This strategy was nuanced by considering a technological distance within the network, the technological effort organisations make to import ideas from the network and the value organisations give to having access to external information. Findings suggest that the level of cross-fertilization is higher

[17] Knowledge and Innovation Community (KIC) Health is a consortium of different stakeholders aimed at increasing industry competitiveness, improving quality of life and improving the sustainability of healthcare systems in Europe. It was designated by the European Institute of Innovation and Technology Governing Board on December 2014 [464].

when there are short or medium technological distances, when organisations make stronger technological efforts and when the access to external information is a very important reason for belonging to the network. These findings could support an open innovation strategy where organisations tend to be aware of and open to what their network could offer, rather than protecting their own knowledge [104], [108], [389], [390].

The second strategy analysed is referred to as the creation of a collaborative network. For this strategy, a previous collaboration and the type of collaboration networks were considered. Findings suggest that neither a previous collaboration, nor a formal collaborative structure supports higher levels of cross-fertilization. Indeed, the authors believe that these considerations could be related to each other by taking into account that since no formal agreements are developed along the value chain, informal and spontaneous interactions are more likely to emerge in this situation. These findings are also consistent with the informal network literature which gives more weight to the trust, commitment and mutual learning from informal dynamics in order to foster the convergence of creative ideas and technologies [450]–[454].

The third strategy was analysed by taking into account the level of orientation to market, customer prioritization and the experience in higher levels of TRLs where pilot production and product demonstration activities are prevalent. Evidence suggests that market-orientated and customer prioritized projects boost higher levels of cross-fertilization of KETs. In contrast, the claim that previous experience with higher levels of technological maturity favours cross-fertilization was not completely supported. This finding may, however, be due to the fact that 56% of the sample develops R&D as a principal activity; meanwhile only 19% is dedicated to production and 6% to commercialization as principal activities.

Another contribution of this work is related to the significant role of nanotechnologies in the cross-fertilization of KETs. In this study, it was identified that organisations who apply nanotechnology knowledge in their organisations are the ones that produce higher levels of cross-fertilization. This result not only confirms the transversal and multidisciplinary nature of nanotechnologies, emphasizing its plasticity among different industries, but more importantly, suggests an essential characteristic of highly cross-fertilized projects.

These results could be used as a guideline for policy makers and project leaders that aim to create innovation on the basis of the cross-fertilization of technologies. In this regard, considering this relationship could be strategic in management and policy making at a cross-fertilized context [300], [365], [455]. Therefore, in order to encourage this process and consequently to leverage innovation projects, this study suggests considering projects where: i) organisations could share technological

knowledge, which should not be too similar, nor too diverse from their partners, ii) organisations could make strong efforts to obtain broad knowledge, iii) having access to external sources of information is considered important, iv) where the network could have an informal collaborative structure, v) with projects with high market orientation and iv) where customers could be prioritized as part of their innovation strategy. Neither a previous collaborative experience, nor an experience in higher levels of TRL seemed to correspond with higher levels of cross-fertilization. Considering these respects, new scientific policies and strategies could be reshaped to address and support the growing industrialization of emergent cross-fertilized KETs.

CHAPTER 4

Conclusions of the thesis

This work has analysed the process and ecosystems of innovation in nanotechnologies by considering the cross-fertilization of KETs in the field of healthcare. For this purpose, two approaches that support innovation have been complementarily taken into account: one, a technological perspective and, on the other side, a management perspective. In this regard, key issues and current concerns of innovation and technology transfer have been addressed. By doing so, this work has sought to extend scientific, industrial and innovation knowledge attempting to answer the new challenges that are facing publicly-funded research.

This thesis has also sought to contribute to a better understanding of regional systems of innovation, which are aimed at solving major economic and societal needs. Accordingly, this research is aligned with the knowledge based economy speech, grounded in the optimal change of the productive matrix of a region through the development of technological activities and the social return of the investments in science. It should be stressed that the objectives of this thesis are also aligned with a traditional expression in Quichua (native language of Ecuador), which is an ancestral community goal: "SUMAK KAWSAY", which means equity and quality of life for all citizens.

Additionally, the relevance of collaborative interaction and the environmental factors associated with the success of a medicine-related emerging technology were highlighted in this thesis by consolidating several actors into a Five-Helix innovation model. This concept emphasises the pressing need to ensure a closer cooperation between engineers, physicians, project and innovation managers, technicians and researchers. It also represents another perspective regarding innovation communities and open innovation literature.

Findings from this research could have implications for evolutionary economics regarding technological diversity creation in innovation systems. The data obtained supports once again the idea that innovation system literature is connected with the social network approaches. In this regard, it has been shown that external collaboration plays an important role in emerging technologies.

Moreover, this thesis exhibits a methodological original contribution, which is the implementation of the probabilistic text modelling method LDA for analysing the degree of a project's multi-disciplinarity. Even this method is well accepted by the research community, text analysis are less frequent and have not been used before for studding technological diversity. Notwithstanding, this is the first work that used topic modelling for analysing technological diversity at nano-related European projects in a convergent scenario of technologies. Additionally, since project information has been used as the source of data, this study offers a differentiated methodology compared with publications and patents, which have been the common source of data used for analysing innovation. Therefore, this work has

considered complementary techniques by utilizing from the increasing power of machine learning and computation.

Having said that, the main conclusions of this thesis are the following:

- The exponential growth of nanotechnologies has become evident over the last decades. In the field of healthcare, findings suggest that diagnosis, therapeutics, and regenerative medicine are the three main areas where nanotechnology is having a promising impact. Advances in POC devices are also gaining relevance in the improvement of sensitivity, selectivity, and the multiplexing capabilities of medical devices.
- Despite these numerous advances, nanotechnology research is still facing the so-called Valley of Death, which limits the successful transference of scientific approaches into the marketplace. In order to address this scenario, European funding initiatives have consecutively integrated additional strategies focusing on the impact of research performance and the assessment of societal needs. In this regard, the introduction of the TRL shows that the current focus of the R&D investment in Europe is in innovative outcomes.
- Four nano-enabled sensor-based devices at different levels of technological maturity have been identified as examples of specific nanotechnology applications within a multi-KET approach. The innovation ecosystem analysed showed that these devices are developed by a multi-disciplinary group of experts. This group was found to be more multi-disciplinary at higher levels of technological maturity.
- Additional findings from the four cases have shown that more KETs are cross-fertilized at lower levels of technological maturity. Involving diverse KETs increased the complexity of technology transfer activities resulting in a difficult commercialization. The consequent deduction for this finding is that innovation management strategies from the beginning of the value chain might not be based on traditional strategies if the aim is to overcome the so-called Valley of Death.
- Innovation and technology transfer challenges of nano-enabled sensor based devices are manufacturing costs, technological barriers and technology-market matching. In addition, limiting factors such as the existence of cheaper and well-positioned alternatives in the marketplace, as well as the lack of market-oriented strategies have been evidenced for all cases.
- On the other side, more intra-organisational collaboration and focused market research strategies have been found in the nanosensor-based device

with higher levels of technological maturity. This case was the one with the greatest possibility to overcome the Valley of Death at a reduced time-to-market. In this regard, it could be concluded that barriers for knowledge and technology transfer are overcome across organisational boundaries though multi-disciplinary participation and customer- and market-oriented managerial strategies.

- The nano-related innovation ecosystem has been subsequently analysed in a European regional context through EU-funded nanotechnology innovation projects. From the system of selected projects, it has been found that most of the projects have been granted to Spain, Germany, Italy, the UK and France. Specifically, Spain and Germany are the countries with major shared cooperation, as evidenced in the network map. In addition, it has been found that more than half of participant organisations are private for-profit entities (principally SMEs), following by higher or secondary education establishments and research organisations. Once again, we conclude that the current H2020 Programme puts the focus on innovation outputs and places the firms as innovating engines for a sustainable and technology-driven economy growth.
- The profile of the stakeholders involved in the process of cross-fertilization of KETs was identified from interviewing project leaders of nanotechnology-related innovation projects. It was identified that the majority of these organisations are principally private-for-profit entities with less than 50 employees (micro- and small-sized). Frequent areas of specialization found in these organisations were life-sciences, materials and pharma, particularly developing R&D and production as principal activities. In addition, KETs with a significant technology domain found were industrial biotechnology and advanced materials, and the majority of the organisations (98%) have participated in previous European Framework Programmes. Regarding main characteristics in project leaders, it has been found that more than half of them are aged between 34 to 54 years old, most of them with Masters or PhDs and having a management-related role at their organisations. Regrettably, gender inequality has been evidenced in the leadership roles of these projects.
- The influence of characteristics of EU-funded nanotechnology projects on the creation of technological diversity was also analysed. In addition to organisational diversity and the network of the project, novel variables that have a plausible influence on diversity creation were included. Results showed that the largest contribution to the creation of technological diversity comes from the multi-disciplinary nature of a project. These findings support the idea that the development of multi-disciplinary projects fosters the long-term success of nanotechnologies. In this regard, the multi-

disciplinary collaboration found in previous findings could be endorsed and suggested for boosting cross-fertilization of KETs.

- The joint knowledge base of project partners and the geographical distance between them were also positively associated with technological diversity creation at the system of projects. The opposite has occurred regarding the number and diversity of organisations and the degree of clustering, which showed a negative association. These results establish that the structure of the network is also essential to be considered for the overall success of nanotechnologies.
- Three innovation management strategies and their influence on the process of cross-fertilization of KETs have been studied. From this analysis, it could be concluded that higher levels of cross-fertilization of KETs are being boosted by customer-concerned and market-oriented projects, in which organisations prioritize the access of external knowledge. It was also found that the network that best boosts the cross-fertilization of KETs has an informal structure, where knowledge is moderately heterogeneous, endorsing previous findings from the case studies. Therefore, these results suggest that factors related with the absorptive capacities and dynamic capabilities of organisations are decisive in a technological convergent approach.
- The suggested innovation ecosystem for developing health-related multi-KETs was confirmed at the empirical study. However, some concepts from this model need to be re-adjusted. For instance, findings from Chapter 2 showed that the multi-disciplinarity of the group was lower at higher levels of cross-fertilization, which could be related with the lower and moderate technological distances found in higher levels of cross-fertilization in Chapter 3. These relations show that even the suggested model included a multi-disciplinary team, considering the *level of multi-disciplinarity* is relevant in order to avoid too much multi-disciplinarity. Additionally, the existence of a previous collaboration from the beginning of the value chain was not completely supported in the empirical study; therefore, more research is needed to endorse the concept of an *integrated mosaic-based* innovation community suggested as the optimal model to transfer multi-KETs to the marketplace.
- Finally, it was also identified that actors with *higher levels of nanotechnology application are correlated with higher levels of cross-fertilization of KETs.* Accordingly, this study confirms the transversal role of nanotechnologies, highlighting the imperative need for the implementation of this technology in the industrial sector.

The conclusions summarized here, and the detailed conclusions of each chapter, could have practical implications for all stakeholders involved in innovation and technology transfer in the nano-field. On one hand, it could be particularly useful for researchers wishing to transfer their basic research, and for the other, industrial entrepreneurs challenged to scale and bring those discoveries into the marketplace. Innovation managers and project leaders could also benefit from the insights presented in this work in order to apply adequate innovation strategies in the development of cross-fertilized products such as medical devices.

Last, but not least, this work could guide policy makers for reshaping and improving nanotechnology related priority lines. In this context, it is suggested that policies could: i) foster an open, collaborative, integrative and balanced ecosystem, ii) influence the level of diversity in groups and projects, and ii) foster excellent science and technological quality, but also strategic innovation management capacities of all the stakeholders at the nano-related innovation ecosystem. With these guidelines, it is expected to contribute with the successful innovation and long-term success of the commercialization of nanotechnologies and, especially, nanomedicines.

4.1 Future steps

This thesis could be considered as the starting point of future research activities. Initial factors to be considered are the sample size and the sample setting. The reduced sample size in the empirical section was the result of the conditions of inclusion considered. Consequently the claims generated are restricted specifically for this sample, and this fact restrains the generalization of the results. It is therefore suggested that future research could include a larger element of analysis in order to obtain more reliable results and statistical power.

Furthermore, establishing a European regional setting could be a strength on one hand, but a weakness on the other. It could be a strength from a European policy perspective aiming to take into account the impact of such policies in the region. However, national and regional initiatives could be hindered in this respect. Moreover, because of the different national priorities regarding technological policies, not all the actors participate with the same density of projects according to each country. Therefore, conclusions in this domain must be handled with care and at a regional context. Assumptions cannot be applied to the entire innovation ecosystem, or even more, outsourced to other systems. In this regard, future research could include national projects and consider national and regional initiatives in order to expand the scope of the research.

Doubtlessly, including other *application areas of nanotechnologies* could be an interesting approach. Since nanotechnology benefits a broad set of fields, future research could include a comparative analysis of the challenges of this technology at different industries such as energy, agro-food, advanced materials, among others. Additionally, this study is suitable to be applied to other *innovation ecosystems or networks*. For instance, it could be applied for studding technological platforms (e.g. the Spanish Technology Platform on Nanomedicine), knowledge and innovation communities (e.g. the KIC Health from the European Institute of Technology), or other regional innovation systems (e.g. the Research Innovation Strategies for Smart Specialization RIS3Cat). In this context, the methodologies applied in this thesis could be practical for these purposes since they have been demonstrated to be appropriate for a better understanding of the technological and management perspectives of innovation in nanotechnologies and other emergent technologies.

CHAPTER 5

Resumen en Castellano

5.1 Introducción

Trasladar los resultados de la investigación básica hacia el mercado es un proceso que no siempre resulta fácil ya que es un camino que está lleno de desafíos. De hecho, muchos de los avances científicos y tecnológicos no logran atravesar el llamado "valle de la muerte", período en el que los emprendimientos fracasan y no continúan hacia el mercado. Éste fenómeno ha sido especialmente identificado en el desarrollo de las Tecnologías Facilitadoras Esenciales (TFEs), consideradas clave por la Comisión Europea para la innovación industrial y la competitividad.

Para hacer frente a este escenario, varias líneas de acción en políticas públicas están siendo re-direccionadas y se están focalizando en el desarrollo industrial de las TFEs [4], [22]–[24], [26]. El Programa Marco Europeo Horizonte 2020 (H2020) es un ejemplo de esta tendencia que, además de buscar la implementación industrial de las TFEs, también impulsa su fertilización cruzada para que se puedan obtener avances científicos más innovadores y de este modo, poder solventar las necesidades sociales y económicas más urgentes de cada la región.

La nanotecnología se encuentra categorizada dentro de las seis TFEs, y dado el gran impacto que ésta tecnología está teniendo en diversas áreas de aplicación y desarrollo económico, su implementación industrial está cobrando cada vez mayor importancia en la actualidad, por lo que superar el valle de la muerte resulta imperioso. Para ello es necesario comprender los procesos y ecosistemas de innovación en los cuales se desarrollarán las nanotecnologías, al igual que identificar los retos que implica la fertilización cruzada entre las TFEs [30], [31].

5.1.1 Objetivo general

En base a lo expuesto, un nuevo paradigma en I+D+i es necesario para alcanzar el retorno social de la inversión en ciencia y tecnología. Siguiendo esta línea, la presente tesis tiene por objetivo general examinar los desafíos de innovación y de transferencia tecnológica para alcanzar la comercialización exitosa de las nanotecnologías en un escenario de convergencia tecnológica.

El análisis de esta tesis se enfoca en el campo de la salud, dado que en ésta área de aplicación las nanotecnologías están teniendo mayor impacto. En este sentido, se pretende ampliar los conocimientos relacionados con los procesos y ecosistemas de innovación necesarios para la culminación satisfactoria del proceso de transferencia tecnológica y de este modo, aportar a la reducción de la brecha existente entre la investigación y el mercado en las tecnologías emergentes.

5.1.2 Objetivos específicos

- **Objetivo 1**: Describir el estado actual de las nanotecnologías aplicadas al campo de la salud, así como también sus procesos innovadores y tendencias de mercado.
- **Objetivo 2**: Identificar aplicaciones específicas de la nanotecnología en el campo de la salud con un enfoque multi-TFEs, con el fin de obtener una amplia perspectiva de los principales retos de la innovación y transferencia tecnológica en el proceso de su fertilización cruzada.
- **Objetivo 3**: Explorar los ecosistemas de innovación y la dinámica de los actores clave involucrados en actividades de transferencia tecnológica y de comercialización de las nanotecnologías aplicadas al campo de la salud, en un proceso de fertilización cruzada de las TFEs.
- **Objetivo 4**: Determinar los principales factores que influyen y fomentan el desarrollo de las multi-TFEs en el campo de las nanotecnologías aplicadas a la salud.
- **Objetivo 5**: Identificar el perfil de las principales organizaciones involucradas en el desarrollo de las multi-TFEs en el campo de las nanotecnologías aplicadas a la salud, y sus estrategias de gestión de la innovación.

5.1.3 Enfoque de la investigación

En base a estos objetivos, la presente investigación considera dos enfoques de manera complementaria:

- Por un lado se enfoca en una **perspectiva tecnológica**, la cual se centra en el análisis de las nanotecnologías teniendo en cuenta la relevancia al ser considerada una TFE, y el complejo proceso que implica su convergencia con otras tecnologías. Dentro de esta perspectiva se analiza la creación de la diversidad tecnológica, factor considerado clave en el éxito a largo plazo de las tecnologías emergentes, como lo es la nanotecnología.
- Por otro lado se enfoca en una **perspectiva de gestión de la innovación**, en la cual se enfatiza la importancia de gestionar el proceso innovador de las nanotecnologías, especialmente cuando se desarrolla dentro de un escenario convergente. En este sentido, una eficiente gestión de la innovación nanotecnológica es considerada en este estudio como una actividad relevante en el proceso de transferencia tecnológica.

5.1.4 Esquema de la tesis

La tesis se divide en cinco capítulos, los cuales se resumen a continuación:

- **Capítulo 1**. En este capítulo se expone el estado del arte de las nanotecnologías en el campo de la salud y se recopilan las bases teóricas acerca de los modelos y sistemas de innovación sobre los que se basa la investigación. Además, se incluye un análisis de la innovación nanotecnológica en Europa en base a los principales indicadores de la región. Este primer capítulo pretende cumplir con el **Objetivo 1**.
- **Capítulo 2**. En éste capítulo se identifican los principales retos de innovación y transferencia tecnológica en el ecosistema donde se desarrollan dispositivos médicos nano-habilitados multi-TFEs. Los retos son identificados a partir de un análisis exploratorio de estudios de caso en diferentes niveles de madurez tecnológica. En base a los hallazgos obtenidos, se propone un ecosistema de innovación fundamentado en un modelo integrado de comunidades de innovación, el cual pretende ser el punto de partida para el análisis de los capítulos subsiguientes. Éste capítulo se focaliza en cumplir los **Objetivos 2 y 3**.
- **Capítulo 3**. En este capítulo se presenta un estudio empírico realizado sobre proyectos de innovación Europeos dentro del programa marco H2020, especialmente aquellos en los que se incentiva la fertilización cruzada de las TFEs. El capítulo está comprendido de dos secciones:
    - **Sección I**: en la cual se identifican las principales características de los proyectos analizados y su influencia en la creación de diversidad tecnológica. El método estadístico utilizado en este capítulo es el Modelo de Regresión Logística Ordinal. Con éste análisis se pretende cumplir con los **Objetivos 3 y 4**.
    - **Sección II**: en la que se analizan las principales características y estrategias de gestión de la innovación de los actores que participan en el proceso de fertilización cruzada de las TFEs. Adicionalmente se identifican aquellas estrategias que fomentan el proceso de fertilización cruzada mediante un Análisis de Correspondencias Múltiples. Mediante éste análisis se pretende cumplir con el **Objetivo 5**.
- **Capítulo 4**. Capítulo en el cual se presentan las conclusiones generales de la tesis y se proponen futuras líneas de investigación que pueden ser derivadas de la misma.
- **Capítulo 5**. Este capítulo presenta el resumen de la tesis en lengua Castellana.

5.2 Capítulo 1. Nanotecnología e innovación: Estado del arte y marco teórico

Sin lugar a dudas, la nanotecnología se ha convertido en una tecnología relevante en diversas áreas de aplicación, entre las que se encuentran la biomedicina, el medio ambiente, la industria textil, la industria energética, la industria alimenticia y la industria de la construcción. Sin embargo, el mayor impacto de la nano-escala está en el campo de la salud, principalmente en el diagnóstico, la terapia y la medicina regenerativa. Entre las principales aplicaciones de mayor crecimiento en este campo se pueden mencionar las nano-partículas para la administración de fármacos, las nano-estructuras para la ingeniería de tejidos, los bio-nano-materiales en medicina regenerativa y la biología sintética [14], [15], [68].

Otra de las aplicaciones con mayor crecimiento de la nano-escala en el campo de la salud son los dispositivos de diagnóstico inmediato (POCs, por sus siglas en inglés para Point-of-Care), dado que se prevé que éstos mejoren su sensibilidad, selectividad y la capacidad de analizar múltiples metabolitos, posibilitando la transición desde los laboratorios hacia los hogares y mejorando la calidad de vida de los pacientes [238]. Estos adelantos permiten pronosticar que el mercado mundial de las nanotecnologías alcance los 3 trillones de dólares para el 2020 [80].

Sobre la base a estas previsiones, los líderes mundiales están fomentando la industrialización de las nanotecnologías, así como de otras cinco TFEs como son la fotónica, la micro y nano-electrónica, los materiales avanzados, la biotecnología industrial y los sistemas avanzados de manufactura [48]. Asimismo, iniciativas como el Programa Europeo Horizonte 2020, están dando mayor énfasis a la innovación basada en la fertilización cruzada de las TFEs, de tal manera que se pueda aumentar la competitividad en la región [153], [172]. Ésta iniciativa adicionalmente implementa estrategias de gestión de riesgos y de gestión de la innovación para que los proyectos puedan concentrar sus esfuerzos en una eficaz transferencia hacía el mercado [171].

Sin embargo, la innovación y transferencia de las TFEs como la nanotecnología, presentan grandes retos para todo tipo de organizaciones. En este sentido se han desarrollado diversos modelos de innovación que pretenden fomentar una adecuada trasferencia tecnológica y de este modo, poder trasladar los productos hacia el mercado. En un principio, el proceso innovador fue visto como un modelo lineal [86], [97], [98]. Actualmente se sabe que este proceso es todo menos lineal, y que está basado más bien en una continua retro-alimentación y re-diseño de conceptos dentro de la cadena de valor. Por otra parte, el modelo de innovación abierta originado por Chesbrough (2003) que es un modelo que prioriza el uso de ideas externas y el flujo de conocimiento a través de redes, ha tenido un mayor impacto en el sector emprendedor en los últimos años [104].

Además de los modelos de innovación adecuados para la transferencia de tecnologías, en las últimas décadas se ha enfatizado la importancia de los sistemas de innovación sectorial, nacional y regional [115]–[118]. Estos sistemas se centran en el papel que juegan diversas organizaciones y su interacción con el ambiente que las rodea, ya sea en un determinado sector, país o región. Estos sistemas tienen su fundamento en la teoría de redes, una rama de la macroeconomía que estudia la dinámica de un grupo de individuos u organizaciones que trabajan colaborativamente persiguiendo un mismo objetivo [36], [121], [123]–[128].

En esta misma línea, el concepto de ecosistemas de innovación se basa en crear un entorno favorable para generar emprendimientos basados en la innovación [134] [135]. En este entorno, por tanto, se concentran e interrelacionan agentes que generan valor al aportar cada uno diferentes puntos de vista y colaborando de manera equilibrada. En base a este concepto surge el "modelo de cinco-hélices", el cual hace referencia al ecosistema que favorece la innovación en el campo de la salud e involucra a los hospitales y a los ciudadanos además del sector empresarial, el sector académico y los centros de investigación, todos ellos impulsados por los parques científicos y tecnológicos, considerados promotores del ecosistema [30]. Éstos conceptos son considerados en los capítulos siguientes y en base a ellos se analizan los retos en los cuales se desarrollan las nanotecnologías aplicadas a la salud, en un contexto de convergencia tecnológica.

5.3 Capítulo 2. Retos en la innovación y la transferencia tecnológica: Una visión a partir de dispositivos basados en sensores nano-habilitados

El proceso de fertilización cruzada se lleva a cabo cuando diferentes tecnologías se hibridan, dando como resultado productos o servicios más innovadores y de gran impacto económico y social [175], [176]. Un ejemplo de este proceso es el caso de los dispositivos nano-habilitados, desarrollados para monitorizar fenómenos tanto físicos como químicos en lugares de difícil acceso. Se estima que éstos dispositivos médicos puedan llegar a tener un gran impacto en los próximos años y que los campos de aplicación con mayor crecimiento serán entre otros, la regeneración de tejidos, las isquemias cardiovasculares y la ingeniería genética [175], [176].

Al igual que otras tecnologías emergentes, el traslado de estos dispositivos hacia el mercado aún se ve enfrentado a superar varios retos relacionados con las barreras tecnológicas y un escaso enfoque hacia las necesidades del mercado. Con el objetivo de dar respuesta a este hecho, en los últimos años ha surgido el concepto de "universidades emprendedoras", el cual hace referencia a un rol de las universidades que va más allá del de producir y transmitir conocimiento. Éste rol se

basa en trasladar al mercado el conocimiento producido y la investigación generada [140], [185]–[189].

En el presente capítulo, este nuevo rol de las universidades es abordado mediante la realización de un análisis exploratorio a diversos dispositivos basados en sensores nano-habilitados desarrollados en un entorno académico. El objetivo es el de identificar los principales retos dentro de los ecosistemas de innovación en los cuales este tipo de dispositivos se están desarrollando. Para ello se seleccionaron cuatro dispositivos basados en sensores nano-habilitados en diferentes etapas de madurez tecnológica (**Figura 5.1**).

La madurez tecnológica de un producto puede clasificarse en base a la escala "Technology Readyness Level" (TRL por sus siglas en inglés), inicialmente desarrollada en 1980 y que está actualmente siendo usada para categorizar tecnologías nuevas y emergentes dentro del programa marco H2020 [225].

Los casos fueron seleccionados a partir de varios criterios. En primer lugar, se consideró que sea un dispositivo que incorpore o en el que se pretenda incorporar nanotecnología en su diseño, desarrollo o fabricación. En segundo lugar, que el dispositivo combine diversas TFEs y que sea un dispositivo con potenciales aplicaciones en campo de la salud. Finalmente, que sea un dispositivo desarrollado en un entorno académico de financiación pública. Los estudios de caso seleccionados fueron los siguientes:

- **Caso I**. Un sistema implantable multi-sensor nano-habilitado para Teragnosis *in vivo.*
- **Caso II**. Un nano-sensor para la detección mejorada de ADN.

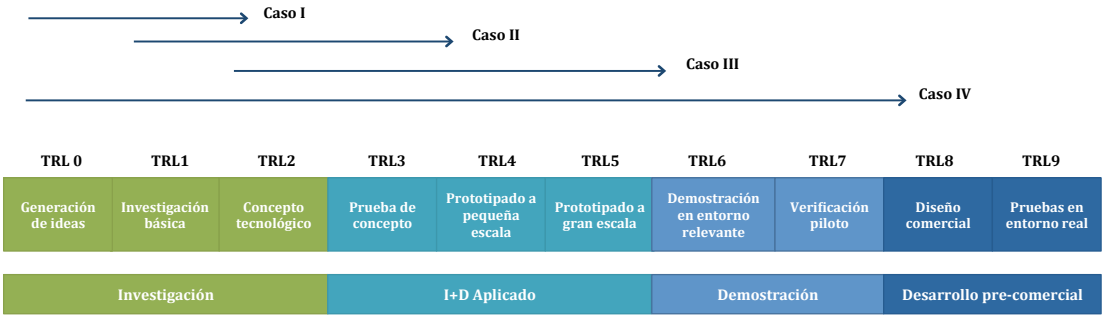

Figura 5.1. Selección de los estudios de caso.

- **Caso III**. Un sensor de análisis bacteriano basado en dielectroforesis e análisis de impedancia.
- **Caso IV**. Un array electroquímico para la detección y monitorización *in vivo* de isquemia gástrica.

Para todos los casos, la información recopilada se obtuvo mediante datos primarios (entrevistas) y fue complementada con datos secundarios (publicaciones, comunicados de prensa, reportes anuales, páginas web, entre otros). De esta manera se pretendió enriquecer el proceso de recolección de información mediante el método de triangulación de datos [230].

El análisis exploratorio de los estudios de caso permitió identificar características comunes para los cuatro casos. Se identificó por ejemplo, que los dispositivos se desarrollan por un grupo multidisciplinario de expertos. Ésta multi-disciplinariedad fue mayor cuanto mayor era la madurez tecnológica del dispositivo. Adicionalmente, en ningún caso se observaron relaciones estrictamente formales o estrictamente informales, haciendo de ésta, una característica en común del ecosistema de innovación.

Entre los desafíos comunes para los cuatro casos se identificaron los altos costos de fabricación y barreras tecnológicas. En este sentido, se evidenció que la existencia de alternativas más baratas y mejor posicionadas, así como la falta de estrategias orientadas al mercado, representan factores limitantes en el desarrollo de este tipo de dispositivos. Adicionalmente, se encontró que más TFEs estaban siendo convergidas en niveles más bajos de madurez tecnológica. Éste hecho, según los desarrolladores de los dispositivos, hace que la complejidad en el proceso de transferencia incremente y por consiguiente, dificulta la entrada del dispositivo al mercado.

A pesar de estas similitudes, se evidenció una mayor participación intra-organizacional y un mayor enfoque hacia el mercado en los dispositivos de mayor madurez tecnológica. En este sentido, el dispositivo con mayores probabilidades de salida al mercado y en un tiempo reducido es el Caso VI. Éste dispositivo se desarrolló dentro de una participación multidisciplinar e intra-organizacional, lo que podría implicar que los obstáculos entre las fronteras tanto disciplinares como organizacionales están siendo superadas en ese caso. Adicionalmente, éste dispositivo demostró un enfoque *comunitario* en el que agentes con perspectivas diferentes trabajan para logar un objetivo común. Por último, éste caso fue el único que realizó un análisis de riesgos y de competidores, así como también de las necesidades de los usuarios finales.

Estos desafíos identificados fueron considerados como la base para la introducción de un modelo de innovación que pretenda superar la brecha entre la investigación y

el mercado. El modelo propone una comunidad de innovación en la que, diversos agentes de otras comunidades de innovación interaccionan y colaboran conjuntamente con una estructura de tipo "mosaico", de tal manera que se facilite el flujo de conocimiento de las diversas áreas tecnológicas (**Figura 5.2**).

La conceptualización de este modelo condujo al objetivo de ser estudiado con mayor profundidad en capítulos siguientes.

En este sentido, la ventaja estratégica se podría conseguir considerando la integración de los diversos agentes desde el comienzo de la cadena de valor. Como consecuencia, técnicos, gestores de la innovación, investigadores, ingenieros, médicos y administradores de proyectos, podrían contribuir con diferentes perspectivas, experiencias y disciplinas que agregan valor al proceso de innovación. Adicionalmente, se podría concluir que la visión completa de la cadena de valor de los procesos de investigación y transferencia de tecnología enfatiza la importancia de la comunidad y en colaboración en el ecosistema innovador en el que el resultado sea la adecuada transferencia y el retorno social de la ciencia.

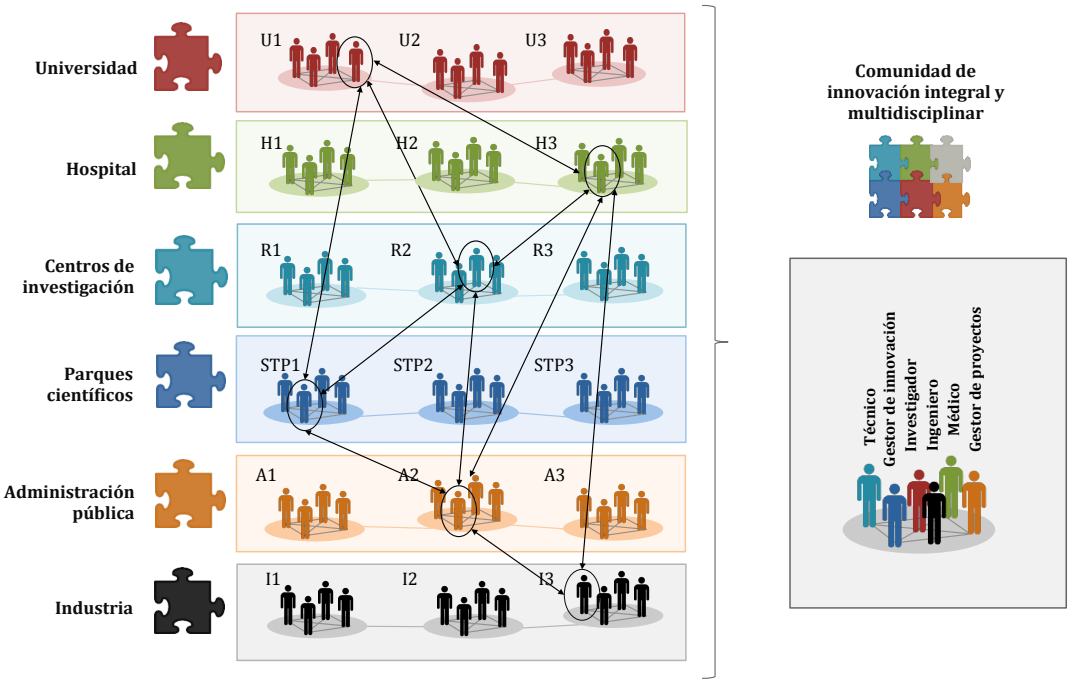

Figura 5.2. Esquema de la comunidad de innovación sugerida para el desarrollo de dispositivos nano-habilitados basados en la fertilización cruzada de TFEs.

5.4 Capitulo 3. Estudio empírico

En el capítulo anterior se exploran los desafíos relacionados con la innovación y transferencia tecnológica en diversos dispositivos médicos nano-habilitados basados en la fertilización cruzada de las TFEs. En base a los hallazgos se sugirió un modelo de ecosistema de innovación multidisciplinar basado en una comunidad integrada. En este capítulo, el objetivo es analizar dicho modelo y estudiar en profundidad dos características halladas en los ecosistemas de innovación, que son el nivel de la multi-disciplinariedad y el nivel de fertilización cruzada de las TFEs.

El capítulo se compone de dos secciones. En la **Sección I** se tiene en cuenta la literatura de la economía evolutiva, la cual establece que el éxito a largo plazo de una tecnología emergente requiere de la suficiente *creación de diversidad tecnológica* entre sus alternativas en el sistema [74], [273], [274]. Una suficiente diversidad tecnológica contribuye a evitar una dependencia tecnológica temprana[18] (llamada en inglés *technological lock-in*), facilita la innovación recombinante, aumenta la resistencia de la tecnología en caso de circunstancias inesperadas, y permite el crecimiento de mercado [273], [275], [276].

Por otro lado, en la **Sección II** se considera el nivel de fertilización cruzada de las TFEs. Como se observó en el **Capítulo 2**, mientras más TFEs estén siendo convergidas, más complejo es el proceso de transferencia tecnológica y comercialización. Este escenario da lugar a sugerir que la forma en que se gestiona este complejo proceso, no puede ser el basado en estrategias convencionales. En este sentido, ésta sección presenta el análisis de las *estrategias de gestión de la innovación* que podrían estar influyendo en el proceso de fertilización cruzada de las TFEs.

Para ambos enfoques, tanto el de creación de diversidad tecnológica como para el de análisis de las estrategias de gestión de la innovación, se seleccionaron como elemento de estudio, proyectos H2020 relacionados con la nanotecnología en el campo de la salud. Se consideraron estos proyectos ya que, en primer lugar, la creación de diversidad tecnológica por lo general se lleva a cabo en proyectos de innovación [273], [282]. En segundo lugar, dado que la fertilización cruzada de las TFEs está siendo incentivada por financiaciones públicas como H2020, el nivel de fertilización cruzada y las estrategias aplicadas para este proceso pueden ser evidenciadas en los proyectos financiados por la UE [112], [280], [281].

Los proyectos fueron seleccionados tomando en cuenta aquellos en los cuales se haya fomentado la fertilización cruzada de las TFEs. Para ello se optó por escoger el

[18] Según Arthur (1989), el *lock-in tecnológico* se produce cuando una sola tecnología domina todo el mercado, evitando la entrada o éxito de otras tecnologías alternativas, las cuales pueden incluso ser potencialmente superiores [457].

Plan de Trabajo 2014-2015 llamado “Liderazgo en Tecnologías Habilitadoras e Industriales” (LEIT, por sus siglas en inglés), en el cual se fomenta la aplicación industrial y la fertilización cruzada de las siguientes TFEs: nanotecnologías, materiales avanzados, biotecnología y manufactura avanzada.

Los datos se obtuvieron a partir del Servicio de Información Comunitario sobre Investigación y Desarrollo (CORDIS, por sus siglas en ingles), el cual es un repositorio público y de acceso abierto que contiene información de los proyectos y los resultados de investigación financiados por la unión Europea. Éstos proyectos pertenece a cuatro categorías dentro del Plan de Trabajo, las mismas que se detallan a continuación:

- Nanotecnología y materiales avanzados para una atención médica más efectiva.
- Aprovechamiento del potencial sectorial transversal de las nanotecnologías y los materiales avanzados para impulsar la sostenibilidad y competitividad.
- Reducción de la brecha entre la investigación y el mercado de las nanotecnologías.
- Procesos industriales basados en biotecnología para impulsar la sostenibilidad y competitividad.

La **Figura 5.3** explica el proceso de selección de los proyectos.

En total se seleccionaron 69 proyectos, desarrollados por 222 organizaciones de diferentes tipos entre las cuales se encontraron centros de educación universitaria, centros de investigación, entidades con fines de lucro y órganos públicos. En la **Sección I** se realizó un análisis del texto descriptivo del proyecto para analizar la diversidad tecnológica en los mismos. Para las 222 organizaciones se realizó un análisis de redes y de patentes.

Posteriormente y como se expone en la **Sección II**, se entrevistaron a 54 líderes de estos proyectos y a partir de la información obtenida, se realizó un análisis descriptivo de las organizaciones y de sus estrategias de gestión de la innovación. Dichas estrategias fueron analizadas en aquellas organizaciones que participaron colaborativamente a través de consorcios (en total 41) mediante un Análisis de Correspondencias Múltiple para determinar su influencia en el grado de fertilización cruzada de TFEs. En este estudio, un consorcio hace referencia al grupo de organizaciones que participan conjuntamente en un mismo proyecto.

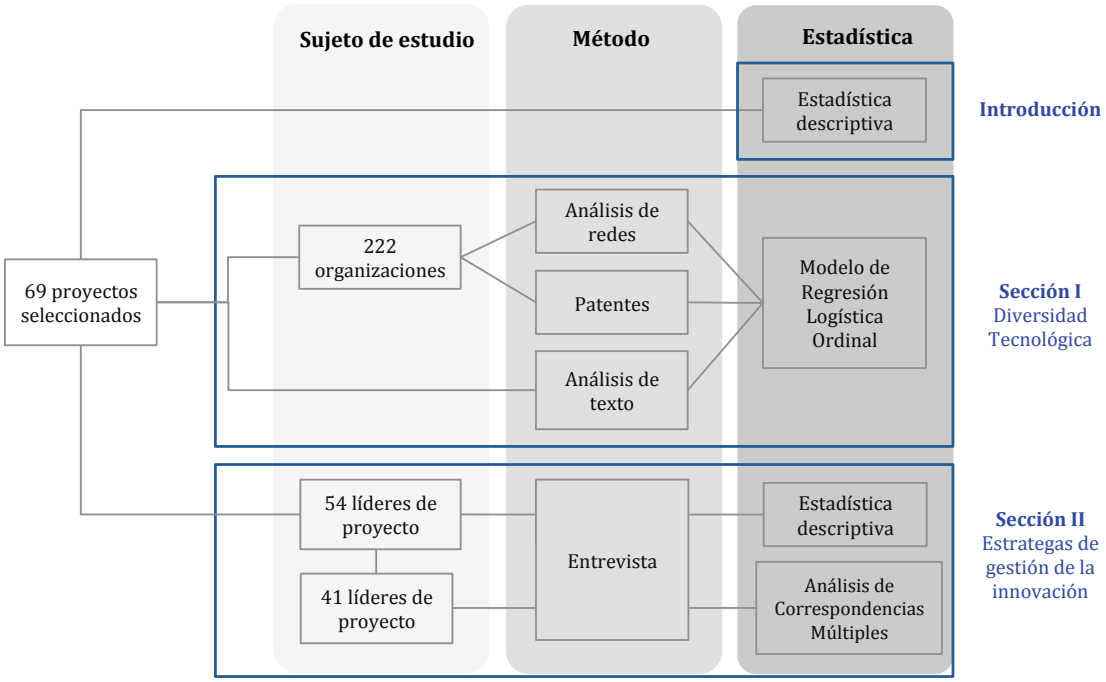

Figura 5.3. Esquema del proceso seguido para el estudio empírico.

5.4.1 Sección I. Enfoque tecnológico

El enfoque tecnológico de esta sección se basa en estudiar la influencia de las características de los proyectos en la creación de la diversidad tecnológica. Para ello, la creación de la diversidad tecnológica fue considerada como variable dependiente, y las variables independientes fueron el grado de multi-disciplinariedad del proyecto, la base de conocimiento nanotecnológico de las organizaciones, el tipo de organizaciones, el grado de agrupación del consorcio, y la proximidad geográfica entre las organizaciones dentro del consorcio.

Para clasificar las alternativas tecnológicas y el grado de multi-disciplinariedad del proyecto, se utilizó el Modelo de Tópicos LDA (Latent Dirichlet Allocation)[456], el cual permite identificar las relaciones latentes entre los tópicos o temáticas de un conjunto de documentos. En base a la diversidad de temas encontrados, se calculó la medida estadística de la entropía de Shannon (**Ecuación 1 en sección 3.6.1**), la cual indica si la diversidad tecnológica en el sistema de proyectos se está creando o reduciendo.

Por otro lado, la base de conocimiento nanotecnológico de los actores se obtuvo cuantificando el número de patentes relacionadas con nanotecnología. Las patentes desde 1980 hasta el 2015, se obtuvieron de la página web de la Oficina Europea de Patentes (EPO, por sus siglas en inglés). Paralelamente se utilizó el programa *AcclaimIP Patent Search and Analysis Software* para asegurar la estandarización de los nombres y las patentes de cada organización.

La diversidad de actores se obtuvo teniendo en cuenta la clasificación establecida por el Programa H2020, en la cual divide a las organizaciones en cinco grupos (detallados en la **Sección 3.2.1**). Por otro lado, la variable grado de agrupación fue obtenida mediante el cálculo del coeficiente de clusterización (del inglés Clustering Coefficient) (**Ecuación 3 en Sección 3.6.6**), el cual representa la probabilidad de que dos organizaciones estén conectadas entre sí mediante la conexión con una tercera organización. La variable distancia geográfica se obtuvo calculando la distancia en kilómetros entre las coordenadas geográficas (latitud y longitud) de las organizaciones de un proyecto y el centro geográfico (o centroide) de todas las organizaciones en un mismo proyecto. Éstos datos fueron calculados mediante los paquetes estadísticos *geosphere* y *fossil* del programa R [359],[360]. Finalmente, las hipótesis planteadas se comprobaron mediante el Modelo de Regresión Logístico Ordinal, en el cual se pudo determinar la relación de influencia de las variables independientes respecto a la variable dependiente.

Los resultados obtenidos mostraron que la mayor contribución a la creación de diversidad tecnológica proviene de la naturaleza multidisciplinar de los proyectos. Las variables que también mostraron una contribución positiva, aunque en menor proporción, fueron la distancia geográfica y la base de conocimiento nanotecnológico. Por el contrario, el grado de agrupación de la red, el número y la diversidad de actores por proyecto, mostraron un efecto negativo en la creación de la diversidad tecnológica.

En base de estos resultados se puede concluir que, debido a que el grado de multi-disciplinariedad de un proyecto influye en gran medida en la creación de la diversidad tecnológica, las políticas públicas de desarrollo de tecnología deben favorecer la diversidad de disciplinas para evitar las dependencias tecnológicas tempranas, favorecer las innovación recombinante, y sobretodo asegurar el éxito de las nanotecnologías. Adicionalmente se puede concluir que al igual que han demostrado otros autores [331], [335], [336], [273], [323], [30], la estructura de la red debe ser un factor considerado en el desarrollo de proyectos tecnológicos, más aún cuando éstos involucren la convergencia de más tecnologías.

5.4.2 Sección II. Enfoque en la gestión de la innovación

En esta sección se estudiaron las estrategias de gestión de la innovación que fomentan la fertilización cruzada de TFEs. En un estudio previo de Maine et al, (2014), en un escenario de convergencia de las nanotecnologías y la biotecnología, se identificó que existen tres estrategias de gestión de la innovación: i) importar ideas a partir de una amplia red de organizaciones, ii) fomentar un entorno colaborativo, y iii) emparejar la tecnología con las necesidades del mercado. La primera estrategia se refiere a la búsqueda y síntesis de conceptos o ideas que pueden ser tomadas a partir de amplias redes con diferentes corrientes tecnológicas. La segunda estrategia consiste en el flujo dinámico de conocimientos entre los grupos de estrecha colaboración y, por último, la tercera estrategia trata sobre vincular la investigación con las necesidades del mercado.

En esta sección, estas tres estrategias son analizadas teniendo en cuenta ciertas características basadas en la capacidad de absorción de las organizaciones, su capacidad dinámica y la teoría de redes. En este sentido, dentro de la primera estrategia, la cual es relativa a importar ideas de amplias redes, se consideraron otros factores como: i) la distancia tecnológica que debe tener la red en cuanto al conocimiento compartido, ii) el esfuerzo tecnológico que las actores deben realizar para importar el conocimiento externo, y iii) la prioridad que los actores dan a pertenecer a una amplia red y por tanto al acceso de información o conocimiento externo. La segunda estrategia, referente al entorno colaborativo, consideró los siguientes factores: i) la colaboración previa, si es que la hubiera, entre los miembros del consorcio, y ii) el tipo de colaboración respecto a su nivel de formalidad. En cuanto a la tercera estrategia que se refiere a vincular la investigación con el mercado, se consideraron los siguientes factores: i) el grado de orientación al mercado, ii) el grado de priorización hacia el consumidor final o paciente, y finalmente iii) la experiencia previa de los actores en actividades de alta madurez tecnológica como, por ejemplo, la producción piloto o prototipo para la demostración de producto.

Para explorar estas estrategias y los indicadores propuestos para el análisis, se llevó a cabo una entrevista dirigida a los líderes de los proyectos. La entrevista tuvo varios formatos: digital, telefónica y presencial. Fue administrada desde el 28 de Mayo hasta el 8 de Julio del 2016, des pués de un proceso previo de pilotaje.

Se realizaron un total de 54 entrevistas, es decir un 26.2% de ratio de respuesta, con un 1.6% de error de muestreo al 95% de confianza. De los 54 entrevistados, 41 de ellos pertenecían a un consorcio colaborativo, por lo que las respuestas de éste grupo de personas fueron aquellas con las que se comprobaron las hipótesis planteadas mediante un Análisis de Correspondencia Múltiple (ACM).

Los resultados mostraron que altos niveles de fertilización cruzada correspondían con distancias tecnológicas cortas o moderadas, un alto esfuerzo tecnológico, una alta priorización del acceso a fuentes externas, un entorno de interacciones informales, una alta orientación al mercado, y un alto grado de priorización hacia el consumidor final. Sin embargo, no se pudo determinar una clara relación entre altos niveles de fertilización cruzada con haber tenido una previa colaboración con los mismos actores dentro del consorcio, ni tampoco haber tenido experiencia previa en actividades relacionadas a la producción piloto o demostración de producto.

Los resultados también reflejaron que los actores con mayor vinculación de conocimientos nanotecnológicos en sus procesos (**Figura 5.4**), se correspondían con mayores niveles de fertilización cruzada (**Figura 5.5**). Éste hallazgo confirma la naturaleza multidisciplinar y transversal de las nanotecnologías en diversas industrias, y lo que es más importante, resalta la relevancia en el proceso de fertilización cruzada.

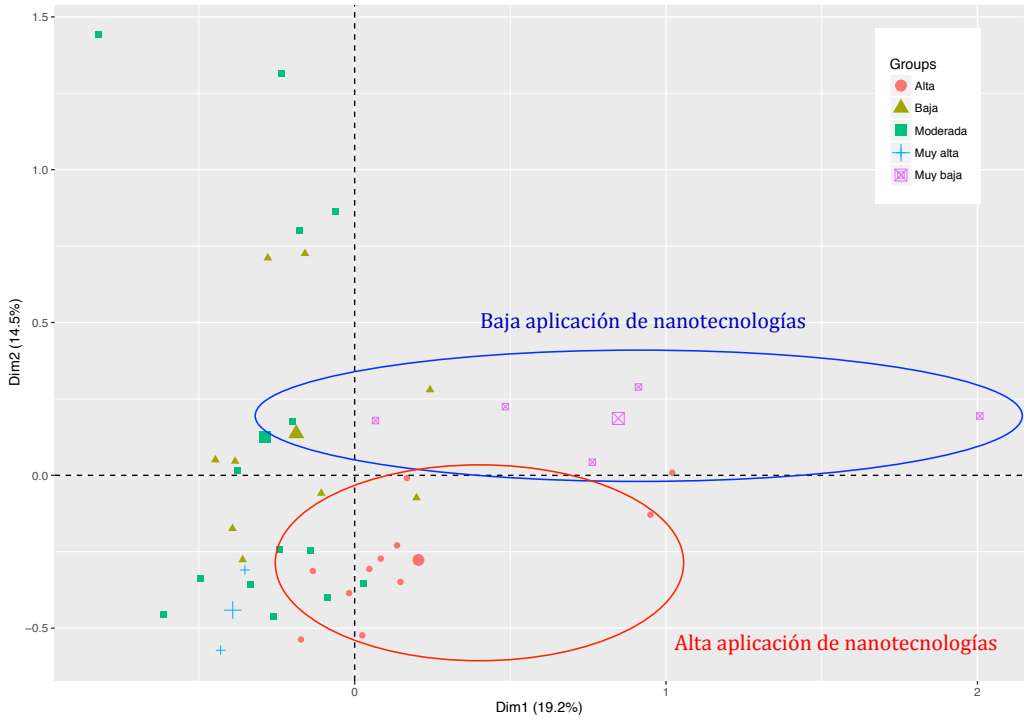

Figura 5.4. Análisis de Correspondencia Múltiple. El gráfico muestra a las organizaciones distribuidas en base al nivel de aplicación de nanotecnologías en sus procesos industriales.

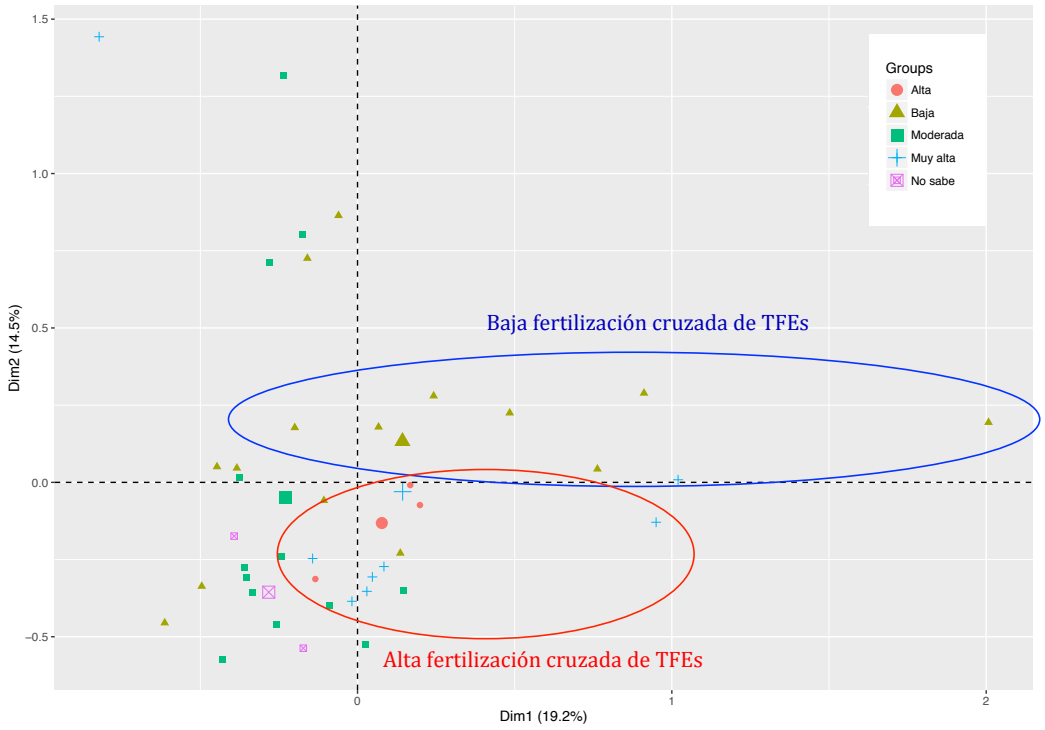

Figura 5.5. Análisis de Correspondencia Múltiple. El gráfico muestra a las organizaciones distribuidas en base al nivel de fertilización cruzada de TFEs.

Se puede concluir por tanto que las tres estrategias previamente identificadas por Maine et al., (2014) influyen en el proceso de fertilización cruzada, y que, dependiendo de ciertas características de la red, actividades o capacidades de las organizaciones, la fertilización cruzada de las TFEs puede ser fomentada en mayor o menor medida. Las aportaciones de este capítulo, por tanto, podrían ser apropiadas para redefinir políticas públicas que busquen innovar a partir de la convergencia de tecnologías.

5.5 Conclusiones de la tesis

En el presente trabajo se analizaron los procesos y ecosistemas de innovación en las nanotecnologías aplicadas al campo de la salud, enfatizando en la fertilización cruzada de las TFEs. Para ello se tuvieron en cuenta dos enfoques complementarios que apoyan la innovación, por un lado una perspectiva tecnológica y, por otro, una perspectiva de gestión de la innovación. En este sentido se han abordado temáticas y prioridades actuales referentes a la innovación y la transferencia de tecnologías

con el objetivo de expandir el conocimiento tanto científico como industrial que den respuesta a los nuevos desafíos que está atravesando la investigación pública.

Los principales resultados hallados indican que la multi-disciplinariedad, tanto en proyectos de innovación nanotecnológicos como en el grupo de expertos que lo desarrollan, tiene una influencia significativa en la creación de diversidad tecnológica y en el nivel de fertilización cruzada de las TFEs. En este sentido se sugiere que ésta característica pueda ser considerada como un factor muy importante a ser tomado en cuenta a la hora superar los retos de transferencia y de fomentar un ecosistema de innovación apropiado para el desarrollo industrial de las nanotecnologías.

Del mismo modo se determinó que las estrategias de gestión de innovación destinadas a incrementar el nivel de fertilización cruzada de las TEFs, deben estar principalmente orientadas hacia el mercado y el consumidor final, y que se deben desarrollar en ecosistemas que promuevan la innovación abierta. En este sentido se puede concluir que los factores relacionados con la estructura de la red, la capacidad de absorción, y las capacidades dinámicas de las organizaciones son decisivos en un escenario de convergencia de tecnologías.

Por otro lado, se encontró que las organizaciones con un alto conocimiento nanotecnológico, medido a través de sus patentes, presentaron una alta influencia en la creación de diversidad tecnológica. Así mismo, las organizaciones con mayor aplicación de las nanotecnologías en sus procesos industriales se correlacionaron con altos niveles de fertilización cruzada de las TFEs. Estos dos importantes hallazgos del estudio empírico confirman el papel transversal de las nanotecnologías y destacan la necesidad de aplicar esta tecnología en el sector industrial.

Por consiguiente, los resultados aquí presentados contribuyen a una mejor comprensión de los sistemas de innovación, los cuales están dirigidos a resolver las principales necesidades económicas y sociales actuales. En este contexto, esta investigación está alineada con el discurso de la economía basada en el conocimiento, la cual pretende cambiar la matriz productiva de una región a través del desarrollo de las actividades tecnológicas y el retorno social de las inversiones en ciencia.

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Appendices

Appendix A: Chapter 1

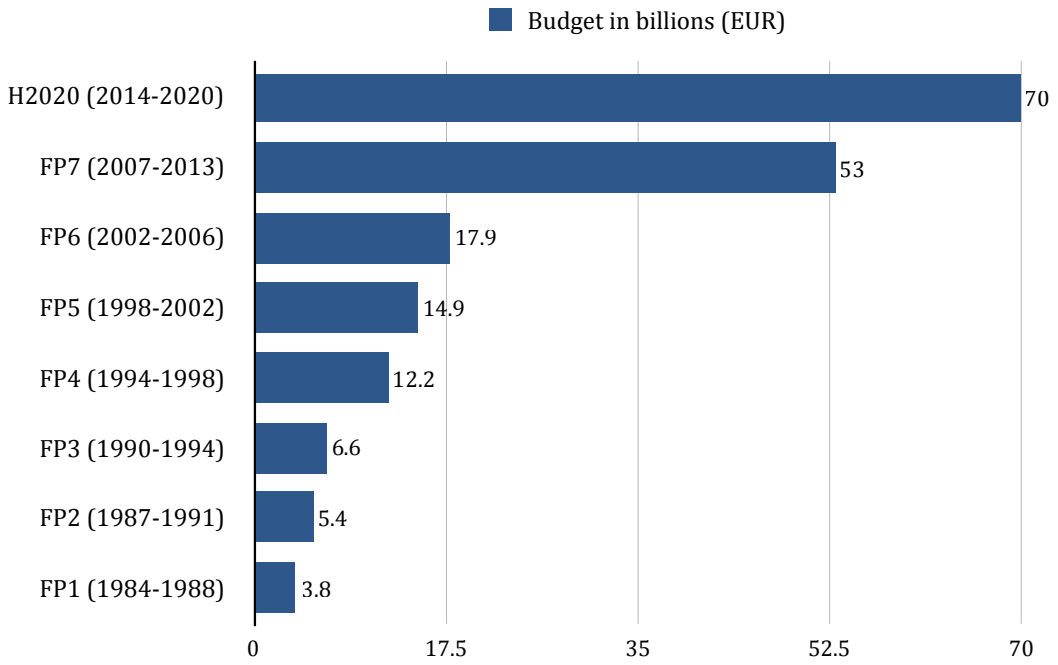

Figure A1. Progress in European Framework Programme's budget (Source: [164]).

Appendix B: Chapter 2

Table A1. Paradigm changes of nanoscale sensors for monitoring human health and behaviour.

	<2000	2000-2010	2010-2020	2020-2030	Medical applications
Pulse oximetry	1-2 cm^3	Attached wired <1 cm^3	Adhered, wearable, wireless reporting 0,1 cm^3	Implanted, embedded, wireless, remote 0,001cm^3	Cardiovascular, ICU, intraoperative surgical monitoring
Accelerometry	External, attached, wired, 1-2 cm^3	Attached wired <1 cm^3	Adhered, wearable, wireless reporting 0,001 cm^3	Implanted, embedded, wireless, remote < 0,001cm^3	Home monitoring, post-operative, geriatrics, orthopedics, neurology (gait analysis), cardiovascular
Pressure	External, attached, wired, 2-4 cm^3	Embedded wireless <1 cm^3	Implanted wireless 0,001 cm^3	Implanted, ingestive, wireless, remote < 0,001cm^3	Ob-Gyn (uterine), intra- & post-operative monitoring, gastro-, intestinal, orthopedics, prosthetics, cardiovascular
Humidity	External, attached, wired, 3-4 cm^3	Attached wired <2 cm^3	Wireless/remote optical sensing 0,001 cm^3	Implanted, ingestive, wireless, remote < 0,001 cm^3	Ob-Gyn (uterine), intra- & post-operative monitoring, gastro-, intestinal, orthopedics, prosthetics, cardiovascular
Galvanic potential (skin)	External, attached, wired, 3-4 cm^3	Attached wired <2 cm^3	Wireless/remote optical sensing 0,001 cm^3	Implanted, ingestive, wireless, remote < 0,001 cm^3	Ob-Gyn (uterine), intra- & post-operative monitoring, gastro-, intestinal, orthopedics, prosthetics, cardiovascular
Impedance (internal)	External, attached, wired, 3-4 cm^3	Attached wired <2 cm^3	Wireless/remote optical sensing 0,001 cm^3	Implanted, ingestive, wireless, remote < 0,001 cm^3	Ob-Gyn (uterine), intra- & post-operative monitoring, gastro-, intestinal, orthopedics, prosthetics, cardiovascular

	<2000	2000-2010	2010-2020	2020-2030	Medical applications
pH	External, attached, wired, 3-4 cm^3	Attached wireless <1 cm^3	Wireless implantable ingestible 0,001 cm^3	Implantable, ingestible, wireless, remote <0,001 cm^3	Gastrointestinal, intra- & post-operative monitoring, urology, wound healing
Glucose Sensors	External sampling	Sampling through skin with nano-needle arrays, implantable MEMS	Long-term implantable MEMS/NEMS with wireless monitoring and feedback for insulin delivery via wearable micropump	Incorporation of nanosensors in integrated artificial pancreas and/or encapsulated live-cell bioreactor	Diabetes, endocrinology, immunology
Fluorescence: nanodots for biomarkers	External (in cell cultures and lab samples)	Internal: IV, injectable; detection with fiberoptic probes, endoscopy(cancer)	Internal: IV, injectable; (detection with wireless spectroscopic probes) (other diseases)	Internal: IV, ingestible, injectable; (detection with wireless spectroscopic probes, external IR through-skin-monitors) (wide variety of diagnostics)	Cancer, infectious diseases, inflammatory, degenerative, genetic diseases
Nanosensors in tissue scaffolding	Concept	Experimental guidance of stem cell and autologous cell growth	Proof-of-concept; 1st prototypes; clinical trials; 1st approved uses	Use in medical practice on-demand generation of live-cell tissue scaffolds	Surgery, nerve, brain, and bone regeneration, joint of a cartilage, heart, burns and wounds
Nanosensors in neurosensory prosthetics	Concept, wireless operation	Experimental prototypes for improved retinal prostheses and cochlear implants with nanosensors	Reduction in size, power requirements; use of power harvesting via nanogenerators	Nanosurface engineering of sensor interfaces for improved bio-compatibility longer lifetime; live-cell integration	Vision, hearing

Source: [83].

Appendix C: Chapter 3. Section I

Nanotechnology-related patents. Research Query:

TS=((nano* OR "atom* scale" OR "atomic layer deposition*" OR "giant magnetoresist*" OR graphen* OR dendrimer* OR fulleren* OR "c-60" OR "langmuir blodgett*" OR mesopor* OR "molecul* assembl*" OR "molecul* wire*" OR "porous silicon*" OR "quantum dot*" OR "quantum well*" OR "quantum comput*" OR "quantum wire*" OR qubit* OR "self assembl*" OR supramolecul* OR supermolecul* OR "ultrathin film*" OR "ultra thin film*" OR monolayer* OR (mono-layer*) OR film* OR quantum* OR multilayer* OR (multi-layer*) OR array* OR pebbles OR NEMS OR Quasicrystal* OR (quasi-crystal*) OR (Scanning tunneling microscop*) OR (Transmission electron microsc*) OR (Atomic force microscop*) OR (Molecular electronic*) OR (Molecular machine*) OR (Molecular manipulat*) OR (Magnetic Resonance Force Microsc*) OR (Buckyball*) OR (Carbon tube*) OR (silicon AND ((light AND emit*) OR (purcell AND effect) OR microcavity OR microdisk OR microtore OR photonic* OR (laser AND detect*) OR Nanophoton* OR (laser AND modulat*))) OR ((Single-electron*) OR (Single electron*)) OR (Lab-on-a-chip*) OR (microarra* OR (DNA chip*)) OR (drug deliver*)) NOT (layer OR Plankton* OR n*Plankton OR m*Plankton OR b*Plankton OR p*Plankton OR z*Plankton OR NanoFlagel* OR NanoAlga* OR NanoProtist* OR Nanofauna* OR Nano*aryote* OR Nanoheterotroph* OR Nanophtalm* OR Nanomeli* OR Nanophyto* OR Nanobacteri* OR nano2* OR nano3* OR nanos_ OR nanog_ OR nanor_ OR nanoa_ OR nanog- OR nanoa- OR nanor- OR nanog OR nanosecond* OR nanomol* OR nanogram* OR nanoplankton* OR Nanometer* OR Nanomolar* OR Nanoliter* OR Nano-second OR Nano-meter OR Nano-molar OR Nano-gram OR Nano-liter)).

Appendix D: Chapter 3. Section II

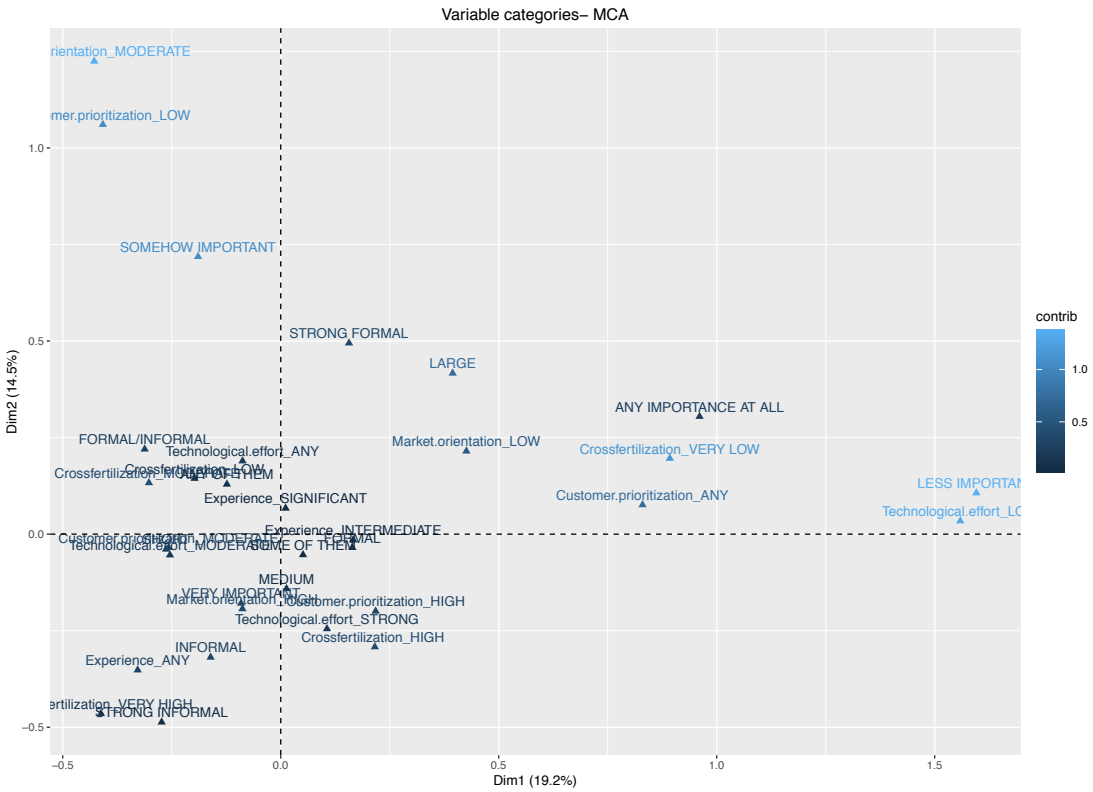

Figure A2. Contribution of each category to the two dimensions.

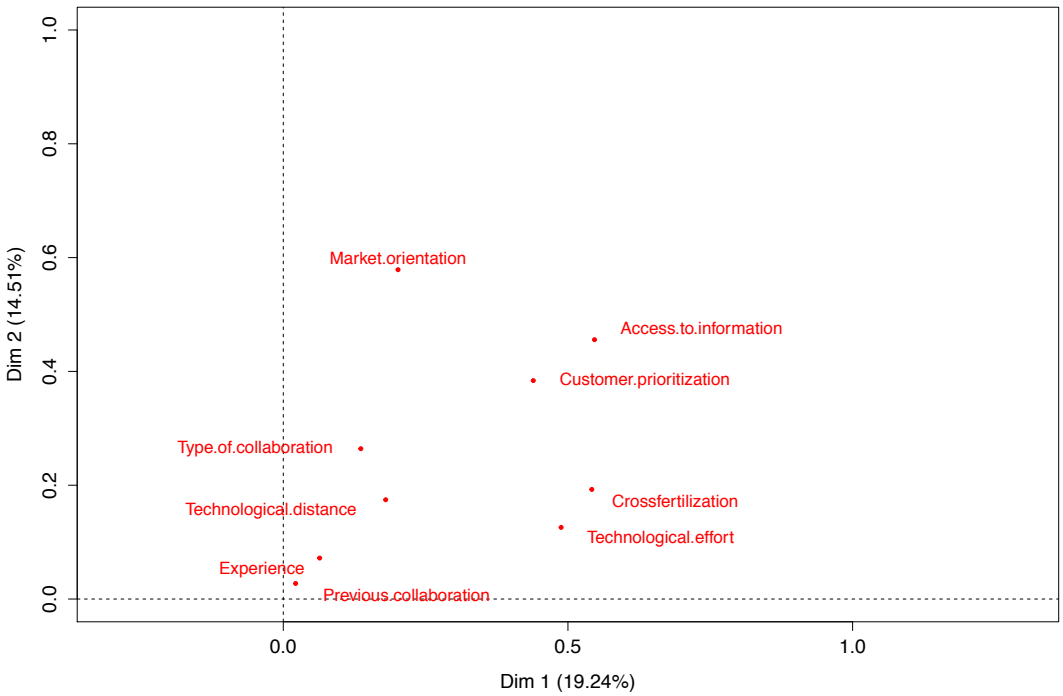

Figure A3. Contribution of each variable to the two dimensions.

Table A2. Characteristics of different formal and informal groups.

	What's the purpose?	Who belong?	What holds it together?	How long does it lasts?
Community of practice	To develop members' capabilities; to build and exchange knowledge	Members who select themselves	Passion, commitment, and identification with the group experience	As long as there is interest in maintaining the group
Informal network	To collect and pass on business information	Friends and business acquaintances	Mutual needs	As long as people have a reason to connect
Project team	To accomplish a specific task	Employees assigned by senior management	The project's milestones and goals	Until the project has been completed
Formal work group	To deliver a product or service	Everyone who reports to the group's manager	Job requirements and common goals	Until the next reorganisation

Source: [256].

Table A3. Decomposition of variability for the first 14 dimensions.

Dimension	Variance	% of variance	Cumulative % of variance
Dim 1	0,08	19,24	19,24
Dim 2	0,06	14,51	**33,76**
Dim 3	0,05	12,41	46,17
Dim 4	0,05	10,62	56,78
Dim 5	0,03	7,56	64,34
Dim 6	0,03	6,86	71,20
Dim 7	0,02	4,67	75,87
Dim 8	0,02	4,34	80,21
Dim 9	0,02	4,05	84,27
Dim 10	0,01	3,27	87,53
Dim 11	0,01	2,26	89,79
Dim 12	0,01	1,94	91,72
Dim 13	0,01	1,69	93,42
Dim 14	0,01	1,53	94,95

Table A4. Coordinates of each variable at the first two dimensions.

Variable	Dim1	Dim2
Cross-fertilization	**0,54**	0,19
Technological distance	0,18	0,17
Technological effort	**0,49**	0,13
Access to information	**0,55**	**0,46**
Previous collaboration	0,02	0,03
Type of collaboration	0,14	0,26
Market orientation	0,2	**0,58**
Customer prioritization	0,44	**0,38**
Experience	0,06	0,07

Appendix E: Interview

Institute for Bioengineering of Catalonia (IBEC); University of Barcelona, Department of Electronics; Bioelectronics and Nanobioengineering Research Group (SIC-BIO); University of Barcelona, Department of Economy; National Secretariat of Higher Education, Science, Technology and Innovation of Ecuador (SENESCYT)

Final version /English
April 2016

Interview: Cross-fertilization of Key Enabling Technologies (KETs) in the field of healthcare.

Interview

Interview addressed to the project leaders of the "Leadership in Enabling and Industrial Technologies" category from the Horizon 2020 Framework

BLOCK 1: GENERAL INFORMATION

Q1. Name of the organisation:

Q2. Name of the respondent (Optional):

Q3. Job title or function:

Q4. Project title or Project ID/reference number:

Q5. Role in the project:

BLOCK 2: ORGANISATION'S PROFILE

Q6. Which is the Size of the organisation?

□ Micro size (< 10 employees)
□ Small size (between 10 and 50 employees)
□ Medium size (between 50 and 250 employees)
□ Large size (at least 250 employees)

Q7. Which is the year of foundation of the organisation?

□ < 2000
□2000-2004
□2005-2009
□ 2010-2012
□ 2013
□ 2014
□ 2015

Q8. Where is the organisation located?

□ University
□ Science and Technology Park
□ Business incubator
□ Hospital

□ Industrial Park
□ Urban framework
□ Rural framework
□ Other (specify): _____

Q9. Which is the area of specialization that bests describes the specialization of the organisation?

□ Life sciences
□ Pharma
□ Materials
□ Manufacturing
□ Electronics and Photonics
□ Health
□ Food and Drink
□ Tools and Instrumentation
□ Education
□ Aerospace
□ Energy
□ Military
□ Other:_____

Q10. Which is the principal activity in the value chain of your organisation? Please, choose one:

□ R+D
□ Production
□ Commercialization
□ Service
□ Consultancy
□ Distribution
□ Formation
□ Transfer
□ Other (specify): _____

Q11. In your organisation, which is the level of application of nanotechnology knowledge?

□ Low (less than 30%)
□ Medium (between 60% -30%)
□ High (between 85% -60%)
□ Very high (over 85% of the products and processes)
□ Unknown

Q12. From the following Key Enabling Technologies (KETs), please rank those in which you consider your company has a significant technology domain.

	(0) Any domain	(1)	(2)	(3)	(4)	(5) Major technological domain
Micro/Nano-electronics	□	□	□	□	□	□
Nanotechnology	□	□	□	□	□	□
Photonics	□	□	□	□	□	□
Advanced Materials	□	□	□	□	□	□
Industrial Biotechnology	□	□	□	□	□	□
Advanced Manufacturing Systems	□	□	□	□	□	□
Other	□	□	□	□	□	□

Q13. Has your organisation participated in previous EU Framework Programmes?

□ Yes
□ No
□ I don't know

BLOCK 3: PROJECT'S INFORMATION

Q14. Which was the starting stage of the project at H2020? Please, select one.

□ Idea generation (TRL 0)
□ Basic research (TRL 1)
□ Technology formulation (TRL 2)
□ Applied research (TRL 3)
□ Small scale prototype (TRL 4)
□ Large scale prototype (TRL 5)
□ Prototype system verified (TRL 6)
□ Pilot system verified (TRL 7)
□ Commercial design (TRL 8)
□ Full commercial application (TRL 9)

Q15. Which is the envisaged final stage of the project at H2020? Please, select one.

□ Idea generation (TRL 0)
□ Basic research (TRL 1)
□ Technology formulation (TRL 2)
□ Applied research (TRL 3)

□ Small scale prototype (TRL 4)
□ Large scale prototype (TRL 5)
□ Prototype system verified (TRL 6)
□ Pilot system verified (TRL 7)
□ Commercial design (TRL 8)
□ Full commercial application (TRL 9)

Q16. Which of the following KETs are being included in the development of the project? Please rank the level of involvement in the project for each KET.

	Not at all	Very little	Somewhat	To a great extent
Micro/Nano-electronics	□	□	□	□
Nanotechnology	□	□	□	□
Photonics	□	□	□	□
Advanced Materials	□	□	□	□
Industrial Biotechnology	□	□	□	□
Advanced Manufacturing Systems	□	□	□	□

BLOCK 4: INNOVATION MANAGEMENT STRATEGIES

Q17. In your opinion, which are the motives to collaborate with partners in the project (beyond the requirements of the collaborative calls)? Please rank them.

	Any importance at all	Less importance	Somehow important reason	Very important reason
Access to competence	□	□	□	□
Access to economic resources	□	□	□	□
Access to technological/knowledge resources	□	□	□	□
Financial risk sharing	□	□	□	□
To speed up innovation process	□	□	□	□
Reduce market risk	□	□	□	□
Previous positive project experience with partners	□	□	□	□
Other specific reasons	□	□	□	□

Q18. Has your organisation previously collaborated with the same current partners in the <u>current project</u> from early stages of development?

□ All of them
□ Some of them
□ Any of them

Q19. If your answer was "all of them" or "some of them", specify in which stage of development the collaboration started. Please select one.

□ Idea generation (TRL 0)
□ Basic research (TRL 1)
□ Technology formulation (TRL 2)
□ Applied research (TRL 3)
□ Small scale prototype (TRL 4)
□ Large scale prototype (TRL 5)
□ Prototype system verified (TRL 6)
□ Pilot system verified (TRL 7)
□ Commercial design (TRL 8)
□ Full commercial application (TRL 9)

Q20. The process of communication or agreement with the partners of the project team has been (*select one*):

□ Very easy
□ Easy
□ Moderate
□ Somewhat difficult
□ Very difficult

Make a comment on your choice here:

Q21. Do you think that all the partners in the project benefit equally from the technological or knowledge recourses in the alliance network?

□ Equal benefit
□ Unequal benefit

Q22. What do you think about the technological knowledge of your organisation compared with the technological knowledge of your partners? It is:

□ Very similar
□ Slightly similar

□ Slightly dissimilar
□ Very dissimilar

Make a comment on your choice here:

Q23. Can you briefly explain which the criterion for selecting your partners was?

Q24. How many people are directly involved in the scientific/technical/managerial activities within the project?

□ < 5
□ 5 – 10
□ 10 – 15
□ 15 – 20
□ >20
□ Unknown

Q25. How the <u>decision making/problem solving</u> process within project is? Select all the appropriate

□ As a collective decision
□ Through a board/coordinator
□ Vertical bilateral
□ Only in consensus meetings
□ Only in informal meetings
□ Other (comment):_____

Q26. Approximately how many hours in a week your organisation spends in activities related to data and knowledge sharing from all participants?

□ Any
□ Less than an hour
□ 1 hour
□ 2 hours
□ 3 hours
□ More than 3 hours

BLOCK 5: COLLECTIVE PURPOSE OF THE PROJECT

Q27. Select the option that best fit to the following parameters regarding the collective purpose of the project (Select only one from each parameter):

The collective purpose of the project is:

□ To develop members' capabilities
□ To deliver a product
□ To accomplish a goal
□ To collect and pass on information
□ Other

Project members are established as:

□ Members who select themselves
□ Everyone who reports to the groups manager
□ Employees assigned by a senior management
□ Friends or business acquaintances
□ Other

The drivers of accomplishing the project are:

□ Passion, commitment and identification with the group's expertise
□ Job requirements and common goals
□ The project`s milestones and goals
□ Mutual needs
□ Economic purposes
□ Other

The relation with partners or team members lasts:

□ As long as there is interest in maintaining the group
□ Until the next reorganisation
□ Until the project has been completed
□ As long as reason to connect exist
□ Other

BLOCK 6: MARKET

Q28. Which activity do you think is predominant in the development of the project? Select one.

□ Use and protect internal knowledge
□ Search for external knowledge and share internal knowledge

Q29. In your opinion, which do you think is the principal driver of the product demonstration/pilot production of the project?

□ Market reasons (e.g. competitive pressure, customer requirements, estimated market potentials, etc.)
□ Information on research activities (e.g. originating from universities, research & technology organisations, universities, customers, competitors, etc.)
□ Access to public subsidies (e.g. tax refunds, investment support)
□ Market regulation activities (e.g. industrial policy, standardization activities, market deregulation, other environmental, or social legislation)
□ Others. (Specify)

Q30. Which is the degree of intensity that market research activities have in the development of the project?

□ Low
□ Moderate
□ High
□ None

Q31. Before or during the development of the project, have any of the scientists or engineers on the project observed customer/clinical practices, or developed ideas about unmet consumer needs?

□ Yes
□ No
□ Do not apply

Q32. During the product demonstration activities, is the final customer/end user being involved?

□ No
□ Yes
□ I don't know

Q33. When prioritizing potential markets for a technology invention, which of these factors, if any, were considered?

□ Potential alliance partners
□ Regulatory hurdles
□ Existing competitors
□ Costumer viability for technology attributes
□ Other

Q34. Has your organisation participated in any other activity in the context of product demonstration or pilot production?

□ Yes
□ No
□ Unknown/Do not apply

Q35. If yes, with whom does your organisation usually co-operate in the context of product demonstration or pilot production? Please select all that apply (multiple answers).

□ Customer
□ Supplier of manufacturing/plant equipment
□ Supplier of product materials/components
□ Universities
□ Other research & technology organisations
□ Engineering services
□ Other
□ Unknown/Do not apply

Q36. How many years of experience do you have with planning, setting up or operating product demonstration/pilot production activities?

□ Up to 1 year of experience
□ Around 2 to 5 years of experience
□ More than 5 years of experience
□ No experiences

BLOCK 7: PROFILE OF THE RESPONDENT

Q37. Please select your gender

□ Female
□ Male

Q38. Your age group is

□ <25
□ 25-34
□ 35-44
□ 45-54
□ 55-64
□ <65

Q39. Which is you educational background? Select all that are appropriate.

□ Engineering
□ Chemistry
□ Material science

□ Biology
□ Medicine
□ Biotechnology
□ Environmental science
□ Nanotechnology
□ Social Sciences
□ Economics and business organisation
□ Others (specify)_____

Q40. Which is your educational degree? Select one.

□ Graduate
□ Technician
□ Engineer
□ Master
□ PhD
□ Medical Doctor
□ Post-Doc
□ Other (specify)_____

Q41. Which is your role in the organisation? Select all that are appropriate.

□ Academic
□ Student/Undergraduate researcher
□ Researcher
□ Management
□ Business development
□ New product development
□ Manufacturing and production
□ Health and Safety
□ Documentation
□ Marketing
□ Other (specify)_____

Confidentiality:
Please select:
□ I accept that the name of the organisation can be published in the study's findings.
□ I do not accept that the name of the organisation can be published in the study's findings.

Study Findings
Please select:
□ I am interested in the study's findings.
□ I am not interested in the study's findings.

We sincerely appreciate your participation in this study.
Thank you very much.

Appendix F: Responses to the open questions

Below it is reproduced verbatim the comments from the open questions of the interview. These are codified according to **Section 3.2.1** and ordered as as follows:

- (Type of organisation_Type of project call_Country)

(Q20) Process of communication or agreement with partners or team members

- (PRC_NG_Spain) Easy. In general, we agree with most of the issues and always trying to keep a good communication network.
- (PRC_NG_Italy) Very easy. Coordination and organisation of the Consortium are very efficient. Some of the partners have already collaborated with our company and this greatly helps the communication.
- (PRC_NM_Spain) Easy. Not too much time. We communicate by mail principally.
- (REC_NG_Spain) Very easy. Because this process is held by a consultory enterprise that was sub-contracted (not an official partner of the consortium) for this job.
- (HES_NM_Ireland) Easy. We had worked with one of the partners previously and this made communication and agreement within the consortium easier than normal.
- (HES_NM_Netherlands) Moderate. Agreement is special difficult. Also the participation of layers in the project.
- (HES_NG_Spain) Easy. We do a lot of networking. We have previously collaborated and partners are previous contacts. All the projects start with confidence, experience and contacts.
- (PRC_BN_Ireland) Moderate. Dependent on the supplier/sub-contractor. Dealing with universities or institutes of technology has been difficult as we own our technology/IP outright but we need to work with some IoT/Unis to develop the prototype and their IP agreements have been quiet onerous.
- (PRC_BN_Spain) Somewhat difficult. Because it is difficult to the team to understand that projects are due long term.

(Q22) Technological knowledge from the organisation compared with the technological knowledge from the network

- (PRC_NG_Spain) Very dissimilar. We belong to the "applied technology" group in the project, and our expertise is more focus in medical devices/cosmetics than in nanotechnology.

- (PRC_BIO_Netherlands) Very dissimilar. Knowledge is very different. Each partner is specialist in his or her part of the project. Our company is more generalist, as we are consultants.
- (PRC_BIO_UK) Very similar. Similar level of knowledge, albeit different types of knowledge.
- (PRC_BIO_Italy) Very dissimilar. Each partner bring different competencies
- Lightly dissimilar. We are the consultant part of the consortium.
- (REC_NG_Spain) Very similar: All the partners in the consortium use the same materials but with different techniques, so we all produce a developed technology.
- (HES_NG_UK) Very dissimilar. Our end application is in a different market space to the other partners in the project and therefore we know our materials and technology the best with there being little input from the other partners. The materials that we are all manufacturing are similar and therefore we all have similar technical knowledge in this aspect. It was difficult to answer the above question when there are two definite aspects to the project - manufacturing and end application.
- (HES_NM_Ireland) Lightly dissimilar. The core technology was developed by our research group and commercialised by another partner will whom we have worked with on previous EU grants. The other partners were service providers who facilitated progression along the commercial pathway.
- (HES_NM_Netherlands) Lightly similar. Difficult to judge.
- (HES_NG_Spain) Very dissimilar. We avoid having overlapping of competences. Each organisation at the consortium knows each's technological knowledge. All of them have a different but complementary domain. At the beginning, not all of us speak the same language but during the development we arrive to do that.
- (PRC_BIO_Slovenia) Lightly similar. Very high expertise and technical knowledge of partners, however on complementing fields.
- (REC_NG_Portugal) Very dissimilar. The project consortium is highly complementary, including partners addressing all the issues of the proposed project from applied research to product development and then to product testing, evaluation demonstration and market dissemination. All the partners have agreed to allocate their most experienced and qualified personnel and the necessary infrastructure to achieve the project objectives. The consortium members bring enough critical mass and complementary expertise to achieve the technical and societal objectives of the project, as well as for spreading knowledge and technologies, and appropriately exploit project results. The contribution of all the partners is therefore crucial for the successful completion of the project.

- (REC_NM_Spain) Very dissimilar. In our project, three different nanopharmaceuticals developed by three partners in the consortium will be scaled up in the pilot plant under GMP.
- (HES_NG_Netherlands) Very similar. We all bring in high-end expertise in a highly complementary manner.

(Q23) Criterion for selecting partners or team members (Only for Coordinators)

- (PRC_BN_Greece) Competence and knowledge.
- (PRC_BIO_Slovenia) High technical expertise on required field and experience with applicative research.
- (PRC_NG_UK) Technology competence, position in the value chain to have complete value chain represented.
- (PRC_NM_Spain) Cover all areas required for the good success of the project
- (PRC_NG_Netherlands) We are a strong team that works well together and has a proven track of producing results during projects.
- (PRC_BN_Norway) Going forward, team members will be collaborating suppliers and acadeics.
- (PRC_BIO_Spain) The process followed for the selection of all the third parties has been made complying with best value-for money and in absence of conflict of interest. For each task to be outsourced we have request for offer to some companies and we have selected the best offer in terms of costs and especially, in terms of their experience in this field.
- (PRC_BN_Spain) Good quality and we have been working with some of them.
- (PRC_BIO_Norway) Complementary Competence, end user market access.
- (PRC_BN_Ireland) Their technical competence as well as their willingness to be fair players.
- (PRC_BN_Ireland) Knowledge and skillsets, availability of equipment, timelines.
- (PRC_BIO_Spain) Complementarity of expertise, interest to develop business and accessibility to end-users.
- (PRC_BN_Spain) They have contracted people to work in the project for different areas such as marketing, regulatory, etc., team members are the ones from the company, and they were selected because of their capacities (people from their own company).
- (PRC_BN_Finland) Knowhow.
- (REC_NG_Portugal) SKHINCAPS consortium was set up based on the project needs in terms of expertise, test facilities and industrial scale-up capabilities. Partners addressing all the issues of the proposed project from applied research to product development and then to product testing, evaluation

demonstration and market dissemination were invited to participate in the consortium, thus combining research capability and industry expertise.

- (REC_NM_Spain) Complementarity, know how on the technologies required in the project, previous experience.
- (REC_NG_Austria) Complementary expertise, access to market/end-users, experience from previous cooperation.
- (REC_BIO_Portugal) Complementary competences.
- (REC_NG_Neetherlands) Complementary know-how and excellence.
- (REC_BIO_Germany) Complementary technologies, competence, trust.

Appendix G: Scientific *curriculum vitae* of the author

Academic degrees

- **MSc. in Pharmaceutics Industry and Biotechnology**
  Pompeu Fabra University (UPF). July 2013. Barcelona, Spain.
- **Biotechnology Engineer**
  Army Polytechnic School University (ESPE). April 2012. Quito, Ecuador.

Outcomes and contributions

Publications

- **Páez-Avilés, C**; Juanola-Feliu, E; Punter-Villagrasa, J; Del Moral Zamora, B; Homs-Corbera, A; Colomer-Farrarons, J; Miribel-Catalá, P; Samitier, J. **(2016)**. Combined Dielectrophoresis and Impedance Systems for Bacteria Analysis in Microfluidic On-Chip Platforms. ***Sensors***. *16*(1514) 1-23.
- **Páez-Avilés, C**; González-Piñero, M; Juanola-Feliu, E; Bogachan, I; Mir M; Samitier, J. **(2015)**. Innovation and Technology Transfer of Medical Devices fostered by Cross-disciplinary Communities of Practitioners*.* ***International Journal of Innovation Management***. *19*(6), 15400121 - 154001227.
- **Páez-Avilés, C**; Juanola-Feliu, E; Ll. Miribel-Català, P; Colomer-Farrarons, J; Samitier-Martí, J. **(2014)**. Teragnosis *in vivo*: Innovación nanomédica fomentada por la convergencia de Tecnologías Emergentes. ***Revista Médica Vozandes*** *25*, 47- 54. ISSN: 1390-1656.
- Punter-Villagrasa, J; Cid, J; **Páez-Avilés, C**; Rodríguez-Villarreal, I; Juanola-Feliu, E; Colomer-Farrarons, J; Miribel-Català, P. **(2015)**. An Instantaneous Low-Cost Point-of-Care Anemia Detection Device. ***Sensors***, *15*(2), 4564-4577.
- Juanola-Feliu, E; Miribel-Català, P; **Páez-Avilés, C;** Colomer-Farrarons, J; González-Piñero, M; Samitier, J. **(2014)**. Design of a Customized Multipurpose Nano-Enabled Implantable System for *in vivo* Theranostics. ***Sensors***, *14*(10), 19275-19306.
- **Páez-Avilés, C**; Van Rijnsoever, F; Juanola-Feliu, E; Samitier, J. Multi-disciplinarity breeds diversity: The influence of innovation project

characteristics on diversity creation in nanotechnology. ***Journal of Technology Transfer***. (Under review).

- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. Cross-fertilization of Key Enabling Technologies: An empirical study of nanotechnology-related projects based on innovation management strategies. ***Journal of Engineering and Technology Management***. (Under review).

Books

- González-Piñero, M; **Páez-Avilés**, **C**; Juanola-Feliu, E; Samitier, J. **(2016)**. Innovation in the Videogames and the Biotechnological Sector. Origin, Evolution Revolution and a Comparative Study. *Lambert Academic Publishing*. ISBN 978-3-659-87185-6.

- **Páez-Avilés, C**; González-Piñero, M; Juanola-Feliu, E; Samitier, J. **(2015)**. Innovation by Cross-cutting KETs: Technology Transfer and Commercialization Challenges for Nanobiotechnology and Nanomedicine. *Lambert Academic Publishing*. ISBN 978-3-659-35932-3.

Oral dissertations in national conferences

- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Cross-cutting KETs: Innovation and Industrialization challenges for Nanobiotechnology and Nanomedicine towards Horizon 2020. *NanoBio&Med Conference 2014*, November 18-21. Barcelona, Spain.

- Juanola-Feliu, E, Miribel-Català, P; **Páez-Avilés, C**; Colomer-Farrarons, J; González-Piñero, M; Samitier, J. **(2014)**. Design of an implantable nano-enabled biomedical device for in-vivo glucose monitoring. *IEEE 2014 Conference on Design of Circuits and Integrated Circuits*, November 26-28. Madrid, Spain. ISBN: 978-1-4799-5743-9/14. (Presented by Juanola-Feliu E.).

- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Nanobiotechnology and Nanomedicine: Innovation and market challenges towards H2020. A multi-KET approach. *5th edition of Trends in Nanotechnology (TNT) International Conference*, October 27-31. Barcelona, Spain.

- Conference Moderator in Plenary Session in the *5th edition of Trends in Nanotechnology (TNT) International Conference*, October 30, 2014. Barcelona, Spain.

- Juanola-Feliu, E; Miribel-Català, P; **Páez-Avilés, C**; Colomer-Farrarons J; J., González-Piñero, M; Samitier, J. **(2014)**. Design of a Customized

Multipurpose Nano-Enabled Implantable device for personalized medicine. *5th edition of Trends in Nanotechnology (TNT) International Conference 2014*, October 27-31. Barcelona, Spain. (Presented by Juanola-Feliu E.)

- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Spanish Innovation and Market on Nanotechnology: An Analysis within the H2020 Framework. *NanoSpain Conference 2014*, March 11-14. Madrid, Spain.

Oral dissertations in international conferences

- **Páez-Avilés, C**; Van Rijnsoever, F. **(2016)**. Multi-disciplinarity breeds diversity: The influence of innovation project characteristics on diversity creation in nanotechnology. *The 2016 Technology Transfer Society Annual Conference*. November 3-5. Phoenix, US. (Presented by Van Rijnsoever, F.).
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2016)**. Nano-enabled medical devices: Mapping the cross-fertilization of key enabling technologies in H2020 projects. *The 8th World Medical Nanotechnology Congress & Expo.* June 8-9. Dallas, US.
- Punter-Villagrasa, J; **Páez-Avilés, C**; Colomer-Farrarons, J; Lopez-Sanchez, J; Juanola-Feliu, E; Miribel-Català, P; Cid, J; Kitsara, M; Aller, N; del Campo, J; Rodrigues-Villarreal, I. **(2015)**. A Portable Point-of-Care Device for Multi-Parametric Diabetes Mellitus Analysis. *Industrial Electronics Society, IECON 2015-41st Annual Conference of the IEEE*. November 09-12. Yokohama, Japan. (Presented by Punter-Villagrasa, J.).
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2015)**. CoPs in innovation and Technology Transfer of Medical devices. *XXVI International Society for Professional Innovation Management (ISPIM) Innovation Conference "Shaping the frontiers of innovation management"*. June 14-17. Budapest, Hungary.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Yachay: An Innovative Case Study Model of University-Company Cooperation in Latin America. *The 31st IASP World Congress 2014*. October 19-22. Doha, Qatar.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Nanobiotechnology and Nanomedicine: Innovation and Commercialization Challenges towards H2020**.** *Proceedings of the NanoBioEurope 2014 Congress***,** June 2-4. Munster, Germany.

Posters

- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2016)**. Cross-fertilization of Key Enabling Technologies: Nanotechnologies in healthcare. *Jornada d'Investigadors Predoctorals Interdisciplinària 2016*. February 2, 2016. Barcelona-Spain.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2015)**. Cross-fertilization of Key Enabling Technologies. Insights from nano-enabled Medical Devices. *NanoBio&Med Conference 2015.* November 18-20. Barcelona, Spain.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Bridging Research and Industrial Production towards H2020: Future challenges for Nanomedicine with a multi-KET approach. *NanoBio&Med Conference 2014*, November 18-21. Barcelona, Spain.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Innovation Ecosystems and Market Challenges in Nanobiotechnology and Nanomedicine: A multi-KET analysis within Horizon2020". *5th edition of Trends in Nanotechnology (TNT) International Conference 2014*, October 27-31. Barcelona, Spain.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Nanomedicine Innovation Ecosystem: An Analysis within the Horizon 2020 Framework. *NanoBioEurope 2014*, June 2-4. Münster, Germany.
- **Páez-Avilés, C**; Juanola-Feliu, E; Samitier, J. **(2014)**. Spanish Innovation and Market on Nanotechnology: An Analysis within the H2020 Framework. *NanoSpain Conference 2014*, March 11-14. Madrid, Spain.

Training collaborations

- *Invited Professor. Master of Nanoscience and Master of Bioengineering at the University of Barcelona.* Contents: innovation systems, innovation theories, indicators, collaborative models, technological diversity, KETs, case studies of nanotechnologies for health. November 2016. Barcelona, Spain.
- *Mentor of the STEM Educational Programme at the Menéndez Pelayo High school.* STEM (Science, Technology, Engineering and Math) is an informal educational initiative promoted by the City Council of Barcelona, in collaboration with the New York Academy of Sciences and the Education Consortium of Barcelona. This initiative connects doctoral students with future scientists. The aim is that students can assimilate curiosity and create knowledge trough science. Contents: Life Sciences Program, including the topics related with the cell, DNA, proteins, the immune system, and genetics. October–December 2015. Barcelona, Spain.

Training courses

- *25th European Doctoral Summer School on Technology Management.* University of Twente and the European Institute for Advanced Studies in Management EIASM. September 2015. Enschede, Netherlands.
- *Training course for Mentors of the STEM Programme for Doctoral Candidates.* Life Sciences. September 2015. Barcelona, Spain.
- *Measuring and Modelling Dynamics in Innovation Systems*. Doctoral Summer School. Utrecht University. August 2015. Utrecht, Netherlands.
- *Diploma in International Business.* Program focused on leadership in Latin America. Organised by Latinomics Org. in collaboration with the United Nations Organisation. June 2015. Vienna - Austria.
- *Science Parks and Areas of Innovation: Fundamentals Seminar.* International Association of Science Parks and Areas of Innovation (IASP). October 2014. Doha, Qatar.
- *Summer School on Management of Creativity in an Innovation Society*. Mosaic. HEC Montreal. June-July 2014. Montreal, Canada and Barcelona, Spain.
- *Introducció a l'Emprenedoria.* Barcelona Institut Emprenedoria. Universitat de Barcelona. (3 ECTs). February-April 2014. Barcelona, Spain.

Project collaboration

- Market research: sensor-based monitor Systems for chronic diseases. Company: Serveis Mèdics Cristòbal – SEMCAT, S.C.L. Principal Researcher: Dr. Pere Miribel Català. No. Of project: FBG 308279. June 2015. Barcelona, Spain.

Award

- Second Edition of the Constest Paraules de la Física**.** Comissió de Dinamització Lingüística de la Facultat de Física. Abril 2015.Barcelona, Spain.

Memberships

- Member of the *Global STEM Alliance: Science Alliance. The New York Academy of Science* since October 2015.
- Member of the *International Society for Professional Innovation Management (ISPIM)* since January of 2014*.*
- Member of the *American Scientific Affiliation (ASA)* since November 2014.