Modeling the Molecular Communication Nanonetworks

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Dedicated to my parents, Josep and Roser,
for their love, support and understanding.

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Abstract

Nanotechnology is a cutting edge investigation area that has come out with new and unlimited applications. The recent explosion of research in this field, combined with important discoveries in molecular biology have created a new interest in bio-nanorobotic communication. This thesis provides a general theoretical understanding of nanonetworks and their multiple possibilities. It describes some basic concepts of architectures that compose nanotechnology topologies, as well as possible designs for the tiny nanonetwork components, the nanomachines. The thesis also reviews some promising methods proposed for communicating and coordinating in these nanonetworks. Molecular communication applied to nanonetworks presents indeed extremely appealing features in terms of energy consumption, reliability and robustness. Nevertheless, it remains to understand the impact of the extremely slow propagation of molecules and the highly variable environments. As a totally unexplored research area, it is important to establish thorough theoretical framework so that the applications and possible solutions can be validated. It is clear that many issues still need to be addressed in order to understand the limiting performance of information communications among nano-scale devices and design optimal and quasi-optimal encoding/decoding strategies. Such issues are believed to be of key relevance for allowing nanotechnologies display their full potential.

Contents

Chapter 1

Introduction

Nanotechnology deals with creation of materials, structures, devices, systems, and architectures of any size by controlling matter at nanometer scale, and more importantly, by taking advantage of novel properties that arise because of the nanoscale. Indeed, properties of materials (physical, chemical, electrical, magnetic, optical, mechanical, etc.) change when going from bulk to nanoscale [23]. Therefore, it is not just about size alone but more about how to harness the change in properties and produce useful functionalities.

1.1 What is Nanotechnology?

Nanotechnology can best be defined as the development and practical applications of technological structures and devices on a nanometer scale, usually ranging from 0.1 to 100 nanometers. This is not to be confused with the "Nanoscience" witch does not describe a practical application but rather the study of the properties of nanometric world. The prefix "nano-" means one billionth (10^{-9}) of something, so nanotechnology refers most generally to technology on the scale of a billionth of a meter, that is, about 1/80,000 of a human hair's diameter, or 10 times the diameter of a hydrogen atom. The dimension of 100 nm is important since under this limit new mater properties appear, mainly due to the law of quantum physics.

Nanotechnology is a multidisciplinary field that covers several diverse technological areas of knowledge including chemistry, physics, molecular biology, material science, computer science and engineering, among others not such representative. Advances in this field have expanded the breadth of potential applications tremendously in recent years. Although its applied use is still limited, nanotechnology has begun to appear in various applications and products, namely nanomaterials.

1.2 What is a Nanomachine?

At the level of atoms and molecules, **nanomachines** can be considered as the most basic functional unit. Nanomachines are biological or artificial created nano-scale devices or components that are capable of performing only very simple tasks of computation, sensing, or actuation (e.g., detection of molecules, generation of motion, or performing chemical reactions) in its very close environment, because of their limited size and limited complexity [1].

Molecular biological systems are themselves nanomachines, constituting an existence proof for molecular nanotechnology; for instance, molecular motors are proteins or protein complexes that transform chemical energy, such as ATP hydrolysis, into mechanical work at the molecular scale. Nanomachines are largely in the

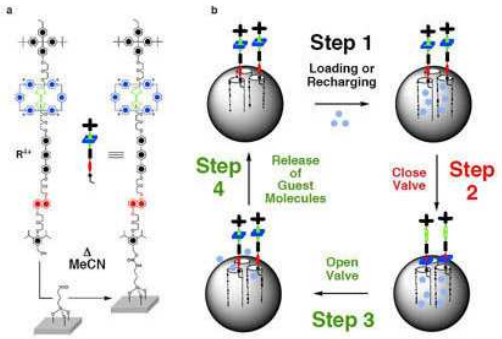

Figure 1.1: **(a)** Shows the structural formula of the rotaxane molecule and the procedure for tethering it to the surface of a tiny piece of glass; **(b)** Shows how the nano-valve opens and closes.

research and development phase, but some primitive molecular machines have been tested. An example is the above illustrated nano-valve created by UCLA chemists, that is capable of controlling the passage of molecules, i.e., the nano-valve can be opened and closed at will to trap and release molecules. It uses switchable rotaxane molecules (redox-activated bistable) as moving parts, the chemical energy that opens and closes the valve is obtained through a single electron, and a luminescent molecule tells wether a molecule is trapped or has been released. Furthermore, nanomachines can be used as building blocks to perform more complex systems, such as nanorobots and nano-computing devices.

Because of its small size, a single nanomachine generates a rather small force in the order of a few piconewtons (10^{-12} newtons). In addition, a single nanomachine is rather sensitive to its environment and is easily perturbed by thermal collisions with the surrounding molecules. It is quite remarkable that biological systems are able to cover very wide range of forces between a few piconewtons and several hundred newtons [1] by combined action of their forces, just as single cells can exert forces in the nanonewton range, and animals can generate forces of hundreds of newtons.

1.3 What is a Nanonetwork?

Hence, if multiple nanomachines communicate, they may execute collaborative and synchronous tasks in a distributed manner so further capabilities and applications will be enabled. Networked nanomachines may also cover larger areas, ranging from meters to kilometers, and expand the limited workspace of a single nanomachine which can only perform nano-scale objectives. Furthermore, if a large number of them cooperate, macro-scale tasks can be executed. However, when deployed over broad areas, interaction with a specific nanomachine is extremely difficult. Nanonetworks will provide the infrastructure and mechanism to enable that communication.

This interaction between nanomachines can be carried out throughout several means: nanomechanical, acoustic, electromagnetic, and chemical or molecular;

In the former, communication between transmitter and receiver is pursued through mechanical contact, more specifically, through hard junctions between linked devices. *Nanomechanical communication* is not suitable in many scenarios because of the contact requirement between transmitter and receiver, and the need of a precise navigation systems for their correct alignment. In *acoustic communication* the message is encoded in ultrasonic waves, meaning pressure variations that move at sound speed; similarly, in *electromagnetic communication*, information is transmitted through modulated electromagnetic waves. The main drawback for both of them is the size and current complexity of the transducer needed to establish that communication, it cannot be easily integrated in the nanomachines. Besides, assuming the integration were possible in the electromagnetic case, the output power of the nanotransceiver would not be enough to guarantee bidirectional communication. Consequently, it could be used to transmit information from micro-devices to nano-devices, but not on the opposite direction or between nanomachines. Last but not least, in *molecular communication* the message is encoded using molecules. Molecular transceivers are able to react to specific molecules, and to release others in response to an internal command. In creating molecular communicating systems, we use existing biological nano-scale communication mechanisms (e.g. intracellular, intercellular communication mechanisms of exchanging molecules) and communication components (e.g. molecular motors, cells with receptors). So far, this is the most promising approach for nanonetworking as later on will be stated.

1.4 Approaches for Nanomachines Development

In his famous talk "There's Plenty of Room at the Bottom" in 1959, novel physicist Richard Feynman pointed out first concepts in nanotechnology, although it was not defined till 15 years later. In that speech, he proposed the prototypical "Top-Down" strategy for building complex nanomachinery. In 1981, K. E. Drexler descried a new "Bottom-Up" approach involving molecular manipulation and molecular engineering in the context of building molecular machines and molecular devices with atomic precision. Research and advances in nanotechnology have been accelerated since the early 21st century.

Up to now, three different approaches for nanomachines development have been defined:

1.4.1 Top-Down Approach

Mechanisms and structures are miniaturized to a nanometric scale, in other words, it is focused on the development of nano-scale machines by means of downscalling current existing devices at micro-scale, involving microelectronics and micro-electro-mechanical technologies, without atomic level control. It has been the most frequent application of nanotechnology up to this point, in particular in the domain of electronics.

To build a nanomachine using Feynman's scheme, the operator first directs a macro-scale machine to fabricate an exact copy of itself but four times smaller in size. After verification of its proper work, this reduced-scale machine would be used to build a copy of itself, another factor of four smaller but a factor of 16 tinier than the original one. This process of fabricating progressively smaller machines proceed until a machine capable of manipulations at nano-scale is produced. The final result is a nanomachine capable of reconstructing itself or producing any other useful nano-scale output[16].

It is becoming clear that the top-down approach is subject to drastic limitations, including a severe cost escalation when the components approach the nanometer dimension. To proceed toward miniaturization at nano-scale, science and technology need to find new avenues. As we go down in size, there are a number of interesting problems that arise: It is not just a matter of scalling in proportion, there is also the problem that materials stick together by the molecular attractions (Van Der Waals).

Recently, progress is being made on Feynman's top-down approach in a relatively new field known as Micro-Electro-Mechanical Systems or MEMS, where devices integrate mechanical components directly with electrical circuitry using advanced manufacturing techniques, such as electron beam lithography and micro-contact printing. Nanomachines as nano-electromechanical systems (NEMS) com-

ponents are being developed using this approach, although manufacturing processes in this approach are still in an early stage.

1.4.2 Bottom-Up Approach

This approach is a promising strategy to exploit science and technology at the nanometer scale, which starts from nano- or subnano-scale objects (namely atoms or molecules) to build up larger structures, using the chemical and physical forces that operate at nano-scale. A theoretical nanomachine build following this philosophy is illustrated in Figure 1.2. The idea that atoms could be used to construct nano-scale machines was first raised by Feynman, *"The principles of physics do not speak against the possibility of maneuvering things atom-by-atom"*, and depicted in a visionary way in the mid-1980s by K. Eric Drexler, who claimed it would be possible to build a general purpose nanorobot, a universal assembler, capable of building almost anything atom-by-atom, including copies of itself.

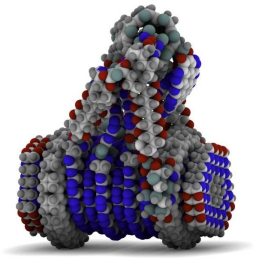

Figure 1.2: A theoretical nanomachine build up atom-by-atom.

The idea of an *atom-by-atom* bottom-up approach to nanotechnology, which seems so appealing to physicists, does not convince chemists who are well aware of the high reactivity of most atomic species, the subtle aspects of atomical bond, and the properties of molecules. Thus, atom-by-atom assembly is considered unrealistic for at least three well-grounded reasons:

1. The fingers of a hypothetical manipulator arm should themselves be made out of atoms, which implies that they would be too fat to have control of the chemistry in the nanometer region.

2. Such fingers would be also too sticky -the atoms of the manipulator hands would adhere to the atom that is being moved, so that it would be impossible to place it in the desired position.

3. The continual shaking to which every nano-scale structure is subject because of collisions with the surrounding molecules would prevent precise nano-engineering.

Later on, in the frame of supramolecular chemistry, the idea that molecules could be much more convenient building blocks than atoms to construct nano-scale devices and machines arose. This idea was based on the following points:

1. Molecules are stable species, whereas atoms are difficult to handle.
2. Nature uses molecules (not atoms) to construct the great number and variety of nanodevices and nanomachines that sustain life.
3. Most laboratory chemical processes deal with molecules (not atoms).
4. Molecules are structures that already exhibit distinct shapes and carry device-related properties.
5. Molecules can self-assemble or can be connected to make larger structures.

Molecular-level devices need energy to operate and signals to communicate with the operator. The *energy* needed for the operation of a *molecular device*[1] or *molecular machine*[2] can be supplied in the form of (i) a chemical reagent, (ii) an absorbed photon, or (iii) addition or subtraction of an electron.

Since a device and a machine have to work by repeating cycles, an important requirement is *reset*. This means that any chemical reaction involved in the operation has to be reversible. Although no chemical reaction is fully reversible, this requirement is met reasonably well by energy transfer, electron-transfer (redox), and proton-transfer (acid-base) processes, and by some types of photoisomerization and metal-ligand coordination reactions.

This Bottom-Up Nanotechnology is called "molecular nanotechnology" or "molecular manufacturing".

To manufacture machines generally requires two primary capabilities: fabrication of parts and assembly of parts. By 1998 at least primitive parts fabrication and parts assembly capability had been demonstrated at the molecular level using three different enabling technologies: biotechnology, supramolar chemistry and scanning proves. So far, many nanomachines, such as molecular differential gears and pumps, have been theoretically designed using individual molecules as building blocks. However, manufacturing technologies able to assemble nanomachines molecule-by-molecule do not exist yet.

[1] A *molecular device* can be defined as an assembly of a discrete number of molecular components designed to achieve a specific function. Each molecular component performs a single act, while the entire supramolar assembly performs a more complex function, which results from the cooperation of the various components.

[2] A *molecular machine* is a particular type of molecular device in which the component parts can display changes in their relative positions as a result of some external stimulus.

1.4.3 Bio-hybrid Approach

Nature has inspired mankind for ages and has been a key source from which we can learn and adapt. As above stated, several biological structures found in living organisms can be considered nanomachines (see Figure 1.3). Some examples found in *cells* include nano-biosensors, nano-actuators, biological data storing components, tools and control units.

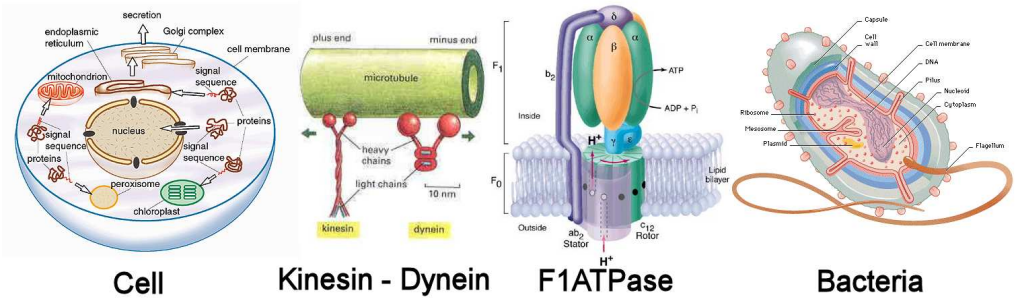

Figure 1.3: Biological Nanomachines.

The underlying principle of *biomimetics* deals with the understanding, conceptualization and mimicking nature's way of handling various problems and situations. Natural processes are extremely efficient in terms of energy and usage of materials, and provide us with many inspiring designs and principles. In nano-scale two levels in biomimetics are considered:

- **Machine-nano-mimetics**: It consists in the creation of artificial nanomachine components *inspired* by the equivalent machine components at nanoscale.
- **Bio-nano-mimetics**: Principle where biological entities, such as proteins and DNA, are *used* to create the nanomachine components.

The field of nanorobotics encapsulate these two mimetic principles, and inherit their various characteristics, design logic and advantages. A general overview of bio-nanomachines will be thoroughly discussed later; Nevertheless, some examples in line with this approach, and illustrated in Figure 1.3, are the use of biological *nano-motor* to power a nano-device or the use of *bacteria* as controlled propulsion mechanisms for the transport of micro-scale objects.

This approach proposes building new nanomachines inspired in these biological structures or use them as building blocks together with manufactured components to perform more complex systems such as *nanorobots*. Next chapter will explore more thoroughly this promising approach for nanomachines development.

1.5 Nanotechnology Applications

Nanotechnology is a cutting edge investigation area that has come out with new and unlimited applications. Private and public research efforts worldwide are developing nanoproducts, some of which have entered the marketplace, more are on the verge of doing so, and others remain more a vision that a reality [21]. The potential for these innovations is enormous and have many applications, just few of them are shown here.

- **Biomedical**

  Terms such as biomedical nanotechnology, bio-nanotechnology, and nanomedicine are used to describe this hybrid field. The most direct applications of nanomachines and nanonetworks are in the biomedical field:

  - **Diagnostic techniques.** Biological tests measuring the presence or activity of selected substances become quicker, more sensitive and more flexible when certain nano-scale particles are put to work as tags or labels. Health monitoring also takes advantage of in-body nano-sensor networks.
  - **Drug delivery.** Overall drug consumption and side-effects can be lowered significantly by depositing an active agent to transport drug molecules to the desired location. NEMS are being investigated for that active release of drugs.
  - **Tissue engineering.** Nanotechnology can help to reproduce or to repair damaged tissue. Tissue engineering might replace todays conventional treatments like organ transplants, artificial implants, or prostheses, although it is closely related to the ethical debate.

- **Chemistry and Environment**

  In short-term perspective chemistry will provide novel "nanomaterials" with tailored features and chemical properties.

  - **Catalysis.** The extremely large surface to volume ratio from nanoparticles benefits catalysis applications that range from fuel cell to catalytic converters and photocatalytic devices.
  - **Filtration.** A strong influence of nanochemistry on *waste-water treatment*, *air purification* and *energy storage devices* is to be expected. Some water-treatment devices incorporating nanotechnology are already on the market, with more in development. Moreover, low-cost nanostructured separation membranes methods have been shown to be effective in producing potable water in a recent study.

- **Energy**

  Advancements in nanotechnology related to energy are: *storage*, *conversion*, *manufacturing improvements* by reducing materials and process rates, *energy saving* by better insulation for example, and enhanced *renewable energy sources*.

- **Information and Communication**

  - **Memory storage and novel semiconductor devices.** The dependence of the resistance of a material on an external field (due to the spin of the electrons) can be significantly amplified for nano-scale objects, and can be used to create a non-volatile main memory for computers, increase in the data storage density of hard disks, etc.
  - **Novel optoelectronics devices.** Analog electrical devices are increasingly replaced by optical or optoelectronic devices due to their enormous bandwidth and capacity, respectively. Two promising examples are photonic crystals and quantum dots.
  - **Displays.** Lower energy consumption could be accomplished using carbon nanotubes (CNT).
  - **Quantum Computers.** Entirely new approaches of quantum mechanics enable the use of fast quantum algorithms for several computations at the same time.

- **Heavy Industry**

  - **Aerospace.** Nanotechnology will provide lighter and stronger materials.
  - **Refineries.** Using nanotech applications, refineries will be able to remove any impurities in the materials they create.
  - **Vehicle manufacturers.** Nanotechnology will provide lighter and stronger materials, as well as more heat-resistant combustion engines.

- **Consumer Goods**

  - **Foods.** Nanotechnology can be applied in the production, processing, safety and packaging of food. Nanocomposite coating process creates active packaging that prolongs food quality and shelf life.
  - **Household.** The most prominent application is self-cleaning or easy-to-clean surfaces.
  - **Optics.** Nanotechnology also offers scratch resistant surface coatings based on nanocomposites.
  - **Textiles.** The use of engineered nanofibers already makes clothes water- and stain-repellent, and wrinkle-free. In mid-term, "smart" clothes can be developed.

- **Cosmetics.** Different products are improved with nanoparticles, such as sunscreens and makeup products.

- **Military Field**

  These applications are similar to some of aforementioned, but they are focused on military requirements.

  - **Nuclear, biological and chemical (NBC) defenses.** Nanonetworks (composed of both nano-sensor and nano-actuator) can be deployed over the battlefield or targeted areas to detect aggressive chemical and biological agents and coordinate the defensive response [1].
  - **Functionalized equipments**. These applications include "smart" uniforms, stronger and lighter armaments.
  - **Battlefield monitoring and actuation.**

Chapter 2

Nanomachines

Nanomachines, both those found in biological systems and artificially created, are small devices or components that perform only simple tasks of computation, sensing or actuation due to their limited size (measured in nanometers) and limited complexity [25]. Nanomachines are largely in the research-and-development phase, but some primitive devices have been tested. An example is a sensor having a switch approximately 1.5 nanometers across, capable of counting specific molecules in a chemical sample.

The first useful applications of nanomachines will likely be in medical technology, where they may be used to identify pathogens and toxins from samples of body fluid. Another potential application is the detection of toxic chemicals, and the measurement of their concentrations, in the environment. More complex nanomachines, such as *nanorobots*, might be designed not only to diagnose, but to treat disease conditions, perhaps by seeking out invading bacteria and viruses and destroying them. As no artificial non-biological nanorobots have yet been created, they remain as a hypothetical concept.

Some advantages of nanomachines are their durability, their microscopic size, their high operational speed, and their tiny amount of energy requirement to operate.

We believe in the bio-hybrid approach, because of that this chapter will be focused in this solution for nanomachines development. One of the main advantages of using nature's machine components is that they are highly efficient, and reliable. Just as conventional macro-machines are used to generate forces and motions to accomplish specific tasks, bio-nanomachines can be used to manipulate nano-objects, to assemble and fabricate other machines or products, to perform maintenance, repair and inspection operations.

There are many complexities that are associated with using bio-components, but the advantages of using them are also quite considerable [22].

- These bio-components offer immense variety and functionality at a scale where creating a man made material with such capabilities would be extremely difficult.
- These bio-components have been perfected by nature through millions of years of evolution and hence they are very accurate and efficient. For instance, F1-ATPase is known to work at efficiencies which are close to 100%. Such efficiencies, variety and form are not existent in any other material found today.
- Another significant advantage in protein-based bio-nanocomponents is the development and refinement over the last 30 years of tools and techniques enabling researchers to mutate proteins in almost any way imaginable. An excellent example of this approach is the use of zinc to control F1-ATPase, which is able to rotate a nanopropeller in the presence of ATP.

A list of the most important components of the typical systems or machines assembly and the equivalence between macro- and potential bio-nanocomponents is depicted in Figure 2.1.

COMPONENT		MACRO-	NANO-
Structural Elements	Links	Metal Plastic Polymer	DNA Nanotubes
	Joints	Metal Plastic Polymer (Revolute, Prismatic, Spherical, Cylindrical)	DNA hinge Molecular bonds Synthetic joints
	Actuators	Electrical, Pneumatic and Hydraulic Motors Smart material based actuators	ATPase protein Flagella motors DNA actuators Viral Protein Motors, etc.
Transmission Elements		Springs (Metal, polyvinyl) Bearings Gears	β Sheets Molecular camshaft design [Smith, 2001]
Sensors		Light, Force, Position, and Temperature Sensors	Rhodopsin Heat Shock Factor

Figure 2.1: “Macro” and “Bionano” equivalence of components used in machines assembly.

2.1 Nanomachines Architecture

According to the bio-hybrid approach, cells have been considered as the reference model to learn from and imitate in order to develop new bio-inspired nanomachines and systems for specific communication purposes. From [1], Figure 2.2 illustrates a components mapping between a generic architecture of a nanomachine and the biological nanomachines found in living cells:

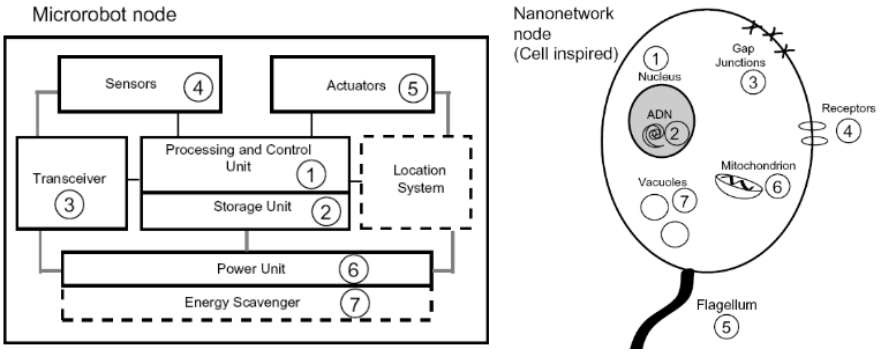

Figure 2.2: Functional architecture mapping between nanomachines of a nanorobot, and nanomachines found in cells [1].

(1) Control Unit. It is aimed at executing the instructions to perform the intended tasks controlling all the other nanomachine's components. It could include a storage unit, in which the information of the nanomachine is saved. In the cell's case, all the instructions to carry out the intended cell functions are contained in the *nucleus*.

(2) Communication Unit. It consists of a transceiver able to transmit and receive messages (molecules) at nano-level. *Gap junctions* and *ligand receptors*, located on the cell membrane, play this role in the cell.

(3) Reproduction Unit. The function of this unit is to fabricate each component of the nanomachine using external elements, and then assemble them to replicate itself. This unit is provided with all the instructions needed to realize this task. In the cellular scenario, the code of the nanomachine is stored in molecular sequences, which are duplicated before the cell division. Each resulting cell will contain a copy of the original DNA sequence.

(4) Power Unit. This unit is aimed at powering all the components of the nanomachine by getting energy from external sources such as light or temperature, and store it for a later distribution and consumption. Cells can include different nanomachines for power generation such as the *mitochondrion*, which generates most of the chemical substances used as energy in many cellular processes, and the *chloroplast*, which converts sunlight into chemical fuel.

(5) Sensors and Actuators. These components act as an interface between the environment and the nanomachine. Several sensors and/or actuators can be included in a nanomachine, e.g., temperature sensors, chemical sensors, clamps, pumps, motor or locomotion mechanisms. Good examples found in cells are the transient receptor potential (taste) and the flagellum (locomotion).

2.2 Features of Nanomachines

Desirable features of future nanomachines are already present in a living cell, some of them include *self-contention, self-assembly and self-replication, locomotion, communication capabilities*, and *interface architecture* [1]:

- Nanomachines will have a set of instructions to realize specific tasks, embedded in their molecular structure. They will be *self-content*.
- *Self-assembly* and *self-replication* enable assemblage at nano-scale and nanomaintenance, without external intervention, which implies the nanomachines will contain the corresponding instructions.
- *Locomotion* enables nanomachines to move.
- *Communication* between nanomachines is required to realize more complex tasks in a cooperative manner, and enable decentralization and distributive intelligence (*swarm intelligence*).
- "Nano" to "macro" world *interface architecture* providing instant access to nanomachines, its control and maintenance.

This main features of nanomachines have been widely addressed in the literature [1], [22], [25]. While all of them being important, there are two characteristics evident in cells that have not been paid enough attention from the communication point of view, which are their *multitasking* capabilities and their *multi-interface* architecture.

- *Multitasking.* A cell can be doing several different actions at the same time. On the one hand, it can take nutrients, convert them into energy, reproduce, breath, etc. On the other, while doing these vital functions, it can be sampling the environment or signalling other cells in the nearby, for instance. Thus nanomachines, as well as cells, should be understood as complex and complete systems.
- From a communication point of view, cells and therefore nanomachines, can be seen as *multiple-interface* devices. Cells have hundreds, or even thousands, of receivers. A single cell is able to communicate using different

channel access techniques: gap junctions, ligand-receptors, molecular motors. In addition, according to the previous feature, cells can be using different communication mechanisms simultaneously.

Furthermore, all cells have specific and highly sensitive **signal transducing mechanisms** [27]: The receptors bind the signal molecule, amplify the signal, integrate it with input from other receptors, and transmit it into the cell. If the signal persists, receptor desensitization reduces or ends the response. These mechanisms are illustrated in Figure 6.4:

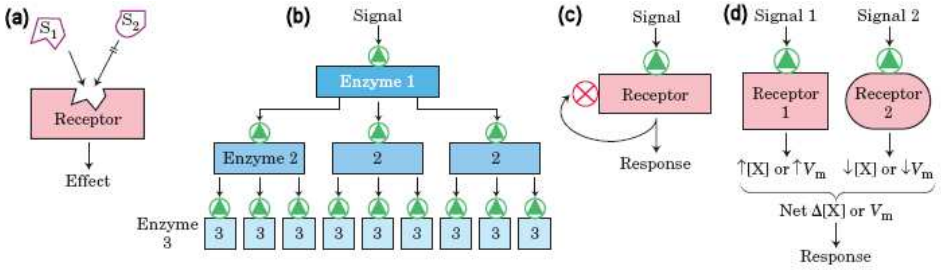

Figure 2.3: Four features of signal-transducing systems: **(a) Specificity**, **(b) Amplification**, **(c) Desensitization**, and **(d) Integration** [27].

(a) Each ligand and each receptor are complimentary. Different ligands attach to different receptors. *Specificity* measures the precision a signal molecule fits on its molecular complementary receptor, where other signals do not fit.

(b) *Amplification* by enzyme cascades results when an enzyme associated with a signal receptor is activated and, in turn, catalyzes the activation of many molecules of a second enzyme, each of which activates many molecules of a third enzyme, and so on. Such cascades can produce amplifications of several orders of magnitude within milliseconds.

(c) The sensitivity of receptor systems is subject to modification. When a signal is present continuously, *desensitization* of the receptor system results; when the stimulus falls below a certain threshold, the system again becomes sensitive.

(d) *Integration* is defined as the ability of the system to receive multiple signals and produce a unified response appropriate to the needs of the cell or organism. For instance, when two signals have opposite effects on a metabolic characteristic (Figure 6.4), the regulatory outcome results from the integrated input from both receptors by reinforcing in more or less degree the different internal metabolic paths.

2.3 Roadmap

As introduced at the beginning of this chapter, nanorobotics refers to the still largely hypothetical nanotechnology engineering discipline of designing and building nanorobots. Nanorobots would be typically devices ranging in size from $0.1 - 10$ micrometers and constructed of artificial or biological nanocomponents. The roadmap for the development of bio-nanorobotic systems for future applications (medical, industrial, environmental, military, and spatial) is shown in Figure 2.4.

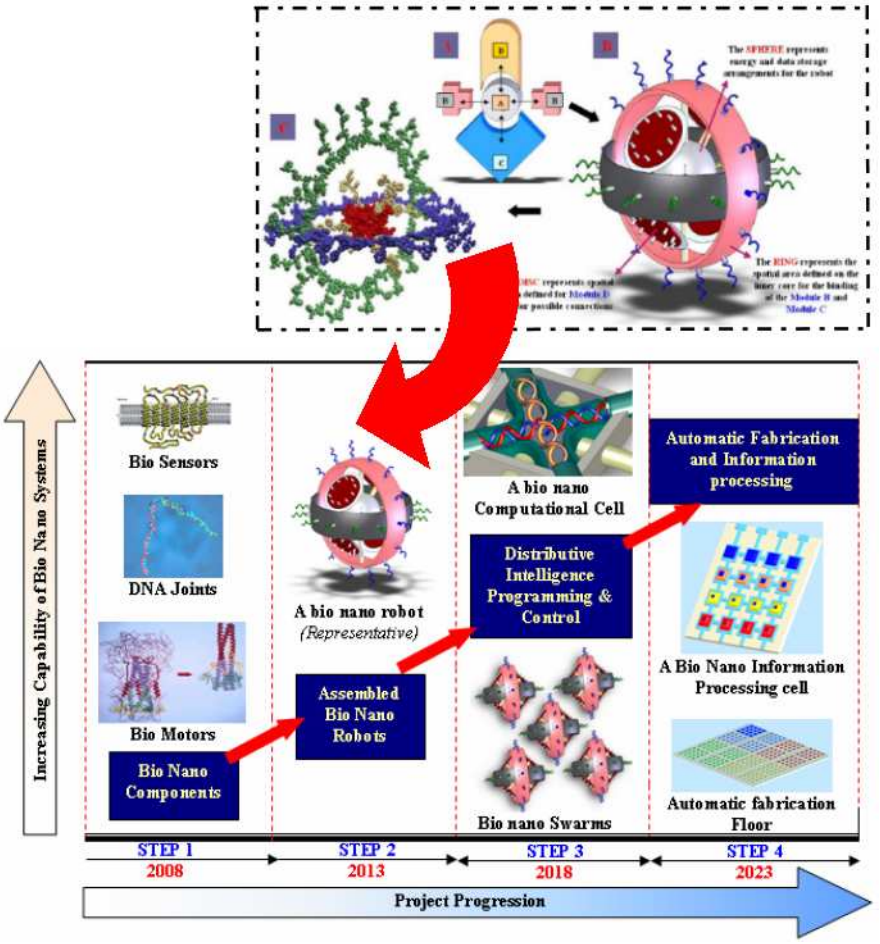

Figure 2.4: The Roadmap, illustrating the system capability targeted as the project progresses [22].

The roadmap progresses through the following main steps:

1. The first research area is in determining the structure, behavior and properties of basic bio-nanocomponents (e.g., proteins).

2. The next step is combining these components into complex assemblies. The figure shows a conceptual representation of *modular organization* of a bio-nanorobot. The modular organization defines the hierarchy rules and spatial arrangements of various modules of the bio-nanorobots such as: the inner core (energy source for the robot); the actuation unit; the sensory unit; and the signaling and information processing unit. By the beginning of this phase a "library of bio-nanocomponents" will be developed, which will include those modular categories: actuation, energy source, sensory, signaling etc.

3. With the individual bio-nanorobots capable of basic functions, concepts of co-operative behavior and distributed intelligence need to be developed, to enable them to collaborate with one another. This design step could lay the foundation towards the concept of *bio-nanoswarms* (distributive bio-nanorobots). Again, it is planed to follow natures path, mimicking the various colonies of insects and animals, and transforming principles learned to our domain.

4. The next step in nanorobotic designing would see the emergence of automatic fabrication methodologies.

The recent explosion of research in nanotechnology, combined with important discoveries in molecular biology have created a new interest in bio-nanorobotic systems. Bio-mimetic (section 1.4.3) and its principles would greatly influence the field of nanorobotics and nanotechnology.

Chapter 3

Communication Among Nanomachines

Multiple nanomachines can be interconnected to work collaboratively and in a distributed manner and, perform complex tasks such as sensing, computation, or actuation. As stated in the previous chapters, the interconnection and communication of functional components at nano-scale is defined with the term *nanonetworks*. Nanonetworks are usually used in two different branches of research (Figure 3.1). On one hand, nanonetworks are used to refer to structures, interconnections of devices, or modified materials at nano-scale (involving dry techniques), and on the other, nanonetworks are used to refer to a novel communication scheme that includes transmitter and receiver devices, information, carrier and medium (this involves wet techniques). Communications take place by different means in dry and wet techniques.

3.1 Dry Techniques

Dry techniques refer to all of the nanotechnologies that deal with the study of fabrication of structures in carbon, silicon and other inorganic materials. It is usually aimed at building nano-scale structures, by scaling down the current micro-scale technology, that then need to be assembled on a chip. Nanowires and nanotubes are good examples of such techniques.

In this context, a basic distinction is commonly used between nanowired communications and wireless optical communications.

3.1.1 Nanowired Communication

A *nanowire* is a structure that have a lateral size constrained to tens of nanometers or less (diameter) and an unconstrained longitudinal size. Typical nanowires exhibit aspect ratios (length-to-width ratio) grater than 1000, as such they are often

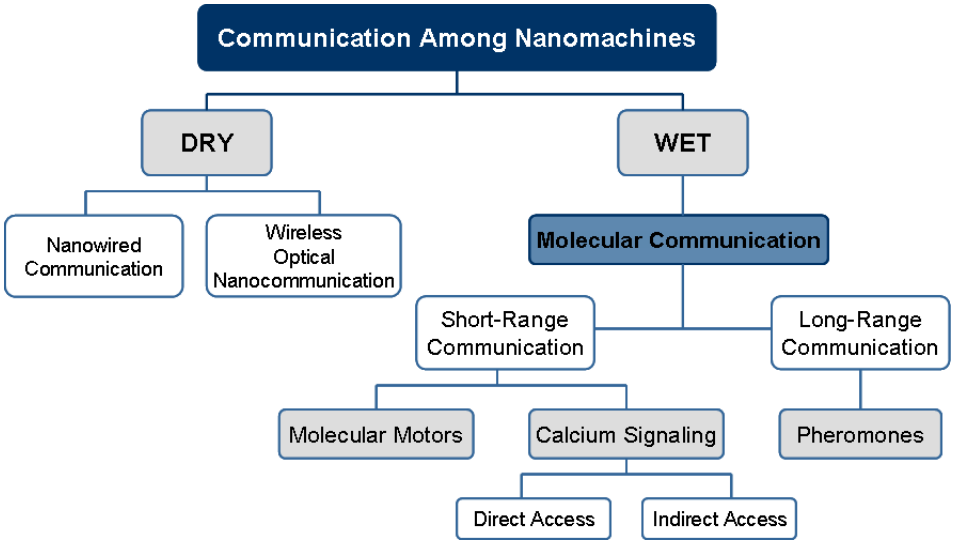

Figure 3.1: Schematic representation of possible Nanonetwork Communication.

referred to as 1-Dimensional materials. As illustrated on Figure 3.2, the diameter of these wires is small, even smaller than the smallest structures that are currently fabricated using lithographic techniques. At these scales, quantum mechanical effects are important.

A variety of organic (e.g. DNA) and inorganic wires have been fabricated. The most prominent examples in inorganic fabrication are silicon nanowires and carbon nanotubes, although metallic wires (e.g., Ni, Pt, Au) and nanofibers of conducting polymers (e.g., polyaniline) have also been produced. Nanowires could be used, in the near future, to link tiny components into extremely small circuits.

Nanowire and carbon nanotube networks have several *advantages* [17] of importance in comparison with other structures, such as thin films for example:

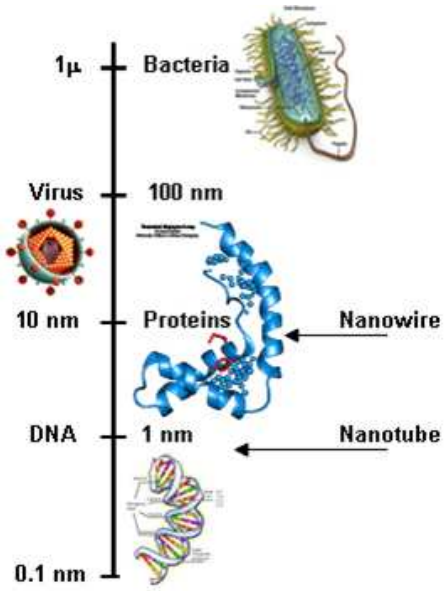

Figure 3.2: The size scale of nano-scale metallic, semiconducting wires with high aspect ratio, as compared with fabricated (CMOS) structure sizes.

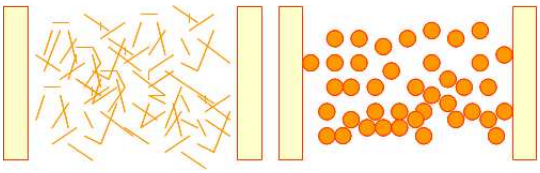

Figure 3.3: The concept of two dimensional random nanowire network (upper part) and networks built of wires and dots (lower figure).

Conductance. The conductivity of the wires is large; The larger the nanowire conductivity, the better the network conductance. Factors like nanowire-nanowire interconnects are also playing an important role as later will be addressed.

Transparency. A network of highly one dimensional wires has very elevated transparency (approaching 100% for truly one dimensional wires) as illustrated on the lower part of Figure 3.3: a wire network with a conducting channel has much higher transparency than the same construction using quantum dots.

Flexibility. A random network of wires has, as a rule significantly higher flexibility that a film of comparable surface coverage, making this architecture eminently suited for flexibility-requiring applications.

Fault Tolerance. Breaking a conducting path leaves many others open. The elec-

tron pathways will be rearranged.

The Individual Components. The ability to make highly perfect wires (with quality superior than that of thin films, for example) is retained in the random nanonets. The individual elements are grown by a variety of techniques, a fact not surprising in the light of the broad variety of nanowires.

Appropriate solubilization, and deposition technologies of such wires (while avoiding bundling) are essential to arrive. These have been solved in certain cases, for example significant effort has been devoted to carbon nanotube solubilization and deposition.

A *carbon nanotube (CNT)* is a cylindrical structure that looks like a rolled up sheet of graphite (Figure 3.4). Its properties depend on how you roll the graphite into the cylinder: by rolling the carbon atoms one way, you can create a semiconductor, whereas rolling them another way can make a material hundreds of times stronger than steel, but six times lighter. The cylindrical nanotube usually has a length-to-width ratio greater than nanowire's, since its diameter is in the order of a few nanometers (approximately 1/50,000th of the width of a human hair), while they can be up to several millimeters in length. Carbon nanotubes have novel properties, ranging from their unique dimensions to an unusual current conduction mechanism, that make them potentially useful in many applications in nanotechnology, electronics, optics, and other fields of materials science, as well as potential uses in architectural fields.

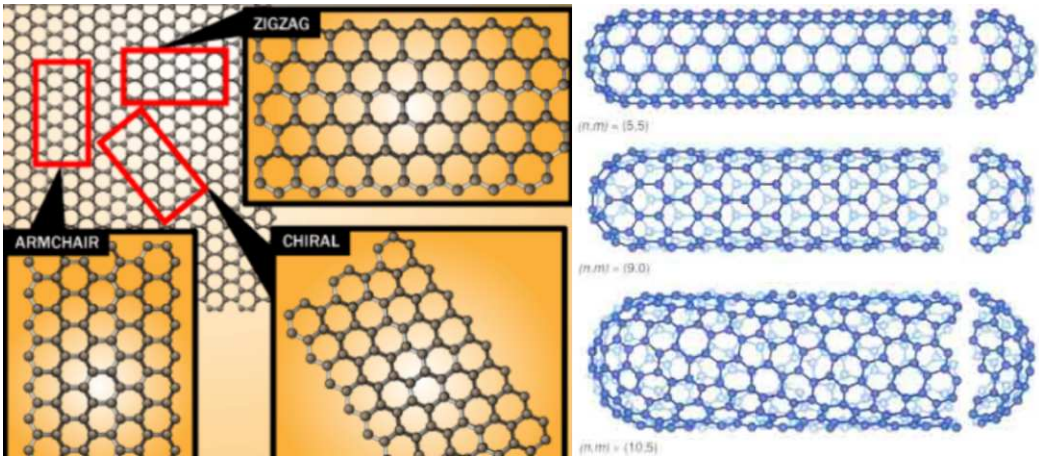

Figure 3.4: If a sheet of carbon is rolled, it creates a carbon nanotube. Depending on the direction the sheet is rolled into, different patterns emerge.

Due to their small size, nanotubes can reach deep into their environment without affecting their natural behavior. For example, a single CNT is small enough to penetrate a cell without triggering its defensive responses.

Individual nanotubes can be used to construct a network of sensing elements with a greater depth and coverage than today's sensor networks. Unfortunately, networking such a collection of sensors using current techniques negates the advantages of CNT size.

Current technology is focused on utilizing an entire CNT network as semiconducting material to construct a single transistor or Field Effect Transistor (FET), and in using individual nanotubes within random carbon nanotube networks (CNT) to carry information among different nano-devices.

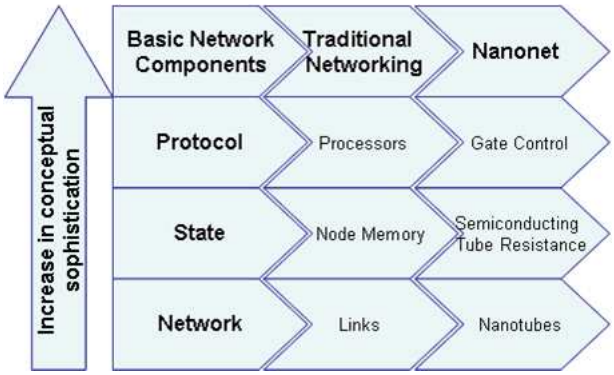

Figure 3.5: Network components for nano-scale networking requires modification of networking concepts to best fit in that tiny environment.

In the case of CNT networks, the traditional networking stack is inverted because, rather than the network layer being positioned above the physical and link layers, the CNT network and routing of information is an integral part of the physical layer [13]. At the bottom level, following the Table 3.5, communication links in CNT networks may be **carbon nanotubes** overlapping at points that will be identified as nodes, instead of the links between hosts and routers found in traditional networks. Data transmission occurs via modulated current flow through the CNT network. **Gate control** is used to induce routes through the CNT network, which is initially divided in different gates or areas (see Figure 3.6). When a gate is turned on, the nanotubes within its area become conducting [12]. The sensing elements, which sense by variation in resistance, may act simultaneously as routing elements. Hence, data must either flow, be switched or routed through nodes, by varying the nanotubes resistance. This is enabled by changing **state**, which may be implemented as a routing table on a router or an electromagnetic field controlling the resistance within the specific area of the CNT network. Finally, a variety of applications will benefit from this technology. The most obvious use for nanowires is in electronics, including transparent electronics, plastic or macro-electronics where mechanical flexibility is essential, etc. But not all nanowire applications are in this field, for instance researchers are also using nanowires to coat titanium implants, reducing the risk of implant failure.

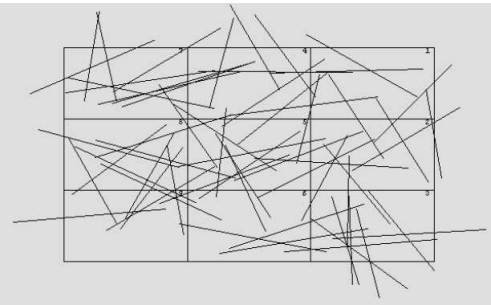

Figure 3.6: Matrix of gates on a random CNT network.

3.1.2 Wireless Optical Communication

In this case, the communication process consists in the emission of photons from a properly excited molecule, which are captured by a predisposed receiver. A possible way to perform such kind of communication is indeed suggested by *plasmonics*, an emerging branch of nanophotonics, which studies properties of collective electronic excitations (known as *surface plasmons*) in thin films or nanostructures of noble metals. It offers an opportunity to merge photonics and electronics at nano-scale dimensions, and to realize very large scale electronics and photonics integration.

A plasmon is a quantum of a plasma oscillation or vibration, that is, a quasiparticle resulting from the quantization of plasma oscillations, just as photons and phonons are quantizations of light and sound waves, respectively. Thus, [29] one can think of a plasmon as a sphere comprised of many discrete, evenly-spaced positive charges, that can be approximated as a positive charge distribution, which at the same time is surrounded by a negative charge distribution consisting of a free electron cloud hovering just on top of the positive charge distribution, but not in contact (Figure 3.7). Hence, they are basically vibrational modes of the electron gas density, oscillating about the metallic ion cores, often at optical frequencies.

Surface plasmons can oscillate at relatively low frequencies for relatively small wavelengths. Some predisposed metallic structures capture specific wavelengths of light and convert an amount of electrical energy back into light that is reflected away, in other words, plasmons couple with a photon to create a third quasiparticle called a *plasma polariton*. This polariton propagates along the surface of the metal until it decays, either by absorption, whereupon the energy is converted into phonons, or by a radiative transition into a photon. Surface plasmons can be excited by both electrons and photons. If light frequency is lower than the plasma's, light is reflected, because the electrons in the metal screen the electric field of the light. Whereas, if light frequency is higher than the plasma's, light is transmitted, because the electrons cannot respond fast enough to screen it.

Plasmons have been considered as a means of transmitting information on com-

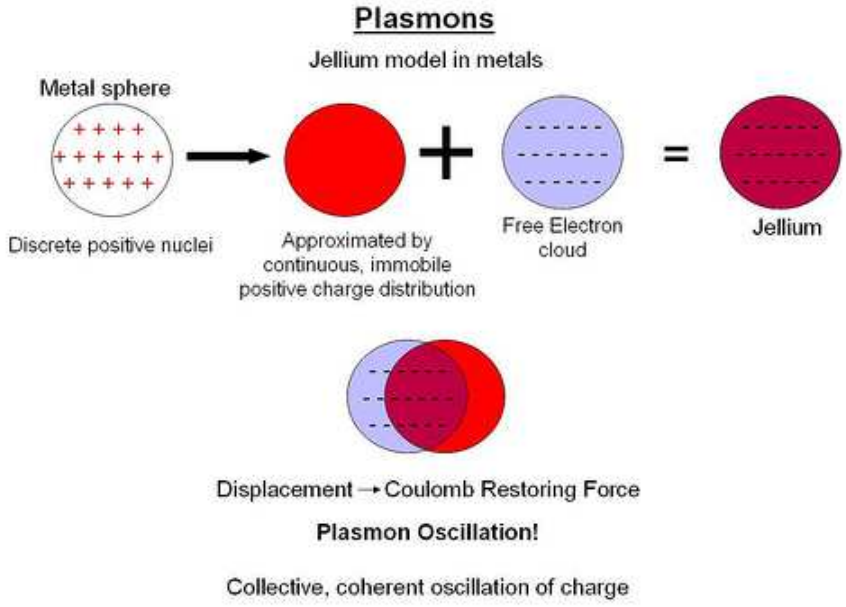

Figure 3.7: "Jellium" model in metals

puter chips, since they can support much higher frequencies (into the 100 THz range, while conventional wires become very lossy in the tens of GHz). Plasmons have also been proposed as a means of high-resolution lithography and microscopy due to their extremely small wavelengths. Both of these applications have seen successful demonstrations in the lab environment. For plasmon-based electronics to be useful, an analog to the transistor, called a "plasmonster", must be invented.

Surface plasmons can be described by macroscopic electromagnetic theory (Maxwells equations) if only if the electron mean free path in the metal is much shorter than the plasmon wavelength, which is usually fulfilled at optical frequencies. Nevertheless, the main drawback in optical molecular communication is that classical mechanic laws do usually fail, due to quantum effects. Furthermore, note that in macroscopic electromagnetic theory, bulk material properties such as dielectric constants, are used to describe objects irrespective of their size. However, for particles of nanoscale dimensions, a more fundamental description of their optical and electronic properties may be required.

3.2 Wet Techniques

Wet techniques refer to the study of biological systems that usually operate in aqueous environment, such as molecular motors, DNA-based systems, etc. Since dealing with biological systems, it is provably a good idea to draw inspiration from

nature in order to design communication systems at such level. In this direction it is been explored the possibility of communicating at the nanometer scale using molecular communication.

3.2.1 Molecular Communication

Molecular communication is a new communication paradigm that was firstly introduced in [16]. It does not use electromagnetic waves but uses molecules to transmit the information. Molecular communication is a new and interdisciplinary field that spans nano, bio and communication technologies.

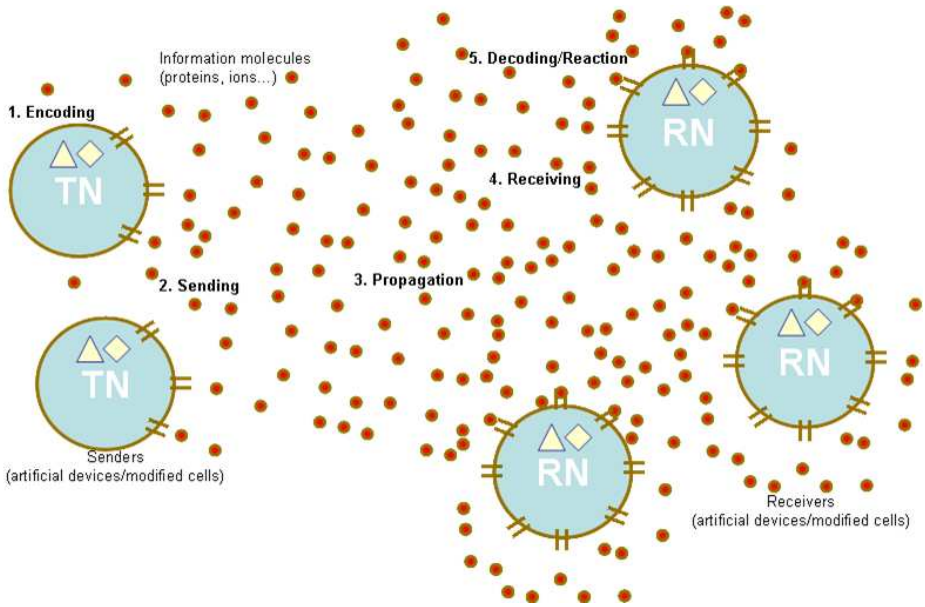

Figure 3.8: Molecular communication process.

Key components of this communication system are depicted in Figure 3.8 and include a transmitter, a receiver, and a propagation system:

1. **Encoding.** The transmitter encodes information onto molecules (called *information molecules*).

2. **Transmission.** The transmitter inserts the message into the medium by releasing the encoded information molecules to the environment or by attaching them to molecular carriers.

3. **Propagation.** Information molecules propagate from the transmitter to the receiver.

4. **Reception.** Information molecules are detected or unloaded from the carriers at a receiver.

5. **Decoding/Reaction.** Upon receiving the information molecules, the receiver decodes the molecular message into useful information such as biochemical reaction, data storing, actuation commands...

Unlike previous communication techniques, the integration process of molecular transceivers in nanomachines is more feasible due to the size and natural domain of molecular transceivers. These transceivers are nanomachines able to react to specific molecules, and to release others, as a response to an internal command. Molecular communication provides means for biological and artificially-created nanomachines to communicate over short and long distances. In the framework of nanonetworks, short-range is understood as the communication process that takes place in the range from nm to few mm, whereas long-range refer to the communication process in which the transmitter and receiver nanomachines range from mm up to km [1].

- **Short-Range Communication using Molecular Motors**

  Most of the intra-cell communications are based on molecular motors. Molecular motors (e.g., kinesin, dynein, and myosin) are proteins or protein complexes that transform chemical energy into mechanical work at a nano-scale. These protein motors can transport a data packet (molecule) from the transmitter to the receiver as described in [1].

  On the transmitter side, the information molecules are loaded on molecular motors, which transport the information along the microtubules to the receiver. The packets can be encapsulated in vesicles[1], which have a twofold objective:

  1. It allows enhancing the compatibility between the information molecule and the molecular motor, enabling the use of diverse types of molecules as information packets.
  2. The encapsulation protects the information molecules avoiding them to react with antagonistic receptors present in the medium.

  The network infrastructure should be deployed prior to the beginning of the communication process. The propagation of molecular motors along a microtubule is unidirectional. The polarity of the microtubule indicates the movement direction of specific molecular motors, e.g., kinesin moves towards the (+) end of the microtubule, and dynein towards the (-) end.

  Basically, the concept of bio-inspired communication through molecular motors (shown in Figure 3.9) can be summarized as follows:

  – For a given network topology, there exists rail molecules (micro-tubules) establishing connections among several nanomachines.

[1] A *vesicle* is a fluid or an air-filled cavity that can store or digest cellular products.

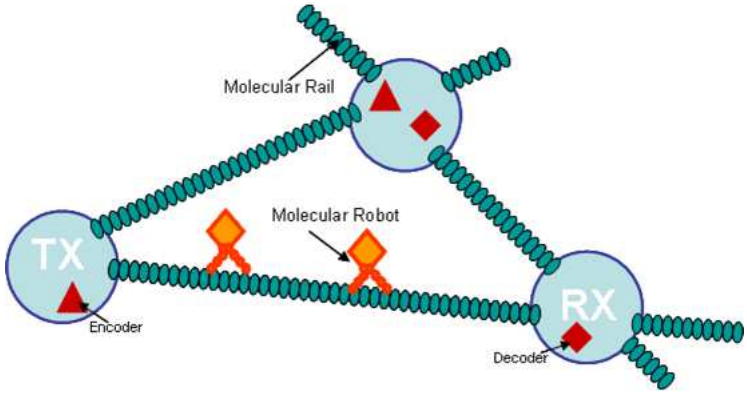

Figure 3.9: System components in molecular motors communication systems.

- When a cell needs to transmit an specific molecule (or even a vesicle), it releases it onto a molecular motor.
- Moving along a pre-established path, the molecular motor will reach the destination.
- The molecule (or vesicle) will either bind to the receiver or be absorbed through a gap junction.

- **Short-Range Communication using Molecular Signals**

  In molecular signaling based communications, the information is transmitted by varying a given concentration of molecules (signals) according to the information that needs to be propagated. Thus, drawing an analogy with the classical wireless communication, the molecule concentration level is considered as the carrier. This carrier may be modulated in frequency (by changing the rate of the molecule concentration) or in amplitude (by changing the number of molecules per unit volume). A good example of this first type of short range molecular communications is calcium signaling [26]. Similar to the natural models, propagation of information can be performed in two different communication schemes depending on the deployment of the nanomachines, as depicted in Figure 3.10:

  - **Indirect Access.** When cells or nanomachines are deployed separately without any physical contact, the bio-inspired approach of the communication scheme can be described as:
    1. Nanomachines and particles in general, suspended in a liquid or gaseous medium, move randomly according to Brownian dynamics.
    2. When a cell or a nanomachine has to transmit some information (for example, something that it has sensed from the environment or

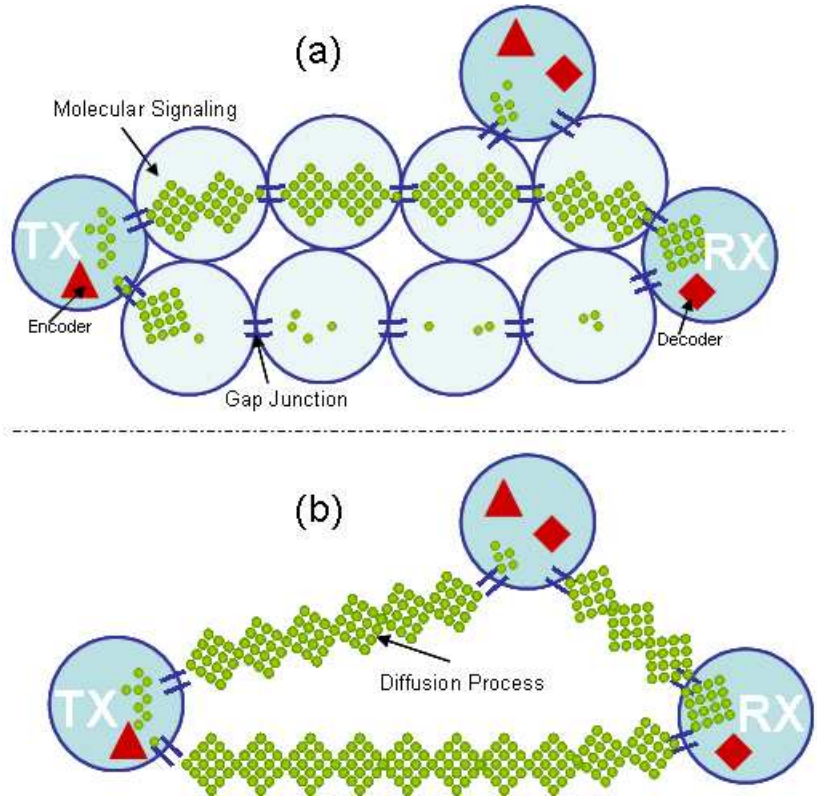

Figure 3.10: Signal propagation in calcium signaling communication systems by (a) gap junctions signal forwarding and (b) by diffusion.

an individual need) it releases a specific type of molecules, which may range in the order of hundreds or even thousands, into the medium. At that moment, the concentration of molecules around the cell increases abruptly.

3. Due to molecular diffusion, these molecules will travel through the medium dispersing themselves randomly. During this propagation phase, other particles in the medium following Brownian dynamics can collide, or even block the movement of these molecules due to noise and interference coming from other molecules being released at the same time.
4. These molecules may finally reach the receptors, which can be also in the order of hundreds or even thousands per cell or nanomachine, located in the cell membrane. These molecules may or may not bind to the receptors, with different affinities.
5. The reaction of a cell will depend on the type of molecule received and different stimulus. Before a cell can transmit again the same molecule, there is an implicit waiting time related to the detaching

phase of the molecules from the receivers.

- **Direct Access.** When cells or nanomachines are physically located one next to the other, in direct contact, then molecular signals propagate through *gap junctions*. A gap junction is a specialized intercellular connection which directly connects the cytoplasm of two cells, allowing various molecules and ions to pass freely between cells. One can think of a gap junction as a gate in the cell's membrane. In this particular case, two different phases within the communication process can be identified: The *approximation phase*, in which a cell or nanomachine physically reaches its target, and the *transmission phase*, in which the following communication process starts:
  1. Two or more cells (nanomachines), being in physical contact, exchange molecules using gap junctions.
  2. One cell can be in contact with different cells and have different gap junctions *open* simultaneously.
  3. While being in contact, ions or molecules will propagate from one cell to another, by following the principles of molecular diffusion resulting from the difference of concentration of a specific molecule type.

- **Long-Range Communication using Pheromones**

  For long-range communication, techniques based on pheromone diffusion can be used [1]. Pheromones can be considered as encoded molecular messages that are released into the medium, such as air or water, and may only be detected by selective nanomachines according to receptor-binding mechanisms. The communication process can be briefly summarized as follows:

  1. When a cell or a nanomachine has to transmit some information (usually to trigger a remote reaction) it releases a specific type of pheromones, into either an aqueous or a gaseous medium. At that moment, the concentration of molecules around the cell increases abruptly.
  2. Due to molecular diffusion, pheromones will travel through the medium dispersing themselves randomly. During this propagation phase, other particles in the medium following Brownian dynamics can collide, or even block the movement of these molecules due to noise and interference. In this scenario physical obstacles should be also taken into account. Moreover, propagation of the information can also be affected by several other factors such as antagonist agents, medium flow, temperature, and dispersion, which can also be considered as sources of noise.
  3. Pheromones may finally reach the receptors which can be located up to several kilometers from the source nanomachines. Also in this case,

pheromones may or may not bind to the receptors and with different affinities. The reaction of a cell will depend on the type of molecule received and different stimulus.

Nanonetworks based on pheromonal communication are good examples of scalable molecular communication, offering a unique opportunity to combine the advantages of nano-scale and long range communication, the "nano" and the "macro" world (see Figure 3.11), since information is encoded at nano-scale, although transmitter and receiver nanomachines can be considered as macro-systems. For instance, on the biological systems found in nature, animals would play the role of nanomachines. However, the communication is still based on nano-transceivers and nano-messages, and therefore it is in line with the definition of nanonetworks [1]. Despite biological nanomachines exhibit a wide variety of mechanisms for exchanging information at the nano and micron scales, nowadays there are no artificial nanomachines capable to carry out the tasks described below, even though they are in the near future prospects.

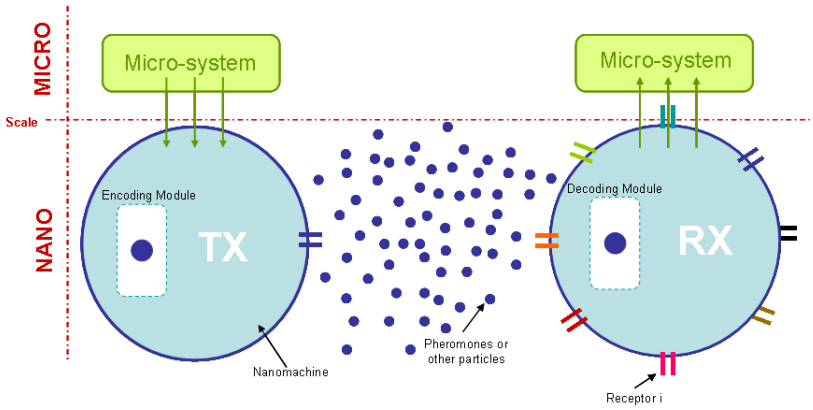

Figure 3.11: Conceptual diagram of a pheromonal communication. Biological models provide a useful example of molecular communication scalability [1].

Long-range communication is further explained on the next chapter.

So far, the following observations make molecular communication the most promising solution for nanonetworking.

On one hand, one of the advantages of using biological systems (e.g. molecular motors to transport molecules, or communication among cells) is that they can address the difficulties of nano-scale communication that the current electrical and optical wave based communication systems may encounter. Biological communication mechanisms have already been naturally selected for functioning at the nano-scale [25]. With the current research emphasis it may become more feasible

in the near future to use and adapt existing components from biological systems (e.g., receptors, nano-scale reactions, communication molecules).

Biocompatibility is another advantage of using biological components as they increase the (bio)compatibility of molecular communication with applications that are sensitive to artificial materials (e.g., require ecological breakdown, biomedical applications).

Existing biological systems also use highly *energy-efficient* processes. single molecular reaction may represent multiple computations, and consumes a relatively small amount of power (e.g., 10,000 times less than a micro-electronic transistor). For example, myosin energy converts ATP to mechanical work with 90 percent efficiency. Thus, molecular communication mechanisms may be able to perform more computation with less energy dissipation than existing electrical components, and would power the nanonetworks nodes and processes. Furthermore, molecular communication may be transmitted over longer ranges while still using the same amount of power and without loss of information.

On the other hand, propagation of information in molecular communication is typically characterized as *low speed* and *highly dependent on the environment conditions* which are very variable compared to standard communication network. These characteristics have repercussions for the design of protocols of molecular communication systems. For example, slow diffusion based processes do not support the creation of high-speed switching functions common in conventional network devices that will require complex queuing mechanisms for packets [32].

The use of molecules to encode and transmit the information represents a new communication paradigm, which demands novel solutions. Nanonetworks are not a simple extension of traditional communication networks at the nano-scale. Their main differences with traditional communication networks can be summarized as follows:

- While in traditional communication networks, the information is encoded in electromagnetic, acoustic or optical signals. In nanonetworks using molecular communication, two different structures can be defined to represent the **information/message**:

  - **Molecules.** Two different and complimentary coding techniques can be considered in this case (Figure 3.12):

    1. The first one uses temporal sequences to encode the information (e.g., molecular signals), such as the concentration of specific molecules in the medium (**concentration encoding**). According to the level of the concentration, i.e., the number of molecules per volume, the receptor decodes the received message.
    2. The second technique, hereinafter called **molecular encoding**, uses internal parameters of the molecules to encode the information. The information transmitted is not a single component, but rather a complex mixture of numerous chemicals in various different percentages of the total. Thus, information may be encoded in the specific molecules used, the chemical structure, relative positioning of molecular elements, polarization, etc. Hence, the information is contained in the molecule itself (receiving a molecule may trigger a specific reaction) [24].

    Molecular communication based on the diffusion process will use molecules to encode the information. More concretely, *short-range communication using molecular signals* will use ions concentration and modulation to encode the information (1), whereas *long-range communication* will use molecular compounds, such as pheromones (2).

  - **Biopolymers.** The information can be encoded inside a biopolymer[2] **(biopolymer encoding)**, such as a DNA sequence. This method will be used in *short-range communication using molecular motors*, where the aforementioned macromolecules will be encapsulated inside vesicles before the transmission process.

[2] *Biopolymers* are a class of polymers, which are large molecules (macromolecules) composed of repeating structural units typically connected by covalent chemical bonds, produced by living organisms. Starch, proteins and peptides, DNA, and RNA are all examples of biopolymers.

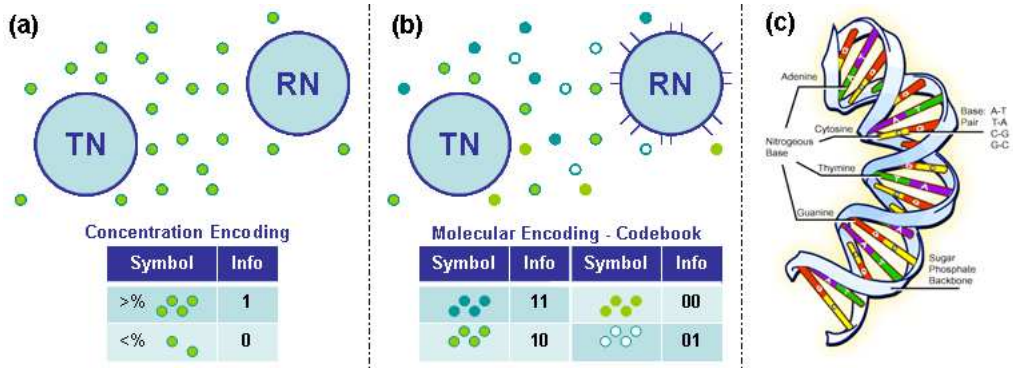

Figure 3.12: Coding techniques: **(a)** Concentration encoding; **(b)** Molecular encoding. For simplicity, both are binary communication; **(c)** DNA-encoding.

- The **propagation speed** of signals used in traditional communication networks, such as electromagnetic or acoustic waves, is much faster than the propagation of molecular messages. In nanonetworks, the information, i.e., the molecules, has to be physically transported from the transmitter to the receiver. In addition, molecules can be subject to random diffusion processes and environmental conditions, such as wind or temperature changes, which can affect the propagation of the molecular messages.

- In traditional communication networks, **noise** is described as an undesired signal overlapped with the signals transporting the information. In nanonetworks, according to the coding techniques, two different types of noise can affect the messages. First, as occurs in traditional communication systems, noise can be overlapped with molecular signals such as concentration level of other molecules. At the same time, in nanonetworks, noise can also be understood as an undesired reaction occurring between information molecules and other molecules present in the environment, which can modify the structure of the information molecules.

- Text, voice and video are usually transmitted over traditional communication networks. By contrast, in nanonetworks the transmitted information is more related to phenomena, chemical states and processes [8].

- In nanonetworks, most of the processes are chemically driven resulting in **low power** consumption. In traditional communication networks the communication processes consume electrical power that is obtained from batteries or from external sources such as electromagnetic induction.

Most of the existing communication networks knowledge is not suitable for nanonetworks due to their particular features. Nanonetworks require innovative networking solutions according to the characteristics of the network components and the molecular communication processes. There is still a lot of work to do

in order to develop efficient molecular communication techniques, such as determining the average speed of different bio-inspired molecular motors in different aqueous media, obtain a propagation model and a channel capacity expression for each type of molecular communications, characterizing and identifying different types of pheromones, etc.

Chapter 4

Long-Range Molecular Communication

Long-range communication is understood as the communication process its efficient distance ranges from millimeters up to kilometers.

Throughout the years technology has been inspired by biology. Natural world life depends on the oldest information communication method: chemical stimuli. Thus animals as well as autonomous robots need to acquire and exchange environmental signals in order to adjust their activity in time and space. These chemical messengers used to convey information between members of the same species to coordinate, cooperate, attract or alert, are commonly termed pheromones. Pheromones can be defined more thoroughly as molecular compounds secreted in minute amounts that trigger a particular behavioral or physiological response (reaction) in another organism of the same species. There are *alarm pheromones*, *food trail pheromones*, *sex pheromones*, and many others. They are widespread used by microorganisms, insects, crustaceans and vertebrates (e.g., motile bacteria, bees, crayfish and bats, respectively), although some fungi and plants also use them. The advantages of pheromone communication are that only minute quantities of chemical are required, it is efficient, easy to broadcast and it is effective at long range [19]. There are single molecule pheromones, but many of them consist of a blend of two or more molecules, which can elicit a grater response than any individual component [11]. Further, one single pheromone may have multiple functions, and, in contrast, a single behavioral response probably involves more than one pheromone.

An example of this bio-inspired technology is the possible application of necrophoric bee behavior for rescuing disabled robots [19]. When bees die, they release a pheromone called oleic acid, and this initiates an hygienic necrophoric behavior in the other bees. Upon detecting the pheromone, worker bees grasp the corpse and move it a certain distance from the hive. This kind of chemically mediated strategy may have several applications in robotic systems such as the rescue robots. In the case a robot suffers a serious problem, a total loss of power for instance, it could broadcast a chemical automatically. The chemical would then be carried away by

the air flow and received by the rescue robots. Finally, the rescue robots would locate the malfunctioning robot and retrieve it cooperatively. Another application in robot swarms is inspired by the queen bee, which releases pheromones throughout the colony to coordinate the actions of its members. Again in the robot case, the robot leader releases different chemicals to guide the swarm members and to elicit different behaviors [18].

4.1 Transport of Molecular Information

The movement of chemicals (e.g., molecules, ions, etc.) from a source to a receiver within a fluid (i.e., liquids and gases) is carried out by convective-diffusive transport, which can occur either by convection due to bulk flow (advection) or by diffusion due to Brownian motion. In *convective transport*, material is transported by the large-scale motion of currents in the fluid along its streamlines at the main velocity of the fluid. On the other hand, *Brownian motion* is the random movement of particles suspended in a liquid or gas, which are subjected to continuous collisions, from all directions, with the surrounding molecules. If the velocities of all molecules were the same all the time, the particle would experience no net movement. However, molecules don't have a single velocity at a given temperature, but rather have a distribution of velocities of varying degrees of probabilities, resulting in an observable random zigzag movement.

At very small size scales this movement of chemicals is driven by random molecular motion (e.g., Microorganisms information exchange) due to particles movement at micron-scale is dominated by viscous forces, not inertial (Reynolds number[1] is below 10^{-2}); cohesion among fluid molecules let them move transversely to the streamlines in response to molecular-scale collision. This case does apply for molecular nanonetworking.

With increasing the size and velocity of organisms (increasing Reynolds number), molecular diffusion loses in importance for the dispersal of chemicals because of its slow rate. Consequently, fluid flow becomes the most effective way in dispersing molecules. So that you can get an idea, molecular diffusion for 1 hour would displace a particle by no more than 5 mm in water and 500 mm in air, whereas in the case of dispersion by fluid flow, particles move at the velocity of the fluid.

Modulating the nearby flow pattern, animals can facilitate the exchange of chemical information with their environment by using undulating, beating, or fanning appendages. Fan organs are widely used in the animal kingdom to propel and direct chemical stimuli away from and toward organisms. Insects, as well as some

[1] *Reynolds number* is a measure of the ratio of inertial forces to viscous forces and, consequently, it quantifies the relative importance of these two types of forces for given flow conditions.

$$Re = \frac{InertialForces}{ViscousForces}$$

vertebrates, use wing-fanning for delivering pheromones to their mates and facilitate pheromones perception by moving nearby molecules to the receptors (e.g., bees, butterflies and bats). Crustaceans, such as the crayfish, are well known for their ability to create directed water currents used for both sending and receiving chemical signals in aquatic environments with stagnant flow conditions. The versatility of the crayfish fan organ has been shown to help terrestrial autonomous robots to locate chemical sources by actively drawing air to their chemical sensor and scanning different directions for the presence of chemicals [10].

4.2 Communication Process using Pheromones

Communication is the process of transferring information from a sender to a receiver with the use of a medium in which the communicated information is understood by both sender and receiver. This requires all parties understand a common language and allows nanomachines/organisms to exchange information by several methods.

In nanonetworks as well as in biological systems, the communication between nanomachines involves the following 5 processes: *encoding*, *transmission*, *propagation*, *reception* and *decoding*.

4.2.1 Encoding

T*his is the process by which a sender encode the information on molecules so that it produces the intended reaction in the receiver.* While in traditional communication networks the message is encoded using a binary system (section 3.2), in long-range nanonetworks information is encoded on the molecule itself by means of *molecular encoding*. The released message is not a single component, but rather a complex mixture of numerous chemicals in various different percentages of the total. Thus, information may be encoded using internal parameters of the molecules, such as he specific molecules used, the chemical structure, relative positioning of molecular elements, polarization, etc.

4.2.2 Transmission

In this process the sender nanomachine emits the encoded information into the environment. This release can be both liquid or gas. Furthermore, according to the message requiring, it can be an *instantaneous* or a *continuous emission*. The instantaneous release of substance, in a single puff, would be the ideal design for communications requiring rapid fade-out. In nature, emission somewhat like this ideal form is approached in the release of alarm substances (alarm-type message); For instance, harvester ants use this kind of alarm communication under certain circumstances. The expanding sphere of diffusing pheromone will remain centered on the animal, if it is in still air, or else be carried along with moving air (or water)

currents. On the other hand, a source of message molecules emitting continuously at a constant rate (message molecules/second) might be useful for status telemetry, navigational beacons or periodic sampling monitors.

It is important to notice that the transmission must be voluntary, otherwise it can not be considered as a communication message [1]. An example of a non-voluntary communication, would be the odors, which can carry information and trigger certain behaviors but usually they are not transmitted voluntarily.

4.2.3 Propagation

Message molecules move through the environment, both dry and wet, from a sender to a receiver. In long-range nanonetworks, the channel can not be considered deterministic neither a physical link between transmitter and receiver because of its high variability. As stated in section 4.1, molecular propagation may occur through fluid flow or by diffusion due to Brownian motion. Propagation through molecular diffusion can be physically described as a net transport of molecules that move from regions of higher concentration towards regions of lower concentration by random molecular motion. This process applies for long-range molecular communication using pheromones released on air, as well as for short-range molecular communication using particles in an aqueous medium (e.g., calcium ions). Molecular diffusion is typically described mathematically using Fick's laws of diffusion[2]. Diffusion of molecules is very sensitive to environmental conditions, once released to the medium, they can be affected by several factors such as temperature, viscosity, medium flow, pressure, dispersion... Antagonist agents also threaten the communication between nano-transducers, since those chemicals bind to the receptor but do not produce a physiological response, blocking the action of those molecules which can produce that response. All those factors that compromise the transmission reliability can be considered as sources of noise, although some of them might be reduced if using artificial messenger molecules.

4.2.4 Reception

This is the process by which a receiver captures carrier molecules propagating in the environment. According to molecular encoding characteristics, the receiver may contain highly selective and sensitive receptors to discriminate the information molecules from others with minimal structural changes, even when the signal-to-noise ratio is very low. These receptors are precise proteins with high binding

[2]**First Law.** Fick's first law relates the molecular flux in a medium with the concentration of molecules, by postulating that the flux of molecules goes from regions of high concentration to regions of low concentration, with a magnitude that is proportional to the concentration gradient.
Second Law. Fick's second law predicts how diffusion causes the concentration of molecules to change with time, in relation again to the variation of molecular concentration.

affinity towards pheromonal messages (information), so that they can detach the information molecule from the carrier and convey the information for a further processing. Receptor proteins are considered as the nanomachine antennas.

This process depends on the environmental conditions and on the receiver structure. In the animal world, pheromonal signaling is mainly detected by the olfactory system. Most mammals possess a well-developed vomeronasal organ that is a blind-ended, mucus-filled tube, located in the nasal septum [11], where the chemical signal is transduced into nervous activity. The olfactory system in insects also approaches the theoretical limit for a detector. They perceive the world through semiochemicals with inordinate sensitivity. As depicted in 4.1, in order

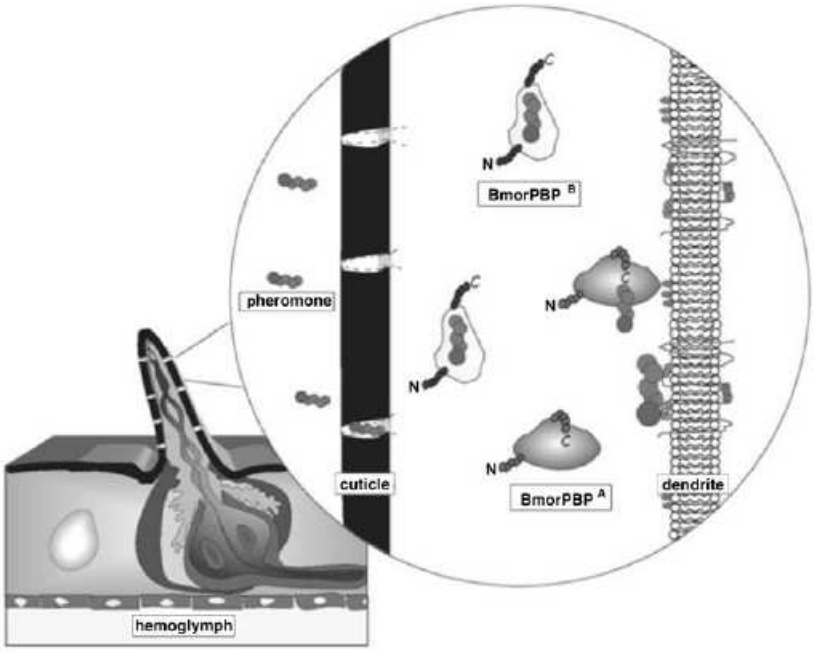

Figure 4.1: Schematic representation of the proposed model for the mode of action of insect PBPs.

to convey their message, pheromones must reach the olfactory receptor proteins, and to achieve it, these particles must cross some discriminating environments: Pheromones (and other semiochemicals) are detected by specialized sensory organs on the antennae. They enter the sensillar wall through pore tubules in the cuticle and cross the first level of discrimination determined by pheromone-binding proteins (PBPs) that assist the *precise pheromones* to cross an aqueous barrier and reach their receptors (the odorant receptors are surrounded by this impenetrable aqueous environment known as the sensillar lymph. Pheromones transport through this barrier is possible thanks to PBPs that encapsulate, solubilize and transport them to the olfactory receptors. Hence, both PBPs and odorant receptors contribute to the specificity of the cell response and lead to the remarkable selectivity

of the insect olfactory system. Bound pheromone molecules are protected from odorant-degrading enzymes, but it is highly unlikely that they interact with the receptors. After interaction with negatively-charged sites, the pheromone molecule is ejected, and it is in that moment when the pheromone molecule itself (not the complex) activates the odorant receptor, triggering a cascade of intracellular events which leads to nervous activity [20].

4.2.5 Decoding

In this process received information is interpreted and processed, and receiver nanomachines invoke reactions in response to it. The design of a reaction is dependent on the application. Continuing with the animal analogy, once a receptor is activated the chemical signal is transduced into nervous activity that is sent to the brain and the whole system (e.g., motor system) is told what to do.

4.3 Ideal Messenger Molecule

Several features have been considered to set the main characteristics the ideal chemical messenger molecule should fulfill:

- Its structure should contain a distinctive "head" or "flag" that permits easy recognition and binding by nanomachine molecular receptor systems so that the entire message need not be read in order to identify the intended recipient.
- It should be relatively bioinactive, thus it does not break down readily by natural processes before the message is received.
- It should be easily eliminated to prevent potentially toxic accumulations; however, the molecule and any likely breakdown products should also be inherently nontoxic in anticipated maximum concentrations.
- It should be recyclable, since some chemicals that are part of the messenger molecule are limited in the particular environment where the communication process takes place, and therefore, the broadcast rate would be limited.
- The molecule should be capable of easy extension to larger sizes, permitting to write significant entire messages on the molecule, since the statistical nature of the transport process implies a relatively long time between assured detections of the messenger molecule.

4.3.1 Another Possible Messenger Candidate: The Partially Fluorinated Polyethylene Molecule

In [16] the *partially fluorinated polyethylene molecule* is considered for chemical broadcast communication in the human body. It was in turn originally suggested by K. Eric Drexler for nanocomputer tape bulk memory systems, although others have been investigated. Such molecules can store one *bit* per carbon atom, using an H atom to represent a "0" and an F atom to represent a "1" on one side of the carbon-chain backbone, with all H atoms occupying the other side of the backbone to facilitate easy reading. The *message* may be a single linear chain or may include branching structures representing prioritizations embedded in the message. Hydrofluorocarbon molecules are characterized by high chemical and biochemical inertness, absence of metabolism, and rapid excretion in the human body.

Assuming molecules are of the form $CH_3(CHX)_nCH_3$, with X=H or X=F atoms (averaging 50%/50% H/F atoms on the read side), and can store 1 bit per unit (with n units/molecule), then the information density of the message is $D_{message}$ $\sim$26 bits/nm^3 (3 bits/nm of linear message molecule length)[3], and therefore the number of bits that can store a messenger molecule of spherical radius $r_{message}$ is approximately

$$I_{message} = \frac{4}{3}\pi r_{message}^3 D_{message} \tag{4.1}$$

For the $(CHX)_n$ core fragment, $I_{message}$=n bits. There might be sent from *simple messages* ($\sim$100 bits), to very *complex messages* of up to $\sim 10^9$ bits/molecule, from which $\sim$1000 bits might be required for message packet flagging or header information, such as recipient identification, time stamping, "destroy by" dating, etc.

4.4 Analysis of Communication Through Molecular Diffusion

The following discussion is from [16], [28], [9], and is presented for determining those parameters of olfactory communication systems most closely related to the diffusion process: rate of emission of the message molecule, the threshold concentration, communication range... Ignoring for the present such problems as variable threshold, instability of diffusion molecules, etc.

Four general cases of diffusion can be found in nature:

1. Instantaneous emission, from a stationary source, of the communicating substance in stationary medium;

[3]By comparison, linear DNA achieves 1 bit/nm^3.

2. Continuous emission, from a stationary source, of the communicating substance in stationary medium;

3. Continuous emission, from a mobile source, of the communicating substance in stationary medium;

4. Continuous emission, from a stationary source, of the communicating substance in nonstationary medium;

These techniques have been applied in the analysis of real communication systems, for instance: alarm communication of the harvester ants, involving cases (1) and (2), case (3) in the analysis of the recruitment trail of the fire ant, and case (4) in the analysis of sex attractant of the gypsy moth. Furthermore, they also may be applied to chemical communication in human body between nano-devices.

The mathematical models and techniques of analysis can be applied equally well to interspecific communication and, with suitable adjustments, to chemical communication *in both air and aqueous medium*. However, diffusion process is greatly complicated by naturally occurring turbulence and it may become a complex analytical problem. A nonstationary transporting medium does more than just move message molecules in the direction of flow, it also may create turbulence in the medium, adding a component of turbulent diffusivity that overwhelms simple Brownian diffusion. Although the study of chemical communication has been accelerating in the past several years, research on nanonetworking is relatively new.

Thus, for simplicity, in the following analysis the medium is taken to be continuous, stationary, isotropic and unbounded, and the communication substance released will come from a *stationary* and isotropic *source* (not mobile).

When it comes to choose between instantaneous or *continuous emission* there is no much hesitation since a continuous transmission requires substantially lower power and correspondingly smaller transmitters than the equivalent instantaneous transmitter. It also provides no delays in the transmitter and faster update rates, which results in faster and better tracking solutions for both transmitter and receiver. Signal modulation is also possible if transmitting continuously, which is another way to carry out discrimination of receivers, users, etc.

4.4.1 Continuous Stationary Source in Stationary Medium

Consider a source of molecules emitting continuously at constant rate through time $Q_{message}(t)$ (message molecules/s) into an idealized stationary medium. The *spatial density of message molecules* (molecules/m^3) as a function of time t and distance r from the point source is given by

$$U(r,t) = \int_0^t \frac{Q_{message}(t^*)}{(4\pi D(t-t^*))^{\frac{3}{2}}} e^{\frac{r^2}{4D(t-t^*)}}\, dt^* \tag{4.2}$$

where $r^2 = x^2 + y^2 + z^2$ (the cartesian coordinate system) and D (m^2/s) is the *Translational Brownian Diffusion Coefficient*, proportional to the velocity of the diffusing particles, and according to the Stokes-Einstein relation, it depends on the temperature *T*, viscosity of the fluid η, and the size of the particles, which are assumed to be roughly spherical with radius *R*.

$$D = \frac{kT}{6\pi\eta R} \tag{4.3}$$

And from 4.3 and 5.4,

$$D = \frac{kT}{\eta}\sqrt[3]{\frac{D_{message}}{162\pi^2 I_{message}}} \tag{4.4}$$

These are only approximations though, because D varies slightly with concentration and the not perfect molecular sphericalness, among other factors. A proper characterization of D will enable to model the characteristics of whatever type of molecule that is being propagated in any medium.

If considering the **simplest case** of release being constant $Q_{message}(t) = Q_{message}$, the density function from 4.2 becomes

$$U(r,t) = \frac{Q_{message}}{4D\pi r} erfc(\frac{r}{\sqrt{4Dt}}) \tag{4.5}$$

which unlike the previous one it is already a closed formula.

As the release of messenger molecules continues for a long time ($t \longrightarrow \infty$), the concentration approaches the steady-state limit,

$$U(r) = \frac{Q_{message}}{4D\pi r} \tag{4.6}$$

In other words, the concentration decreases linearly with distance from the source.

The detection of molecules by the receptor is based in chemical sensors, hence a minimum threshold concentration C_{th} is required in some minimum waiting time t_{sensor}, given by

$$C_{th} = \frac{N_{encounters}}{r^2_{message} I_{sensor}} \sqrt{\frac{I_{message} MW_{unit}}{4\pi kTN_A}} \tag{4.7}$$

Where $N_{encounters}$ is the number of random ligand-receptor encounters necessary to ensure binding, that is the number of elements or nano-antennae that will be activated in the receiver. MW_{unit} (Kg/mole) is the message molecule Molecular Weight ($MW_{message} \sim nMW_{unit}$) and N_A is known as the Avogadro's Number ($N_A = 6.023 \cdot 10^{23}$ molecules/mole) is the Avogadro's Number. As C_{th} depends

on the nano-receiver and it doesn't exist yet, it will be considered as a constant and will have orientating values, since nano-receptors will be designed according to this requirement and some others.

The concentration of message molecules is an expanding diffusive sphere that increases through time to a maximum size and, as the density function is monotonic, concentration is above threshold within this sphere and nowhere else. Thus, the radius of this sphere containing concentrations above the threshold value corresponds to the maximum effective distance for chemical communication associated with long-term release from the source.

$$R_{max} = \frac{Q_{message}}{4\pi C_{th} D} \tag{4.8}$$

The exact solution of the time that it takes for the threshold sphere to reach some proportion, p, of its maximum radius involves the complementary error function, but can be reasonably well approximated by

$$t_R = (\frac{pQ_{message}}{p^* 4\pi C_{th} D^{\frac{3}{2}}})^2 \simeq (\frac{1.1 f_R Q_{message}}{8\pi C_{th}(1-f_R) D^{\frac{3}{2}}})^2 \tag{4.9}$$

where $erfc(p^*) = p$ and f_R is the fractional radius expansion of the message sphere ($0 <\sim f_R <\sim 1$).

All these results assume that the messenger molecules are free to diffuse infinitely in all directions, corresponding to the source not being near to any reflecting plane or ground. However, in the majority of biological situations the source is at the ground (reflecting plane at $z = 0$), and the additional condition that $U = 0$ for all $z < 0$ is imposed. Hence, if applied in all the aforementioned formulae, the rate of emission at the ground should be twice the solution in infinite space.

4.4.2 Numerical Analysis and Results

In this section, a comparison between some of these concepts in the three general environments (air, water and human body) is performed.

First of all, it is necessary to set the ranges of the possible or most common *diffusion coefficient* values in each environment in a set temperature and pressure, as well as an orientating rate of messenger molecules released in the medium and threshold concentration. It is important to take into account that this is orientating data, since these values vary according to several factors (only some of them are contemplated: pressure, the medium where the communication takes place, characterized by its viscosity[4], and its temperature).

[4]Some general tentative viscosity values can be found at the appendix in Table A.

All these orientating values are gathered in the following Table.

Table 4.1: Orientating Values for Diffusion Coefficient

Medium	**T (K)**	D_{range} **(cm^2/s)**
Air	298	[0.08 - 0.8]
Water	295	[10^{-7} - 10^{-4}]
	310	[10^{-10} - 10^{-5}]
Blood Plasma	310	[10^{-7} - 10^{-9}]

- Data in *air* is taken from [28], [9] and from Table A.1 at the appendix.
- In dilute *aqueous solutions* diffusion coefficients of most ions are similar and have values that at room temperature[5] are in the range of $0.6 \cdot 10^{-5}$ to $2 \cdot 10^{-5}$ cm^2/s. For biological molecules, diffusion coefficients normally range from 10^{-7} to 10^{-6} cm^2/s. Besides, Table A.2 gives the measured diffusion coefficients in water for various molecules of physiological interest, converted to human body's average temperature 310 K (37°C). Find it at the appendix.
- In the *human body* environment just the particular case of the partially fluorinated polyethylene molecule will be analyzed, and data for both simple and complex messages is taken from [16].

Considering a continuous release of messenger molecules through time, the maximum communication range R_{max} from a continuous point source versus the ratio of number of molecules released to the threshold density Q/C_{th}[6], for various coefficients of diffusion D and for a source away from the ground [7]is graphed below in Figure 4.2, as well as the time at which the radius $R = f_R R_{max}$ is reached. In this case, the maximum communication range (since $f_R = 1$ has been taken).

[5]For scientific calculations, *room temperature* is taken to be 293 to 296 K, or 20 to 23.5 °C

[6]Only the ratio Q/C_{th} is of interest with respect to the diffusion process, and not the absolute values of Q and C_{th}, which of course are important to the study of other communication features.

[7]For a source in the ground, Q should be doubled in applying the graph.

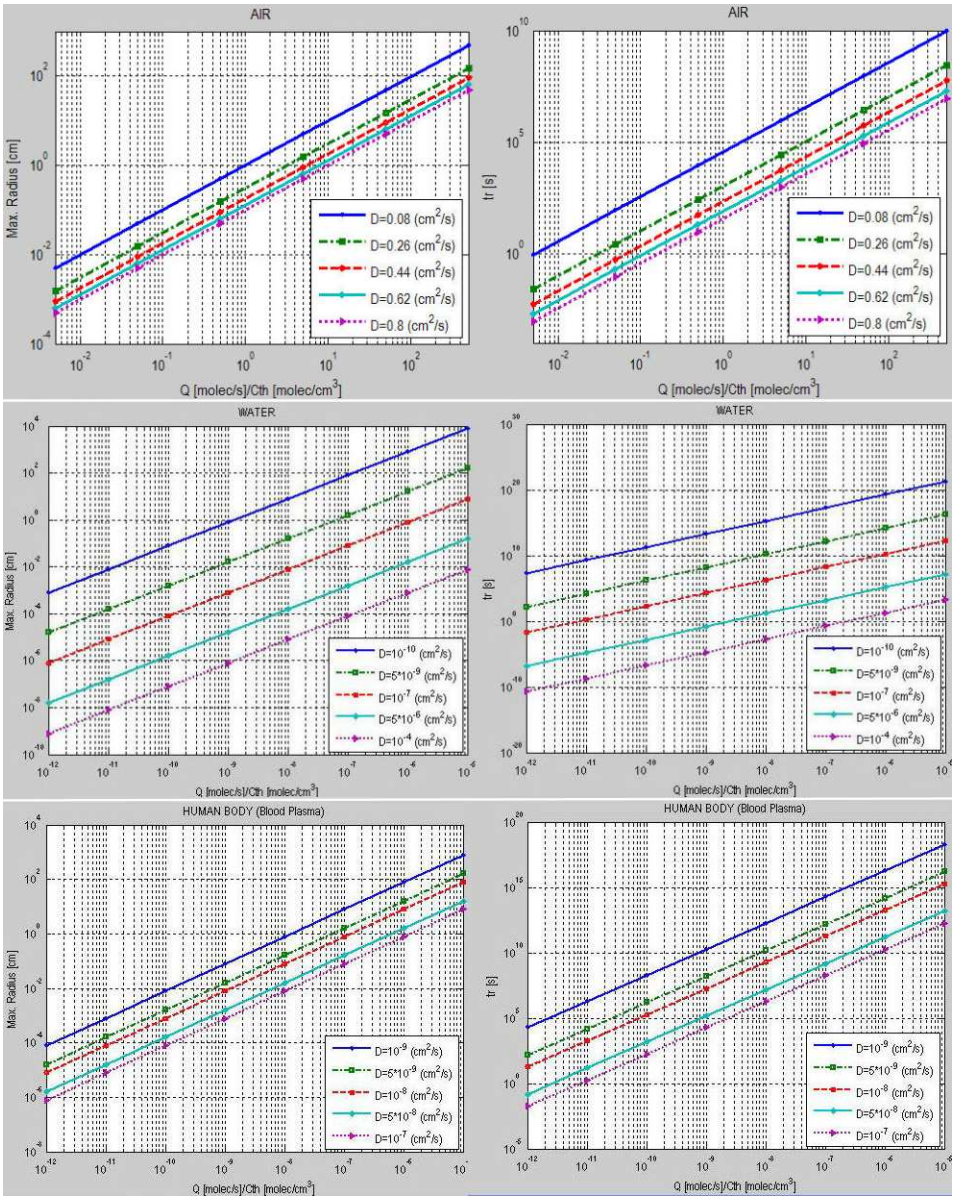

Figure 4.2: R_{max} vs. Q/C_{th} and t_R vs. Q/C_{th} in Air, Water and Blood Plasma.

On the other hand, if $Q_{message}(t) = Q_{message}$, the closed density function $U(r,t) = \frac{Q_{message}}{4D\pi r} erfc(\frac{r}{\sqrt{4Dt}})$ can be used, which makes the calculation process much easier and faster.

Concentration of molecules versus time for different distances from the source, is plotted in Figure 4.3. Set values of *diffusion coefficient*, *threshold concentration*, and *rate of messenger molecules released*, are taken according to their common

values in each medium (Table 4.2).

Table 4.2: Set values used in the analysis of $U(r,t)$ for each environment.

Medium		**D** (cm^2/s)	$Q_{message}$ (molecules/s)	C_{th} (molecules/cm^3)
Air		0.43	$2.8 \cdot 10^{14}$	10^{12}
Water		10^{-6}	$4 \cdot 10^{4}$	10^{12}
Blood Plasma	Simple msg.	$2.2 \cdot 10^{-7}$	$4 \cdot 10^{4}$	10^{12}
	Complex msg.	$1 \cdot 10^{-9}$	10	$9 \cdot 10^{10}$

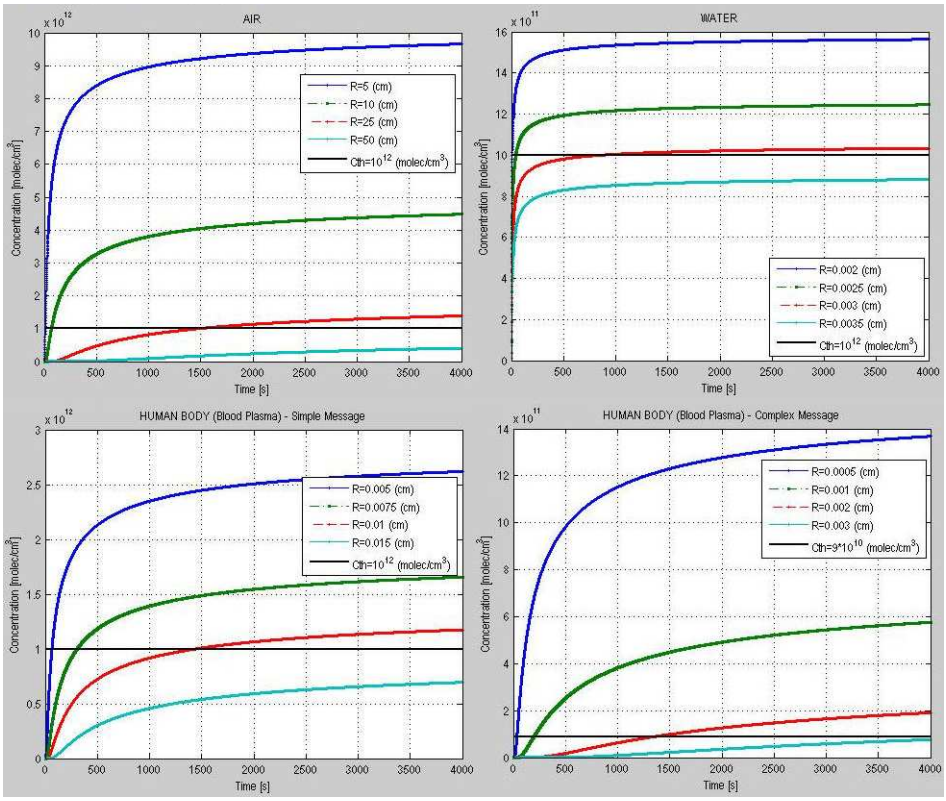

Figure 4.3: Concentration of molecules vs. time for different distances from the source.

Note that in the four plots, the longest distance simulated is not within the communication range since concentration of molecules at such distance is not enough to be detected by the receiver. Remember that the threshold concentration, C_{th}, is a design parameter that can be differently set depending on the application, as well

as the rate of molecules release.

What does it happen when the rate of molecules released is not constant through time? Does it make possible a modulated transmission of information? If the transmitter releases molecules in an oscillating or pulsed rate, can the receiver detect it?

For this case the most general function of *spacial density* is needed

$$U(r,t) = \int_0^t \frac{Q_{message}(t^*)}{(4\pi D(t-t^*))^{\frac{3}{2}}} e^{\frac{r^2}{4D(t-t^*)}} dt^* \tag{4.10}$$

This function may be considered as one solution of Fick's law under certain constraints:

- Static nodes/nanomachines.
- Point source.
- Continuous emission.
- Ideal medium: without accounting for noise, interferences, obstacles, turbulences, etc.
- Isotropic diffusion.

This brought some problems when implementing because it is not a closed function and a huge amount of samples are needed even when it comes to simulate very little time of transmission. As following commented, several codes where implemented and tested but most of them failed.

1. In the first attempt, Matlab commands for integration were used to solve it, but calculation took extremely long time and the program always got hung up.
2. In the second attempt it was tacked with numerical methods, but it had the same unfortunate result as the previous one.
3. Then, reconsidering the real case of the *Pogonomyrmex badius* alarm system

   > When a worker is alarmed it emits alarm substance which attract nearby workers. As the others attain the original source they begin releasing substance themselves. If the arrival of the other workers is fairly uniform in time we might assume the total emission near the original source is approximately continuous and constant [9].

and taking the solution from an instantaneous source $U(r,t) = \frac{Q_{message}}{(4\pi D)^{\frac{3}{2}}} e^{\frac{r^2}{4D}}$, the principle of superposition was used to obtain the solution for the continuous case.

Indeed, to obtain a continuous and constant response the sum of multiple instantaneous sources, each one emitting every dt, was considered. Hence, it was just a matter of adding, after each interval dt, the new release of molecules to the previous delivered molecules which concentration was decaying according to the function above. As the total emission had to be approximately continuous, a really small dt was required, and consequently the same problems happened again: the number of samples exceeded the array or the program got hung up.

4. Finally, a new interpretation of the function made possible to solve it, since Matlab would not need to work with so many samples:

   Convolution is defined as the integral of the product of two functions after one is reversed and shifted

   $$[f * g](t) = \int_0^t f(\tau) g(t-\tau) d\tau \tag{4.11}$$

   From where

   $$U(r,t) = \int_0^t \frac{Q_{message}(t^*)}{(4\pi D(t-t^*))^{\frac{3}{2}}} e^{\frac{r^2}{4D(t-t^*)}} dt^* = [f * g](t) \tag{4.12}$$

   if

   $$f(t) = Q_{message}(t) \tag{4.13}$$

   $$g(t) = \frac{e^{\frac{r^2}{4D(t)}}}{(4\pi D(t))^{\frac{3}{2}}} \tag{4.14}$$

   In this case, the calculation time was still long, but not so much though, and did not get hung up. The definitive code can be found at the appendix (Figure B.3). Note that concentration of molecules cannot have negative values, thus a carrier is needed to force positive values which in this case a baseband carrier is used (offset) and the modulated signal is added over it. This means there is always a constant concentration in the environment nearby the receivers which is desired to be as homogeneous as possible.

Once at these point, the next step was running some simulations and check if the receptor could indeed detect the oscillations or pulses of the release pattern. As the most direct applications nanonetworks are in the biomedical field, simulation medium is blood plasma. Figure 4.4 shows that amplitude modulation can be detected at the receiver side within a specific radius and frequency range, which dependence will be studied in the next chapter.

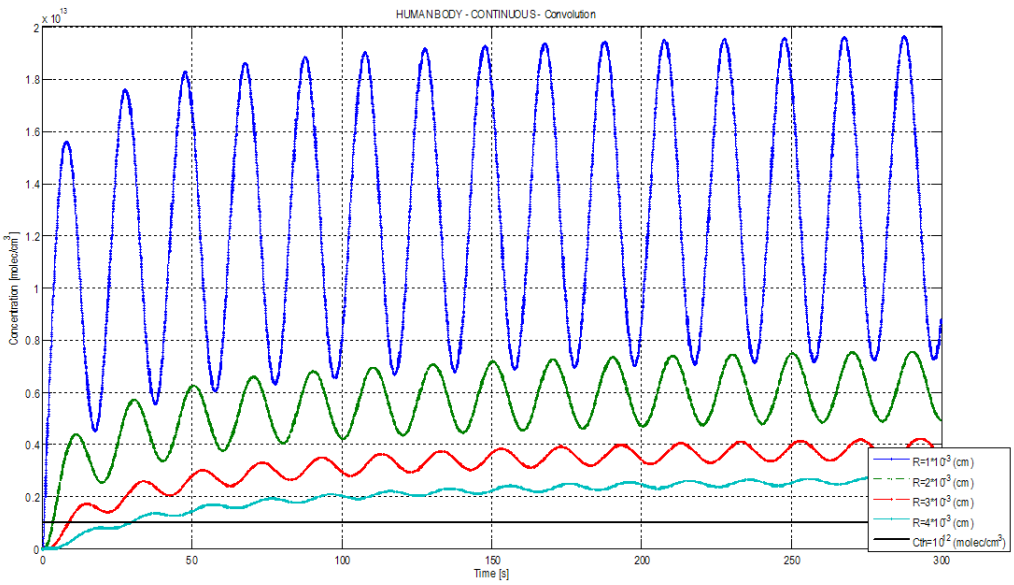

Figure 4.4: Concentration of molecules nearby the receiver when the released rate is modeled following a sinusoidal wave (amplitude modulation).

4.5 Advantages and Drawbacks of Communication through Molecular Diffusion

Pheromone communication for nanomachines has a number of advantages that are not available with other alternatives. However, it also has a bunch of disadvantages. Thus, it will depend on the application to be worth using it or not.

When communication is carried out through diffusion, the channel can not be considered deterministic. It is very complicated by naturally occurring turbulence, since it overwhelms simple Brownian motion and requires complex mathematical methods of treatment not familiar to most biologist. Additionally, diffusion of molecules is *greatly subjected to environmental conditions*, which threaten to delay, block, or break down the communication between nanomachines. This may involve several factors such as pressure, viscosity, antagonist agents... and this effect is even stronger with temperature.

Another important week point is the *slowness* of transmission, except in non-stationary medium and across short distances.

Some advantages of diffusion are that not only it is an efficient method and easy to broadcast, but also it is effective at long range. Moreover, only by taking advantage of the movement of the environmental medium itself, such as wind or water currents, the communication effective range is even far greater, although it

needs a much more complex treatment.

A main advantage of diffusion propagation is that just minute quantities of chemical are needed to succeed. Nevertheless, however it requires the receiver to contain highly sensitive and selective receptors to detect and discriminate the information even when signal-to-noise ratio is very low.

Last but not least, it is quite remarkable, however, that there are no artificial nanomachines capable of carry out the required tasks yet.

Chapter 5

Channel Modeling in Molecular Communication

In this chapter an information theoretical approach for nano-scale communications will be developed, together with some possible molecular channel modeling. In order to make it more understanding let me first review the basic concepts in Shannon information theory valid at macro-scale, since as classical mechanics laws usually do not fail at the nano-scale, parallels between information theoretic and physics interpretation of some parameters as entropy, information and free energy still hold true in that tiny setting.

5.1 Shannon Information Theory Fundamentals

Information theory is based on probability theory and statistics. The most important quantities of information are entropy, the information in a random variable, and mutual information and the amount of information in common between two random variables. The former quantity indicates how easily message data can be compressed while the latter can be used to find the communication rate across a channel.

The choice of logarithmic base in the following formulae determines the unit of information entropy that is used. The most common unit of information is the bit, based on the binary logarithm.

The Shannon *information* associated to an event occurring with probability p

$$I(p) = -lnp \tag{5.1}$$

The *entropy* represents the average information associated to the event whose occurrence is modeled by the random variable X, or $X|Y$ when *conditional entropy* with alphabet $\mathcal{A}$ and $\mathcal{B}$

$$H(X) = -\sum_{x \in \mathcal{A}} p_i lnp_i \tag{5.2}$$

$$H(X|Y) = -\sum_{x\in\mathcal{A}}\sum_{y\in\mathcal{B}} p(x,y)lnp(x|y) \tag{5.3}$$

The mutual information between two random variables X and Y can be written as

$$I(X;Y) = H(X) - H(X|Y) = H(Y) - H(Y|X) \tag{5.4}$$

If these random variables X and Y, respectively, represent the input and output of a noisy communication channel (see figure 5.1) the mutual information can be interpreted as the information flow of the channel (how much uncertain we are left on X after observing Y).

Figure 5.1: Block scheme of a communication channel with conditional law $p(y|x)$.

Hence, the channel capacity will be given by the maximum information flow

$$C = \max_{p_i} I(X;Y) \tag{5.5}$$

which can also be expressed as following if AWGN model

$$C = B \cdot log_2(1 + SNR) \tag{5.6}$$

B representing the channel bandwidth and SNR being the signal-to-noise ratio

5.2 Molecular Channel Models

Since nanomachines are limited in their size and capabilities, the traditional wireless communication based on electromagnetic waves cannot be possible to communicate with each other. As stated before, molecular communication is the most promising paradigm to make it viable. Thus, it is essential to find out molecule delivery capacity of a molecular channel between two nanomachines based on molecular communication parameters such as temperature of environment, concentration of emitted molecules, distance between nanomachines and duration of molecule emission. Next, three different models for molecular communication channels are presented and developed, and a closed form expression for capacity is derived for each one.

In traditional communication networks with many senders and many receivers communicating with each other, there are mainly three types of communicating channels called as multiple-access, broadcast, and relay channels. Similarly, in

a nanonetwork with many Transmitter Nanomachines (TNs) and many Receiver Nanomachines (RNs) communicating with each other, we define three kinds of molecular channels called as:

- **Molecular Multiple-Access Channel**, in which multiple TNs transmit molecular information to a single RN.
- **Molecular Broadcast Channel**, in which a single TN transmits molecular information to multiple RNs.
- **Molecular Relay Channel**, in which a single TN transmits molecular information to an RN using at least one nanomachine as a relay node.

5.2.1 Molecular Communication Model

Before introducing each channel model, the molecular communication model used must be defined. Thus, according to the model given in [2], the following assumptions need to be taken:

- The kind of nanomachine considered is analogous to the biological mechanisms.
- An artificial ligand-receptor binding model is used. According to that, ligand molecules are emitted and diffused in the environment till they bind the receptors R found at the receiver surface with concentration N ($\mu mol/liter$). These bound molecules allow the receiver to understand the biological information. According to the ligand-receptor binding reaction kinetic, when molecules A encounter receptors R on RN, A bind R and constitute complexes C (bound receptors) which generate the concentration in RN.

$$A + R \longrightarrow^{k_1} C \tag{5.7}$$

As well as the binding reaction, it is possible to release molecules A from R

$$A + R \longleftarrow^{k_{-1}} C \tag{5.8}$$

where k_1 ($\mu mol/liter/s$) and k_{-1} ($1/s$) are the binding and release rates, respectively. While the binding rate heavily depends on the molecular diffusion parameters from TN to RN such as diffusion coefficient, temperature of environment ($k_1 \propto$ 2T) and distance between TN and RN ($k_1 \propto 1/\alpha$), the release rate depends on some environmental factors such as interaction range and temperature. It is analytically modeled as follows

$$k_{-1} = k_{-1}^0 e^{\frac{\alpha f}{k_B T}} \tag{5.9}$$

where k_{-1}^{0} is the zero-force release rate, which is related with the capability of molecule capturing of RN and it can be experimentally predicted. α is the distance between TN and RN , k_B and T are the Boltzmann constant and absolute temperature, respectively. f is the applied force per bound and it is related with the energy of the emitted molecules, the distance between TN and RN, and the environmental factors.

- TN emits molecules called A via square pulses with amplitude L_{ex} ($\mu mol/liter$) during t_H seconds

$$L(t) = \begin{cases} L_{ex} & \text{with probability } P_A \text{ in } (jt_H \leq t \leq j+1)t_H, \qquad j = (0, 1, ...) \\ 0 & \text{with probability } (1 - P_A) \text{ otherwise} \end{cases}$$

- In this duration, concentration of bound receptors C(t) ($\mu mol/liter$) rises exponentially, and after t_H, it starts to decay

$$C(t) = \begin{cases} C_\infty(1 - e^{-t(k_{-1}+k_1 L_{ex})}) & \text{for } 0 \leq t \leq t_H \\ C_{t_0} e^{-k_{-1}(t-t_H)} & \text{for } t \geq t_H \end{cases}$$

  where C_∞ is the steady state level of bound receptors $C_\infty = \frac{k_1 L_{ex} N}{k_{-1}+k_1 L_{ex}}$

- In traditional digital communication, information sequences are transmitted via two bits, logic 1 and 0. A receiver will decide that a transmitter sends a logic 1 if the voltage level detected is grater than a prescribed voltage in the channel, otherwise the receiver will interpret a logic 0. A similar scheme can be used in the molecular communication paradigm, during the interval t_H TN can emit either molecules A (corresponding to a logic 1 in digital communication) or transmit no molecule (corresponding to a logic 0); Resulting in 2 molecular bits called A and 0. Consequently, if a RN senses a concentration of molecules A which is greater than a prescribed concentration called *S* ($\mu mol/liter$), RN decides TN has transmitted molecular bit A during t_H. Conversely, if that concentration is less than *S*, RN decides TN transmitted molecular bit 0.

- Nevertheless, it may be also possible to detect erroneous molecular communication bits at the RN side, by detecting a logic 1 when TN intended to transmit a logic 0, or vice versa. During molecular communication, molecules A are emitted and continuously diffuse to surrounding environment, such that they always exist in the environment, which makes possible for RN to receive A although TN transmits molecular bit 0. Besides, it may also happen due to the delay in diffusion of molecules A to RN, which may receive a molecular bit 0 although A has been transmitted. Several factors can affect the molecular diffusion between TN and RN, and cause these channel errors: temperature of the environment, concentration of emitted molecules A, distance between TN and RN, duration of molecule emission, binding and release rates, and number of receptors on RN.

- Thus, the *molecule delivery capacity* is defined as the maximum number of non-erroneous molecular bits which can be delivered within a specific time duration [2].

First of all, single molecular communication channel will be defined, since it is used for modeling of molecular multiple-access, broadcast and relay channels and to derive their capacity expressions.

5.2.2 Single Molecular Communication Channel

In every time when TN transmits a molecular bit, concentration of delivered molecules determines success of the transmission. If TN transmits molecular bit A, with probability P_A, at least S number of molecules[1] must be delivered to RN within t_H, and conversely, if TN intends to transmit a molecular bit 0, with probability (1-P_A), number of molecules received by RN within t_H must be less than S. Therefore, it is imperative to know how many molecules are delivered during each interval t_H, so that a threshold value to determine success of the molecular bit transmission from TN to RN can be taken.

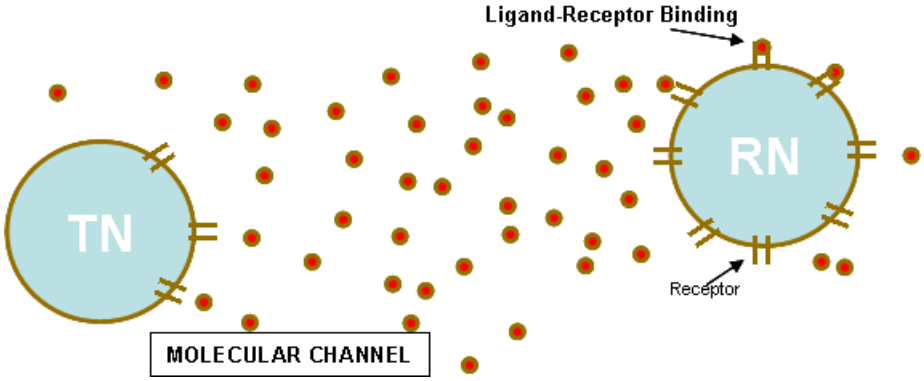

Figure 5.2: Block scheme of a communication channel with conditional law $p(y|x)$.

For the case that TN emits A during t_H,using concentration of bound receptors $C(t)$, number of delivered molecules A within t_H (N_A) is given by

$$NA = \int_0^{t_H} \frac{k_1 L_{ex} N}{k_{-1} + k_1 L_{ex}} (1 - e^{-t(k_{-1}+k_1 L_{ex})}) dt \tag{5.10}$$

[1]Either number of molecules or concentration of molecules can be used, since concentration of molecules ($\mu mol/liter$) can be converted to number of molecules by simply multiplying Avogadro constant ($N_A = 6.023 \cdot 10^{23}$)

Since TN is continuously emitting every t_H, the previous delivered bits affect the number of molecules A in the current interval, but due to the exponential decay of number of complex according to 5.2.1, just the last molecular bit emitted affects the current transmission. Hence, the number of complexes coming from the previous interval (NP) that still remain in the current interval can be given as follows

$$NP = P_A NA \int_0^{t_H} e^{-k_{-1}t} dt \tag{5.11}$$

Therefore, the expected value of total number of delivered molecules A during t_H, i.e., $E[S_A]$

$$E[S_A] = NA + NP \tag{5.12}$$

and consequently, the probability of having success in transmission of a molecular bit A is bounded by

$$p_1(S_A \geq S) \leq \frac{E[S_A]}{S} \tag{5.13}$$

Hence, $p_1 = \frac{E[S_A]}{S}$ is the maximum probability of having success in the communication between TN and RN when molecular bit A is sent, and (1-p_1) the probability for receiving the erroneous molecular bit 0.

According to [4] S_A is assumed to be normally distributed random variable with the distribution N($E[S_A], \sigma_A^2$), and since S_A cannot be negative, $\mu_A = E[S_A]$ and $\sigma_A = E[S_A]/3$. As a result, the probability of having success in transmission of a molecular bit A can be also given as follows

$$p_1(S_A \geq S) = \int_S^{\infty} \frac{1}{2\pi\sigma_A} e^{-\frac{(x-\mu_A)^2}{\sigma_A^2}} dx \tag{5.14}$$

On the other hand, for the transmission of molecular bit 0 during t_H, number of delivered molecules A only depends on the lastly emitted bit concentration, since no molecules are transmitted during the current interval. Therefore, the expected value of total number of delivered molecules within t_H is given by

$$E[S_0] = NP \tag{5.15}$$

where similar to S_A, S_0 is also assumed to be normally distributed N($E[S_0], \sigma_0^2$), where $\mu_0 = E[S_0]$ and $\sigma_0 = E[S_0]/3$.

For the successful delivery of molecular bit 0, with probability p_2, TN must deliver to RN a number of molecules such that is less than *S*.

$$p_2(S_0 \leq S) \leq \frac{E[S_0]}{S} \tag{5.16}$$

$$p_2(S_0 \leq S) = \int_0^{S} \frac{1}{\sigma_0 2\pi} e^{-\frac{(x-\mu_0)^2}{\sigma_0^2}} dx \tag{5.17}$$

Hence, TN achieves to deliver molecular bit 0 successfully with probability $p_2 = \frac{S}{E[S_0]}$ and, it does delivers it incorrectly with probability (1-p_2).

According to P_A, p_1 and p_2, the channel can be modeled as a symmetric channel. Considering that TN emits molecular bit X and RN receives molecular bit Y (see figure 5.1), then the *transition matrix of the molecular channel* can be given as follows

$$\mathbf{I}(\mathbf{X};\mathbf{Y}) = \begin{pmatrix} p_1 P_A & (1-p_2)(1-P_A) \\ (1-p_1)P_A & p_2(1-P_A) \end{pmatrix}$$

From where is given the following *mutual information* $I(X;Y)$ between X and Y, which states the number of distinguishable molecular bits, i.e., ***M***

$$M = I(X;Y) = \Big(H\Big(p_1P_A + (1-p_2)(1-P_A), (1-P_1)P_A + p_2(1-P_A)\Big)\Big) - \Big(P_A H(p_1, 1-p_1) + (1-P_A)H(p_2, 1-p_2)\Big)$$

Finally, the **capacity** of the **single molecular channel** between TN and RN, that is the maximum number of non-erroneous molecular bits delivered within t_H, i.e., SC, can be expressed as

$$SC = \max(I(X;Y)) \tag{5.18}$$

Next, using single molecular communication channel and the assumptions presented above, molecular multiple-access, broadcast and relay channels will be modeled.

5.2.3 Molecular Multiple-Access Channel

In this case, multiple TNs ($TN_1, ..., TN_n$) send molecular information to a single RN, as depicted in Figure 5.3. It is assumed that each nanomachine has a self-identifying label and attaches this label to the emitted molecules, providing a very simple addressing scheme. It is also assumed that TN_i delivers molecular bit A with probability P_{Ai} and concentration L_{ex} using the binding and release rates k_1^i and k_{-1}, respectively. And last but not least, no contention among TNs to access the molecular multiple-access channel is considered.

Using 5.10 and 5.11, the expected total number of molecules delivered when transmitting molecular bit A and 0, i.e., $E[S_A^i]$ and $E[S_0^i]$, respectively, can be computed by

$$E[S_A^i] = NA + P_{Ai} NA \int_0^{t_H} e^{-k_{-1}t} dt \tag{5.19}$$

$$E[S_0^i] = P_{Ai} NA \int_0^{t_H} e^{-k_{-1}t} dt \tag{5.20}$$

where NA is computed using 5.10, k_1^i, k_{-1} and L_{ex}. Once again, similar to S_A, S_A^i and S_0^i are also normally distributed random variables with distribution

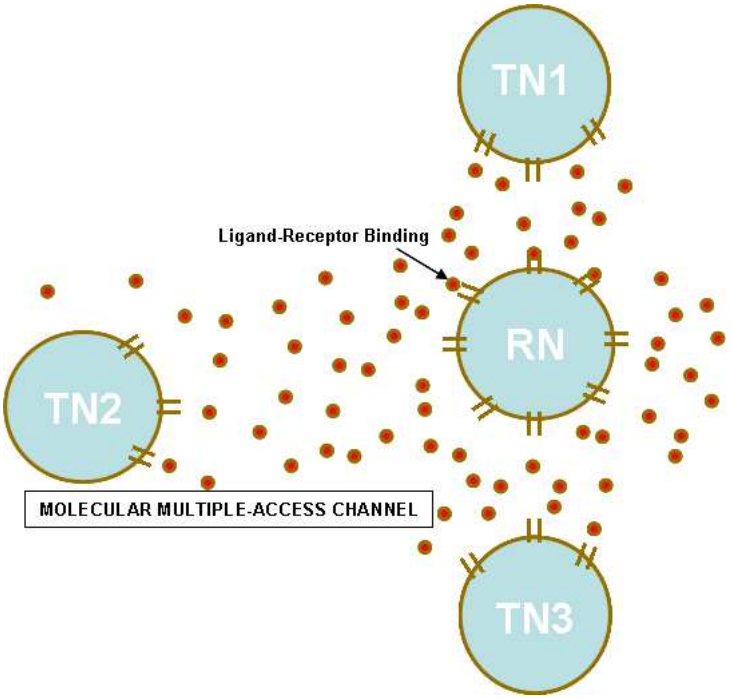

Figure 5.3: Molecular multiple-access channel with three transmitter nanomachines and one nanoreceiver.

N(μ_{Ai}, σ^2_{Ai}), where $\mu_{Ai} = E[S^i_A]$ and $\sigma_{Ai} = E[S^i_A]/3$ for the case of molecular bit A, which is the same for molecular bit 0.

S^i_A and S^i_0 are the concentrations of molecules delivered by the *n* TNs. Since there are *n* nanomachines transmitting in the same channel to a single RN, the amount of molecules delivered by each TN_i must be reduced. For the case of transmitting a molecular bit A and 0, respectively, the molecular concentration delivered by TN_i, i.e., M^i_A and M^i_0, can be expressed as

$$M^i_A = KS^i_A \tag{5.21}$$

$$M^i_0 = KS^i_0 \tag{5.22}$$

where K is a constant reducing factor that can be expressed as follows for the case in which different molecules bind to a single kind of receptors with a constant concentration N ($\mu mol/liter$) on RN.

$$K = \frac{N}{N + \sum j \neq n \left(P_{Aj} E[S^j_A] + (1 - P_{Aj} E[S^j_0]) \right)} \tag{5.23}$$

$N + \sum j \neq n \left(P_{Aj} E[S^j_A] + (1 - P_{Aj} E[S^j_0]) \right)$ denotes the average molecule

concentration delivered by other TNs.

Notice that since K is a constant and S_A^i has normal distribution, M_A^i and M_0^i also have the normal distribution N($K\mu_{Ai}, (K\sigma_{Ai})^2$) and N($K\mu_{0i}, (K\sigma_{0i})^2$), respectively.

Hence, the maximum bound for probabilities p_{1i} / p_{2i} that TN_i achieves to deliver molecular bit A/0 successfully is modified as follows

$$p_{1i}(M_A^i \geq S) = \int_S^\infty \frac{1}{K2\pi\sigma_A} e^{-\frac{(x-K\mu_{Ai})^2}{(K\sigma_{Ai})^2}} dx \tag{5.24}$$

$$p_{2i}(M_0^i \leq S) = \int_0^S \frac{1}{K\sigma_0 2\pi} e^{-\frac{(x-K\mu_{0i})^2}{(K\sigma_{0i})^2}} dx \tag{5.25}$$

Considering that TN_i emits molecular bit X and RN receives molecular bit Y and according to P_{Ai}, p_{1i} and p_{2i}, the channel can be modeled similar to a symmetric channel and *mutual information* $I^i(X;Y)$ between X and Y can be computed by 5.4.

Based on $I^i(X;Y)$, capacity of the molecular channel between each TN_i and RN, i.e., MC_i, can be expressed as

$$MC_i = \max(I^i(X;Y)) \tag{5.26}$$

Hence, the total **capacity** of the **molecular multiple-access channel**, i.e., MC, is given by

$$MC = \max\left(\sum_{i=1}^{n} I^i(X;Y)\right) \tag{5.27}$$

5.2.4 Molecular Broadcast Channel

In this case, a single TN communicates with multiple RNs ($RN_1, ..., RN_n$) as shown in figure 5.4. It is also assumed that TN attaches its label on the molecules to enable RNs to infer which nanomachine transmits its molecules to them. Moreover, it is considered that molecules emitted by TN uniformly diffuse in all directions, and therefore, each RN_i receives a molecule concentration independent of other RNs in the channel such that RNs do not interfere with each other.

Hence, the molecular channel between TN and any RN_i has the same molecule delivery capability with the single molecular channel, such that RN_i can independently receive any molecule concentration (different from the others) according to its binding rate k_1^i and release rate k_{-1}, which are strongly affected from the locations of RNs with respect to TN. Consequently, the capacity of the molecular channel between TN and any RN_i, i.e., BC_i, can be directly found using the mutual information of single molecular channel $I^i(X;Y)$ as follows

$$BC_i = \max(I^i(X;Y)) \tag{5.28}$$

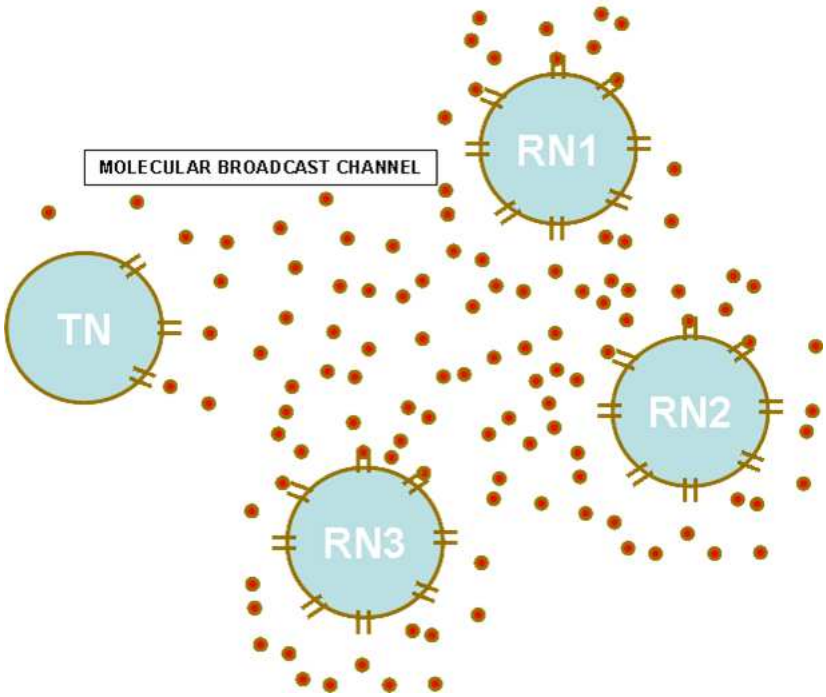

Figure 5.4: Molecular broadcast channel with one transmitter nanomachine and three receiver nanomachines.

Consequently, the total **capacity** achieved in the **molecular broadcast channel** from TN to *n* number of RNs, i.e., BC, can be given by

$$BC = \sum_{i=1}^{n} \max(I^i(X;Y)) \tag{5.29}$$

5.2.5 Molecular Relay Channel

In the molecular relay channel, a single TN sends molecular information to a single RN, using at least one nanomachine as a relay node as shown in 5.5. Here, it is assumed that there is just one nanomachine as a relay node, denoted by H, such that it has the capability of molecule emission and reception. This way, it can receive the molecular information from TN thanks to the receptors on its surface with concentration N ($\mu mol/liter$), and then forward the received information to RN following the emission pattern given in section 5.2.1. It is also assumed that both TN and H attach their self-identifying label on the emitted molecules, as well as that H foreknows next molecular bit, which will be emitted by TN. Using this information, H emits the same molecular bit with TN in each transmission interval t_H, helping, this way, the molecular communication between TN and RN.

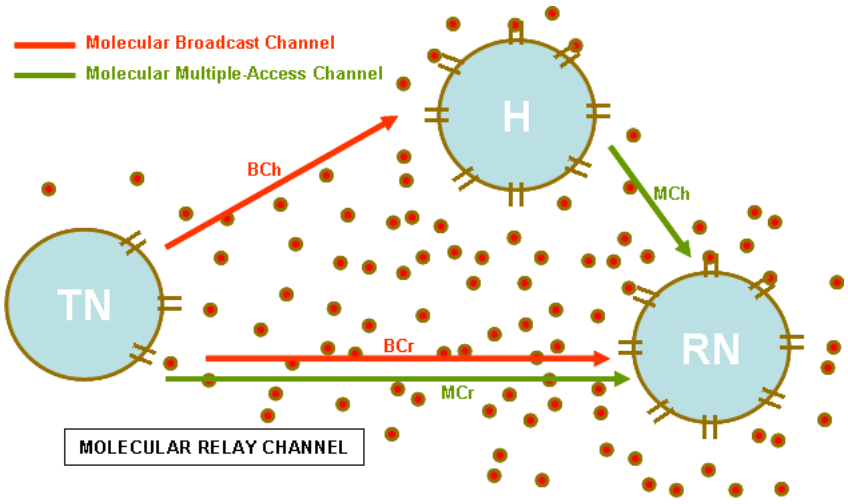

Figure 5.5: Molecular relay channel between TN and RN with one relay node.

Molecular relay channel consists of one *molecular broadcast channel* and one *molecular multiple-access channel*. In the broadcast channel, TN transmits molecular information to H and RN, and in the multiple-access channel, TN and H deliver the information to RN. Thus, using the corresponding sections, 5.2.3 and 5.2.4, each single channel capacity can be computed. As depicted in figure 5.5, capacities from TN to H and RN are denoted as BC_h and BC_r, respectively; while capacities from H and TN to RN are denoted as MC_h and MC_r.

A satisfactory solution for capacity of simple molecular relay channel with a single relay node is achieved using the *max-flow min-cut theorem*[2]. According to that, the molecular relay channel with a single relay node H has two cut sets. The first cut set includes the molecular broadcast channel, (TN,H) and (TN,RN), and the second includes the molecular multiple-access channel, (H,RN) and (TN,RN). Therefore, the capacity of the molecular relay channel, i.e., RC, is equal to the minimum capacity of these cut sets

$$RC = min(max(BC_h, BC_r), \overline{MC}) \tag{5.30}$$

where $\overline{MC}$ is the capacity of molecular multiple-access channel from TN and H to RN. Although they emit the same molecular bit in each t_H, they contend on the receptors of RN. What follows is used to compute $\overline{MC}$.

If TN and H did not contend as in single channel, expected concentration of molecules delivered to RN by TN and H, i.e., $E[S^T N_A]$ and $E[S_A^H]$, would be

[2]The *max-flow min-cut theorem* is a statement in optimization theory about maximum flows in flow networks. It states that: "The maximum amount of flow is equal to the capacity of a minimal cut". In other words, the theorem states that the maximum flow in a network is dictated by its bottleneck.

computed as in section 5.2.3. However, concentration of molecules delivered is reduced due to the contention,

$$M_A^{TN} = K_{ATN} S_A^{TN} \quad , \quad M_A^H = K_{AH} S_A^H \tag{5.31}$$

according to the constant reducing factors K_{ATN} and K_{AH} [**?**], which are different from 5.23 because this time TN and H release the same bit during t_H

$$K_{ATN} = \frac{N}{N + E[S_A^H]} \quad , \quad K_{AH} = \frac{N}{N + E[S^T N_A]} \tag{5.32}$$

Hence, $\overline{MC}$ is given by

$$\overline{MC} = max(I^{mc}(X;Y)) \tag{5.33}$$

where $I^{mc}(X;Y)$ may be computed using P_A, 5.14 and 5.17, where $(K_{ATN} + K_{AH})\mu_{Ai}$ and $((K_{ATN} + K_{AH})\sigma_{Ai})^2$ are the mean and variance of the distributed random variable $M_A^{TN} + M_A^H$. Similar computation would apply for molecular bit 0.

Finally, using BC_h, BC_h, and $\overline{MC}$, molecular **capacity of molecular relay channel** can be computed using 5.33.

5.2.6 Adaptive Molecular Error Compensation

Numerical results from [4] and [3] reveal that high molecular communication capacity can be achieved in both molecular multiple-access and broadcast channels by selecting the appropriate molecular communication parameters such as concentration of emitted molecules (L_{ex}), duration of the pulses (t_H) and molecular bit transmission probability (P_A). As a combination of these two channels, molecular relay channel can also improve the molecular communication capacity between two nanomachines using a relay node.

As previously stated, molecular capacity of a channel is defined as maximum number of non-erroneous molecular bits which can be delivered within a specific time duration, so it is imperative to compensate the errors by detecting and correcting them to achieve higher communication capacity. Limited computational and storage capabilities of nanomachines make traditional channel coding techniques not feasible in nanonetworks, since they need high computational power and efficient processors. Therefore, molecular communication needs simple proactive error compensation schemes, which do not require any computational processing to compensate the possible errors on the molecular channel.

In [3] an Adaptive Molecular Error Compensation (MEC) scheme is proposed, which according to the numerical analysis, provides more than 100% capacity improvement by selecting the most appropriate molecular transmission probability (P_A) with respect to some changing environmental factors that heavily affect the error rate in molecular communication such as temperature (T), binding rate (k_1) and distance between nanomachines (α).

Theoretically, it is possible to find a molecular transmission probability, which minimizes the errors on molecular communication channel and maximizes the molecular communication capacity.

The first step in the scheme proposed in [3] consists on defining an interval such that it provides the minimum error rate and maximizes the molecular communication capacity. According to the molecular communication model previously introduced, to successfully deliver molecular bit A TN must transmit at least *S* number of molecules to RN. Therefore, next condition is imposed

$$E[S_A] = NA + NP > S \tag{5.34}$$

after substituting NP by 5.11 in 5.34, a lower bound for P_A, i.e., LB, can be given

$$P_A > \frac{S - N_A}{NA \int_0^{t_H} e^{-k_{-1}t} dt} = LB \tag{5.35}$$

$NA \int_0^{t_H} e^{-k_{-1}t} dt$ will be denoted as N_{ex} and it states concentration of molecules A that are received by RN within an exponential decaying phase after TN transmits molecular bit A. This integral operation is impossible for TN to practically compute due to its very limited computational power. Here, it is assumed that similar to molecular communication from TN to RN, molecular communication from RN to TN can also be possible[3]. It is also assumed that RN computes the concentration within an exponential decaying phase after TN transmits a molecular bit A and it communicates this concentration to RN before initiating the molecular communication.

$$LB = \frac{S - N_A}{N_{ex}} \tag{5.36}$$

In order to get the upper bound, the other condition for successfully deliver molecular bit 0 is expressed next, which states that the number of molecules delivered to RN must be less than *S*

$$E[S_0] = NP \leq S \tag{5.37}$$

And after the appropriate substitutions,

$$P_A \leq \frac{S}{NA \int_0^{t_H} e^{-k_{-1}t} dt} = UB \tag{5.38}$$

the upper bound is given as

$$UB = \frac{S}{N_{ex}} \tag{5.39}$$

[3]It is not assumed full duplex molecular communication since they cannot simultaneously deliver and receive. Hence, it is assumed half duplex molecular communication between TN and RN.

Finally, the interval for selection of the most appropriate P_A that minimizes the channel errors in the molecular communication can be stated as

$$LB < P_A \leq UB \tag{5.40}$$

$$\frac{S - N_A}{N_{ex}} < P_A \leq \frac{S}{N_{ex}} \tag{5.41}$$

But once the interval is given, which value of P_A provides the highest molecular communication capacity?

When increasing P_A, number of delivered molecules also increases. Therefore, higher P_A decreases errors of molecular bit A, but increases the errors of molecular bit 0. However, as long as P_A value is lower than the UB, errors of molecular bit 0 are disabled. As a result, P_A should be selected as high as possible for non-erroneous molecular bit A and lower than UB for non-erroneous molecular bit 0. Hence, the selected P_A value should be closest to UB since $P_A \cong$ UB can provide higher molecular communication capacity.

The regulation of P_A to compensate the errors needs some coordination between TN and RN to periodically conduct the adaptive Molecular Error Compensation (MEC) of the channel. Once the basic theory is already stated, to finally understand how this MEC works, the following pseudo-code is given [3].

Algorithm: MEC

1. TN sets P_A as $\overline{P_A}$
2. TN initiates the molecular communication
3. **foreach** P_A **do**
4. RN detects the increasing error rate
5. RN emits BS_1
6. TN terminates the molecular communication
7. TN emits BS_2
8. RN computes N_{ex} and UB
9. RN selects P_A, ($P_A \cong$ UB)
10. RN informs TN about the selected P_A
11. TN updates P_A as the selected P_A
12. TN emits BS_3
13. TN again initiates the molecular communication
14. **end**

1. Initially, TN sets the molecular bit transmission probability P_A to an initial value, denoted as $\overline{P_A}$, within the theoretical interval previously computed. TN initiates the molecular communication.

2. If error rate increases, RN detects it [4].

[4]Error detection mechanisms have not been developed yet, but are assumed as possible.

3. Then, RN emits a fix molecular bit stream, denoted as BS_1[5], to terminate the current molecular communication with TN and to start the Molecular Error Compensation scheme.

4. Once BS_1 is received by TN, it immediately emits the molecular bit stream BS_2[6].

5. RN selects P_A as a value closest to UB ($P_A \cong$ UB).

6. RN informs TN about the selected P_A[7].

7. TN sets the new P_A and emits the molecular bit stream BS_3[8] to again initiate the molecular communication. Then, it initiates the molecular communication according to the updated P_A, which minimizes the error rate and maximizes the molecular communication capacity.

[5] BS_1 is a fixed molecular bit stream, which may be determined in the design stage of the molecular communication system. It is a special stream that as soon as it is received by TN, it terminates the molecular communication and it infers the initiation of MEC scheme. For example, A0A might be selected as BS_1.

[6] BS_2 is a fixed molecular stream, which enable RN to compute N_{ex} and UB. Since N_{ex} is the number of molecules delivered within an exponential decaying phase after TN emits A, a BS_2 such as A0000A0000 could be appropriate.

[7] It is not assumed that RN sends the actual P_A value, which is possibly a floating point number, but RN emits specific molecular bit patterns (corresponding to different level of molecular bit transmission probability) such that TN can infer the actual P_A value.

[8] BS_3 is also a fixed molecular bit stream determined in the design stage. For example, 0A0 might be selected as BS_3.

5.3 Discussion

On our opinion the theoretical approach that is developed in [2], [4] and [3], for statistically modeling the channel in molecular diffusion communication, is unrealistic.

There, a binary model using an amplitude modulation based on concentration of molecules at the receiver (Figure 5.6) is proposed.

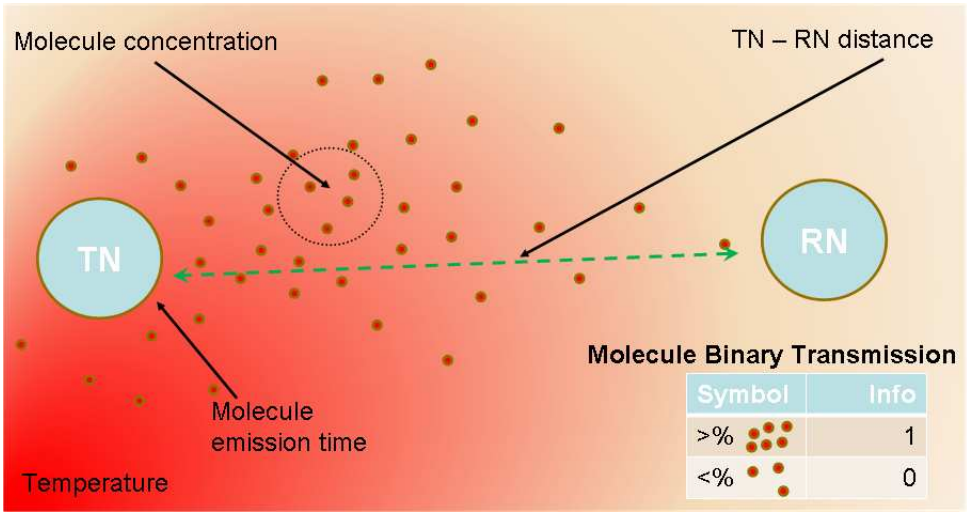

Figure 5.6: Binary model based on concentration encoding.

From our point of view, new channel models should be developed since those already proposed have some flaws and take nonsense assumptions that will be next discussed.

First of all, let us structure their model schematically (Figure 5.7) and start the discussion from there.

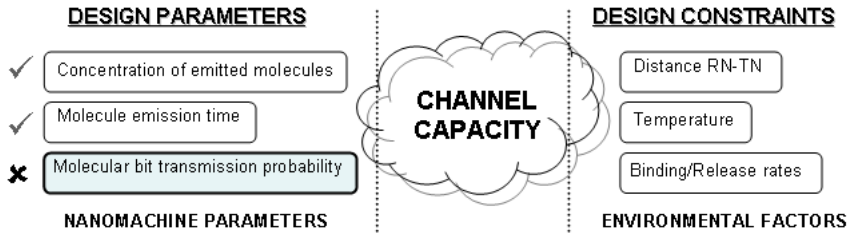

Figure 5.7: Model Scheme. We do not have control over P_A, it depends on the information itself.

For one thing is clear that the probability for TN of transmitting molecular bit A (logical bit 1), P_A, cannot be a parameter we have control over, since it intrinsically depends on the information itself which is an entropic entity. Therefore, it is not

possible to know that value, however, if using code words when transmitting, a given mean, $E[P_A]$, could be obtained. Working with source coding entails higher robustness but also a bite-rate decrease, or code-rate in this case, and as a result lower bandwidth. Moreover, higher computation capabilities are required which nanomachines cannot fulfill up to now.

Nevertheless, source coding is not the best solution, indeed the parameter that should be controlled to optimize the channel capacity is the concentration of molecules at the TN, L_{ex}, which would not be an unrealistic perfect pulse as in the model presented above, but it would account for other parameters (e.g., transmitting delay, distance between the receptor and the transmitter, etc) and for an emission pattern with slopes to simulate the linear release of molecules.

Note that the amount of substance delivered during the intervals depends on the ligand-receptor affinity, which results from greater or lower force between the ligand and its receptor. High affinity ligand binding implies that a relatively low concentration of a ligand is required to trigger the receiver response and, on the contrary, low affinity ligand binding needs relatively high concentration of a ligand to achieve the aimed response [27]. Taking into account that these molecules should be detached from the receiver before being able to process new ones, it is not clear which option would certainly provide us with higher information rates or channel capacities. In biological nanomachines, binding is mediated by noncovalent interactions (hydrogen bonding, hydrophobic, and electrostatic) between the complementary surfaces of ligand and receptor. Receptor-ligand interaction brings about a conformational change that alters the chemical activity of the receptor. Hence, this binding depends on the concentrations of the interacting components and can be described by an equilibrium constant:

$$A + R \rightleftharpoons_{k_{-1}}^{k_1} C \tag{5.42}$$

Therefore, binding and release rates depend on the chemical characteristics of the molecules and the receptors. On the contrary, in the model that [2], [4] and [3] propose (Figure 5.8), these rates are considered as design constraints, when they are not, and define them dependent on non-related parameters such as the distance between the transmitter and the receiver.

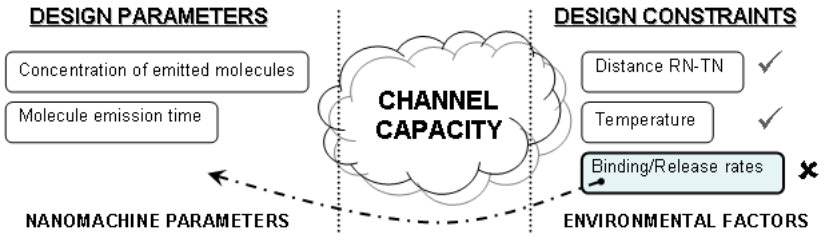

Figure 5.8: Model Scheme. Binding/Release rates are design parameters. They depend on the chemical characteristics of the molecules and the receptors.

As aforementioned, they propose a binary model using amplitude modulation where the information received does not depend on what is transmitted, but if a concentration level is exceeded or not (Figure 5.9). In other words, the information is not encoded in the particle itself but *concentration encoding* is used (Section 3.2), thus the receptor decodes the received information according to the comparison between the level of concentration of the temporal sequences it receives and a previously set threshold. This coding technique entails cheaper transceivers and less computational requirements since particles are all the same, which means they do not have to be specifically encoded and decoded. However and very important, to carry out this coding/decoding system some parameters need to be taken into account, which this model overlooks: *Synchronization* between TN and RN, *bit-time* (t_H), *bit-rate*, *propagation delay*, etc.

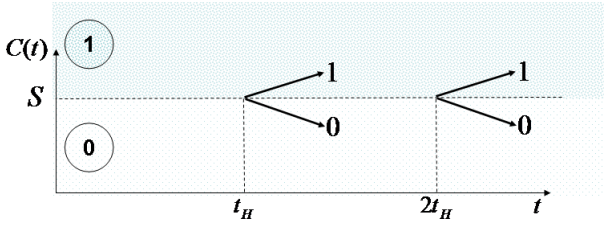

Figure 5.9: Binary model using concentration encoding.

On the other hand, a simple error correction technique is also proposed and is based on the adaptation of P_A to reach the maximum channel capacity. This adaptive process requires the RN to detect erroneous bits, to recalculate new P_A values, and to send certain bit streams to TN when necessary. For one thing is clear that RN is unable to know when a bit is right or not, since according to this model all particles are the same, without coding, and therefore, without any FEC code (e.g., CRC), which at the same time it would result unfeasible for nanomachines computational constraints. On top of that, sending bit streams to a specific TN to communicate a new P_A value is also impossible due to the nature of isotropic diffusion process and more important, because not addressing mechanisms are contemplated neither to select an specific receiver, nor to distinguish which TN is sending the erroneous bits. Note that each RN would need different P_A.

When it comes to the more complex channel models (i.e., broadcast, multicast access, and relay) they start talking about "labeled molecules", that means that as each sender codes their emitted molecules differently, TN can distinguish each of them. This idea differs from the main concept that these models involve, since its coding/decoding system is based on concentration encoding with same type of molecules, and consequently cheaper transceivers. Furthermore, the three models are only valid for unidirectional simplex communication: Multiple-access molecular channel model only takes into account one RN, broadcast molecular channel model only considers one TN, and relay molecular channel model is only conformed by one TN, one RN and one relay. To top it all, this last model breaks with

the concept of relay networks by assuming that the relay node H knows in advance the exact transmission pattern of TN, so they both send the same bits simultaneously. As above stated, the transmitted information cannot be known a priory since it is an entropic entity. Moreover, a delay exist between TN-H, H-RN, and TN-RN.

Last but not least, these models are just developed for ideal conditions, without accounting neither for turbulences, nor the effect of noise (present in the medium) and interference's (coming from other users transmitting at the same time). Furthermore, they should also consider the propagation model given by Fick's laws and include the effect of having different types of obstacles in the communication pathway.

On balance, new models for molecular channels need to be developed taking into account the different molecular communication techniques, and consequently all the constraints and parameters each of them entail separately. That will give cause to develop more complex models on top of them considering more specific factors (e.g., Doppler effect), protocols, architecture topologies, etc...

Do we need a new perspective on Shannon theory?

As addressed in the literature, entropy, information and free energy hold true in the nano-setting, which means that the same formulas can be used to model the communication in that scenario. However, we will need to model some parameters such as the "information sources" and the noise, so we can talk about Signal to Noise Ratio (SNR) for example, and other similar concepts. To sum up, the problem we have to afford mainly concerns to analytical characterization of the parameters at the nano-communications scenario since the mathematical basis proposed by Shannon will still be the same.

5.4 Channel Simulation

One of the firsts things needed in nanotechnology from the communicating point of view is to have a channel model. As it has to be done from scratch the most general and simple setting is taken: pheromone diffusion in still air. In other to be able to use Robert's law, simulation is conducted under certain constraints:

- Static nodes/nanomachines.
- Point source.
- Continuous emission.
- Ideal medium: without accounting for noise, interferences, obstacles, turbulences, etc.
- Isotropic diffusion.

The first step to get the channel spectrum, and consequently its bandwidth, is to estimate the impulsional response of the molecular diffusion (Figure 5.10). The

aim of studying the impulsional response of the channel is that it will help us for a better understanding of the channel spectrum, since it is no more no less than the representation of Robert's law kernel 4.10.

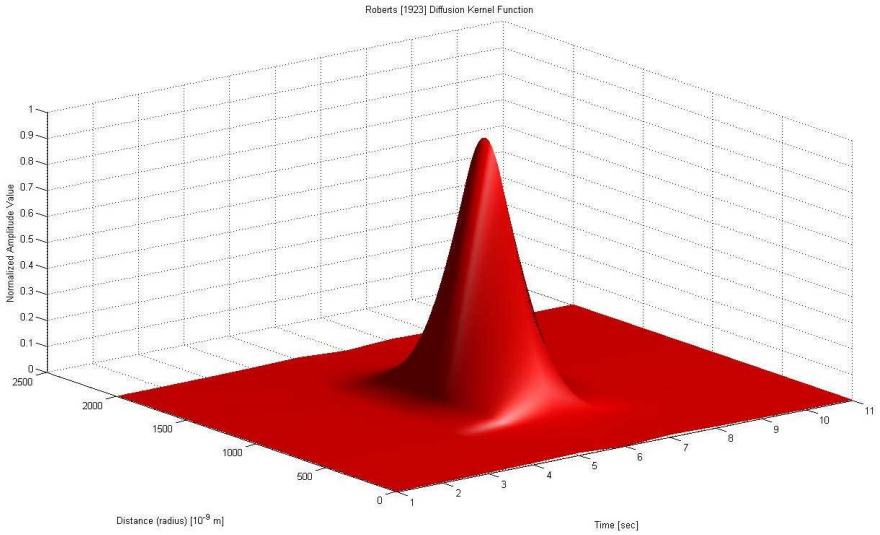

Figure 5.10: Impulse response of the channel. Robert's law kernel.

Impulsional response is not our main concern though, because in the case of molecular channels it makes no sense modeling them without including the receivers effect. According to [2], receivers are modeled as "chemical antennas" that follow the ligand-receptor theory. Indeed, the model used is simplified by only accounting for the binding and release rates. Unlike the E.M. antennas, these reception processes take some time and also modify the detected information.

On top of that, *amplitude modulation* is used to transmit the information, but unlike E.M. we cannot have negative values for concentration of molecules, thus a carrier is needed to force positive values which in this case a baseband carrier is used (offset) and the modulated signal is added over it. This means there is always a constant concentration in the environment nearby the receivers which is desired to be as homogeneous as possible.

Summing up, the channel model consists of two parts:

1. **Molecular diffusion.** Since the olfactory system model is considered to be suitable in our case, Robert's laws [9] can be used for modeling it.

2. **Chemical processes at the receiver side**. We proceed modeling the receivers, and more concretely, their chemical antennas (receptors) and their properties using the simple model proposed in [2].

This way, we manage to model and simulate the channel saving some of the previously discussed issues, by accounting for both molecular diffusion and chem-

ical reception (Figures 5.11 and 5.12).

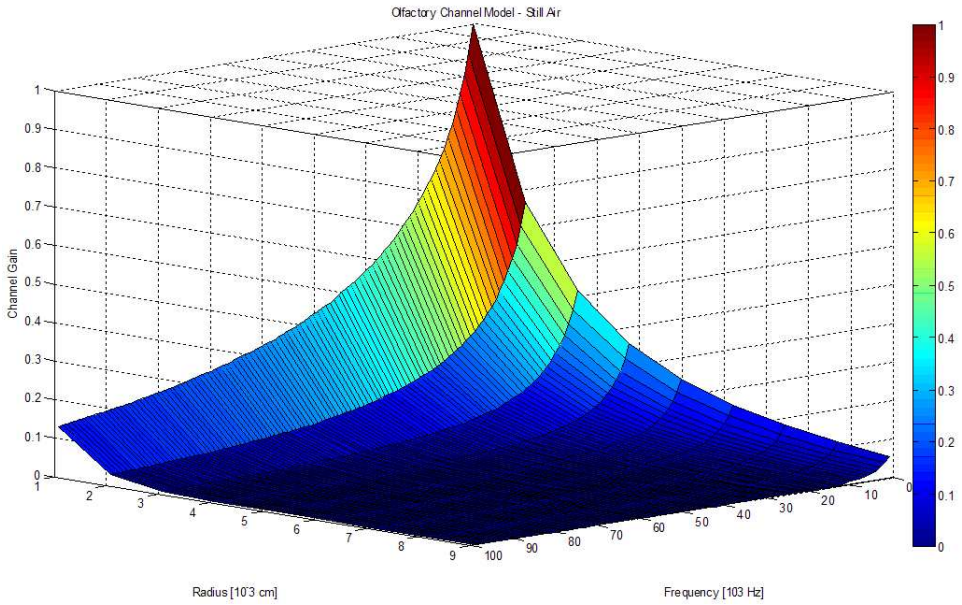

Figure 5.11: Channel spectrum. Channel's Gain vs. Radius vs. Frequency.

The figures show the gain of the channel, with respect to frequency and to the distance between the transmitter and the receiver, as well as the frequency vs. radius dependence:

Gain vs. Radius

Gain, and therefore concentration of molecules, decreases in an exponential fashion with the radius. This behavior is expected because of the negative exponential and it is due to the diffusion process: the closer comes the transmitter to the receiver, the more concentration of molecules is detected. On the contrary, if the receiver is too far from the transmitter, it will detect less concentration of molecules, and even that concentration cannot be enough to enable the detection.

Note that this exponential behavior is more pronounced at shorter ranges, and there exist an area were that behavior is quasi-linear.

Gain vs. Frequency

There is not a linear behavior between gain and frequency either, which shows that the channel distorts the signal. This may be caused by a frequency dispersion behavior, therefore given a distance a different delay exists for each frequency. Thus, the receiver does not detect the same that has been transmitted. In other words, if the transmitter sent a specific pulse "shape", due to the channel's distortion, the received "shape" would be different. This problem is similar to radar's, which has been solved using the "chirp" function. The chirp is a frequency variation in time and, as channel's behavior happens to have dispersion, this would compensate for

the distortion in frequency as time and space vary. Therefore, the transmission of a chirped pulse may be able to equalize the channel effect. This research work is still in progress.

Radius vs. Frequency

As expected, the lower is the frequency which information is transmitted, the farther the detection can be performed, and viceversa.

0.7cm

The values used for the simulations have been taken from the study presented in section 4.4.2 and from [4], [3] and [31], which are considered to be common and adequate values. These (A), together with the corresponding codes (B) can be found in the appendix.

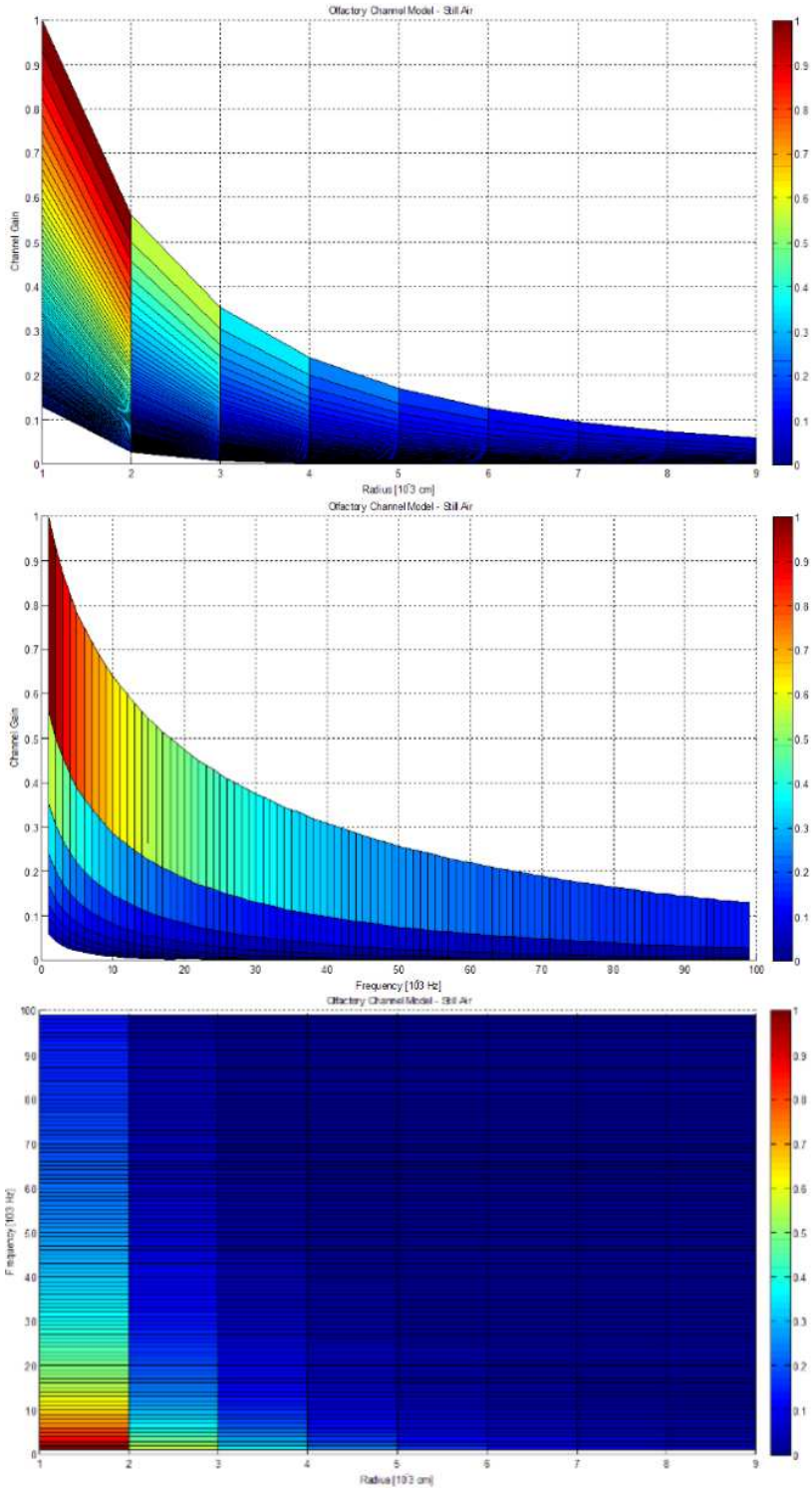

Figure 5.12: (a) Gain vs. Radius; **(b)** Gain vs. Frequency; **(c)** Radius vs. Frequency.

Chapter 6

Molecular Automata Model for Short-Range Communicating Nanomachines

Nanomachines are molecular cell-sized artificial devices or engineered organisms capable of performing very simple tasks such as actuation or sensing. According to the previous chapters, construction of such nanomachines seems to be within the reach of current nano- and bio-technologies and so communication among these nanomachines becomes an important problem. While other chapters deal with a low level view of molecular communication, this one will present some algorithmic aspects of the respective communication process.

In what follows is presented the molecular automata model and a biological cell-based communication model proposed by [32]. This solution specifies biomolecule address encoding, link switching mechanisms and error correction for molecular communication processes. Nanomachines are modeled as cell-based automata and cell-based computing is used to implement those solutions.

6.1 Molecular Automata Model of a Nanomachine

Generally an automaton consists of

1. A data tape divided into cells, each one containing a symbol selected from the tape alphabet

2. A finite-state device driven by transition rules.

Depending on the symbol read and the internal state, a transition rule instructs the device to write a new symbol, change state, or move one cell to the left or to the right.

Biomolecular automata are essentially simple automata operating on digital information encoded in directional biopolimers[1]. They are capable of autonomous conversion of an input encoded molecule to an output molecule according to a set of rules defined by a molecular program. In other words, biomolecular automata are molecular scale, programable, autonomous computing devices in which the input, output, software and hardware are made of biological molecules.

For instance, in the molecular realization of the automata proposed in [30] the input is encoded as a single DNA[2] molecule, transition rules (software) are encoded by another set of DNA molecules, and the hardware consists of DNA-manipulating enzymes. Computation takes place when all molecular components are present in solution and the input molecule is processed in steps performed by the hardware molecules, which follow the instructions of the software molecules. The result of the computation is encoded in the output molecule.

Hence, an automaton operates by scanning a tape of symbols, one symbol at a time, possibly modifies one symbol in each step, moving to an adjacent symbol and changing its state according to a predefined set of the transition rules. The tape of symbols may be naturally encoded in a polar biopolymer such as DNA or RNA. The transition rules of the machine may be encoded by transition molecules similar to tRNA, and transitions may be accomplished by a combination of different processing enzymes [6]. DNA and RNA polymerases, the ribosome, and recombinases can all be viewed as simple molecular automata, and their nucleotide bases as an information unit with four possible values. For example, RNA polymerase is, mathematically speaking, a so-called finite state transducer, which translates a string over the alphabet A, T, C, G into a string over the alphabet A, U, C, G according to a simple translation table. Concretely, a *finite-state automata* is unidirectional read-only, utilizes the energy stored in the chemical bonds of its DNA input molecules instead of relying on ATP as energy source, and its software molecules are reusable. An example of a molecular finite automata structure with two states and an alphabet of two symbols is depicted in 6.1, where details and operation mechanisms of the molecular finite automaton from [7] are shown.

[1] *Biopolymers* are a class of polymers, which are large molecules (macromolecules) composed of repeating structural units typically connected by covalent chemical bonds, produced by living organisms. Starch, proteins and peptides, DNA, and RNA are all examples of biopolymers.

[2] DNA, the "universal" information molecule, is a long polymer made from repeated units called nucleotides. There are four nucleotide bases: adenine (A), cytosine (C), guanine (G) and thymine (T), complimentary two by two.

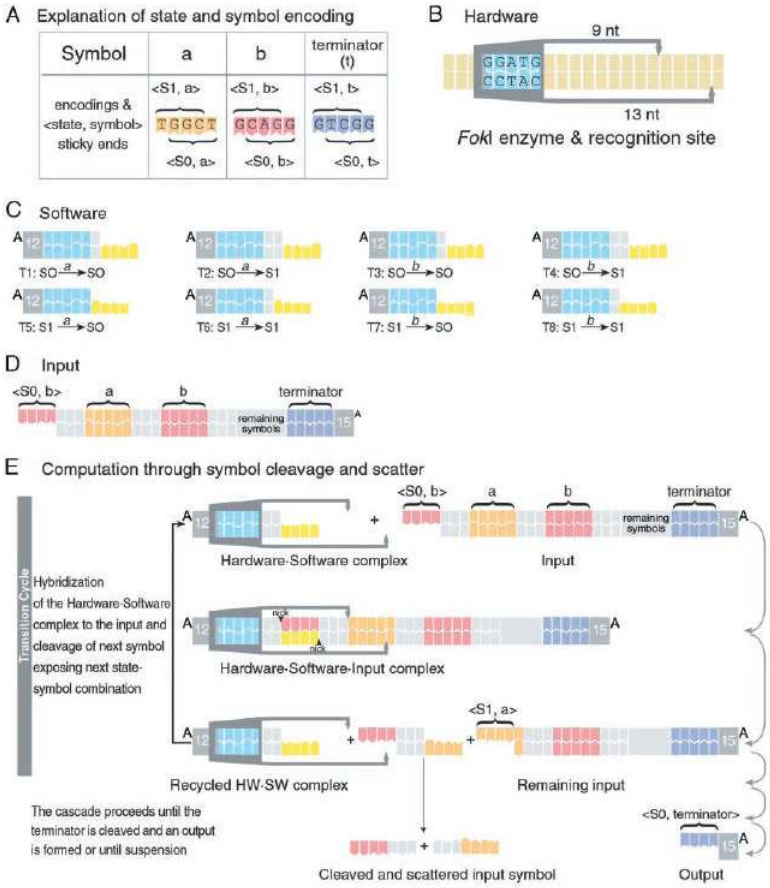

Figure 6.1: Details and Operation Mechanisms of Molecular Finite Automaton [30].

(A) Encoding of a, b, and terminator (sense strands) and the $< state, symbol >$ interpretation of 4-nucleotide (nt) sticky ends. The leftmost representing the current symbol and the state S1, similarly the rightmost for S0. **(B)** *Hardware*: The FokI restriction enzyme, which recognizes the sequence GGATG and cleaves 9 and 13 nt apart. **(C)** *Software*: Each DNA molecule realizes a different transition rule by detecting a current state and symbol, and determining a next state. It consists of a $< state, symbol >$ detector (yellow), a FokI recognition site (blue), and a spacer (gray) of variable length that determines the FokI cleavage site inside the next symbol, which in turn defines the next state. Empty spacers effect S1 to S0 transition, 1-base pair (bp) spacers maintain the current state, and 2-bp spacers transfer S0 to S1. **(D)** *Input*: The exposed sticky end encodes the initial state and first symbol. Each symbol is encoded with 5 bp separated by 3-bp spacers. **(E)** Suggested mechanism of operation of the automaton. The computation proceeds via a cascade of transition cycles, each cleaving and scattering one input symbol, exemplified with the input molecule bab in the initial state S0 and the transition $S0 \rightarrow^{b} S1$. Both hardware and

software molecules are recycled.

According to [30], for some applications such as biomedical, a stochastic biomolecular automaton would be more suitable because of the stochastic nature of the biomolecular systems. In stochastic molecular automaton, stochastic choice is realized by means of competition between alternative biomedical pathways, and choice probabilities are programmed by the relative molar concentrations.

6.2 Nanonetwork Architecture

A static multiple overlapping ring topology is proposed for a given nanonet with pre-defined rate of traffic in [32]. This way, routing complexities are minimized since routing tables can be static and routing process is only performed at the interconnection nodes between different rings.

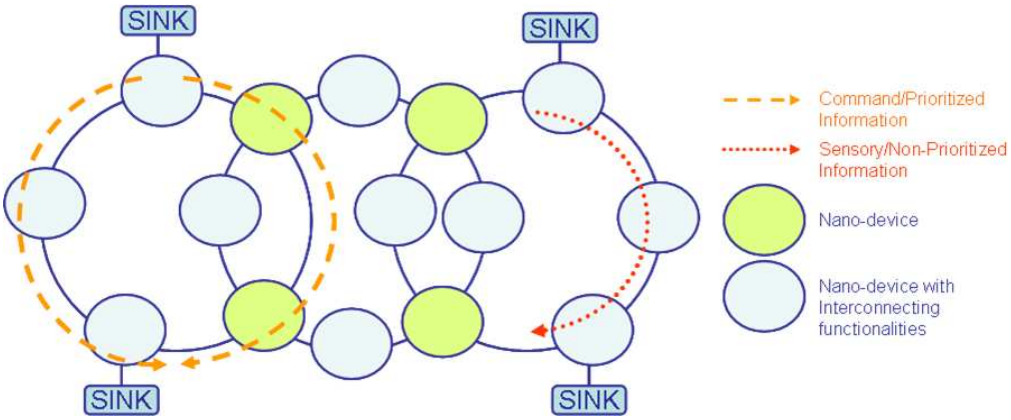

Figure 6.2: Overlapping Ring Network Topology for Bionanomachines.

Two types of information are considered, each receiving different treatment depending on its nature: *Sensory data* (data collected from bionanodevices) and *command/prioritized data* (instructions for bionanodevices). As depicted in Figure 6.2, the former is transmitted through single paths with no error corrections while prioritized information is sent through redundant paths with error correction capabilities (e.g., FEC).

The solution combines two molecular computing techniques: DNA and enzyme computing. There are some differences between the two types of cell-based computation, where each has certain advantages and disadvantages. Firstly, DNA is the universal ”information molecule” and an obvious choice for encoding information as a sequence of biochemical symbols. DNA computing is a newly emerging computing paradigm that is able to outperform the state-of-art digital computer in communication speed, power consumption, storage space and cost. As previously introduced, the basic idea consist in long DNA input molecule processed repeatedly by a restriction enzyme, whose operation is controlled by short

DNA "rule" molecules. The computational complexity and speed associated to DNA computing is not attainable using enzyme-based computation, which in turn requires short computation time and thus, it is more suitable for simpler circuits. In short, enzymatic computation is most suitable in performing small size logic

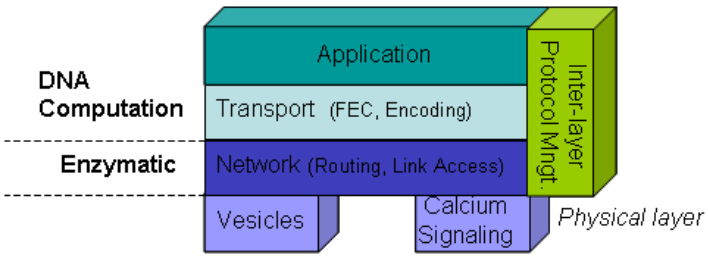

Figure 6.3: Protocol Stack for Molecular Communication.

circuits with high-speed computation due to their limited time requirement, what makes it best for switching between different link layers and routing (see Figure 6.3). On the other hand, the transport and application layers require higher complexity computation and is usually not required to be time sensitive. Such computations include FEC, addressing and encoding/decoding. In between the two layers will be the Inter-layer protocol management, which triggers the process of computation.

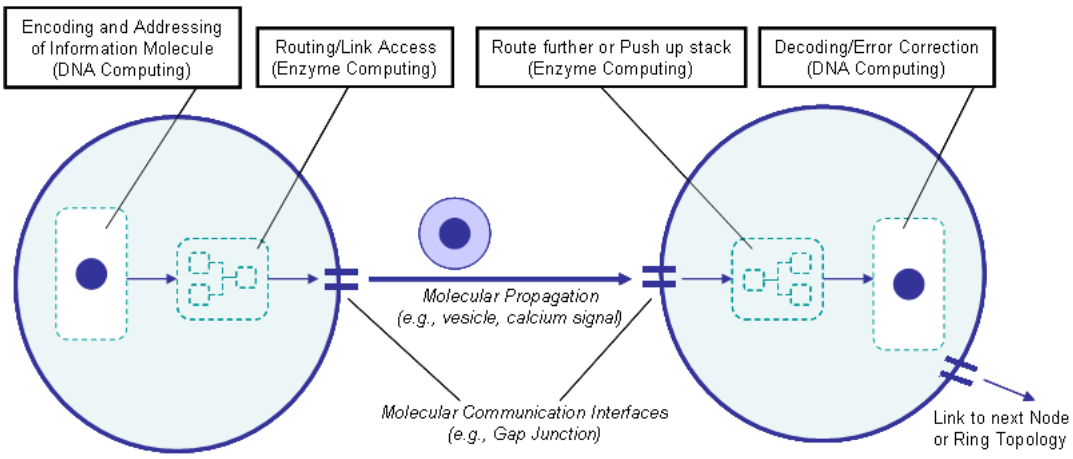

Figure 6.4: Mechanism of Transmission for Single Link Molecular Communication.

The communication process for a single link works as follows (Figure 6.4):

1. *Data encoding process*: data is encoded in DNA molecules using a DNA-

automaton[3].

2. *Address encoding process*: Encoded biomolecule is further encoded with the intended destination address using an address table.

3. *Inner molecular interface control*: Encoded biomolecule is switched to the correct molecular communication interface link.

4. *Molecular motors*: Once the encoded biomolecule reaches the physical layer it is transported to the next node using a suitable molecular communication mechanism, such as molecular motors or calcium signalling. This process is further descrived in section 3.2.1.

5. *Decoding and Forward Error Correction*: Once the message is received it is correctly decoded, even though encoding errors exist in the message molecule.

6.2.1 Data Encoding and Address Encoding Process

How each message molecule is encoded as a unique sequence of nucleotide bases and each encoded message is "framed" to include the addressing information is shown in Figure 6.5. The upper leftmost "sticky end" represents the current state of the automaton. Each rule molecule has a recognition site to which a restriction enzyme can bind.

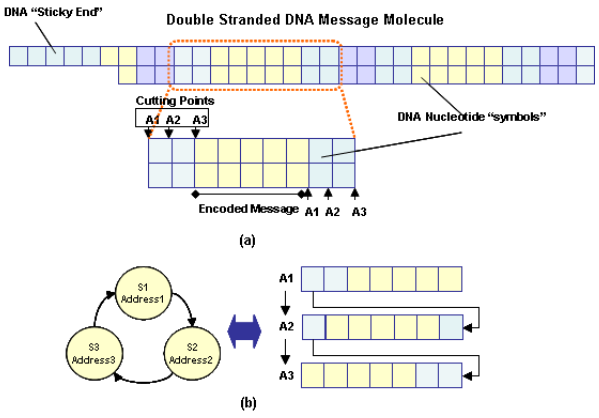

Figure 6.5: (a) Double Stranded DNA Molecule Indicating Restriction Cut Points for Address Encoding. (b) State Representation of Address Encoding Transitions.

During the address encoding process, the DNA message molecule is repeatedly cut by a restriction enzyme which cuts off the leftmost segment of the molecule.

[3]DNA-automaton is a class of molecular automaton, further explained in 6.1, that uses DNA to encode the information, instead of other biopolymers.

This precise cleavage of input message molecule that encodes or "frames" the message is a key characteristic of computation. The segment that is cut away is separated into two single strand DNA(ssDNA) molecules, as indicated in Figure 6.6, the lower ssDNA molecule is the address-encoded message with its rightmost end complimentary to the new sticky-end of the DNA message molecule, which reveals the next state of the automaton.

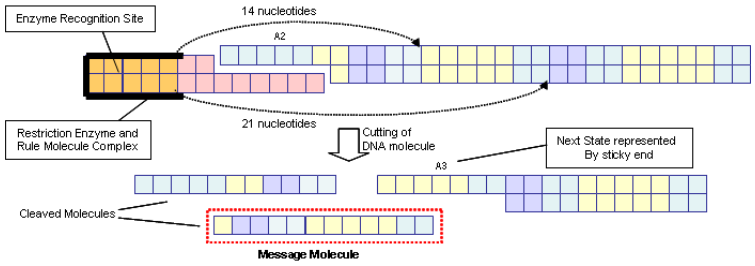

Figure 6.6: Mechanism of State Transition from Address 2 to Address 3 using Benenson's Molecular Automata.

The nanodevice can control computation by releasing molecules that selectively activate DNA "rule molecules". Theoretically, this mechanism can be extended to encode multitude of unique address locations and any number of messages during computation.

6.2.2 Molecular Interface Control

It provides the ability to switch the address-encoded molecule to the corresponding communication interface based on the addressing state diagram shown in Figure 6.7. More specifically, the interface selection is achieved using the mes-

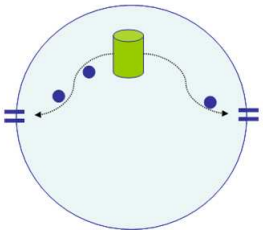

Figure 6.7: Schematic Diagram of Cell With Two Molecular Interfaces.

sage molecule as input to the enzymatic reaction circuit [5], which alters a chemical signal that "switches" the message molecule to the correct interface. This biochemical implementation is given by adjustment of the total concentration of the species relative to the range of concentrations of the input molecule.

6.2.3 DNA Decoding and Forward Error Correction

The solution proposed in [32] is based on Benenson DNA-based automata design [6] and uses "protector strands" to control the enzymes operation (initially these protector strands are bound to the transition strands) [5]. The **decoding mechanism** works as follows (see Figure 6.8):

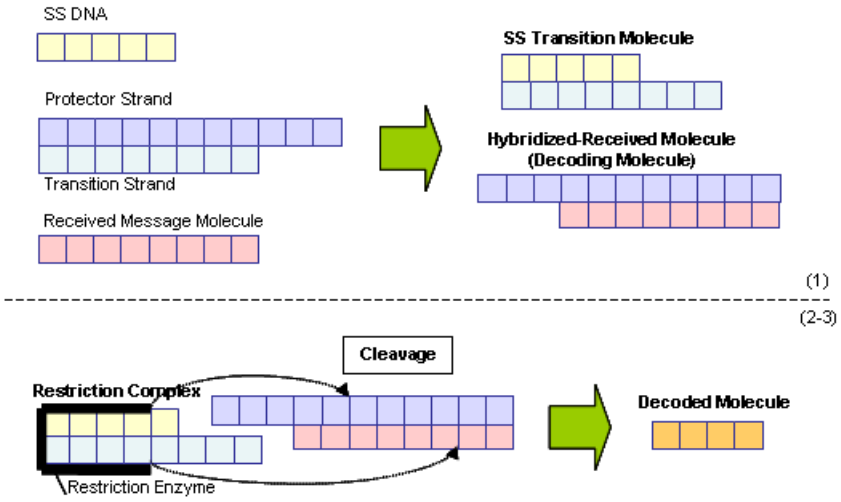

Figure 6.8: Decoding and Forward Error Correction Mechanism.

1. Firstly, the protector strands are designed to have a strong affinity to received message molecules. Hence, when a molecule is received it causes the corresponding protector strand to separate from the transition strand and hybridize with the message molecule. At the same time, this allows the formation, and thus activation, of a double-stranded transition molecule, similar to the encoding process.

2. Double-stranded transition molecule combines with restriction enzyme forming the restriction complex that will cleave the corresponding hybridized received molecule.

3. After the cleavage the decoded DNA molecule is released.

To sum up, the hybridization of the received message molecule by recognizing protector strands, results in the successful release of the decoded message after the cleavage of the restriction enzyme complex.

This solution combines the decoding process with error correction mechanism. The proposed Forward Error Correction (FEC) is based on including redundancy in the encoding process, and as a result each message molecule is composed of

several repeated, identical nucleotide sequences. To make the mechanism easy understood it will be presented through an example following Fedichkin et al. ideas [15], where short oligonucleotide[4] sequences (about 10 bases)are used as encoded molecules. For instance, base T will be used to encode "1" and base C will be used to encode "0". Conclusively, an oligonucleotide composed of n ($n = 10$ in this example) repeated T (or C) bases will encode "1" (or "0") with n repetitions. These oligonucleotides could include some other bases that would represent errors in the encoded sequence. Magnetic nanoparticles functionalized with single oligonucleotide chains (A_n and G_n) complementary to those that are used for encoding "1" and "0", respectively, can be use to recognize the encoded oligonucleotide and to correct error appearing in the sequences. This is illustrated in Figure 6.9.

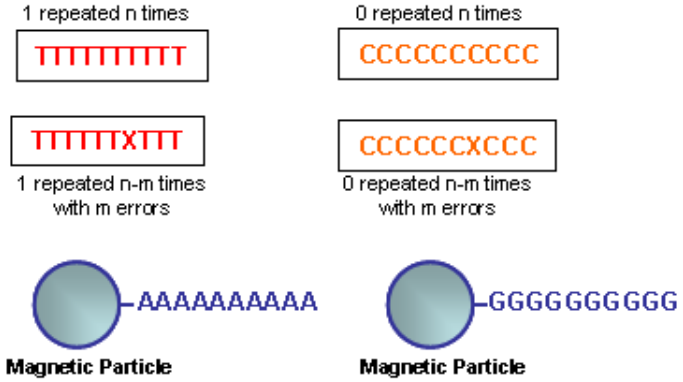

Figure 6.9: Chemical Materials Used for the Error-Correction in the Encoded Oligonucleotides.

The present example will demonstrate the error correction process in the poly-T-oligonucleotide (encoded "1" repeated $n - m$ times) with m errors represented by X (foreign bases). A similar process should be used to make error-correction in the poly-C-oligonucleotide. Since the encoded signal coming to the system is unknown in advance, it is supposed to be ready to read any of them, thus the system should include both poly-A- and poly-G-functionalized magnetic nanoparticles. The poly-A-functionalized magnetic nanoparticles will be responsible for the hybridization and recognition of poly-T-oligonucleotide, while poly-G-functionalized magnetic nanoparticles will hybridize with poly-C-oligonucleotide.

The hybridization will proceed only if the "melting" point[5] of the double-stranded (ds) oligonucleotide is higher than the temperature of the reaction solution. The "melting" point depends on the number of errors in the poly-T (or poly-C) sequence -when the number of errors is higher the hybridized complex is less stable and the "melting" point is lower. The change of the "melting" point for short

[4] An oligonucleotide is a short segment of RNA or DNA, typically with twenty or fewer bases.

[5] 'melting" point is the temperature corresponding to the dissociation of the ds-DNA complex).

ds-oligonucleotide sequences could be $10°C$ per one error in the sequence. Thus, by selecting different temperatures for the hybridizing solution, we can control the number of errors in the encoded sequence that will still allow the hybridization process proceed.

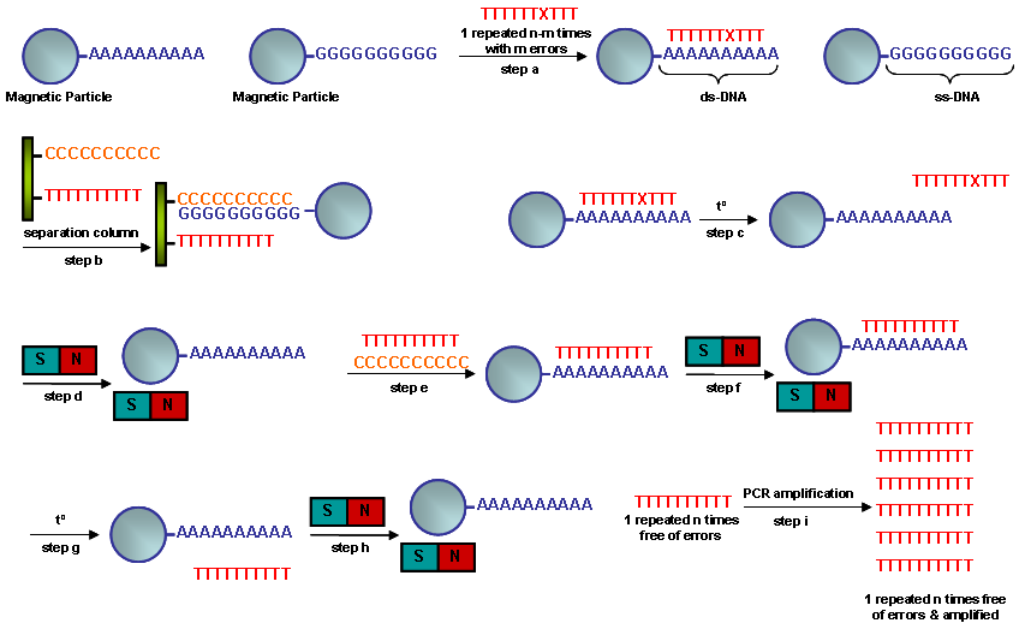

Figure 6.10: Scheme Showing the Steps of the Recognition, Error Correction and Amplification of the Encoded DNA Signal.

The following reaction steps, depicted in Figure 6.10, will be used to recognize the encoded signal, to correct errors in the signal and to amplify it.

a. Hybridization process between poly-T-oligonuleotides (with m errors) and the complimentary poly-A-functionalized magnetic nanoparticles. This process will result in the formation of double-stranded oligonucleotides (poly-T/polt-A) bound to the magnetic nanoparticles.

b. All the magnetic nanoparticles with non-hybridized oligonucleotides will be absorbed by the column due to the hybridization with the complementary strands, and only the magnetic nanoparticles with the ds-oligonucleotides will go through the column.

c. The solution ds-poly-T/poly-A is heated. This will release the original poly-T oligonucleotide (that still contains errors in the sequence) from the poly-A-functionalized magnetic nanoparticle.

d. The magnetic nanoparticles will be separated from the solution using an external magnet, washed from the absorbed poly-T, and placed in a solution.

e. Since it is not known in advance what kind of the encoded oligonucleotide was added (poly-T or poly-C) and thus it is not known what kind of functionalized magnetic nanoparticles is obtained in the previous step, a mixture of poly-T and poly-C oligonucleotides will be added to the solution[6]. The complimentary oligonucleotide (poly-T in the present example) will hybridize with the oligonucleotide (poly-A) bound to the magnetic nanoparticles.

f. The ds-oligonucleotide-functionalized magnetic nanoparticles will be again collected with the external magnet, washed from non-hybridized oligonucleotdes, and re-dispersed in a solution.

g. The solution will be heated again to dissociate the ds-oligonucleotide.

h. Magnetic nanoparticles will be collected and separated from the solution with the external magnet.

k. Finally, **the solution will contain the error-corrected equivalent to the initial encoded input.** This sample may be subjected to polymerase chain reaction amplification to generate numerous copies of the error-free encoded oligonucleotide.

In a fixed and final form, error correction may be incorporated into the decoding process by including redundancy in the encoding process. Hybridization can occur even though both single strand DNAs involved are not exactly complementary, fact that enables messages to be correctly decoded even though encoding errors exist in the message molecule. The output loop (figure 6.8) is the corrected message molecule in this case.

6.3 Discussion

In this chapter molecular automata model has been briefly introduced. Nowadays, current development on molecular automata seems to be hampered by the lack of DNA- and RNA- manipulating enzymes. Moreover, another important issue is symbol encoding since current experimental realizations utilize artificial alphabet of predesigned DNA sequences. However, the nanomachine should "understand" natural alphabets of either single nucleotides or amino acid codons to be biologically relevant. Designing even the simplest finite automaton capable to operate on an arbitrary DNA sequence remains a major challenge.

On the other hand, the communication model proposed is based on how DNA and enzymatic computing can perform a molecular automata capable to encode different information in DNA sequences, send them (or reroute them) through the corresponding interfaces and decode them with error correction mechanisms. It is

[6]Note that these oligonucleotides are different from the initial encoded inputs, which contained errors. These are error-free.

clear that the biggest portion of the solution proposed is basically descriptive and mainly theoretical, but it is a first step in a cutting edge technological paradigm.

Obviously, many questions arise, and a bunch of challenges need to be studied in order to get to improved solutions.

Firstly, in what it is proposed it is assumed that coding the information using nucleotides of a DNA sequence (DNA coding) is theoretically possible, but the fact is that in the real world application a lot of questions still need to be answered, above all when it comes to the communication point of view: How many nucleotides should the ideal sequence contain? Would it be possible to set some keywords or default sequences? How should delimiters be defined? More importantly, robustness of DNA sequences in front of different agents should be thoroughly analyzed (there is not noise, but Ultra-Violet light can alter DNA for example).

Another important issue is to define which ways of propagating the information (molecular motors, calcium signaling, molecular diffusion) make sense when it comes to DNA encoding, in other words, which molecular propagation techniques can take advantage of having information encoded in their inner structure. It is clear noticed that transmitting DNA-encoded information through calcium signaling is not feasible, although it is suggested in the preceding solution, since a calcium ion is exactly a calcium atom that has lost 2 electrons (a positively charged ion); and when we talk about DNA, we are talking about macromolecules! Therefore, in this solution it is only suitable to communicate the different nodes by molecular motors since calcium signaling cannot encode information in its structure (its communication process consists in receiving or not receiving calcium ions in the targeted nanodevice), and using molecular diffusion in a nanonet with ring topology makes no sense, because molecules propagate unidirectionally through all the nanonet reaching all nodes progressively instead of being directionally rerouted from node to node.

After this overall review, let me talk about the proposed solution from the communicating point of view.

There are a number of factors that must be taken into account when it comes to protocols for nanonetworks. Firstly, propagation of information in molecular communication is typically characterized as *low speed* and it takes place in an *environment* where the link condition is *highly variable*. These characteristics have repercussions for the design of protocols for molecular communication systems. Slow speed diffusion does not allow high-speed switching functions, and at the same time, due to the high variability of the environment, the use of acknowledgments, retransmission of messages in the event of loss or corrupt messages, and signalling information may not lead to improved performance.

The protocol previously presented is suitable for static nanonets with pre-defined rate of traffic between nodes, since routing tables used are static. It is this way because of the limited capabilities of the nanomachines, in this case molecular automata. All this together makes the protocol not much flexible and supposes one of the main constrains that it entails. On the other hand, it allows an addressed

transmission of the information messages. DNA-automata can encode the destination address into the molecule and the molecular interface control is responsible for rerouting the message or keep it and sending it to the decoding mechanism. But, how many addresses can a molecular nanomachine store? Could this solution be used to interconnect a large number of nodes?

Note that if different type of information (prioritized and non-prioritized) is considered, channel differentiation will be needed in order to avoid possible collisions. For instance, consider the nanonet shown in Figure 6.11, a collision would happen if node B sends information to C, and at the same time C sends prioritized information to another node. A possible solution for channel differentiation using molecular motors would be having two different molecular rails (microtubules), one for each direction.

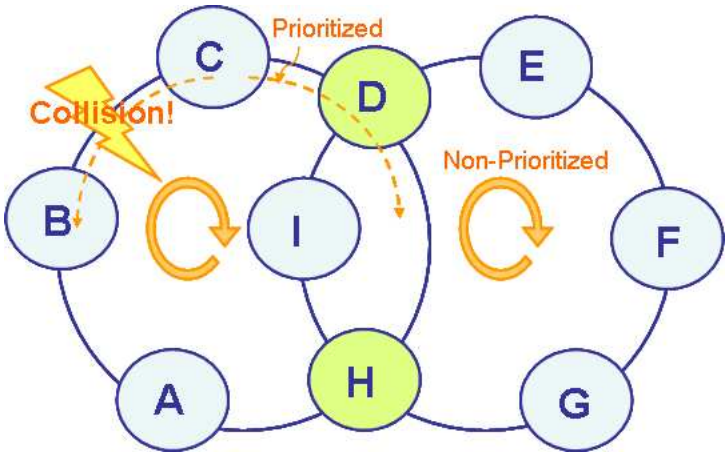

Figure 6.11: Nanonet with Overlapped Ring Topology

More questions arise when thinking about the nanomachines requirements. This solution also demands that nanomachines interconnecting interfaces, besides being able of sending and receiving simultaneously, they also should be capable of receiving information through two different interfaces at the same time and process it correctly. That may lead to another requirement: a queuing mechanism. A possible situation where this third requirement can be considered is when node C sends information to E, F, or G nodes and, at the same time, node I also sends information to any of those nodes. Anyhow, node D will have to reroute information from C and I to the same interface (towards node E) at the same time. Then a queuing mechanism will be needed. If we take into account the current development on molecular automata, where the final goal is to make them as powerful and similar to the cell as possible. Considering the cell properties such as multitasking, parallel computation, multiple full duplex transceivers, prioritization of the information capability, etc. The requirements demanded for the nanomachines are in line with the current research.

Finally, it is worth to highlight that the introduced solution is one of the first that

proposes such a physical mechanism and talks about using the idea of molecular automata for molecular nanonetworks. As a very cutting edge research area it makes sense that it is basically proposed from a theoretical point of view, with more or less flaws, but it will help to get to an improved novel mechanism.

Chapter 7

Time Finite-State Automata Model for Short & Long Range Communicating Nanomachines

This chapter presents a computational model of molecularly communicating mobile nanomachines that are randomly distributed in an aqueous environment, which are called random nanonetworks. The solution defined is inspired in amorphous computing and population protocols and means to answer some open questions such as: What happens if there are several nanomachines communicating concurrently? Would it be necessary to synchronize them so that one would act as a sender and the other as a receiver? How does the transmitter nanomachine know that the target machine has received its signal? If a finite number of different signals (types of molecules) exist, what happens if a machine having several receptors detects different signals at different receptors at the same time? What happens when a target receiving machine is actually sending a signal?

In what follows a computational model of molecularly communicating mobile nanomachines proposed by [34] is defined. The scenario considered is a closed liquid environment in which nanomachines form an autonomous system without external control (Figure 7.1). In other words, the system consists of a finite number of nanomachines freely "floating" in their environment, resulting in a random distribution of nanomachines (i.e., random nanonetwork), that interact via molecular communication. In this case, nanomachines are modeled by a variant of finite-state automata, so called timed probabilistic automata.

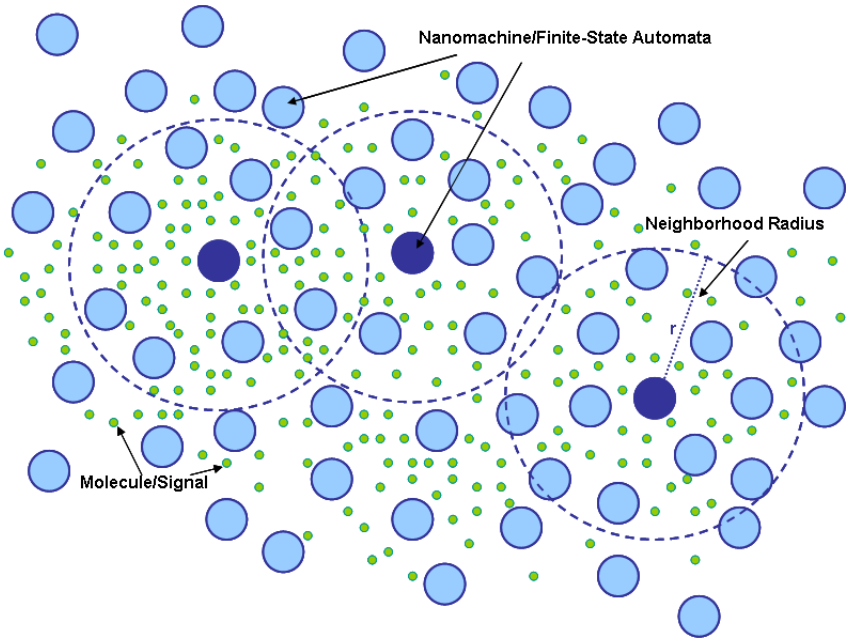

Figure 7.1: Dynamic wireless nanonetwork using molecular communication.

7.1 Automata Computational Model for Random Nanonetworks with Mobile Nanomachines

This version of probabilistic timed automaton [34] will in fact be a probabilistic timed transducer (Mealy automaton)[1] having a finite number of input ports (receptors) and output ports (emitters). The signal molecules will be represented by elements of automaton's finite working alphabet.

The following assumptions are taken to make the underlying molecular mechanism as simple as possible while capturing the constraints imposed on molecular communication:

1. Each automaton is able to work in two modes: in the **receiving mode**, reading (in parallel) the symbols (molecules) from its input ports, and in the **sending mode**, writing the same symbols to its output ports, in other words, releasing the signal molecules of the same kind through all its output ports. Information is *received successfully* if and only if all symbols read at all input ports are identical, otherwise a *communication collision* occurs and all the symbols are released.

2. In their life time, signal molecules can travel, by diffusion, in average a certain maximal distance called *communication radius*. After that time, they

[1] *Mealy machine* is a finite state machine (and more accurately, a *finite state transducer*) that generates an output based on its current state and an input.

disintegrate into other molecules which are not longer interpreted by automata as signal molecules.

3. The automata work asynchronously – there is no global clock in the system. Each automaton is equipped by a finite set of timers (clocks) that are not synchronized and can be independently reset to 0. Therefore, each automaton action is governed by its own local clock.

4. The automata have no identifiers (anonymity of nanomachines).

Note that the previous restrictions are quite restrictive:

Condition 1 means that a nanomachine cannot be in the receiving and sending mode simultaneously; If signal molecules reach the input ports of an automaton in the sending mode, they won't be detected. Furthermore, if a broadcast from one automaton is "jammed" by the broadcast from a different nanomachine sending different signals, the receiving nanomachine will not detect any of them.

Condition 2 ensures that signal molecules cannot roam forever in the environment, neither reach possible toxic levels. Besides, it also ensures that new information prevails over the old one.

Condition 3 says that automata do not switch their sending and receiving modes synchronously, which together with the fact that they can move in their environment either passively (e.g., in a bloodstream) or actively like some bacteria, prevents whatever kind of "acknowledgements" of received messages.

7.2 Properties of Random Nanonetworks

Consider a nanonet with a communication graph *G* whose nodes are nanomachines (automata) and edges[2] connect those automata which are within the communication radius of each other. Topology of *G* is dynamic and depends on time since automata are in continuous movement. Its size is measured in the number *n* of its nodes. The properties which are of importance in this case are graph *diameter* $D(n)$, which bounds the length of longest communication path, and the *maximal degree* of its nodes Q (i.e., the maximal neighborhood size of a node) which determines the collision probability on the communication channel. Although the requirements put on this type of nanonetworks with dynamic topology are quite strong and can hardly be fulfilled in practice, they are needed for analyzing the correctness and efficiency of this protocol. They are not so nonsensical assumptions

[2]The existence of an edge between two nodes is a random event depending on the random positions of the nodes. The probability of edge presence is higher with larger communication radius *r* and is lower when the nodes are spread over a larger area A [33].

since the protocol is sufficiently robust in order to operate correctly on nanonetworks that occasionally, for short time, deviate from their well-behaved properties.

7.3 Asynchronous Communication Protocol

7.3.1 Protocol Send

A node is to send a signal s, with probability of failure $1 > \varepsilon > 0$, *from a node to any other node of the nanonet within the communication radius of the sending node.*

The protocol is designed to work correctly under the assumption that all nodes work concurrently, asynchronously, using the same protocol and therefore possibly interfering with each other's broadcast. Each node has a timer measuring timeslots of length 2T, being T the time to transfer a signal between any two neighbor nodes. The idea is that each node during its own timeslot can either to listen till the end or to send a signal at the very beginning of it and then listen till the end. The probability of a node sending *s* is controlled by the transition probability of the respective probabilistic automaton and will be repeated $k = O(Qlog(1/\epsilon))$ subsequent timeslots. In order to enable each automaton to send the signal k times, its timer must be set to the interval kT, which is the time that a node must be in the sending node. As demonstrated in [33] $O(Qlog(1/\epsilon))$ is the time it takes to receive *s* by any node within the communication radius.

7.3.2 Broadcast Protocol

In order to send a signal s *from a node to any other node of the nanonet which is not in the communication radius of the sending node.*

The main idea consist in "flooding" the network by that signal, i.e., broadcasting *s* to all nodes of the network. To achieve it all nodes of the nanonet are used as a "retranslation station", i.e., every node reached by a given signal *s* will further retransmit it through the network using *Protocol Send*. Once the node has retransmitted the signal, it locks itself with respect to that signal, that is, it will remain in the receiving mode until it detects any other signal different from the last received. Then the node will lock itself with respect to that other signal after retransmitting it. This locking mechanism will be implemented straightforwardly: each node remembers the last sent signal and ignores it if received again - the node "locks itself" with respect to that signal.

Note that this time, in order to achieve the failure probability ε for the broadcasting, *protocol send* must be performed with a probability of error ε/n, and consequently sending algorithm will be repeated $k = O(Qlog(n/\epsilon))$ times. Again, in [33] is shown that the broadcasting algorithm sends *s* to any node of the nanonet that has not been locked with respect to *s* yet in time $O(DQlog(n/\epsilon))$, after that, every node of the nanonet will be locked with respect to *s*.

7.4 Discussion

Molecular diffusion is initially understood as a broadcast technique and is one of the most frequently used among cells for communicating. This technique apply for both: short-range molecular communication using molecules in an aqueous medium, and long-range molecular communication using pheromones on air. Therefore, everything discussed for any of these cases will implicitly apply for the other.

As explained in chapter 4, particles released in a liquid or gaseous medium move randomly following Brownian kinetics and freely disperse themselves following Fick's laws of diffusion. During this propagation they may experience non-deterministic effects due to the presence of other molecules, which may collide, block or react with the transmitted molecules altering their normal diffusion behavior. These effect coming from concurrent communication, or even just dust, can be described as interference and noise, respectively.

Furthermore, information can be contained either in the molecule itself (receiving a molecule may trigger a specific reaction), or inside a macromolecule (such as DNA sequence). In this solution it is used the former case, although the transmission of macromolecules encapsulated in vesicles would also be possible, but it would involve longer delays and major difficulties since they contain higher information than single molecules.

These molecules may finally reach the receptors (hundreds or even thousands per nanomachine) and following the receptor-ligand behavior, they may bind or not to the receptors. The reaction will depend on the molecule received and different stimulus.

In section 7.1 a simple nanomachine is computationally modeled using a mealy machine. Simple automata models can be useful in the initial stage, but taking into account the properties reviewed in 2.2, such assumptions simplify too much their complexity and powerfulness of nanomachines. A clear example is defining that information is successfully received if and only if all the inputs are the same. This statement does not take into consideration the multitasking and multi-interface mechanisms that nanomachines involve, which enable processing the information simultaneously according to the following pattern:

- If they receive the *same molecule*, they simply react as expected. For example, when more than one nanomachine/cell senses an increase in temperature, they may inform other nanomachines/cells of this. Therefore, instead of colliding, they reinforce one to each other.
- If they receive *different molecules*:
  - If these molecules do not interfere in terms of meaning one with each other, different actions may be taken at the same time (nanomachines/cells are multi-interface and multitask).

– If these molecules do interfere between them, different internal operations take place that work out as priority mechanisms among molecules allowing to reinforce with more or less degree each received information.

As stated, information may be transmitted in DNA-encoded macromolecules, which provably will be encapsulated inside a vesicle, and in the molecules themselves, which is the case this protocol applies for. It is assumed that there is no addressing in the information and therefore, all the users look the same from the receiver's view. But, although in the early stage it is not so necessary to know who sent what, working with molecules opens new possibilities.

Channel in computer networks has usually been thought from two different points of view: time domain and frequency domain, mainly CDMA (code domain). In molecular communications, a new dimension may be proposed: Using the receptor-ligand binding properties it may be possible to identify ("label") different users or groups of users by assigning different ligand molecules to each one. Moreover, this may also enable that some receptors with different nano-receivers ignore the information coming from some specific users, that is to say, a single nanomachine may have different binding mechanisms that can react or not to different molecules. At the same time, each one can generate several different selective ligand molecules. This multiple access channel technique can be defined as Molecular Division Multiple Access (MDMA). There are a lot of things to be studied yet: molecule assignment mechanisms, network topologies, capacities for these systems, definition of common control channels, broadcast channels, users channels, which correspond to different molecules in a centralized scheme, or developing random access techniques that exploit these unique characteristics.

On the other hand, note that in the preceding protocol as soon as a node senses a signal, it retransmits it and gets lock to itself with respect to that signal. After sending, in order to avoid interfering one with each other's broadcast (collision), any node has to wait for $cDQlog(n/\varepsilon)$ time units (for some constant $c > 0$) until the next signal can be sent, which is the time that the farthest nanomachine will receive the signal (with probability $1 - \varepsilon$). The transmitting nanomachine will obtain the response for the signal emitted after $2cDQlog(n/\varepsilon)$ time units.

Following this line, each assumption taken in 7.1 is discussed next:

Condition 1 This solution states that nanomachines cannot be sending and receiving simultaneously. However, automata are supposed to be capable of carry on several computing processes in parallel (multitasking).

Condition 2 It is also guessed that molecules cannot roam forever in the environment, which in molecular diffusion process it is naturally happening, due to

the molecular propagation model[3]. When a type of molecule is not released anymore its presence is progressively reduced till completely disappear.

Condition 3 Assuming that automata work asynchronously also makes sense, since each automaton is completely independent and works as an autonomous machine, as cells do. They do not need to synchronize with each other, although for some specific applications it might be interesting. For example, coordinating their access to the medium.

Condition 4 Unidentified information does not turn out to be a problem in the communication process. Although, assigning different types of cells to each automata or group of automata may be a possible way to identify/differentiate the communicating nanomachines.

Along this discussion, those open questions initially presented have already been solved in a broad sense:

1. *What happens if there are several nanomachines communicating concurrently?*

   As stated, nanomachines are multitask and multi-interface devices, so they can be "processing" different information at the same time through their hundreds, or even thousands, of receivers. Moreover, Molecular Division Multiple Access gives the possibility to "label" different users and offers selectivity at the reception.

2. *Would it be necessary to synchronize them so that one would act as a sender and the other as a receiver?*

   This random, mobile, and wireless nanonet works asynchronously. However, it would be suitable to use an implicit Time Division Multiple Access (TDMA) between receiving and transmitting modes. In other words, each nanomachine should be in the receiving mode by default, and jump to the transmitting mode if information has to be sent.

3. *How does the transmitter nanomachine know that the target machine has received its signal?*

   Two types of acknowledgments may be considered:

   - *Implicit Acknowledge*, which is the reaction produced in the receiver once the information has been detected. This reaction is then sensed by the transmitter and the surrounding nanomachines.
   - *Explicit Acknowledge*, which idea is equivalent to the traditional ACK message. The receiver sends a specific molecular message to the transmitter to let it know the information has been correctly received.

[3]In the one dimension case: $J = -D\frac{d\phi}{dx}$, where J is the diffusion flux (amount of substance) $[length^{-2}time^{-1}]$

For example, consider a nanonet that is aimed to keep a room in a fixed temperature. In this particular scenario, when a nanomachine senses the temperature gets colder it immediately sends a message to the others telling to increase the temperature. For the case of implicit acknowledge, the nanomachine will know its message has been received when it senses a warmer temperature, otherwise the nanomachine will wait until receiving the "ACK message". If no ACK is received, the nanomachine will re-send the information again.

4. *If a finite number of different signals (types of molecules) exist, what happens if a machine having several receptors detects different signals at different receptors at the same time?*

   It has also been commented in this section. If the information is the same, instead of colliding they reinforce one to each other. On the other hand, if the information received is different but do not interfere between them, the different information will be processed separately at the same time; on the contrary, if they do interfere the priority mechanisms will decide.

5. *What happens when a target receiving machine is actually sending a signal?*

   Nanomachines have several interfaces working asynchronously and autonomously as a complete system (it refers to multitasking and multi-interface properties).

Nanomachines are aimed to be as accurate as possible to biological nanomachines, the cells. Taking into account their multiple input/output behavior, nanomachine models may be seen as complex mealy machines. Hence, a **multi-automata model** is envisioned: each nanomachine may be composed of different subsystems, each one being described at the same time as a finite-state machine (FSM). Furthermore, each subsystem may have multiple input and multiple output signals and they do interact among them.

Chapter 8

Open Issues in Nanonetworks and Conclusions

Most of the existing communication networks knowledge is not suitable for nanonetworks due to their particular features. Nanonetworks require innovative networking solutions according to the characteristics of the network components and the molecular communication processes. We should learn of and use existing nanomachines and biological nanonetworks to develop the basis for this new and challenging communication paradigm.

8.1 Open Issues in Nanonetworks

From the discussions presented in the previous chapters, it is clear that many issues still need to be addressed in order to understand the limiting performance of information communications among nano-scale devices and design optimal and quasi-optimal encoding/decoding strategies. Such issues are believed to be of key relevance for allowing nanotechnologies display their full potential.

The first step necessary for moving forward towards a theory of communications among nanomachines consist in the **characterization of the channels properties** in such setting. This includes, for instance, the characterization of current propagation in nanotubes/nanowires, as well as the characterization of biological diffusion processes and ligand-receptor model for molecular communications.

In this case, an identification and classification of the noise and possible interferences for each molecular communication technique is needed right after the characterization of their physics. In other words, on the one hand, a propagation model needs to be developed for molecular diffusion and particularized for *short-range communication using molecular signals*, both through aqueous medium and gap junctions, and for *long-range communication using pheromones*. This last one involves a characterization of different ligands-receptor couples and their affinity, as well as their characterization in terms of selectivity. Furthermore, different types of pheromones and other possible molecular compounds need to be identified and

characterized. Once at this point, this can be used to determine the transmission delay and the propagation range for any given type of compound and communication technique using molecular diffusion.

On the other hand, a propagation model for *short-range communication using molecular motors*, based onto Brownian motors models and communication using vesicles, also needs to developed. Additionally, an information model for DNA coding is essential. All this together with a review of different wired topologies can help to classify the suitableness and usefulness of these nanonetworks for different specific applications.

Once the channel models for each molecular communication technique have been developed, an expression for the channel capacity can be obtained for each of them.

Based on the unique characteristics of the different molecular communication mechanisms, a big step in nano-scale networking would be defining different **channel access techniques** and **Medium Access Control protocols**, both for deterministic and random network topologies. For those applications in which routing is feasible and necessary, new reliable and energy **routing techniques** should also be developed.

Nevertheless, the basic nanonetwork components need to be defined in the first instance. Therefore, above all, the existing biological nanomachines, their specific functions and characteristics, and the way in which they communicate, must be identified and described. So later on, this information can be used to implement different sets of feasible features in **nanomachines**. At the same time, **molecular automata**, and even multi-automata, models can also be designed based on the previous study and on DNA coding models.

As a last resort, despite the current existence of simulation tools for molecular assembly, and biological and genetic systems, there is none for nanonetworks up to now. Therefore, a **simulation tool**, integrating all these models, should be developed for nanonetworking. It should be able to properly model: nanonetwork components (nanomachines), molecular communication processes, network traffic, noise sources, etc.

8.2 Conclusions

Nanotechnology is a cutting edge investigation area that has come out with new and unlimited applications. The recent explosion of research in this field, combined with important discoveries in molecular biology have created a new interest in bio-nanorobotic communication. Moreover, bio-mimetic (section 1.4.3) and its principles will greatly influence the field of nanorobotics and nanotechnology. Hence, a continuous advancement in bio-nanotechnology is expected for the next decades (see Figure 8.1).

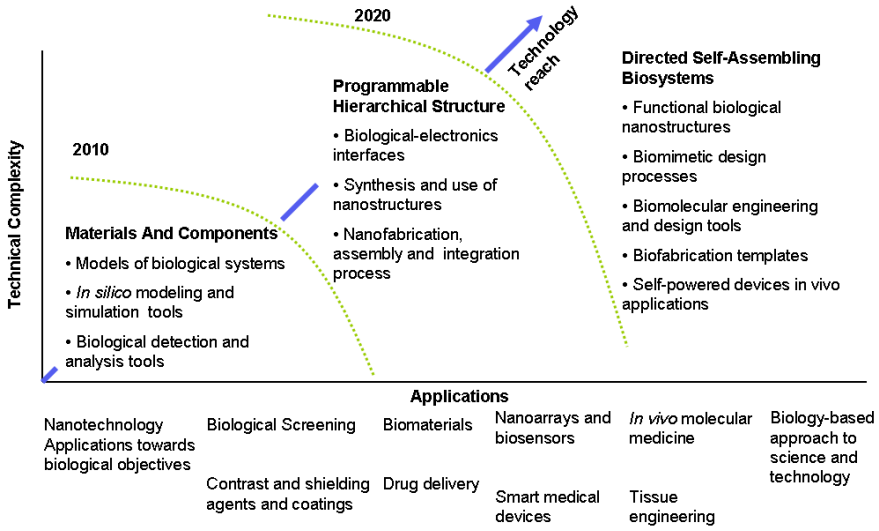

Figure 8.1: A Continuum of Opportunity for Nanotechnology in the Life Sciences. Source: SRI Consulting Business Intelligence (SRIC-BC; Menio Park, CA, USA).

This thesis provides a general theoretical understanding of nanonetworks and their multiple possibilities. It describes some basic concepts of architectures that compose nanotechnology topologies, as well as possible designs for the tiny nanonetwork components, the nanomachines. The thesis also reviews some promising methods proposed for communicating and coordinating in these nanonetworks. As a totally unexplored research area, it is important to establish thorough theoretical framework so that the applications and possible solutions can be validated.

Molecular communication applied to nanonetworks presents indeed extremely appealing features in terms of energy consumption, reliability and robustness. Nevertheless, it remains to understand the impact of the extremely slow propagation of molecules and the highly variable environments. Anyhow, innovative results are expected in terms of novel communications and networking strategies for networked nano-scale systems.

Appendix A

Data Tables

Table A.1: Common viscosity values in air, water and blood plasma, in a set temperature. Note that temperature plays the main role in determining viscosity.

$\eta_{air} = 18.27 \cdot 10^{-6} Pa = 182.7 \mu P$	$at 291 K$
$\eta_{water} = 8.94 \cdot 10^{-4} Pa = 0.894 cP$	$at 298 K$
$\eta_{BloodPlasma} = 1 \cdot 10^{-3} Pa = 1 cP$	$at 310 K$

Figure A.1: Diffusion coefficient of several compounds at 298.2 K (25 °C) and 1 atm pressure from [14].

Compound	Infrared frequency (cm^{-1})	No. of data	Diffusion coefficients in $cm^2\ s^{-1}$	
			Experimental	Calculated
Ethane	2950	6	0.1531 ± 0.0038	0.1453
Ethene	3123	6	0.1655 ± 0.0021	0.1543
Ethyne	3307	5	0.1457 ± 0.0015	0.1597
Cyclopropane	1028	6	0.1277 ± 0.0012	0.1219
Propene	2953	6	0.1318 ± 0.0017	0.1204
Propadiene	1969	6	0.1392 ± 0.0018	0.1160
Propyne	3346	6	0.1316 ± 0.0011	0.1236
Butane	2965	8	0.1021 ± 0.0013	0.0981
1-Butene	2969	6	0.1092 ± 0.0016	0.1019
2-Methylpropene	2963	6	0.1072 ± 0.0032	0.1000
cis-2-Butene	3036	6	0.1087 ± 0.0013	0.1011
trans-2-Butene	961	6	0.1131 ± 0.0012	0.1091
1,3-Butadiene	3110	6	0.1158 ± 0.0018	0.1039
1-Butyne	3340	6	0.1163 ± 0.0020	0.0945
2-Methylbutane	2967	6	0.0935 ± 0.0020	0.0876
2,2-Dimethylpropane	2957	6	0.0877 ± 0.0021	0.0883
Cyclopentane	2967	6	0.0919 ± 0.0025	0.0920
1-Pentene	2967	6	0.0958 ± 0.0011	0.0926

Figure A.2: Transitional brownian diffusion coefficients for physiologically important molecules suspended in water at 310K.

Diffusing Particle in Water	Mol. Wt. (gm/mole)	Diff. Coeff. D (m^2/sec)
H_2	2	5.4×10^{-9}
H_2O	18	2.31×10^{-9}
O_2	32	2.0×10^{-9}
Methanol	32	1.5×10^{-9}
HCl	36.5	3.6×10^{-9}
CO_2	44	1.9×10^{-9}
NaCl	58.5	1.5×10^{-9}
Urea	60	1.3×10^{-9}
Glycine	75	1.0×10^{-9}
KCl	75	2.0×10^{-9}
α-Alanine isomer	89	9.5×10^{-10}
β-Alanine isomer	89	9.7×10^{-10}
Glycerol	92	8.8×10^{-10}
$CaCl_2$	111	1.2×10^{-9}
Glucose	180	7.1×10^{-10}
Mannitol	182	7.1×10^{-10}
Citric acid	192	6.9×10^{-10}
Sucrose	342	5.4×10^{-10}
Milk lipase	6,669	1.5×10^{-10}
Ribonuclease	13,683	1.3×10^{-10}
Insulin	24,430	7.7×10^{-11}
Scarlet fever toxin	27,000	1.0×10^{-10}
Somatotropin	27,100	9.4×10^{-11}
Carbonic anhydrase Y	30,640	1.1×10^{-10}
Plasma mucoprotein	44,070	5.6×10^{-11}
Ovalbumin	43,500	8.1×10^{-11}
Hemoglobin	68,000	7.3×10^{-11}
Serum albumin	68,460	6.5×10^{-11}
Transferrin	74,000	6.2×10^{-11}
Gonadotropin	98,630	4.7×10^{-11}
Collagenase	109,000	4.5×10^{-11}
Actin	130,000	5.3×10^{-11}
Plasminogen (profibrolysin)	143,000	3.1×10^{-11}
Ceruloplasmin	143,300	5.0×10^{-11}
γ-Globulin	153,100	4.2×10^{-11}
Immunoglobulin G (IgG)	158,500	4.2×10^{-11}
Hyaluronic acid	177,100	1.3×10^{-11}
Glucose dehydrogenase	190,000	3.6×10^{-11}
Fibrinogen	339,700	2.1×10^{-11}
Collagen	345,000	7.3×10^{-12}
Urease	482,700	3.7×10^{-11}
Cytochrome a	529,800	3.8×10^{-11}
α-Macroglobulin	820,000	2.5×10^{-11}
β-Lipoprotein	2,663,000	1.8×10^{-11}
Ribosome	4,200,000	1.3×10^{-11}
Viral DNA	6,000,000	1.4×10^{-12}
Urinary mucoprotein	7,000,000	3.4×10^{-12}
Tobacco mosaic virus	31,340,000	5.6×10^{-12}
T7 Bacteriophage	37,500,000	9.5×10^{-12}
Polyhedral silkworm virus	916,200,000	2.3×10^{-12}
1-μm spherical nanodevice	$\sim 8 \times 10^{-11}$	4.1×10^{-13}
Platelet (~2.4 μm)	$\sim 4 \times 10^{-12}$	1.6×10^{-13}
Red Blood Cell (~5.6 mm)	$\sim 6 \times 10^{-13}$	6.8×10^{-14}

Table A.2: Set values used in the Cannel Simulation.

Qmax	$2.8 \cdot 10^{14}$
D	0.43
Radius	10^{-3}-10^{-2}
Frequency	$2 \cdot 10^{-6}$-$4 \cdot 10^{-4}$
Time	$5 \cdot 10^{5}$

Appendix B

Codes

Figure B.1: Code for Channel Simulation.

```
% SCRIPT FILE FOR NEUS EXPERIMENTAL ANALYSIS
clc;
clear all;
close all;

%% Radius range

r=1e-3:1e-3:1e-2;

%% Frequency range

f = 0:0.000002:((0.000002)*200);

%% Output matrix building

OUT = zeros(length(f), length(r));

%% Simulation cycle

% Display a waitbar that shows what percentage of a calculation is complete, as the calculation proceeds
h = waitbar(0, 'Loading data set, please wait...');
n = 1;

f_max_index_previous = 10;
for f_index = 1:length(f)


    parfor (r_index = 1:length(r))

       u_bf = Up(1,2.8e14,f(f_index),5e5,50,r(r_index),0.43);
       u = Cr(u_bf,5e5,50,r(r_index));

       U = fft(u(1,:),[],2);
       U_magnitude = abs(U);
       U_phase = angle(U);
       U_magnitude_diff = diff(U_magnitude,1,2);
       U_magnitude_diff_shift = [U_magnitude_diff(1,2:end) 0];
       f_pos_index = find((U_magnitude_diff>0) & (U_magnitude_diff_shift<0)) + 1;
```

```
        if isempty(f_pos_index)
            OUT(f_index, r_index) = 0;
        else
            OUT(f_index, r_index) = U_magnitude(f_pos_index(1));
        end
    end

    waitbar(n/(length(f)),h);

    n = n+1;

end

close(h);

figure
surf(OUT(3:end,:)/(16e8)); figure(gcf)
xlabel('Frequency [0.000002 Hz]');
ylabel('Radius [10^-3 cm]');
zlabel('Concentration Signal Amplitude [transmitted power = 3/2*4*10^4]');
title('Olfactory Channel Model - Still Air');
```

Figure B.2: Code for receptor chemical effect.

```
function Crx = Cr(conc,tend,step,r)

    % Crx [molecules/cm^3]

    % Time vector Creation
    t=[0.00001:step:tend];
    jend=length(t);      % Number of ___seconds

k0=0.08;
f0=1e-12;
KB=1.3806503e-23;
T=310;
microNA=6.02214179e17;
N=0.005*microNA;

      %k1=prop*2*T/r;
      %k_1=k0*exp(((r/100)*f0)/(T*KB))
      k1=0.3*microNA;
      k_1=0.08;

      for j=1:jend
        Cinf=((k1/conc(1,j))*N)/(k_1+k1/conc(1,j));
        Crx(1,j)=Cinf*(1-1*exp(-t(j)*(k_1+k1/conc(1,j))));
      end
```

Figure B.3: Code for general spacial function $U(r,t)$.

```
function U = Up(Q_num,Q_Ampl,f,tend,step,r,D,Cth)

    % U : [molec/cm^3] : Spatial Density of message molecules (m.m.)

    % Q_num : Q function
    % Q_Ampl : Q function Amplitude, i.e., maximum Q.
    % Q : [molec/s] : Rate of Molecules released, each one carrying
    %                 I bits/molec.
    % f : frequency
    % tend  : [s] : Source Emitting time (simulation time)
    % step : Time division [1 second step = 1]
    % r : [cm] : distance between TN and RN.
    % D : [cm^2/s] : Brownian Translational Diffusion Coeff. for m.m.
    % Cth : Minimum threshold concentration of m.m. that can be detected by
    %       a chemical sensor in some minimum waiting time teq.

  %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

    % Time vector Creation
    t=[0.00001:step:tend];
    jend=length(t);     % Number of ___seconds


    Q(1:jend)=0;

    switch Q_num
        case (0)
            for j=1:jend
                Q(j) = Q_Ampl;
            end
        case (1)
            for j=1:jend
                offset=Q_Ampl;
                Q(j) = offset+Q_Ampl*sin(2*pi*f*t(j));
            end

    end

    set(0,'defaultaxesfontname','Arial Narrow');
    figure;
    plot(Q);
    grid on;
    xlabel('Time [s]');
    ylabel('Concentration Rate [molec/s]');
    title('HUMAN BODY - Concentration Rate');

  %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
iend = length(r);
for i=1:iend
    for j=1:jend
        func(j) = (1/(4*pi*D*t(j))^(3/2)).*exp(-(r(i)^2)/(4*D*t(j)));
    end
u = step*conv(Q,func);
U(i,:) = u(1:jend);
end

i=i+1;
U(i,1:jend) = Cth;

% Figure Settings
set(0,'defaultaxesfontname','Arial Narrow');
figure;

% Plot Graphs
for i=1:iend

    switch i
        case {1,6}
            c = '-*';
        case {2,7}
            c = '-.s';
        case {3,8}
            c = '--o';
        case {4,9}
            c = '-d';
        otherwise
            c = ':>';
    end

    h(i)=plot(t,U(i,:),c,'LineWidth',1,'MarkerSize',1);
    hold all;
end
i=i+1;
h(i)=plot(t,U(i,:),'k-','LineWidth',2,'MarkerSize',2);
hold all;
grid on;

% Introduce D values
legend(h,'R=10^(-2) (cm)','R=3*10^(-2) (cm)','R=6*10^(-2) (cm)',
'R=9*10^(-2) (cm)','Cth=10^(12) (molec/cm^3)',4);
% axis([t(1),t(l),U(1),U(l)]);
xlabel('Time [s]');
ylabel('Concentration [molec/cm^3]');
title('HUMAN BODY - CONTINUOUS - Convolution');
hold off;
```

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