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ON THE DESIGN OF KNOWLEDGE TRANSFER MECHANISMS: APPLYING THE INCOMPLETE CONTRACTS MODEL TO DEVELOPMENTS IN BIOTECHNOLOGY

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ABSTRACT

This paper proposes a framework on how different mechanisms for knowledge transfer can be linked to the underlying technological life-cycle. Drawing on recent insights from the organizational economics literature, we analyze the design of knowledge transfer mechanisms and structures from an incentive point of view. The basic version of the incomplete contracts model (or property rights model) was adapted to include knowledge as an asset. Several empirical hypotheses can be derived from this model. They are contrasted with other theoretical approaches to model organizational growth and development, as we are specifically interested in the use of new ventures creation as a technology transfer mechanism. Using this framework as a starting point, a limited empirical test is conducted in two sub-fields of modern biotechnology: monoclonal antibodies and protein engineering. The results are interesting: the property rights model may add to current insights on spin-offs as a mechanism for knowledge transfer as well as to a better understanding of the incentive structures that influence an organization's decision to enter a technological collaboration with a university or another biotech firm.

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INTRODUCTION

In most Western economies, governments are stimulating the transfer of the fundamental knowledge available in their public research laboratories and universities for commercial application and purpose (e.g. Aldrich and Sasaki, 1995; Roberts and Malone, 1996; Van Dierdonck and Debackere, 1988). Academic institutions all around the world have developed a myriad of mechanisms to appropriate the benefits from the creativity of their researchers and research groups (Van Dierdonck, Debackere and Engelen, 1990). On the demand side, rapid technological change and the increased complexity of knowledge have enhanced the interest of established firms to design and to enter into research collaborations with academia (Debackere et al., 1996; Rogers and Gibson, 1994). As a consequence, both industry and academia have constructed a broad range of governance mechanisms to underpin their collaborative research activities. However, practice shows that those initiatives have met with mixed success. Research consortiums such as MCC in micro-electronics or SEMATECH in semi-conductors were successful in a limited number of research fields, mostly those where the technology was most mature (Rogers and Gibson, 1994). The use of patent offices to set up license contracts seems to have little effect in most scientific domains (Nelsen, 1991). Finally, policies aimed at stimulating entrepreneurial behavior have resulted in successes that are often ambiguous (Roberts and Malone, 1996; Roberts, 1991). As a result, those "practice" results demand for a better understanding of the factors that determine the boundaries of research between universities and industry.

Given this growing number of approaches to knowledge transfer, and taking into account the many difficulties they encounter, an increasing number of scholars have directed their attention towards explaining the causes and consequences of research collaborations. A first stream of research builds on the neo-classic economic premises and treats the choice to collaborate as a function of the appropriability regime (Grossman and Shapiro, 1985; Katz, 1986; Kesteloot and DeBondt, 1993; Levin and Reiss, 1988; Ordover and Willig, 1985; Sinha and Cusumano, 1991). These studies often adopt a rather static approach and focus on pre-competitive research collaboration among rivals that already compete in existing markets. The results of these studies tend to be sensitive to the restricting assumptions underlying the model[2], which limits their practical relevance in studying the optimization of various forms of knowledge transfer.

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[2] Most studies focus on the incentives to collaborate that *rivals* have in a *symmetric* industry. This means that it is hard to extrapolate their results to university-industry collaborations or to collaborations between very small and large companies.

A second research agenda draws upon the insights transaction cost economics offers to understand the evolution towards new structures of research governance (Ouchi and Bolton, 1988; Tapon, 1989; Williamson, 1975). Unlike the neo-classic stream which focuses on firms as production functions and considers the existing market structure to be a main determinant of know-how transfer, transaction cost economics stresses the importance of the costs of organizing and transacting knowledge exchanges as a determinant of the research boundaries between industry and universities (Besanko et al., 1995). Pisano (1990) was among the first to empirically address some of the insights offered by this stream of thought. He explores the research boundaries of large firms in the pharmaceutical industry. Among other results, he finds that the 'number of suppliers available' to conduct biotechnology research (namely the small biotech companies) within a certain application area, influences the make-or-buy decision within large pharmaceutical companies. Based on this observation, he concludes that small-numbers bargaining stemming from specialized R&D capabilities is one of the driving forces behind the decision to do in-house research. The transaction cost framework relies heavily on market imperfections which make collaboration between self-interested parties difficult or almost impossible. Although this framework offers a possibility to analyze collaborations between small and large firms, its application to the analysis of knowledge transactions in which one or both partners are public research institutes, remains limited. Clearly, when the research boundaries of the firm are changing, as witnessed by the growing number of transfer mechanisms and institutional arrangements that foster research collaborations, additional theoretical insights are needed.

In the meanwhile, the institutional economic debate on the theory of the firm has ventured into models that explain the boundaries of the firm in terms of the incentives resulting from asset ownership (Hart, 1989) as well as the complementarities that arise amongst asset ownership, job design and incentive systems as intra-firm practices (Holmstrom and Milgrom, 1994). While addressing the incentives issue related to asset ownership, Grossman, Hart and Moore (1986, 1990) introduced the 'incomplete contracts model.' The model shows how the inability to write complete contracts determines the distribution of asset ownership among various agents. It has been further elaborated by Brynjolfsson (1994) to include information as an asset. Adopting Brynjolfsson's (1994) approach, we model knowledge as a separate asset to better understand the genesis of different modes of knowledge transfer. This stance opens new perspectives for the analysis on the incentives to transfer know-how and it will be used throughout this paper as a starting point for analyzing the 'optimal' application of different modes of technology transfer.

In addition to modeling knowledge as a separate asset, we also address the "static" nature of most knowledge transfer models developed sofar. As shown previously, technological progress is a dynamic process in which the nature of the technology or knowledge changes over time. Continuous changes are often related to progress along a technological trajectory defined by a technological paradigm while discontinuities are associated with the emergence of a new paradigm (Dosi, 1982). It is likely that the diffusion of knowledge and the optimal governance modes to stimulate this knowledge transfer will be

different in the different stages of technological development. Therefore, we explicitly incorporate the stage of technological development as an explanation for differences in knowledge transfer.

The remainder of the paper is structured as follows. We begin with a brief literature review and an elaboration of the incomplete contracts model to include knowledge as an asset. Subsequent sections discuss the hypotheses which can be derived from this basic model and describe the data on which the empirical test of the model is based. Finally, we analyze the results and draw conclusions for further research.

LITERATURE REVIEW AND MODEL SPECIFICATION

From Neo-Classic Economics towards Property Rights Models: An Overview. As mentioned in the introduction, one reason why theories fail to provide an insight into the motives for research collaborations or knowledge transfer lies in their more fundamental weakness of explaining the research boundaries of the firm. For instance, neo-classic economic theory views the firm as a production function. A particular firm is assumed to choose the optimal level of R&D expenditure based on its own probability of success in R&D, that of its rival firm and the exact nature of the project, measured in terms of appropriability (Katz, 1986; Sinha and Cusumano, 1991). Success in R&D is usually measured in terms of a certain "prize," which is often approximated by the expected net present value of future profits. However, in practice, basic research seems not to be solely driven by the firm's profit motive, but to a large extent by the logic of scientific advance as perceived by the scientists (Rappa and Debackere, 1993&1995; Tapon, 1989:199).

The transaction cost model turns the attention from an analysis of production costs towards the coordination or transaction costs of internal organization. The fundamentals of transaction cost theory date back to Coase (1937), who stated that organizations exist because, in certain circumstances, they minimize *transaction* costs in a more efficient way than spot markets do. An important aspect of the theory is that the nature of the transaction[3] will influence the costs associated with it and hence determine the optimal way of organizing this transaction (with hierarchies and spot markets as two extreme forms of organization). Translated to a research environment, the nature of the "know-how" which is transferred from university to industry will determine the costs associated with this transaction. Because of the complex nature of knowledge, the large amount of uncertainty involved with it and the relatively long-term orientation of research, Teece (1988) concluded that transaction costs involved in

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[3] Building on Williamson's (1985) summary, Milgrom and Roberts (1992:30) distinguish five attributes of transactions which may influence transaction costs: (a) the level to which the investments associated with the transaction are **specific** to this transaction; (b) the **frequency** with which similar transactions occur and the **duration** or period of time over which they are repeated; (c) the **complexity** of the transsaction and the **uncertainty** about what performance will be required; (d) the **difficulty of measuring performance** in the transaction and (e) the **connectedness** of the transactions involving other people.

knowledge transfer may make in-house research the only viable alternative. Unfortunately, neither Williamson (1985), who championed the theory into management research, nor Teece (1988) who applied it to analyze transactions on the market for know-how have defined the exact nature of these costs.

In addition to the transaction cost model, the principal-agent model has become increasingly important over the past fifteen years (Holmstrom, 1979). In contrast to transaction cost economics, which focuses on the "transaction" as the main unit of analysis, principal-agency theory builds on the neo-classic assumptions to explain managerial decisions *within* the firm (Eisenhardt, 1989; Holmstrom, 1979). Rooted in information economics and risk sharing theory, the principal-agent model uses information asymmetry as a crucial element in explaining owner-manager or supervisor-employee relations. Because the principal is not able to observe directly the amount of effort spent by an agent, an incentive problem arises[4]. Quite recently, Holmstrom (1989), using an extended version[5] of this model, derived the hypothesis that smaller firms have a competitive advantage over large firms in conducting highly innovative research. Larger firms have a mix of highly innovative and highly routine tasks which introduce incentive problems according to this model. Small firms avoid these problems by focusing solely on highly innovative tasks. Notwithstanding the interesting results derived from the principal-agent models discussed so far, these models do not yet get to the core of the knowledge transfer problem because their results do not depend on the organizational location of the agency relation (Holmstrom, 1989).

Hence, each of the economic theories described above, needs additional elaboration to help explain the technology transfer decision. Or to use Hart's (1989: 1764) words:

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[4] In a basic principal-agent model, the agent's performance can be written as: $X = E + \varepsilon$ with X as a measure of the agents performance, E is the amount of effort an agent puts in the project and ε is a normally distributed error term of which the variance v is beyond the control of the agent. The principal is unable to observe E, but can measure X. An incentive contract specifies the payment $s(X)$ when X occurs. The net benefit of the contract for the principal depends on the total performance of the agent X minus the amount the principal pays for it in an incentive contract, namely $s(X)$. The net benefit for the agent is a function of his incentives $s(X)$ and the cost of effort c(E), modified by a parameter of absolute risk aversion, r. Assuming that the agent has an exponential utility function, his net benefit takes the form of $\exp\{-r(s(X)-c(E))\}$. The incentive problem with which the manager is confronted with, then boils down to choose s so that it optimizes the agents efforts without burdening him too much with risk. The reduced linear form of such an optimal incentive contract can be written as $s(X) = ax+b$ with a is a piece rate contingent upon his performance and b is a flat salary component, which basically serves to make the agent participate in the project. Optimizing the net benefit for agent and principal gives the following result: $a = (1+kr\sigma^2)^{-1}$. The intuition behind this result is: the agent's commission (variable component) and hence his share to the profits is higher, when his aversion to risk is lower (lower r), when the variance of the error term is lower (lower σ^2) and when his openness to incentives is lower (lower k).

[5] The extended version allows an agent to perform various 'activities.' The basic insight derived from this model is that mixing activities with a different variance in the error term (in other words some of which are easy to measure and some of which are difficult to measure), introduces incentive problems. In an optimal setting, both activities should be carried out by different persons. We refer to Holmstrom and Milgrom (1989) for a detailed discussion of this model.

"All the theories discussed so far suffer from the same weakness: while they throw light on the nature of contractual failure, none explains in a convincing or rigorous manner how bringing a transaction into the firm mitigates this failure."

In order to build a more comprehensive theory on the boundaries of the firm, Hart together with Grossman (1986) and Moore (1990), elaborated the "property rights model." A key assumption of this model is that in practice, unlike in agency theory where the principal aims to write an optimal incentive contract, most contracts written by organizations are incomplete. A number of elements make it impossible to write complete contracts: First, the managers who write contracts are confronted with what Simon (1957) has defined as "bounded rationality." This means that on the one hand new contingencies may arise which are not specified in the contract or on the other hand companies may simply find it too costly to specify all existing contingencies in a contract. Next, it might be impossible to measure the performance of the transactions specified in the contract. Especially knowledge transfer might only have results which can be observed on the long term. The complexity of such a transfer makes it impossible to capture it in a contract. Hence, the scope of the contract will generally be a negative function of the complexity of the subject and the probability of unexpected contingencies during the term of the contract (uncertainty). In other words, certain rights will be specified in the contract, but there remain *"residual rights"* that are not contracted for. In general, when these residual rights relate to the use of an asset, the owner of that asset will retain control over them. For instance, if a research contract between a university lab and a biotechnology firm says nothing about 'updating' the equipment used, then it is the owner of that equipment who decides whether to update it or not.

Property Rights: Modeling Knowledge as a Separate Asset. The discussion in the previous paragraph suggests that the party that holds the residual rights to some of the essential assets or, more specifically, that is the owner of these assets will increase its *ex-post* bargaining position in the deal. In our example, the owner of the medical equipment will decide whether to update it or not. If, for instance, the owner is the university lab and if an update of its medical equipment significantly increases the value of the output for the other party, i.c. the biotechnology firm, then the ex-post bargaining power of the university lab will be inefficiently large. Basically, the biotech firm will rely on the goodwill of the lab to update its equipment (under the assumption that no comprehensive contract can be written to deal with this problem). If, on the other hand, the owner of the equipment is the biotech firm and if the update of the equipment is most beneficial for this firm, then the university lab will bear the risk of going unpaid for the re-training of its researchers to work with this new equipment. This situation is called the incentive dilemma under incomplete contracts. The Grossman, Hart and Moore framework (further abbreviated as GHM) suggests that this dilemma can be mitigated if those parties that control the most essential means of production are given an essential amount of ex-post bargaining power resulting from asset ownership.

The initial framework only includes the physical, non-human assets such as machines or equipment. Of course, in many high technology industries not only the physical assets may play an important role in producing value. Also 'knowledge assets' will be an important part of the value creating chain. Following Brynjolfsson's (1994) work[6], we have extended this initial model to include these knowledge assets in the property rights framework. Including knowledge as a separate asset in the model though, introduces the question of alienability. Physical assets are almost by definition alienable. One can always trade the rights of ownership to that asset. For knowledge assets, alienability is not that straightforward. A key question that should be addressed is then as follows: under what circumstances is knowledge alienable and what are the underlying social and technical dimensions that make it alienable?

Only if knowledge is alienable, one can consider the full option of jointly owning the physical and knowledge assets. When there is a high degree of complementarity between both assets, this may be considered as the most efficient way of organizing. The relative price at which one asset then can be transferred towards the owner of the other asset, will determine whether it is more efficient to transfer the know-how assets towards the owner of the physical assets or vice versa. However, if knowledge is not alienable, one can only pose the question whether the party that has the knowledge should own the physical assets as well or whether another party should have the ownership rights to them. Under conditions of high complementarity between both assets, this single ownership option may be a second-best alternative to the joint ownership option. Brynjolfsson (1994, pp. 1652) calls the difference between the values created between the two alternatives *"the value of alienability."* Both the alienability of knowledge as an asset and the complementarity between the physical and knowledge assets are now hypthesized to shape the organizational structures and subsequently, the research boundaries of the firm, in modern biotechnology research.

A Dynamic View on the Property Rights Model. A second dilemma facing many models used to assess research collaborations (or the boundaries of R&D) is their static nature. This is in sharp contrast to the empirical studies which suggest that technology evolution is best described by a punctuated equilibrium model (Anderson and Tushman, 1990; Tushman and Anderson, 1986). Using data from a number of industries, Tushman and Anderson (1986 & 1990) show that technology evolves through periods of incremental change punctuated by technological breakthroughs that for the existing firms can be either competence enhancing or competence destroying. Periods of technological breakthroughs are often associated with the emergence of a new technological paradigm; while incremental changes are related to progress along a technological trajectory defined by a technological paradigm (Dosi, 1982). Technology distinguishes itself from basic science in the pre-paradigmatic phase in the sense that it includes the search for an optimal set of heuristics to develop a new commercializable product, whereas basic scientific work aims to solve problems of scientific relevance not necessarily taking the

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[6] Brynjolfsson extended the property rights model with information assets as a variable.

commercial side into account (Debackere et al., 1994). Characteristic for the pre-paradigmatic stage is that knowledge is difficult to communicate. Different research groups 'compete' to find the right set of solutions to further develop the technology. Once this set of solutions is found, a technological paradigm emerges which can be both competence enhancing or competence destroying. Competence enhancing means that the new technology enforces the value of the complementary assets in hands of the existing firms, while competence destroying means that new complementary assets are needed to commercialize the technology (Abernathy and Clark, 1985).

Modeling Knowledge Transfers. Based on the discussion in the previous paragraph, we conclude that changes in the "alienability" of knowledge and changes in the complementarity between the physical and knowledge assets are both good candidates to model technical progress from a property rights perspective.

We depart from the initial situation in which knowledge is not alienable and there exists an optimal degree of complementarity between the knowledge and physical assets. This means that both the physical assets and knowledge assets cannot create any value when they are not used in combination with each other. One can think of such situations in the pre-paradigmatic phases of technological development (Dosi, 1982). The knowledge assets are strongly tied with the top scientists or engineers that perform the research. The complementary physical assets[7] are embodied in the (in some cases highly specialized) equipment these people use. Without the equipment, the scientists or engineers can not make any progress. The equipment itself does not add any value in the process of technological development unless it is used by those who control the knowledge assets.

Consider now the case in which these both assets are controlled by different agents. In the pre-paradigmatic phase of technological development, it is very difficult to predict the "outcome" of one's research efforts. In terms of the property rights model, there are too many contingencies involved to write a comprehensive contract. In the absence of such a contract, the engineer or scientist who creates some potential value is subject to hold-up by the agent who controls the physical assets. For instance, the university or company in which the researcher is employed can threaten to withhold the necessary equipment and use it for other purposes. On the other hand, also the employer faces a hold-up problem because the engineer or scientist can leave the company or university which makes the equipment obsolete. Therefore, both parties will bargain for the division of the total marginal benefit created by their marginal efforts (under Nash bargaining, each party gets 1/2 of the marginal value). In the equilibrium, each party will invest till the marginal cost of the investment equals the marginal benefits. The property rights model, which includes knowledge as an asset then generates the following first order conditions (the top scientists are indexed by 1 and the other party by 2):

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[7] It should be noted that in the pre-paradigmatic phase the complementary assets do not include the distribution channels and other assets needed to 'commercialize' the technology, but the equipment used to develop this technology.

$$1/2v^1(A_P, A_K) + 1/2v^1(A_K) = c'_1(x_1) \qquad \text{(1a)}$$

$$1/2v^2(A_P, A_K) + 1/2v^2(A_P) = c'_2(x_2) \qquad \text{(1b)}$$

with A_P, = physical assets and A_K = knowledge assets
v^1 and v^2 the marginal benefit for each of the parties
and c'_1, c'_2 the marginal cost of investment each of the parties faces.

As the second term in equation (1a) and (1b) is zero (the physical assets and the knowledge assets are useless when they are not used in combination with each other), each party faces the total marginal cost of investment but only captures half of the marginal benefits. Therefore both parties will under-invest and asset ownership should be given to one of them.

From an incentive point of view, ownership on both assets should be given to either one of the parties. Which one ultimately depends upon the relative value of the physical assets versus the value of the technology. In the pre-paradigmatic stage, where knowledge is highly inalienable, it is clear that the best option would be to give the residual ownership rights to that party which possesses the knowledge as well, i.c. the engineers or scientists. In other words, the analytic model developed in equations (1a) and (1b) indicates that, in the pre-paradigmatic phase, engineers or scientists will have optimal incentives to develop a technology if they receive the residual ownership rights to the physical assets as well. A practical implication of this analysis is that technology transfer, in such a pre-paradigmatic stage, should be realized through stimulating spin-off companies, in which the key researchers own the physical assets (von Glinow and Mohrman, 1991).

Once a technological paradigm has emerged and knowledge becomes alienable at a decreasing price, the model changes. Then, the relevant question is not anymore *who* should jointly own the knowledge and the physical assets, but which part of the knowledge or physical assets can "in an optimal solution" be transferred to a second party. Let us take the example of a new technology based firm which wants to pursue three research projects. It has the choice between "outsourcing" one of the projects to an agent who has the most up to date knowledge to finish this project (e.g. a research lab at the university) or to perform them all in-house. When research lab 1 owns the 'research project' or knowledge asset A_{K1} then the first order conditions for this research lab are[8]:

$$1/3v^1(a_i, A_{K1}, A_{PK2}, A_{PK3}) + 1/6v^1(a_i, A_{PK1}, A_{PK2}) + 1/6v^1(a_i, A_{K1}, A_{K3}) + 1/3v^1(a_i, A_{K1}) = c'_1(x_1) \qquad \text{(2a)}$$

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[8] The division of bargaining power is calculated by using the Shapley value (Shapley, 1953). The Shaply value in the three agent case can be derived as follows: Agent 1 can be in four coalitions: {1,2,3}, {1,2},{1,3} and {1}. The probability of being in each of those coalitions is 1/3, 1/6, 1/6 and 1/3, respectively.

with A_{K1} = knowledge asset for research project 1
and a_i= private information
v^1 the marginal benefit for party 1
and c'_1 the marginal cost of investment party 1 faces.

Alternatively, if all the "knowledge" is owned by the biotechnology firm, then the first order condition for the research lab can be written as:

$$1/2v^1(a_i, A_{K1}, A_PK2, A_PK3) = C'_1(x_1) \qquad (2b)$$

Again, in those cases where the knowledge which can be obtained from the research project is only "weakly complementary" with the other knowledge assets (other research programs) of the technology based firm, then it is beneficial from an incentive point of view to out-source the project while the specialized research lab itself retains the property rights to the knowledge involved in the latter project. One might think of such a situation as a research collaboration between a university and a new technology based firm in which the technology based firm licenses or out-sources a part of its research program to the university. From the point of view of the university, this means that technology transfer becomes possible through patent vehicles.

Figure 1 gives a schematic overview of the most important policy insights which can be derived from the property rights model. The two key dimensions which play in the model are: (a) the degree of complementarity between the physical and knowledge assets or among the knowledge assets themselves and (b) the alienability of knowledge. The reasoning is as follows: in the pre-paradigmatic stages of technology development, knowledge is not alienable. If, in these stages, the physical assets to generate or further develop the technology are of crucial importance, then these assets should be in hands of the scientists or engineers that embody the knowledge assets (equations (1a) and (1b)). If not, the residual rights are in hands of the organization which owns the physical assets, which in turn creates disincentives for the researchers. Hence, in the early stages of technological development, stimulating spin-off companies might be the most appropriate choice of technology transfer[9].

Once the technology becomes more mature (e.g. once a technological paradigm is established), knowledge turns out to be alienable through the use of property rights[10]. At this stage, equations (2a)

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[9] Note that this argument does not depend on whether industry or universities are the main institutional sources of this technology. Spin-offs occur from both types of organizations. In practice, the semi-conductor industry is an example where spin-offs mainly resulted from existing electronics companies, whereas the biotechnology industry represents a context where spin-offs were mainly university driven.

[10] Patents are only one form of property rights which guarantee knowledge alienability. Other property rights which are determined by common law include property rights and to a lesser extent trade secrets (that are covered by the trade secret law). Still other property rights do not find their roots in common law; though in a mutual respect by the industrial partners or consumers (Kay, 1993). Reputation and to a lesser extent trademarks are an example of these kinds of property rights. We refer to Besen and

and (2b) suggest that new technology based firms have an incentive to look for other partners to perform their basic research activities with as long as the knowledge involved in these new activities is only 'weakly' complementary to the existing physical assets and to the existing knowledge assets. One can think of new technology based companies which have developed or commercialized their core technologies and now look for universities or specialized firms to supply knowledge which is complementary to but not too much entangled with the core knowledge they have in-house and with the different physical assets which they have accumulated. In these technical sub-fields, universities can set up patenting offices to commercialize their technology. In other words, research laboratories that want to perform contract research for existing companies should take into account that, from an incentive point of view, these companies will be most willing to out-source projects which belong to the technological sub-fields outlined above.

The analytic model also suggests two corollaries. First, in a pre-paradigmatic stage of technology development, it is less optimal to stimulate research collaboration between university and industry. The reason is straightforward: every time a research laboratory or a university department has developed a sufficient critical mass, the researchers have an optimal incentive to spin off their own company. Attempts from the university to commercialize their knowledge through research may create ex ante disincentives to invest in the development of this knowledge. On the other side, collaboration efforts undertaken by the industrial partners do not succeed because the researchers lack the incentive to collaborate on a long term basis. Second, once knowledge becomes alienable, this does not mean that spin-off companies are not fruitful anymore. The model only suggests that there is an incentive to collaborate, maybe in specialized sub-domains, either with other new technology based companies or with the universities themselves. One can think of universities that choose to bundle their knowledge resources and form a semi-independent company that acts as a catalyst between the 'generalist' companies that already existed and the university laboratories themselves.

These ideas are summarized in Figure 1 below. In this model, we further assume that when the technology is still in its pre-paradigmatic stage and the complementarity of assets is low, participation in informal technological communities and the researcher networks that develop in their context, might be the better solution to the knowledge transfer process. In case technology is well-articulated and complementarity of assets is high, the (multi-partner) consortia are hypothesized to provide a viable transfer mechanism. Hence the four quadrants modeled in Figure 1. However, in the context of this paper, we will focus on the trade-off between the formation of a new venture (the so-called "spin-off" company) and the development of a research collaboration, as indicated by the direction of the arrow drawn in Figure 1.

Raskind (1991) for an oversight of the intellectual property rights and their impact on economic activity.

Figure 1: Technology Transfer From A Property Rights Point of View
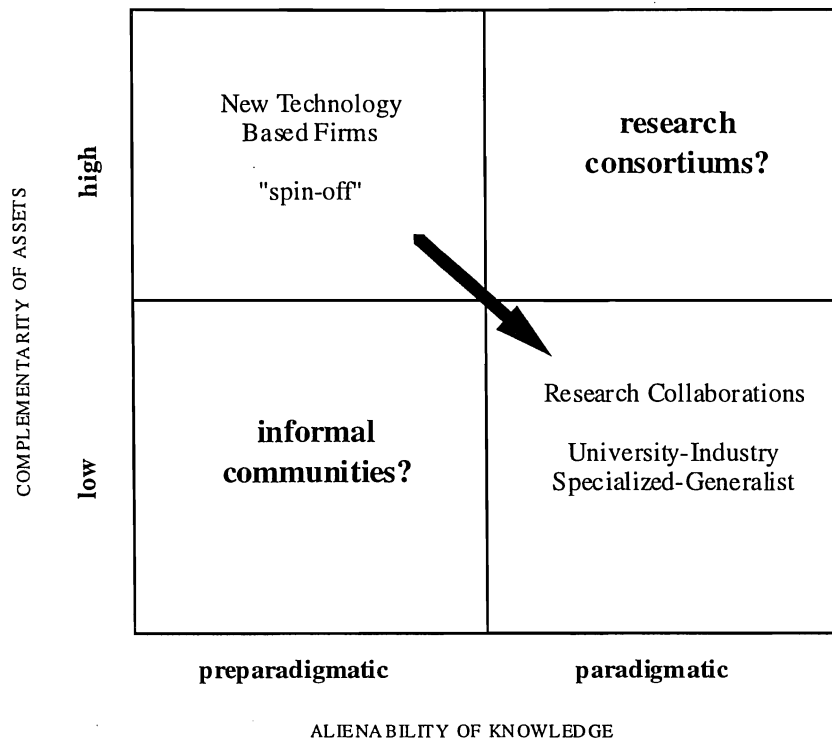
So far, we specified how the incomplete contracts model might contribute to an increased insight in the process of knowledge transfer, defined from an incentives perspective. The analytic model now generates a set of empirically testable hypotheses, that are further developed in the next session.

HYPOTHESIS DEVELOPMENT

One of the first insights derived from the property rights model is the relationship between the stage of technology development and the number of foundings in the industry. The underlying rationale is that in the pre-paradigmatic stages of technology development, the knowledge associated with this technology is inalienable. From an incentive point of view, the model shows that in this case the scientists or engineers who develop the knowledge should own the physical assets needed to develop it. In other words, they are stimulated to found their own technology based company. Once that knowledge becomes more alienable, we might hence expect less foundings based on the technology. Hence, a negative relationship is supposed between the number of new technology based foundings in a technological community and the alienability of knowledge in that community.

In order to empirically test this relationship, we should control for competing explanations that have been developed in the literature as (community-level) explanations for organizational founding. The

most extensive and most elaborated among them is 'organizational ecology.' Organizational ecologists have incorporated the study of founding as a focal topic in their research agenda (see Table 1, for an overview). Their main argument is that population-level dynamics shape the patterns of founding. In the early eighties, Delacroix and Carroll (1983) empirically investigated this hypothesis in a population of Argentine New Papers. They found a curvilinear relationship between population density, measured as the number of organizations at any period in time, and the founding rates in the populations under study. The theoretical explanation is as follows: organizational density is determined by the prior failures and the prior foundings in a population. Both dimensions have this curvilinear relationship with founding patterns. Prior failures, at first hand, create free-floating resources which could be accessed by newly founded organizations. However, this positive influence has an upper limit beyond which an even larger number of failures would signal that the environment is hostile towards potential entrepreneurs. Similarly, foundings initially encourage potential entrepreneurs because in a similar population or niche because they signal that the environment is fertile. But as the number of foundings increases, an upper limit is reached beyond which competition for resources in this environment discourages further foundings.

-- Insert Table 1 about here --

This initial hypothesis has been further elaborated as the 'density-dependence' hypothesis. The density dependence hypothesis states, in general, that initially population density legitimates the organizational form of a new population and helps to increase the founding rate of this new population. However, as the population density further increases, the legitimacy process becomes dominated by the competition effect and founding rates start decreasing. As a result, one expects an inverted U-shaped relationship between population density and founding rates. This hypothesis has been validated in a large number of different populations, ranging from the US Brewery Industry towards US Semiconductor companies and even the US biotech industry. As shown by Table 1, in most of these different populations, the density-dependence hypothesis has received empirical support. Therefore, we conclude that the evidence in support of the non-monotonic pattern is very strong and should be controlled for in our study of the effect of knowledge alienability on organizational foundings.

Based on the discussion of the previous paragraphs, a first hypothesis or research proposition derived from the model is as follows:

> *Hypothesis 1: after controlling for population density, the alienability of knowledge*
> *in a new technological domain, will have a negative effect on the*
> *number of foundings in that domain .*

As a corollary to this, the model also predicts that the number of research collaborations in a particular technological domain will be a negative function of these organizational foundings. Organizations

which want to collaborate with research groups do not have the possibility to do so, because the existing groups do not have enough incentives. On the contrary, once a research group obtains a critical mass of knowledge, it has an optimal incentive to spin-off its own company. Concluding, we can formulate the following corollary:

Corollary 1: there is a negative relationship between the number of foundings in a particular domain and the number of research collaborations in that domain.

The property rights model does not only focus on foundings as a viable strategy of technology transfer. Equation (2a) and (2b) show that, once knowledge has become alienable, new technology based firms have an incentive to enter research collaborations with external partners in those technological sub-fields where the knowledge involved is only weakly complementary to their physical assets and the knowledge assets within the company. In line with the core competence literature, new technology based companies are assumed to enter a research collaboration in those technological sub-fields in which they do not have their core knowledge or physical assets.

Based on this, we argue that, before an organization is willing to enter a research collaboration (be it with a university or another biotech firm), the organization should already have developed a more or less coherent set of 'knowledge' and a well-elaborated set of physical assets which form the 'core competence' of the company (Prahalad and Hamel, 1990). As a consequence, we state that the decision to enter a research collaboration is a positive function of the resources which a particular company has accumulated, both in terms of knowledge and physical assets. Hypothesis 2, derived from the property rights model, is then formulated as follows:

Hypothesis 2a: after controlling for the level of knowledge alienability, the decision of a new technology based firm to enter a research collaboration is a positive function of its accumulated stock of knowledge in the technology.

Hypothesis 2b: after controlling for the level of knowledge alienability, the decision of a new technology based firm to enter a research collaboration is a positive function of its accumulated stock of physical assets.

RESEARCH SITE: GENETIC ENGINEERING AND HYBRIDOMA TECHNOLOGY IN THE BIOTECHNOLOGY COMMUNITY

The Cohen-Boyer invention in 1973 has been characterized as the breakthrough that turned the "basic science" of molecular biology into an industry, known as "biotechnology" (Kenney, 1986). Gene-splicing technology or rDNA would, after several years of discussion, lead in 1981 to the now famous Cohen-Boyer patent. In short, rDNA is the technology used to cut and paste DNA strings. Although this was the pivotal starting point for biotechnology, two subsequent technological breakthroughs would

alter the face of the domain. In 1975, Millstein and Kohler developed the hybridoma-technology, which is used to produce monoclonal antibodies for diagnostic purposes. Much later, in the early eighties, the biotech community started to focus on "protein engineering" which combines both the "hybridoma"' and "rDNA" technology. Protein engineers basically make use of gene splicing and cell fusion technology to develop proteins or polypeptides with desirable therapeutic characteristics.

It is important to note that biotechnology is a heterogeneous set of biological techniques, which are used for a variety of purposes. The property rights model described above is not an a priori 'industrial' model, but a technology related one. Hence, not the industry, but the 'technological domain' or, to use organizational ecology terminology, the homogenous population of companies that are interested in the development or commercialization of the same technology form the appropriate unit of analysis (Gray, 1985). For the purpose of this paper, we divided biotechnology in a number of homogenous technological sub-fields.

We did so in two steps. First, we traced all companies which were active in biotechnology research with therapeutic purposes (see Table 2 for a description of how this population is constructed and a definition of the technological sub-fields identified below). Within this biopharmaceutical population, a number of different technological sub-fields can be distinguished (OTA, 1991). Based on a careful analysis of the relevant scientific journals in the field (see Table 2 for a list of the journals we have screened) and in line with industry reports such as OTA (1991) and Ernst & Young (1995), we were able to distinguish between seven technological subfields: (a) monoclonal antibodies, using hybridoma technology, (b) protein engineering using rDNA systems, (c) drug delivery systems, (d) anti-sense technology, (e) gene therapy, (f) intracellular receptors and (g) rational drug design (using computerized methods).

-- Insert Table 2 about here --

Within those technological sub-fields, there are very different types of organizations involved. According to Clarysse and Debackere (1996)[11], 65% of all research and development groups in plant genetic engineering (rDNA) are housed in universities. Government funded labs account for about 10%. New biotechnology firms account for another 10% and about 15% is accounted for by large established chemical or seed companies. The division of "research labor" in the biopharmaceuticals is more difficult to assess because the "research boundaries" are less clear to define. Debackere and Clarysse (1995) estimated that for a particular stream of research, namely Hepatitis C, 70% of the research groups are based in universities and university-related hospitals. Another 20% was performed by government-related laboratories; while 5% resulted from the efforts of new biotechnology companies and another 5% is performed by large companies. Since we are interested in the foundings of

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[11] This study focuses on the use of rDNA techniques to genetically manipulate plant varieties.

independent new firms, we will focus on new biotech companies. Figure 2 shows the relative importance of each technological sub-field (in 1994) for the new biotechnology start-ups.

Figure 2: New Biotech Companies in Each Technological Sub-Field as a Percentage of the Total Population in 1994 (168 companies)
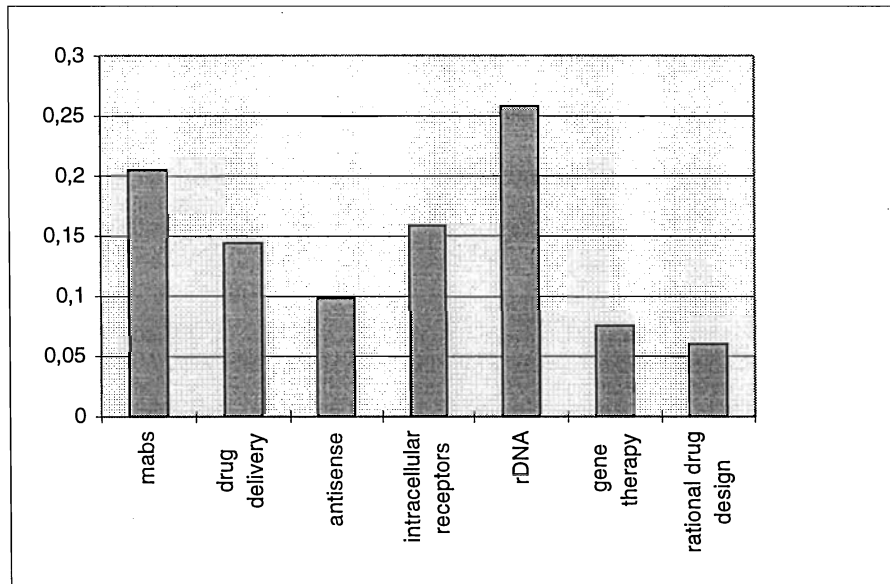

Legend: When a Biotech Company was involved in more than one technological sub-field, it was given credit for that one in which the majority of its research efforts were.

As shown in Figure 2, the technological sub-field of monoclonal antibodies (MABS) and genetic engineering of proteins (rDNA) are by far the largest biotechnology. Together, they account for about 45% of the new technology based companies involved in biopharmaceutical development. Although rational or structure-based drug design has become a very popular concept in drug development, relatively little biotechnology start-ups focus on this sub-field. Increasingly popular are the domains of anti-sense technology and gene therapy. Gene therapy consists of the development of 'therapies' in relation to the recombinant drugs which are helpful in treating chronic diseases such as Cystic Fibrosis. Anti-sense technology is the newest sub-field and targets the RNA instead of DNA strings. By using this kind of technology, companies hope to be able to inhibit the replication of viruses. So far, only a couple of leads derived from anti-sense technology have entered clinical trials. Drug delivery companies focus on the development of novel delivery systems for biologics and genes. Most of these companies either focus on the use of liposomes (especially the older companies among them) or the use of ligands. Finally, quite recently, a whole stream of biotech companies has started to specialize their activities in the recombinant development of receptors (intracellular receptors). These companies are not interested in the development of real 'drug agents,' but in the targets which enable the pharmaceutical companies to develop drug agents.

Because the sub-fields of Monoclonal Antibodies (Hybridoma technology) and Genetic Engineering (rDNA technology) both really were at the origin of biotechnology as an industry, they show a similar life cycle. Moreover, as illustrated in Figure 2, together they include over 45% of the new technology based companies involved in biopharmaceutical research. Therefore, we decided to focus in this paper on these two technological sub-fields as a population of organizations. Figure 3 lists the foundings and dissolutions in this population. It is clear that the "big wave" of start-ups in this population is in the early eighties. From the mid-eighties on, an increasing number of the first generation companies disappear from the population. Most of these 'exits' are the result of mergers and acquisitions.

**Figure 3 : Foundings of New Biotech Companies
in Monoclonal Antibodies and Genetic Engineering of Proteins**
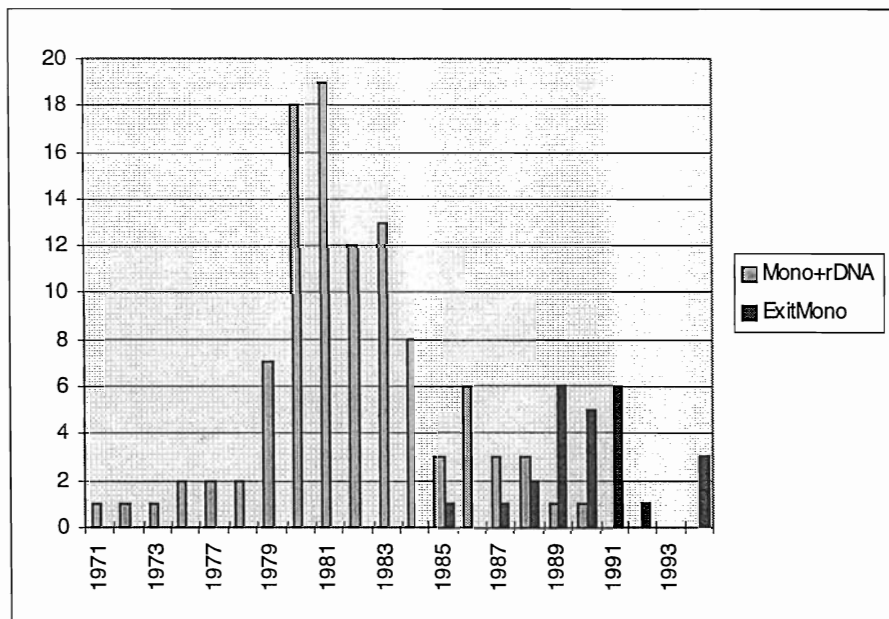
Legend: Number of company foundings in each year on the vertical axis.

MODEL SPECIFICATION

Hypothesis 1 and hypothesis 2 are situated at different levels of analysis and thus they need a different approach. To investigate hypothesis 1, we adopt the approach by organizational ecology studies, which have mostly used a Poisson model (see Table 1, for an overview of the models which have most frequently been used in the organizational ecology studies of founding). We first briefly motivate why a Poisson version is an appropriate way to model foundings in a population or technological community.

Model Specification for hypothesis 1. When modeling the founding of organizations in a population, the level of analysis is the population (Hannan and Carroll, 1992:236). We have to do with repeated events (Allison, 1984:51) occurring to one level of analysis: the population of interest; this kind of process is easily modeled as an arrival or a point process (Cox and Isham, 1980:2). The entry rate is the

dependent variable in the analyses. The baseline model for comparison is always the constant rate, time independent Poisson model, also called the exponential model (Allison, 1984:23), describing a series of events, distributed randomly across time. If we knew the dates of foundings of biotechnology firms with a great degree of precision (e.g. day and month of founding), then we would be able to model the entry rates as a continuous process, using a hazard model. If one uses the hazard model (or a related accelerated failure time model) to model the process of foundings, then one assumes that the time between two founding dates is the dependent variable of interest. In other words, one defines a founding as a discrete event which takes place at a well-known, well-defined point of time. Of course, both from a conceptual and an empirical point of view, this assumption is very difficult to hold. Which date is "the" date? The founding of an organization seems to be more of a process than of an exact event. Hence, it makes more sense to estimate the number of organizational foundings that are expected to occur *within a certain time interval*, than to model the exact date.

As shown by Barnett and Amburgey (1990), a Poisson process then provides a natural baseline model for organizational founding. The basic Poisson model for event count data can be described as in equation 6:

$$\Pr(Y_t = y_t) = e^{-\lambda(x_t)} \left[\frac{\lambda(x_t)^{y_t}}{y_t!} \right]$$
(3)

The Poisson model holds the strong assumption that both the variance and the mean of the number of events are equal. This assumption is often found to be too stringent in an analysis of founding rates (see Ranger-Moore et al., 1991). Unobserved heterogeneity in the model always leads to overdispersion. A first way to correct for this heterogeneity would be to adopt a 'fixed effects approach' by including dummy variables which are niche-specific (e.g. a dummy variable for each of the different geographic locations or market niches). The fixed effects approach is very attractive when no real conceptual model is available which explains the distribution of the heterogeneity. However, the main disadvantages of these models are (1) they absorb a lot degrees of freedom (one for each dummy variable) and (2) parameters of the co-variates, if any, contaminate with the dummy variables and are therefore very difficult to estimate. Hausman, Hall and Griliches (1984) have proposed to overcome these problems by letting λ vary randomly across individual units. A common way to do so is by including equation 4 in equation 3 (the Poisson model), or if overdispersion is a problem, by incorporating equation 4 in the negative binomial specification which can be derived from the baseline model (see Hausman, Hall and Grilliches, 1984:921):

$$\lambda_{it} = \exp(p' x_{it}) \varepsilon_{it}$$
(4)

where the error term ε_{it} is assumed to follow a gamma distribution, i can be the number of different niches or populations and t is the time variable. Of course, the value of this random effects largely

depends on the assumption that the errors really follow a gamma-like distribution, or in other words, that the errors will be larger for larger values of λ_{it} (in this case the number of foundings/niche/period of time).

Model Specification for hypothesis 2a and 2b. In these hypotheses, we study a classic make or buy decision. To study these decisions, previous research has used a Probit or Logit specification (Pisano, 1990). In line with this research, we choose to use a *probit normal probability* model. This model belongs to the family of binary choice models. It suggests the use of a cumulative probability function, which is normally distributed. This probability function can be written as equation (5):

$$P_i = F(a+bX_i) = F(Z_i) \qquad (5)$$

where Z_i is a non-observable variable. Translated in terms of our unobserved continuous variable Z_i, we assume that Y takes the value of 1 if the value of Z_i is larger than a certain "critical" cut-off point Z_i^* and Y takes the value of 0 if the value of of Z_i is smaller than or equal to a certain "critical" cut-off point Z_i^*. The probit model assumes that this cut-off point is a normally distributed variable so that the probability that our unobserved continuous variable is larger than Z_i, can be computed from the cumulative normal probability function, which can be written in a standardized form as equation (6):

$$P_i = F(Z_i) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z_i} e^{-s^2/2} ds \qquad (6)$$

where s is a normally distributed random variable (mean=0 and variance=1). By definition, the variable P_i lies in the (0,1) interval. The model can be interpreted as the probability that a certain organization enters research agreements, conditioned upon the value of the explanatory variables.

CONSTRUCT OPERATIONALIZATION AND EMPIRICAL RESULTS

The variables used in this study are explained in Table 3. In Tables 4 and 5, the results of the analyses are presented.

-- Insert Table 3 about here --

Hypothesis 1 and Corollary 1. The operationalization of the density variable is straightforward: the number of organizations in the population (see Figure 4). As shown in Figure 4, the number of organizations exponentially increases in the early eighties to reach a summit in 1988. From then on mergers and acquisitions decrease the number of organizations in both technological communities.

Knowledge alienability is more difficult to operationalize than organizational density. Arrow (1962) has defined three characteristics which are typical for resource allocation on knowledge markets:

indivisibility, *uncertainty* and *appropriability*. Indivisibility means that sometimes parts of the knowledge cannot be separated from other parts or even from the owner of that knowledge. Uncertainty refers to the fact that investing in knowledge does not result in a straightforward manner in output. Hence, existing firms may under-invest in knowledge because of the risk associated with it. Finally, knowledge appropriability refers to the extent that the owner of the knowledge is able to extract economic value from it. All three characteristics are related to the intangible or tacit nature of this knowledge. Arrow (1962: 615) argued:

> "...with suitable legal measures, information[12] may become an appropriable commodity. Then the monopoly power can indeed be exerted. However, no amount of legal protection can make a thoroughly appropriable commodity of something so intangible as information ... Mobility of personnel among firms provides a way of spreading information. Legally imposed property rights can provide only a partial barrier ..."

**Figure 4: Number of Organizations in the
Genetic Engineering or Hybridoma Technological Community**
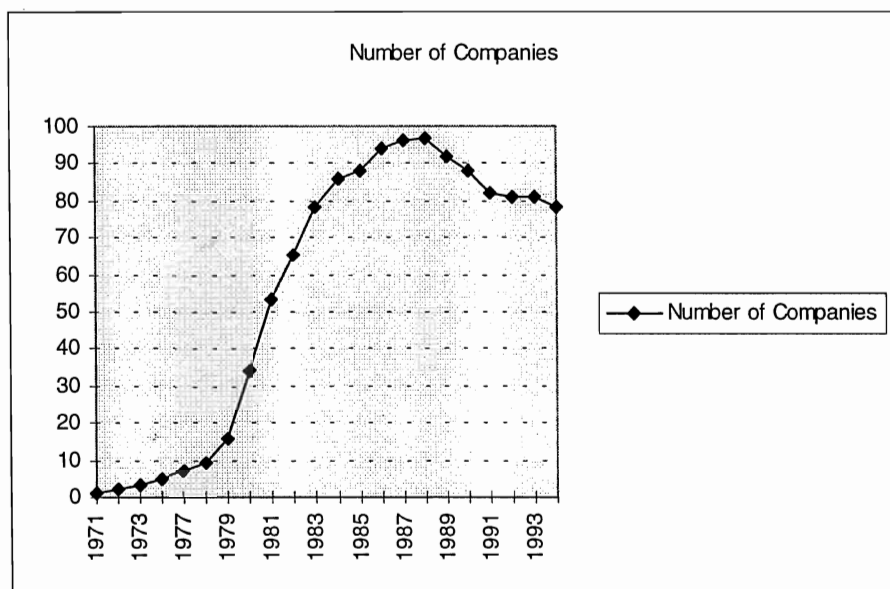
Legend: Number of new biotech firms in genetic engineering or hybridoma technologies on the vertical axis.

The property rights model as defined in equations (1a) and (1b) is consistent with this statement in a sense that it predicts the use of equity ownership of the personnel as a first "inner circle of protecting knowledge." However, the more knowledge looses its intangible or tacit character, which means the more it becomes codified, the better it can be traded on the spot market (von Hippel, 1994).

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[12] We define knowledge assets in the way he defines information.

Hence, the codification of knowledge may be a good proxy for its alienability at any point in time. In pharmaceuticals, patents have since long been a legal mechanism which was very useful both for information protection and codification. In Teece's (1986) terms, we can say that the market for know how in pharmaceuticals has a tight appropriability regime. Figure 5, for instance, illustrates how many percent of the drugs introduced in the US market were also originated by the same firm.

**Figure 5: Percentage of NME's Introduced in the US Market, Period 1960-1989
With Manufacturing Company Different From the Originating Company**
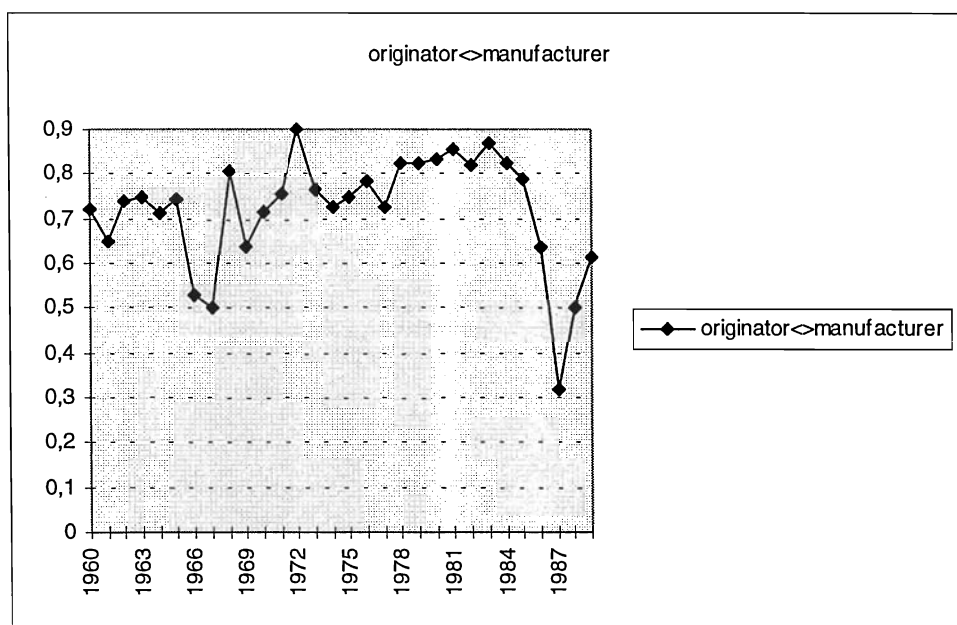
Legend: Compiled from De Haen's Non-Proprietary Index & Drug Product Index, period 1960-1989.

The data in Figure 5 indicate what percentage of the New Molecular Entities introduced to the US market in that particular year of observation are *not* manufactured by the company that has discovered them. It is clear from this figure that already since a long time, there is a difference between organizations which "discover" the new entities and those which "manufacture" them and/or eventually market these NMEs. Only in 1987, the percentage of NMEs introduced on the US market which were manufactured by the companies that had really discovered them was smaller than the percentage of NMEs originated by a different company. We can conclude from these results that, in economic terms, the appropriability regime in traditional pharmaceuticals should be rather tight.

It is a realistic assumption that this appropriability regime is more or less driven by the well-functioning of the legal protection system, the patents. The question which remains to be answered then is: does this patent system also hold for the protection of living organisms or other products derived from the application of new biotech techniques? As extensively described by Kenney (1986), the patent controversy came to an end with the 1980 decision of the Supreme Court in the Diamont vs.

Chakrabarty case that a live genetically engineered microorganism constitutes patentable subject matter within the meaning of section 101. In other words, from 1980 on it was *legally* possible to receive patents on a genetically manipulated micro-organism. Figure 6 shows then the number of patents filed in the US which can be classified as 'biotech patents'[13]. In 1994, the biotech patents filed for the genetic engineering of proteins make up over half of the total biotech patents population. Although the initial 'start' of this genetic engineering of proteins (better known as protein engineering) was possible from the 1975 on (discovery of the hybridoma technique), it took until the early eighties before it was further commercialized. The first patents are filed in 1977 (although it took over five years for these patents to be granted). Patent activity for protein engineering and monoclonal antibodies grew exponentially respectively in the mid- and early eighties.

Figure 6: Patent Activity in rDNA, Monoclonal Antibodies and Total Biotechnology
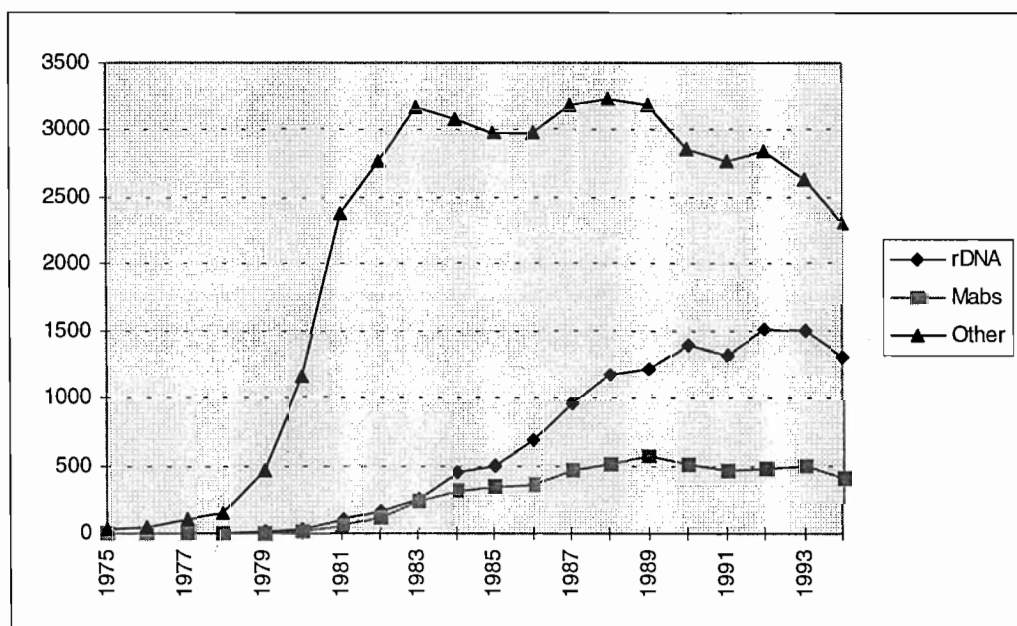
Legend: Annual Number of US Patents Filed in Genetic Engineering (rDNA), Monoclonal Antibodies (MABS) and other biotech domains.

Table 4 shows the results of the models in both the technological community of 'protein engineering companies' and the one of 'monoclonal antibody based' companies. Models (1) and (4) test the density-

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[13] These patents are drawn from Derwent's Biotechnology Patents file. First, we selected all US Biotech patents from this file through selecting on the priority date. Only US patents have this priority date, which makes a selection of them straightforward. The search strategy to select those patents related to monoclonal antibodies was: (monoclon*) and (antibod*). In other words, in order to be selected in the database, the patents should include both terms either in the title or in the abstract of the document. A similar search strategy was formulated to select the 'genetic engineering', including the terms ((recombin*) or (rDNA)) and (protein*). Again patents which had one of the two first terms *and* the third term either in the abstract or the title were selected from Derwent's biotech file. All others were considered as biotech patents which were related to other technical fields.

dependence model in these communities. Consistent with the large stream of organizational ecology research, both equations support the inverted-U relationship between the number of organizations that already exist in this industry and the number of foundings. Adding the knowledge alienability variable[14] (see models (2) and (5)) to the model, considerably increases the explanatory power. In the case of monoclonal antibodies, the likelihood ratio increases with about 44% (the accompanying R' changes from 0.08 to 0.47); while in the case of protein engineering, the likelihood changes with 13% (the accompanying R^2 changes from 0.28 to 0.37). Also the individual signs of the coefficients point into the expected direction and are significantly different from 0.

In an auxiliary model, we also included a time trend in model (2) and model (5). Even after controlling for this time trend (which was significant in both cases), the results did not change. The slope of the PATENTS variable in model (5) was slightly smaller (-0.008) but that did not change its impact. In order to test to what extent these results are sensitive to the econometric specification we used, we used a negative binomial specification to check the stability of the results. The coefficients in models (3) and (6) remain largely the same with slightly inflated standard errors. In none of both models was the overdispersion parameter statistically significant. The implications of these results are twofold. First, they provide an empirical test of a slightly modified version of the property rights model[15]. Second, even after controlling for the most widely tested hypothesis on organizational foundings, the density-dependence model, the knowledge alienability hypothesis adds to the explained variance of the model.

-- Insert Table 4 about here --

Qualitative research on the incentive systems used in biotechnology start-ups confirm the empirical conclusions drawn from our quantitative models in the sense that they propose equity ownership as an important incentive. Kenney (1986: 96), for instance, argued that leading researchers or "founding" professors were given up to 10% of the initial equity. In addition to this, the remaining researchers were given stock options as incentives. Data on the motivations of those professors to spin-off a new company also reveal that the equity shares and, related to this, the huge amounts of money that could be earned in case of a success are ranked as a primary reason for their "entrepreneurial activity." Moreover, cases in which the ownership of physical and knowledge assets remained separate, clearly highlight examples of under-investment on both sides (Kenney, 1986). Based on the same data, he describes how research laboratories at universities complain that they have not the necessary equipment to keep ahead of the biotechnology start-ups, whereas the established pharmaceutical and chemical firms were very skeptical towards the new biotechnology challenge.

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[14] Measured as the annual patent activity in each technological community.
[15] The reader should note that this test is only a first step in the right direction. The degrees of freedom in each of the models is too small to draw strong conclusions from them.

We also stated, as a corollary, that we expected a positive correlation between the intensity of patent activity and the number of research collaborations[16] in the domain. Unfortunately we were not able to split this variable up between the monoclonal antibodies and protein engineering. As a first indication, we calculated the Pearson point correlation between the number of research collaborations (between biotechnology companies and universities/other biotechnology companies) in which they are involved over the period 1982-1994. This correlation coefficient is 0.74, which provides (be it limited) evidence in support of the corollary.

Hypothesis 2a and 2b. The dependent variable is the same for both hypotheses, namely a dummy variable which takes on the value of 1 if the company has entered a research collaboration in that particular year (see Table 3 for a description of this variable).

-- **Insert Table 5 about here** --

Hypothesis 2a states that the accumulated stock of knowledge influences the decision to enter a research collaboration in a positive direction. We have a direct measure of this accumulated stock of knowledge through the cumulated number of patents indicator (CUMPAT). Previous research has used this measure as an indicator of the knowledge stock in the company (Henderson and Cockburn, 1994). However, no direct measure is available to capture the amount of physical assets a biotech company has invested in. Instead, we use the number of projects this company has in clinical trials (CLINICAL) as a proxy. Previous research on biotechnology has argued that having products in clinical trials make it necessary to invest heavily in the physical assets needed to carry the clinical trials. For instance, Dr. Howard Simons, Director of Central Research at du Pont (Brown, 1982:9, in Kenney 1986) argued:

> "Recombinant DNA is just a way to synthesize things ... as soon as you've inserted the gene, it's identical to what you would do in the chemical industry anyway...development needs investments which cost 20 time as much as research ..."

Before testing these hypotheses, we controlled for a number of competing explanations. First, we included the total level of knowledge alienability by measuring the patenting activity during any given year. This variable is highly correlated with the time trend variable so that we omitted the latter one from the final analyses to avoid multicollinearity problems. We also controlled for the size of the company by using the number of employees in each company as a proxy (SIZE) and for the age of the company, measured as the number of years elapsed since company founding (AGE). Models (7) and (9) are respectively a Probit and a Logit estimation of this baseline model. As expected, it is mainly the patent variable which explains the probability of entering a research collaboration. AGE has a slightly significant and positive sign, which indicates that it are especially the more mature organizations which tend to enter such collaborations.

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[16] We refer to table 3 for a description of how this variable is constructed.

After controlling for AGE, SIZE and PATENTS, we included the explanatory variables in the model. The knowledge assets which organizations have accumulated in the field have a significant positive effect on the probability that these organizations enter a research collaboration, which supports hypothesis 2a. The effect of the number of projects each organization has in clinical trials (CLINICALS) is slightly less, but still significant in the expected way. Hence, also hypothesis 2b receives support. Of course, the variables which we use in the model are only proxies for the constructs developed in the property rights model. Moreover, we have no variable which captures the degree of interrelatedness between the different knowledge assets on the one hand and the knowledge and physical assets on the other hand. We also have no indication on how homogenous the existing knowledge base is and, related, how much it reflects a core competence in a certain domain.

Qualitative analysis of the data sources, however, revealed that in many cases research collaborations are formed between more mature companies involved in protein engineering and monoclonal antibodies and the newer biotech companies or university laboratories that are involved in newer technologies such as gene therapy and anti-sense technology, which confirms the direction of the hypothesis.

CONCLUSIONS AND DIRECTIONS FOR FUTURE RESEARCH

In this paper, we analyzed how recent developments in organizational economics can help us understand the complex process of technology transfer. The GHM incomplete contracts or property rights model, which has been the basis for many recent developments in principal-agency theory towards a full theory of the firm (Holmstrom, 1994), was used as a starting point to explain inter-organizational knowledge transfers.

The GHM model focuses on the incentives that agents have to cooperate or not, given the status of ownership of the complementary assets. We analytically modeled "knowledge" as an asset. When knowledge is not alienable, the model shows that those who possess the knowledge have the best incentive to develop this knowledge further if they also have the rights to the physical assets needed to develop this knowledge. Linking this result to the theories of technological evolution, this means that before a technological paradigm is established or, put differently, in the beginning of the technological life cycle (Foster, 1986), technology transfer should be stimulated through the spin-off of new technology based companies in which the key researchers receive equity rights.

Once knowledge becomes alienable, the model gives an insight in *what kind* of knowledge will be outsourced by *which* companies. The model and subsequent analyses suggest that probably the more mature companies that have already developed a research portfolio, have the highest incentive to out-source these knowledge assets that are only weakly interrelated with either their existing portfolio or the physical assets they have invested in order to further develop this portfolio. There are two conclusions which can be drawn from this insight. First, research laboratories that want to perform contract research

with existing companies should invest in this kind of knowledge. Second, high-tech companies that belong to a second wave of foundings have an incentive to specialize in these technological sub-fields and act as brokers between universities and the more mature biotech or pharmaceutical companies.

In addition to these analytic derivations, we also made an attempt at analyzing how reality matches the predictions of the property rights model. Therefore, a hypothetical framework was developed. To empirically analyze the first hypothesis, we contrasted the predictions of the property rights model with the competing explanations derived from organizational ecology. The empirical results, derived from two biotechnology sub-fields are comforting. The knowledge alienability variable explains up to 39% of the yearly variation in the number of foundings, after controlling for the generally accepted density-dependence model. Of course, we should take some caution in interpreting these results because of the limited degrees of freedom in each model[17]. Still, the results open some directions for further research on the incentive systems used in new technology based companies. In the empirical operationalization, we assume that the key researchers receive equity ownership in these new companies. How does this degree of equity ownership change over time? Does it discriminate between successful and less successful new technology based companies? Is it a substitute for property rights in the initial stages of technological development? The incomplete contracts model, and its elaborated version analyzed by Holmstrom (1994), offers some strong, testable hypotheses for these questions.

The second set of hypotheses were more difficult to analyze (2a and 2b), because we have no data on the degree of inter-relatedness between the different knowledge and physical assets, nor of the homogeneity of the existing knowledge base. The results are therefore indications rather than empirical tests. These indicators confirm direction of the hypothesis: companies which have accumulated a larger knowledge base and hence, have built more competencies in a certain core technology are more likely to enter a research collaboration (in what we assume to be a weakly related new technology) than those that did not accumulate this knowledge base yet. These results invite further research. Collaboration and more specifically outsourcing in basic research might be desirable from an incentive point of view. Further studies should go inside the firm and collect data at the project level so that the degree of inter-relatedness between the different kinds of assets can be taken into account.

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[17] We only cover the period 1971-1994, which leaves us with 24 observations of the dependent variable.

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Table 1: Organizational Ecology Studies of Founding

DATASET/STUDY	KEY VARIABLES	MODEL USED
Day Care Centers in Toronto, 1971-1989 ; Baum and Singh (1994)	**Dependent Variable** foundings **Independent Variables** *overlap density:* (-) *nonoverlap density:* (+)	Negative Binomial Regression, random effect (only time) with gamma distribution
Argentine News Papers, 1800-1900 ; Delacroix and Carroll (1983)	**Dependent Variable** foundings **Independent Variables** *density:* inverted-U shaped relationship (significant)	Poisson and Negative Binomial Regression, random effect (only time) with gamma distribution
US Brewing Industry, 1633-1988 ; (Carroll and Swaminathan, 1989)	**Dependent Variable** foundings **Independent Variables** *density:* inverted-U shaped relationship (significant)	Poisson and Negative Binomial Regression, random effect (only time) with gamma distribution
Transgene Plant Community, 1974-1994, Debackere and Clarysse, (1997).	**Dependent Variable** foundings of research groups, Dutch venture capital firms. **Independent Variables** *Clique Membership:* relative number of organizations that belong to an industry-wide exchange network (-) *Mimetic Isomorphism :* concentration of network prestige (+) *Density:* inverted-U shaped relationship (significant) **Control Variables** *environment specific variables.*	Poisson and Negative Binomial for transgene plants, random effects only for the time dimension; Hazard model (loglinear) for Dutch venture capital foundings
US Biotech Industry, 1974-1987 ; Shan, Singh and Amburgey (1991)	**Dependent Variable** foundings of new biotech firms. **Independent Variables** *Density:* inverted-U shaped relationship (significant) **Control Variables** venture capital availability (+) GNP (n.s.) NYSE (n.s.)	Loglinear Hazard Model
Rural Cooperative Banks in Italy, 1964-1988 ; Lomi (1995)	**Dependent Variable** foundings **Independent Variables** *aggregated density effect:* inverted-U shaped relationship (significant) *geographic density:* density in well-defined geographic niches (+) **Control variables** general economic and social conditions such as Agricultural employment (n.s.) Core Bank's share (+)	Semi-parametric Random Effect Poisson Models (taking into account both unobserved heterogeneity along the time dimension and between the niches)
Pennsylvania Telephone Companies, 1877-1933, Barnett and Amburgey (1990)	**Dependent Variable** foundings **Independent Variables** *mass:* sum of the sizes of all organizations in the population (+) *density effect:* inverted-U shaped relationship (significant)	Negative Binomial Regression, random effect (only time) with gamma distribution

Legend:
(+) means a statistically significant (p<.05) positive sign.
(-) means a statistically significant (p<.05) negative sign.
(n.s.) means not significant at the .05 level.

Table 2: Selection of the Biotech Community and the Different Subdomains

Step 1.
In a first step, a list of journals was selected that covered the underlying sciences in Biochemistry and Molecular Biology. According to the Science Citation Index, these fields have 157 journals, 10% of which we selected. These 10% were the top 10% ranked by their impact factor as listed in the Science Citation Index. In each of these journals we screened the "review" articles to explore emerging technological subfields. Each of these journals is displayed in the table below.

List of Journals

FIELD	JOURNAL	RANKING
Biochemistry and Molecular Biology (157)	Annu Rev Biochem	35.5
	Cell	33.6
	Annu Rev Cell Biol	22.7
	Faseb J.	18.2
	Annu Rev Bioph Biom	15.8
	Embo J	12.6
	Rev Physiol Bioch P	12.2
	Crit Rev Biochem Mol	10.3
	Adv Enzymol Ramb	10.2
	Prog Nucleic Acid Re	9.7
	Mol Cell Biol	8.3
	Proteins	6.8
	J. Biol Chem	6.7
	Plant Cell	6.3
	Mamm Genome	6.3
Biotechnology and Applied Microbiology (43)	Mamm Genome	6.3

In these journals, we identified 7 distinct technological subdomains in pharmaceutical research: (a) **monoclonal antibodies** which are generated through the hybridoma technology and most often used for diagnostic purposes; (b) **protein engineering** or the recombinant synthesis of polypeptides or proteins; (c) **drug delivery systems** which mainly boil down to the use of Liposomes or Ligands to enhance the activity of genes or biologics; (d) **anti-sense technology** which focuses on the recombinant manipulation of RNA strings instead of the classic DNA; (e) **gene therapy** which is the development of protocols to insert genes with therapeutic characteristics directly in the body; (f) **recombinant receptors** or the recombinant construction of drug targets instead of drug agents and (g) **rational drug design** or the structured modeling of molecules according to the receptor characteristics making use of computerized methods such as X-ray crystallography.

Step 2. A population of biotech companies was defined using the broadest definition as described in Appendix A. The definition of Biopharmaceutical companies was as follows:

New Biotech Based Companies which are involved in biopharmaceutical research and development *and* not fully owned (i.e. at least 75% equity position) by another company. Companies are identified and selected from a number of secondary datasources including BioScan, American Healthcare and Marketplace Guide, NDA-pipeline, Bio\Technology annual review of...

Step 3. Each of the companies that was identified in step two was traced back in the sample of journals as described above. Using the information from the articles in these journals, we classified each company in an appropriate category. If a company belonged to more than one of these categories, we selected that one in which most of the articles were published. An average biotech company publishes about 22 articles/year.

Table 3: Variable Names and Sources

Variable Name	Data Construction and Description
RPATENTS	number of US patents filed during that year of observation. The Derwent patent data base is used as the 'population'. This database is easily accessible through the ON-LINE hosts of DIALOG and ORBIT. First, we selected a restricted population of US patents based on the priority information included in each patent. Then, we used a search strategy to select the subsample of US patent filings concerning protein engineering.
MPATENTS	number of US patents filed during that year of observation. The Derwent patent data base is used as the 'population'. This database is easily accessible through the ON-LINE hosts of DIALOG and ORBIT. First, we selected a restricted population of US patents based on the priority information included in each patent. Then, we used a search strategy to select the subsample of US patent filings concerning monoclonal antibodies (hybridoma technology).
FOUNDINGS	Foundings of New Biotech Based Companies which are involved in biopharmaceutical research using techniques of protein engineering or monoclonal antibodies (*in vitro* diagnostic assays excluded) *and* not fully owned (i.e. at least 75% equity position) by another company. Companies are identified and selected from a number of secondary datasources including BioScan, American Healthcare and Marketplace Guide, NDA-pipeline, Bio\Technology annual review of... 10-K reports and the NDA-pipeline were used to identify the strategic interest (genetic engineering/monoclonal antibodies) of the companies.
RESEARCH COLLABORATIONS	The research collaboration variable is a variable collected from information available in the full text version of the NDA-pipeline (accessible through Dialog). This database contains detailed information on the drugs in development and their status of progress. For a detailed description of the sample from which this variable is drawn and the underlying data sources, we refer to appendix C, where a dummy version of the variable is described into detail.
RESCO	Dummy variable variant of the RESEARCH COLLABORATIONS variable described in the previous paragraph.
CLINICALS	The number of projects this particular company has in clinical trials during the period of observation. This variable is computed from the NDA-pipeline data for the sample of companies described in Appendix C.
CUMPAT	Cumulative number of patents for each of the companies in our sample. This variable is drawn from DERWENT's database on biotech patents. A patent is granted to a company in the year that company filed the patent. Again this variable is computed for the sample of companies described in Appendix C.
AGE	Number of Years that the company exists.
SIZE	average size of the company in number of employees at each year of observation. A detailed description of how this variable was constructed is included in Appendix C.

Table 4: Determinants of New Tech Foundings
Poisson Regression/Negative Binomial. Dependent Variable= Number of NDA/PLAs.

	RDNA sample			Mabs sample		
	(1)	(2)	(3)	(4)	(5)	(6)
NUMBER {number of companies in the sample}	0.27** (0.052)	0.197** (0.056)	0.197** (0.056)	0.166** (0.0625)	0.114* (0.053)	0.119* (0.005)
NUMBER2 {number of companies squared in the sample}	-0.006** (0.001)	-0.003* (0.0015)	-0.003* (0.0015)	-0.004* (0.002)	-0.004* (0.002)	-0.005* (0.002)
PATENTS {number of patent filings}		-0.002** (0.000)	-0.002** (0.000)		-0.017** (0.003)	-0.017** (0.004)
CONSTANT	-0.929 (0.477)	-0.623 (0.459)	-0.624 (0.459)	-0.532 (0.449)	-0.723 (0.492)	-0.747 (0.529)
Overdispersion parameter		N/A	-9.243 (71.90)	N/A	N/A	-3.428 (4.984)
Log-likelihood	-39	-33.9	-33.9	-47.9	-27.76	-27.74
R^2	0.28	0.37	0.24	0.08	0.47	0.32

*: means significant at the 0.05-level
**: means significant at the 0.01-level
standard errors in parentheses

Table 5: Determinants of the Decision to Enter a Research Collaboration
Probit/Logit Model. Dependent Variable = 1 if involved in a Research Collaboration. 557 obs.

	Probit Regression		Logit Regression	
	(7)	(8)	(9)	(10)
PATENTS {total number of biotech patents}	0.001** (0.000)	0.001** (0.000)	0.008** (0.000)	0.002** (0.000)
SIZE {number of employees}	0.006 (0.003)	-0.006 (0.000)	-0.001 (0.000)	0.005* (0.002)
AGE {number of years elapsed since company founding}	0.072* (0.0287)	-0.035 (0.0244)	0.053* (0.0143)	-0.067 (0.043)
CUMPAT {cumulative number of patents filed}		0.0095** (0.0025)		0.0176** (0.0047)
CLINICALS {number of projects the organization has in clinical trials}		0.052* (0.0225)		0.0894* (0.0379)
CONSTANT	-2.482** (0.389)	-2.304** (0.407)	-4.270** (0.725)	-3.995** (0.767)
Log-likelihood	-316	-288	-316	-288
R^2	0.05	0.10	0.05	0.10

*: means significant at the 0.05-level
**: means significant at the 0.01-level
standard errors in parentheses