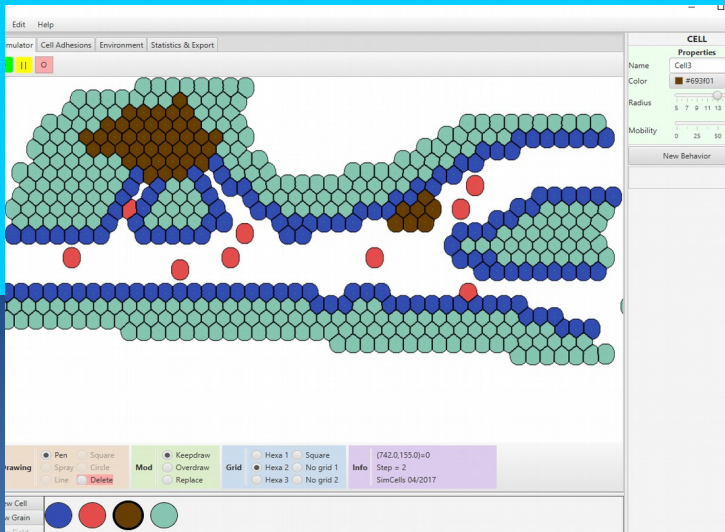


SimCells

<http://virtulab.univ-brest.fr>



User Guide

MULTICELLULAR SIMULATION

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SUMMARY

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1. AGENTS

- CELLS
- GRAINS
- FIELDS

2. BEHAVIOURS

- PRINCIPLES
- CONDITIONS
- ACTIONS

3. EXAMPLES

- PROSTATE

4. DATA ANALYSIS

- DIAGRAMS
- EXPORT
- VIDEO CAPTURE

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INTRODUCTION

SimCells allows the creation of virtual multicellular systems without coding.

The biological problems are described thanks to an agent-based system (agents + behaviours + environment) and are facilitated by a graphical user interface.

Four scale levels are modelled:

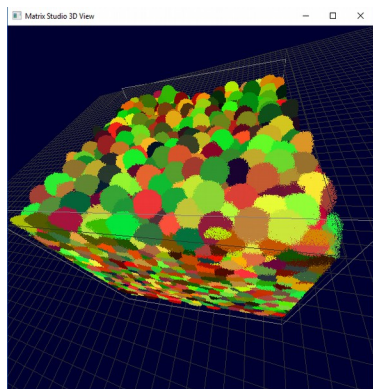
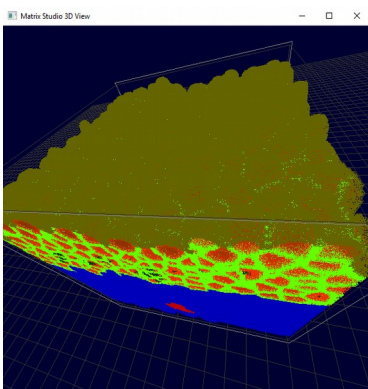
- the multicellular scale (tissues => $1 \times 1 \times 1 \text{ mm}^3$)
- the cell scale ($10 \times 10 \times 10 \text{ } \mu\text{m}^3$)
- the macromolecular (called grain) scale ($1 \times 1 \times 1 \text{ } \mu\text{m}^3$)
- the molecular (called field) scale ($1 \times 1 \times 1 \text{ nm}^3$)

The environment is represented by a 3D matrix where all the agents evolve and interact.

The physical engine of SimCells uses the computational power of multi-cores graphical card, allowing the simulation of millions of cells.

This guide shows the possibilities of SimCells from the point of view of the user.

The 3D is inherent to SimCells. A 3D modeller is on the way:





1

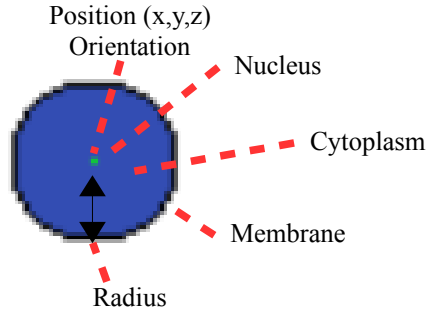
AGENTS

The main entities are the Cells, Grains and Fields. They are the main agents of all multicellular simulations in SimCells. For each entity, parameters can be changed and behaviours can be added (see part 2 - BEHAVIOURS).

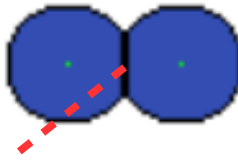


CELLS

A single cell



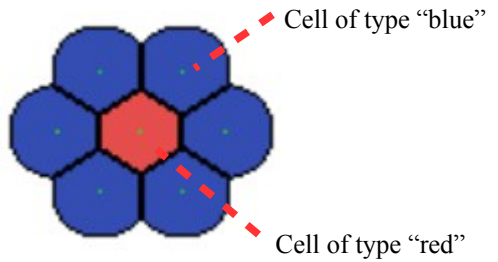
Two interacting cells



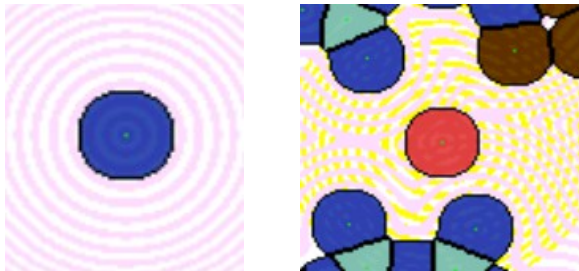
Cell adhesion:

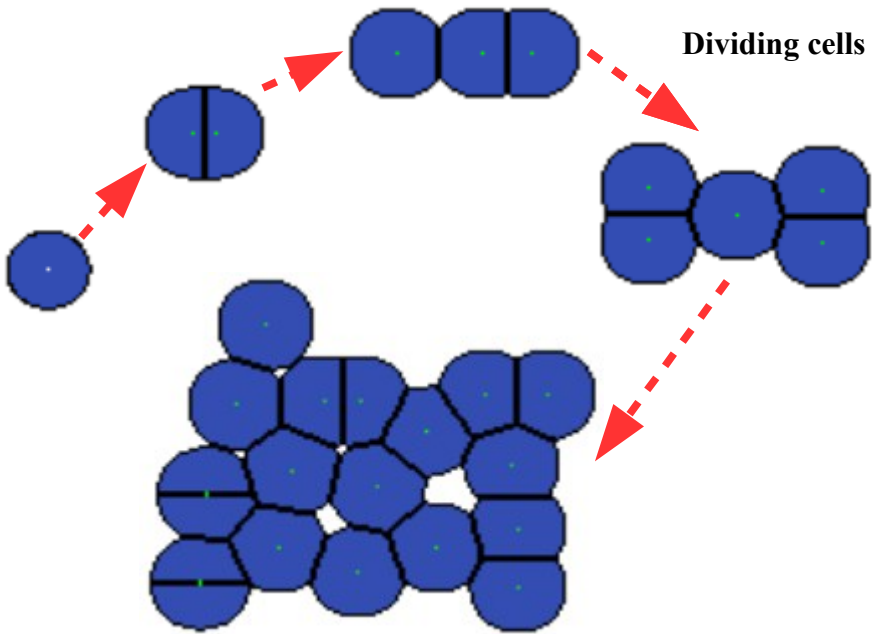
- can be changed for each type (more or less)
- the surface of exchange can be calculated and used in behaviours

Multiple interacting cells



Cells emitting signals





Migrating cells

Other parameters

Age, Pressure, Cell contacts and Membrane flexibility

CELL	
Properties	
Name	Cell2
Color	■ #e64d4d
Radius	<input type="range" value="13"/>
Mobility	<input type="range" value="50"/>
New Behavior ^ v	
... OK	Signal <input checked="" type="checkbox"/>
... OK	Chemotactism <input checked="" type="checkbox"/>

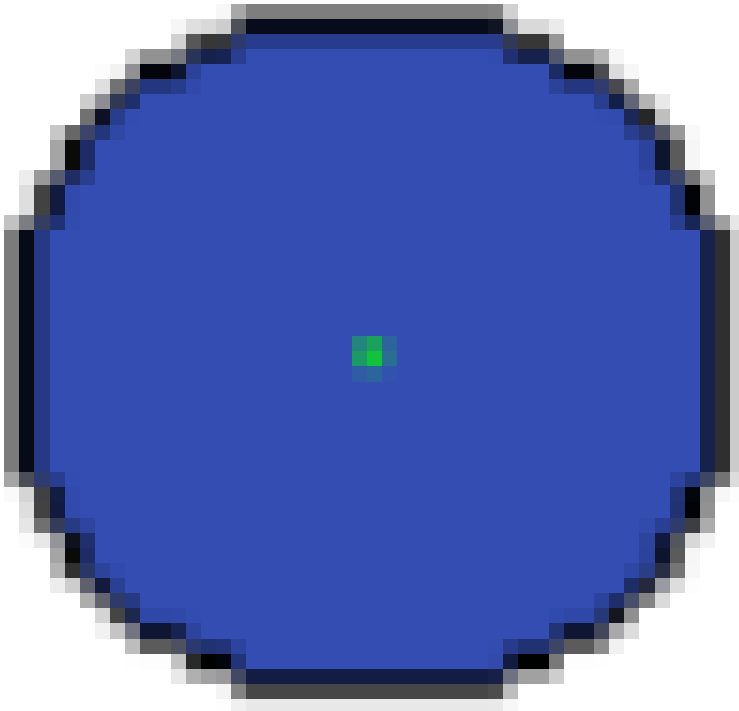
GRAINS

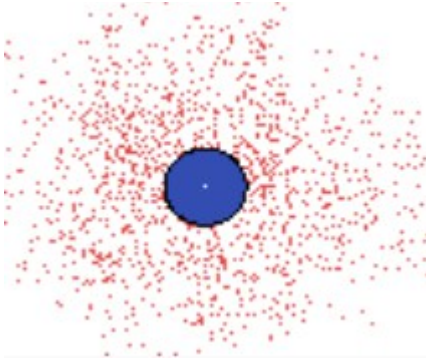
Position (x,y,z)

A single grain



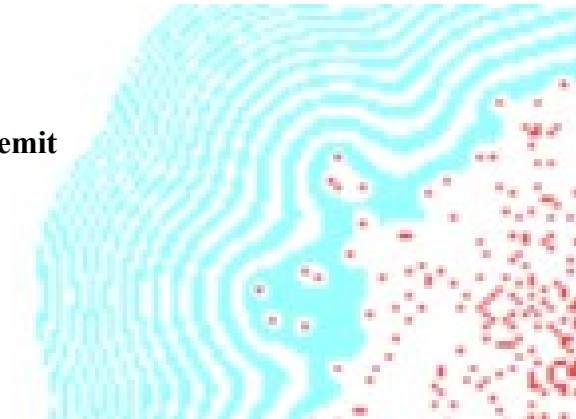
A grain as compared with a single cell





A cell can produce and consume grains

Grains can, like cells, emit signals.



Grains have roughly the same abilities as cells: signalling, migration, division, deletion, differentiation, transformation (grain => cell or cell => grain).

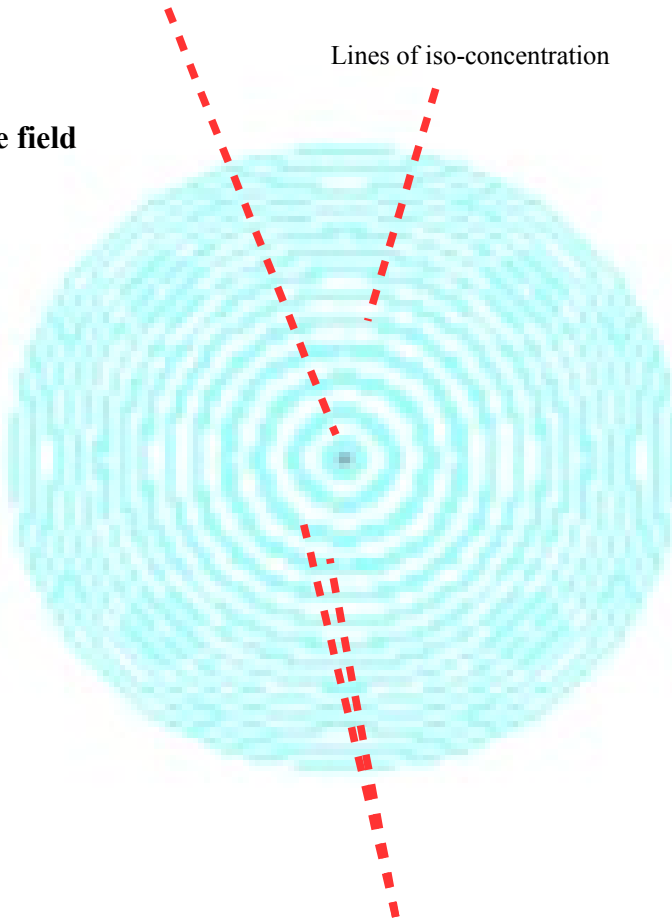
The behaviours are described using the same graphical manner.

FIELDS

Source of a field:
a grain or a cell nucleus

Lines of iso-concentration

A single field



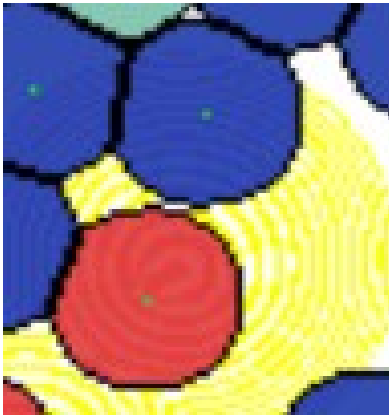
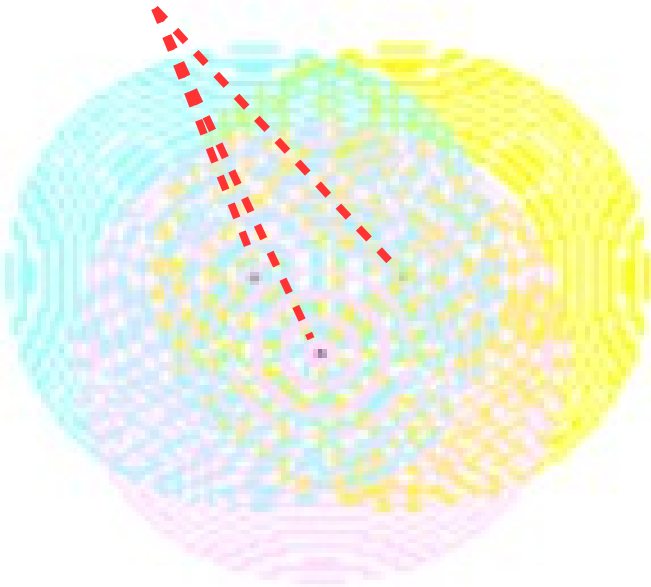
Between 2 successive lines
of iso-concentration, there
are 2 order of magnitude

A field has:

- a concentration per matrix element,
- a diffusion rate and
- a degradation rate

3 sources of field

**Independent fields
can overlap.**



Cells and grains use fields

The fields can be detected by
grains or cells to differentiate,
move, divide or die.



2

BEHAVIOURS

Each agent can have one or more behaviours. A behaviour is made of a set of conditions THEN a set of actions.

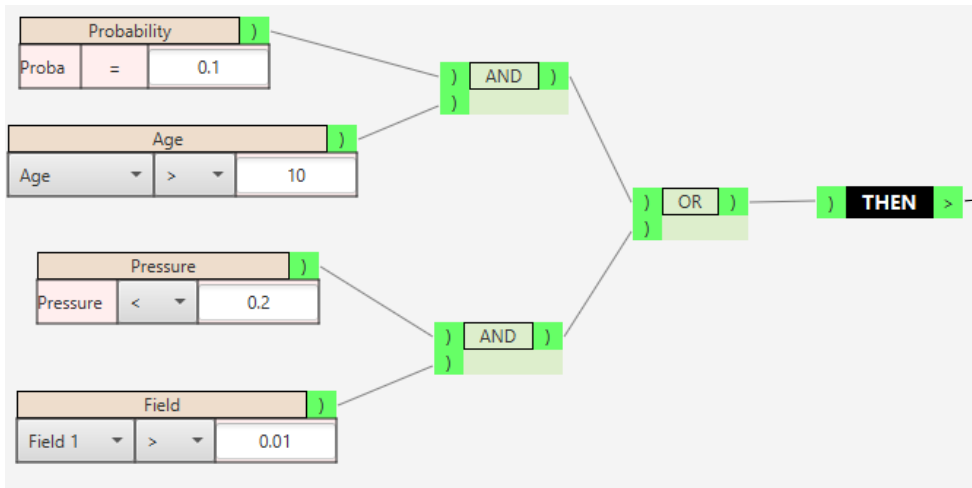


PRINCIPLES

Each cell and grain can have zero, one or more behaviours.

A behaviour is made of

- a set of **conditions**, linked by logical gates (AND, OR, NOT)
- a succession of **actions** (after the THEN box)



>	Absorb Field		>
Field 2	sub	0.01	

>	Reaction		>									
Cell1	==>	Cell1										
0	<table border="1"> <tr> <td></td> <td>+</td> <td>X</td> </tr> <tr> <td>-</td> <td></td> <td>-</td> </tr> <tr> <td>o</td> <td>+</td> <td></td> </tr> </table>		+	X	-		-	o	+		Cell1	
	+	X										
-		-										
o	+											

> **END**

CONDITIONS

Probability)
Proba	=	1	

Age)
Age	▼	=	▼
			10

Pressure)
Pressure	<	▼	
			0.2

Field)
Field 1	▼	>	▼
			0.01

Contact)
Cell2	>	20	%	

Cell on ECM Concentration)
Concentration	<	10.0	mg/mL	

Difference ECM & Cell Orientation)
Angle	<	180	°	

)	AND)
)		

)	OR)
)		

)	NOT)
)		

ACTIONS

> Reaction >											
Cell1	==>	Cell1 ▾									
Grain2 ▾	<table border="1"><tr><td></td><td>1</td><td>X</td></tr><tr><td>-</td><td></td><td>-</td></tr><tr><td>0</td><td>1</td><td></td></tr></table>		1	X	-		-	0	1		Cell1 ▾
	1	X									
-		-									
0	1										

> Put Field >		
Field 1 ▾	add	0.01

> Absorb Field >		
Field 1 ▾	sub	0.01

> Chemotaxis >			
Attracted by ▾	Field 1 ▾	speed=	0.1

> Add Langevin Force >	
Fmax	0.1

> Add Force >	
Fx	0.1
Fy	0.1
Fz	0.1

> Cell Rotates To ECM Orientation >		
Rapprochement	1	% per Step

> Cell Changes ECM Concentration >		
Absorb ▾	0.1	mg / mL per Step

> ECM Rotates To Cell Orientation >		
Rapprochement	1	% per Step

> OpenCL >		
Name	Initialisation of glucosis	
Code	<pre>if (step == 0) { MatField1[p] = (sin(x) + cos(y)) / 2.0 ; }</pre>	
Info	WARNING Only for developers	<>

3

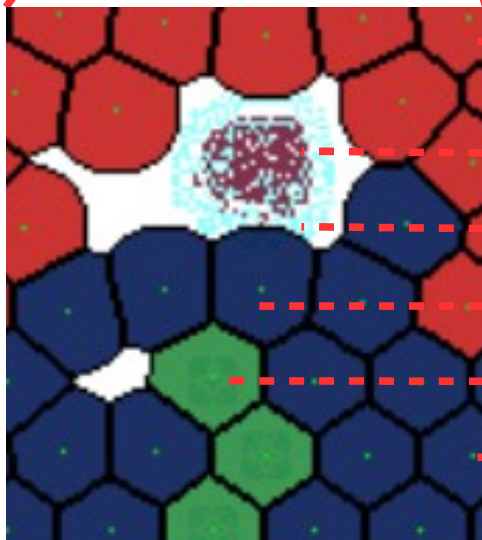
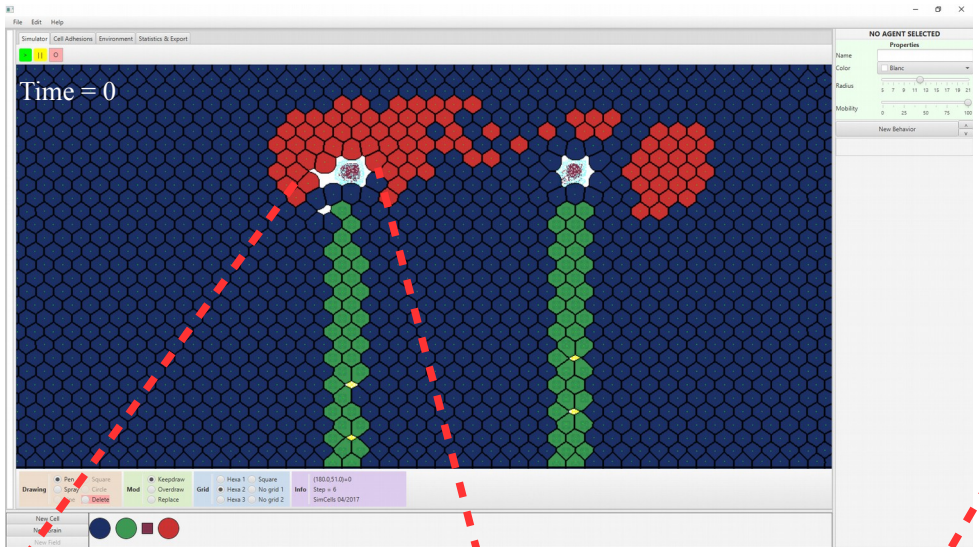
EXAMPLES

Many kind of cellular simulations are possible with SimCells. One example is described here.



PROSTATE EXAMPLE

Simulation of the prostate tissue inflammation after surgery.



Cancerous cells

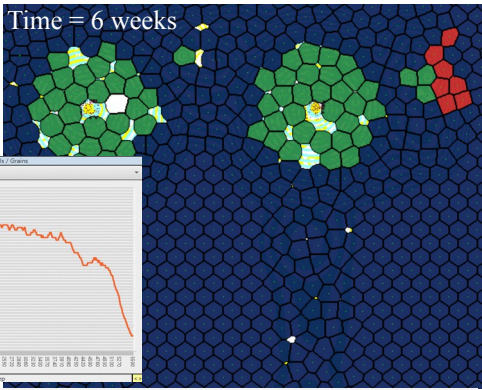
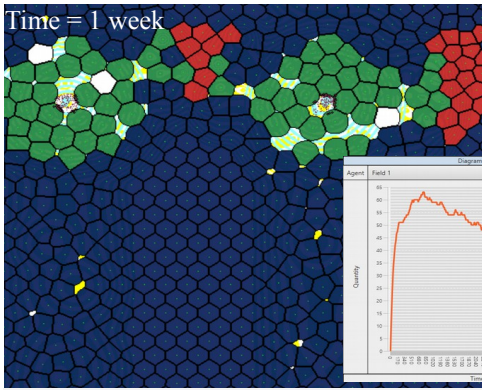
Radioactive grains

Radioactive field (2)

Inflammation field (1)

damaged cells

Healthy cells



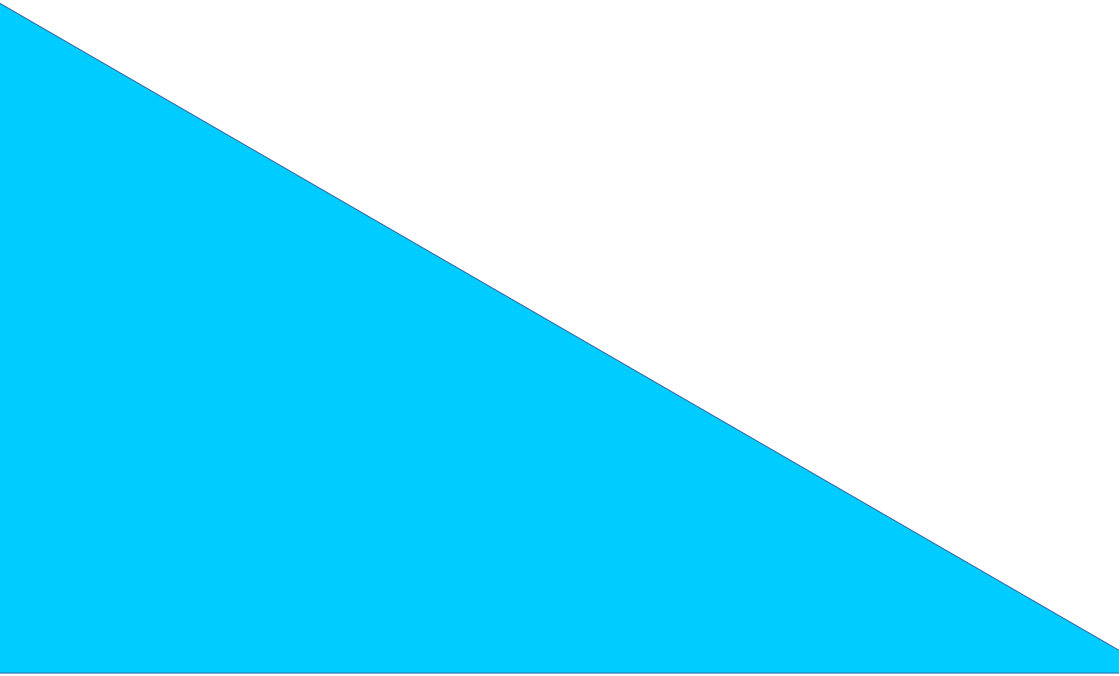
Probability)	AND)	THEN	>	Reaction	>	END
Proba	=	0.01				Tumeur	==>	Tumeur
Pressure	<	0.2				0		Tumeur
Field)	THEN	>	Reaction	>	END		
Field 2	>	1.0E-15		Tumeur	==>	Prostate Inflamm@e		
				*		*		
Probability)	THEN	>	Put Field	>	END		
Proba	=	1.0		Field 2	add	0.01		
Probability)	THEN	>	Reaction	>	END		
Proba	=	0.001		Grain Radioactif	==>	0		
				*		*		
Probability)	THEN	>	Put Field	>	END		
Proba	=	1.0		Field 1	add	0.01		
Probability)	THEN	>	Reaction	>	END		
Proba	=	0.01		Prostate Inflamm@e	==>	0		
				*		*		
Field)	THEN	>	Reaction	>	END		
Field 2	>	1.0E-7		Prostate	==>	Prostate Inflamm@e		
				*		*		
Pressure)	THEN	>	Reaction	>	END		
Pressure	<	0.01		Prostate	==>	Prostate		
				0		Prostate		

4

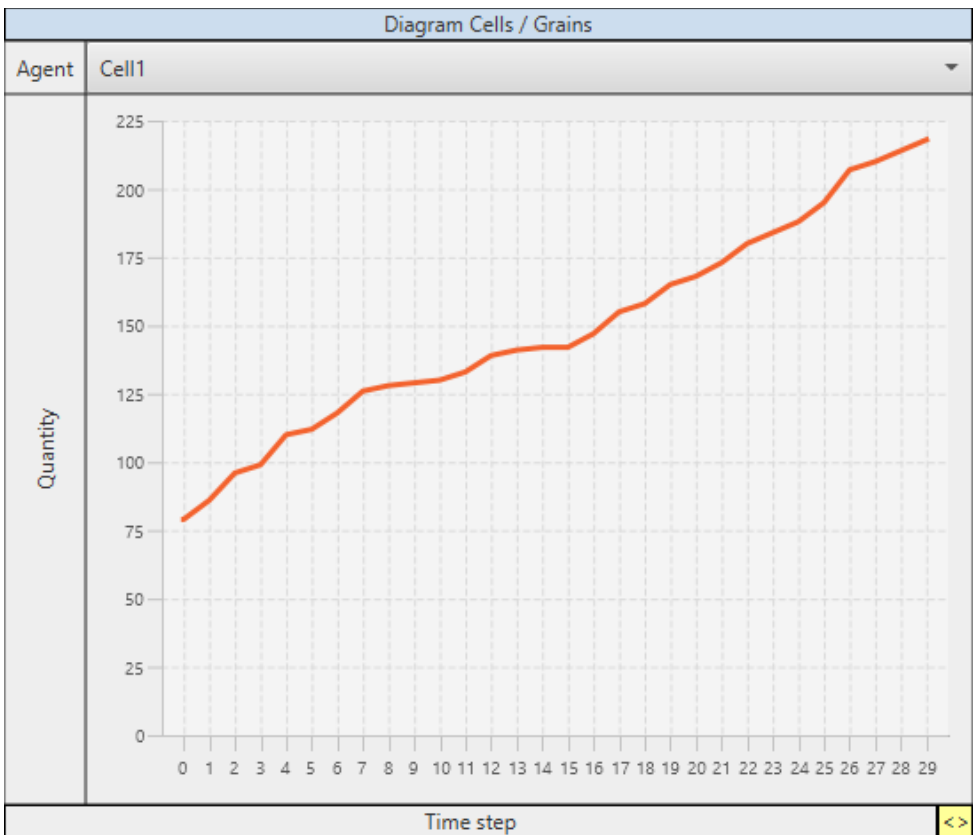
DATA ANALYSIS

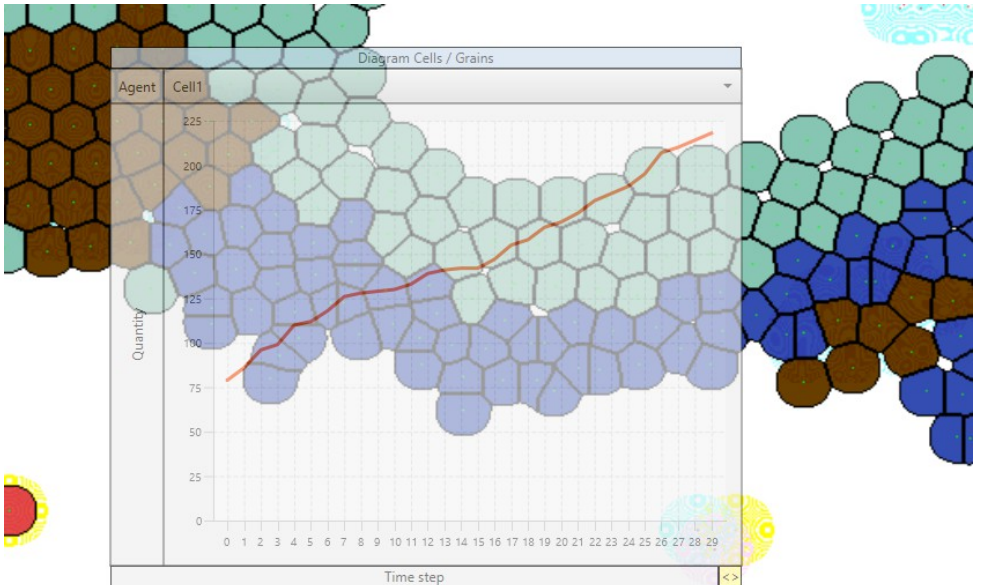
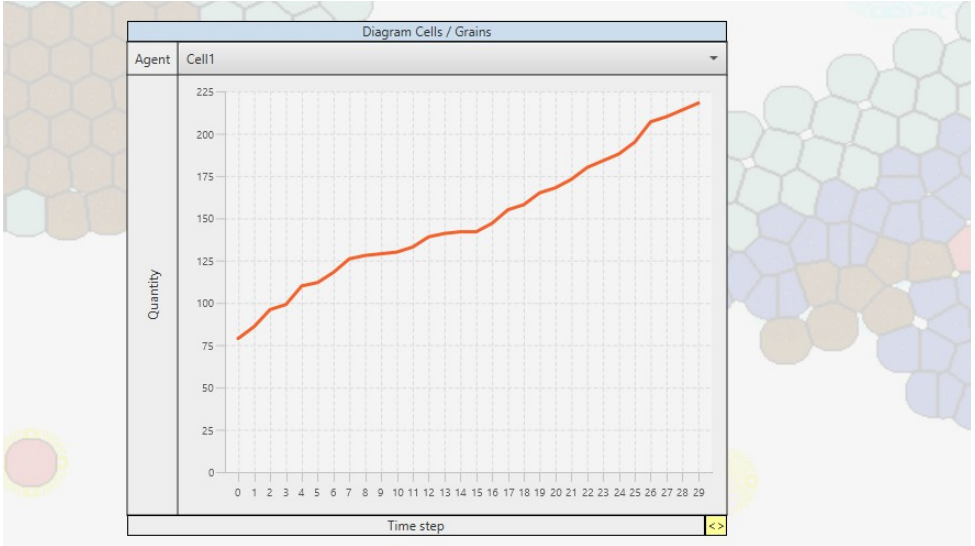
The number of cells, grains and field evolving during a simulation can be displayed thanks to dynamic diagrams. All this data can be exported to a text file and used in any spreadsheet software like Excel.

A video AVI file can be created in order to share and analyse the multicellular pattern evolutions.



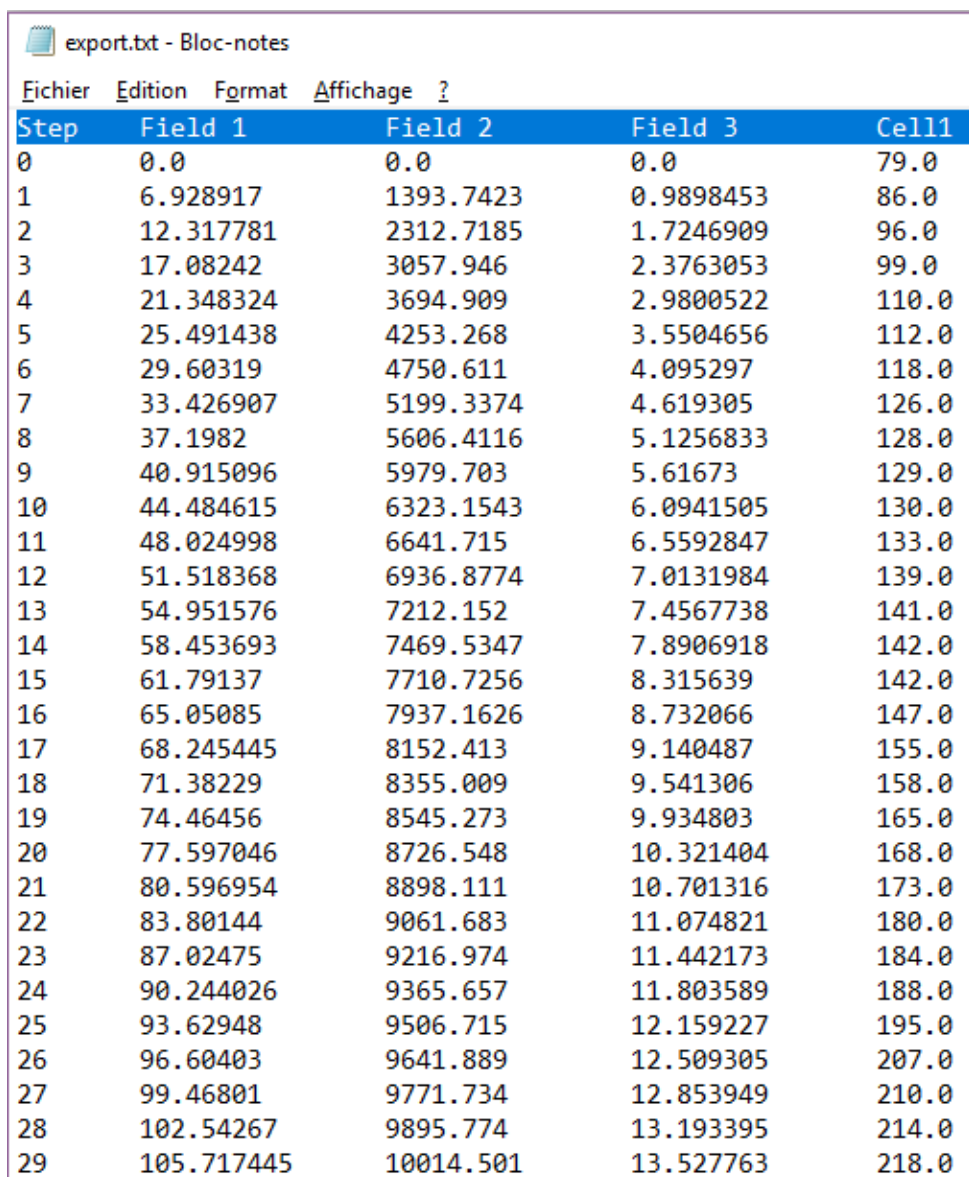
DIAGRAMS





DATA EXPORT

The data can be exported in text format and imported in any spreadsheet software.

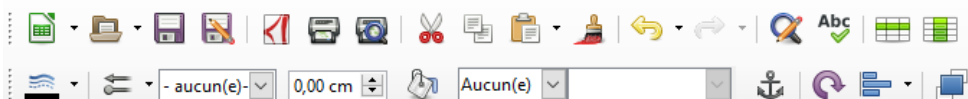


export.txt - Bloc-notes

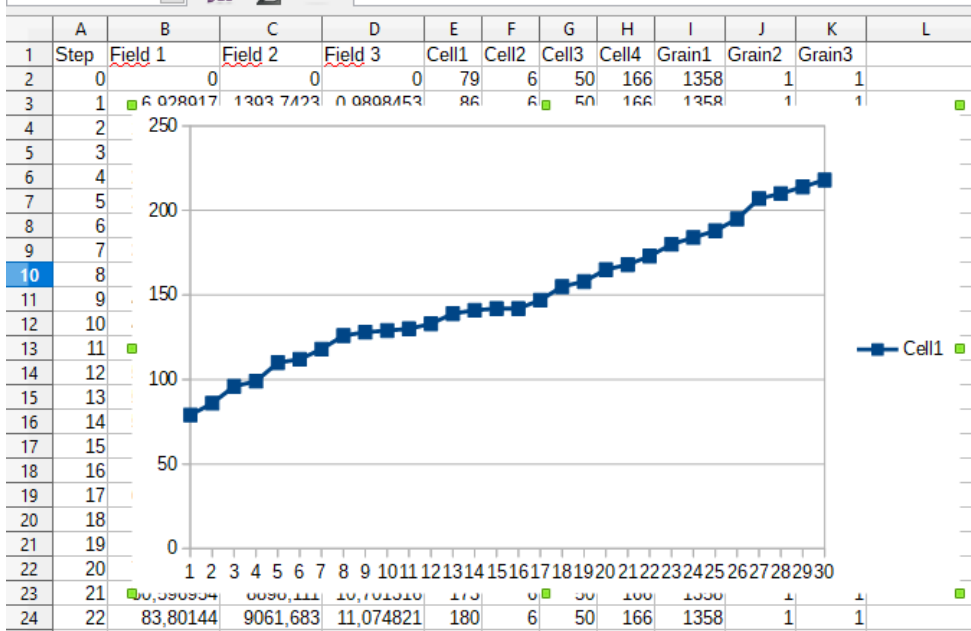
Step	Field 1	Field 2	Field 3	Cell1
0	0.0	0.0	0.0	79.0
1	6.928917	1393.7423	0.9898453	86.0
2	12.317781	2312.7185	1.7246909	96.0
3	17.08242	3057.946	2.3763053	99.0
4	21.348324	3694.909	2.9800522	110.0
5	25.491438	4253.268	3.5504656	112.0
6	29.60319	4750.611	4.095297	118.0
7	33.426907	5199.3374	4.619305	126.0
8	37.1982	5606.4116	5.1256833	128.0
9	40.915096	5979.703	5.61673	129.0
10	44.484615	6323.1543	6.0941505	130.0
11	48.024998	6641.715	6.5592847	133.0
12	51.518368	6936.8774	7.0131984	139.0
13	54.951576	7212.152	7.4567738	141.0
14	58.453693	7469.5347	7.8906918	142.0
15	61.79137	7710.7256	8.315639	142.0
16	65.05085	7937.1626	8.732066	147.0
17	68.245445	8152.413	9.140487	155.0
18	71.38229	8355.009	9.541306	158.0
19	74.46456	8545.273	9.934803	165.0
20	77.597046	8726.548	10.321404	168.0
21	80.596954	8898.111	10.701316	173.0
22	83.80144	9061.683	11.074821	180.0
23	87.02475	9216.974	11.442173	184.0
24	90.244026	9365.657	11.803589	188.0
25	93.62948	9506.715	12.159227	195.0
26	96.60403	9641.889	12.509305	207.0
27	99.46801	9771.734	12.853949	210.0
28	102.54267	9895.774	13.193395	214.0
29	105.717445	10014.501	13.527763	218.0

export.txt - LibreOffice Calc

Fichier Édition Affichage Insertion Format Outils Données Fenêtre Aide

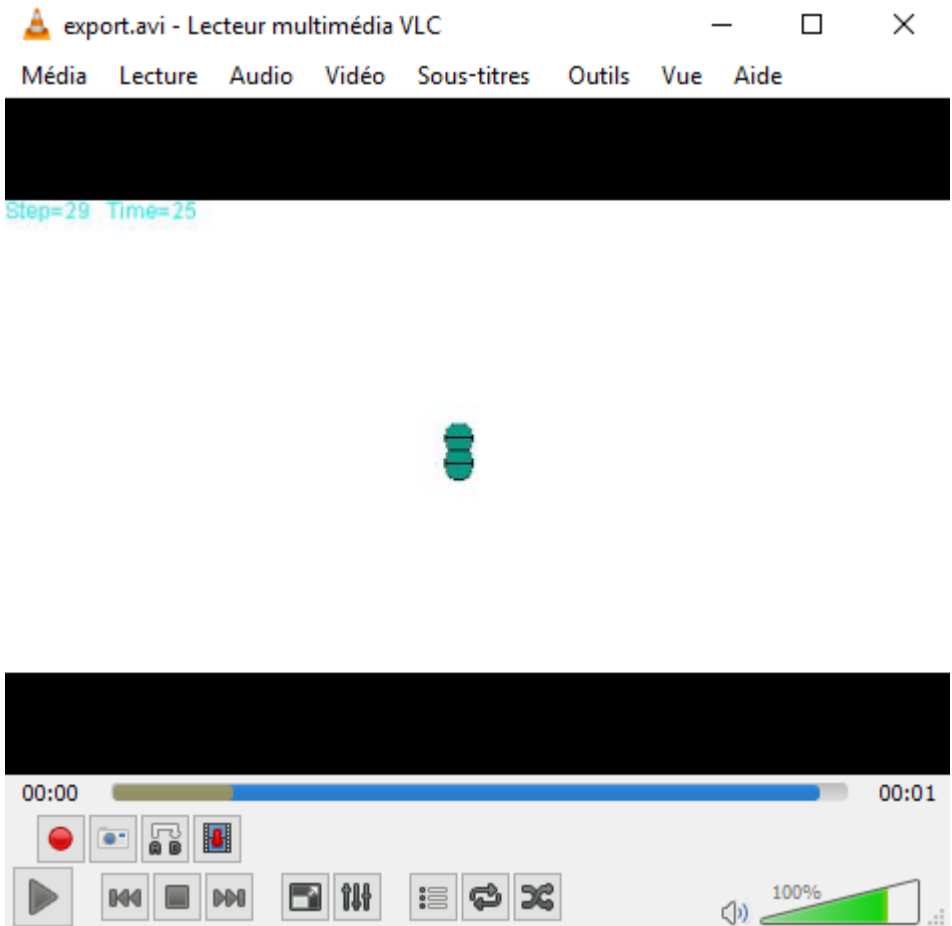


Q10



VIDEO CAPTURE

Simulation steps can be exported to an AVI video file.



CONCLUSION

SimCells is a software made to create multicellular simulations.

It has 3 kinds of agents: cells, grains and fields, allowing multiscale simulations.

Behaviours can be added to the agents thanks to a graphical programming language.

Exports can be made to treat the data in specialised software like Excel or LibreOffice Calc.

A video capture is possible to observe in fast or slow motion a simulation.

