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Nanonetworking Center in Catalunya

Automata Modeling of Quorum Sensing for Nanocommunication Networks

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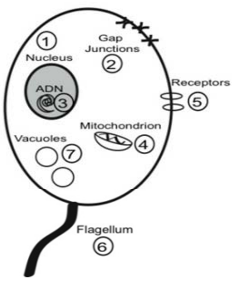
- Quorum Sensing
- Automata Modeling of Quorum Sensing Bacteria
- Nanomachine Design Based on Quorum Sensing Bacteria
- Concluding Remarks

Introduction: Nanotechnology and Nanomachines

I. F. Akyildiz, F. Brunetti, and C. Blázquez, ***"Nanonetworking: A New Communication Paradigm,"*** Computer Networks (Elsevier) Journal, Vol. 52, pp. 2260-2279, August, 2008.

- ***Nanotechnology*** is enabling the development of devices in a scale ranging from one to a few hundred nanometers.
- A ***nanomachine*** is the most basic functional unit, which is consisting of nanoscale components and which is able to perform a specific task at nano-level, such as computing, data storing, sensing or actuation.



Introduction: Interaction between Nanomachines

- WHY?

  Due to the reduced size of the nanomachines, their limitations are clear:

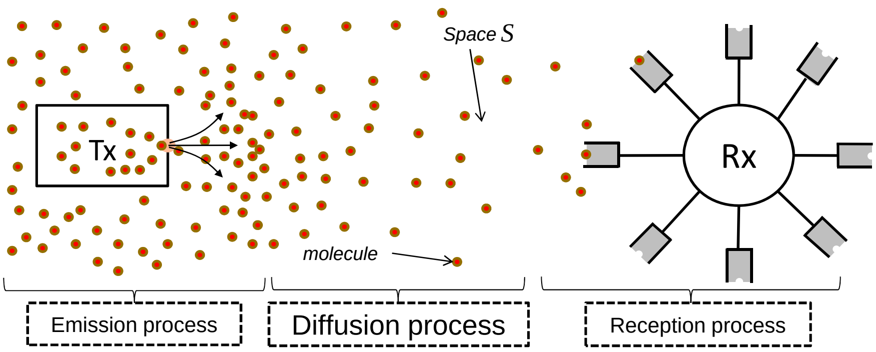
  - Range
  - Complexity

  NaNoNetworks expand the possibilities of nanomachines, increasing the complexity and range of operation of the system.

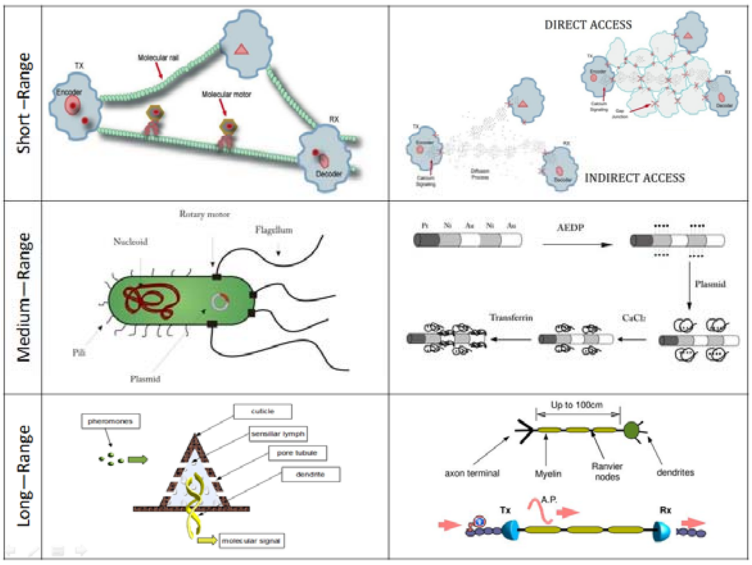
- HOW?
  - Molecular Communication

Introduction: Molecular Communication (I)

I. F. Akyildiz, F. Brunetti, and C. Blázquez, ***"Nanonetworking: A New Communication Paradigm,"*** Computer Networks (Elsevier) Journal, Vol. 52, pp. 2260-2279, August, 2008.
M. Pierobon, I. F. Akyildiz, **" A Physical End-to-End Model for Molecular Communication in Nanonetworks,"** IEEE Journal of Selected Areas in Communications (JSAC), May 2010.



Introduction: Molecular Communication (II)



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Quorum Sensing

J. Henke and B. Bassler, **"Bacterial social engagements,"** *Trends in Cell Biology*, vol. 14, 2004, pp. 648-656.

- ### What?

  Quorum Sensing is a mechanism used by bacteria to coordinate their behavior in a colony, as a function of their population.

- ### Why?

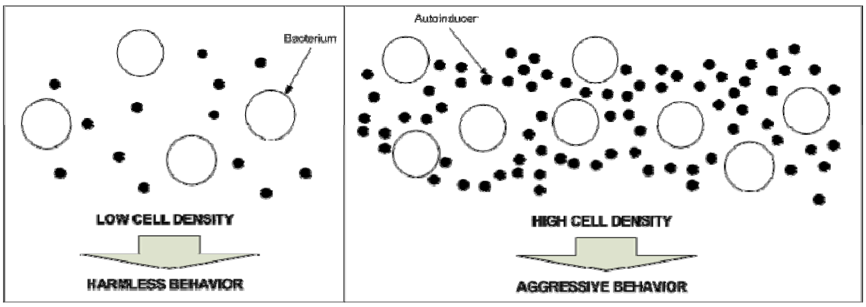
  Processes controlled by Quorum Sensing are unproductive when undertaken by an individual bacterium but become effective when undertaken by the group.

- ### How?

  Quorum Sensing is achieved through the production, release, and subsequent detection of and response to a threshold concentration of ***autoinducers.***

Quorum Sensing: Principles and Mechanisms (I)

- When the population of bacteria grows, the extracellular concentration of autoinducers increases as well.
- If this concentration reaches the activation threshold, it means that a certain population has been achieved, and the group responds to it with a population-wide change of behavior.



Quorum Sensing: Principles and Mechanisms (II)

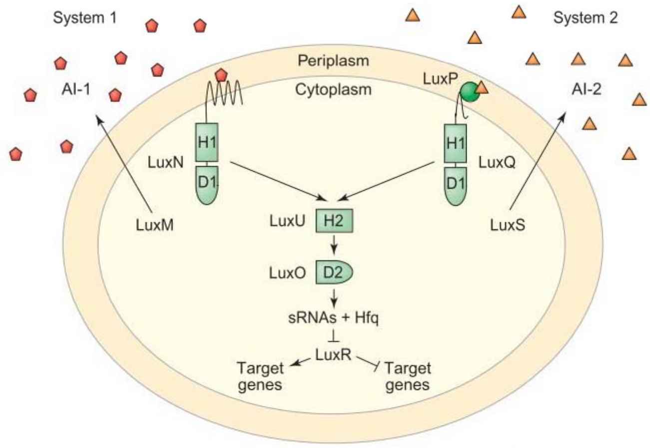
- Autoinducers are the key of the process.
- Tiny molecules (smaller than 1nm) that trigger an autocatalytic reaction: trigger the release of more particles of the same kind.
- There is a vast variety of autoinducers, enabling:
  - ***Intraspecies communication:*** when only bacteria of one species is able to receive that autoinducer.
  - ***Interspecies communication:*** when chemosensors of many species of bacteria are able to sense that autoinducer *(LuxS).*

Quorum Sensing: Complex Systems

- Some bacteria count on more than one Quorum Sensing system.
- For instance, *vibrio harveyi* bacteria activate only with the presence of two different types of autoinducers at the same time.
- Nanomachines can mimick this feature to achieve a higher level of complexity.

Quorum Sensing: Complex Systems (II)

J. Henke and B. Bassler, **"Bacterial social engagements,"** *Trends in Cell Biology*, vol. 14, 2004, pp. 648-656.



Quorum Sensing: Communication Aspects

- Quorum Sensing is a special case of Molecular Communication.
- All bacteria are transmitters and receivers.
- The message is collective, modulated by the concentration of autoinducers in the environment.
- The message is encoded in the chemical composition of those autoinducers.

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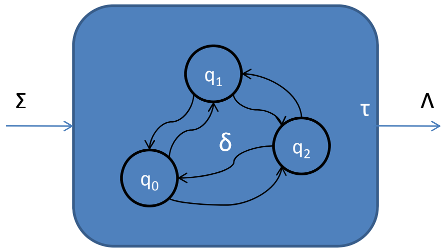
Automata Modeling: Motivation

- The need for a functional model of Quorum Sensing bacteria (not biological model).
- The need for a model that integrates Quorum Sensing and the behavior after reaching quorum.
- The need for a model easily implementable to use it in future nanomachines and coordinate their actions.

Automata Modeling: Definitions

- A Moore machine is a Finite State Machine represented by the six-tuple {Q, Σ, Λ, δ, τ, q_0}.
  - Q: finite set of internal states.
  - Σ: finite alphabet of inputs.
  - Λ: finite alphabet of outputs.
  - δ: transition function.
  - τ: output function.
  - q_0: inital state.



Automata Modeling of Quorum Sensing Bacteria (I)

- The alphabet of inputs maps different levels of concentration of autoinducers sensed by the bacteria. **Σ**

- The alphabet of outputs models different signals that modify the emission of autoinducers, mainly. **Λ**

- We will divide the model in two parts:
  - **Pre-Quorum section:** in which the bacteria have not reached the critical population to activate.
  - **Post-Quorum section:** after reaching quorum, bacteria activate their “aggressive” behavior.

Automata Modeling of Quorum Sensing Bacteria (II)

PRE-QUORUM SECTION

- In the pre-quorum section the bacteria:
  - **Sense the environment:** in order to know the concentration of autoinducers. *(S states)*
  - **Emit autoinducers:** in order to let the other bacteria be aware of one's presence. *(E states)*
- The emission of autoinducers depends on the amount sensed.
  - **Basal rate.** *(state E1, output y1)*
  - **Autocatalytic rate.** *(state E2, output y2)*
- The transitions are selected based on that dependance, leaving the section when the activation threshold is surpassed.

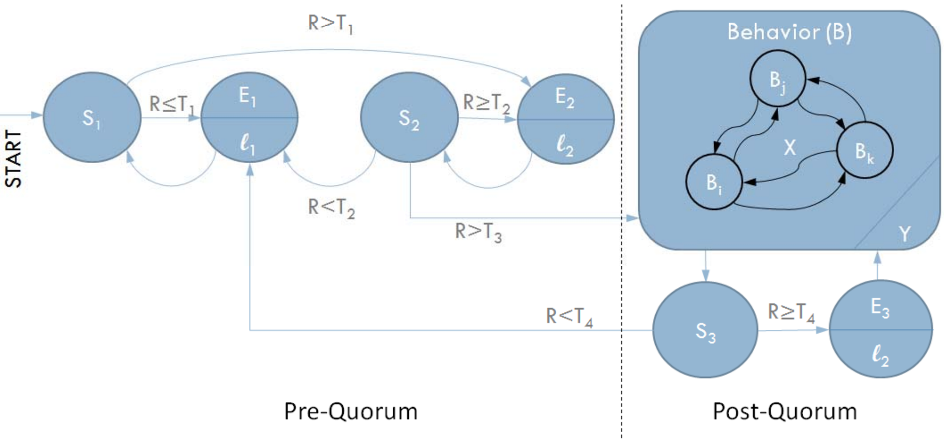
Automata Modeling of Quorum Sensing Bacteria (III)

POST-QUORUM SECTION

- In the post-quorum section the bacteria:
  - **Activate their collective behavior.** *(B states)*
  - **Sense the environment (***S state)*
  - **Emit autoinducers.** *(E state)*
- The collective behavior has to be modeled for each case (e.g. virulence, bioluminiscence).
- Sensing and emission states help to deactivate the new behavior if the population falls.

Automata Modeling of Quorum Sensing Bacteria (IV)

COMPLETE MODEL



Simulations of Quorum Sensing Bacteria

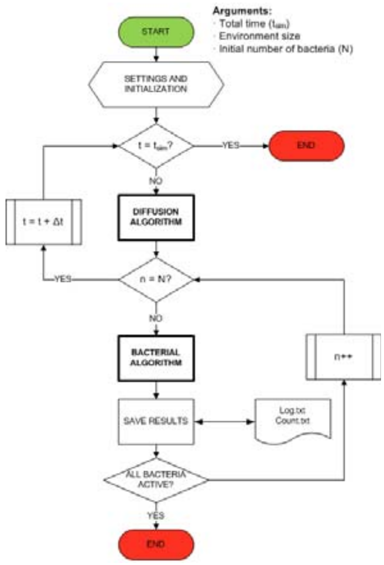
- The diffusion of autoinducers in the environment is a key factor in Quorum Sensing.
- It is modeled following Fick's second law:

$$\frac{\partial c(\bar{x},t)}{\partial t} = D\,\nabla^2 c(\bar{x},t)$$

- To implement it, we need apply the finite differences method:

$$\frac{c(\bar{x},t+\Delta t)-c(\bar{x},t)}{\Delta t} = D\,\frac{c(\bar{x}-\Delta\bar{x},t)-2c(\bar{x},t)+c(\bar{x}+\Delta\bar{x},t)}{(\Delta\bar{x})^2}$$

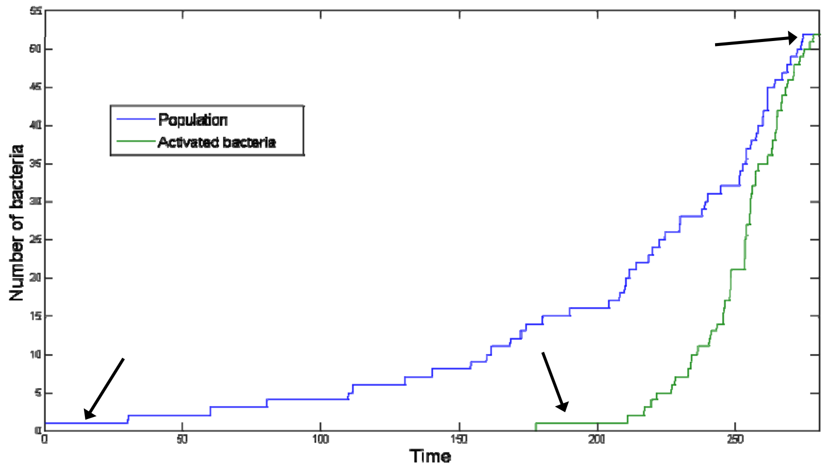
Simulations of Quorum Sensing Bacteria (II)



- DIFFUSION ALGORITHM
  - Implementation of second Fick's Law of diffusion.
- BACTERIAL ALGORITHM
  - Implementation of the Moore machine presented + reproduction.

Results (I)

VALIDATION



Results (II)

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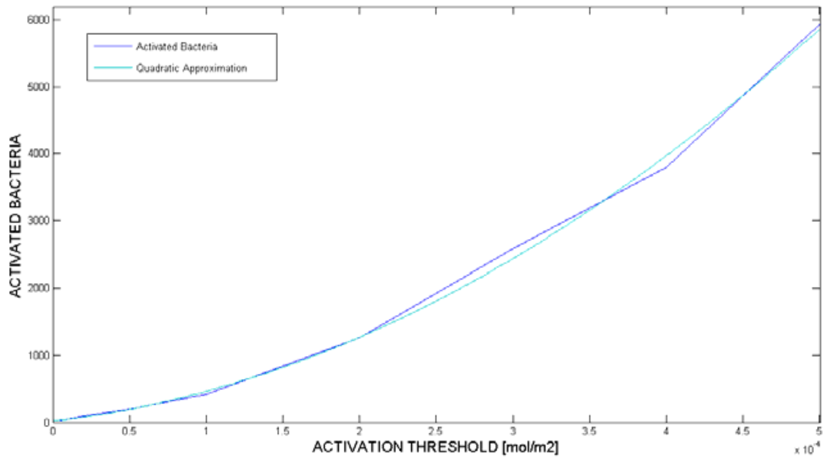
ACTIVATION THRESHOLD



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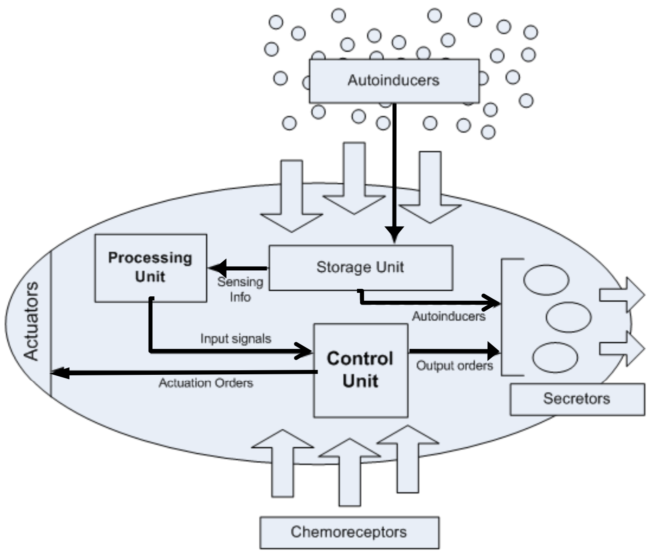
Architecture for Quorum Nanomachines



Implementation of Quorum Nanomachines

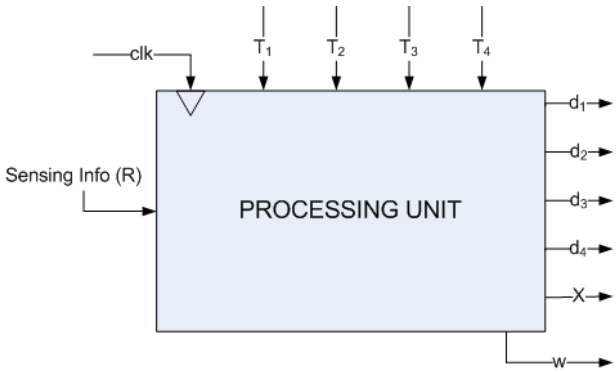
- Collective Activity Synchronization
- Collective actuation after Localized Sensing

Implementation of Quorum Nanomachines

- **Collective Activity Synchronization**
  - **Direct application of Quorum Sensing**
    - **Tissue Repairing**
    - **Drug Release**
- Collective actuation after Localized Sensing

Collective Activity Synchronization: Processing Unit

- The outputs of the PU are inputs of the CU:
  - ***d_{1-4}:*** comparison of the concentration sensed (R) with different thresholds (T_{1-4}).
  - ***w:*** waiting signal.

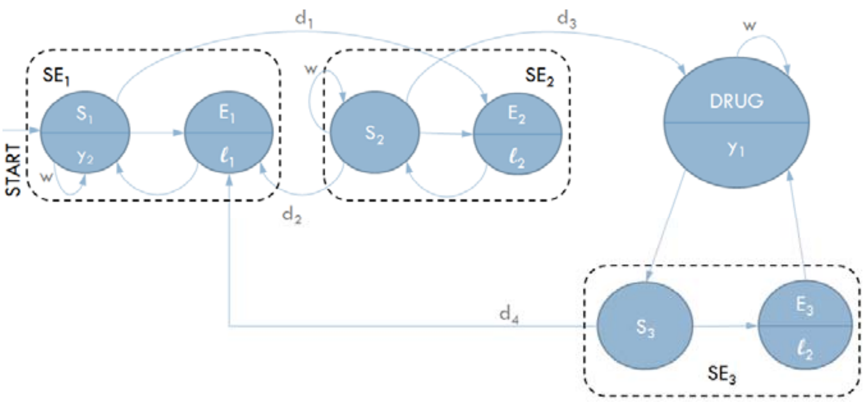


Relaxation Time

- Bacteria have ways to differentiate their own autoinducers from autoinducers released by other individuals. Nanomachines do not.
- It is an important issue to avoid erroneous activations.
- Nanomachines **NEED TO WAIT** until their autoinducers diffuse away before sensing the environment again.
  - HOW?
    - With the wait signal.
  - HOW MUCH?
    - $t_{MIN} \approx (\frac{8\pi p}{3})^{\frac{2}{3}} \frac{R^2}{4\pi D}$

Collective Activity Synchronization: Control Unit

- Modifications:
  - Use of the waiting signal to implement relaxation time.
  - Post-Quorum states adapted to a specific case.

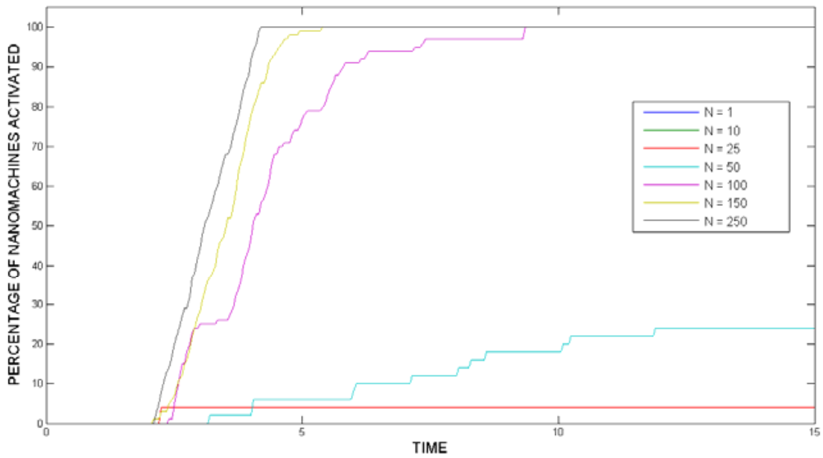


Collective Activity Synchronization: Simulations

- Several differences with the simulations involving bacteria:
  - Deployment of a given number of nanomachines.
  - No reproduction.
  - Application of post-Quorum behavior.

Collective Activity Synchronization: Results

VALIDATION (pre-Quorum)



Collective Activity Synchronization: Results (II)

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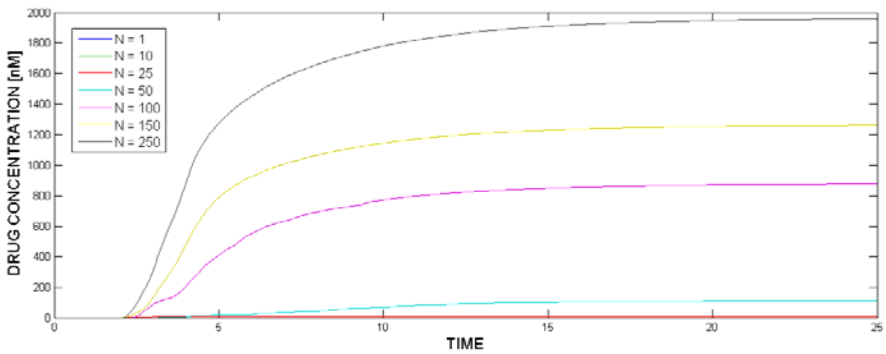
VALIDATION (post-Quorum)



Collective Activity Synchronization: Results (III)

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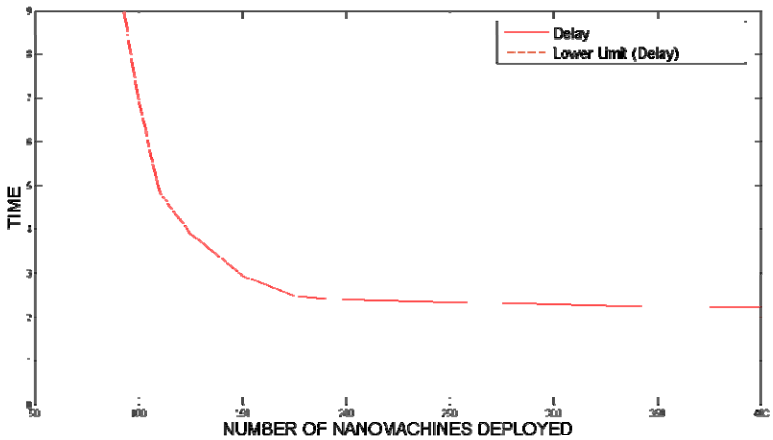
DELAY OF ACTIVATION



Implementation of Quorum Nanomachines

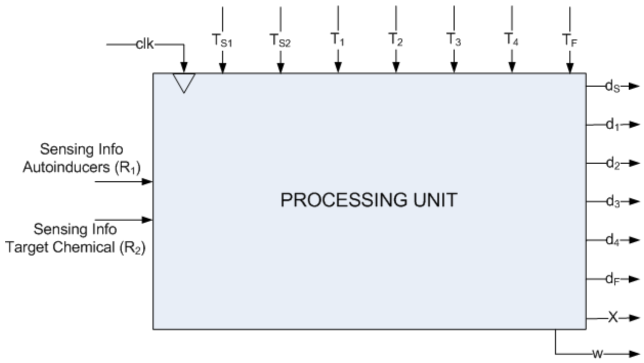
- Collective Activity Synchronization
- **Collective Actuation after Localized Sensing**
  - **Reaction to a certain localized event**
    - **Cancer Detection**
    - **Antibiotic purposes**

Collective Actuation after Localized Sensing

- A cluster of nanomachines is deployed in the environment.
- Their behavior is as follows:
  - If <u>at least one</u> of the nanomachines senses a certain event, all of them must activate by means of Quorum Sensing.
  - If not, they must remain dormant.
- In the simulations, the concentration of a certain chemical will be monitored.

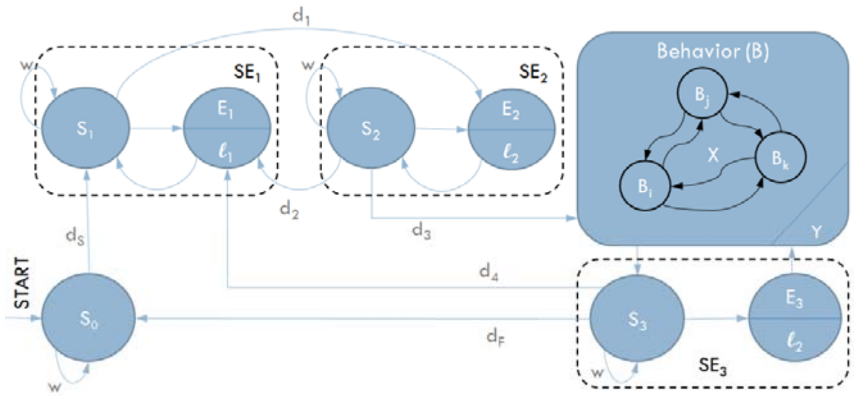
Collective Actuation after Localized Sensing: Processing Unit

- New thresholds and signals:
  - ***d_S:*** starting signal for Quorum Sensing $R_1>T_{S1}$ || $R_2>T_{S2}$
  - ***d_F:*** ending signal for the actuation $R_2<T_F$



Collective Actuation after Localized Sensing: Control Unit

- Modifications:
  - New initial state (S_0), also called "dormant state".
  - d_s is the starting signal.



Collective Actuation after Localized Sensing: Results (I)

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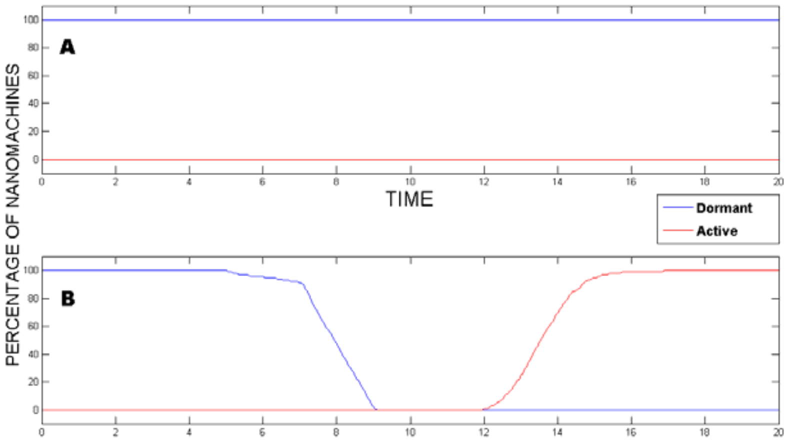
VALIDATION



Collective Actuation after Localized Sensing: Results (II)

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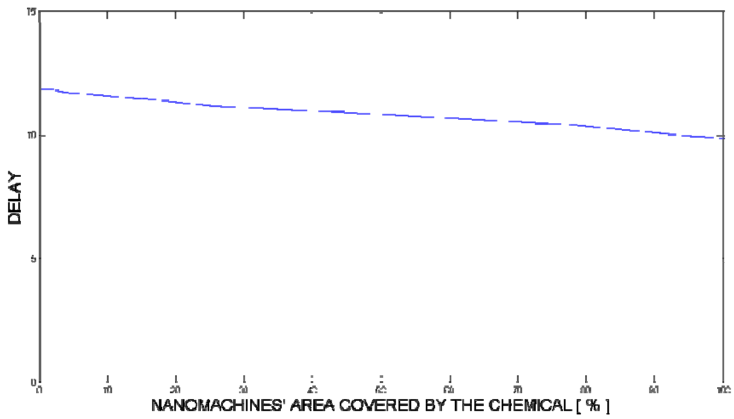
DELAY OF ACTIVATION



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Concluding Remarks

- Conclusions:
  - Quorum Sensing can be used to coordinate or synchronize the action of nanomachines.
  - An automata model has been presented and simulated for Quorum Sensing bacteria.
  - This model can be used as the central control unit of nanomachines that perform Quorum Sensing.
  - Two different implementations have been simulated and delay results have been extracted.

Thank you!

Thank you very much for your attention.

Any question?