The SRSim Software for Spatial and Combinatorially Complex Reaction Systems

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We want a Simulation System for (biochemical) reactions, with:
We want a simulation system for (biochemical) reactions, with:

- individual particles
- in continuous 3d space

MD Simulator LAMMPS
coarse grained, brownian movement
We want a simulation system for (biochemical) reactions, with:

- individual particles
- in continuous 3d space
- reactions defined implicitly
- allow combinatorial complexity

BioNetGen, Kappa, etc...
Imagine we have a complex molecule:
Rule-Based Modelling

imagine we have a complex molecule:

composed of elementary molecules.
Rule-Based Modelling

Some complex molecules...

What's common?
Rule-Based Modelling

Same reaction possible

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SRSim – Rules in Space
Rule-Based Modelling

Intro
Features
Membranes
Thanks
Rule-Based Modelling

How to describe a molecule?

A B B A A
A B A A
A A
How to describe a molecule?

Binding site / Component

A(x,x,y)
Rule-Based Modelling

How to describe a molecule?

A(x,x,y)
Rule-Based Modelling

How to describe a molecule?

A(x,x!1,y).A(x!1,x,y)
How to describe a molecule?

\[ A(x, x!1, y!2).A(x, x!2, y!3).B(z!3, z!4).B(z!4, z!5).A(x!5, x!6, y).A(x!6, x!7, y!8).A(x, x!7, y).A(x, x, y!8) \]

\[ A(x, x!1, y).A(x!1, x, y) \]
Adding Geometry

Size & Weight
Adding Geometry

For any site:

Size & Weight

Bond

Distance & Forces
Adding Geometry

For any site:
- Size & Weight
- Bond Distance & Forces
- Bond Angles & Forces

For any pair of sites:
- Bond Distance & Forces

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SRSim – Rules in Space
Adding Geometry

For any site:
- Size & Weight
- Bond Distance & Forces
- Bond Angles & Forces
- Dihedral Angles & Forces

For any pair of sites:
Features of SRSim

What can we do with the software?
Features of SRSim

+ Infinitely Sized Reaction Systems
Features of SRSim
e.g. Infinite Polymerization

+ Infinitely Sized Reaction Systems

**Molecule Definition:**

very simple molecules 'A'
each with **two active components 'a':**

![Diagram of molecule 'A' with site 'a' and 180° notation]
Features of SRSim

e.g. Infinite Polymerization

+ Infinitely Sized Reaction Systems

\[ A(a) + A(a) \leftrightarrow A(a!1).A(a!1) \quad k_{on}, k_{off} \]
Features of SRSim

e.g. Infinite Polymerization

+ Infinitely Sized Reaction Systems

Sounds boring...

But no cycles are possible!
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
Features of SRSim

e.g. Assembly of Microtubules

+ Infinitely Sized Reaction Systems
+ Self – Assemblies

A completely deterministic structure:
Features of SRSim
e.g. Assembly of Microtubules

+ Infinitely Sized Reaction Systems
+ Self – Assemblies

02-MTgrow...mpg
Features of SRSim

e.g. Assembly of Microtubules

+ Infinitely Sized Reaction Systems
+ Self – Assemblies

But: we wouldn't need any geometry here...
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies

Now, with non-deterministic structures:
Features of SRSim
e.g. Assembly of Spheres

+ Infinitely Sized Reaction Systems
+ Self – Assemblies

**Molecule Definition:**

more complex 'monomers', composed of six basic units:

see movies:

03-spheres1.mpg
04-spheresBig.mpg
05-spheresSmall.mpg
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions

Microtubules again... now with dynamics...
Features of SRSim

e.g. Microtubule Dynamics

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
Molecule Definition:

- filament dimers:
- motor-protein dimers:
- filament chain:
Rule Definition

delete rear bond A/Pa:

form new bond A/Pa:

delete current rear bond B/Pb:

form new bond B/Pb:

...
# use the 'kill' modification to delete bonds (used by the next four rules)

\[
\begin{align*}
A(a!1).Pa(a!1~\text{kill}) & \rightarrow A(a) + Pa(a~\text{kill}) \\
Pa(a~\text{kill}) & \rightarrow Pa(a~n) \\
B(a!1).Pb(a!1~\text{kill}) & \rightarrow B(a) + Pb(a~\text{kill}) \\
Pb(a~\text{kill}) & \rightarrow Pb(a~n)
\end{align*}
\]

# transform the bonds

\[
\begin{align*}
A(a!2,x!1).B(x!1,a!4).Pa(a!2~n,x!3).Pb(x!3,a!4) & \rightarrow A(a!2,x!1).B(x!1,a!4).Pa(a!2~\text{kill},x!3).Pb(x!3,a!4) \\
A(a,x!1).B(x!1,a!2).Pb(a!2,x!3).Pa(x!3,a) + A(a,x!1).B(x!1,a) & \rightarrow A(a,x!1).B(x!1,a!2).Pb(a!2,x!3).Pa(x!3,a!4).A(a!4,x!5).B(x!5,a) \\
A(x!1).B(x!1,a!2).Pb(a!2~n,x!3).Pa(x!3,a!4).A(a!4,x!5).B(x!5) & \rightarrow A(x!1).B(x!1,a!2).Pb(a!2~\text{kill},x!3).Pa(x!3,a!4).A(a!4,x!5).B(x!5) \\
A(a!+,x!1).B(x!1,a) + Pa(a!+,x!3).Pb(x!3,a) & \rightarrow A(a!+,x!1).B(x!1,a).Pa(a!+,x!3).Pb(x!3,a!2)
\end{align*}
\]

# attach new motor-proteins to the filaments

\[
\begin{align*}
A(a,x!1).B(x!1,a,o!+).Pa(a,x!3).Pb(x!3,a) & \rightarrow A(a!2,x!1).B(x!1,a,o!+).Pa(a!2,x!3).Pb(x!3,a)
\end{align*}
\]

# release motor-proteins

\[
\begin{align*}
\text{Fin(o!1).B(a!2,o!1).Pa(a,x!3).Pb(x!3,a!2)} & \rightarrow \text{Fin(o!1).B(a,o!1) + Pa(a,x!3).Pb(x!3,a)}
\end{align*}
\]
Features of SRSim

... Simulate Molecular Machines

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions

Microtubules...

Dreaming of:

ATP Synthases...
Ribosomes...
Polymerases...
etc...

Image from Wikipedia
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations
Features of SRSim

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Assembly Logics: Sierpinski Triangles
Features of SRSim
e.g. Building Sierpinski Triangles

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations

Molecule Definition:

a) tile naming convention
X xor Y = Z

b) '0' and '1' tiles

'1' tiles
0 0
0 0
1 1
0 0
1 1
1 1

'0' tiles

Z tiles
1 0 1
1 0 1
0 0
0 0

b) '0' and '1' tiles

match

ABCD

mismatch

Conventions:

'0' tiles

'1' tiles

X xor Y = Z

U UVU

D DD

'Z' tiles

08-sierp.mpg
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
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+ Logic Operations

Assembly Logics: Sierpinski Triangles

NeuNeu: Artificial Chemical Neurons
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
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+ Logic Operations

Assembly Logics: Sierpinski Triangles

NeuNeu: Artificial Chemical Neurons
Similarity to spiking neural P-Systems?

www.neu-n.eu
Features of SRSim

- e.g. Chemical Artificial Neurons

+ Infinitely Sized Reaction Systems
+ Self-Assemblies
+ Molecular Functions
+ Logic Operations

Example: Count The Number of Inputs
Features of SRSim

- e.g. Chemical Artificial Neurons

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations
Features of SRSim

e.g. Chemical Artificial Neurons

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Introduction:

- Chemical Artificial Neurons
- Infinitely Sized Reaction Systems
- Self-Assemblies
- Molecular Functions
- Logic Operations

Features of SRSim:

- Chemical Artificial Neurons
- Infinitely Sized Reaction Systems
- Self-Assemblies
- Molecular Functions
- Logic Operations

09-neuneu2.mpg
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations
+ anything else... ?
Features of SRSim

+ Infinitely Sized Reaction Systems
+ Self – Assemblies
+ Molecular Functions
+ Logic Operations
+ anything else... ?

Open source, GPL
Available at:

www.biosys.uni-jena.de
Connections to Membrane Computing

Why might you be interested... 🌟
Connections to Membrane Computing

- Implicit / explicit membranes can be built/used...

- Membranes for Constraining / Structuring Processes/Reactions

- What about Membrane Systems with Geometry? What about Rule-Based Modelling with Membranes?

- Spiking neural P-Systems
Thanks to...

you for not falling asleep

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the nice Bio Systems Analysis Group