Nano Communication Networks 4 (2013) 181–188

Contents lists available at ScienceDirect

Nano Communication Networks

journal homepage: www.elsevier.com/locate/nanocomnet

DIRECT: A model for molecular communication nanonetworks based on discrete entities

Deniz Demiray [a,b,*], Albert Cabellos-Aparicio [a], Eduard Alarcón [a], D. Turgay Altilar [c], Ignacio Llatser [a], Luca Felicetti [d], Gianluca Reali [d], Mauro Femminella [d]

[a] Nanonetworking Center in Catalonia (N3Cat), Universitat Politècnica de Catalunya, c/Jordi Girona, 1-3, 08034 Barcelona, Spain

[b] Istanbul Technical University, Informatics Institute, ITU Ayazaga Campus, 34469 Maslak, Istanbul, Turkey

[c] Istanbul Technical University, Faculty of Computer & Informatics, ITU Ayazaga Campus, 34469 Maslak, Istanbul, Turkey

[d] Department of Electronic and Information Engineering, University of Perugia, Via G. Duranti 93, 06125 Perugia, Italy

ARTICLE INFO

Article history:
Received 3 January 2013
Received in revised form 19 August 2013
Accepted 20 August 2013
Available online 30 August 2013

Keywords:
Nanonetworks
Discrete resources
Confined operating environment
Molecular communication
Diffusion

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.

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 [2,24,23,15], 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 [20]. Diffusion-based molecular communication encompasses several techniques, such as calcium ion (Ca^{2+}) signaling [25], one of the most important communication mechanisms among living cells, and pheromonal communication [26].

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

* Corresponding author at: Istanbul Technical University, Informatics Institute, ITU Ayazaga Campus, 34469 Maslak, Istanbul, Turkey. Tel.: +90 2122857455.

E-mail addresses: demirayde@itu.edu.tr, ddemiray@gmail.com (D. Demiray), acabello@ac.upc.edu (A. Cabellos-Aparicio), eduard.alarcon@upc.edu (E. Alarcón), altilar@itu.edu.tr (D.T. Altilar), llatser@ac.upc.edu (I. Llatser), luca.felicetti@diei.unipg.it (L. Felicetti), gianluca.reali@unipg.it (G. Reali), mauro.femminella@unipg.it (M. Femminella).

1878-7789/$ – see front matter
http://dx.doi.org/10.1016/j.nancom.2013.08.004

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 [36,37]. 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 modeling 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 organized as follows. In Section 2, we provide the 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 analyzed. 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 [21]. 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 [9,8,28]. This may happen through the modulation of the released ions in terms of frequency, amplitude and spatial–temporal patterning [5,28,35]. 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 [21,17], 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 [33,29,35]. 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 [22]. 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 [10]), analogously to the extracellular concentration (1–2 mM), whereas the cytosolic concentration is very low, in the order of nM range (resting state: 100 nM). This means that the gradients across their membranes (ER and plasma membrane) are very similar [28,35,7].

The ER channels can be activated by second messengers (such as InsP3 and cADPr) [8] that promote the calcium release into the cytoplasm, with a following drop in the intra-organelle Ca^{2+} concentration of several hundred μM. The cytoplasmic 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 signaling is terminated, the Ca^{2+} ions re-uptake into the internal organelles [16].

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 μM [28].

Once the Ca^{2+} ions have triggered the desired behavior, 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 [35].

An important role in sequestering calcium ions from the cytosol and on intracellular signaling is covered by the Endoplasmic Reticulum and the Mitochondria, which are typically located in close proximity to each other [29,28,22]. 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 [12]. 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 [28,27]. Microscopy observations show that about 20% of the mitochondrial surface is in direct contact with the ER [22].

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 [24], whereas others use molecular motors [23], and ligand receptors [11].

Another group of researchers are focused on proposing models and defining capacities from an information theoretical perspective [3,4,32,31].

An energy model for molecular communications is introduced in [18], 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 [37]. [34] refers to the information capacity of such networks.

Compared to the research available in the 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. 1(a)) 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.

An unconfined operating environment (Fig. 1(b)) 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. 1(c)) 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.

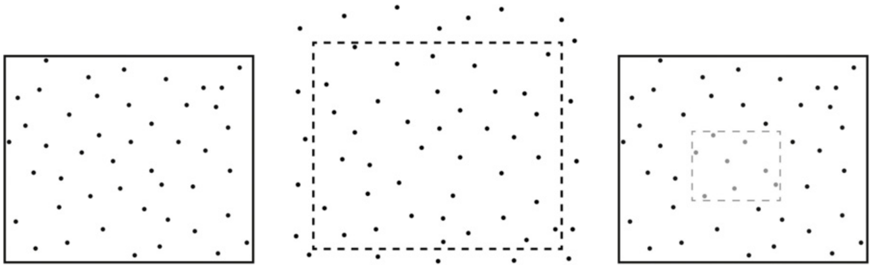
In this paper, we consider a confined operating environment in which the total amount of resources remains constant over the network lifespan. The constant number of resources in a confined operating environment can theoretically make the network indefinitely operational in terms of resources, if proper 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 nanomachines [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



(a) Confined environment. (b) Unconfined environment. (c) Locally unconfined environment.

Fig. 1. Different operating environments.

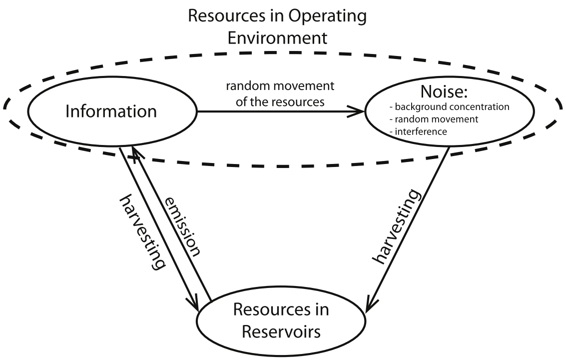


Fig. 2. Resource recirculation.

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 the information, or they can be considered as noise. The information in DIRECT is represented by a group of discrete resources, whereas in electromagnetic communication, the 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, the information is encoded using resources (emission), although a node can harvest resources from the information. There is a complete overlap between the 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 the information and noise. Thus, DIRECT proposes the 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. [13,19]. 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 Eq. (1), where D is the diffusion coefficient of the operating environment [6,30].

An interested reader can find more information about PBM in [13,19]:

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

Experiments are performed using N3Sim [14], 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.

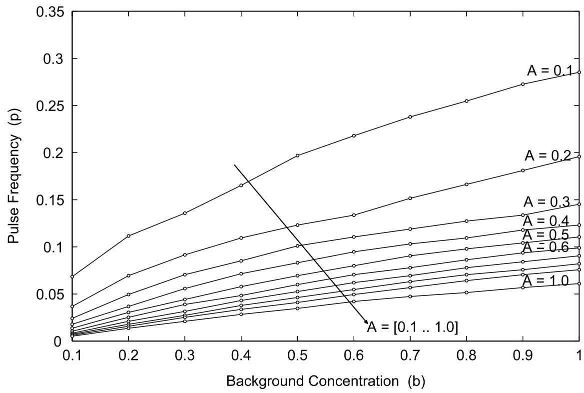


Fig. 3. *Pulse frequency* (p) for different *background concentration* (b) and *pulse amplitude* (A) for $n = 1$.

In the first set of experiments, we investigate the maximum *pulse frequency* as a function of *background concentration* and *pulse amplitude* Eq. (2), the results can be seen in Fig. 3. Please note that we used normalized values for parameters and metric, and we fixed the *number of nodes* to 1. Lines in Fig. 3 represent different *pulse amplitude* values, and they are arranged from the 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*:

$$p = f(b, A) \;\Big|_{n=1}. \tag{2}$$

As we fixed the *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*:

$$p = f(b, n) \;\Big|_{A=0.5}. \tag{3}$$

In the second set of tests, we monitored the *pulse frequency* against the *number of nodes* and *background concentration* Eq. (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 the higher *number of nodes* values.

Nodes in Fig. 4 are homogeneously spread over the environment, forming a grid shape, and they concurrently

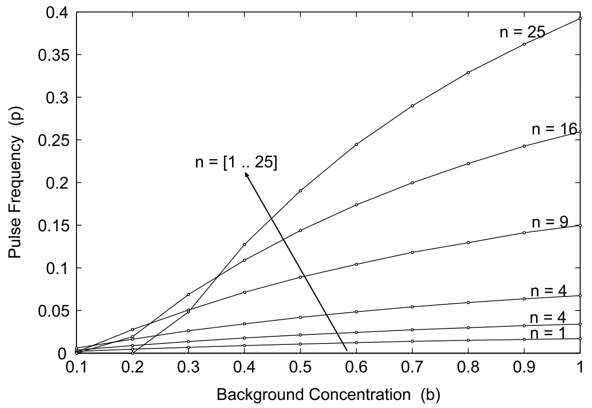


Fig. 4. *Pulse frequency* (p) for different *background concentration* (b) and *number of nodes* (n) for $A = 0.5$.

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.

The higher *number of nodes* values represent more nodes, concurrently emitting pulses, and they inherently increase *pulse frequency*. More nodes emit more pulses, and 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 $n = 25$ in Fig. 4 has zero *pulse frequency* for *background concentration* $b = 0.1$ and $b = 0.2$ because of the lack of the resources. Furthermore, for a *background concentration* value $b = 0.3$, only 9 out of the 25 nodes are operational; as a consequence, the pulse frequency in a scenario with 25 nodes is very similar to the case $n = 9$. 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 the *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* Eq. (4) (Fig. 5). Note that a fixed *background concentration* value is used during this set of simulations. Lines in Fig. 5 represent a different *number of nodes* values, the one at the bottom represents the lowest *number of nodes*, whereas upper lines represent the higher *number of nodes* values:

$$p = f(A, n) \Big|_{b=0.5} . \tag{4}$$

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 the *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 the 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 analyze 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.

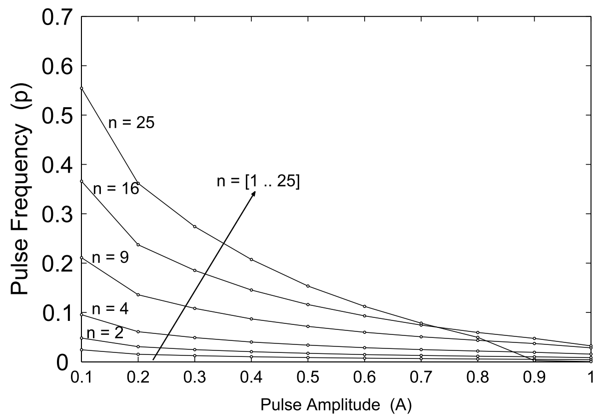


Fig. 5. *Pulse frequency* (p) for different *pulse amplitude* (A) and *number of nodes* (n) for $b = 0.5$.

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 the 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.

Acknowledgments

This work has been supported by the The Science Fellowships and Grant Programmes Department (BIDEB) of The Scientific and Technological Research Council of Turkey (TUBITAK).

References

[1] I.F. Akyildiz, F. Brunetti, C. Blázquez, Nanonetworks: a new communication paradigm, Computer Networks 52 (12) (2008) 2260–2279.
[2] I.F. Akyildiz, F. Fekri, R. Sivakumar, C.R. Forest, B.K. Hammer, Monaco: fundamentals of molecular nano-communication networks, IEEE Wireless Communications 19 (5) (2012) 12–18.
[3] B. Atakan, O.B. Akan, On molecular multiple-access, broadcast, and relay channels in nanonetworks, in: Proceedings of the Third International Conference on Bio-Inspired Models of Network, Information, and Computing Systems, Bionetics 2008, 2008.
[4] B. Atakan, O.B. Akan, Deterministic capacity of information flow in molecular nanonetworks, Nano Communication Networks 1 (1) (2010) 31–42.
[5] M.J. Berridge, P. Lipp, M.D. Bootman, The versatility and universality of calcium signalling, Nature Reviews Molecular Cell Biology 1 (2000) 11–21.
[6] W.H. Bossert, E.O. Wilson, The analysis of olfactory communication among animals, Journal of Theoretical Biology 5 (3) (1963) 443–469.
[7] F.L. Bygrave, A. Benedetti, What is the concentration of calcium ions in the endoplasmic reticulum? Cell Calcium 19 (6) (1996) 547–551. Pearson Professional, 1996.
[8] E. Carafoli, Calcium signaling: a tale for all seasons, Proceedings of the National Academy of Sciences, PNAS 99 (3) (2002) 1115–1122.
[9] M.A. Carrasco, E. Jaimovich, U. Kemmerling, C. Hidalgo, Signal transduction and gene expression regulated by calcium release from internal stores in excitable cells, Biological Research (ISSN: 0716-9760) 37 (4) (2004) Biol. Res., Santiago.
[10] E.F. Corbett, M. Michalak, Calcium, A Signaling Molecule in the Endoplasmic Reticulum? Elsevier Science, 2000. 0968-0004/00, PII: S0968-0004(00)01588-7.
[11] A. Einolghozati, M. Sardari, F. Fekri, Capacity of diffusion-based molecular communication with Ligand receptors, in: IEEE Information Theory Workshop, 2011, pp. 85–89.
[12] J. Garca-Sancho, The coupling of plasma membrane calcium entry to calcium uptake by endoplasmic reticulum and mitochondria, in: Physiology and Pathophysiology. Bioscience Birthday, Symposium for Ole Petersen. Cardiff, 6–7 March 2013.
[13] N. Garralda, I. Llatser, A. Cabellos-Aparicio, E. Alarcón, M. Pierobon, Diffusion-based physical channel identification in molecular nanonetworks, Nano Communication Networks 2 (4) (2011) 196–204.
[14] N. Garralda, I. Llatser, A. Cabellos-Aparicio, M. Pierobon, Simulation-based evaluation of the diffusion-based physical channel in molecular nanonetworks, in: IEEE Conference on Computer Communications Workshops, INFOCOM WKSHPS, 2011, pp. 443–448.
[15] A. Guney, B. Atakan, O.B. Akan, Mobile ad hoc nanonetworks with collision-based molecular communication, IEEE Transactions on Mobile Computing 11 (3) (2012) 353–366.
[16] A.M. Hofer, Another dimension to calcium signaling: a look at extracellular calcium, Journal of Cell Science 118 (2005) 855–862. http://dx.doi.org/10.1242/jcs.01705.
[17] Y.S. Kanwar, L. Sun, Shuttling of calcium between endoplasmic reticulum and mitochondria in the renal vasculature, Department of Pathology, Northwestern University, Chicago, Illinois.
[18] M.S. Kuran, H.B. Yilmaz, T. Tugcu, B. Ozerman, Energy model for communication via diffusion in nanonetworks, Nano Communication Networks 1 (2) (2010) 86–95.
[19] I. Llatser, E. Alarcón, M. Pierobon, Diffusion-based channel characterization in molecular nanonetworks, in: IEEE Conference on Computer Communications Workshops, INFOCOM WKSHPS, 2011, pp. 467–472.
[20] I. Llatser, A. Cabellos-Aparicio, E. Alarcón, Networking challenges and principles in diffusion-based molecular communication, IEEE Wireless Communications 19 (5) (2012) 36–41.
[21] I.A. Lukyanets, E.N. Yavorskaya, S.L. Tokar, E.A. Lukyanetz, Roles of the mitochondria and endoplasmic reticulum in calcium elevation during osmotic shock in adrenocortical cells, Neirofiziologiya/Neurophysiology 34 (2–3) (2002) 192–194.
[22] O. Martins de Brito, L. Scorrano, An intimate liaison: spatial organization of the endoplasmic reticulummitochondria relationship, The EMBO Journal 29 (2010) 2715–2723. European Molecular Biology Organization.
[23] M. Moore, A. Enomoto, T. Nakano, R. Egashira, T. Suda, A. Kayasuga, H. Kojima, H. Sakakibara, K. Oiwa, A design of a molecular communication system for nanomachines using molecular motors, in: Fourth Annual IEEE International Conference on Pervasive Computing and Communications Workshops, PERCOMW'06, 2006, pp. 554–559.
[24] T. Nakano, T. Suda, T. Koujin, T. Haraguchi, Y. Hiraoka, Molecular communication through gap junction channels, Transactions on Computational Systems Biology X (2008) 81–99.
[25] T. Nakano, T. Suda, M. Moore, R. Egashira, A. Enomoto, K. Arima, Molecular communication for nanomachines using intercellular calcium signaling, in: 5th IEEE Conference on Nanotechnology, July 2005, pp. 478–481.
[26] L. Parcerisa Giné, I.F. Akyildiz, Molecular communication options for long range nanonetworks, Computer Networks 53 (16) (2009) 2753–2766.
[27] A.B. Parekh, Mitochondrial Regulation of Store-Operated CRAC Channels, Elsevier, 2008 http://dx.doi.org/10.1016/j.ceca.2007.12.006.
[28] S. Patergnani, et al., Calcium signaling around mitochondria associated membranes (MAMs), Cell Communication and Signaling 9 (2011) 19.
[29] O.H. Petersen, A. Tepikin, M.K. Park, The endoplasmic reticulum: one continuous or several separate Ca^{2+} stores? Trends in Neurosciences 24 (5) (2001) 2001 Elsevier Science Ltd.
[30] J. Philibert, One and a half century of diffusion: fick, Einstein, before and beyond, Proceedings of Diffusion Fundamentals 4 (2005) 1–19.
[31] M. Pierobon, I.F. Akyildiz, A physical end-to-end model for molecular communication in nanonetworks, IEEE Journal on Selected Areas in Communications 28 (4) (2010) 602–611.
[32] M. Pierobon, I.F. Akyildiz, Information capacity of diffusion-based molecular communication in nanonetworks, Proceedings IEEE INFOCOM 59 (6) (2011) 506–510.
[33] J.W. Putney, Calcium Signaling, second ed., CRC Press, 2005.
[34] R. Rajesh, V. Sharma, P. Viswanath, Information capacity of energy harvesting sensor nodes, in: 2011 IEEE International Symposium on Information Theory Proceedings, July 2011, pp. 2363–2367.
[35] R. Rizzuto, et al., Ca^{2+} transfer from the ER to mitochondria: when, how and why, Biochimica et Biophysica Acta 1787 (11) (2009) 1342–1351. http://dx.doi.org/10.1016/j.bbabio.2009.03.015.
[36] A. Seyedi, B. Sikdar, Modeling and analysis of energy harvesting nodes in wireless sensor networks, in: 46th Annual Allerton Conference, Allerton House, Illinois, USA, 2008.
[37] S. Sudevalayam, P. Kulkarni, Energy harvesting sensor nodes: survey and implications, IEEE Communications Surveys and Tutorials 13 (3) (2011) 443–461.

Deniz Demiray was born in Istanbul in 1982. He graduated from Kocaeli University with a degree in Computer Engineering in 2005. He received a M.Sc. degree from Istanbul Technical University in 2008 in Computer Science. During October 2011–October 2012 he worked at Nanonetworking Center in Catalunya (N3Cat) at UPC as a visiting researcher, and joined N3Cat. He is currently pursuing a Ph.D. in Computer Science at Istanbul Technical University. His research interests are nanonetworking, molecular communication, nature inspired computing and swarm intelligence.

Albert Cabellos-Aparicio received a B.Sc. (2001), M.Sc. (2005) and Ph.D. (2008) degree in Computer Science Engineering from the Technical University of Catalonia (www.upc.edu). In 2004 he was awarded with a full scholarship to carry out Ph.D. studies at the Department of Computer Architecture, Technical University of Catalonia (UPC), Spain. In September 2005 he became an assistant professor of the Computer Architecture Department and as a researcher in the Broadband Communications Group (http://cba.upc.edu/). In 2010 he joined the NaNoNetworking Center in Catalunya (http://www.n3cat.upc.edu) where he is the Scientific Director. He is an editor of the Elsevier Journal on Nano Computer Network and member of the Project Management Committee of the LISPmob opensource initiative (http://lispmob.org). His main research interests are future architectures for the Internet and Nanonetworks.

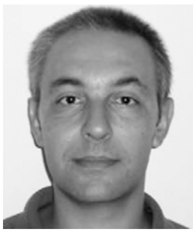
Eduard Alarcón received the M.Sc. (National award) and Ph.D. degrees (honors) in Electrical Engineering from the Technical University of Catalunya (UPC BarcelonaTech), Spain, in 1995 and 2000, respectively. Since 1995 he has been with the Department of Electronic Engineering at UPC, where he became Associate Professor in 2000. He is the scientific co-director of N3CAT, the center for Nanonetworks at UPC. During the period 2006–2009 he was Associate Dean of International Affairs at the School of Telecommunications Engineering, UPC. From August 2003 to January 2004, July–August 2006 and July–August 2010 he was a Visiting Professor at the CoPEC center, University of Colorado at Boulder, USA, and during January–June 2011 he was Visiting Professor at the School of ICT/Integrated Devices and Circuits, Royal Institute of Technology (KTH), Stockholm, Sweden. He has co-authored more than 250 international scientific publications, 4 books, 4 book chapters and 4 patents, and has been involved in different National, European and US (DARPA, NSF) R&D projects within his research interests including the areas of on-chip energy management circuits, energy harvesting and wireless energy transfer, and communications at the nanoscale. He is the PI of the Guardian Angels EU FET flagship project at UPC. He has given 25 invited or plenary lectures and tutorials in Europe, America and Asia, and was appointed by the IEEE CAS society as a distinguished lecturer for 2009–2010 and lectures yearly MEAD courses at EPFL. He is elected member of the IEEE CAS Board of Governors (2010–2013) and member of the IEEE CAS long term strategy committee. He was recipient of the Myril B. Reed Best Paper Award at the 1998 IEEE Midwest Symposium on Circuits and Systems. He was the invited co-editor of a special issue of the Analog Integrated Circuits and Signal Processing journal devoted to current-mode circuit techniques, and a special issue of the International Journal on Circuit Theory and Applications. He co-organized special sessions related to on-chip power management at IEEE ISCAS03, IEEE ISCAS06 and NOLTA 2012, and lectured tutorials at IEEE ISCAS09, ESSCIRC 2011, IEEE VLSI-DAT 2012 and APCCAS 2012. He was the 2007 Chair of the IEEE Circuits and Systems Society Technical Committee of Power Systems and Power Electronics Circuits. He was the technical program co-chair of the 2007 European Conference on Circuit Theory and Design—ECCTD07 and of LASCAS 2013, Special Sessions co-chair at IEEE ISCAS 2013, tutorial co-chair at ICM 2010 and ISCAS 2013, Demo Chair of BodyNets 2012, track co-chair of the IEEE ISCAS 2007, IEEE MWSCAS07, IEEE ISCAS 2008, ECCTD'09, IEEE MWSCAS09, IEEE ICECS'2009, ESSCIRC 2010, PwrSOC 2010, IEEE MWSCAS12 and TPC member for IEEE WISES 2009, WISES 2010, IEEE COMPEL 2010, IEEE ICECS 2010, IEEE PRIME 2011, ASQED 2011, ICECS 2011, INFOCOM 2011, MoNaCom 2012, LASCAS 2012, PwrSOC 2012, ASQED 2012, IEEE PRIME 2012, IEEE iThings 2012 and CDIO 2013. He served as an Associate Editor of the IEEE Transactions on Circuits and Systems—II: Express briefs (2006–2007) and currently serves as Associate Editor of the Transactions on Circuits and Systems—I: Regular papers (2006-), Elsevier's Nano Communication Networks journal (2009-), Journal of Low Power Electronics (JOLPE) (2011-) and in the Senior Editorial Board of the IEEE Journal on IEEE Journal on Emerging and Selected Topics in Circuits and Systems (2010-).

D. Turgay Altilar received his Ph.D. degree in 2002 from Queen Mary, University of London. He was involved with several EU projects related to parallel multimedia processing during his Ph.D. research. He has been assigned as an Associate Professor in 2012 at the Computer Engineering Department of Istanbul Technical University. Dr. Altilar's research interests are related to wireless sensor networks, cognitive radio, real-time systems, pervasive computing, parallel, distributed and grid computing. The current research interests are nanonetworking, routing protocol design in cognitive radio networks, data dissemination on multimedia sensor networks, MAC and routing protocol design for multichannel sensor networks, resource management Grid Computing and naturally tolerant parallel algorithm design and heterogeneous network-based GPGPU computing. He has served as technical program committee chair, technical program committee member, session and symposium organizer, and workshop chair in several conferences. Dr. Altilar is a member of IEEE.

Ignacio Llatser was born in Vinaròs (Spain) in 1984. In 2008, he graduated with a double M.S. degree in Telecommunication Engineering and Computer Science from the Technical University of Catalonia (UPC). He completed his Master Thesis on game-theoretical protocols for vehicular networks in the Laboratory for Computer Communications and Applications, at the École Polytechnique Fédérale de Lausanne (EPFL). In 2009, he joined the Nanonetworking Center in Catalunya (N3Cat) at UPC, where he is currently pursuing a Ph.D. in Computer Architecture. His research interests lie in the fields of nanonetworks, molecular communication and graphene-enabled wireless communications.

Luca Felicetti received the master degree in Information and Telecommunication Engineering from University of Perugia in 2011. Now, he is a Ph.D. student at the Department of Electronic and Information Engineering, University of Perugia. His current research interests focus on nano-scale networking and communications.

Gianluca Reali has been an Associate Professor at the University of Perugia, Department of Information and Electronic Engineering (DIEI), Italy, since January 2005. He received the Ph.D. degree in Telecommunications from the University of Perugia in 1997. From 1997 to 2004 he was a researcher at DIEI. In 1999 he visited the Computer Science Department at UCLA. His research activities include resource allocation over packet networks, wireless networking, network management, and multimedia services.



Mauro Femminella received both the master degree and the Ph.D. in Electronic Engineering from University of Perugia in 1999 and 2003, respectively. Since November 2006, he has been Assistant Professor at the Department of Electronic and Information Engineering, University of Perugia. His current research interests focus on nano-scale networking and communications, middleware platforms for multimedia services, location and navigation systems, and network and service management architectures for the future Internet.