

ActinSimChem  
MANUAL

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## Installation

To install the program ActinSimChem:

- Download the file *ActinSimChem.exe* .
- Place the program into your work folder.
- Launch the file *ActinSimChem.exe*.

## System Requirements

Software is developed for the Windows operating system (Windows 98 or further versions are required). Program was tested on the computer: processor Intel Pentium (CPU 1400 MHz), RAM 512 MB. Up to 50 MB of free space of hard drive is recommended.

## Description

ActinSimChem is the stand-alone software package for the Monte Carlo simulation of actin polymerization processes. ActSimChem integrates the nSRF and SRF models (*cf.* the manuscript). ActSimChem provides:

- Input and modification of the model parameters.
- Real-time simulation of actin polymerization.
- Graphical representation of simulation results.
- Storage of the results.

The main work window of the ActSimChem, shown in Figure 1, is divided into four informational units (sub windows and panels marked in red): **Command Panel**, **Input Parameters**, **Current Systems Parameters**, and **the Plots of Simulation Results**.

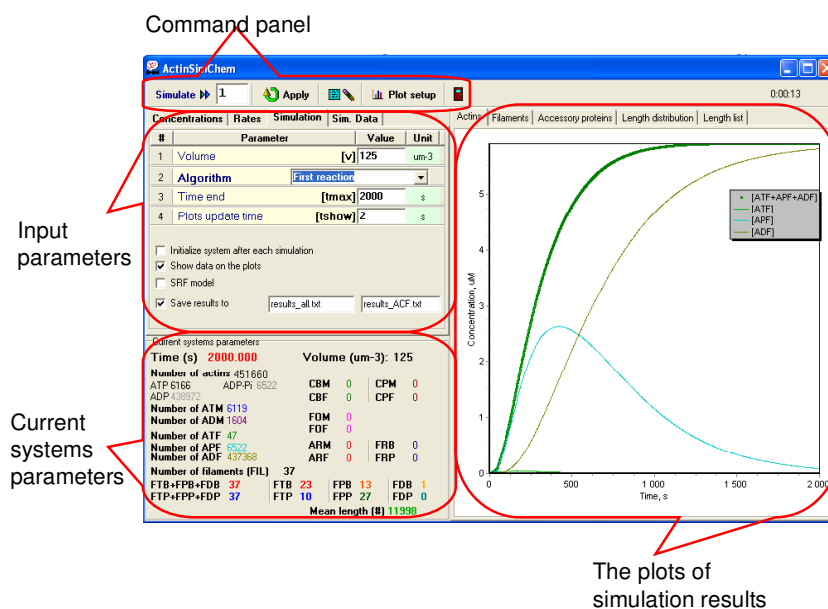



Figure 1. Main window of the ActinSimChem.

## Command Panel

The Command Panel contains the buttons providing the control of the program activities:

- Button [**Simulate**] runs simulation procedure. If simulation is in the process, this button appears as [**Stop**] button. Press it if the termination of unfinished simulation is requested.
- Field [**Number of runs**], situated next to the button [**Simulate**], is used to input the number of model launches with the same initial parameters as defined in the multi-scale table **Input Parameters** for further statistical averaging.
- Button [**Apply**] uploads the systems parameters.
- Button [**Clear**] () cleans all plots and lists from the results of previous simulations.
- Button [**Plot setup**] opens a subwindow for activating the concentration curves in the plots.
- Button [**Close**] let exit the program.

## Input Parameters

The **Input Parameters** is the multi-scale table of input model parameters: the initial molecular concentrations (the tab **Concentrations**), the chemical rate constants (the tab **Rates**), and the technical simulation parameters (the tab **Simulation**); and simulation results (the tab **Sim.Data**).

- Tab **Concentrations** (Figure 2) – input values for the [ATM], [ADM], [CBM], [CPM], [FOM], [ARM] concentrations (*cf.* Table 1, the manuscript).  $\mu\text{M}$  is  $10^{-6}$  M.
- Tab **Rates** (Figure 2) is divided into several subtabs:
  - **Nucleation** – input of the nucleation rates  $k_{SNUC}$ ,  $k_{FNUC}$ ,  $k_{CBNU}$ ,  $k_{CPNU}$ ;
  - **Associations** – input of the rate constants for actin association reactions  $k_{ASTB}$ ,  $k_{ASDB}$ ,  $k_{ASTP}$ ,  $k_{ASDP}$ ;
  - **Dissociations** – input of the rate constants for actin dissociation reactions  $k_{DITB}$ ,  $k_{DIPB}$ ,  $k_{DIDB}$ ,  $k_{DITP}$ ,  $k_{DIPP}$ ,  $k_{DIDP}$ ;
  - **ATP/ADP** – input of the rate constants for the reactions of aging and recharge of actin units  $k_{TTOP}$ ,  $k_{PTOD}$ ,  $k_{DTOD}$ ;
  - **Capping** – input of rate constants for capping-protein-related reactions  $k_{ASCB}$ ,  $k_{DICB}$ ,  $k_{ASCP}$ ,  $k_{DICP}$ ;
  - **Formin** – input of rate constants for formin-related reactions  $k_{ASFB}$ ,  $k_{DIFB}$ ,  $k_{FASB}$ ;
  - **Fragmentation/Annealing** – input of rate constants for spontaneous fragmentation and annealing reactions  $k_{FRGM}$ ,  $k_{ANNL}$ ;
  - **ARP2/3** – input of rate constants for ARP2/3-related reactions  $k_{ASRT}$ ,  $k_{DIRP}$ .

Concentrations		Rates	Simulation	Sim. Data
#	Concentration of	Value	Unit	
1	ATP associated G-actin [ATM]	6	uM	
2	ADP associated G-actin [ADM]	0.1	uM	
3	Barbed-end capping prot. [CBM]	0.01	uM	
4	Pointed-end capping prot. [CPM]	0.01	uM	
5	Formin [FOM]	0.001	uM	
5	ARP2/3 [ARM]	0.01	uM	

Concentrations		Rates	Simulation	Sim. Data
Capping		Formin	Fragmentation/Annealing	ARP2/3
Nucleations		Associations	Dissociations	ATP/ADP
#	Parameter	Value	Unit	
1	Dissociation of ATF (barbed) [DITB]	0.9	s-1	
2	Dissociation of APF (barbed) [DIPB]	0.9	s-1	
3	Dissociation of ADF (barbed) [DIDB]	1.5	s-1	
4	Dissociation of ATF (pointed) [DITP]	0.19	s-1	
5	Dissociation of APF (pointed) [DIPP]	0.19	s-1	
6	Dissociation of ADF (pointed) [DIDP]	0.26	s-1	

Figure 2. The tabs **Concentrations** and **Rates**.

Notations and default values for the parameters are taken from the Table 1 of the manuscript.

- Tab **Simulation** (Figure 3) determines the parameters of simulation procedure.
  - **Volume** – input of the simulated volume (in  $\mu\text{m}^{-3}$ ).
  - **Algorithm** – selection of the Monte Carlo modelling algorithms.
  - **[Time end]** – the end time for simulation of chemical processes.
  - **[Plots update time]** is a resolution channel of the time scale in the plots.
  - Checkbox **[Initialize system after each simulation]** is used for automatic uploading of the parameters. If it is unchecked then simulations go on from the current systems state.
  - Checkbox **[Show data on the plots]** is used to draw results of simulation in the plots. If it is off – simulations run faster.
  - Checkbox **[Save data to]** is used to store the simulation results into text files (*.txt*). Two output files with the names, which are shown in fields next to checkbox, are created in the folder where the program is located. Names and locations of these files could be changed if it is required. The first file (*results\_all.txt*) represents the time dependence of the reagent concentrations. The columns in the file are organised as following: **[Time] [ATM] [ADM] [ATF] [ADF] [FTB] [FDB] [FTP] [FDP] [CBM] [CBF] [CPM] [CPF] [FOM] [FOF] [ARM] [ARF]**.  
 In the second file (*results\_ACF.txt*) the time dependence of the filamentous actin is stored, being averaged over iterations (column 1 is time, column 2 is a concentration of the filamentous actin).
  - Checkbox **[SRF model]** turns switch from the nSRF model to the SRF model. If it is unchecked – the nSRF model is on.

#	Parameter	Value	Unit
1	Volume	[v] 125	um-3
2	Algorithm	First reaction	
3	Time end	[tmax] 2000	s
4	Plots update time	[tshow] 2	s

Initialize system after each simulation  
 Show data on the plots  
 SRF model  
 Save results to

Figure 3. Tab Simulation.

- Tab [Sim. Data] (Figure 4) provides the time dependence of the filamentous actin total concentration. First column represents the time, others – corresponding filamentous actin concentrations for each statistical iteration (the same information is stored in the file results\_ACF.txt).

Time	[ATF+ADF]		
5.00	0.38155	0.16441	0.19399
10.00	1.06872	0.59134	0.62602
15.00	1.81090	1.08775	1.20962
20.00	2.57483	1.65285	1.87814
25.00	3.23282	2.26745	2.51120
30.00	3.77629	2.85310	3.07396
35.00	4.23724	3.35592	3.56128
40.00	4.61549	3.79713	3.99657
45.00	4.94171	4.18517	4.36321
50.00	5.21951	4.52444	4.67903
55.00	5.44380	4.81190	4.94636
60.00	5.62577	5.05391	5.17299
65.00	5.77597	5.26153	5.37065

Figure 4. Tab Sim. Data. Three iterations are used.

### Current Systems Parameters

The window **Currents Systems Parameters** visualizes the values of model parameters at time  $t$  during a simulation run. The quantities of proteins are given in numbers of molecules per volume.

### Plots of Simulation Results

The multi-window **Plots of Simulation Results** exhibits the results of simulations: concentrations of actines (the tab **Actins**), filaments (the tab **Filaments**), and associated proteins (the tab **Associated proteins**), the distributions of the filaments lengths (the tab **Length distribution**), the filaments length list (the tab **Length list**) Plots contain legends describing the corresponding curves.

### Example

1. Start the program ActinSimChem. Then the main window appears (Figure 1).
2. Initialise the simulation parameters. Go to the subtab **Simulation** (Figure 3) and select:
  - $v = 500\mu\text{m}^3$ .

- **Algorithm** = direct method Gillespie.
  - $t_{\max} = 1000$  s.
  - $t_{\text{show}} = 5$  s.
  - **Initialize system after each simulation** = unchecked
  - **Show data on the plots** = checked.
  - **Save data to** = checked.
  - **SRF model** = unchecked.
3. Determine initial concentrations of proteins (Figure 2, the tab **Concentrations**). Type in a set of systems parameters, for example:
- $[\text{ATM}] = 6 \mu\text{M}$
  - $[\text{ADM}] = 0.5 \mu\text{M}$
  - $[\text{CBM}] = 0.1 \mu\text{M}$
  - $[\text{CPM}] = 0.1 \mu\text{M}$
  - $[\text{FOM}] = 0.001 \mu\text{M}$
  - $[\text{ARM}] = 0.01 \mu\text{M}$
4. Keep a *default* set of the rate constants for the reaction rates in the Tab **Rates**.
5. Test 3 iterations of simulation procedure. Type 3 into the field [**Number of runs**], which is situated next to the button [**Simulation**].
6. Press the button [**Plot setup**] to check variables visualized in the plots. Panel will appear, Figure 5. Change the states of checkboxes as shown in Figure 5 and press the button [**Accept**].

Actins	
<input type="checkbox"/> ATM+ADM	<input checked="" type="checkbox"/> ATF+APF+ADF
<input type="checkbox"/> ATM <input type="checkbox"/> ADM	<input checked="" type="checkbox"/> ATF <input checked="" type="checkbox"/> ADF
	<input checked="" type="checkbox"/> APF
Filaments	
<input checked="" type="checkbox"/> Number of filaments	
<input checked="" type="checkbox"/> FTB+FPB+FDB	<input checked="" type="checkbox"/> FTP+FPP+FDP
<input type="checkbox"/> FTB <input type="checkbox"/> FDB	<input type="checkbox"/> FTP <input type="checkbox"/> FDP
<input type="checkbox"/> FPB	<input type="checkbox"/> FPP
Accessory proteins	
<input checked="" type="checkbox"/> CBF <input checked="" type="checkbox"/> CPF	<input checked="" type="checkbox"/> FOF <input checked="" type="checkbox"/> ARF
<input type="checkbox"/> CBM <input type="checkbox"/> CPM	<input type="checkbox"/> FOM <input type="checkbox"/> ARM
Length distribution	
Number of bins in length distribution <input type="text" value="10"/>	
<input checked="" type="button" value="Accept"/>	<input type="button" value="Cancel"/>

Figure 5. Panel Plot Setup.

7. Press the button [**Apply**] to up-load the parameters.
8. Press the button [**Simulation**] to start simulation.
9. Wait till the end of simulation. During simulation process you may look at the interactive changes in the plots and in panel **Current systems parameters**.

10. After simulation has been finished – you may want to analyze results of simulation, represented on the plots and output sheets.

11. Go to the folder where your program is stored. Open the text files and analyze your data in the Notepad, MS Word, Excel or in any other stat. processing program.

12. Remember the time of computing required for this task, which is represented in the right top of simulation window.

13. Perform simulation described above using the SRF model:

- press the button [**Clear**] to erase plots from the results of previous simulations.
- Change the names of output files (for example, results\_all\_s.txt and results\_ACF\_s.txt).
- Press the button [**Apply**] to upload new parameters.
- Press the button [**Simulate**] to start simulation.

Compare results and computing time of simulation according two models.

14. Note, the systems parameters correspond to the final time moment of the simulation. Change [**Number of runs**] value to 1 and run simulation by pressing [**Simulate**] button (don't press [**Apply**] in this case). Note, the parameter [**Time end**] is doubled and the simulation is continued till the end of a new time limit.