

## *Inteligencia computacional y algoritmos bio-inspirados: sistemas víricos*

Pablo Cortés

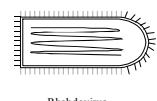
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- Viral systems foundations
  - Artificial Intelligence algorithms based on trajectories
  - Artificial Intelligence algorithms based on populations
  - Particle swarm optimization
  - Immune systems
  - Multi-agent systems



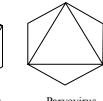
Reovirus



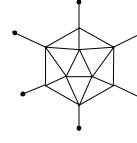
Rhabdovirus



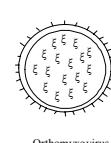
Picornavirus  
(poliovirus)



Parvovirus



Adenovirus



Orthomyxovirus  
(influenza)

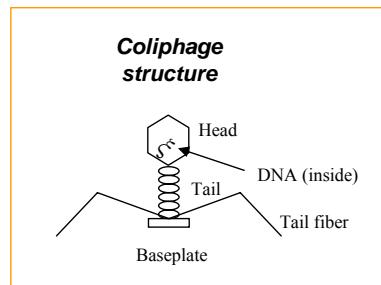


Herpesvirus

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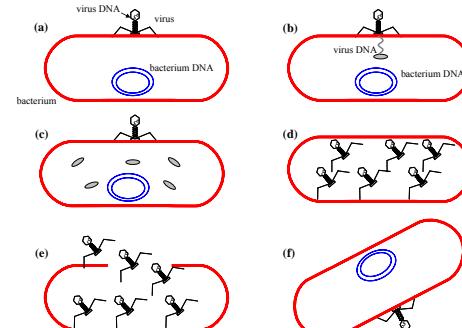
- Viruses are intracellular parasites shaped by nucleic acids, such as DNA or RNA, and proteins.
- The protein generates a capsule, called a capsid, where the nucleic acid is located. The capsid plus the nucleic acid shape the nucleus-capsid, defining the virus.
- One of the main characteristics of viruses is the replication mechanism. The phage (a common type of virus) does follow lytic replication process.



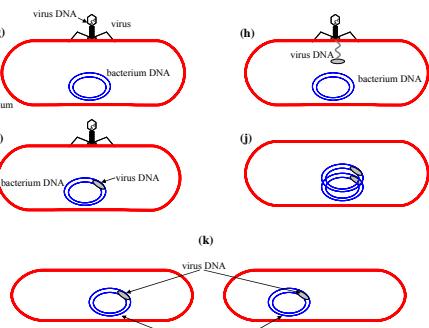
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## Lytic replication



## Lysogenic replication



- The virus is **adhered to the border** of the bacterium. Virus **penetrates the border** being injected inside this one, (a) and (b)
- The infected cell stops the production of its proteins, beginning to produce the phage proteins, **starting to replicate copies** of the virus nucleus-capsids, (c) and (d)
- After **replicating a number of nucleus-capsids**, the bacterium **border is broken**, and **new viruses are released**, (e) which can infect near cells, (f)
- The virus **infects the host cell**, being lodged in its genome, (g) and (h)
- The virus **remains hidden inside the cell** during a while until it is **activated by any cause**, for example ultraviolet irradiation or X-rays, (i)
- The **replication of cells altered, with proteins from the virus**, starts → Similar to a mutation process.

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1.	<b>Virus component</b>
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- VS are defined by three components: a set of viruses, an organism and an interaction between them:  

$$VS = \langle Virus, Organism, Interaction \rangle$$
- Virus component** of the VS is a set consisting of single viruses:  

$$Virus = \{Virus_1, Virus_2, \dots, Virus_n\}.$$
- Each virus is defined in four components:  

$$Virus_i = \langle State_i, Input_i, Output_i, Process_i \rangle$$
- State<sub>i</sub>**, defines the cell infected by the virus. It is typically the mathematical encoding of the solution in computational terms, which we also call genome.
- Input<sub>i</sub>**, identifies the information that the virus can collect from the organism (sensor). It represents the input's interaction with the organism. It corresponds to the neighbourhood of the cell in computational terms.
- Output<sub>i</sub>**, identifies the actions that the virus can take (actuator). It corresponds to the selection mechanism of the type of virus replication in computational terms.
- Process<sub>i</sub>**, represents the autonomous behaviour of the virus, changing the **State<sub>i</sub>**. It corresponds to the replication operator process in computational terms.

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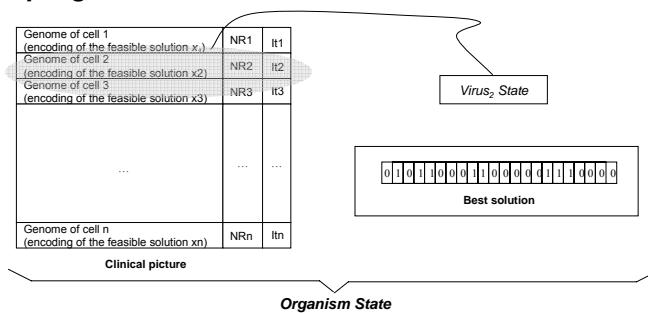


$$VS = \langle Virus, Organism, Interaction \rangle$$

- Organism component** of the VS is defined by two components:::  

$$Organism = \langle State_o, Process_o \rangle$$
- State<sub>o</sub>**, characterizes the organism state in each instant. The set of feasible solutions in a specific space  $\mathbb{R}^n$  is given by the problem constraints  

$$K = \{x : g_i(x) \leq 0, \forall i = 1, \dots, n\}$$
- Each feasible solution  $x \in K$  is called a cell. The genome is the mathematical encoding of each cell or feasible solution. The total amount of infected cells constitutes the infected part of K for each time instant, and it is named **clinical picture**. The **clinical picture consists of every three-tuple genome-NR-IT**.

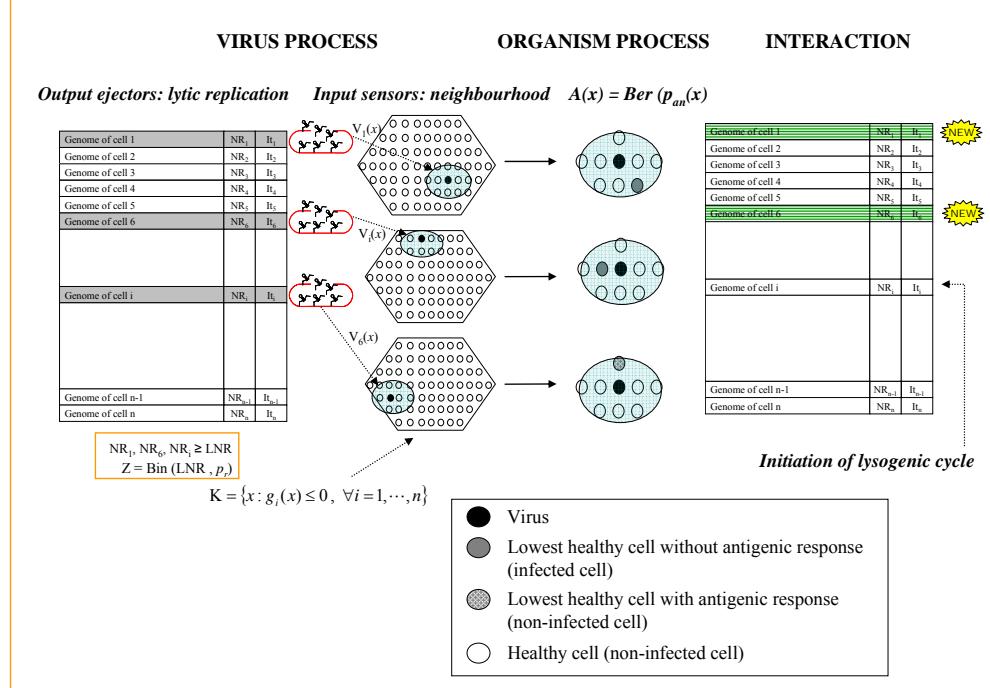


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- **Organism component** of the VS is defined by two components::  
 $\text{Organism} = \langle \text{State}_o, \text{Process}_o \rangle$
  - **Process<sub>o</sub>**, represents the autonomous behaviour of the organism that tries to protect itself from the infection threat, consisting of antigen liberation.
    - An antigen is any substance that elicits an immune response. The antigens generate an immune response by means of antibodies trying to fight the virus infection.
    - The computational mission of the antigens is to liberate space in the population of infected cells (clinical picture), trying to maintain free record memory in the clinical picture to incorporate new infected cells (new feasible solutions).
- $\text{VS} = \langle \text{Virus}, \text{Organism}, \text{Interaction} \rangle$
- **Interaction component** of the VS is conditioned by the *Input* and *Output* actions that lead to a Process of every virus and the corresponding Organism response.
    - A Virus;process implies a resulting change in the organism, and the same applies for an Organism's process.
    - The interaction is the union of both actions.

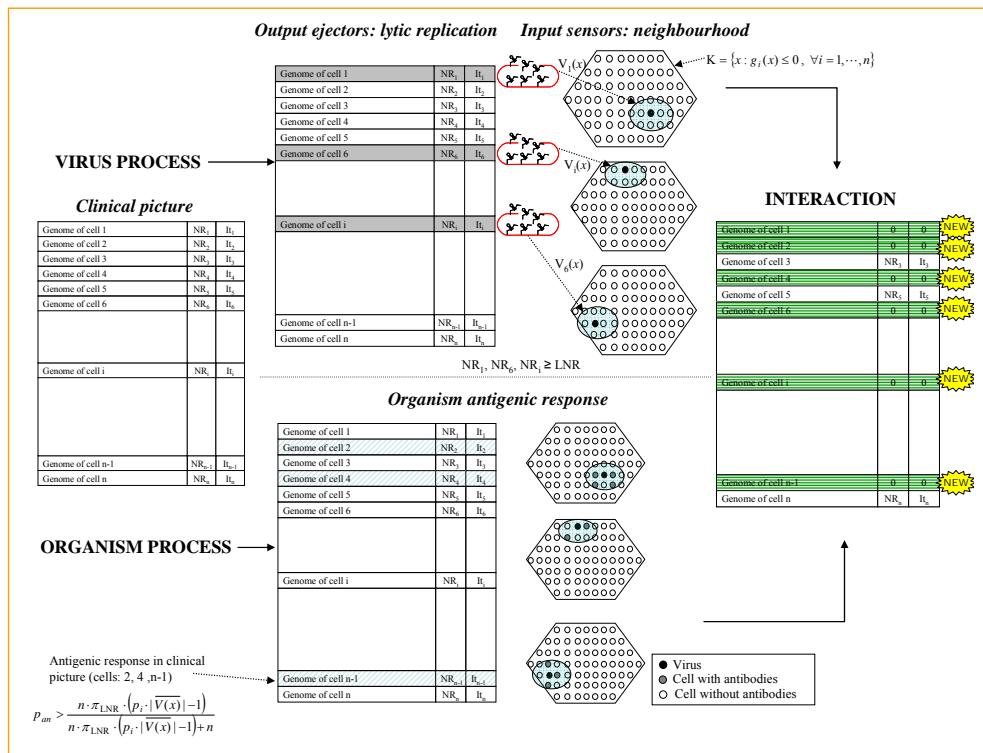
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  2. Massive infection
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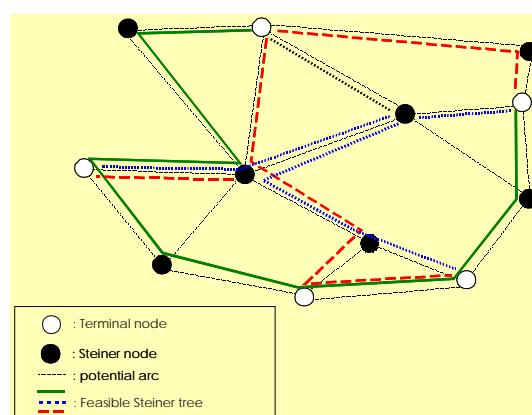
1. Introduction
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  1. Selective infection
  2. Massive infection

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## Adapting VS to the Steiner problem

- **Organism State** is given by the feasibility region:
 
$$K : X(\delta(W)) \geq 1, \forall W \subset N, W \cap T \neq \emptyset, ((N \setminus W) \cap T \neq \emptyset)$$

$$0 \leq x_{ij} \leq 1, \forall (i, j) \in A; x \text{ integer}$$
- **Organism process**: antigenic response from cells
- **Virus state** is the three-tuple:
  - Genome: a bit string with the Steiner nodes that are in the tree
  - number of replicated nucleus-capsids (lytic replication)
  - Number of hidden generations (lysogenic replication)
- **Output ejector**: type of replication
- **Input sensor**: neighbourhood → constant and N-T sized
- **Virus process**: new cells infected (mapping the feasibility region)

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- Trials: OR-Library J.E. Beasley Imperial College (series C, D & E) <http://people.brunel.ac.uk/~mastjib/jeb/info.html>
- Series C: 500 nodes, arcs varying from 625 to 12,500, and terminals from 5 to 250
- Series D: 1,000 nodes, arcs varying from 1,250 to 25,000 , and terminals from 5 to 500
- Series E: 2,500 nodes, arcs varying from 3,125 to 62,500 , and terminals from 5 to 1,250
- Comparison to:
  - **Tabu Search**: Gendreau, M., Laroche, J.-F., Sansò, B. A tabu search heuristic for the Steiner tree problem. Networks 1999; 34 (2):162-172.
  - **Genetic Algorithms**: Esbensen, H. Computing near-optimal solutions to the Steiner problem in a graph using genetic algorithm. Networks 1995; 26, 173-185.
  - **Genetic Algorithms**: Voss, S. and Gutenschwager, K. A chunking based genetic algorithm for the Steiner tree problem in graphs. In Pardalos, P.M., Du, D., (Eds.) Network Design: Connectivity and Facilities Location, DIMAC series in Discrete Mathematics and Theoretical Computer Science 40, AMS, Providence, 1999. p. 335-355.
- Steiner problems categories:
  - Steiner group 1: % terminals < 15% (shortest path approaches provide good solutions)
  - Steiner group 2: % terminals between 15% and 30% (more difficult cases)
  - Steiner group 3: % terminals >30% (MST approaches provide good solutions)

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	Stein-C: group 1			Stein-C: group 2			Stein-C: group 3		
Parameter	Coefficient	t-ratio	P( T > t )	Coefficient	t-ratio	P( T > t )	Coefficient	t-ratio	P( T > t )
ER	-.1627359097E-01	-17.938	.0000	-.1273674287E-01	-17.102	.0000	-.6201052638E-02	-33.383	.0000
DB	.6196468609E-02	6.830	.0000	.5878508007E-02	7.893	.0000	.2075200906E-02	11.172	.0000
LITI	.9859702694E-02	-10.868	.0000	-.1150348920E-01	-15.446	.0000	.7409459177E-02	-39.889	.0000
DL	.3670145379E-03	-.405	.6879	.2385351693E-03	-.314	.7551	.2033251897E-03	1.095	.2799
LT	.6165346813E-02	6.796	.0000	.1751795994E-02	2.352	.0234	.4951710153E-03	2.666	.0109
Z	.1663867492E-03	-.183	.8554	.2691466718E-04	-.036	.9713	.5265526171E-04	-.283	.7782
ER_POB	.7003059497E-02	-7.719	.0000	.5167419501E-02	-6.938	.0000	-.1364551560E-02	-7.346	.0000
ER_PLI	.8558958037E-02	9.434	.0000	.9824820706E-02	13.192	.0000	.5792756906E-02	31.186	.0000
ER_LNR	.7465536683E-04	.082	.9348	.2547066287E-03	.342	.7341	.6346707768E-04	.342	.7343
ER_LIT	.6091337370E-02	-6.714	.0000	-.1309931377E-02	-1.759	.0859	.2162974302E-03	-1.164	.2508
DR_PZ	.1520681087E-03	.168	.8677	.4128354307E-04	.055	.9561	.7542575442E-04	-.406	.6868
DB_PLIT	.3592776392E-02	-3.960	.0003	-.4961598593E-02	-6.662	.0000	-.1731482463E-02	-9.321	.0000
DB_LNR	.7503267980E-03	-.827	.4129	-.5292303695E-04	-.071	.9437	.9390983973E-05	.051	.9599
DR_LIT	.2544590461E-02	2.805	.0076	.3891250128E-03	.522	.6041	.2019797493E-03	1.087	.2831
DR_PZ	.6631948513E-03	-.731	.4688	.1516643456E-03	.204	.8396	.6409390469E-04	-.345	.7318
LITI_LN	.2567051887E-03	.283	.7786	.200066744E-03	.271	.7875	.1561495836E-03	-.841	.4053
LITI_LI	-.1712201851E-02	-1.887	.0660	-.1237158692E-02	-1.661	.1041	-.3410432235E-03	-1.836	.0734
LITI_PZ	.6425612504E-03	-.708	.4827	.1878275183E-03	.252	.8021	.1438668444E-03	.772	.4445
NR_LIT	-.8883046612E-03	-.979	.3331	-.2012397331E-03	-.270	.7883	.8122341766E-04	.437	.6642
NR_PZ	.6213004108E-03	-.685	.4972	.3794939438E-04	.051	.9596	.1411620695E-03	.760	.4515
TPZ	.2776950650E-04	.031	.9757	.9490056945E-04	.127	.8992	.1452575337E-03	-.782	.4386

## Adequate parameters selection

	Group 1		Group 2		Group 3	
Parameters	1 <sup>st</sup> set	2 <sup>nd</sup> set	1 <sup>st</sup> set	2 <sup>nd</sup> set	1 <sup>st</sup> set	2 <sup>nd</sup> set
ITER	50,000 (+)	10,000 (-)	50,000 (+)	50,000 (+)	10,000 (-)	50,000 (+)
POB	100 (+)	50 (-)	100 (+)	50 (-)	50 (-)	50 (-)
PLITI	0.7 (+)	0.7 (+)	0.7 (+)	0.7 (+)	0.7 (+)	0.7 (+)
LNR	15 (~)	15 (~)	15 (~)	15 (~)	10 (-)	10 (-)
LIT	10 (-)	10 (-)	20 (+)	10 (-)	10 (-)	10 (-)
Pz	0.5 (~)	0.5 (-)	0.5 (~)	0.5 (-)	0.5 (~)	0.5 (-)

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Steiner series C							
Problem	Optimum	GA-E	GA-V	MPH	P-Tabu	F-Tabu	VS
C1	85	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C2	144	1,67%	0,83%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C3	754	0,13%	0,13%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C4	154	0,14%	0,04%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C5	1579	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C6	55	0,73%	1,09%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C7	102	1,76%	2,75%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C8	509	0,63%	0,51%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C9	707	1,05%	1,30%	0,99%	0,14%	0,14%	<b>0,00%</b>
C10	1093	0,26%	0,27%	0,09%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C11	32	1,88%	1,88%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C12	46	1,30%	0,43%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C13	258	1,01%	1,32%	0,78%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C14	323	0,87%	0,68%	1,24%	0,31%	0,31%	<b>0,00%</b>
C15	556	0,22%	0,24%	0,12%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C16	11	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C17	18	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
C18	113	0,71%	0,71%	5,31%	0,88%	0,00%	0,00%
C19	146	0,41%	0,82%	4,79%	0,68%	<b>0,00%</b>	<b>0,00%</b>
C20	267	<b>0,00%</b>	<b>0,00%</b>	0,37%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
Best approach	5	5	5	11	0,00%	0,00%	0,00%
				16	18	20	

Steiner series E							
Problem	Optimum	GA-E	MPH	P-Tabu	F-Tabu	VS	
E1	111	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
E2	214	0,93%	0,12%	0,42%	0,32%	0,24%	
E3	4013	<b>0,00%</b>	1,07%	0,42%	0,32%	0,24%	
E4	510	0,02%	0,14%	0,42%	0,32%	0,24%	
E5	8128	<b>0,00%</b>	0,02%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	
E6	73	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	
E7	145	<b>0,00%</b>	2,07%	2,07%	<b>0,00%</b>	<b>0,00%</b>	
E8	2640	<b>0,23%</b>	1,63%	0,49%	0,42%	1,14%	
E9	3604	0,19%	1,17%	0,42%	<b>0,14%</b>	0,47%	
E10	5600	<b>0,00%</b>	0,21%	0,04%	0,04%	0,14%	
E11	34	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	
E12	67	1,49%	1,49%	1,49%	1,49%	1,49%	<b>0,00%</b>
E13	1280	0,70%	1,88%	0,78%	<b>0,63%</b>	1,33%	
E14	1732	<b>0,23%</b>	1,04%	0,29%	<b>0,23%</b>	0,64%	
E15	2784	<b>0,00%</b>	0,22%	0,11%	0,11%	<b>0,00%</b>	
E16	15	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	
E17	25	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	
E18	564	3,37%	7,62%	2,66%	<b>1,60%</b>	2,66%	
E19	758	1,26%	4,35%	1,19%	1,19%	<b>1,18%</b>	
E20	1342	<b>0,00%</b>	0,67%	<b>0,00%</b>	<b>0,00%</b>	0,15%	
Best approach	12	6	6	9	14	12	

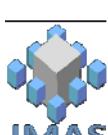
## Steiner series D

Problem	Optimum	GA-E	GA-V	MPH	P-Tabu	F-Tabu	VS
D1	106	0,57%	0,88%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D2	220	<b>0,00%</b>	0,73%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D3	1565	0,92%	1,25%	0,77%	0,26%	0,06%	<b>0,00%</b>
D4	1935	0,52%	0,63%	0,16%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D5	3250	0,12%	0,19%	0,06%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D6	67	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D7	103	1,94%	3,62%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D8	1072	1,55%	2,28%	1,59%	0,47%	<b>0,37%</b>	0,47%
D9	1448	0,50%	1,15%	0,83%	0,41%	<b>0,21%</b>	0,69%
D10	2110	0,13%	0,44%	0,38%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D11	29	2,07%	1,84%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D12	42	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D13	500	0,56%	1,28%	2,08%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D14	66	0,70%	0,78%	0,75%	0,15%	<b>0,45%</b>	0,15%
D15	1116	0,16%	0,30%	0,36%	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D16	13	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D17	23	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>	<b>0,00%</b>
D18	223	1,26%	1,43%	6,28%	1,35%	<b>0,90%</b>	<b>0,90%</b>
D19	310	1,03%	1,20%	5,81%	0,65%	<b>0,32%</b>	0,65%
D20	537	0,15%	0,16%	0,19%	<b>0,00%</b>	<b>0,00%</b>	0,37%
Best approach	5	5	4	8	15	19	16

## Computational Time analysis

Set of Problems	Group	Best Case	Worst Case
Stein-C	1	1	2
Stein-C	2	71	205
Stein-C	3	54	112
Stein-D	1	4	13
Stein-D	2	1,471	4,329
Stein-D	3	166	750
Stein-E	1	6	33
Stein-E	2	4,692	19,892
Stein-E	3	480	3,292

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OR-Library	Group 1	Group 2	Group 3
Trials	C{1,2,6,7,11,12,16,17}	C{8,9,13,14,18,19}	C{13,4,5,10,15,20}
	D{1,2,6,7,11,12,16,17}	D{8,13,14,18,19}	D{3,4,5,9,10,15,20}
	E{1,2,6,7,11,12,16,17}	E{8,13,14,18,19}	E{3,4,5,9,10,15,20}
Average value	MPH : 0,15% GA-V : 0,88% GA-E : 0,60% P-Tabu : 0,15% F-Tabu : 0,06% VS-S : 0,00%	MPH : 2,88% GA-V : 1,13% GA-E : 0,95% P-Tabu : 0,63% F-Tabu : 0,39% VS-S : 0,57%	MPH : 0,35% GA-V : 0,37% GA-E : 0,17% P-Tabu : 0,08% F-Tabu : 0,04% VS-S : 0,10%
Standard Deviation	MPH : 0,50% GA-V : 1,08% GA-E : 0,78% P-Tabu : 0,50% F-Tabu : 0,30% VS-S : 0,00%	MPH : 2,32% GA-V : 0,49% GA-E : 0,73% P-Tabu : 0,66% F-Tabu : 0,46% VS-S : 0,72%	MPH : 0,35% GA-V : 0,39% GA-E : 0,23% P-Tabu : 0,15% F-Tabu : 0,09% VS-S : 0,19%
Maximum error	MPH : 2,07% GA-V : 3,62% GA-E : 2,07% P-Tabu : 2,07% F-Tabu : 1,49% VS-S : 0,00%	MPH : 7,62% GA-V : 2,28% GA-E : 3,37% P-Tabu : 2,66% F-Tabu : 1,60% VS-S : 2,66%	MPH : 1,17% GA-V : 1,25% GA-E : 0,92% P-Tabu : 0,42% F-Tabu : 0,32% VS-S : 0,69%

## Difficulties for Steiner group 2:

% terminals between 15% and 30%

## VS massive infection

Problem	Optimum	% terminals	MPH	GA-Voss	GA-Esh	P-Tabu	F-Tabu	VS-select	VS-massive
C8	509	20,4%	0,00%	0,51%	0,63%	0,00%	0,00%	0,00%	0,39%
C9	707	29,7%	0,99%	1,05%	0,14%	0,14%	0,00%	0,00%	0,00%
C13	258	16,7%	0,78%	1,32%	1,01%	0,00%	0,00%	0,00%	0,00%
C14	323	25,1%	1,24%	0,68%	0,87%	0,31%	0,31%	0,00%	0,00%
C18	113	16,6%	5,31%	0,71%	0,88%	0,00%	0,00%	0,00%	0,00%
C19	146	25,0%	4,79%	0,82%	0,41%	0,68%	0,00%	0,00%	0,00%
D8	1072	20,7%	1,59%	0,72%	0,47%	0,37%	0,47%	0,47%	0,47%
D13	500	16,7%	2,00%	1,48%	0,56%	0,00%	0,00%	0,00%	0,20%
D14	667	25,1%	0,75%	0,75%	0,30%	0,15%	0,15%	0,15%	0,00%
D18	223	16,7%	6,28%	1,43%	1,26%	1,35%	0,90%	0,90%	0,00%
D19	310	25,0%	5,81%	1,20%	1,03%	0,65%	0,32%	0,65%	0,00%
E8	2640	21,1%	1,63%	--	0,23%	0,49%	0,42%	1,14%	1,78%
E13	1280	16,7%	1,88%	--	0,70%	0,78%	0,63%	1,33%	0,55%
E14	1732	25,0%	1,04%	--	0,23%	0,29%	0,23%	0,64%	0,29%
E18	564	16,7%	7,62%	--	3,37%	2,66%	1,60%	2,66%	0,35%
E19	758	25,0%	4,35%	--	1,26%	1,19%	1,19%	1,18%	0,00%
			MPH	GA-Voss	GA-Esh	P-Tabu	F-Tabu	VS-select	VS-massive
Average		2,88%	1,13%	0,95%	0,63%	0,39%	0,57%	0,25%	
Stand. Deviation		2,							

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- A new approach is presented based on a virus infection analogy
- Perspective from the opposite side to Artificial Immune systems
- Very promising approach outperforming very good approaches such as Gendreau et al TS, Voss et al GA or Esbensen GA.
- Further research:
  - We are testing VS in other NP-Hard problems in production (scheduling) context.
  - We are analysing other virus behaviour different from phages to analyse alternative replication cycles and alternative antigenic responses from organisms → Library of different viruses (Ebola, AIDS, Smallpox, etc.)
  - Parallel programming computation (population of computers). A virus in each computer = Trajectories + Population
  - MAS perspective: virus—agent, communication between virus , virus collaborative infection, alien nation

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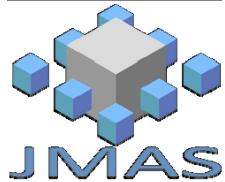
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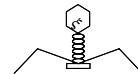
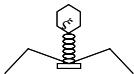


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## *Inteligencia computacional y algoritmos bio-inspirados: sistemas víricos*



**Pablo Cortés**