

User Interface Crash Course

Insert Model Name here, special character (e.g. \$%^&) cannot be used.

Box for inserting metabolites' information (name, initial concentration and boundary condition*) within the model

*boundary condition TRUE would make the concentration fixed and vice versa

***NUMBERS indicate ideal information entering order.
***ADD and DELETE button lets users add/delete information count for each boxes.

The screenshot shows the 'Convenient Modeller' window. At the top is a 'File' menu and a 'Model Name:' text box. Below this are three main panels: 'Reacting Species', 'Enzymes', and 'Reactions'. The 'Reacting Species' panel has a table with columns 'No.', 'Species', 'Concentration', and 'Boundary'. The 'Enzymes' panel has a table with columns 'No.', 'Enzyme', and 'Concentration'. The 'Reactions' panel has a table with columns 'No.', 'Enzyme', 'Activator', 'Inhibitor', and 'Reaction'. At the bottom, there are buttons for 'Add' and 'Delete' for each panel, and a 'Model Fitting' section with buttons for 'Generate Header File', 'Insert Fitting Data', 'Run Parameter Estimation', and 'Save'. Red circles with numbers 1, 2, and 3 are placed over the 'Reacting Species', 'Enzymes', and 'Reactions' panels respectively. Red dashed arrows point from these circles to the corresponding text boxes on the right. A red box on the left points to the 'Reacting Species' panel. A red box at the top left points to the 'Model Name' text box.

No.	Species	Concentration	Boundary
1			<input type="checkbox"/>

No.	Enzyme	Concentration
1		

No.	Enzyme	Activator	Inhibitor	Reaction
1	N/A	N/A	N/A	

Box for inserting enzyme information (name & concentration).

Box for inserting reaction information (enzyme that catalyses it*, activator/inhibitor, product and substrates**)

*if enzyme involved are unknown, pseudo name and concentration of 1 can be used.

**to add product and substrates users need to double click on the reaction cell for a different interface to appear.

Generate Header File

Insert Fitting Data

Run Parameter Estimation

Save

Example use of Convenient Modeller

Step 1: Add all known metabolites and its initial concentration (if they are unknown, concentration of 0.1 is suggested)

*concentration unit used in this software is up to the user's choosing (not explicitly stated in software), they should however be standardised across metabolite, proteins and flux.

The screenshot displays the 'Convenient Modeller' software interface. At the top, there is a 'File' menu and a 'Model Name' input field with the placeholder text 'Insert Model Name'. The 'Reacting Species' section contains a table with columns 'No.', 'Species', 'Concentration', and 'Boundary'. The table lists six species: 1 IN, 2 OUT, 3 A, 4 B1, 5 B2, and 6 C. The concentrations are 10, 10, 18, 41, 9, and 52 respectively. The 'Boundary' column has checkboxes, with the first two (IN and OUT) checked. Below the table, it shows 'Number of Species: 6' and buttons for 'Add' and 'Delete'. The 'Enzymes' section has a table with columns 'No.', 'Enzyme', and 'Concentration'. It currently shows one enzyme with 'No.' 1 and 'Enzyme' blank. Below this, it shows 'Number of Enzymes: 0' and buttons for 'Add' and 'Delete'. The 'Reactions' section has a table with columns 'No.', 'Enzyme', 'Activator', 'Inhibitor', and 'Reaction'. It currently shows one reaction with 'No.' 1, 'Enzyme' N/A, 'Activator' N/A, 'Inhibitor' N/A, and 'Reaction' blank. Below this, it shows 'Number of Reactions: 0' and buttons for 'Add' and 'Delete'. At the bottom, there is a 'Model Fitting' section with buttons for 'Generate Header File', 'Insert Fitting Data', 'Run Parameter Estimation', and 'Save'.

No.	Species	Concentration	Boundary
1	IN	10	<input checked="" type="checkbox"/>
2	OUT	10	<input checked="" type="checkbox"/>
3	A	18	<input type="checkbox"/>
4	B1	41	<input type="checkbox"/>
5	B2	9	<input type="checkbox"/>
6	C	52	<input type="checkbox"/>

No.	Enzyme	Concentration
1		

No.	Enzyme	Activator	Inhibitor	Reaction
1	N/A	N/A	N/A	


Step 2: Add all known enzymes and its concentration (if they are unknown, concentration of 1 is suggested)

*if enzyme for an reaction is unknown OR if it is a pseudo reaction, a pseudo name can be used.

Convenient Modeller

File

Model Name:



Reacting Species

No.	Species	Concentration	Boundary
1	IN	10	<input checked="" type="checkbox"/>
2	OUT	10	<input checked="" type="checkbox"/>
3	A	18	<input type="checkbox"/>
4	B1	41	<input type="checkbox"/>
5	B2	9	<input type="checkbox"/>
6	C	52	<input type="checkbox"/>

Enzymes

No.	Enzyme	Concentration
1	IMPORT	50
2	Diverge	11
3	Converge	22
4	Export	35.0

Number of Species: 6

Add

Delete

Number of Enzymes: 4

Add

Delete

Reactions

No.	Enzyme	Activator	Inhibitor	Reaction
1	N/A	N/A	N/A	

Number of Reactions: 0

Add

Delete

Model Fitting

Generate Header File

Insert Fitting Data

Run Parameter Estimation

Save

Step 3: Add reaction information. Drop down menu for enzyme/activator/inhibitor*.

*Enzyme information is compulsory, while activator and inhibitor are optional

**Double click on the reaction cell to access interface to select substrate and production, as well as their stoichiometry

The screenshot displays the SML Convenient Modeller interface. The top panel shows the 'Model Name' field and two tables: 'Reacting Species' and 'Enzymes'. The 'Reacting Species' table has columns for 'No.', 'Species', 'Concentration', and 'Boundary'. The 'Enzymes' table has columns for 'No.', 'Enzyme', and 'Concentration'. The bottom panel shows the 'Reactions' table with columns for 'No.', 'Enzyme', 'Activator', 'Inhibitor', and 'Reaction'. A red arrow points from the 'Reactions' table to the 'Please build your reaction' dialog box. The dialog box has a 'Substrate(s)' section with 'IN' selected and a 'Product(s)' section with 'A' selected, both with a stoichiometry of 1. The bottom panel shows the updated 'Reactions' table with 4 reactions.

No.	Species	Concentration	Boundary
1	IN	10	<input checked="" type="checkbox"/>
2	OUT	10	<input checked="" type="checkbox"/>
3	A	18	<input type="checkbox"/>
4	B1	41	<input type="checkbox"/>
5	B2	9	<input type="checkbox"/>
6	C	52	<input type="checkbox"/>

No.	Enzyme	Concentration
1	IMPORT	50
2	Diverge	11
3	Converge	22
4	EXPORT	35

No.	Enzyme	Activator	Inhibitor	Reaction
1	IMPORT	N/A	N/A	
2	Diverge	N/A	N/A	
3	Converge	N/A	N/A	
4	EXPORT	N/A	N/A	

Please build your reaction

Substrate(s): IN, Stoichiometry: 1

Product(s): A, Stoichiometry: 1

Cancel OK

No.	Enzyme	Activator	Inhibitor	Reaction
1	IMPORT	N/A	N/A	R2: (1) IN <-> (1) A
2	Diverge	N/A	N/A	R4: (1) A <-> (1) B1 + (1) B2
3	Converge	N/A	N/A	R3: (1) B1 + (1) B2 <-> (1) C
4	EXPORT	N/A	N/A	R5: (1) C <-> (1) OUT

Number of Species: 6, Number of Enzymes: 4, Number of Reactions: 4

Model Fitting: Generate Header File, Insert Fitting Data, Run Parameter Estimation, Save

Step 4: Make the fitting data file. (example used here are for steady state data, for time course data, a column would be added to indicate time point)

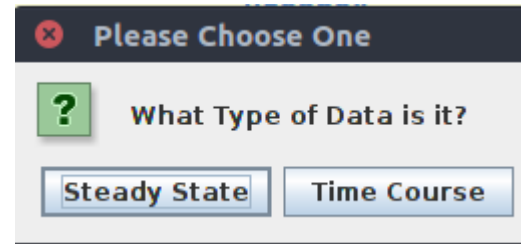
4a: click on generate header file for fitting data.

4b: move the names and IDs to a spreadsheet to edit the information much more easily.

4c: keep only IDs and expected values for metabolites/flux.

NOTE: move the data back into a text file and make sure there isn't any trailing new lines

4a:



What header file looks like in a text file.

```
Copy to Excel.
Remove the Names.
Keep only the IDs.
Paste data back into txt file to be inserted into Convenient Modeller, make sure to avoid empty lines.
If there is no known value for flux/enzyme/metabolites, delete its respective ID from the text.

IN      S1
OUT     S2
A       S3
B1      S4
B2      S5
C       S6
IMPORT  R1
Diverge R2
Converge      R3
EXPORT  R4
```

4b:

	A	B	C
1	IN	S1	10
2	OUT	S2	N/A
3	A	S3	6.40291
4	B1	S4	32.2015
5	B2	S5	0.201489
6	C	S6	0.00152386
7	IMPORT	R1	0.544777
8	Diverge	R2	N/A
9	Converge	R3	0.544777
10	EXPORT	R4	0.544777

4c:

	A	B
1	S1	10
2	S3	6.40291
3	S4	32.2015
4	S5	0.201489
5	S6	0.00152386
6	R1	0.544777
7	R3	0.544777
8	R4	0.544777

Step 4d: OPTIONAL

If an enzyme concentration value is given to the steady state fitting data, Convenient Modeller would use the value to change the model's selected enzyme values during parameter estimation process.

This is useful for providing fitting data that has multiple conditions, which normally affect protein concentration within the system to an extent, and result in different metabolite and flux output.

As seen in the example, some information can be left out for the fitting process.

	A	B	C	D	E	F
1	E1	50	60	30	58	58
2	E2	11	15	22	15	15
3	E3	22	15	11	16	16
4	E4	35	42	29	32	32
5	R1	0.544777	0.676	0.569	N/A	0.79
6	R2	0.544777	0.676	0.569	N/A	0.79
7	R3	0.544777	0.676	0.569	N/A	0.79
8	R4	0.544777	0.676	0.569	N/A	0.79
9	S1	10	10	10	10	15
10	S2	10	10	10	10	8
11	S3	6.40291	6.27	N/A	6.27	8
12	S4	32.2015	0.2734	N/A	0.31	0.39
13	S5	0.201489	32.27	N/A	32.3	32.4
14	S6	0.00152386	0.0016	N/A	0.002	0.0023

Step 5: After inserting fitting data, user can run the parameter estimation process.

5a: Select the hyperparameters for the genetic algorithm.

Population: Number of models to be solved (high values would lead to longer parameter estimation time)

Max Generations: Maximum number of generations to go for before stopping even if optimal parameters aren't found. (high values would lead to longer parameter estimation time)

Plateau limit: Number of generations where there is no further increase in fitness score. After reaching the given number, the process would stop.

Plague: Process of removing unfit individuals and maintaining only the initial population size at given number of generation.

*After the process is done as seen in the example where it says 'Estimation Complete!', user can click the 'Save' button to save the model with estimated parameters.

No.	Species	Concentration	Boundary
1	IN	10	<input checked="" type="checkbox"/>
2	OUT	10	<input checked="" type="checkbox"/>
3	A	18	<input type="checkbox"/>
4	B1	41	<input type="checkbox"/>
5	B2	9	<input type="checkbox"/>
6	C	52	<input type="checkbox"/>

No.	Enzyme	Concentration
1	IMPORT	50
2	Diverge	11
3	Converge	22
4	EXPORT	35

No.	Enzyme	Activator	Inhibitor	Reaction
1	IMPORT	N/A	N/A	R2: (1) IN <-> (1) A
2	Diverge	N/A	N/A	R4: (1) A <-> (1) B1 + (1) B2
3	Converge	N/A	N/A	R3: (1) B1 + (1) B2 <-> (1) C
4	EXPORT	N/A	N/A	R5: (1) C <-> (1) OUT

Parameters for Genetic Algorithm

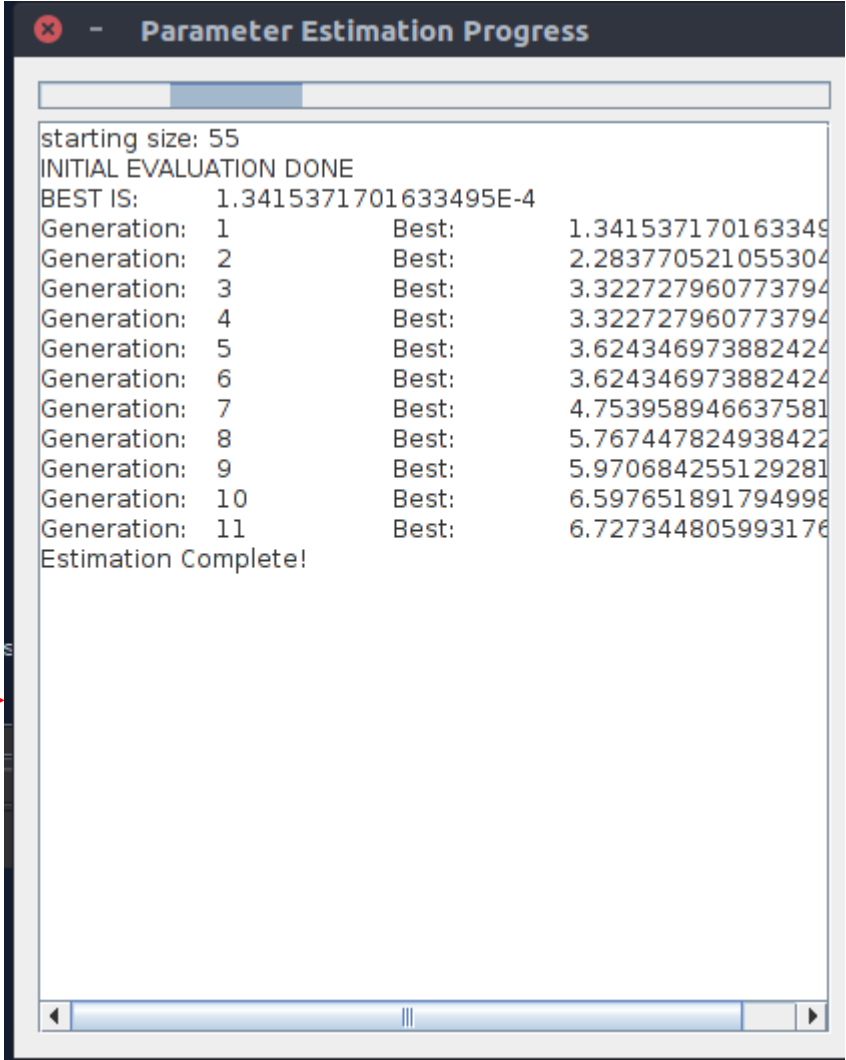
Starting Population: 100

Max Generations: 10000

Plateau Limit: 225

Plague at every N Generation: 5

Run Cancel



TSV format

- This is an example made in a spreadsheet for clarity, it should be in a text file.
- The text is read in row by row by the software.
- A '#' sign denotes start of a new element being read into the system.
- 'B.C' stands for boundary condition, a function in SBML that makes a metabolite's concentration fixed if stated to be 'TRUE' (and vice versa), becoming either an output or input for the system being modelled.
- The column following either metabolites or enzymes are concentrations for the respective compounds.
- For the reactions, users must first set an enzyme that catalyses the reaction, and if needed activators and/or inhibitors for the reaction in the proceeding columns.
- In the following columns, substrates come first, then a '=' sign to separate them from the products, which comes in the next columns.
- For stoichiometries of reactions, users can add numbers followed by '*' preceding the substrates/products (e.g. 2*G6P)

	A	B	C	D	E	F	G	H
1	#METABOLITES	CONC:	B.C.					
2	GLCo	50	TRUE					
3	GLCi	0.1	FALSE					
4	G6P	3.8	FALSE					
5	F6P	0.74	FALSE					
6	F16P	11.8	FALSE					
7	ATP	4.29	FALSE					
8	ADP	1.29	FALSE					
9								
10	#ENZYMES							
11	GLT	0.002						
12	HXK	0.013						
13	PGI	0.15						
14	PFK	0.16						
15								
16	#REACTION ENZYMES	ACTIVATOR	INHIBITORS					
17	GLT	N/A	G6P	GLCo	=	GLCi		
18	HXK	N/A	T6P	GLCi	ATP	=	G6P	ADP
19	PGI	N/A	N/A	G6P	=	F6P		
20	PFK	N/A	ATP	F6P	ATP	=	F16P	ADP

** Text file can then be imported to GUI by clicking:
File (top right corner) -> Tsv to Model