Applications of membrane systems in population biology and ecological modelling

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- P Systems → modeling framework
  - Ecosystems
- Randomness → probabilistic strategies

Simulation algorithms

- Reproduce the behaviour of the models
- Validation
- Virtual experimentation

Software

- Implements the algorithms
- GUI for the end-user

- Ordinary Differential Equations (ODEs)

- Petri Nets (Goss, 1998)
- Agent Based Systems (Holcombe, 2003)
- Process Algebra, π–calculus (A. Regev, E. Shapiro, 2004)
- Bioambients (L. Cardelli, E.M. Panina, A. Regev, W. Silvermann, E. Shapiro, 2004)
- Brane Calculus (L. Cardelli, 2005)

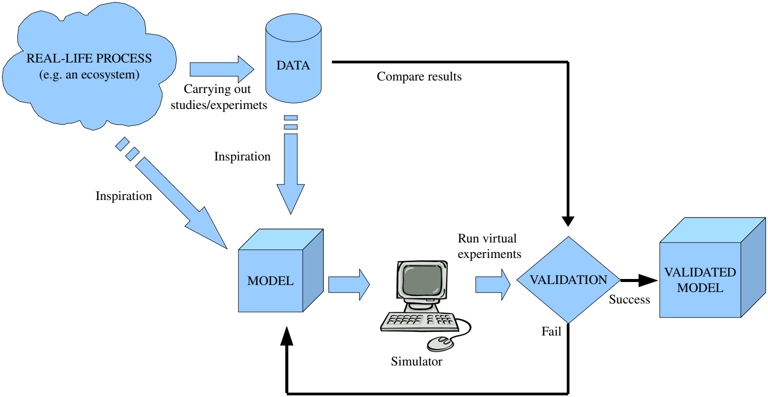
- Relevance
- Understandability
- Extensibility
- Computability / treatability

P systems

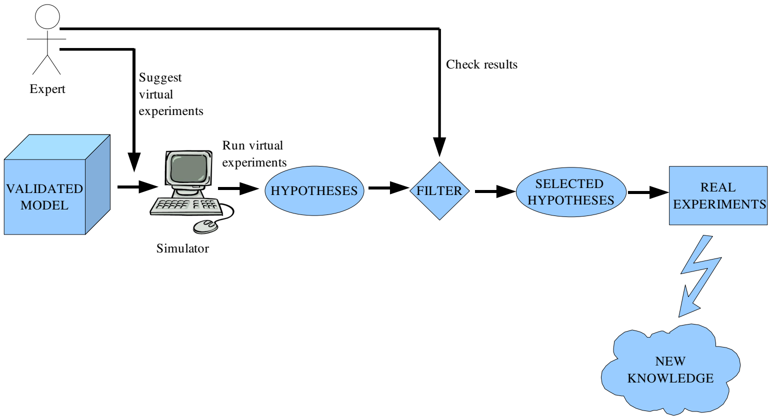
Modeling framework that meets these requirements.

Modeling ecosystems

Validation process



Virtual Experiments



Need to define a new variant of P Systems

- Cooperation
- Randomness
- Communication between environments
- Membrane polarization

A P system based modeling framework

- A skeleton of an extended P system with active membranes of degree q ≥ 1,

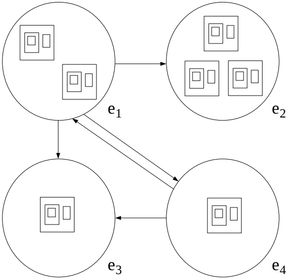
$$(\Gamma, \mu, R)$$

- A probabilistic functional extended P system with active membranes of degree q ≥ 1, taking T time units,

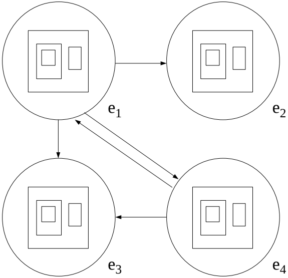
$$\Pi = (\Gamma, \mu, R, T, \{f_r : r \in R\}, M_0, \dots, M_{q-1})$$

- A multienvironment probabilistic functional extended P system with active membranes of degree (m, q) taking T time units,

$$(\Sigma, G, R_E, \Gamma, \mu, R, T, \{f_{rj} : r \in R_\Pi, 1 \leq j \leq m\}, M_{ij} : 0 \leq i \leq q-1, 1 \leq j \leq m)$$



Stochastic aproximation



Probabilistic aproximation

Functions related to rules

Stochastic aproximation

- Kinetic constants
- Stochastic constants
- Propensity

Probabilistic aproximation

- Probabilistic functions

Environment rules

$$(x)_{e_j} \xrightarrow{p_{(x,j,j')}} (y)_{e_{j'}} \qquad \text{y} \qquad (\Pi_k)_{e_j} \xrightarrow{p_{(k,j,j')}} (\Pi_k)_{e_{j'}}$$

Multienvironment P systems

Functional extended with active membrane

Simulation algorithms ← **Take the semantics of the model**

Stochastic aproximation

- Multicompartimental Gillespie Algorithm [1]
- Time wait algorithm [1]

Probabilistic Aproximation

- *Uniform Random Distribution Algorithm* [2]
- *Binomial Random Distribution Algorithm* [2]
- *DNDP: Direct non deterministic with probabilities algorithm* [3]
- *BDD-CB: Block based direct distribution for consistent blocks*

1 M.J. Pérez-Jiménez, F.J. Romero-Campero. P systems, a new computational modelling tool for Systems Biology. *Transactions on Computational Systems Biology VI*. Lecture Notes in Bioinformatics, 4220 (2006), 176–197

2 M. Cardona, M.A. Colomer, A. Margalida, A. Palau, I. Pérez-Hurtado, M.J. Pérez-Jiménez, D. Sanuy. A Computational Modeling for Ecosystems Based on P Systems. *Natural Computing*, in press.

3 M.A. Martínez-del-Amor, I. Pérez-Hurtado, M.J. Pérez-Jiménez, A. Riscos-Núñez, M.A. Colomer. A new simulation algorithm for probabilistc P systems. *Proceedings of the 2010 IEEE Fifth International Conference on Bio-Inspired Computing: Theories and Applications BIC-TA*, 2010, 59–68

Applications

Stochastic aproximation

- Quorum Sensing (Vibrio Fischeri) [1]
- Signaling pathways (FAS, EGFR) [2, 3]
- Gene regulation in prokaryotes (Lac Operon) [4]

1 F.J. Romero, M.J. Pérez-Jiménez. A model of the Quorum Sensing System in Vibrio Fischeri using P systems. *Artificial Life*, 14, 1 (2008), 95-109.

2 S. Cheruku, A. Paun, F.J. Romero, M.J. Pérez-Jiménez, O.H. Ibarra. Simulating FAS-induced apoptosis by using P systems. *Progress in Natural Science*, 17, 4 (2007), 424-431.

3 M.J. Pérez-Jiménez, F.J. Romero. A study of the robustness of the EGFR signalling cascade using continuous membrane systems. *Lecture Notes in Computer Science*, 3561 (2005), 268-278.

4 F.J. Romero, M.J. Pérez-Jiménez. Modelling gene expression control using P systems: The Lac Operon, a case study. *BioSystems*, 91, 3 (2008), 438-457.

Applications

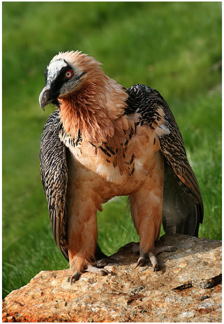
Probabilistic aproximation

- A real ecosystem related to the bearded vulture [1,2]
- A real ecosystem related to the zebra mussel [3]

1 M. Cardona, M. A. Colomer, M.J. Pérez–Jiménez, D. Sanuy, A. Margalida. Modelling ecosystems using P systems: The Bearded Vulture, a case of study. *Lecture Notes in Computer Science*, 5391 (2009), 137–156.

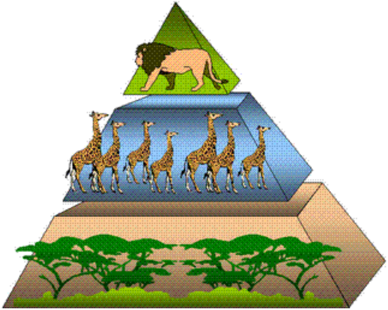
2 M. Cardona, M.A. Colomer, A. Margalida, I. Pérez-Hurtado, M.J. Pérez-Jiménez, D. Sanuy. A P system based model of an ecosystem of some scavenger birds. *Lecture Notes in Computer Science*, 5957 (2010), 182-195.

3 M. Cardona, M.A. Colomer, A. Margalida, A. Palau, I. Pérez-Hurtado, M.J. Pérez-Jiménez, D. Sanuy. A Computational Modeling for Ecosystems Based on P Systems. *Natural Computing*, in press.



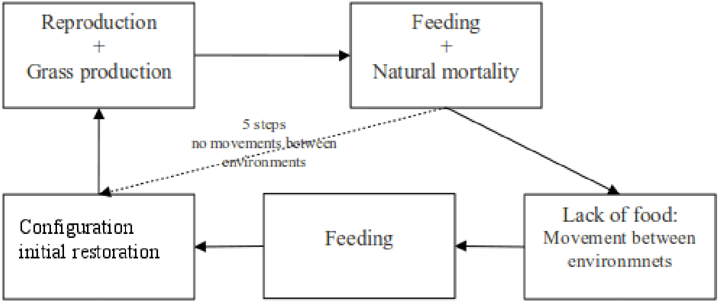
- **Modeling Ecosystems using P systems: The Bearded Vulture, a case study**. Cardona et al. *LNCS*, 2009. Vol IV, 137–156.
- **P System Based Model of an Ecosystem of the Scavenger Birds**. Cardona et al. *LNCS*, 2010. Vol IV, 182–195.
- **A Computational Modeling for real Ecosystems based on P systems**. Cardona et al. *Natural Computing*, 2010. on-line version.

Example: Tritrophic Interactions



- Simplification of a real ecosystem
- Three trophic levels
  - (3) Carnivores
  - (2) Herbivores
  - (1) Grass
- The model
  - 5 modules
  - 9 steps per cycle
  - 10 areas

Tritrophic Interactions

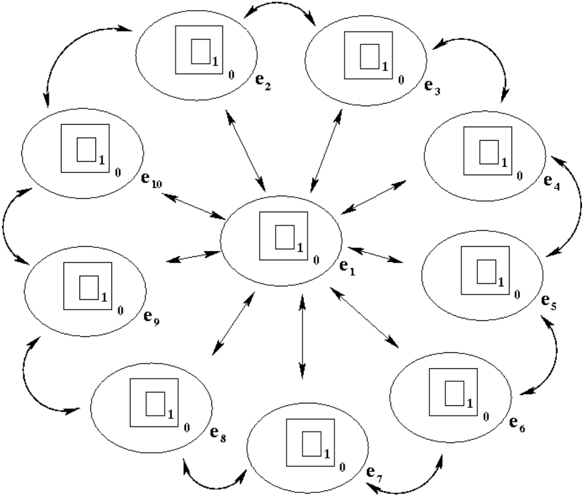


Tritrophic Interactions

$$(G, \Gamma, \Sigma, \Pi, R_E, \{f_{r,j} : r \in R_\Pi, 1 \le j \le 10\}, \{\mathcal{M}_{ij} : 0 \le i \le 1, 1 \le j \le 10\})$$

- $G = (V, S)$
- $\Gamma = \{X_i : 1 \le i \le 7\} \cup \{X'_i, Y_i : 2 \le i \le 7\} \cup \{R_i : 0 \le i \le 6\} \cup G.$
- $\Sigma = \{X_i, X'_i : 2 \le i \le 7\}.$
- $\Pi = (\Gamma, [[\,]_1]_0, R_\Pi).$
- $R_E = \{(X_i)_{e_k} \xrightarrow{p_{k,s,i}} (X'_i)_{e_s} : 1 \le k \le 10, 1 \le s \le 10, 2 \le i \le 7\}$
- $\{f_{r,j} : r \in R_\Pi, 1 \le j \le 10\}$
- $\{\mathcal{M}_{ij} : 0 \le i \le 1, 1 \le j \le 10\}$
  - $\mathcal{M}_{0j} = \{X_1^{q_{1,j}}, R_0 : 1 \le j \le 10\}.$
  - $\mathcal{M}_{1j} = \{X_2^{q_{2,j}}, \ldots, X_7^{q_{7,j}} : 1 \le j \le 10\}.$
- $R = R_E \cup R_\Pi$

Tritrophic Interactions



- Grass production

  $r_{1,j} \equiv X_1[\ ]_1^0 \xrightarrow{m_j} [X_1, G^{h_j}]_1^+,\ 1 \le j \le 3$

- Females which reproduce and generate d_i offsprings.

  $r_{2,i} \equiv [X_i]_1^0 \xrightarrow{k_{i,1} \cdot 0{,}5} [X_i^{1+d_i}]_1^+, 2 \le i \le 7$

- Females and males which don't reproduce.

  $r_{3,i} \equiv [X_i]_1^0 \xrightarrow{1-k_{i,1} \cdot 0{,}5} [X_i]_1^+, 2 \le i \le 7$

- P system synchronization.

  $r_4 \equiv R_0[\ ]_1^0 \rightarrow [R_0]_1^+$

Tritrophic Interactions
Feeding + Natural mortality

- Animals which feed and survive.

  $r_{5,i} \equiv [X_i G^{f_i}]_1^+ \xrightarrow{1-k_{i,2}} [Y_i]_1^-, 2 \leq i \leq 6$

  $r_{6,i} \equiv [X_7 X_i^{f_7}]_1^+ \xrightarrow{1-k_{7,2}} [Y_7]_1^-, 2 \leq i \leq 6$

- Animals which feed and don't survive.

  $r_{7,i} \equiv [X_i G^{f_i}]_1^+ \xrightarrow{k_{i,2}} [\,]_1^-, 2 \leq i \leq 6$

  $r_{8,i} \equiv [X_7 X_i^{f_7}]_1^+ \xrightarrow{k_{i,2}} [\,]_1^-, 2 \leq i \leq 6$

- P system synchronization.

  $r_9 \equiv [R_0]_1^+ \rightarrow [R_0]_1^-$

Tritrophic Interactions

Lack of food: movement between environments

- The objects related to species which have not eaten go to the skin membrane.

  $r_{10,i} \equiv [X_i]_1^- \longrightarrow X_i[\ ]_1^-, 2 \leq i \leq 7$

- The objects in the skin go to the environment.

  $r_{11,i} \equiv [X_i]_0^0 \longrightarrow X_i[\ ]_0^0, 2 \leq i \leq 7$

- Movement of objects between environments.

  $r_{12,k,s,i} \equiv (X_i)_{e_k} \xrightarrow{p_{k,s,i}} (X_i')_{e_s},$
  $1 \leq k \leq 10, 1 \leq s \leq 10, 2 \leq i \leq 7$

- The object X' goes into the skin membrane.

  $r_{13,i} \equiv X_i'[\ ]_0^0 \longrightarrow [X_i']_0^0, 2 \leq i \leq 7$

- The object X' goes into the inner membrane.

  $r_{14,i} \equiv X_i'[\ ]_1^- \longrightarrow [X_i']_1^-, 2 \leq i \leq 7$

- P system synchronization.

  $r_{15,l} \equiv [R_l]_1^- \longrightarrow [R_{l+1}]_1^-, 0 \leq l \leq 4$

Tritrophic Interactions

Feeding

resources in the new area $\rightarrow$ possibility to feed and survive.

$$r_{16} \equiv [X'_i G^{f_i}]_1^- \xrightarrow{1-k_{i,2}} [Y_i]_1^0, 2 \leq i \leq 6$$

$$r_{17} \equiv [X'_7 X'^{f_7}_i]_1^- \xrightarrow{1-k_{7,2}} [Y_7]_1^0, 2 \leq i \leq 6$$

$$r_{18} \equiv [X'_7 Y_i^{f_7}]_1^- \xrightarrow{1-k_{7,2}} [Y_7]_1^0, 2 \leq i \leq 6$$

$$r_{19} \equiv [X'_i G^{f_i}]_1^- \xrightarrow{k_{i,2}} [\ ]_1^0, 2 \leq i \leq 6$$

$$r_{20} \equiv [X'_7 X'^{f_7}_i]_1^- \xrightarrow{k_{7,2}} [\ ]_1^0, 2 \leq i \leq 6$$

$$r_{21} \equiv [X'_7 Y_i^{f_7}]_1^- \xrightarrow{k_{7,2}} [\ ]_1^0, 2 \leq i \leq 6$$

$$r_{22} \equiv [R_5]_1^- \longrightarrow [R_6]_1^0$$

$$r_{23,i} \equiv [Y_i]_1^0 \longrightarrow [X_i]_1^0, 2 \leq i \leq 7$$

$$r_{24} \equiv [R_6]_1^0 \longrightarrow [R_0]_1^0$$

$$r_{25} \equiv [X_1]_1^0 \longrightarrow X_1[\;]_1^0$$

$$r_{26,i} \equiv [X_i']_1^0 \longrightarrow [\;]_1^0, 2 \leq i \leq 7$$

$$r_{27} \equiv [G]_1^0 \longrightarrow [\;]_1^0$$

- Strategy based on the binomial distribution
- Blocks of rules with the same left-hand side
  - Probabilities summing 1
  - Consistent charges in right-hand side
- Each simulation step is composed by
  (1) Selection micro-step
  (2) Execution micro-step

This simulation algorithm is useful for the most of the cases but it has the next disadvantages:

- It needs to classify the rules by its left-hand-side.
- It does not handle rules with intersections on their left-hand-sides.
- It does not check the consistency of charges in the selection of rules.
- It does not evaluate probabilistic functions related to rules.

Simulation algorithms

Direct non-deterministic distribution algorithm with probabilities (DNDP)

Input: A multienvironment functional P system with active membranes of degree (q, m) with $q \geq 1,\ m \geq 1$, taking T time units, $T \geq 1$, and a natural number $K \geq 1$.

```
for t ← 0 to T − 1 do
    C_t ← configuration of the system at the moment t
    C'_t ← C_t
    initialization
    First selection phase. It generates a multiset of consistent applicable rules.
    Second selection phase. It generates a multiset of maximally consistent
    applicable rules.
    Execution of selected rules.
    C_{t+1} ← C'_t
end for
```

Simulation algorithms

DNDP Algorithm: Initialization

$R_\Pi \leftarrow$ ordered set of rules of Π
for $j \leftarrow 1$ to m **do**
  $R_{E,j} \leftarrow$ ordered set of rules from R_E related to the environment j
  $A_j \leftarrow$ ordered set of rules from $R_{E,j}$ whose probability at the moment t is > 0
  $M_j \leftarrow$ ordered set of pairs $\langle label, charge \rangle$ for all the membranes from C_t contained in the environment j
  $B_j \leftarrow \emptyset$
  for each $\langle h, \alpha \rangle \in M_j$ (following the considered order) **do**
    $B_j \leftarrow B_j \cup$ ordered set of rules $u[v]_h^\alpha \leftarrow u'[v']_h^\beta$ from R_Π whose probability at the moment t is > 0 for the environment j
  end for
end for

Simulation algorithms

DNDP Algorithm: First selection phase (*consistency*)

for $j \leftarrow 1$ to m **do**
    $R^1_{sel,j} \leftarrow$ *the empty multiset*
    $R^2_{sel,j} \leftarrow$ *the empty multiset*
    for $k \leftarrow 1$ to K **do**
        $D_j \leftarrow A_j \cup B_j$ with a *random order*
        for each $r \in D_j$ (following the considered order) **do**
            if r is *consistent* with the rules in $R^1_{sel,j}$ **then**
                $n \leftarrow$ applications(r,j)
                if $n > 0$ **then**
                    $C'_t \leftarrow C'_t - n \cdot l(r)$
                    $R^1_{sel,j} \leftarrow R^1_{sel,j} \cup \{< r, n >\}$
                else
                    $R^2_{sel,j} \leftarrow R^2_{sel,j} \cup \{< r, n >\}$
                end if
            end if
        end for
    end for
end for

Simulation algorithms

DNDP Algorithm: First selection phase (*applications* function)

$n \leftarrow 0$
$N' \leftarrow$ max{number of times that r is applicable to C'_t}
if $N' > 0$ **then**
    if $p_{r,j}(t) = 1$ **then**
        $n \leftarrow F_b(N', 0{,}5)$
    else
        $N \leftarrow$ max{number of times that r is applicable to C_t}
        $n \leftarrow F_b(N, p_{r,j}(t))$
        if $n > N'$ **then**
            $n \leftarrow N'$
        end if
    end if
end if
return n

Simulation algorithms

DNDP Algorithm: Second phase of rules selection (*maximality*)

for $j \leftarrow 1$ to m **do**

  $R_{sel,j} \leftarrow R^1_{sel,j} + R^2_{sel,j}$ *with an order by the rule probabilities, from highest to lowest*

  for each $< r, n > \in R_{sel,j}$ (following the selected order) **do**

    if $n > 0 \vee$ (r is *consistent* with the rules in $R^1_{sel,j}$) **then**

      $N' \leftarrow$ max{number of times that r is applicable to C'_t}

      if $N' > 0$ **then**

        $R^1_{sel,j} \leftarrow R^1_{sel,j} \cup \{< r, N' >\}$

        $C'_t \leftarrow C'_t - N' \cdot l(r)$

      end if

    end if

  end for

end for

Simulation algorithms

DNDP Algorithm: Execution of selected rules

for each $< r, n > \in R^1_{sel,j}$ **do**
    $C'_t \leftarrow C'_t + n \cdot r(r)$
    Update the electrical charges of C'_t according to $r(r)$
end for

Simulation results

Software used

- P-Lingua: programming language to define P systems

    `http://www.p-lingua.org`

- pLinguaCore: Java library $\rightarrow$ P-Lingua parser + simulation algorithms
- A specific Java GUI over pLinguaCore
    - Input
        - Initial ecosystem parameters
        - Number of years (complete cycles) to simulate
        - Number of simulations per year
    - Output
        - Evolution of the populations
        - Tables and graphs

Simulation results

Number of animals of each species and grass surface

Tritrophic Interactions [beta]

Ecosystem Edit Model Simulation Help

Parameters | Simulation | Debug console

Animals | Grass | Populations | Movements

Species	Area 1	Area 2	Area 3	Area 4	Area 5	Area 6	Area 7	Area 8	Area 9	Area 10
Grass	5.000	20.000	5.000	15.000	7.000	5.500	4.000	15.000	9.000	22.000
Species 2	500	1.000	200	2.000	1.000	1.250	980	575	580	1.450
Species 3	500	400	100	450	375	400	300	250	375	200
Species 4	500	250	200	150	400	675	225	350	450	200
Species 5	500	600	400	500	780	550	800	775	525	675
Species 6	25	30	50	60	50	25	12	35	75	100
Species 7	2	0	0	0	4	0	0	0	0	0

P SYSTEM USER **(dndp2 simulation algorithm K=1, check left-hand-rule sides)**

Data: C:\Users\Usuario\Desktop\tritrophicSimulador\escenari1.ec2 (unsaved)

Model: C:\Users\Usuario\Desktop\tritrophicSimulador\Tritrophic6especies.pli

Simulated years: 100

Simulations by year: 50

Steps by year: 9

0% (0.0 s)

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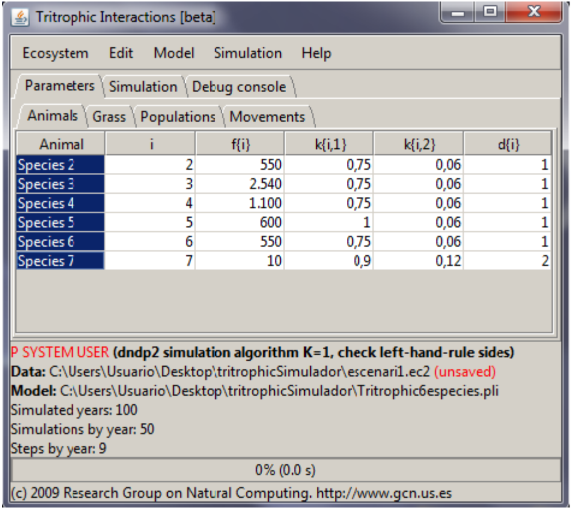
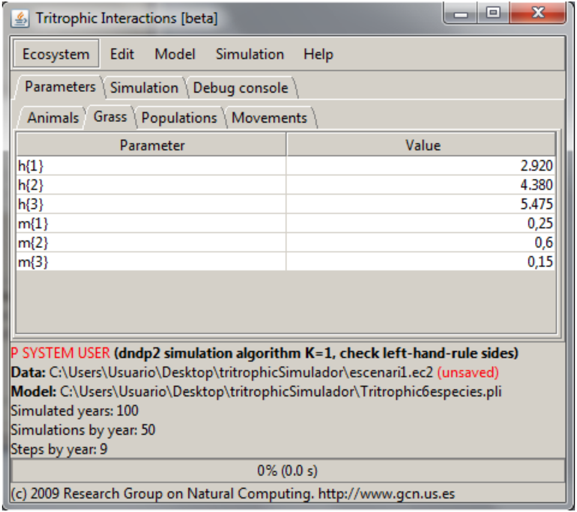
Simulation results

Biological parameters



Simulation results

Parameters related to grass



Simulation results

Probabilities of species movement

Tritrophic Interactions [beta]

Ecosystem Edit Model Simulation Help

Parameters | Simulation | Debug console

Animals | Grass | Populations | Movements

Movement	Species 2	Species 3	Species 4	Species 5	Species 6	Species 7
p{1,1,i}	0,91	0,91	0,91	0,91	0,91	0,01
p{1,2,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,3,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,4,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,5,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,6,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,7,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,8,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,9,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{1,10,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{2,1,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{2,2,i}	0,97	0,97	0,97	0,97	0,97	0,01
p{2,3,i}	0,01	0,01	0,01	0,01	0,01	0,11
p{2,4,i}	0	0	0	0	0	0,11
p{2,5,i}	0	0	0	0	0	0,11
p{2,6,i}	0	0	0	0	0	0,11
p{2,7,i}	0	0	0	0	0	0,11

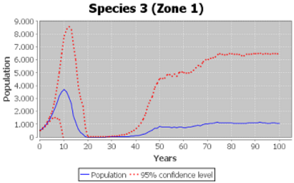
P SYSTEM USER **(dndp2 simulation algorithm K=1, check left-hand-rule sides)**

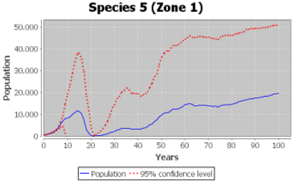
Data: C:\Users\Usuario\Desktop\tritrophicSimulador\escenari1.ec2 (unsaved)

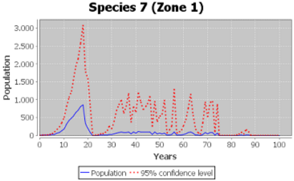
Model: C:\Users\Usuario\Desktop\tritrophicSimulador\Tritrophic6especies.pli

Simulated years: 100

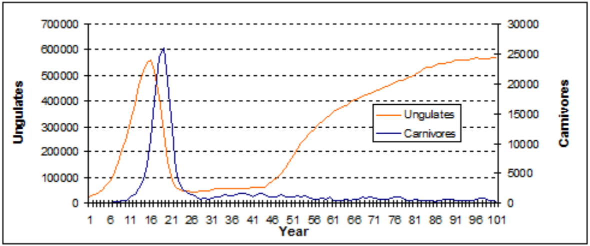
Simulation results



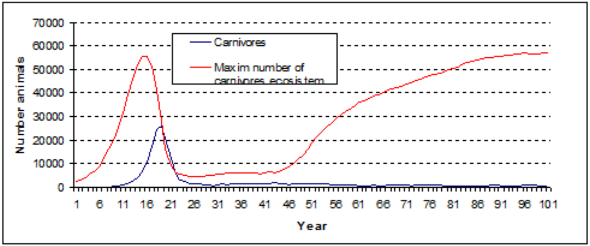




Simulation results



Simulation results



Simulation results

	Scenario 1		Scenario 2	
Algorithm	**Binomial**	**Dndp**	**Binomial**	**Dndp**
Simulation 1	58,41	54,94	63,62	57,81
Simulation 2	58,57	55,10	61,56	58,58
Simulation 3	58,29	56,05	61,39	57,22
Simulation 4	58,19	56,31	62,81	58,19
Simulation 5	58,75	55,21	61,20	58,75
Simulation 6	57,56	55,19	62,86	57,17
Simulation 7	58,13	54,62	61,92	58,68
Average	58,27	55,35	62,19	58,06
Deviation	0,38	0,61	0,91	0,67

Conclusions

- P systems provide a high-level modeling framework for ecosystems
- Software tools based on membrane computing can be used by ecologists
  - Bearded vulture
  - Zebra mussel
- It has been designed simulation algorithms
- A software framework based on P-Lingua has been provided
- A virtual ecosystem has been used as an example

Future work

- Design new simulation algorithms
- Develop simulators based on High Performance Computing (GPUs)
- Design a common protocol to communicate simulators and user interfaces
  - Using different platforms for simulators
  - Codyfing P systems on a standard format file
- Extend the software framework to cover more types of P systems
- Design more efficient and standard GUIs for final users

Thanks!