Bio-Inspired Synchronization for Nanocommunication Networks

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***Abstract*—Nanonetworks are networks of devices inherently working and communicating at a scale ranging between one and hundreds of nanometers. The motivation behind these nanonetworks is to enhance the complexity and range of operation of the system, as the nanomachines that will be part of these networks have significant limitations in terms of size and power consumption. Neither classical communication schemes nor protocols used in conventional networks are valid in this new scenario. For instance, synchronization between nodes is a feature commonly required to build a network architecture. In this paper, we propose Quorum Sensing as a valid tool to achieve synchronization in a cluster of nodes of a nanonetwork by means of molecular communication, and in a distributed manner. Quorum Sensing is a mechanism by which bacteria coordinate their behavior, based on the emission and reception of molecules called autoinducers. The authors present the communication aspects of this natural phenomenon, as well as some simulation results that show the performance of Quorum Sensing-enabled entities. As a conclusion, some possible applications are outlined.**

***Index Terms*—Quorum Sensing; Synchronization; Nanonetworks; Bio-inspired; Molecular Communication;**

I. INTRODUCTION

Nanotechnology promises new solutions for many applications in the biomedical, industrial and military fields, as well as in consumer and industrial goods [2]. Recent breakthroughs in nanotechnology are allowing the development of nanomachines, which are devices in a scale ranging from one to hundreds of nanometers. At this scale, novel nanomaterials and nanoparticles show new properties and behaviors not observed at the macroscopic level [3]: the incredibly reduced size of nanomachines enhances their bio-compatibility, thus enabling the use of nanomachines in non-invasive intrabody networks, for instance. Also, nanosensors are able to detect chemical compounds in extremely low concentrations [19].

On the other hand, nanomachines have significant limitations related to their size. However, communication between devices underlying in the nanoscale greatly expands the possible applications, increasing the complexity and range of operation of the system [2]. The resulting nanocommunication networks (nanonetworks) can be used to coordinate tasks and realize them in a distributed manner, covering a greater area and reaching unprecedented locations.

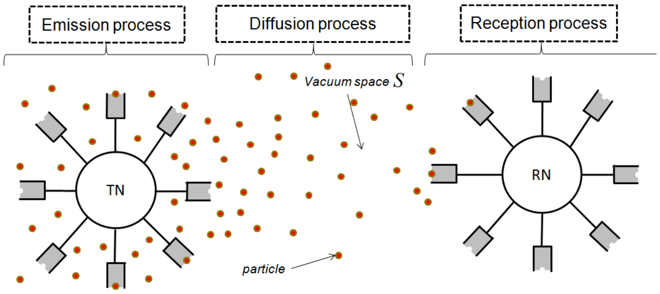

Fig. 1. The three steps present in diffusion-based molecular communication.

Molecular communication is a novel and promising way to achieve communication between nanodevices by encoding messages inside molecules. Three processes appear in this new paradigm: emission, propagation, and reception. First, emitters release molecules as a response to a certain command. These particles propagate through the medium either by following pre-defined pathways, guided diffusion flows, or simply by means of spontaneous diffusion [18]. Finally, receivers count on specific signal transducing mechanisms that react to specific particles. Solutions have been proposed for short-range (distances up to micrometers) [22], medium-range (up to millimeters) [8] and long-range (up to several meters) [16] nanonetworks. Figure 1 shows the processes that are present in molecular communication based on spontaneous diffusion [18].

Given the change of scenario, the classical communication paradigms are no longer valid. The modeling of different molecular communication mechanisms, or the development of new architectures and protocols for nanocommunication networks are some of the new research challenges.

For instance, synchronization between nodes is a feature commonly required to build any network architecture. A considerable effort has been put in order to achieve time synchronization in different scenarios, e.g. wireless sensor networks [10], [20], [13]. However, to the best of our knowledge, this research topic has not been addressed in the case of nanocommunication networks. Synchronization between the elements of a nanonetwork is not easy to accomplish, mainly due to the complexity and energy constraints of nanodevices. Moreover, information propagates at very low speeds in molecular communication, rendering the traditional solutions invalid for this scenario.

The main contribution of this paper is the proposal Quorum Sensing as a valid tool to achieve synchronization in a cluster of nodes of a nanonetwork, by means of molecular communication. We followed the bio-inspired approach, as it has successfully provided robust and adaptable solutions in a wide range of topics (see [14] for a comprehensive review). Briefly stated, Quorum Sensing is a mechanism by which bacteria coordinate their behavior, based on the emission and local reception of molecules called autoinducers. We strongly believe that this phenomenon can be applied to nanomachines with communication capabilities, in order to enable coordination with the nodes in its close environment.

The rest of the paper is organized as follows. In Section 2, further details about the principles of Quorum Sensing can be found. Moreover, we point out some communication aspects about Quorum Sensing. In Section 3, the performance results of some simulations are evaluated. Finally, the conclusions lead to the proposal of several applications for Quorum Sensing. Complementary work, which focuses on the modeling of Quorum Sensing bacteria by means of automata theory, can be found in [1].

II. QUORUM SENSING

Quorum Sensing is a biological process that enables bacteria to communicate using secreted signaling molecules called autoinducers [9]. The concentration of these autoinducers in the environment increases proportionally as the population of bacteria grows. This way, bacteria are able to sense their cell population density, making them capable to regulate their gene expression in a collective manner. Thus, by means of Quorum Sensing, different groups of bacteria “exhibit cooperative behavioral patterns” [7], as the gene expression determines the behavior and functions of a living organism.

Quorum Sensing is a widespread phenomena in the bacterial world, and its importance is indisputable. Actually, it has been described as “the most consequential molecular microbiology story of the last decade” [11]. The reason behind this ubiquity in the bacterial world is considered to be evolutionary. Quorum Sensing enables the control of bacterial functions or processes that are unproductive when undertaken by an individual bacterium but become effective when undertaken by the group; processes that are generally crucial for the species survival.

Many behaviors controlled by Quorum Sensing can be found in the literature [9], [26]. For instance, bacteria species commonly need to activate virulence factors in order to survive or spread. If a bacterium alone launches an attack, host’s defenses will eliminate the threat immediately. Whereas if a large group of bacteria launches an attack, the success rate rises enormously. Several other examples of behaviors that are controlled by Quorum Sensing are: motility, DNA processing, antibiotic biosynthesis, biofilm formation or bioluminescence, as seen in species such as the *Salmonella, Vibrio, Bacillus* and *Escherichia coli* families.

Biologists have also made remarkable discoveries about the way of quenching Quorum Sensing by means of hampering the diffusion of autoinducers [9], [6], [5]. For example, some enzymes act as autoinducer antagonists, destroying them and avoiding the bacteria to reach quorum. This way, the development of new types of antibiotics can be addressed, due to the direct connection of Quorum Sensing with virulence factors in some species of bacteria, and the apparition of mutant varieties of bacteria resistant to antibiotics [23].

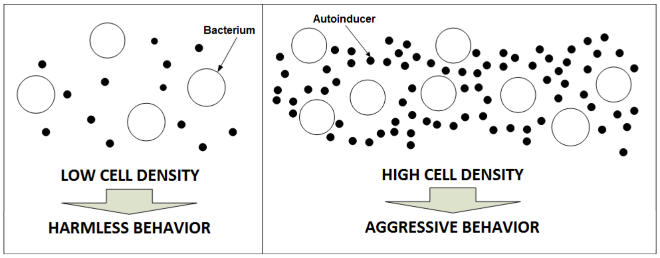

Fig. 2. Quorum Sensing behavior for low and high cell densities.

In our case, we believe that Quorum Sensing is a powerful tool that can be used to coordinate the course of action of several nanomachines. The Quorum Sensing mechanism is a way to achieve global synchronization by means of molecular communication, in a fully distributed manner. Moreover, bacteria follow a rather simple algorithm with no apparent need of configuration, two characteristics that might be critical if we take into account the intrinsic limitations of nanomachines.

A. Principles and Mechanisms

Quorum Sensing is achieved through the production, transmission, and subsequent reception of and response to *threshold* concentrations of *autoinducers* [4]. Indeed, bacteria produce and emit a special kind of particles, which diffuse in the medium and reach other bacteria. As their name implies, autoinducers have the ability of triggering the release of more particles of the same kind, when received. Owing to this property, there exists a certain relationship between the population of bacteria and the extracellular concentration of autoinducers. If, at a certain point, this concentration reaches a critical threshold, it means that a concrete population has been attained. That situation is sensed by the group, which responds with a population-wide change of behavior.

The main qualitative reasoning behind the global activation of the bacteria colony is as follows. Generally, the tendency of the molecules is to diffuse from areas of higher concentration to areas of lower concentration [17]. Thus, as time passes, the inhomogeneity in terms of autoinducer concentration decreases, even in presence of punctual emissions. In the end, all the nodes will be sensing a similar concentration and will activate (or not) at a similar time.

Thresholds: As commented above, Quorum Sensing bacteria activate when the concentration of autoinducers surpasses a fixed threshold. Actually, there exist two critical levels after which bacteria show different behaviors. Namely:

- **Activation Threshold:** the colony performs a population-wide regulation of the gene expression upon reaching a certain critical concentration of autoinducers. Therefore, all the bacteria of the colony will change its behavior at the same time. From now on, we will refer to this critical value as "activation threshold".

- **Autocatalytic Threshold:** which is related to the emission of autoinducers. It has been observed that bacteria synthesize autoinducers at a rate called nominal or basal rate, when the cell density is low. However, as the bacterial population increases, bacteria are reported to synthesize autoinducers by means of autocatalysis, emitting them at a dramatically higher rate. We consider the "autocatalytic threshold" as the level beyond which bacteria start secreting autoinducers at this second rate.

Autocatalysis is a widely known type of chemical reaction. The reaction product is itself the catalyst for that reaction, thus creating a positive feedback loop. This serves as an explanation of how an autoinducer triggers the synthesis and emission of more particles of the same kind, and how the rate of emission in the autocatalytic phase is much higher than the nominal rate.

B. Combination of Quorum Sensing Systems

The number of species of bacteria living in the human digestive tract or any other environment is extremely high, and some studies suggest that they live in complex and highly ordered communities. For instance, some species that use Quorum Sensing need information about their population and the population of other species in order to adjust their behavior, like in the case of competence regulation. Actually, it has been reported that some bacteria are able to react to different autoinducers sequentially or in parallel, constructively or destructively. This means that some species contain several Quorum Sensing systems. Some examples are:

- *Pseudomonas aeruginosa*: this species makes use of two overlapping systems. Moreover, these systems act in series to regulate two overlapping subsets of genes, meaning that different changes of behavior are accomplished sequentially [21].
- *Vibrio Harveyi*: in this case, bacteria are able to sense two different types of autoinducers, the reaction of which converge to regulate a common set of target genes [15]. The key point is that both autoinducers are complementary in terms of the reaction that triggers the change of behavior. Consequently, bacteria activate upon the activation of both Quorum Sensing systems.
- *Bacillus subtilis*: the competence behavior in this species of bacteria is controlled by two parallel Quorum Sensing systems. In contrast to the previous case, the accepted autoinducers have inverse chemical consequences inside the cell, meaning that one is able to cancel the other. Therefore, the competence behavior is controlled by the level of autoinducers "A" only if the other type, "B", is not sensed [12].

These examples make us think that Quorum Sensing schemes can be combined to implement complex interactions between groups of nanomachines, significantly expanding the possible applications of these systems. Moreover, the series or parallel configurations are perfect for the engineering or assembly of distributed and synchronized logic circuitry for systems based on the principles of Quorum Sensing. For instance, if the levels of autoinducers A and B are seen as digital 'high' and 'low' levels, the parallel systems described above would both act as AND gates of the two levels (AB for the *Vibrio harveyi* family and $A\overline{B}$ for *Bacillus subtilis*), achieving a synchronized response of a group of entities. However, inspecting this possibility is out of the scope of this paper and remains as future work.

C. Communication Aspects

The Quorum Sensing phenomenon can be regarded as a communication mechanism. Each bacterium encodes the message through the synthesis of autoinducers and transmits it by means of secretion. The autoinducers propagate following spontaneous diffusion until they arrive to a destination, which will receive it through ligand-binding mechanisms.

One of the differences of molecular communication with respect to the traditional communication paradigms is the concept of *global message*. Molecular messages can be achieved by the accumulation of the contributions of several transmitters, in a process of inherent data aggregation. In the particular case of Quorum Sensing, the global message is encoded in the concentration of particles, which is later decoded and understood as a node density. From the communication perspective, we could define Quorum Sensing as a *collective communication*.

Also, special cases of noise, signal attenuation, and interferences have to be identified when considering Quorum Sensing as a particular case of molecular communication. For example, autoinducer-destroying enzymes can be considered a source of noise, since they diminish the concentration of autoinducers that a node will sense, therefore affecting the global message.

Addressing: Addressing in Quorum Sensing-enabled networks is directly connected with the autoinducers. The chemical structure of these particles determines which receivers will be able to sense them. On one hand, a huge variety of autoinducers enable *intraspecies cell to cell communication*, meaning that only nodes of the same species of the transmitter will be capable of receiving the message. From the addressing perspective, the address encoded in this type of autoinducers is inherently multicast. On the other hand, some particles are considered as some kind of universal signals (i.e. LuxS [4]), enabling *interspecies cell to cell communication*. The address encoded in this type of autoinducers can be considered as broadcast, as the message can be received by any node in the environment.

III. SIMULATION RESULTS

In this paper, we have presented the phenomenon of Quorum Sensing and proposed it as a valid option in order to achieve global synchronization between the nodes of a nanonetwork. This section is devoted to show the delay and percentage of activation for a group of nodes that perform Quorum Sensing.

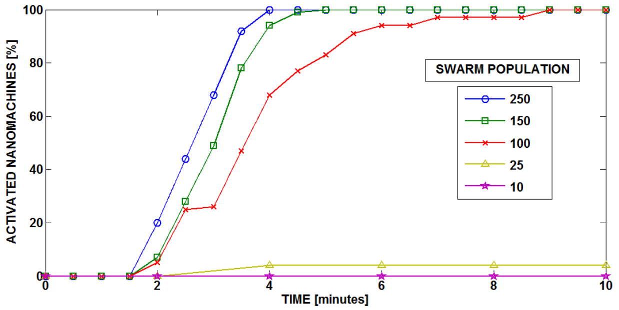

Fig. 3. Evolution over time of the percentage of activated nanomachines by means of Quorum Sensing, for different node densities.

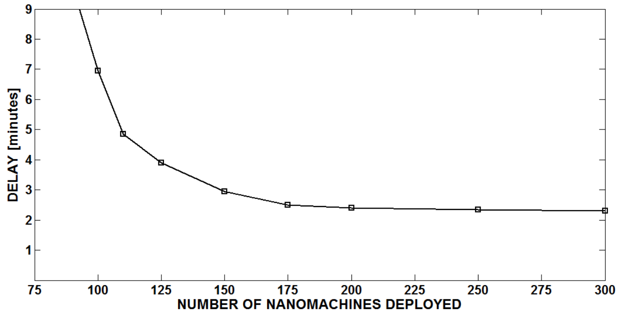

Fig. 4. Activation delay of nanomachines performing Quorum Sensing as a function of the node density.

This performance results are obtained through simulation, using the model developed in [1].

The scenario is the following: a certain number of nanomachines is deployed in a fluidic medium, close to a group of infectious agents. The nanomachines are able to perform Quorum Sensing by secreting and sensing concentrations of autoinducers. Upon activation, these nanomachines will release a drug in order to combat the infection. The objective is to extract conclusions about the activation of the “swarm” of nanomachines, as a function of the number of nodes deployed. Other parameters that could affect the activation of the swarm remain fixed, e.g. medium characteristics or activation threshold of each node.

The simulator introduces a given number of nanomachines in a bounded space of fixed size and keeps track of their state. Basically, the states considered are “non-activated” or “activated”, depending on the level of autoinducers sensed. Obviously, the simulator has to calculate the diffusion of particles in order to monitor the concentration of autoinducers in the environment, so that the state of each nanomachine can be determined. The diffusion of particles is implemented by using the Fick’s Laws of diffusion [17].

A. Activation

The Quorum Sensing principles imply that a given number of nodes is needed in order to reach the minimum concentration of autoinducers required to activate the whole cluster. In our case, this behavior has been indeed identified in the simulations, as shown in Figure 3. The percentage of activated nanomachines is represented as a function of time, for different populations. Since the simulation space dimensions are fixed, an increase in population means an increase in node density.

We can observe that the percentage of activation is negligible for low node densities (swarms of 10 or 25 nanomachines). On the other hand, the group reaches full activation when the number of deployed nanomachines is bigger (over 100 clustered units). Moreover, in the cases of 100% activation of the colony, the delay is observed to drop as the number of arranged nanomachines increases. The reason behind that behavior is that while the activation threshold remains fixed, the concentration of autoinducers will increase faster due to the bigger number of nanomachines in the environment. In light of these results, it seems that Quorum Sensing shows good properties in terms of scalability.

B. Delay

We define the activation delay as the time elapsed between the first autoinducer secretion and the full activation of the group of nanomachines. As it has been pointed out above, there is a connection between this delay and the node density, for a given activation threshold. The behavior of the activation delay is shown in Figure 4.

Coherently with the definition provided, cases in which full activation is never reached will yield an infinite delay. This explains the asymptotic behavior of the delay curve when the population of deployed nanomachines is low. Another interesting result is that the delay of the process decreases if the number of nanomachines deployed is increased. As pointed out above, the concentration of autoinducers will increase faster due to the bigger number of nanomachines in the environment, thus surpassing the fixed activation threshold in less time. Finally, the delay has a lower limit that is related to the capacity of nanomachines to switch from emission to sensing states. More details about this can be found in [1].

In conclusion, we could shorten the activation delay by deploying bigger swarms, resulting in a faster synchronization and actuation. However, it remains unclear if the cost of manufacturing and deploying these nanomachines will be affordable. A compromise between these two factors must be reached, if the results shown in Figure 4 were to be confirmed through physical implementation.

IV. CONCLUSIONS AND FUTURE WORK

In this paper, we have described Quorum Sensing and determined its potential main use in the nanonetworking context. The phenomenon is quite simple: bacteria emit autoinducers and react to them *(1)* by secreting more autoinducers and *(2)* by activating when the particle concentration reaches a certain threshold, which is encoded in the bacterium’s DNA. Despite of its simplicity, this methodology enables the coordination of colonies of bacteria in a decentralized manner. The solution is robust, scalable, and energy efficient. For instance, if we consider that bacteria consume energy when they secrete autoinducers, the presence of an autocatalytic threshold inherently protects the cells of spending more energy than needed when they are isolated.

In light of these features, several applications inspired in Quorum Sensing have been proposed in computer networks. In [24], Quorum Sensing has been proposed to coordinate the behavior among multiple instances of a computer worm clustering. In [25], a clustering algorithm featuring based on Quorum Sensing is depicted.

In our case, we strongly believe that Quorum Sensing is an efficient method to achieve global synchronization in a way that nodes only interact with their close environment. The simulation results have shown how a group of nanomachines that perform Quorum Sensing activates or not depending on its population. Moreover, the system shows a good behavior in terms of scalability, as the activation delay is even reduced when the number of nanomachines deployed increases. Nonetheless, many biological aspects regarding Quorum Sensing are still relatively unknown and have to be studied in depth to fully understand this phenomenon. A detailed study of those aspects will enable the obtaining of more reliable results.

Some concrete applications could benefit from the achievement of coordination between the nodes of a nanonetwork. As commented in Section II-B, Quorum Sensing schemes can be combined to implement more complex interactions between nanomachines, significantly expanding the possibilities of these systems. Our future work will be focused on developing Quorum Sensing-based solutions for sensing reliability, molecular signal amplification and detection of complex events on molecular communication networks. For example, sensing reliability consists on using Quorum Sensing to determine that a certain number of nodes have detected the same event. This process might result in a decrease of false-positive results, given the redundancy applied to the detection.

As Quorum Sensing relies on the emission and reception of molecules, we have intuitively considered that it fits perfectly as a synchronization solution for molecular communication networks. Nevertheless, we envisage that the principles of Quorum Sensing will provide useful insights in order to develop novel synchronization or reliability techniques in other scenarios, such as wireless sensor networks. This point will be also addressed in future work.

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