DIRECT: A Model for Molecular Communication Nanonetworks Based on Discrete Entities

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Abstract
A number of techniques have been recently proposed to implement molecular communication, a novel method which aims to implement communication networks at the nanoscale, known as nanonetworks. A common characteristic of these techniques is that their main resource consists of molecules, which are inherently discrete. This paper presents DIRECT, a novel networking model which differs from conventional models by the way of treating resources as discrete entities; therefore, it is particularly aimed to the analysis of molecular communication techniques. Resources can be involved in different tasks in a network, such as message encoding, they do not attenuate in physical terms and they are considered 100% reusable. The essential properties of DIRECT are explored and the key parameters are investigated throughout this paper.

Keywords:
Nanonetworks, Discrete Resources, Confined Operating Environment, Molecular Communication, Diffusion

1. Introduction
With the introduction of nanoscale communication networks, or nanonetworks [1], molecular communication has become an alternative approach to
electromagnetic communication at the nanoscale. Although different communication protocols have been proposed to implement molecular communication [2, 3, 4, 5], they all rely on the use of small molecules, including ions and hormones, which are physically transported from the transmitters to the receivers. For instance, in diffusion-based molecular communication, the transmitted particles propagate by means of diffusion in a fluid medium [6]. Diffusion-based molecular communication encompasses several techniques, such as calcium ion ($\text{Ca}^{2+}$) signaling [7], one of the most important communication mechanisms among living cells, and pheromonal communication [8].

This paper introduces DIRECT, a general model which allows the analysis of molecular communication techniques by modeling the molecules used to encode messages as resources. Formally, DIRECT can be defined as a set of techniques, models and protocols developed to efficiently operate a network which utilizes and relies on discrete entities, i.e., resources. These resources are used to encode messages and they act as information carriers over a medium in a confined environment.

Most of the previous work on molecular communication treats molecules as entities which disperse in an unconfined environment. As opposed to this, DIRECT considers a closed environment where a group of transmitter and receiver nanomachines communicate by exchanging a finite set of molecules, which are interpreted as resources. Since the amount of resources is fixed and remains constant throughout the network lifespan, nanomachines need to harvest resources in order to transmit new messages. This harvesting need of nanomachines represents the main idea behind DIRECT and, as it is later shown, it represents one of the main constraints of the performance of the nanonetwork.

If properly harvested, any resource in a molecular communication nanonetwork located in a confined space can be reused. This allows the infinite recirculation of resources, i.e., the continuous use and harvest cycle, and naturally introduces the concept of resource conservation in a nanonetwork based on molecular communication. In an ideal case, the harvesting of resources by nanomachines would allow the perpetual operation of the network without the need of creating new resources. Our intention with DIRECT is to model the recirculation of resources in a molecular communication nanonetwork, to investigate its properties and to define its limits and capacity.

The issue of resource harvesting has been widely studied in the electromagnetic communication domain [9, 31]. However, the concept of electromagnetic energy does not completely overlap with the concept of resources in DIRECT, since electromagnetic waves attenuate as they propagate throughout space (for instance, because of absorption by obstacles in the wave path). Therefore, we think that DIRECT is the first model that will allow modelling the recirculation of resources in molecular communication nanonetworks. Please note that this document provides an introduction to DIRECT, explaining general concept and main properties as well as constitutional elements of the model. Some preliminary results from experiments and related observations are given in order to constitute the first steps of a future analytical model.

The rest of this document is organised as follows. In Section 2, we provide
information about the usage of $Ca^{2+}$ ions in molecular communication and how ER and Mitochondria harvests $Ca^{2+}$ for future use. In Section 3 the state of the art and related works are briefly explained by stressing the differences with respect to DIRECT. In Section 4, different operating environments are introduced and the importance of a confined environment is explained. In Section 5, the formal definitions and explanations for resources, nodes, lifespan and capacity are given. In Section 6, a case study for DIRECT in a molecular communication nanonetwork using pulse based modulation is analysed. A number of tests are performed in order to observe the interdependencies between the essential parameters that define the environment, and simulation results are discussed. We conclude the paper in Section 7, where a path for future work is also given.

2. Molecular Harvesting in Biological Systems

Calcium ions play an important role in the cell life as a fundamental second messenger in signal transduction pathways [15]. The variations of cytosolic $Ca^{2+}$ concentration are important regulatory factors for the control of cellular functions. In fact, an increase in intracellular $Ca^{2+}$ concentration, in response to extracellular signals, can trigger and modulate several events (such as muscle contraction, cell growth, proliferation and many others [11, 12, 18]. This may happen through the modulation of the released ions in terms of frequency, amplitude and spatial-temporal patterning [13, 18, 20]. These signals are generated by the cells by using both internal and external sources of $Ca^{2+}$. The internal sources are represented by the several intracellular organelles that act also as $Ca^{2+}$ storages. These storages accumulate, release and buffer $Ca^{2+}$ ions constantly, during specific cellular events. The Mitochondria and the Endoplasmic Reticulum (ER) are the main ones [15, 16], so in what follows are introduced the main features of these two organelles, but also the Golgi Apparatus and the Nucleus can be involved too in different scenarios [10, 14, 20]. All of these organelle can absorb high levels of ions in order to keep low the cytoplasmic concentration.

The ER is an important cellular organelle, placed near the nucleus, occupying at least the 10% of the cell volume [24]. It is a dynamic reservoir of calcium ions which can be activated by both electrical and chemical cell stimulation and it can store an high amount of calcium ions, in the order of mM range (1-3 mM [23]), analogously to the extracellular concentration (1-2 mM), whereas the cytosolic concentration is very low, in the order of nM range (resting state: 100nM). This means that the gradients across their membranes (ER and plasma membrane) are very similar [18, 20, 21].

The ER channels can be activated by second messengers (such as InsP3 and cADPr) [12] that promote the calcium release into the cytoplasm, with a following drop in the intra-organelle $Ca^{2+}$ concentration of several hundred $\mu$M. The cytosolic $Ca^{2+}$ elevates from the resting value up to 1000 nM, so a great part of this $Ca^{2+}$ is rapidly extruded by the plasma membrane pumps (PMCA and Na/Ca exchangers) into the extracellular medium. When the InsP3
signalling is terminated, the $Ca^{2+}$ ions re-uptake into the internal organelles [22].

The propagation of $Ca^{2+}$ is based on a positive feedback process, where the released $Ca^{2+}$ ions trigger the near stores to release more ions (known as Calcium Induced-Calcium Release process). As introduced above, the first release may occur from the second messenger InsP3, and then the process will go on autonomously, depending only on: a) the $Ca^{2+}$ diffusion coefficient, b) the distance between the stores and c) their sensitivity. The release of the InsP3 is due to the binding of an external ligand to its specific receptor on the plasma membrane, and then it diffuses to the ER, where it causes the opening of the $Ca^{2+}$ channels. The following release of the previously sequestered calcium rise sharply the cytosolic concentration to about 10 $\mu$M [18].

Once the $Ca^{2+}$ ions have triggered the desired behaviour, they have to be rapidly removed from the cytosol, to restore the resting conditions. This may happens through the combined activity of $Ca^{2+}$ extrusion mechanism, such as the plasma membrane pumps (PMCA and NCX) and the refilling processes of the internal stores, such as the sarco-endoplasmic reticulum ATPase (SERCA) pumps [20].

An important role in sequestering calcium ions from the cytosol and on intracellular signalling is covered by the Endoplasmic Reticulum and the Mitochondria, which are typically located in close proximity to each other [14, 18, 24]. The first one is normally filled with ions that can be released to generate or reinforce $Ca^{2+}$ signals, the last ones is normally empty and can store large amounts of ions, that can be buffered, used to increase the energy production or even released in the cytosol. The mitochondrial $Ca^{2+}$ accumulation is usually transient and follows the cytosolic $Ca^{2+}$ spikes which arises during cell activation [17]. Indeed the mitochondrion is able to sequester $Ca^{2+}$ rapidly during the development of the $Ca^{2+}$ signal and then releases it back slowly during the recovery phase. This uptake of $Ca^{2+}$ by the mitochondrion is important in shaping both the amplitude and the spatio-temporal patterns of $Ca^{2+}$ signals.

The calcium released by the ER is closely coupled to mitochondrial uptake, because several micro-domains of high $Ca^{2+}$ concentration are generated in their proximity and they are fundamental for the correct interactions between the two organelles, enabling a direct and highly efficient transmission channel. This lets the mitochondria to buffer the local $Ca^{2+}$ released effectively and consistently [18, 19]. Microscopy observations show that about 20% of the mitochondrial surface is in direct contact with the ER [24].

3. State of the Art

Molecular communication has been an attractive topic for researchers after the introduction of the nanoscale communications. Numerous potential applications of nanonetworks make molecular communication even more appealing. These potential applications range from biomedical applications, such as intelligent drug delivery and health monitoring systems, to military and environmental applications such as air pollution monitoring [1].
A number of different models have been proposed to describe molecular encoding, channel and transmission. Some of these models use gap junctions [3], whereas others use molecular motors [4], and ligand receptors [25].

Another group of researchers are focused on proposing models and defining capacities from an information theoretical perspective [26, 27, 28, 29].

An energy model for molecular communications is introduced in [30], providing biological background of the energy consumption of different elements of the process.

A broad study for energy harvesting in electromagnetic communications is given in [31]. [32] refers to the information capacity of such networks.

Compared to the research available in literature, DIRECT can be considered as an abstract model defining general rules for different models, with similar or common properties. Our intention in DIRECT is to state common properties, like the use of discrete resources in a confined environment, and define and model a system through some related features such as communication capacity and its limits. In this paper we investigate a way of defining a system by stating relations between resource concentration, number of nodes and communication capacity in a confined environment.

4. Operating Environments

Considering the use of discrete resources in DIRECT, operating environments (or working spaces) can be classified into three categories according to the scope of the particle movement due to the existence of the boundaries: confined, unconfined and locally unconfined (Fig.1).

A confined operating environment (Fig.1a) is a closed working environment, bounded with reflective borders. Any resource reaching to the boundaries, reflects back into the environment. Thus, the number of total resources within the environment remains the same at any time.

A unconfined operating environment (Fig.1b) has no boundaries and any resource can pass through the virtual borders of the monitored environment through time. Thus the total amount of discrete resources can vary in the environment.
A locally unconfined operating environment (Fig.1c) is a special case of a confined operating environment, where the environment dimensions are extremely large such that we can consider a relatively small portion of the environment as unconfined.

In this paper, we consider a confined operating environment in which the total amount of resources remains constant over the network lifespan. The constant number of resources in a confined operating environment, can theoretically make the network indefinitely operational in terms of resources, if proper harvesting and emitting mechanisms are applied. During operation, the network may temporarily stop functioning due to the lack of local resources. However, that could be overcome by harvesting over time, since resources naturally diffuse from higher density locations to the lower density ones. On the other hand, in an unconfined operating environment, the network may become permanently not operational as a result of resource dispersal.

5. Resources and Nodes

In DIRECT, a resource is a discrete physical entity which is required by a task, such as modulation of the signal, within the network. Resources can be considered as the atomic entities within the network. They are perpetual and reusable, they do not disperse or attenuate. If proper harvesting mechanisms are applied, resources are 100% reusable. \( Ca^{2+} \) is an analogous example of a resource involved in molecular communication.

Nodes are autonomous agents, and they constitute the basic functional unit, capable of processing/storing data, sensing and actuating. They are either organic or electromechanical nano machines [1], with communication capabilities. We assume that, every node operating in DIRECT includes proper harvesting mechanisms and an internal reservoir to keep resources within for future use. Any harvesting operation fills a node’s reservoir, whereas a communication operation drains it.

The harvesting mechanisms in DIRECT differ from the ones in electromagnetic communication. Nodes in DIRECT harvest resources by absorbing discrete particles into the node’s reservoir. In electromagnetic communication, instead, the harvesting operation usually refers to the energy harvesting from different sources such as sunlight, body heat or vibration, all of which are produced as a result of external incidents that cannot be controlled within the system. The harvested energy is consumed by the nodes. However, in DIRECT, resources are reusable.

This reusability property allows the recirculation of resources in DIRECT. A resource can be found either inside a node’s reservoir (in a pure resource form) or at large in operating environment (Fig.2).

Resources in operating environment can have two different forms. They can be used to encode information, or they can be considered as noise. Information in DIRECT is represented by a group of discrete resources, whereas in electromagnetic communication, information is modulated using electromagnetic...
waves. Because of the random movement of the resources during the propagation process, some of the resources may change their functionality and turn into noise. These resources can be seen as the attenuated parts of the propagating signal. Note that no resource would be lost because of such a functionality change. Moreover, the emitted signal may attenuate during propagation.

Every resource in operating environment, which is not used for information encoding, are considered as noise. Noise can be generated from random movement of the resources, interference from other transmitters or can be initially given to the environment as background noise, to supply resources to the nodes. In electromagnetic communication, instead, noise is a fluctuation or a random signal added to the original signal from an outside source.

As seen in Fig.(2), information is encoded using resources (emission), although a node can harvest resources from information. There is a complete overlap between information and resources, which we call duality of the resources. Duality of the resources also exists between resources and noise in a similar manner. A node can harvest resources from noise; however, noise is itself made of resources.

The duality of the resources provides a 100% recycling of resources in the form of both information and noise. Thus, DIRECT proposes reusable information and noise which, to the best of our knowledge, is a unique property that cannot be found in any other communication paradigm.

Theoretically, the infinite recirculation of resources can provide an infinite lifespan to the DIRECT network, in terms of resources. The lifespan comes to an end when there is not a single node left that is capable of communicating in infinite time. During the network lifespan, there might be some intervals in
which the network may not be operational due to the lack of resources. However, nodes may continue harvesting until they collect sufficient resources from the operating environment and resume with their operation.

The resource recirculation is broken if and when:

- The working environment is not confined.
- There are not sufficient resources to be harvested by the nodes which yields starvation.
- Deployment of an excessive number of nodes which yields starvation.
- Nodes are not supplied with proper harvesting mechanisms.

Definition of capacity in DIRECT is different than in any other communication paradigm. Considering the previously introduced properties, the capacity in DIRECT can be defined as the maximum number of nodes which can be supported for a given amount of resources in infinite lifespan. From a different perspective, the capacity can be given as a function of the optimum amount of resources to obtain infinite lifespan for a given number of nodes.

6. Experiments

A set of experiments has been performed to observe the behavior of DIRECT in modeling molecular networks. Three essential parameters are investigated during experiments, and the relationship between them is studied. These parameters are:

1. **Pulse amplitude** ($A$) is the number of resources that constitute an emitted pulse initially.
2. **Background concentration** ($b$) is the initial concentration of resources over the operating environment.
3. **Number of nodes** ($n$) is the total number of nodes available in the operating environment.

The **Pulse frequency** ($p$), which is the ratio of the number of pulses emitted per unit time, is the essential metric which is monitored according to the variations of the given parameters. **Pulse frequency** is an important metric for communication performance because it represents the number of pulses (i.e., information bits) per unit time which can be emitted by a node in the network.

A pulse based modulation (PBM) is recently applied to molecular communication as a modulation scheme by Llatser et al [33, 34]. In our experiments, we used PBM because its properties and behavior are already studied.

In PBM, in order to represent 1 bit of information, the sender must instantaneously emit a pulse which comprises of $Q$ discrete resources. To emit a pulse, a sender node should have already harvested at least $Q$ resources from the operating environment assuming that it possesses none initially. The emitted pulse will propagate through the environment, like the ripples in water, eventually
reaching the receiver’s location. The concentration of a pulse at time \( t \) at a
distance \( x \) is given by (1), where \( D \) is the diffusion coefficient of the operating
environment [35, 36].

An interested reader can find more information about PBM in [33] and [34].

\[
\rho(x, t) = \frac{Q}{4\pi Dt} e^{-x^2/4Dt}
\] (1)

Experiments are performed using N3Sim [37], a previously developed simulation software for nanonetworks with transmitter, receiver and harvester nodes
using diffusion-based molecular communication. N3Sim models the movement
of the resources according to Brownian Motion and takes into account the inertia
of the particles and collisions between them. Transmitter nodes encode the
information by emitting a group of resources, i.e increasing their local concentration on the simulation environment. Harvester nodes gather resources from
the environment within their range and store them for future use. Receiver
nodes decode the information by counting the resource concentration within
their range. N3Sim acts according to a simulation scenario provided by a configuration file. As a discrete-time simulator, at each time step N3Sim follows these steps:

1. N3Sim emits resources (if there is an active emitter node at this time step
   according to the configuration file)
2. Counts resources on receiver nodes
3. Calculate next position of each resource according to Brownian dynamics
4. Solve collisions between resources (if required by configuration file)
5. Update positions of the resources

In the first set of experiments, we investigate the maximum pulse frequency
as a function of background concentration and pulse amplitude (2), the results
can be seen in Fig.3. Please note that we used normalized values for parameters
and metric, and we fixed number of nodes to 1. Lines in Fig.3 represent different
pulse amplitude values, and they are arranged from highest pulse amplitude
value to lowest. Lines at the bottom, which represent a high pulse amplitude
value, result in a low pulse frequency, whereas the upper lines, which represent
a low pulse amplitude, result in a high pulse frequency.

\[
p = f(b, A)|_{n=1}
\] (2)

As we fixed number of nodes in Fig.3, we observe the impact of background concentration over pulse amplitude, and vice versa. A higher background concentration value provides more resources to the environment, whereas a low background concentration value provides low resources. In order to emit pulses with higher amplitudes, a node requires more resources, thus it requires high background concentration values. On the other hand, pulses with a low amplitude require less resources. To obtain a higher pulse frequency, the environment must provide a high resource concentration, and the pulse amplitude must remain low. This claim is confirmed in Fig.3, in which the maximum value of the
background concentration parameter combined with the lowest pulse amplitude value gives the highest pulse frequency. Contrarily, we observe a minimum pulse frequency at the point for maximum pulse amplitude and minimum background concentration.

![Graph showing pulse frequency (p) for different background concentration (b) and pulse amplitude (A) for n = 1.](image)

Figure 3: Pulse frequency (p) for different background concentration (b) and pulse amplitude (A) for n = 1

\[ p = f(b, n) |_{A=0.5} \]  

In the second set of tests, we monitored the pulse frequency against number of nodes and background concentration (3) (Fig.4). Note that a fixed pulse amplitude value is used during this set of simulations. Each line in Fig.4 represents a set of tests for a different number of nodes parameter. They are arranged in such a way that the one at the bottom stands for the lowest number of nodes, whereas upper lines designate higher number of nodes values.

Nodes in Fig.4 are homogeneously spread over the environment, forming a grid shape, and they concurrently harvest resources from different regions of the environment. As we fixed the pulse amplitude, we observe the relationship between background concentration and number of nodes values.

Higher number of nodes values represent more nodes, concurrently emitting pulses, and they inherently increase pulse frequency. More nodes emit more pulses, thus require more resources. If the environment cannot feed nodes with the necessary resources, they cannot harvest enough resources to emit pulses. We can observe this fact in Fig.4 as a minimum at the origin. Lack of resources has a significant effect if more nodes operate concurrently, for instance the line
Figure 4: Pulse frequency \((p)\) for different background concentration \((b)\) and number of nodes \((n)\) for \(A = 0.5\)

\(n = 25\) in Fig.4 have zero pulse frequency for background concentration \(b = 0.1\) and \(b = 0.2\) because of the lack of the resources. Furthermore, for background concentration value \(b = 0.3\) not all of the 25 nodes but 9 of them are operational, as a consequence pulse frequency can be reached is very similar to \(n = 9\) value. Contrarily, for background concentration values greater than 0.3, all of the 25 nodes are operational. We can observe a maxima at the highest values of number of nodes and background concentration. To operate more nodes, the environment must provide more resources.

In the third set of tests, we monitored pulse frequency against pulse amplitude and number of nodes (4) (fig.5). Note that a fixed background concentration value is used during this set of simulations. Lines in Fig.5 represent different number of nodes values, the one at the bottom represents lowest number of nodes, whereas upper lines represent higher number of nodes values.

\[
p = f(A, n) \bigg|_{b=0.5}
\]

(4)

Pulses with higher pulse amplitude contain more resources than pulses with lower pulse amplitude. Similarly, the need for resources increases if more nodes concurrently operate in the network. However, concurrently operating nodes involve higher pulse emissions per unit time. A high pulse frequency can be achieved if a high number of nodes operate concurrently, and each node releases pulses with low pulse amplitude. Please note that, the operating environment
cannot feed an unlimited number of nodes, especially if they are emitting pulses with high pulse amplitude. This fact can be observed in Fig.5 as a minimum for the highest value of pulse amplitude. Furthermore, for number of nodes n = 25 and pulse amplitude $A = 0.9$, we still observe zero pulse frequency because of the lack of resources. For pulse amplitude $A = 0.8$, only 9 of 25 of the nodes are operational and resulting pulse frequency value is very similar to $n = 9$ case.

7. Conclusion and Future Work

Molecular communication presents fundamental differences with respect to traditional wireless communications. Among these, the use of molecules as information carrier is probably the most relevant one. As a consequence, an analytical framework that takes this unique characteristic into account is needed in order to analyse the performance of molecular communication nanonetworks.

This paper presents DIRECT, a networking model which can be used to understand the general properties of molecular communication nanonetworks. DIRECT models molecules as discrete entities, representing resources in a confined environment. According to this model, a nanonetwork could achieve an infinite network lifespan if proper resource harvesting mechanisms were applied, even though the network might be temporarily inactive during the harvesting periods.
As a result of this analysis, it has been observed that harvesting operations have a considerable effect over the signal measured by receivers in a molecular communication nanonetwork. For instance, both a higher background molecular concentration and a higher number of transmitting nodes cause an increase in the maximum data rate at which information can be successfully transmitted.

As future work, the capacity of DIRECT, and the upper and lower bounds of the network capacity for a given amount of resources will be investigated. Next steps will also consider the equations which establish a connection between the harvesting and receiving operations.

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