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Nanonetworks: A new communication paradigm

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ABSTRACT

Nanotechnologies promise new solutions for several applications in biomedical, industrial and military fields. At nano-scale, a nano-machine can be considered as the most basic functional unit. Nano-machines are tiny components consisting of an arranged set of molecules, which are able to perform very simple tasks. Nanonetworks. i.e., the interconnection of nano-machines are expected to expand the capabilities of single nano-machines by allowing them to cooperate and share information. Traditional communication technologies are not suitable for nanonetworks mainly due to the size and power consumption of transceivers, receivers and other components. The use of molecules, instead of electromagnetic or acoustic waves, to encode and transmit the information represents a new communication paradigm that demands novel solutions such as molecular transceivers, channel models or protocols for nanonetworks. In this paper, first the state-of-the-art in nano-machines, including architectural aspects, expected features of future nano-machines, and current developments are presented for a better understanding of nanonetwork scenarios. Moreover, nanonetworks features and components are explained and compared with traditional communication networks. Also some interesting and important applications for nanonetworks are highlighted to motivate the communication needs between the nano-machines. Furthermore, nanonetworks for short-range communication based on calcium signaling and molecular motors as well as for long-range communication based on pheromones are explained in detail. Finally, open research challenges, such as the development of network components, molecular communication theory, and the development of new architectures and protocols, are presented which need to be solved in order to pave the way for the development and deployment of nanonetworks within the next couple of decades.

1. Introduction

The concepts in nanotechnology was first pointed out by the 1965 nobel laureate physicist Richard Feynman in his famous speech entitled "*There's Plenty of Room at the Bottom*" in December 1959. The main focus of his speech was about the field of miniaturization and how he believed humans would create increasingly tinier and powerful devices in the future. The term "nanotechnology" was first defined by [59] 15 years later as: "Nanotechnology mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or by one molecule". In the 1980s, the basic idea of this definition was explored in much more depth by [26] who took the Feynman concept of a billion tiny factories and added the idea that they could replicate themselves, via computer control instead of control by a human operator. Activity surrounding nanotechnology began to slowly increase and the advancements really began to accelerate in the early 2000s.

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Nanotechnology enables the miniaturization and fabrication of devices in a scale ranging from 1 to 100 nanometers. At this scale, a nano-machine can be considered as the most basic functional unit. Nano-machines are tiny components consisting of an arranged set of molecules which are able to perform very simple computation, sensing and/or actuation tasks [57]. Nano-machines can be further used as building blocks for the development of more complex systems such as nano-robots and computing devices such as nano-processors, nano-memory or nano-clocks.

Nano-machines can be interconnected to execute collaborative tasks in a distributed manner. Resulting nanonetworks are envisaged to expand the capabilities and applications of single nano-machines in the following ways:

- Nano-machines such as chemical sensors, nano-valves, nano-switches, or molecular elevators [4], cannot execute complex tasks by themselves. The exchange of information and commands between networked nano-machines will allow them to work in a cooperative and synchronous manner to perform more complex tasks such as in-body drug delivery or disease treatments.
- The workspace of a single nano-machine is extremely limited. Nanonetworks will allow dense deployments of interconnected nano-machines. Thus, larger application scenarios will be enabled, such as monitoring and control of chemical agents in ambient air.
- In some application scenarios, nano-machines will be deployed over large areas, ranging from meters to kilometers. In these scenarios, the control of a specific nano-machine is extremely difficult due to its small size. Nanonetworks will enable the interaction with remote nano-machines by means of broadcasting and multihop communication mechanisms.

Communication between nano-machines can be realized through *nanomechanical, acoustic, electromagnetic and chemical or molecular communication* means [31].

Nanomechanical communication is defined as the transmission of information through mechanical contact between the transmitter and the receiver. In *acoustic communication*, the transmitted message is encoded using acoustic energy, i.e., pressure variations. *Electromagnetic communication* is based on the modulation of electromagnetic waves to transmit information. *Molecular communication* can be formally defined as the use of molecules as messages between transmitters and receivers.

Molecular communication is the most promising approach for nano-networking based on the following advantages:

- Due to the size and principles of traditional acoustic transducers and radiofrequency transceivers, their integration at molecular or nano-scale is not feasible [31]. By contrast, molecular transceivers are intrinsically conceived at nano-scale. These are nano-machines which are able to emit and receive molecules.
- In nanomechanical communication, transmitters and receivers need to be in direct contact. This is not a restriction for molecular communication over large areas, where transmitters and receivers can be remotely located as long as the transmitted molecules reach the intended receiver.

In the recent literature, the term "nanonetworks" refers to electronic components and their interconnection within a single chip on a nano-scale [12]. This concept is also known as Network on Chip (NoC). This term is also referred to as the network-like interconnection of nanomaterials as well, e.g., carbon nanotubes arrays [38,15]. In this paper, we use the term "nanonetworks" strictly for the interconnection of nano-machines based on molecular communication.

This paper follows the bio-inspired approach to explore, from a telecommunication point of view, the potential of molecular communication for nanonetworks. First, in Section 2, we present the nano-machines including the state-of-the-art in research and current approaches for their development. In Section 4, we explain nanonetwork features and their advantages and disadvantages over traditional communication networks. In Section 3, we explain potential applications of nanonetworks. We explore existing biological models and techniques for molecular communication for short and long-ranges in Sections 5–7, respectively. Finally, we outline open research issues and contrast them with traditional communication network challenges in Section 8. We conclude the paper in Section 9.

2. Overview of Nano-machines

A nano-machine is defined as "*an artificial eutactic mechanical device that relies on nanometer-scale components*" [24]. Also the term "*molecular machine*" is defined as "*a mechanical device that performs a useful function using components of nanometer-scale and defined molecular structure; includes both artificial nano-machines and naturally occurring devices found in biological systems*".

In general terms, we define a nano-machine as "*a device, consisting of nano-scale components, able to perform a specific task at nano-level, such as communicating, computing, data storing, sensing and/or actuation*". The tasks performed by one nano-machine are very simple and restricted to its close environment due to its low complexity and small size.

There are three different approaches for the development of nano-machines as depicted in Fig. 1. In the *top-down approach*, nano-machines are developed by means of downscaling current microelectronic and micro-electro-mechanical technologies without atomic level control. In the *bottom-up approach*, the design of nano-machines is realized from molecular components, which assemble themselves chemically by principles of molecular recognition arranging molecule by molecule. Recently, a third approach called *bio-hybrid* is proposed for the development of nano-machines [63]. This approach is based on the use of existing biological nano-machines, such as molecular motors, as components or models for the development of new nano-machines. In Fig. 1, different systems are mapped according to their origin, biological or man-made

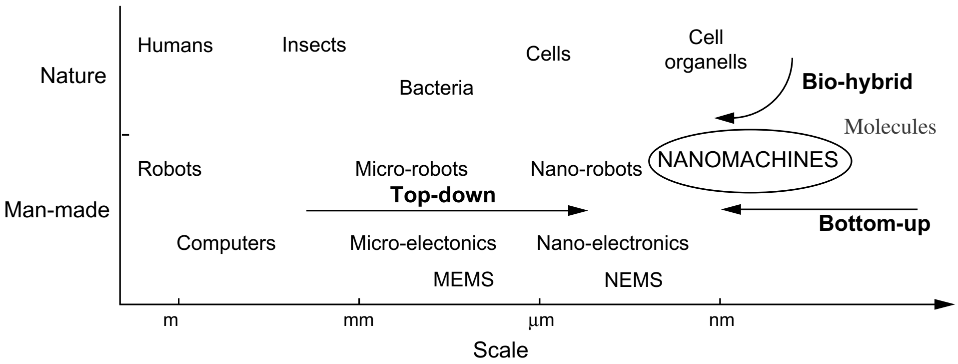

Fig. 1. Approaches for the development of nano-machines.

systems, and to their size, ranging from nanometers to meters. In the future, nano-machines will be obtained following any of these three approaches. However, the existence of successful biological nano-machines, which are highly optimized in terms of architecture, power consumption and communication, motivate their use as models or building blocks for new developments.

2.1. Development of nano-machines

2.1.1. Top-down approach

Recently, newest manufacturing processes, such as the 45 nm lithographic process, have made the integration of nano-scale electronic components in a single device possible [39]. The *top-down* approach is focused on the development of nano-scale objects by downscaling current existing micro-scale level device components. To achieve this goal, advanced manufacturing techniques, such as electron beam lithography [61] and micro-contact printing [42], are used. Resulting devices keep the architecture of pre-existing micro-scale components such as microelectronic devices and micro-electro-mechanical systems (MEMS).

Nano-machines, such as nano-electromechanical systems (NEMS) components, are being developed using this approach [19,34,45]. However, the fabrication and assembly of these nano-machines is still at an early stage. So far, only simple mechanical structures, such as nano-gears [66], can be created following this approach.

2.1.2. Bottom-up approach

In the *bottom-up* approach, nano-machines are developed using individual molecules as the building blocks. Recently, many nano-machines, such as molecular differential gears and pumps [51], have been theoretically designed using a discrete number of molecules. Manufacturing technologies able to assemble nano-machines molecule by molecule do not exist, but once they do; nano-machines could be efficiently created by the precise and controlled arrangement of molecules. This process is called molecular manufacturing [24].

Molecular manufacturing could be developed from current technologies in couple decades if adequate resources are invested. Current development of nano-machines using this bottom-up approach, such as molecular switches [5] and molecular shuttles [6], are based on *self-assembly* molecular properties [7].

2.1.3. Bio-hybrid approach

Several biological structures found in living organisms can be considered as nano-machines. Most of these biological nano-machines can be found in cells. Biological nano-machines in cells include: nano-biosensors, nano-actuators, biological data storing components, tools and control units [25]. Expected features of future nano-machines are already present in a living cell, which can be defined as a *self-replicating* collection of nano-machines [63]. Several biological nano-machines are interconnected in order to perform more complex tasks such as cell division. The resulting nanonetwork is based on molecular signaling. This communication technique is also used for inter-cell communication allowing multiple cells to cooperate to achieve a common objective such as the control of hormonal activities or immune system responses in humans.

The *bio-hybrid* approach proposes the use of these biological nano-machines as models to develop new nano-machines or to use them as building blocks integrating them into more complex systems such as nano-robots. Following this approach, the use of a biological nano-motor to power a nano-device has been reported in [56]. Another example in line with this approach is the use of bacteria as controlled propulsion mechanisms for the transport of micro-scale objects [10].

2.2. Expected features of nano-machines

The main constraint in the development of nano-machines is the lack of tools which are able to handle and assemble molecular structures in a precise way. However, given the rapid advances in manufacturing technologies, efficient fabrication of more complex nano-machines will be possible in the near future. They are expected to include most of the functionalities of existing devices at micro-scale. In addition, nano-machines will present novel features enabled by molecular properties of the materials that can be exploited at nano-scale. The most important and expected features of future nano-machines can be described as follows:

- Nano-machines will be intrinsically *self-contained*. This means that each nano-machine will contain a set of instructions or code to realize the intended task. These instructions or sequence of operations can be embedded in the molecular structure of nano-machines, or can be read from another molecular structure in which the instruction set is stored.
- *Self-assembly* is defined as the process in which several disordered elements form an organized structure without external intervention, as a result of local interactions between them. At nano-level, *self-assembly* is naturally driven by molecular affinities between two different elements. *Self-assembly* will leverage the development of nano-machines and will allow them to interact with external molecules in an autonomous way.
- *Self-replication* is defined as the process in which a device makes a copy of itself using external elements. This potential process will enable the creation of large number of nano-machines to realize macroscopic tasks in an inexpensive way [43]. Similar to the first feature, *self-replication* implies that the nano-machine contains the instructions to create a copy of itself.
- *Locomotion* is the ability to move from one place to another. Nano-machines are aimed to accomplish specific tasks, which are usually described by a spatial-temporal actuation. This means that a nano-machine should be located in the right place at the right time to accomplish the task. However, no single nano-machine is able to move towards a previously identified target. More complex systems could use embedded nano-sensors and nano-propellers to detect and follow specific traces of the target. *Locomotion* will enable the use of nano-machines in applications where mobile actors are needed, e.g., nano-robots for disease treatments [18].
- *Communication* between nano-machines is needed to allow them to realize more complex tasks in a cooperative manner. At this level, as explained in Section 1, the most promising technique is based on molecular communication. Further advances in nano-sensors and nano-actuators are expected to enable the integration of molecular transceivers into nano-machines.

2.3. Nano-machine architecture

A nano-machine could consist of one or more components, resulting in different levels of complexity, which could be from simple molecular switches to nano-robots [18]. The most complete nano-machines will include the following architecture components:

(1) *Control unit*. It is aimed at executing the instructions to perform the intended tasks. To achieve this goal, it can control all the other components of the nano-machine. The control unit could include a storage unit, in which the information of the nano-machine is saved.
(2) *Communication unit*. It consists of a transceiver able to transmit and receive messages at nano-level, e.g., molecules.
(3) *Reproduction unit*. The function of this unit is to fabricate each component of the nano-machine using external elements, and then assemble them to replicate the nano-machine. This unit is provided with all the instructions needed to realize this task.
(4) *Power unit*. This unit is aimed at powering all the components of the nano-machine. The unit will be able to scavenge energy from external sources such as light, temperature and store it for a later distribution and consumption.
(5) *Sensor and actuators*. Similar to the communication unit, these components act as an interface between the environment and the nano-machine. Several sensors and/or actuators can be included in a nano-machine, e.g., temperature sensors, chemical sensors, clamps, pumps, motor or locomotion mechanisms.

Currently such complex nano-machines cannot be built. However, there exist systems found in the nature, such as living cells, with similar architectures. According to the bio-hybrid approach these biological models, i.e., the cells, can be used to learn and understand the principles governing the operation of nano-machines and their interactions. This knowledge is expected to contribute to the development of new bio-inspired nano-machines and systems for specific purposes. In Fig. 2, we show a component mapping

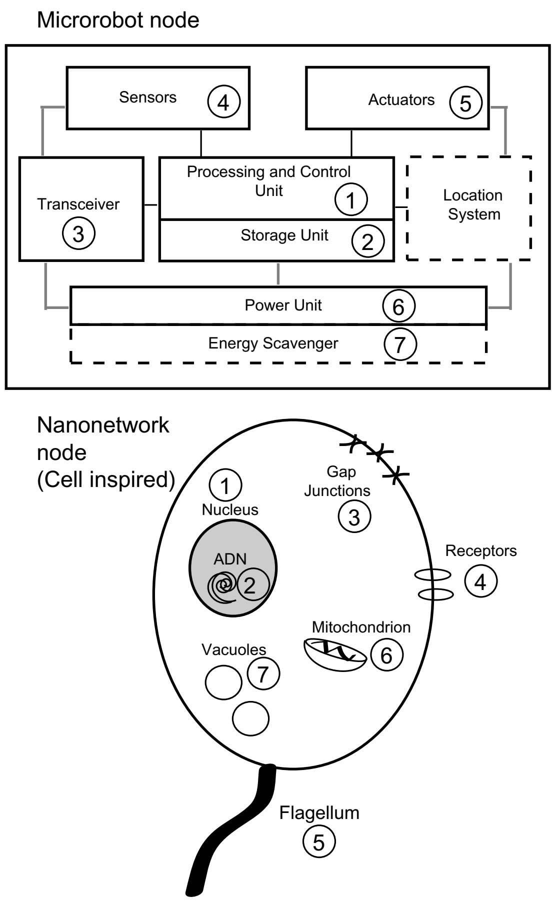

Fig. 2. Functional architecture mapping between nano-machines of a micro or nano-robot, and nano-machines found in cells.

between a generic architecture of a nano-machine and a living cell, including its biological nano-machines. Similar to the architecture of a nano-machine, a cell contains the following components:

(1) *Control unit*. The nucleus can be considered as the control unit of the cell. It contains all the instructions to realize the intended cell functions.
(2) *Communication*. The gap junctions and hormonal and pheromonal receptors, located on the cell membrane, act as molecular transceivers for inter-cell communication.
(3) *Reproduction*. Several nano-machines are involved in the reproduction process of the cell such as the centrosome and some molecular motors. The code of the nano-machine 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*. Cells can include different nano-machines for power generation. One of them is the *mitochondrion* that generates most of the chemical substances, which are used as energy in many cellular processes. Another interesting nano-machine is the *chloroplast*, which converts sunlight into chemical fuel.
(5) *Sensors and actuators*. Cells can include several sensors and actuators such as the *Transient Receptor Potential* channels for tastes and the *flagellum* of the bacteria for locomotion. The *chloroplast* of the plants can also be considered as an actuator since it transforms water to oxygen that is later released to the environment.

A *bio-hybrid* approach cannot only be used to develop novel nano-machines, but also to understand their interactions in larger systems such as cells. These interactions, exclusively enabled by molecular communication techniques, are essential since this is the only way to explore their capabilities to achieve more complex tasks in a cooperative manner.

In this paper, we expand the bio-hybrid approach beyond the models for novel nano-machines in order to study and develop molecular communication techniques for their interconnection.

3. Nanonetworks applications

The potential applications of nanonetworks are unlimited. We classify them in four groups: biomedical, environmental, industrial and military applications. However, since nanotechnologies have a key role in the manufacturing process of several devices, nanonetworks could be used extensively in many other fields such as consumer electronics, life style and home appliances among others.

3.1. Biomedical applications

The most direct applications of nano-machines and nanonetworks are in the biomedical field. Biological models inspire and encourage the use of nanotechnologies to interact with organs and tissues. The advantages provided by nanonetworks are clearly in terms of size, biocompatibility and biostability, enabled by the control of system components at molecular level. These are some of the envisaged applications:

- *Immune system support*. The immune system is composed by several nano-machines that protect organism against diseases. These nano-machines are a collection of nano, micro and macro systems, including sensors and actuators, acting in a coordinated way to identify and control foreign and pathogen elements. Nano-machines can be used to help the detection and elimination procedures. They could realize tasks of localization and response to malicious agents and cells, such as cancer cells [20,32], resulting in a less aggressive and invasive treatments compared to the existing ones.
- *Bio-hybrid implants*. These are aimed at supporting or replacing components such as organs, nervous tracks or lost tissues [24,30]. Nanonetworks can provide friendly interfaces between the implant and the environment. Restoration of central nervous system tracks is a possible application of bio-hybrid implants.
- *Drug delivery systems*. These are another specific type of implants. For instance, these systems could help to compensate metabolism diseases such as diabetes. In this sense, nano-sensors and smart glucose reservoirs or producers can work in a cooperative manner to support regulating mechanisms [29]. Drug delivery systems could also help to mitigate the effects of neurodegenerative diseases by delivering neurotransmitters or specific drugs [64].
- *Health monitoring*. Oxygen and cholesterol level, hormonal disorders, and early diagnosis are some examples of possible applications that can take advantage of in-body nano-sensor networks [22,30]. The information retrieved by these systems must be accessible by relevant actors. Thus, nanonetworks must provide the proper level of connectivity to deliver the sensed information.
- *Genetic engineering*. Manipulation and modification of nano-structures such as molecular sequences and genes can be achieved by nano-machines. The use of nanonetworks will allow expanding the potential applications in genetic engineering.

3.2. Industrial and consumer goods applications

Nanonetworks will be used not only the intra-body but also in industries. Nanonetworks can help with the development of new materials, manufacturing processes and quality control procedures. More specifically, these applications have already been proposed:

- *Food and water quality control*. Similar to health monitoring applications, food and fluids quality control can take advantage of nanonetworks. *Nano-sensor networks* can help detecting small bacteria and toxic components that can affect to the product quality and cannot be detected

using traditional sensing technologies [3]. Advanced self-powered *nano-sensor networks* can be used to detect very small amount of chemical or biological agents installed in water supplies across the country.
- *Functionalized materials and fabrics*. Nanonetworks can be included in advanced fabrics and materials to get new and improved functionalities. Antimicrobial and stain-repeller textiles are being developed using nano-functionalized materials [60]. For instance, nano-actuators can help to improve the airflow in smart fabrics. These nano-actuators can communicate to nano-sensors to control the proper reaction based on the external conditions.

3.3. Military applications

Nanotechnologies can also have several applications in the military field. While in the applications pointed out before, the range covered by nanonetworks is short, in military field the deployment range of nanonetworks can be widely variable depending on the application. Battlefield monitoring and actuation demand a dense deployment of nanonetworks over large areas, while systems aimed at monitoring soldier performance are deployed in smaller areas, i.e., human body. Among the military applications, we can mention:

- *Nuclear, biological and chemical (NBC) defenses*. This is a classic application for large area deployment. Nanonetworks can be deployed over the battlefield or targeted areas to detect aggressive chemical and biological agents and coordinate the defensive response [55]. The overall system can be compounded of nano-sensors and nano-actuators, which would detect and control the hostile agents. Nano-sensor networks could also be deployed into cargo containers to detect the unauthorized entrance of chemical, biological or radiological materials.
- *Nano-functionalized equipments*. These applications are similar to those found in consumer goods field, but it is focused on military equipment. Advanced camouflage as well as army uniforms can take advantage of nanonetworks. For instance, equipments can be manufactured using advanced materials containing nanonetworks that self-regulate the temperature underneath soldiers clothes [27] and even detect whether the soldier has been injured.

3.4. Environmental applications

Since nanoneworks are inspired in biological systems found in nature, they can also be applied in environmental fields achieving several goals that could not be solved with current technologies. Some environmental applications are:

- *Biodegradation*. There is an existing and growing problem with garbage handling around the world. In this line, nanonetworks could help with the biodegradation process in the garbage dumps. Nanonetworks can help the biodegradation process by sensing and tagging different materials that can be later located and processed by smart nano-actuators.
- *Animals and biodiversity control.* Nanonetworks can be also used in natural environments to control several species. For instance, as seen in nature, nanonetworks using pheromones as messages can trigger certain behaviors on animals. As a result it is possible to interact with those animals and also to control their presence in particular areas.
- *Air pollution control.* Similar to the quality control applications, air can be monitored using nanonetworks. Moreover, nano-filters can be developed to improve the air quality by removing harmful substances contained in it [35].

4. Communication among nano-machines

Among all of the expected features of future nano-machines, the communication capabilities are also very important. This is the only feature that enables them to work in a synchronous, supervised and cooperative manner to pursuit a common objective.

Nano-machines communication can include the two following bidirectional scenarios:

(1) Communication between a nano-machine and a larger system such as electronic micro-devices, and
(2) Communication between two or more nano-machines.

Different communication technologies, such as electromagnetic, acoustic, nanomechanical or molecular; have been proposed for each scenario in [31].

Communication based on *electromagnetic waves* is the most common technique to interconnect microelectronic devices. These waves can propagate with minimal losses along wires or through air. However, given the size of nano-machines, wiring a large quantity of them is unfeasible. As an alternative, wireless solutions could be used. To establish a bidirectional wireless communication, a radio-frequency transceiver should be integrated in the nano-machine. Nano-scale antennas could be developed for very high frequency communication. However, due to the size and current complexity of the transceivers, they still cannot be easily integrated into nano-machines. In addition, if the integration were possible, the output power of the nano-transceiver would not be enough to establish a bidirectional communication channel [31]. As a consequence, electromagnetic communication could be used to transmit information from a micro-device to a nano-machine, but not from nano-machines to micro-devices, nor among nano-machines.

At nano-level, *acoustic communication* is mainly based on the transmission of ultrasonic waves. Similar to the communication based on electromagnetic waves, the acoustic communication implies the integration of ultrasonic transducers in the nano-machines. These transducers should be capable to sense the rapid variations of pressure produced by ultrasonic waves and to emit acoustic signals accordingly. Again, the size of these transducers represents the major barrier in their integration in the nano-machines.

In *nanomechanical* communication, the information is transmitted through hard junctions between linked devices at nano-level. The main drawback of this type of communication is that a physical contact between the transmitter and the receiver is required. Moreover, this coupling should be precise enough to guarantee that the desired mechanical transceivers are aligned correctly. This communication technique is not suitable in many application scenarios where nano-machines are deployed over large areas without any direct contact between them. In addition, without precise navigation systems in nano-machines, their positioning for a correct nanomechanical communication is a major barrier.

Molecular communication is defined as the transmission and reception of information encoded in molecules. Molecular communication is a new and interdisciplinary field that spans nano, bio and communication technologies [46]. Unlike previous communication techniques, the integration process of molecular transceivers in nano-machines is more feasible due to the size and natural domain of molecular transceivers, i.e., nano-scale framework. These transceivers are nano-machines which are able to react to specific molecules, and to release others as a response to an internal command.

Molecular communication can be used to interconnect multiple nano-machines, resulting in nanonetworks as defined in Section 1. Nanonetworks expand the capabilities of single nano-machines in the following terms:

- More complex objectives can be achieved if multiple nano-machines cooperate. Nanonetworks enable this cooperation by providing mechanisms to exchange information between different nano-machines such as molecular motors or nano-switches.
- Single nano-machines can only perform tasks at nano-level, and therefore their workspace is very limited. However, if a large number of nano-machines are interconnected, they can pursuit macro-scale objectives, and work over larger areas, such as treatment of cancer tumors or air pollution monitoring.
- If multiple nano-machines are deployed over large areas, the interaction with a specific nano-machine is extremely difficult due to its small size. This interaction includes procedures such as nano-machines activation/deactivation, configuration of parameters, data acquisition or actuation commands. Nanonetworks will enable this interaction by providing the infrastructure and mechanism to broadcast the information over these areas. In addition, two nano-machines could interact indirectly by using other nano-machines as repeaters.

Besides expanding capabilities of single nano-machines, nanonetworks represent a potential solution for some applications where available communication networks and micro-devices are not suitable. Compared to current communication network technologies, nanonetworks have the following advantages:

- The *reduced size* of nano-machines and the resulting nanonetwork components can be an advantage in many applications where the dimension of the involved systems is critic. For instance, in the biomedical field, nano-machines can be used for intra-body applications allowing nanonetworks to lead to nano-invasive and more selective treatments.
- *Biocompatibility* is defined as the quality of a device to operate accordingly in biological environments without affecting them negatively. In some biomedical applications, many electronic devices have to cope with hostile environments as well as many organisms reject implants and drugs. Nanotechnologies can be used to enhance the compatibility between nano-machines and natural organs or tissues by means of more friendly materials and interfaces. For instance, bio-hybrid nano-machines compound by biological elements can interact with natural processes without any side effect. In addition, nano-machines and molecular messages may also be programmed to deactivate after completing the nanonetwork task preventing removal procedures. Nanotechnologies, allow the control of materials at molecular level. Using these materials, we can design nanonetworks nodes according to specific environmental conditions improving the biocompatibility of the system.
- Chemical reactions are highly efficient in terms of *energy consumption* [47]. These reactions will power the nanonetworks nodes and processes. Chemical reactions can also represent complex computation and decision processes, which in traditional communication could mean multiple operations.

4.1. Nanonetworks versus Traditional communication networks

Nanonetworks are not a simple extension of traditional communication networks at the nano-scale. They are a complete new communication paradigm, in which most of the communication processes are inspired by biological systems found in nature. Nanonetworks have the following differences with traditional communication networks:

- In nanonetworks, the *message is encoded using molecules*; while in traditional communication networks, the information is encoded in electromagnetic, acoustic or optical signals. Two different and complementary coding techniques can be considered to represent the information in nanonetworks. The first one uses temporal sequences to encode the information, such as the temporal concentration of specific molecules in the medium. According to the level of the concentration, i.e., the number of molecules per volume, the receptor decodes the received message. For instance, this technique is used by the Central Nervous System to propagate the neural impulses. This technique can be considered similar to those used in traditional networks where time-varying sequences transport the information. The second technique, hereinafter called *molecular encoding*, uses internal parameters of the molecules to encode the information such as the chemical structure, relative positioning of molecular elements or polarization [46]. In this case, the receiver must be able to detect these specific molecules to decode the information. This technique is similar to the use of encrypted packets in communication networks, in which only the intended receiver is capable to read the information. In nature, molecular encoding is used in pheromonal communication, where only members of the transmitter specie can decode the transmitted message.

- 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., 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 temperature, 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 molecules. This means that another source emits the same molecules used to encode the message, therefore they affect the concentration sensed by the receiver. In nanonetworks, noise can also be understood as an undesired reaction occurring between information molecules and other molecules present in the environment. These reactions can modify the structure of the information molecules and therefore the receiver would not be able to detect the transmitted message.
- Text, voice and video are usually transmitted over traditional communication networks. By contrast, in nanonetworks, since the message is a molecule, the transmitted information is more related to phenomena, chemical states and processes [11].
- 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.

We summarize nanonetworks and traditional communication network features in Table 1 [37]. 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.

4.2. Nanonetwork components

The first models of nanonetworks are based on those used in Information and Communication Technologies (ICT) for telecommunication networks. In Fig. 3, we show the general concepts of nanonetworks versus existing telecommunication systems. Nanonetworks components are functionally similar to those found in traditional networks.

In nanonetworks, we can identify five different components: the transmitter node, the receiver node, the messages, the carrier, and the medium. Each of these components affects the overall communication process, which includes the following steps as Fig. 3b depicts:

(1) The transmitter encodes the message onto molecules.
(2) The transmitter inserts the message into the medium by releasing the molecules to the environment or attaching them to molecular carriers.
(3) The message propagates from the transmitter to the receiver.
(4) The receiver detects the message.
(5) The receiver decodes the molecular message into useful information such as reaction, data storing, actuation commands, etc.

4.2.1. Transmitters and receivers

The transmitter role is played by a nano-machine such as a modified living cell, a biomedical implant, or a nanorobot. In most of traditional communication networks, the nodes encode the information by modulating electromagnetic signals. In nanonetworks the nodes encode the information by modifying molecules by means of chemical reactions. Nano-machines also play the receiver role. The receiver should be able to extract the message from the medium. Since nano-machines are very simple, and the message is basically a molecule, handling this message could not be a trivial task. The message contains useful information that is going to be used by the receiver. At molecular level, this can mean to forward the message, to store it, or to react to it. Nanonetwork nodes transmit and receive molecules. These molecules are a finite source.

Table 1
Main differences between traditional communication networks and nanonetworks enabled by molecular communication [37]

Communication	Traditional	Molecular
Communication carrier	Electromagnetic waves	Molecules
Signal type	Electronic and optical (Electromagnetic)	Chemical
Propagation speed	Light (3×10^8 m/s)	Extremely low
Medium conditions	Wired: Almost immune Wireless: Affect communication	Affect communication
Noise	Electromagnetic fields and signals	Particles and molecules in medium
Encoded information	Voice, text and video	Phenomena, chemical states or processes
Other features	High energy consumption	Low energy consumption

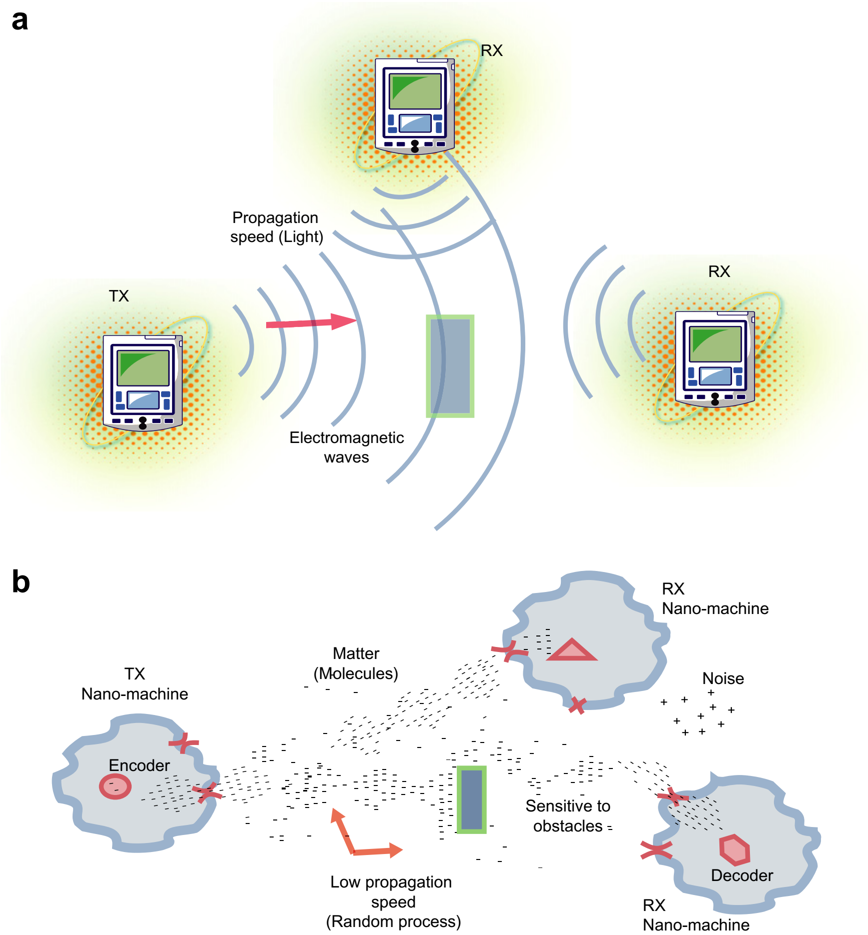

Fig. 3. Overview of (a) traditional communication systems and (b) nanonetworks: energy transmission vs. molecular transmission.

This has two consequences. First, the transmitter nano-machines should be able to obtain, from an external source, raw molecules and store them for a later use as messages. Second, the receiver nano-machines should be able to buffer a limited number of molecules, and also include release mechanisms to empty this molecular buffer to be ready for the next messages.

4.2.2. Message

In traditional computer networks, the information is represented using a binary system and the transmitted message is usually a set of bits. In molecular communication, the message is a molecule. This molecular message will have three important characteristics [31]. First, it will present a predefined external structure that will allow an easy recognition at the receiver. Second, it will be inactive. This means that molecular messages will not be prone to react to other molecules in the medium. Finally, molecular messages should easily be eliminated without any side effect once they are decoded at the receiver nano-machine. In [37], some molecular features such as polarity, motion, magnetization, and structures, are suggested for information coding. A potential candidate for molecular messaging is the partially fluorinated polyethylene proposed in [24]. This molecule can be compounded by a sequence of hydrogen and flour atoms, resulting in a binary sequence able to store digital data [9].

4.2.3. Carrier

In classical communication paradigm, a carrier is used to transport the message. The carrier is used because of its signal feature advantages, especially in terms of propagation. In traditional computer networks, the carriers also allow creating multiple communication channels. In nanonetworks, the carriers are particular molecules which are able to transport chemosignals or molecular structures containing the information. The aim of the molecular carriers is to enhance the propagation features of single information molecules, to create more reliable communication by protecting molecules from external noise sources, and finally to enable the creation of multiple independent channels using the same medium. The use of molecules as information carriers in molecular communication was observed in biological systems. According to these observations, two potential types of carriers have been identified: *the molecular motors and the calcium ions* [50]. *Molecular motors, e.g., kinesin, dynein and myosin, are proteins* that can generate movements using chemical energy. These protein motors can transport a data packet, i.e., molecule, from the transmitter to the receiver as described in [49]. The second type of carrier consists of *calcium ions* (Ca^{2+}). The transmitter can modulate the concentration of these ions in amplitude and frequency to encode the information [17].

4.2.4. Medium

Wireless communication networks have been developed for almost every type of media found in nature such as airborne, waterborne, and underground. Many wireless transmission technologies have also been applied successfully to communicate with implantable devices. The propagation of typical network signals, such as acoustic, optical or electromagnetic, can be affected by the medium conditions. In molecular communication, the medium can be wet or dry, e.g., in-body or environmental monitoring nanonetworks, and the propagation is even more dependent on the medium conditions. The speed of the medium, which is faster than the propagation speed of the molecules, can affect the communication between nano-machines. In addition, physical obstacles on the signal pathway can impede the propagation of the molecules, which can go through solid objects. These radical changes oblige the review of many common communication concepts such radiation, range, as well as the development of new propagation models.

5. Short-range communication using molecular motors

First nanonetworks models are inspired by molecular communication schemes observed in biological systems. Biological nanonetworks are used for intra-cell, inter-cell and intra-specie communication. Intra-cell and inter-cell communication are referred as short-range techniques due to the size of living cells and their internal components. Thus, in the framework of nanonetworks, we classify as short-range the communication process that takes place in a range from nm to few mm. Complementarily, we classify as long-range communication, the interconnection of two nano-machines in a range of mm to km as occurs in pheromonal communication.

Most of the intra-cell communications are based on molecular motors. Molecular motors, e.g., dynein, are proteins or protein complexes that transform chemical energy into mechanical work at a nano-scale [16]. Their use as information shuttles or communication carriers for nano-machines within a short-range has been widely proposed [21,46,54]. These molecular motors can be found in eukaryotic cells in living organisms.

Inside the cells, molecular motors are aimed at transporting essential particles among organelles during different stages of the cell life cycle. They travel or move along molecular rails called microtubules. These microtubules are widely deployed setting a complete railway network for intra-cell substance transportation. The microtubules go from the centrosome, i.e., cell organelle, outwards the cell membrane resembling a star topology in communication networks.

Specific molecular motors able to carry other molecules use these intracellular molecular rails. Depending on the cargo, molecular motors move at a speed up to 400 mm/day. The ability to move molecules makes molecular motors a feasible way to transport information packets, i.e., molecules, from the transmitter to the receiver nano-machine. As an additional advantage, molecular motors and microtubules can be used as a bio-hybrid communication interface between man-made nano-machines and biological structures. For instance, nano-machines could use this communication interface to interact with cell organelles to achieve specific tasks, such as drug delivery.

The deployment of the microtubules, i.e., network infrastructure, to support the movement of the molecular motors is a key issue. Two different solutions could be used for the deployment of the network infrastructure. The first one is based on natural mechanisms found in cells, in which microtubules can be developed by means of molecular self-assembly [62]. The second solution is based on the development of lithographic tracks of molecular motors to interconnect nano-machines. These tracks, which are made of molecular motors attached to a surface, can move structures similar to the microtubules from one point to another [36]. In this solution, the information molecule is not attached to the molecular motor but to the microtubule or a structure with similar characteristics [48].

The concept behind these two solutions is the same. In both solutions, the movement created by molecular motors is used to transport the information molecules. Further description of this molecular communication technique will consider the scenario according to the first solution. The scenario is assumed to include system components such as pre-deployed microtubules between nano-machines and traveling molecular motors. These components, shown in Fig. 4, should present specific features to support all of the communication processes between the nano-machines.

5.1. Communication features

Molecular communication enabled by molecular motors takes place in aqueous medium. The environment should include the necessary components at biologically appropriate conditions [28], such as temperature, humidity, medium viscosity and pH. Due to the organic and chemical nature of the involved nano-machines and information packets, the nanonetwork is highly sensitive to these conditions and the communication process can be negatively affected by sudden variations of the environmental conditions.

In molecular communication based on molecular motors, the communication process includes one transmitter and only one receiver. When the communication process occurs, the information molecule is altered and the encoded information is lost. Therefore the molecule information restricts the communication process to one receiver. The outcome is similar to a point-to-point physical communication link in traditional communication networks. To implement more complex communication schemes including multihoping techniques, the receiver nano-machines should be able to amplify, decode and redirect the information.

On the transmitter side, the information molecules are loaded on molecular motors, which transport the

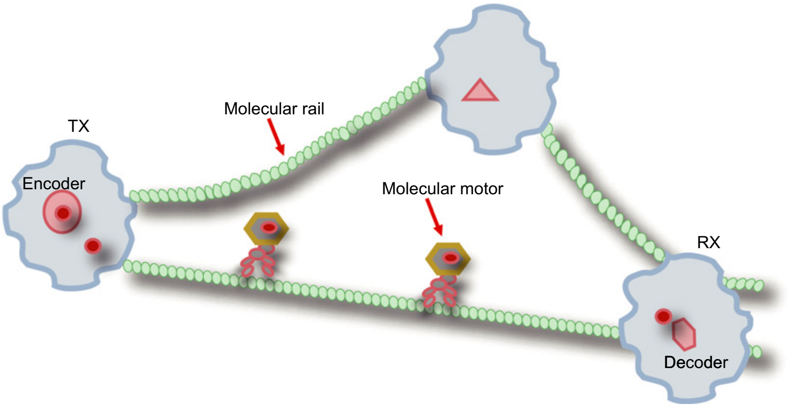

Fig. 4. System components in molecular motors communication systems.

information along the microtubules to the receiver. The packets can be encapsulated in vesicles. A vesicle is a fluid or an air-filled cavity that can store or digest cellular products [1]. The objective if this encapsulation of the information is twofold [48]. First, it allows enhancing the compatibility between the information molecule and the molecular motor, enabling the use of diverse types of molecules as information packets. Second, 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. Several microtubules could be deployed to interconnect one node, i.e., nano-machine, with many others. Depending on the nanonetwork infrastructure, a transmitter nano-machine will be able to use unicasting or multicasting mechanisms. To implement the first mechanism, the transmitter should be able to select a specific molecular rail to transmit the information molecule to the intended receiver. To achieve a multicast transmission, the transmitter could release several molecules, containing each one the same data, which are self-assembled onto molecular motors traveling on different molecular rails and hence different destinations. 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. Thus, bidirectional communication links can be obtained using different molecular motors or a pair of opposite microtubules between two nano-machines.

5.2. Communication process using molecular motors

Molecular motors are used to carry vesicles containing information molecules that are transmitted from the transmitter to the receiver. To facilitate the reception, the transmitter uses protein tags that bind to specific receptors on receiver nano-machines. Once the infrastructure is deployed between the transmitter and receiver nano-machines, the process includes the following tasks [46]:

- *Encoding*. This task involves the generation of the information molecules. When an external stimulus is applied to transmitter nano-machines, they generate these information molecules. The encoding process consists of selecting the right molecules that represent the information or the reaction to be invoked at the receiver. Thus, it is possible to control the reaction at the receiver by selecting the proper stimulus applied to the transmitter nano-machine.
- *Transmission*. This is a key task in this scenario and further research is needed to establish the process to attach the information packet to carrier molecules in an accurate way. The feasibility of this process is based on ligand-receptor binding process [41]. A ligand molecule, usually a protein, can bind to another larger molecule referred as receptor according to the affinity between them. In chemical terms, affinity is defined as the trend of dissimilar elements to form chemical compounds based on their electronic properties. The transmitter nano-machine should guarantee the high affinity between the information molecules and the molecular motors. If this affinity exists, the information molecule can bind to the molecular motors to start the propagation process. Encapsulation techniques can be used to ensure the affinity between the information molecule and the molecular motors. Vesicles are biological capsules with high affinity with molecular motors, therefore, they can be used as standard interfaces between different information molecules and molecular motors. Other biological process such as cell fission, reproduction or pore formation could also be used to release information packet to the medium [48].
- *Propagation*. This part of the process refers to the movement of the information molecules through the medium. Microtubules or molecular rails interconnecting nano-machines restrict the movement to themselves. As a result, molecules move in the direction of these rails instead of diffusing or moving randomly through the medium. In this scenario, the propagation is similar to propagation of electrical signals through conducting materials. The difference lies on the propagation speed, which will depend on the information molecule, the molecular motors and the molecular rail. The natural

domain for molecular motors is intra-cell communication. However, new advances in biomolecular science can enable inter-cell and bio-hybrid scenarios, as reported in [36].

- *Reception.* It is the process in which molecular motors containing information molecules arrive at the receiver nano-machine. The information molecules are detached from the molecular motors. This is achieved thanks to the affinity between the protein tags or the molecular encapsulation and receptors at the receiver. A receiver can have several reception properties in order to detach different information molecules from the molecular rails. Similar to the transmission, the extraction of information from a vesicle can also be done through different cellular processes such as fusion or pore formation [58].
- *Decoding.* The receiver nano-machine invokes the desired reaction according to the received information molecule. These biological reactions depend on the information molecule sent by the transmitter nano-machine. A nano-machine can be equipped with several receptors. Each receptor would be able to react to a specific information molecule. The decoding can be highly associated to these specific receptors. For instance, each receptor can be mapped to a specific action of the receiver nano-machine. Another option is to decode the information molecules inside the nano-machines. In this case the nano-machine could have one receptor and the different messages should use a common interface such as vesicles. As we can see, molecular motors just provide a means to transport the information from one point to another. Nano-machines will have to include all the mechanisms to support traditional network tasks such as message coding/decoding, multi-hopping and routing.

6. Short-range communication using calcium signaling

Inter-cell communication based on calcium signaling is one of the most well-known molecular communication techniques. It is responsible for many coordinated cellular tasks such as fertilization, contraction or secretion [11]. Calcium signaling is used in two different deployment scenarios. It can be used to exchange information among cells physically located one next to each or among cells deployed separately without any physical contact. Depending on the scenario, the propagation of the chemosignals includes different messengers such as ATP substance, calcium ions (Ca^{2+}) or inositol 1,4,5-triphosphate (IP_3) among others.

The description of the sequential propagation of the chemosignals driven by different messengers is known as the chemosignal pathway. One messenger transports the information until certain point of the pathway where the information is transferred to another messenger. The information transfer from one messenger to another continues until the information reaches its destination. This multi-messenger propagation scheme presents two advantages. First, the signal can be amplified at different levels of the chemosignal pathway. The amplification is usually done when the information is transferred among messengers. Second, we could use a set of messengers, i.e., chemical agents, to obtain different signal transduction and decoding results. The combination of different messengers could lead to different results and could be used to adapt the propagation parameters to a specific environment. The ligand-receptor binding principle is one of the most important processes participating in the information transfer among messengers. This process consists in the bounding of two molecules resulting in a local reaction, which in turn can trigger other processes.

If cells are deployed separately in the chemosignal pathway, as it is shown in Fig. 5b, the information molecule, i.e., the ligand, binds to a molecular receptor located on the external membrane of the cell. This binding generates an inner cell signal, which can be decoded by cell components. In this case, the ligand is considered as the *first messenger* while the inner signal molecules are considered as *second messengers* of the chemosignal pathway. *First messengers* are molecules that transport the information outside the cell. Complementarily, *second messengers* transport the information inside the cells. Membrane receptors convert the *first messenger* signals into *second messenger* signals by chemical reactions.

When cells are located next to each other, as it is shown in Fig. 5a, they can be connected through gap junctions. These biological gates allow different molecules and ions to pass freely between cells [1]. In this deployment scenario, the signal travels along cells using second messengers, such IP_3 and without the intervention of first messengers. The IP_3 is a messenger that provokes the release of calcium ions by cell organelles. Thus, the diffusion of IP_3 through gap junctions propagates a Ca^{2+} wave along the interconnected cells.

Several cellular components participate in the flux regulation of Ca^{2+} that makes signal propagation possible. The storage of Ca^{2+} inside the cell is enabled by certain proteins of the cytoplasm and organelles such as the endoplasmatic reticulum that can act as Ca^{2+} buffers or reservoirs. Extracellular mechanisms, such as ion channel located on the cell membrane, are also involved in this process in order to maintain this finite resource.

Calcium signaling provides a mean to interconnect neighboring cells. Unlike communication based on molecular motors and molecular rails, as explained in Section 5, calcium signaling provides more flexible transmission schemes. Using calcium signaling, all the surrounding nano-machines can receive a message sent by a unique transmitter. This communication technique is similar to broadcast networks in which all the transceivers located in the transmission range of the transmitter can sense the electromagnetic signal.

6.1. Communication features

Calcium signaling can be used for short-range communication among several nano-machines [50]. Similar to natural models, nano-machines should be near each other. Similar to the natural models, the propagation of the information can be performed in two different schemes depending on the deployment of the nano-machines:

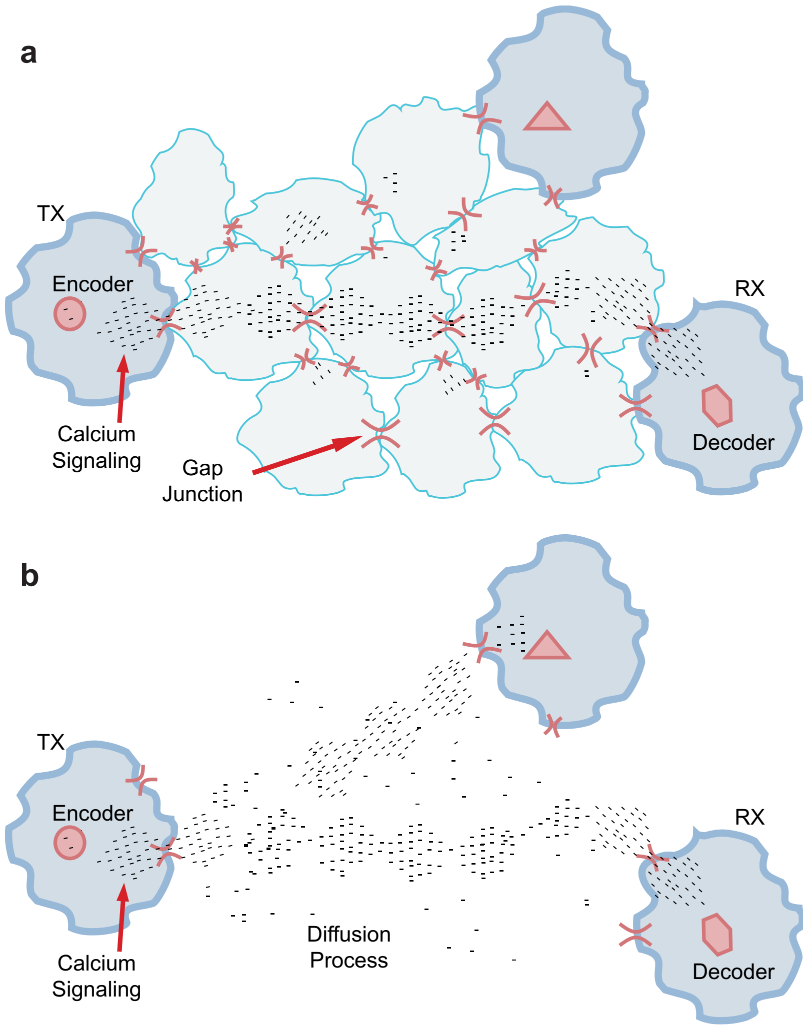

Fig. 5. Signal propagation in calcium signaling communication systems by (a) gap junctions signal forwarding and (b) by diffusion.

- *Direct access.* If nano-machines are physically connected, Ca^{2+} signals travel from one nano-machine to the next one through the gates, as shown in Fig. 5a. These gates should work similarly to the gap junctions allowing the flux of ions and molecules from one nano-machine to the interior of another nano-machine.
- *Indirect access.* If the nano-machines are not in direct contact, the transmitter nano-machine should be able to release the information molecules to the medium as first messenger in the chemosignal pathway. Information molecules will move through the medium following a diffusion process. They will generate a calcium signal inside the receiver nano-machine. Transmitters can encode the information varying the concentration of first messengers as shown in Fig. 5b. Biological systems encode the information on frequency and amplitude of concentration changes, usually referred to as Ca^{2+} oscillation and Ca^{2+} spikes [11].

These two propagation schemes enable the formation of networks supporting multicast or broadcasting transmission mechanisms. The overall communication system could work as follows: transmitter and receiver nano-machines are connected to each other through a signaling network consisting of interconnected nodes, which propagate the information using Ca^{2+} signals.

Due to the close interaction between nano-machines, the propagation of the information is not affected by the natural speed of the medium. However, the channel is not expected to be noiseless. Ca^{2+} can bind easily to charged particles that can be found in the network medium. A nanonetwork could use several different messengers to design the chemosignal pathway according to the working conditions. Nanonetworks should also be aware of potential communication process running in the environment. One of the potential drawbacks on using calcium signaling is the interference that can be caused in biological process such as muscle contractions or neurosignals.

6.2. Communication process within calcium signaling

For a better description of the communication process, we use two different network scenarios as shown in Fig. 5a and b, respectively. The direct access scenario contains one transmitter nano-machine and many other cells or similar nano-machines that are able to propagate the signal, i.e., the message. These components are physically located one next to each other and they are interconnected through functional gates or gap junctions. The receiver nano-machine, to which the message is addressed, can be any of these nano-machines members of the network. The indirect access scenario includes nano-machines that are deployed separately and where the signals propagate along the medium where the nano-machine are deployed.

In these two scenarios, the communication process based on calcium signaling includes the following steps:

- *Encoding*. This task refers to the generation of the information molecules. If neighboring nano-machines are used for the propagation of the signal as occurs in direct access scenario, the transmitter nano-machine encodes the information using Ca^{2+}. The information is precisely encoded in amplitude and frequency of the function describing the concentration of Ca^{2+} signal. These encoding methods are known as amplitude modulation (AM) and frequency modulation (FM). In the indirect access case, the transmitter should encode the information in the molecule to be used as a first messenger. The first messengers could also be encoded using AM and FM techniques. An external stimulus can be used to start the generation encoding process. For instance, it has been reported that some mechanical stimulus applied to cells provoke the generation of IP3 substance inside the cell. The presence of IP_3 unleashes the release of Ca^{2+}.
- *Transmission*. This task involves the signaling initiation. In direct access scheme, transmitter nano-machines stimulate neighboring cells and consequently the signaling process starts. The signaling generates the initiation of propagation of Ca^{2+} waves. IP_3, which was generated previously in the transmitter nano-machine, starts flowing into neighboring cells through the gates or gap junctions. Thus, neighboring nano-machines would release more Ca^{2+} driven by the presence on IP_3 substance. In the indirect access case, transmitters may initiate signaling by releasing substances to the environment. Similar processes to cell fission or pore formation could be used by nano-machines to release the information molecules to the medium.
- *Signal propagation*. When nano-machines use direct access, IP_3 transmitted to neighboring cells or nano-machines induces the release of Ca^{2+} from the IP_3-sensitive Ca^{2+} stores. The diffusion of the IP_3 substance continues to new neighboring nano-machines inducing again the release of Ca^{2+} on these nano-machines. This chain reaction provokes an increase of the Ca^{2+} concentration and as a result, the Ca^{2+} wave propagates across the networked nodes affected by IP_3. This propagation can be controlled varying the permeability of the gates or gap junctions. When nano-machines use indirect access, the propagation of first messengers containing the information can be described by using diffusion or Brownian motion models. When these information molecules bind to the receptors of the receiver nano-machines, they are translated into Ca^{2+} internal signals. The indirect access is much more sensitive to the medium conditions than the direct access. Transmitter nano-machines should consider the medium conditions such as wind, flow, temperature and noise to ensure that the information molecules will arrive to the intended receiver.
- *Reception*. When using direct reception, receiver nano-machine establishes gap junctions with the neighboring cells and perceives the Ca^{2+} concentration from inside of these cells. Once the message is received, receiver nano-machine can stop the IP_3 propagation by closing the gates or gap junctions connecting with other nano-machines. In the case of indirect reception, the receptor plays the most import role. They have to translate the information molecule into internal Ca^{2+} signals. A nano-machine could be equipped with several receptors capable to detect different information molecules. This can be used to establish several parallel communication channels among different nano-machines.
- *Decoding*. The receiver nano-machine reacts to the internal Ca^{2+} concentration. The concentration depends on the influx of IP_3 and Ca^{2+} that arrives to the receiver or on the bindings occurred between information molecules and nano-machines receptors. The Ca^{2+} signal can be encoded in amplitude and frequency enabling the activation of different processes. The basic difference between the receiver and those nano-machines or cells participating in the signal propagation is that the receiver can decode the message, while other nano-machines just receive the signal and forward it. Since calcium signaling can be considered as a broadcast scheme, multiple receivers can decode the same message.

7. Long-range communication using pheromones

Long-range communication is referred to as the communication process in which the distance between transmitter and receiver nano-machines ranges from millimeters up to kilometers. Control and communication of nano-machines in long-range communication can be useful in many applications, such as the military field or environmental monitoring.

Nanonetworks in long-range communication scenario are also inspired in biological systems found in nature. Ants, butterflies, bees and many mammals use molecular messages, i.e., pheromones, to communicate with members of the same species. Pheromones can be defined as molecular compounds containing information that can only be decoded by specific receivers and can invoke certain reactions in them. Pheromonal communication is used to build complex networks including micro and macro-scale mobile actors. For instance, in ants colony, the communication between members is based on pheromones and a whole set of social behavior primitives is encoded in these nano-messages. Another example is the long-distance communication between butterflies using pheromones where molecular messages can reach the range of a few kilometers [65].

7.1. Communication features

Communication using pheromones is similar to the short-range techniques described in Section 5 and 6. The communication is based on the release of molecules that can be detected by a receiver. In long-range nanonetworks the channel cannot be modeled as a deterministic neither a physical link between transmitter and receiver. Thus, concepts like diffusion, flows and molecules concentration in the medium play a key role in the communication process.

Regarding the medium, molecular communication using pheromones can be used in dry [14] and wet [40] environments. Once the molecules are released to the medium, they can be affected by several factors, such as antagonist agents, medium flow and temperature, and dispersion. All those factors can be considered as sources of noise, similar to those found in traditional communication channels, and they can compromise the transmission reliability.

A key feature in long-range communication using pheromones is the coding system. While in traditional communication networks the message is encoded using a binary system, the information in long-range nanonetworks is encoded on the molecule itself. Since messages consist of molecules, there is a huge quantity of possible combinations that can be used to transmit data. Moreover, messages can be compounded by several different molecules allowing even more combinations to encode the information.

The reception of the transmitted molecules is realized by molecular receptors located on the receiver, as depicted in Fig. 6. This phenomenon is based on the ligand-receptor binding process as occurs within calcium signaling triggered by first messengers. A ligand is a molecule that interacts with a protein, by specifically binding to this one. In molecular communication using pheromones, the receptor proteins can be considered as the receiver nano-machine antenna or transducer, which transforms energy contained in the message into a reaction at the receiver.

Nanonetworks based on pheromonal communication are good examples of scalable molecular communication systems. In biological communication systems based on pheromones, the information is encoded on molecules at nano-scale, although the transmitter and receiver nano-machines, i.e., animals, can be considered as macro-systems. However, the communication is still based on nano-transceivers and nano-messages and therefore is in line with the definition of nanonetworks. In these biological systems, complex neural networks and hormonal systems act as the interface among these macro entities, e.g., brain, and the nano communication system.

7.2. Long-range pheromonal communication process

The communication process includes five tasks similar to those found in short-range communication techniques. Currently, there are still no artificial nano-machines capable of executing the tasks described in this section but they are expected to be available in the near future. The objective of the following description is to identify the existing biological communication processes and to map them into those communication processes found in traditional communication networks. This knowledge mapping can help to understand the biological communication mechanisms and to develop solutions for future nano-machines.

- *Encoding*. This process includes the selection of the specific pheromones or appropriate molecules to transmit the information and produce the reaction at the intended receiver. On the biological systems found in nature, animals release specific pheromones to invoke certain reactions at the receivers. For instance, the female Douglas-fir beetle releases pheromones to attract the male to the host tree. When the male detects these pheromones, it transmits an acoustic signal to stop the sexual pheromones production and also releases Douglas-fir anti-odors to avoid the detection of the host by other males. Another example of coding through molecules can be found in colonies of bees. Honeybees use up to 15 known glands in their molecular communication process. The released message is not a single component but rather a complex molecular structure compound by different chemicals. Different pheromones can be used as sexual, alarm, marking, attraction or aggregation and orientation messages.
- *Transmission*. This process consists of releasing the selected pheromones during the encoding process to the medium. Since pheromones can be released to the medium through physiological fluids, molecular

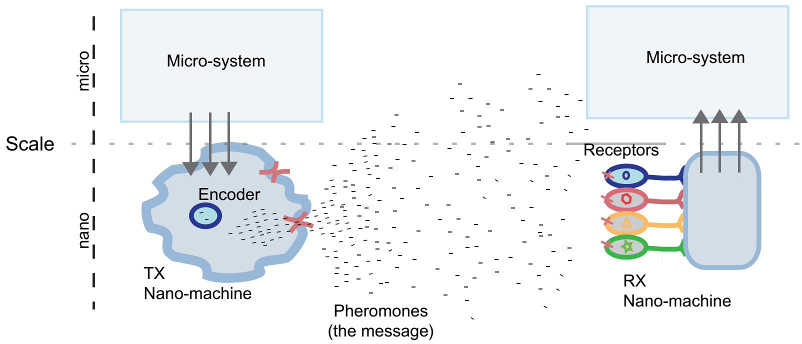

Fig. 6. Conceptual diagram of a pheromonal communication. Biological models provide a useful example of molecular communication scalability.

messages can be in liquids or gases. The transmission of information is defined as a voluntary action of the transmitter. It is important to emphasize the voluntary character of the transmission, otherwise it is not considered as a communication message. For instance, odors can contain information and can trigger specific behaviors at the receivers, but usually they are not transmitted voluntarily and therefore they cannot be considered as an example for nanonetwork communication.

- *Propagation*. The propagation of pheromones, from the transmitter to the receiver nano-machine, can be modeled using diffusion processes where each molecule is subjected to Brownian motion. The diffusion of molecules or propagation is very sensitive to environmental conditions such as temperature, viscosity and pressure. Antagonist molecules present in the medium can also affect the propagation negatively by modifying the information molecules before they reach the destination. In biology, the reception of pheromonal messages is studied by measuring the concentration level of pheromones near the intended receiver [13]. These communication models based on concentration level and diffusion models, can help to determine some parameters, such as the sensitivity needed in the receptor to detect the molecular messages. The model can also help to develop channel-multiplexing mechanisms and to assess the channel capacity according to the propagation characteristics.
- *Reception*. Once the information message reaches the receiver, it can use receptor proteins to detach the molecule from the carrier. These receptors can be located on the physical surface of the receiver. Receptors are proteins with a high molecular affinity to pheromonal messages, so that they can bind to them. The ligand-receptor binding process also depends on the environmental conditions. Special structures can be included in nano-machines for this task, e.g., the vomeronasal organ that acts as the receiver for pheromonal communication in most mammals [14]. This biological organ is a blind-ended mucus-filled tube, located in the nasal septum [23]. The vomeronasal sensory neurons (VSNs) transform these received molecules into bioelectric signals that are transmitted to the brain and later decoded into a specific reaction.
- *Decoding*. This process is referred to the interpretation of the information transmitted or the reaction invoked by the received message. For instance, in some insects the reception organs includes many different receptors that can be sensitive to different molecules or messages. The molecular receptor of the fruit fly is its antennae and the maxillary palps that include 1300 olfactory receptor neurons (ORNs). These ORNs, which are connected to the brain, can decode 40 different odors. The decoding system is embedded in the reception organs and can be expressed as spatial-temporal activation patterns of the receptors.

8. Research challenges in nanonetworks

The interest in nanotechnologies is growing while more applications are being proposed. The potential impact of these technologies leverages the continuous development of new tools, such as simulators [18], scanning probe microscopes [44], or lithography machines able to pattern nano-metric structures.

Over the last years, novel molecular manufacturing techniques are enabling the development of more advanced nano-machines. Using nanonetworks, these nano-machines can be interconnected to realize more complex tasks in a coordinated and complementary manner. First developments in nanonetworks are inspired by biological systems based on molecular communication.

Recently, two molecular communication schemes have been proposed based on natural models. These schemes are based on inter and intra-cell molecular communication techniques [57]. Additionally, in this paper we propose a third communication scheme based on pheromones. These three communication schemes are examples for short or long-range molecular communication observed in nature. They are proposed as basic models for the development of future nanonetworks.

Nanonetworks are not only related to the molecular communication techniques, but also to nano-machines, which are able to communicate at this level. The nanonetworks development roadmap includes several stages, in which an interdisciplinary scientific approach is needed to address all the posted research challenges.

8.1. Development of nano-machines, testbeds and simulation tools

One of the first phases in the nanonetworks roadmap is aimed at developing nano-machines including molecular transceivers. Latest efforts on nanotechnologies enabled the creation of functional nano-structures that introduce switching, memory, and light-emitting behaviors [8]. These are still very simple but they will lead to more complex nano-machines, which will be capable of performing specific communication processes. Future nano-machines are expected to operate autonomously, and also to include self-assembly, self-replication, locomotion and communication capabilities as described in Section 4.

Despite the current existence of simulation tools for molecular assembly, and biological and genetic systems, there is none for nanonetworks up to now. Simulation tools should allow the use of different nanonetwork topologies and molecular communication schemes such as calcium signaling or networks based on molecular motors. It should also include the medium parameters that affect the propagation of the information molecules, and allow the selection of different carriers to transport the information.

Simple nano-machines or molecular transducers can be considered for the development of first nanonetworks testbeds for molecular communication solutions. This is the case of robotic micro-noses, which could be used to measure concentration level of certain molecules in the environment [33], and therefore act as molecular receivers. Using molecular releasers as transmitters, and systems like the robotic noses, developments in signal modulation, channel models, and medium access could be tested.

8.2. Theoretical approach: basis for a new communication paradigm

A typical communication process includes the following phases:

- The encoding phase in which the transmitter forms the information molecule.
- The transmission or release of these molecules to the environment.
- The propagation of the information molecules trough the medium.
- The reception of the information molecules.
- The decoding of the received information molecules.

First nanonetworks are based on many biological communication processes. However, the communication tasks occurring among these biological components are still not completely understood.

When talking about nanonetworks, the first questions that arise are regarding the information encoding and later decoding. Based on the three bio-inspired communication schemes presented in Sections 5–7, we can identify two different methods to encode the information in molecular communication. The first method encodes the information in the information molecule itself, e.g., structure or polarity. Depending on the molecular structure the message will bind only to specific receptors, resulting in a channel defined by these information molecules and proper receptors. Thus, the communication system could use different molecules and receptors to encode the information as spatial-temporal activation patterns of the receptors, e.g., decoding of odors in fruit flies. The second method encodes the information in the fluctuations of the concentration of ions, similar to amplitude and frequency modulation methods used in traditional telecommunication systems. How nano-machines decode these different fluctuations is still uncertain although the activation of some cellular processes according to these variations has already been proven [11].

The transmission and reception of information molecules is more related to the nano-machines, more specifically with the molecular transceiver. There are many open questions regarding the transmission and reception such as (i) how to acquire new molecules and modify them to encode the information, (ii) how to manage the received molecules, and (iii) how to control the binding processes to release the information molecules to the medium. In [52], models for flux and concentration detectors are presented. Such models demonstrate the dependence of the binding process on the medium conditions. This kind of models can help to understand the interaction between the receptors and the information signal, and to assess some transceivers features such as the molecule release rate or the sensitivity of the receptor.

The propagation of the communication signals in nanonetworks is totally different than in classical communication networks. Nanonetworks use molecules instead of electromagnetic or acoustic waves. The propagation of these molecules, which is subject to different medium parameters such as viscosity, temperature or pH, can be described using a particle diffusion model. Uncontrolled medium conditions such as rain, obstacles, wind or tide, can also affect the communication pathway. Prior to the development of communication mechanisms or protocols, it is important to develop, analyze and understand the channel model and the molecular signal propagation features. Brownian motion models were successfully used to describe the free movement of particles in fluids [53]. Using similar models, the communication based on diffusion of pheromones in ant colonies has been described in [13]. These models can help to develop the channel and propagation models for nanonetworks. Transmitter and receiver binding features can be added to these propagation models to assess the molecular channel capacity [2]. Similar models, but including molecular propagation principles, can be used to explore more complex encoding techniques for molecular transmissions, such as AM and FM. If molecular motors are used as carriers, the propagation is restricted to the nanonetwork infrastructure and therefore the communication process can be considered to be more deterministic. The signal propagation speed using this physical channel as well as the reliability of the transmission using molecular rails still need to be measured.

8.3. Knowledge transfer: architectures and protocols

Once the basic nanonetwork components are built, the transmission is controlled and the propagation is understood, advanced networking knowledge can be applied to design and realize more complex nanonetworks. The development of the nanonetworks can be done using a layered architecture including medium access protocols, routing schemes and application interfaces.

A medium access control (MAC) protocol is needed to define and apply mechanisms to ensure a fair use of transmission channel. In biological molecular communications, most of the channel access schemes are based on code division. In nanonetworks, many molecular coding schemes could be used to transmit the information while these molecules do not interfere with each other and do not affect the medium, e.g., changing the viscosity. An example of biological channel access based on different codes can be found in pheromonal communication. In this example, each communication channel uses different information molecules that can only be decoded by intended receivers, resulting in multiple communication channels over the same medium, one per species. Another medium access technique used by biological systems is based on the modulation in frequency (FM) and amplitude (AM) of the molecular signal. According to these last techniques, the communication channels among nano-machines can be established using different frequencies or signal amplitudes. Each frequency and amplitude channel can be decoded by specific nano-machines.

For more complex networks, an addressing scheme is needed. The packet should include the information about its origin and destination to allow bidirectional and multi-hop communications. How to include this information in an information molecule is still an open issue. However, according to natural models of nanonetworks, the information is usually encoded and broadcast without including a specific address of the transmitter nano-machine. In biological nanonetworks it is assumed that only the authorized transmitters can have access to the channel and send the encoded message. When this message arrives at the receptor, it reacts according to the molecular information ignoring its origin. Thus, these nanonetworks can be considered as data centric networks. This behavior can be observed in pheromonal communication, or in living cell networks using calcium signaling. In these examples, the reactions at the receiver are triggered by the molecular signal itself, which does not contain any specific data about the origin. This principle is also the basis for drugs delivery and the use of supplementary hormones in healthcare. By contrast, the destination address is crucial in data centric networks. Nano-machines participating in the propagation pathway should be able to route a packet towards the right receptor based on the destination address. Addressing and routing schemes are not trivial, and solutions will be developed according to the level of complexity of nano-machines participating in the propagation of the molecular signals. In natural models encoded signals are broadcast in a medium where the intended receivers are located. This simple mechanism is used to reach the intended receivers of the network.

Nanonetworks are developed for a specific purpose or application. The objectives are described in a main controller or are distributed in the internal code of the participating nano-machines. All the interfacing aspects between the controller of a nano-machine, in which the application tasks are described, and the nanonetwork must be explored. Standard interfaces should be defined including protocols and primitives to start a transmission using nano-machines and translate the received molecules into information relevant to the application. These interfaces should be available for macro-systems participating in the nanonetworks, such as monitoring computer networks in biomedical or military fields.

Communication reliability is another key issue in nanonetworks. Some applications demand reliable mechanisms to monitor or interrupt selective transmissions or on-going processes. Some molecular communication schemes are subject to random processes; as a result, the reception of a transmitted message by the right receiver cannot be guaranteed. The communication reliability should be investigated by considering random communication features and particular infrastructures in molecular communication.

9. Conclusions

The development of nanotechnologies will continue and will have a great impact in almost every field. The use and control of these technologies will be a major advantage in economics, homeland security, sustainable growth and healthcare. Intrinsic technological burdens will limit the use of more advanced and smart materials, sensors, actuators and devices at nano-scale, if they are not able to communicate to cooperate to perform more complex tasks. This need for a communication network will be more plausible with the increased complexity of developed nano-devices.

Molecular communication seems to provide efficient mechanisms for networking of nano-machines. It represents a complete new communication paradigm in which the information is encoded into molecules. In this paper the term "nanonetwork" was defined as the interconnection of multiple nano-machines using molecular communication. Nanonetworks demand innovative solutions to create reliable molecular communication channels among nano-machines. First developments are bio-inspired by existing biological nanonetworks. At nano-level, many components and communication process has been studied from a biological or chemical point of view.

Despite being a novel communication paradigm that requires an interdisciplinary approach, information and communication technologies (ICT) are called to be a key contributor for the evolution of the nanonetworks. Network architectures, channel models, nano-machines and transceivers architectures, medium access control and routing protocols are some of the contributions that are expected from the ICT field.

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