José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

VRAIN Valencian Research Institute for Artificial Intelligence

UNIVERSITAT POLITÈCNICA DE VALÈNCIA

DSIC DEPARTAMENTO DE SISTEMAS INFORMÁTICOS Y COMPUTACIÓN

The 24th Conference on Membrane Computing (CMC 2023) Opava, Czech Republic

Membrane computing: A wonderful framework for systems and computational biology

José M. Sempere, PhD
jsempere@dsic.upv.es
Valencian Research Institute for Artificial Intelligence
Department of Informatics Systems and Computation
Universitat Politècnica de València

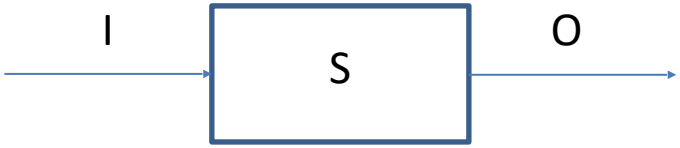
José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Outline

1. Systems biology. A modeling scheme
2. Membrane computing/systems biology: a virtuous cycle
3. ARES and LOIMOS
4. Objects, membranes and rules
5. Inference algorithms
6. Other works
7. Conclusions

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

A look to systems biology



Three primary uses of models in science:

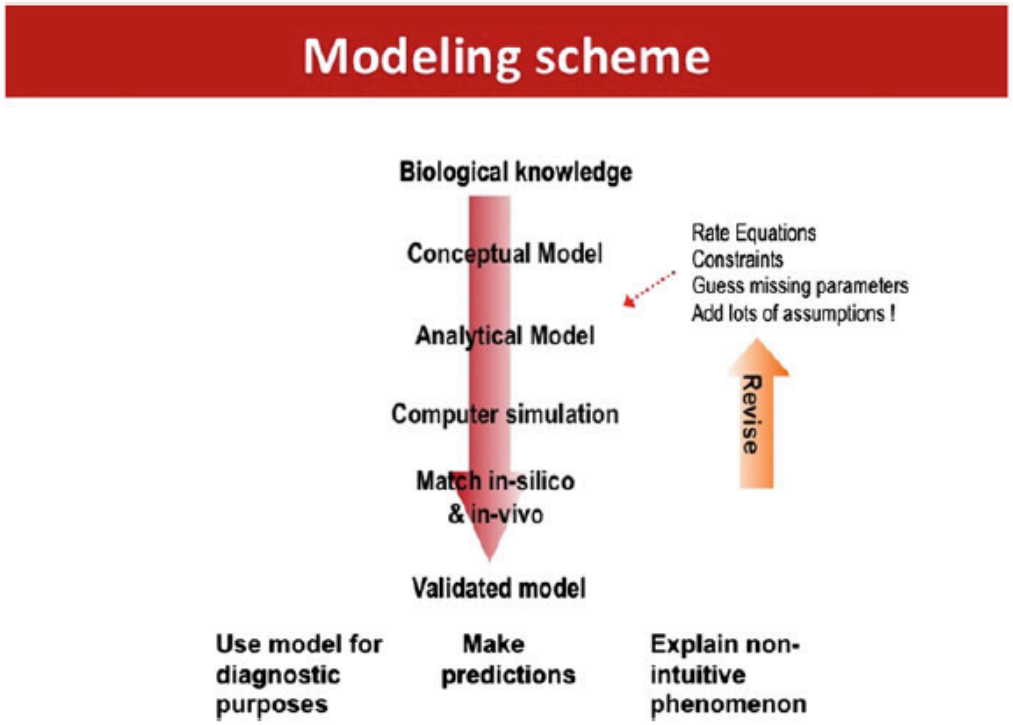
- Understanding (of a real physical or logical system)
- Prediction (of currently unknown future states of the system)
- Control (to manipulate the system to produce a desirable condition)

Problem type	Given …	Find	Use of the model
Synthesis	I and O	S	Understanding
Analysis	I and S	O	Prediction
Instrumentation	S and O	I	Control

- A **system** is made up of different elements and is defined by the field of research in which it is developed.
- A **model** is a formal or abstract representation of a system, usually in the form of a set of objects and the relationship between them.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

A general modeling scheme



V. Singh, P. K. Dhar (eds.), Systems and Synthetic Biology,
DOI 10.1007/978-94-017-9514-2_1

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

… are ODEs based systems the best approach?

The use of ODE systems poses a number of problems for modeling scenarios, which can be listed as follows:

- Systems based on ODEs describe the system deterministically through average values of the state variables, without taking into account the variance (heterogeneity and variation) of the populations.
- In the modeling of populations, the simultaneous temporal and spatial distribution of model elements influences their evolution. This problem is not easily solved using ODEs.
- The ODEs are deterministic and, from the outset, they renounce the degree of indeterminism (stochasticity) inherent in the real world systems.
- Negative or real-valued solutions of ODE systems are meaningless in systems of discrete nature and positive values.
- In some models, the number of ODEs can be very complex and the high number of parameters is not easy to evaluate and adjust. It requires the use of hyper-optimization techniques with high computational costs.

© Zulueta E., González A., López-Guedea, J., Isidro Calvo I. (2011) Simulación basada en SMA de sistemas originalmente representados con EDO. Revista Iberoamericana de Automática e Informática Industrial RIAI, Vol . 8, Núm. 4, pp 232-333

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

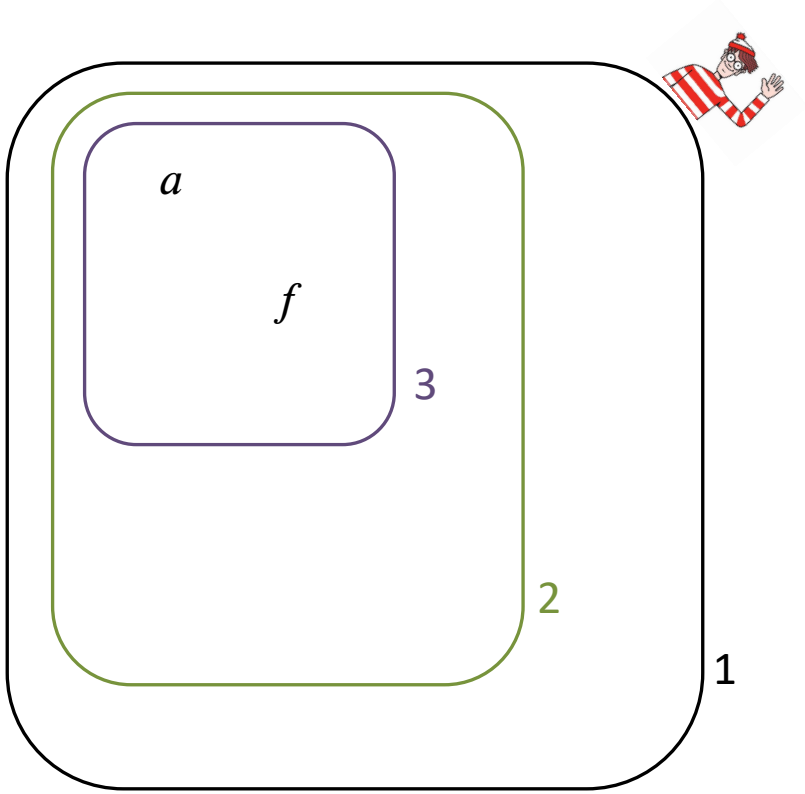
Membrane computing : *the computer that believed itself to be a eukaryotic cell*

$$\Pi = (O,\ H, \mu, w_1, w_2, w_3, R,\ i_o)$$

- $O = \{a, b, d, e, f\}$
- $H = \{1,2,3\}$
- $\mu = [\,[\,[\,]_3]_2]_1$
- $w_1 = \lambda,\ w_2 = \lambda,\ w_3 = af$
- Rules and priority relationships

$$[d]_1 \longrightarrow d[\,]_1$$
$$[b]_2 \longrightarrow [d]_2$$
$$[d]_2 \longrightarrow [de]_2$$
$$[ff]_2 \longrightarrow [f]_2 > [f]_2 \longrightarrow \lambda$$
$$[a]_3 \longrightarrow [ab]_3$$
$$[a]_3 \longrightarrow b$$
$$[f]_3 \longrightarrow [ff]_3$$

- $i_0 = 1$



A transition P system

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

P systems: An analytical model for systems biology.

Some variants of P systems

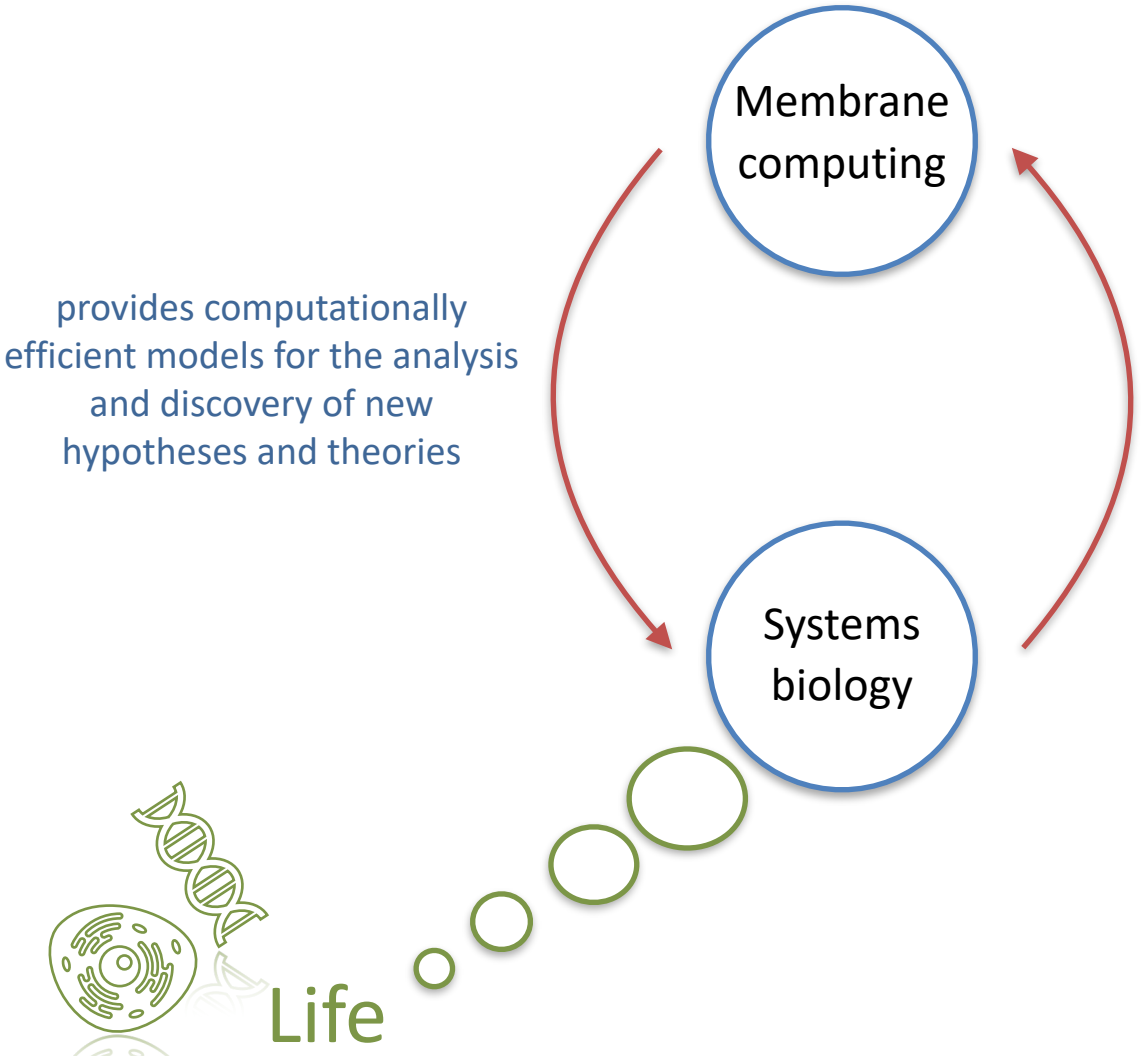
- Transition P systems

- P systems with active membranes

- Tissue P systems
- Catalytic P systems
- P systems with communication rules
- P automata
- P systems with worm objects (strings)
- Splicing P systems
- Conformon P systems
- Metabolic P systems
- P systems with proteins in the membranes
- Spiking neural P systems
- Stochastic and probabilistic P systems
- P colonies
- etc, etc.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Virtuous cicle of membrane computing/systems biology



José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Nine reasons why P systems are a good choice (if not the best) for systems biology (specially for ecology and epidemics)

1. P systems allow a degree of granularity adapted to the model (from unique entities, as viruses and hosts, to populations).
2. The rules of behavior can evolve depending on the physical environment that is always changing.
3. Model simulation engines allow a stochastic/probabilistic approach.
4. Each element of the system can influence the others depending on its hierarchy, which can be simulated from the nested membrane structure of the P system.
5. The evolution of the system can be determined from temporary events that are not necessarily synchronous.
6. The results obtained can be self-explanatory from the traces of the system, which allows its debugging as well as its design through successive refinements.
7. The simulation of P systems can be carried out in high-performance computing environments, which allows simulating highly complex systems that would be unapproachable through conventional computing.
8. The specification of the system by means of rules allows scientists to rigorously express those behaviors that they wish to reflect in the system. In addition, the rules themselves constitute an explicit explanation of the functioning of the model that, in no case, behaves like a black box (which is a pernicious effect in some modeling systems based on machine learning and deep learning).
9. Obtaining quantitative information is done naturally by "counting" those elements of the system that we are interested in studying.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

From the beginning, models for systems biology have been proposed in membrane computing.

- Simulation of Photosynthesis (Nishida 2001)
- Leukocyte Selective Recruitment (Franco, Manca 2003)
- Dynamics of HIV infection (Frisco, Wolfe 2006)
- The Bearded Vulture ecosystem (Cardona, Colomer, Pérez-Jiménez, Sanuy, Margalida 2008)
- Study of Latent CD4+ T Cell Activation (Jack, A. Paun, Rodríguez-Patón 2008)
- KaiABC Oscillator (Hinze, Lenser, Escuela, Heiland, Schuster 2009)
- Thermoreceptor Model (Hinze, Kirkici, Sauer, Sauer, Behre 2015)
- Plant development (Sosík, Smolka, Bradík, Garzon 2018)
- …

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Ecosystems biology in membrane computing: Some works by RGNC (Univ. of Sevilla)

Bearded Vulture

Tritrophic

Pyrenean Chamois

Zebra mussel

Pieris Oleracea

Population Dynamic P systems (PDP)

Probabilistic Guarded P systems (PGP)

BBB
DNDP
DCBA
multicompartment Gilllespie
deterministic with waiting time

Ecosystems

Multienvironment P systems

Inference engines

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

ARES A membrane computing simulator of the evolution of antibiotic resistance

VRAIN
Valencian Research Institute for Artificial Intelligence

Biotechvana

SEVENTH FRAMEWORK PROGRAMME

instituto ramón y cajal de investigación sanitaria irycis

DSIC
DEPARTAMENTO DE SISTEMAS INFORMÁTICOS Y COMPUTACIÓN

EvoTAR
Evolution and Transfer of Antibiotic Resistance

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Antibiotic resistance

31 July 2020

Key facts

- Antibiotic resistance is one of the biggest threats to global health, food security, and development today.
- Antibiotic resistance can affect anyone, of any age, in any country.
- Antibiotic resistance occurs naturally, but misuse of antibiotics in humans and animals is accelerating the process.
- A growing number of infections – such as pneumonia, tuberculosis, gonorrhoea, and salmonellosis – are becoming harder to treat as the antibiotics used to treat them become less effective.
- Antibiotic resistance leads to longer hospital stays, higher medical costs and increased mortality.

Public Health & Policy > Public Health

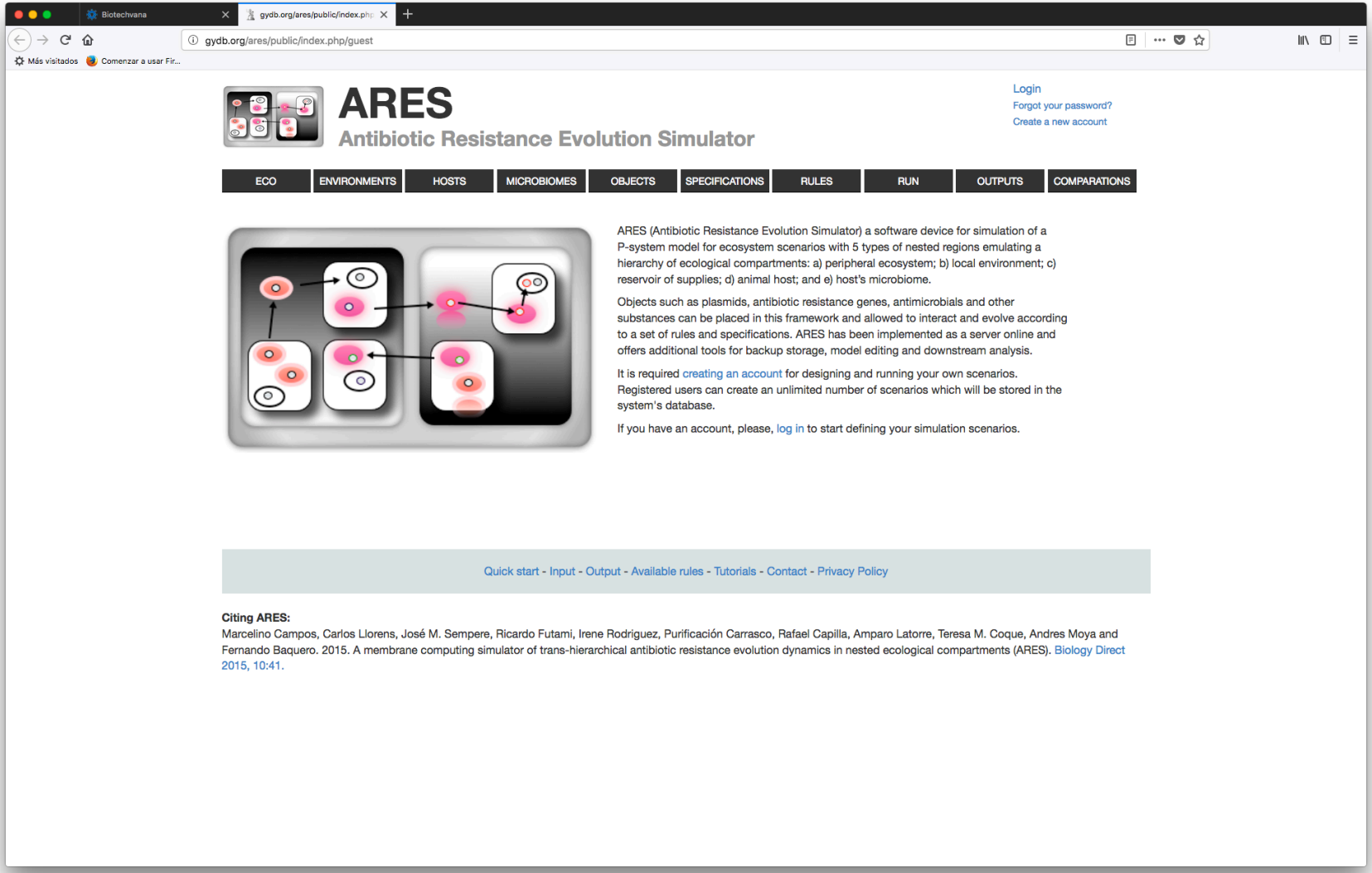
Antibiotic Resistance Could Be a Top Cause of Death by 2050, Experts Say

— Can targeted investments rebuild the antibiotic pipeline?

by Shannon Firth, Washington Correspondent, MedPage Today May 25, 2022

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

The ARES simulator



http://gydb.org/ares/public/index.php/guest

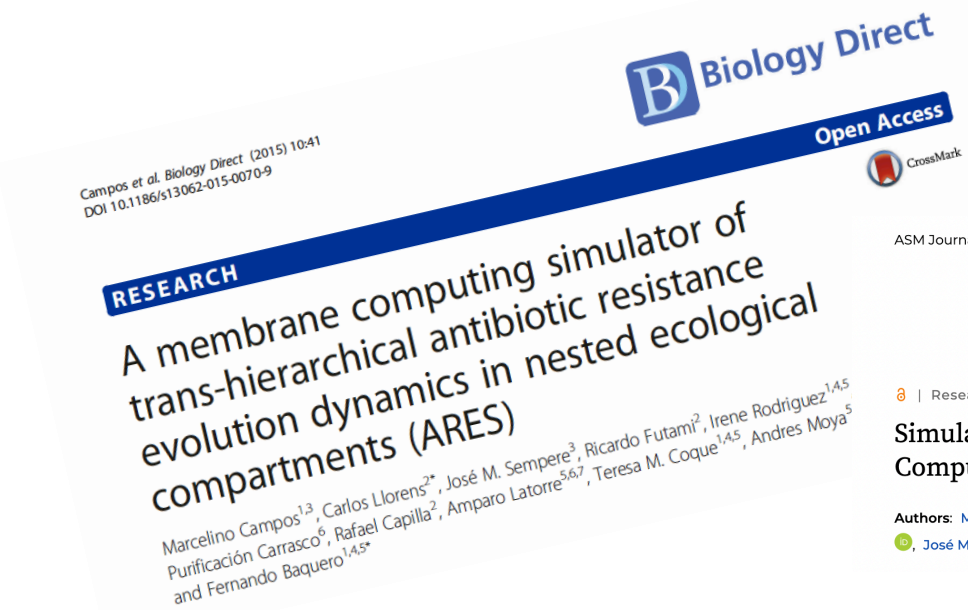
José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

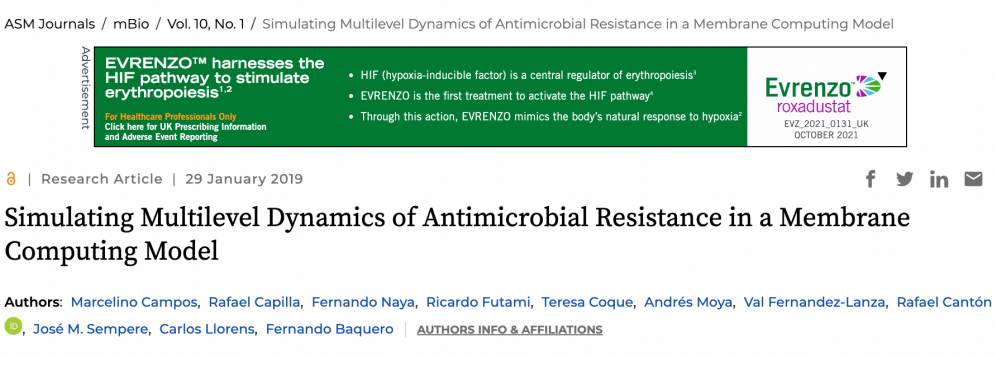
VRAIN Valencian Research Institute for Artificial Intelligence

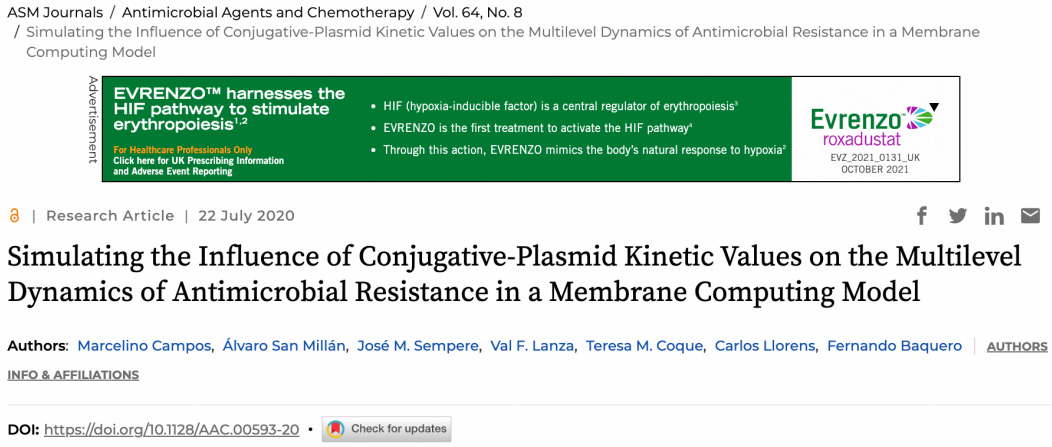
UNIVERSITAT POLITÈCNICA DE VALÈNCIA

DSIC DEPARTAMENTO DE SISTEMAS INFORMÁTICOS Y COMPUTACIÓN

Antibiotic Resistance Evolution Simulator (ARES)

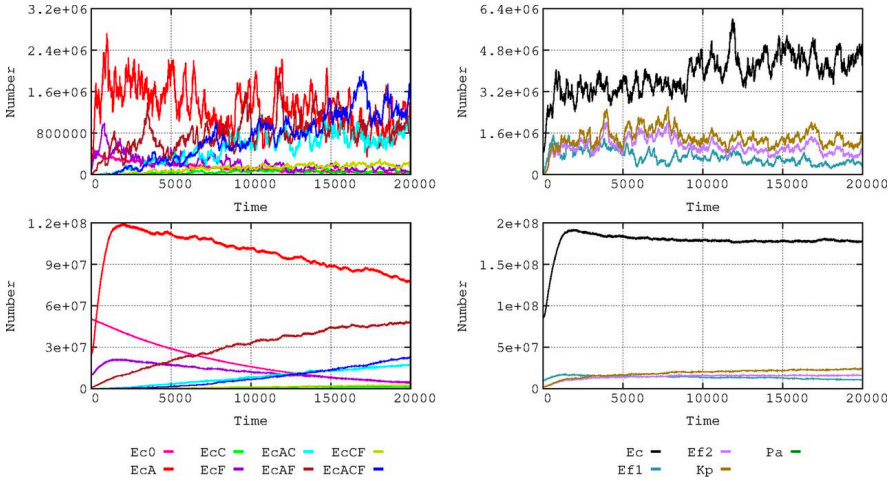




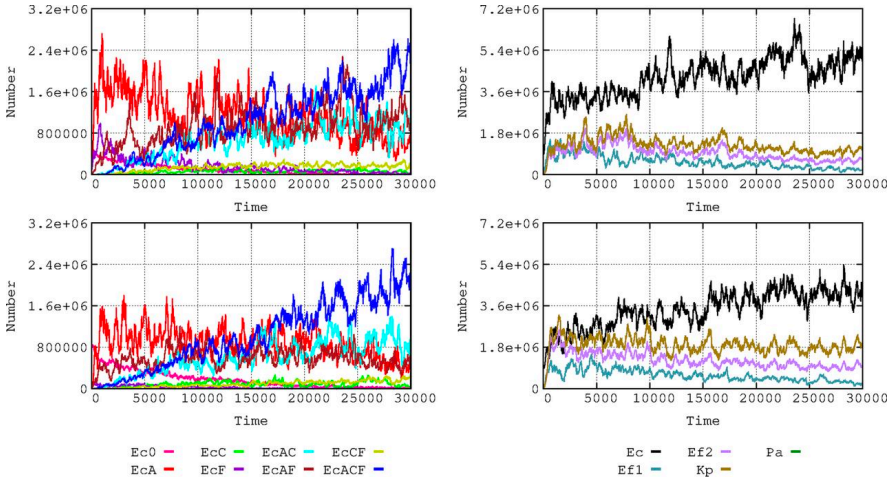


José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

ARES graphics



Comparative dynamics of *E. coli* phenotypes in the hospital (up, left) and the community (down, left). In the right part, species dynamics in the hospital (up) and the community (down): *E. coli* (black), *K. pneumoniae* (yellow green), *E. faecium* AbAS (dark green), and *E. faecium* AbAR (violet). *P. aeruginosa* is not visible in this representation (low numbers).



Influence of baseline *E. coli* resistance phenotype composition on the dynamics of bacterial species. On the left, data represent comparative dynamics of *E. coli* phenotypes in the basic hospital scenario (top) and with reduced numbers of resistant phenotypes (bottom).On the right, data represent comparative dynamics of bacterial species in the basic model (top) and the reduced basal resistances (bottom)

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

VRAIN Valencian Research Institute for Artificial Intelligence

UNIVERSITAT POLITÈCNICA DE VALÈNCIA

DSIC DEPARTAMENTO DE SISTEMAS INFORMÁTICOS Y COMPUTACIÓN

LOIMOS A membrane computing simulator of the COVID-19 dynamics

IMCS 2021 Application of the Year Award

Regular Paper | Published: 29 October 2021

P systems in the time of COVID-19

Fernando Baquero, Marcelino Campos, Carlos Llorens & José M. Sempere

Journal of Membrane Computing **3**, 246–257 (2021) | Cite this article

386 Accesses | **1** Altmetric | Metrics

VRAIN Valencian Research Institute for Artificial Intelligence

Volume 2
2021

Simulating the impact of non-pharmaceutical interventions limiting transmission in COVID-19 epidemics using a membrane computing model

M Campos, J M Sempere, J C Galán, A Moya, C Llorens, C de-los-Angeles, F Baquero-Artigao, R Cantón, F Baquero

microLife, Volume 2, 2021, uqab011, https://doi.org/10.1093/femsml/uqab0

Published: 09 September 2021 **Article history**

Biotechvana

instituto ramón y cajal de investigación sanitaria irycis

Volume 3
2022

JOURNAL ARTICLE

Simulating the efficacy of vaccines on the epidemiological dynamics of SARS-CoV-2 in a membrane computing model

Marcelino Campos, José M Sempere, Juan C Galán, Andrés Moya, Rafael Cantón, Carlos Llorens, Fernando Baquero

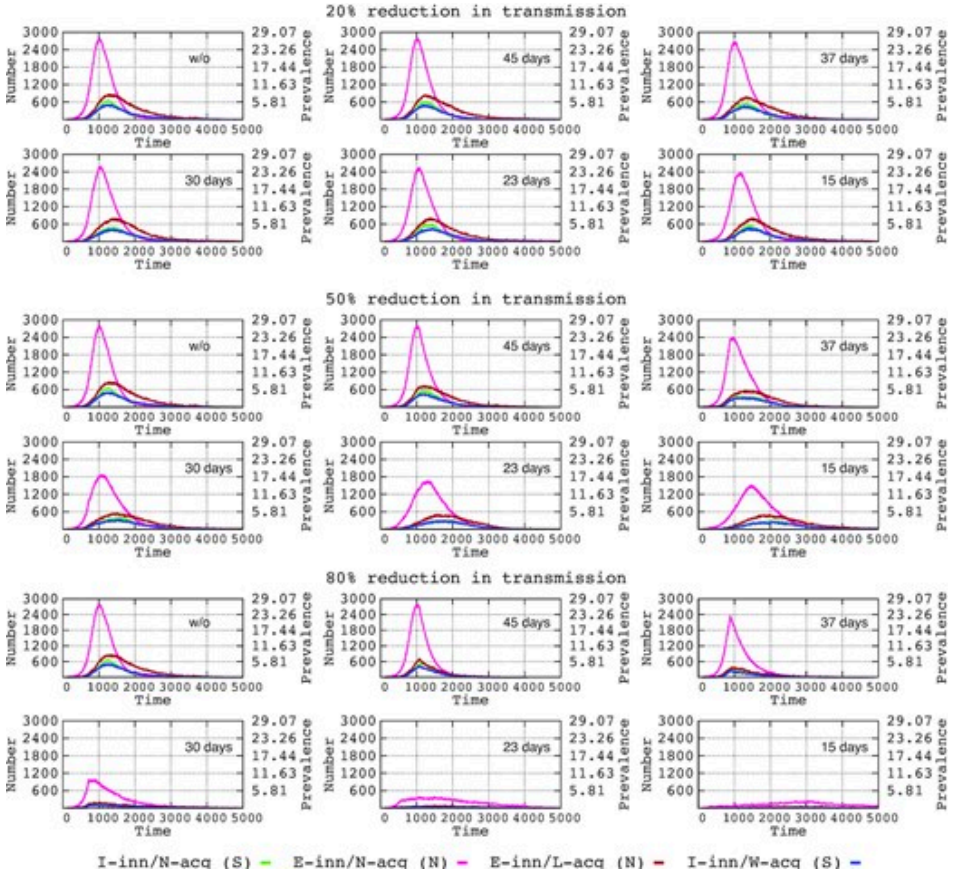
microLife, Volume 3, 2022, uqac018, https://doi.org/10.1093/femsml/uqac018

Published: 16 September 2022 **Article history**

DSIC DEPARTAMENTO DE SISTEMAS INFORMÁTICOS Y COMPUTACIÓN

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

LOIMOS graphics

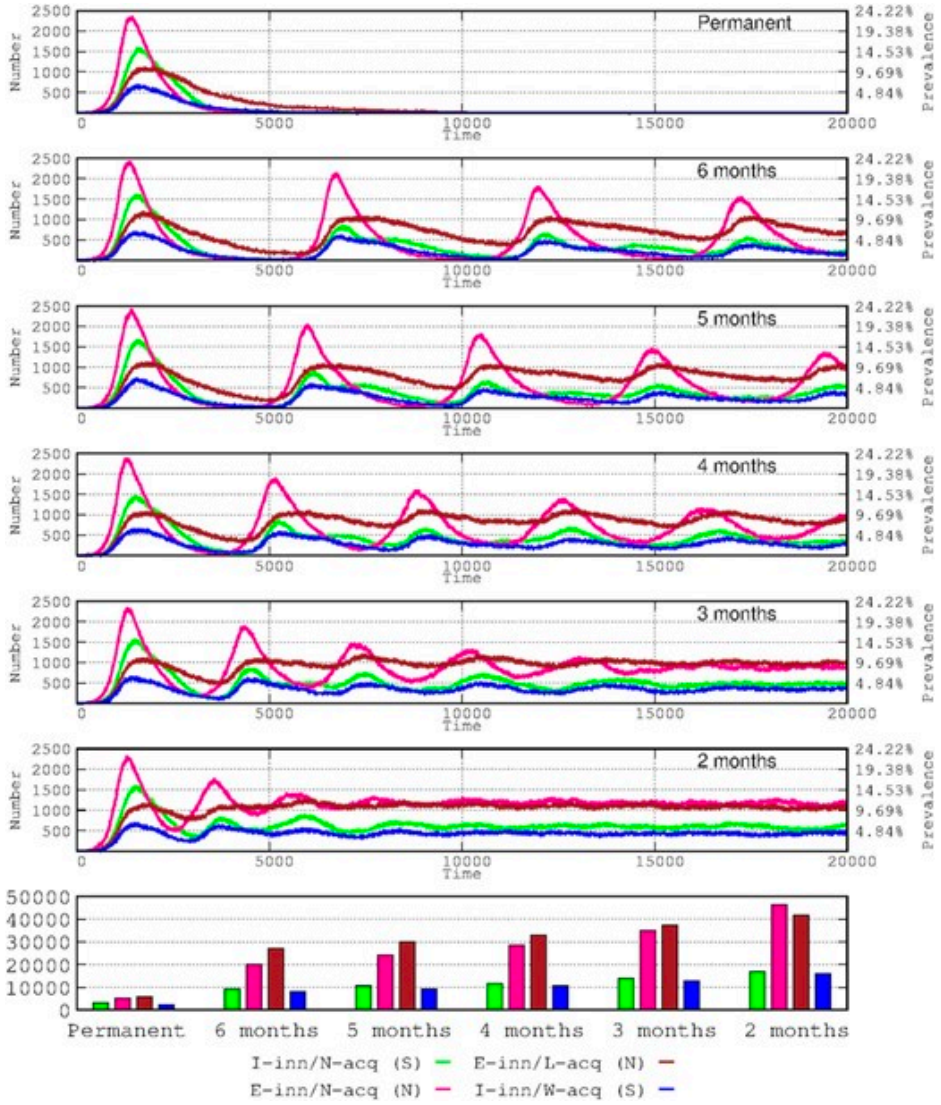


Influence of interventions (time of adoption and intensity of reduction in transmission) on the number of individuals in the host populations with varying response to the COVID-19 infection.

I-inn/N-acq/S (symptomatic): insufficient innate immunity, normal acquired immunity (green line); E-inn/N-acq/N (non-symptomatic): efficient innate immunity, with normal acquired immunity (pink); E-inn/L-acq/N (non-symptomatic): efficient innate immunity, lacking or with very weak acquired immunity due to poor antigenic challenge, violet and I-inn/N-acq (S, symptomatic): insufficient innate immunity, weak acquired immunity (dark blue). Steps in the time scale represent hours after the onset of the epidemics (approximately 1000 h, 42 days, approximately 5000 h, 7 months).

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

LOIMOS graphics



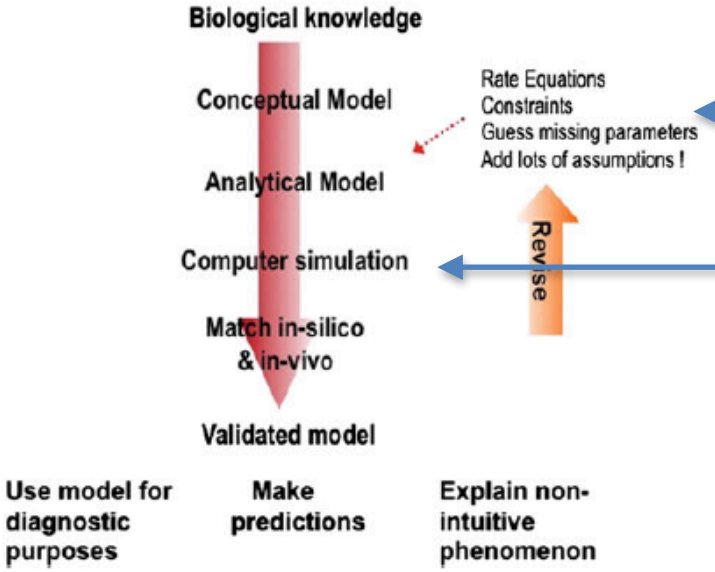
Duration of immunological protection following infection.

Successive panels represent the duration of immunological protection after infection (symptomatic or not) in the number of hosts of the 4 immune-response groups in the various waves. This simulation reflects successive scenarios where the natural immune-protection is permanent or there is loss of protection 6, 5, 4, 3, and 2 months after the infection. The bar graph at the bottom of the figure reflects the total number of infected cases after 20 000 time points (2.28 years) in the 4 immune-response groups.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a methodology to model biological systems by membrane computing

Modeling scheme

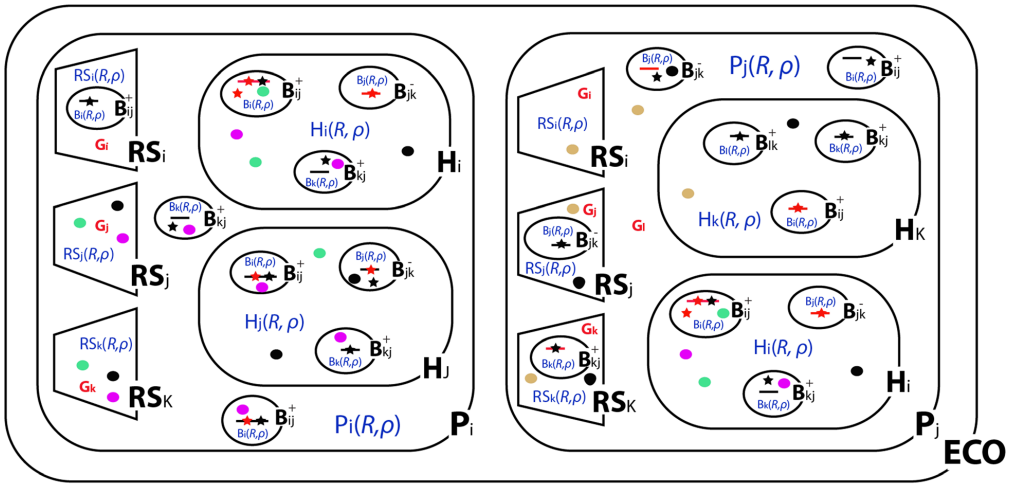


Define the objects, the membranes and the rules

Select the inference algorithms and an efficient running scheme

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

ARES proof of concept: Defining the components.



Membranes

ECO = skin

P_i = environment/area i
P_j = environment/area j

RS_i = reservoir i
RS_j = reservoir j
RS_k = reservoir k

H_i = host i
H_j = host j
H_k = host k

B_{ij}^+ = gram + bacteria belonging to lineage i and GEC j

B_{jk}^- = gram - bacteria belonging to lineage j and GEC k

B_{kj}^+ = gram + bacteria belonging to lineage k and GEC j

B_{lk}^+ = gram + bacteria belonging to lineage l and GEC k

Objects

⋆ = resistance geneARi
⋆ = resistance gene ARj

— = plasmid PLi
— = plasmid PLj
⋆— = plasmid PLi ARi
⋆— = plasmid PLi ARj
⋆— = plasmid PLj ARi
⋆— = plasmid PLj ARj
⋆⋆— = plasmid PLi ARj ARi
⋆⋆— = plasmid PLj ARj ARi

● = antibiotic substance Ai
● = antibiotic substance Aj
● = insecticide substance Ak
● = insecticide substance Al

Gi = clock to create object Ai
Gj = clock to create object Aj
Gk = clock to create object Ak
Gl = clock to create object Al

Rules

$P_i(R,\rho)$ = set of rules for environment Pi
$P_j(R,\rho)$ = set of rules for environment Pj

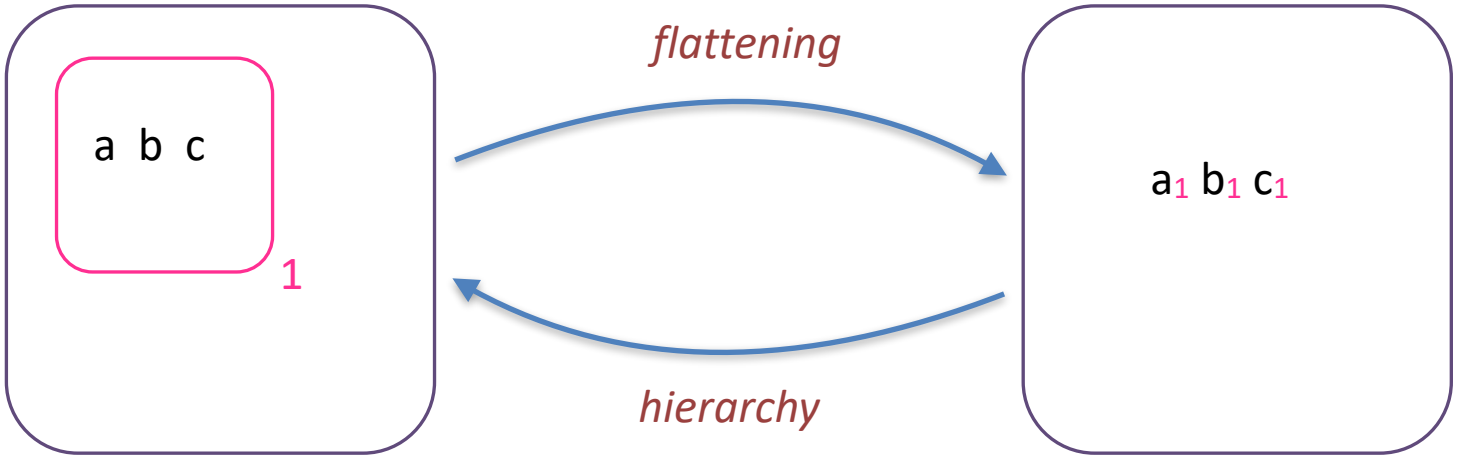
$RS_i(R,\rho)$ = set of rules for reservoir RSi
$RS_j(R,\rho)$ = set of rules for reservoir RSj
$RS_k(R,\rho)$ = set of rules for reservoir RSk

$H_i(R,\rho)$ = set of rules for host Hi
$H_j(R,\rho)$ = set of rules for host Hj
$H_k(R,\rho)$ = set of rules for host Hk

$B_i(R,\rho)$ = set of rules for cells of lineage i
$B_j(R,\rho)$ = set of rules for cells of lineage j
$B_k(R,\rho)$ = set of rules for cells of lineage k
$B_l(R,\rho)$ = set of rules for cells of lineage l

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

membranes or objects ?



👍 Explainability 👎

👎 running time efficiency 👍

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system : Rules

- Substitution rules

$$[\ u_i]_j^{\alpha} \rightarrow\ [u_i']_j^{\alpha'}$$

- Inner communication rules

$$[\ u_i[\ ]_j^{\alpha}]_k^{\beta} \rightarrow\ [[u_i']_j^{\alpha'}]_k^{\beta'}$$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system : Rules

- External communication rules

$$[\,[u_i\,]_j^{\alpha}]_k^{\beta} \rightarrow [\,u_i'[\,]_j^{\alpha'}]_k^{\beta'}$$

- Inter-membrane communication rules

$$[\,[u_i\,]_j^{\alpha}\,[\,]_k^{\beta}\,]_p^{\omega} \rightarrow [\,[\,]_j^{\alpha'}[u_i'\,]_k^{\beta'}]_p^{\omega}$$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system : Rules

- Membrane dissolution rules with content removal

$$[\,[u_i\,]_j^{\alpha}]_k^{\beta} \rightarrow [\,]_k^{\beta'}$$

- Membrane dissolution rules with permanence of contents

$$[\,[u_i\,u_j]_k^{\alpha}]_p^{\beta} \rightarrow [\,u_j\,]_p^{\beta'}$$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system : Rules

- Internal membrane communication rules

$$[\ ]_i^{\alpha}[\ ]_j^{\beta} \rightarrow\ [[\ ]_i^{\alpha}\ ]_j^{\beta'}$$

- External membrane communication rules

$$[\ [\ [\ ]_i^{\alpha}]_j^{\beta}]_k^{\omega} \rightarrow\ [[]_i^{\alpha}[]_j^{\beta'}]_k^{\omega'}$$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system : Rules

- Inter-membrane membrane communication rules

$$[\,[\,]_i^{\alpha}\,]_j^{\beta}[\,]_k^{\omega} \rightarrow [\,]_j^{\beta'}[\,[\,]_i^{\alpha}\,]_k^{\omega'}$$

- Membrane replication rules

$$[\,[\,]_i^{\alpha}]_j^{\beta} \rightarrow [[\,]_i^{\alpha'}[\,]_i^{\alpha''}]_j^{\beta'}$$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

A definition of the P system

- The objects of the P system objects can occupy the membrane capacity (V_c) or not occupy it at all (V_{nc})
- The objects of the P system can either duplicate according to a membrane replication (V_d) or not duplicate (V_{nd})
- A membrane *k* can contain α elements and we represent it as $[\ ]_k^{\alpha}$

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

An specification of the scenario

- One calculation step is equivalent to one hour in reality.
- There are two populations, a hospital with one hundred hosts and a community with ten thousand hosts.
- Every four steps (four hours) the hospital and the community exchange one host.
- We work with gut bacteria. The five types of bacteria studied are EC, EF1, EF2, KP and PA. These bacteria represent 1% of all bacteria in the gut.
- In this scenario, there are three types of antibiotics: A1, A2 and A3.
- A course of antibiotics consists of one dose every 6 hours for seven days. Each dose attempts to kill 30 % of the bacteria studied in the first hour and 15 % in the second hour.
- Twenty percent of the hosts in the hospital are on treatment and 1.3 percent of the community as well.
- In the hospital, 30 % of the treatments are antibiotic A1, 40 % antibiotic A2 and 30 % antibiotic A3. In the community, 75% of treatments are antibiotic A1, 5% antibiotic A2 and 20% antibiotic A3.
- Whenever a host is treated with antibiotic A1, 25 % of the bacteria in the intestine die, with antibiotic A2 20 % die and for antibiotic A3 10 % die. These bacteria take two months to recover their normal number. In the meantime, this space can be occupied by EC, EF1, EF2, KP and PA.
- A bacterium can have two different types of resistance, a static resistance (resistances in the genome) or mobile resistance (resistances in plasmids or transposons).
- A bacterium can only contain two mobile resistances.
- Static resistance AR1 resists antibiotic A1, AR2 resists antibiotic A2 and AR3 resists antibiotic A3.
- PAR1 mobile resistance resists A1, PAR2 resistance resists A1 and A2 if the resistance is in EC, KP or PA, and only A2 if it is in EF1 or EF2.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Towards a modeling of a real scenario: ARES hospital-external community

An specification of the scenario

- Each host starts with the configuration of bacteria shown in the table

Table of bacteria configuration

Bacteria	number	static resistence	movable resistence
EC	5000	no resistence	no resistence
EC	2500	no resistence	PAR1
EC	1000	AR3	no resistence
EC	100	AR3	PAR1
EF1	995	AR2	no resistence
EF2	200	AR2 and AR3	PAR1
KP	200	AR1 and AR3	PAR2
PA	5	AR1	PAR2

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

A definition of the P system : modes of computation

- $\psi = 1$ (maximal parallelism with capacity restriction)

  Any rule that can be executed is executed if after the application of the rule, the capacity limit of the membrane is not exceeded.

- $\psi = 2$ (maximal parallelism without capacity restriction)

  When a rule is applied if a membrane exceeds its capacity to receive objects or membranes, these elements are lost.

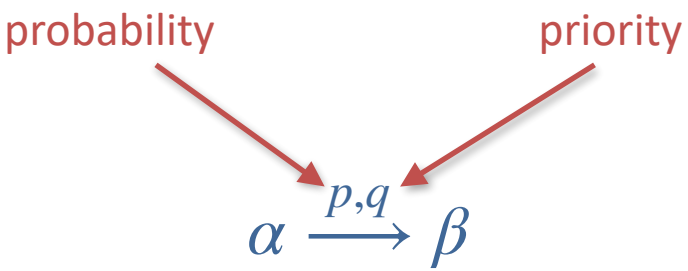
- $\psi = 3$ (maximal parallelism with capacity correction)

  All rules that can be applied, are applied without checking the capacity of the membranes. At the end of a calculation step the membranes with their capacity exceeded delete objects and membranes proportional to their quantity until the capacity is no longer exceeded.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Inference algorithms: applying probabilities

Any rule can be expressed in the following way



There are different algorithms to select the rules at every computation step

- ARES (PLingua + DCBA flavour)
- Gillespie
- k-Gillespie
- random (pure roulette strategy)

… and also the implementation of Markov sources (Sempere,2023) (JMC *accepted*)

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Inference algorithms: applying probabilities

"Evaluation of algorithms for the stochastic simulation of epidemics through P systems" Bachelor's Degree Thesis, ETSINF UPV. Sergio Gómez (author), José M. Sempere and Marcelino Campos (supervisors), 2023

Different experimental scenarios:

- Baseline1
- Baseline 2
- Two environments (cell-like embedding)
- Chainning
- Nesting
- Ring

Different algorithms

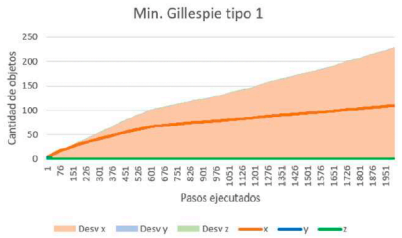
ARES
random
Gillespie (max,min)
k-Gillespie (max,min) (k=3,5)

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

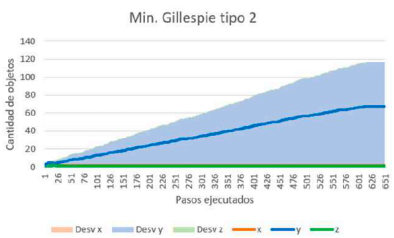
Inference algorithms: applying probabilities

"Evaluation of algorithms for the stochastic simulation of epidemics through P systems" Bachelor's Degree Thesis, ETSINF UPV. Sergio Gómez (author), José M. Sempere and Marcelino Campos (supervisors), 2023

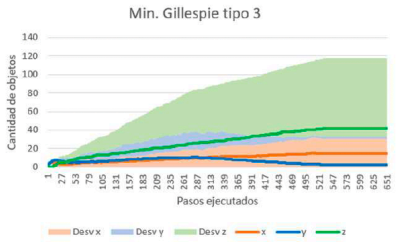
30 different simulations (scenarios, type of rules, algorithms)



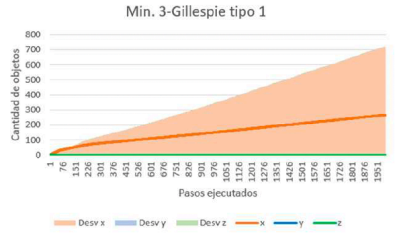
Frecuencia de aparición: 50%



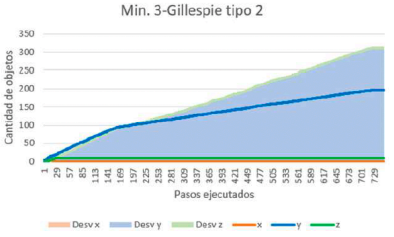
Frecuencia de aparición: 13%



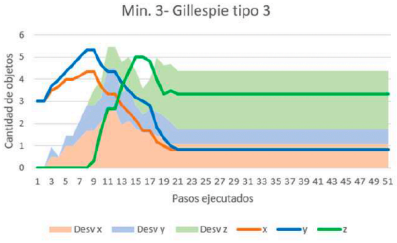
Frecuencia de aparición: 23%



Frecuencia de aparición: 48%

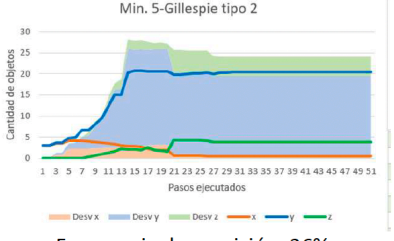


Frecuencia de aparición: 28%

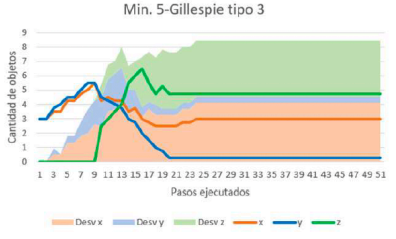


Frecuencia de aparición: 24%

Frecuencia de aparición: 59%

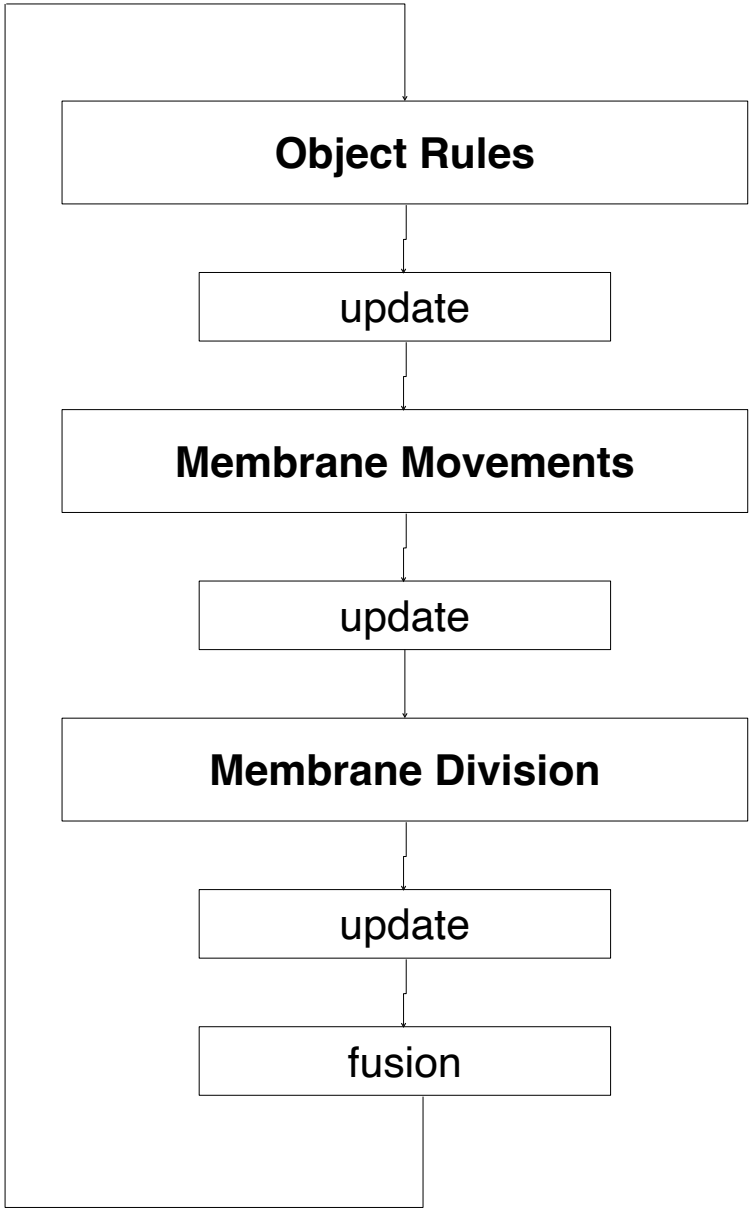


Frecuencia de aparición: 26%



Frecuencia de aparición: 15%

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

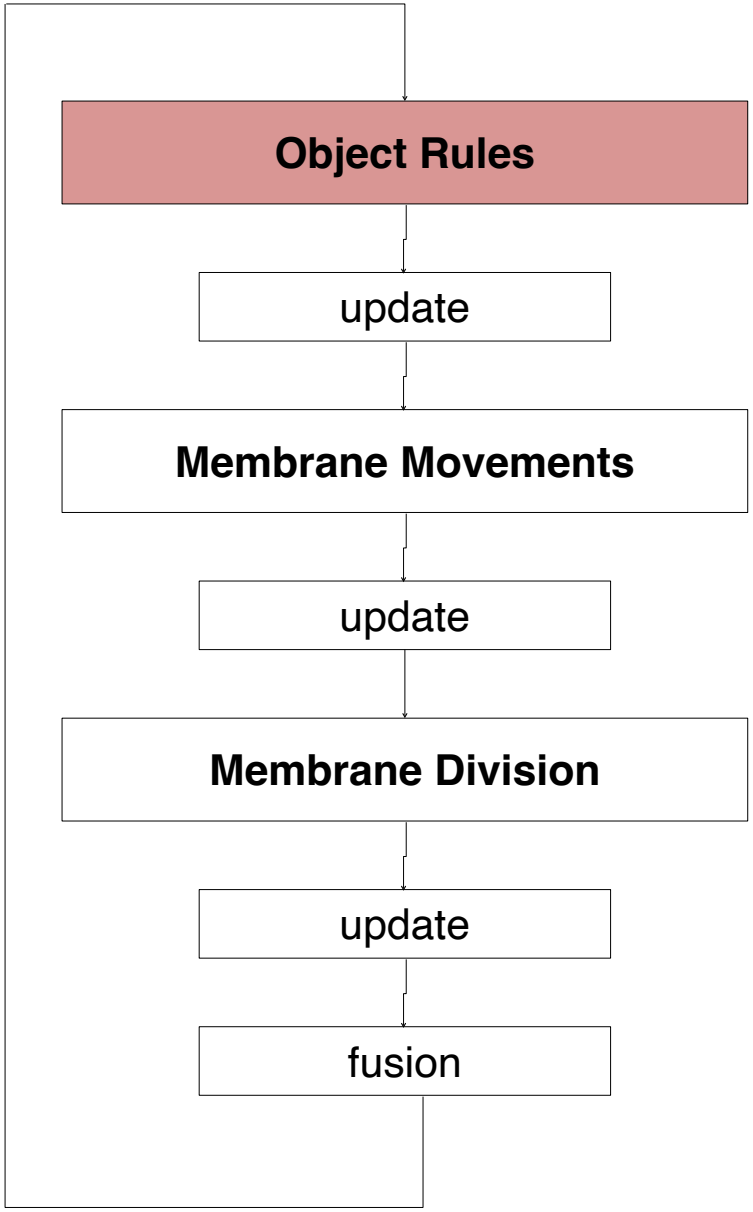


Running the simulator

The computation consists of the repetition, in a loop, of three main steps,

- **Object Rules**
- **Membrane Movements**
- **Membrane Division**.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

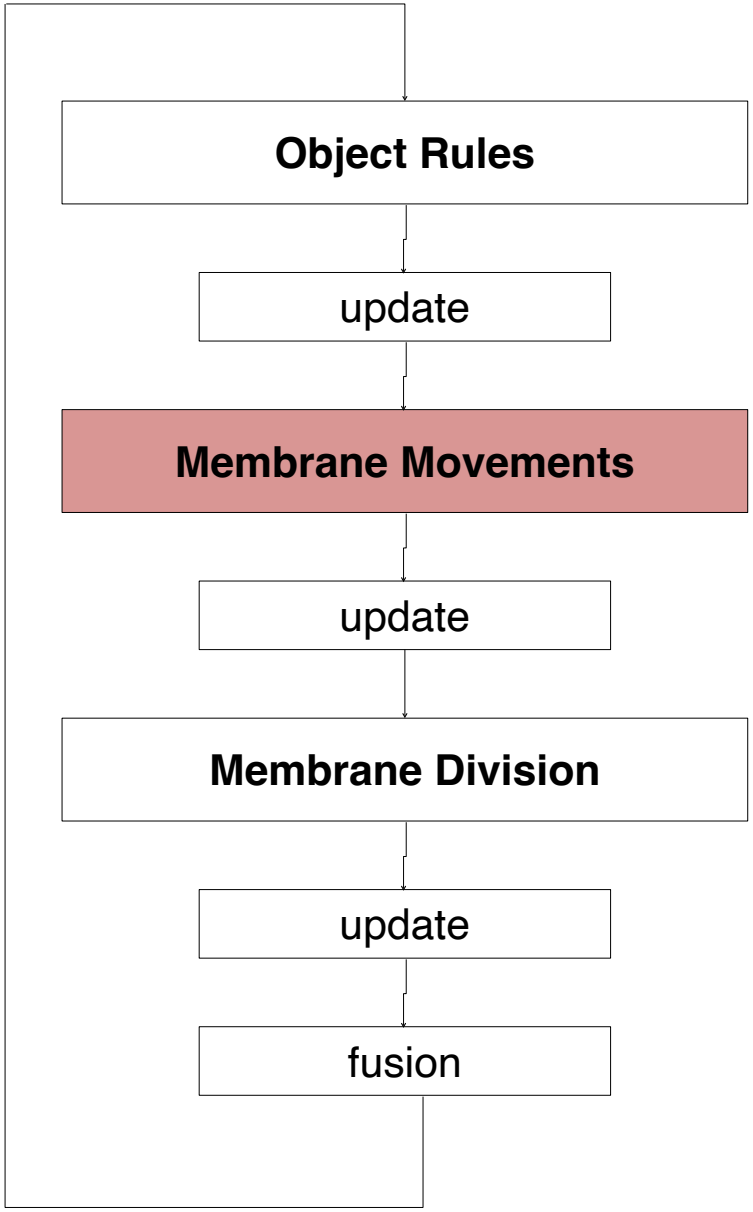


Running the simulator

This step consists of the manipulation and communication of the objects within the membranes.
Depending on the type of rule used, the result of the operation will be located in one membrane or another.
This step also includes the dissolution rules.

- HERE RULE: The result of applying the rule remains in the membrane containing it.
- OUT RULE: The result of applying the rule is ejected to the outer region (parent region).
- IN RULE: The result of applying the rule is introduced in a membrane contained in the region that has the rule (daughter region).
- MEM RULE: The result of applying the rule is inserted in a membrane at the same level as the region with the rule.
- DISS RULE: The membrane is dissolved.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

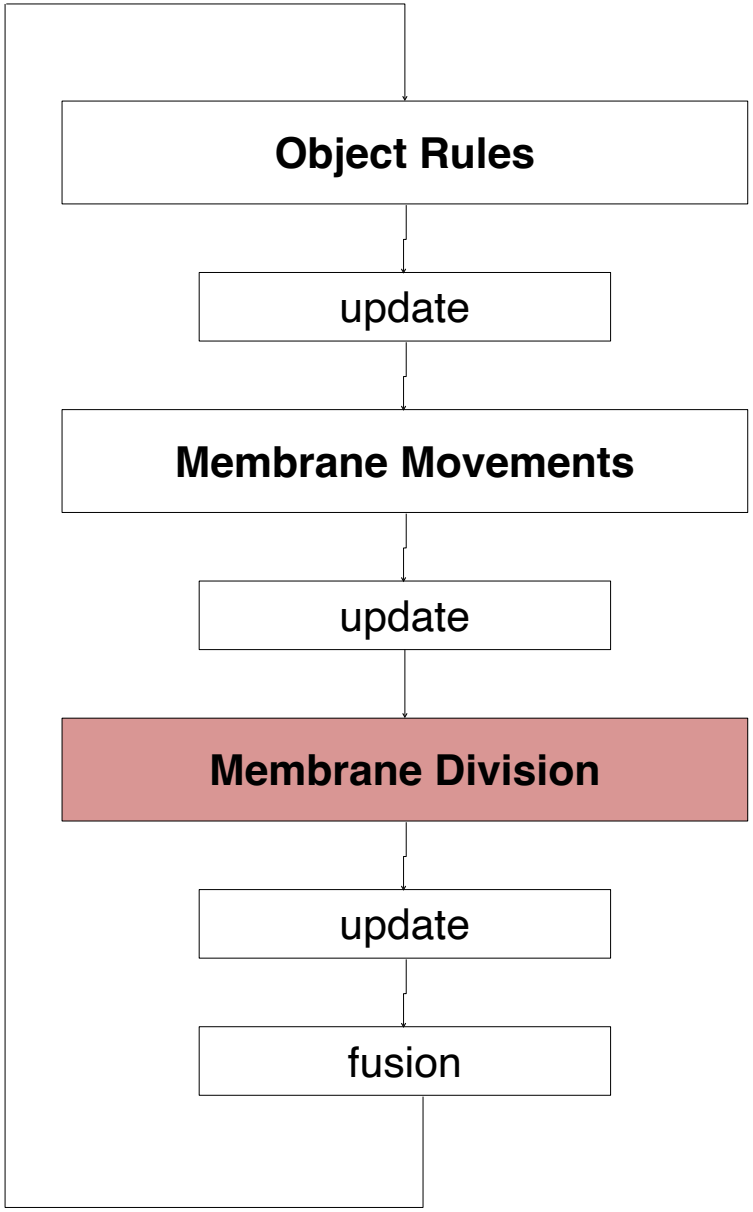


Running the simulator

In this step, membrane movements between different regions are applied. The destination of these membranes depends on the type of rules used.

- OUT RULE: The membranes move to the region immediately outside (parent region).
- IN RULE: The moving membranes are introduced in a region contained in the region possessing the rule (daughter region).
- MEM RULE: Membranes move between regions that are at the same level and in the same region.
- MEMWC: It consists of a movement of membranes between neighboring regions (MEM RULE) but the transmitter keeps a copy of the membranes to be transmitted.
- MEMTRANS RULE: A particular case of the previous one. it only allows the application of one rule per sender/receiver (initially designed to represent plasmid transfer).

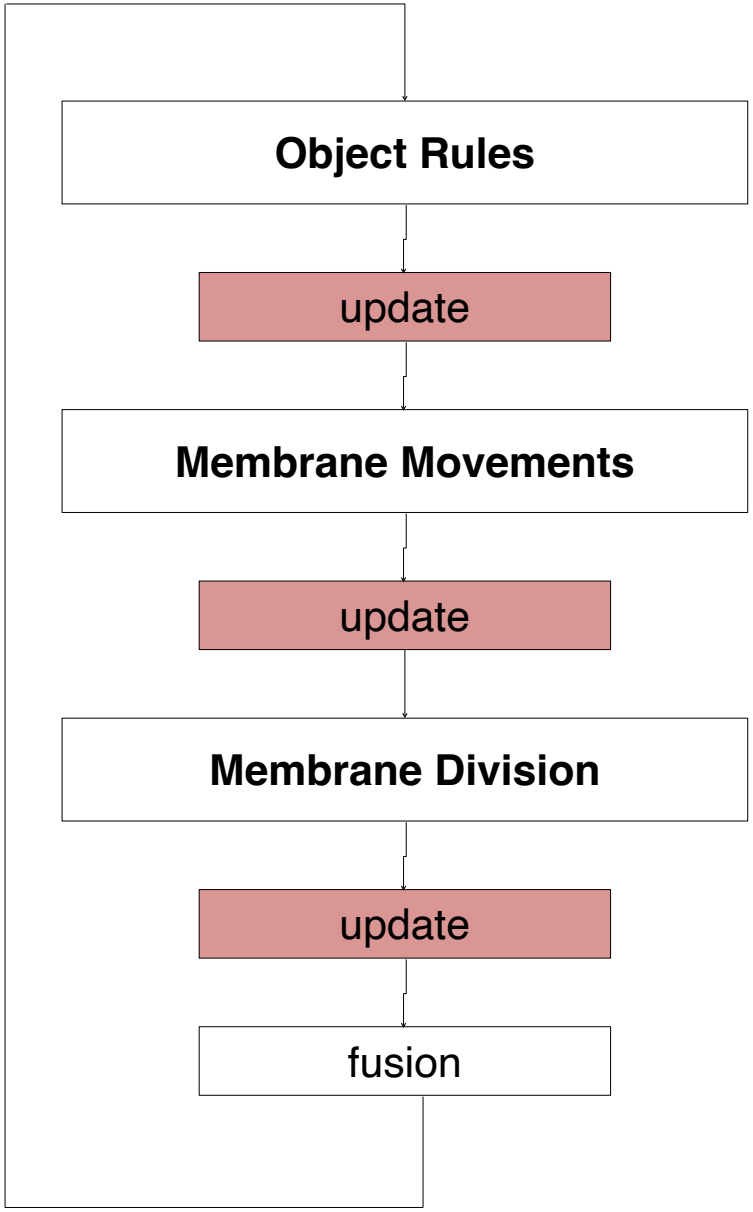
José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/



Running del simulador

This step is used to represent the "growth" or "division" of the membranes. After this step all membranes that have a defined growth rate will grow in number (the inner membranes are doubled, but the basic objects are split).

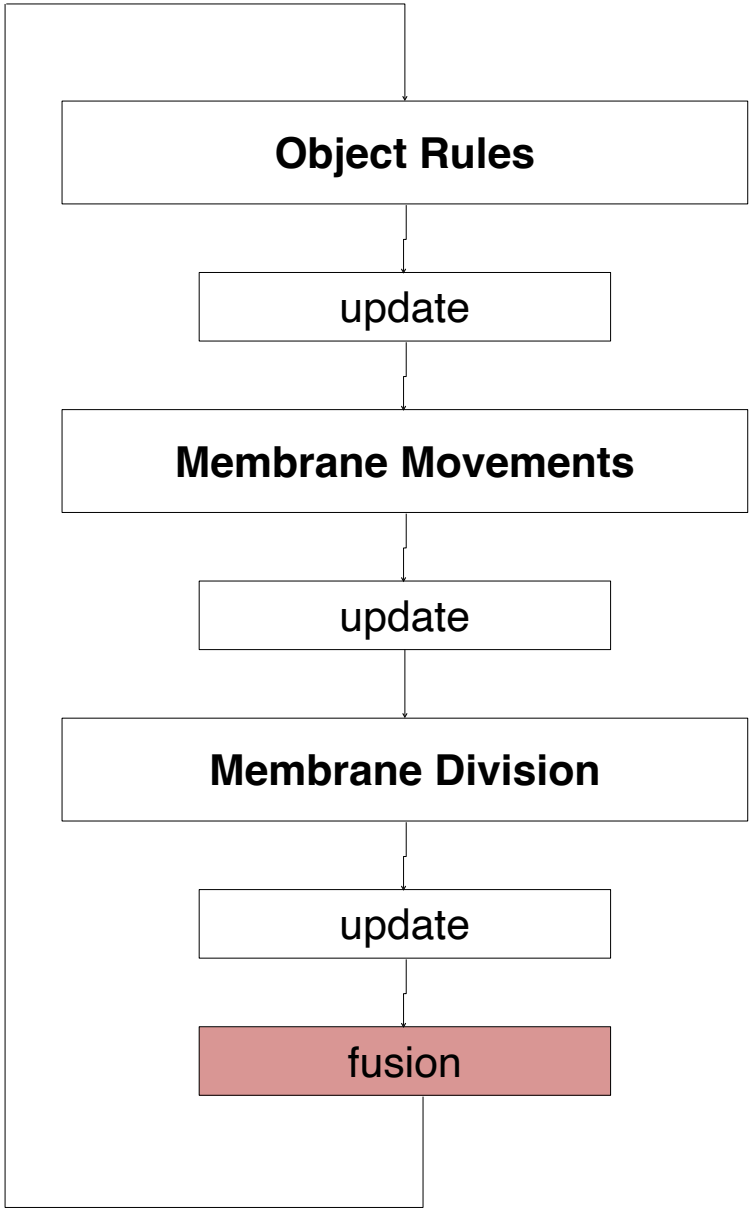
José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/



Running the simulator

These auxiliary steps are used to update the model information after each main step (Object Rules, Membrane Movements and Membrane Division). More specifically we use buffers for basic objects and membranes whose purpose is that they cannot be used several times in the same step.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/



Running the simulator

The model we use works with clusters of membranes, i.e. membranes that are the same and are in the same region are represented by a single object (and a multiplicity).

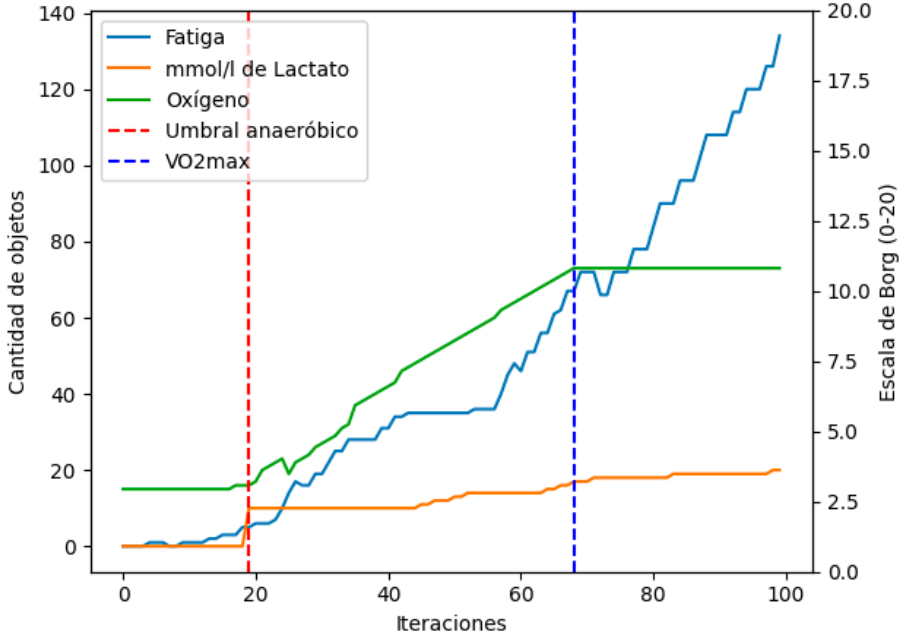
As a result of the application of the different steps of the whole execution process different membranes equal to others in the same regions may appear. This step ensures that the representation of these membranes is done with a single object by joining them together (and adding their multiplicities). The objective is to reduce computational costs.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Recent works

"Modeling of changes in physiological markers during sports practice through membrane computing." Bachelor's Degree Thesis, ETSINF UPV. Marc Mestre (author), José M. Sempere (supervisor), 2023

Goal: A tool to predict the evolution of physiological markers during sports practice

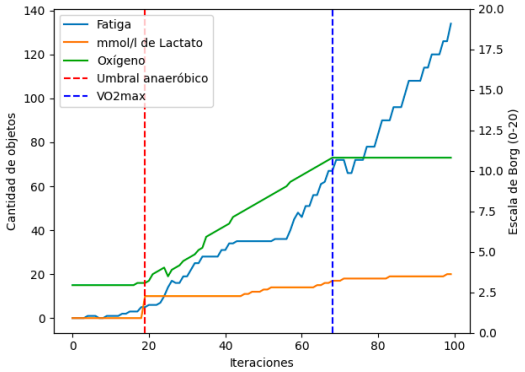


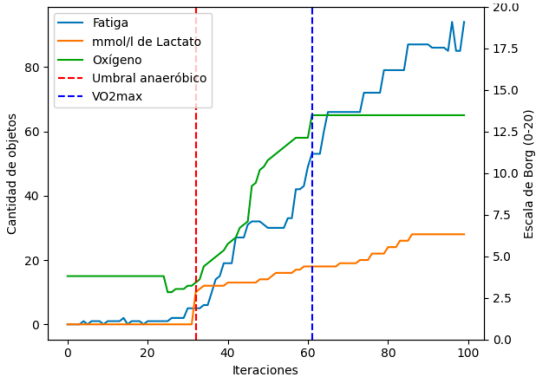
Fatigue
Lactate
Oxygen
Anaerobic threshold
Maximum oxygen consumption

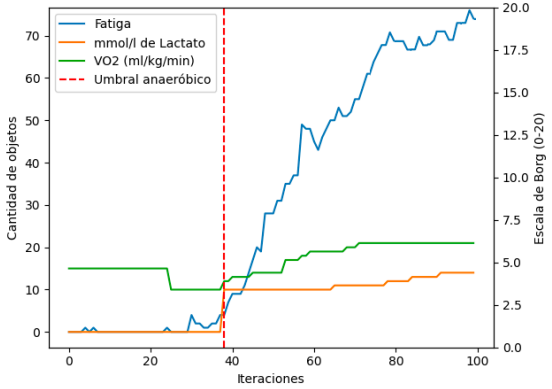
José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

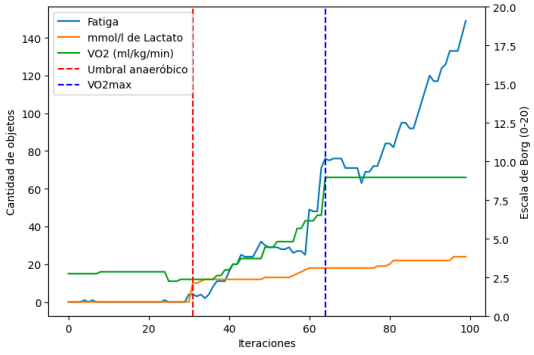
Recent works

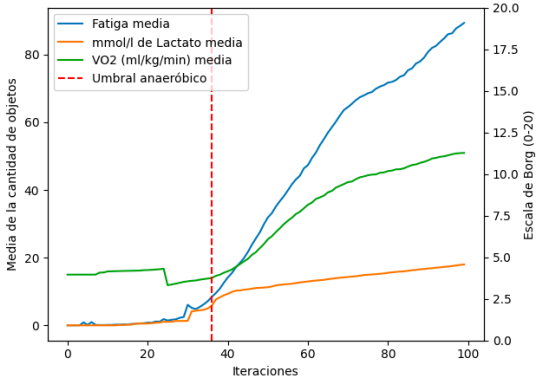
"Modeling of changes in physiological markers during sports practice through membrane computing." Bachelor's Degree Thesis, ETSINF UPV. Marc Mestre (author), José M. Sempere (supervisor), 2023

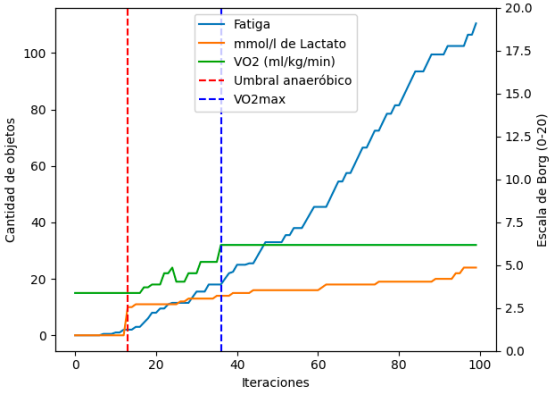










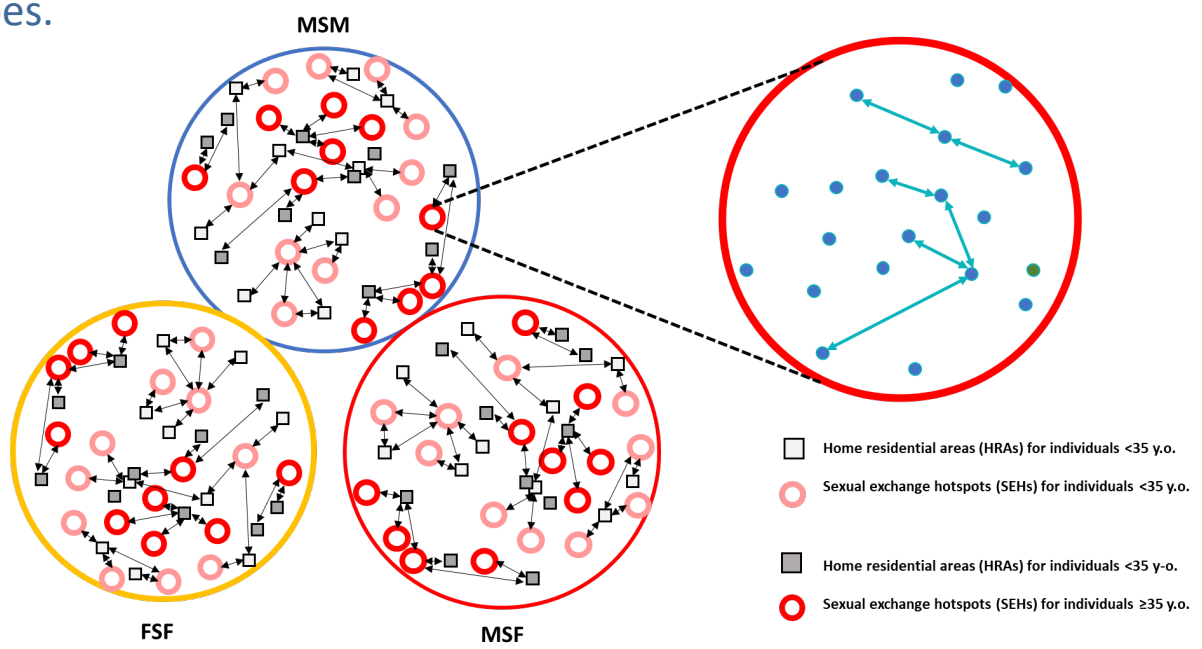


José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Recent works

"Membrane Computing Simulation of Sexually Transmitted Bacterial Infections in Hotspots of Individuals with Various Risk Behaviors" M. Campos, J.C. Galán, M. Rodríguez-Domínguez, J.M. Sempere, C. Llorens, F. Baquero (submitted)

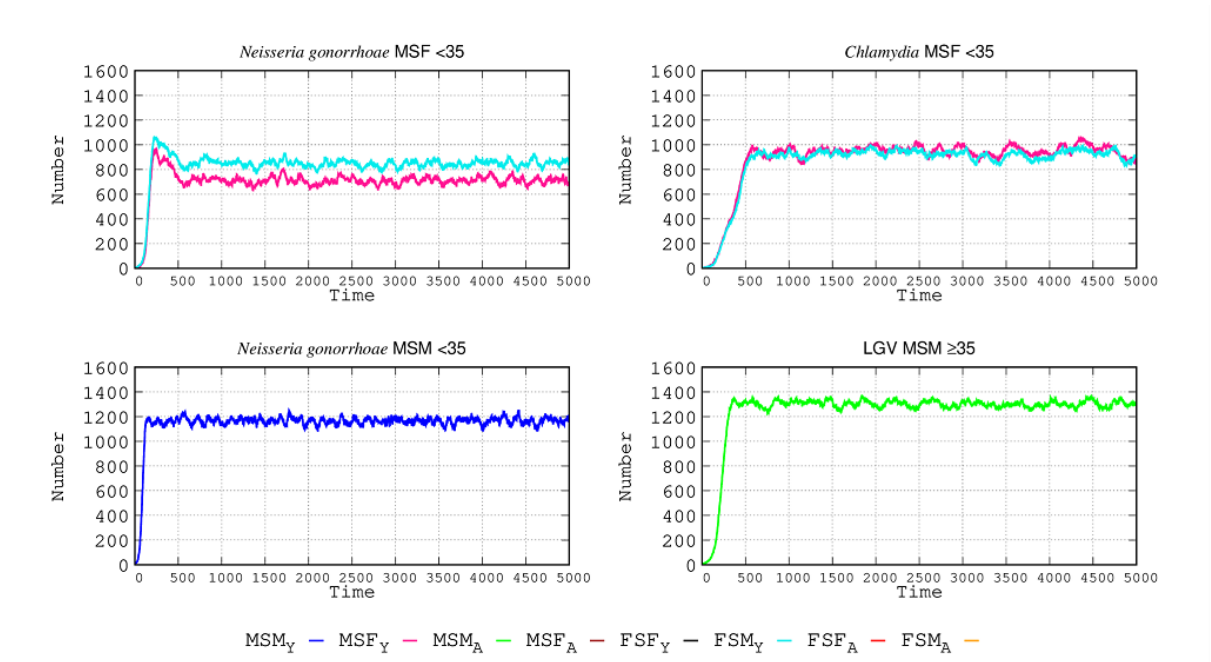
Goal: We propose the use of a simulation technology based on membrane computing, mimicking in silico sexually transmitted bacterial Infections epidemics under various local conditions. This approach allows us to evaluate the relative weight of the various epidemic drivers in various populations at risk and the possible outcomes of interventions in particular epidemiological landscapes.



José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Recent works

"Membrane Computing Simulation of Sexually Transmitted Bacterial Infections in Hotspots of Individuals with Various Risk Behaviors" M. Campos, J.C. Galán, M. Rodríguez-Domínguez, J.M. Sempere, C. Llorens, F. Baquero (submitted)



Epidemiology of STIs in the simulated populations. In upper panels, in the MSF group, males are represented in by the red line and females by the light blue line. In the lower panels, in the MSM group the dark blue line corresponds to <35 y.o. individuals male and green line to ≥35 y.o. males. Only the groups having infected cases are represented.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Some conclusions

- Membrane computing has been shown to be a suitable environment for creating highly useful simulation tools in computational and systems biology.
- P systems provide great flexibility when it comes to creating new rules that are extremely useful in the explainability of biological systems.
- The different running architectures for the simulators (i.e. CUDA, MECOSIM, ...) are a competitive and efficient alternative to the classic systems based on ODEs.

José M. Sempere
email: jsempere@dsic.upv.es
url: http://jsempere.webs.upv.es/

Thank you for your attention !!

Děkuji vám za Váš čas !!