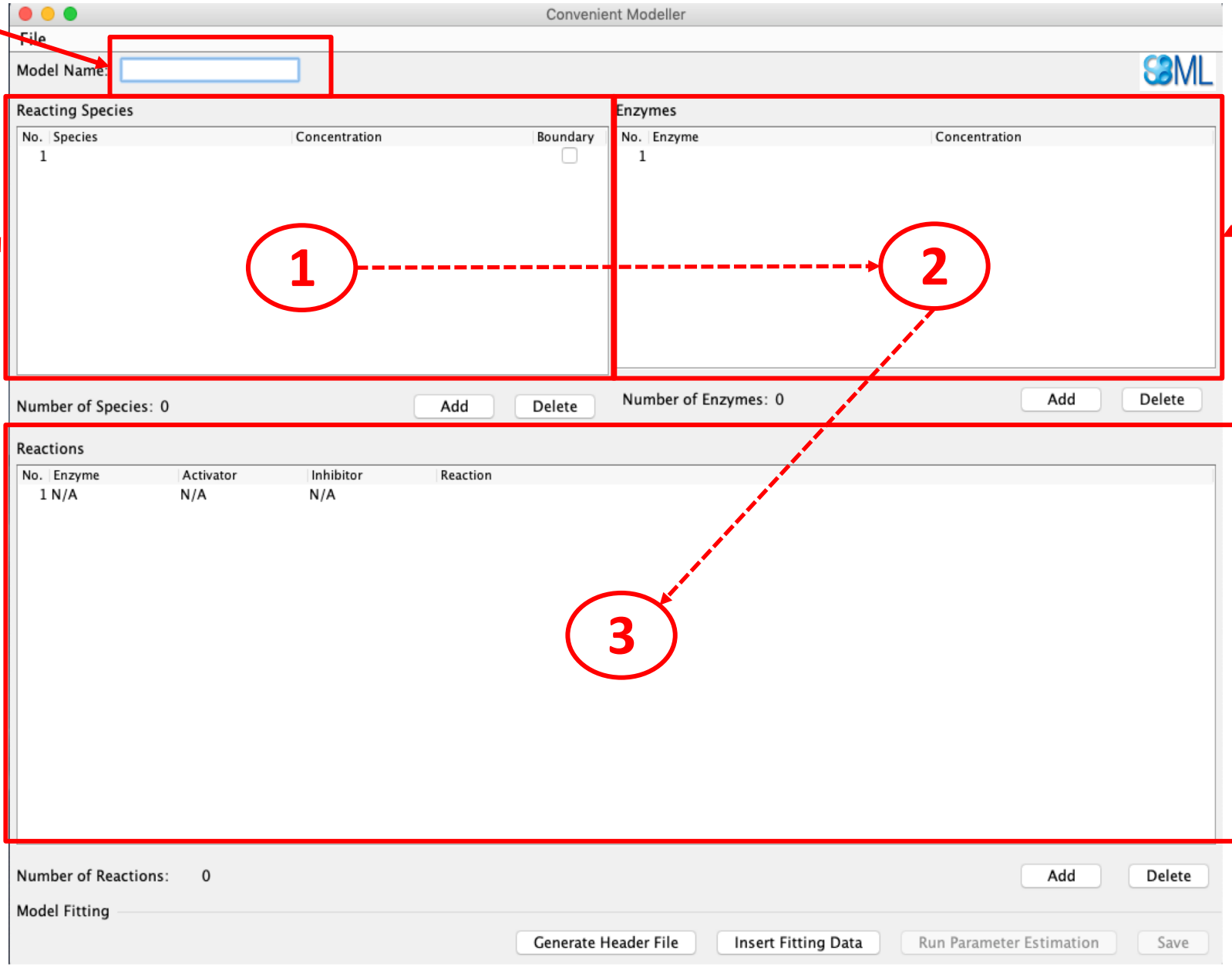
User Interface Crash Course

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

Box for inserting enzyme information (name & concentration).

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

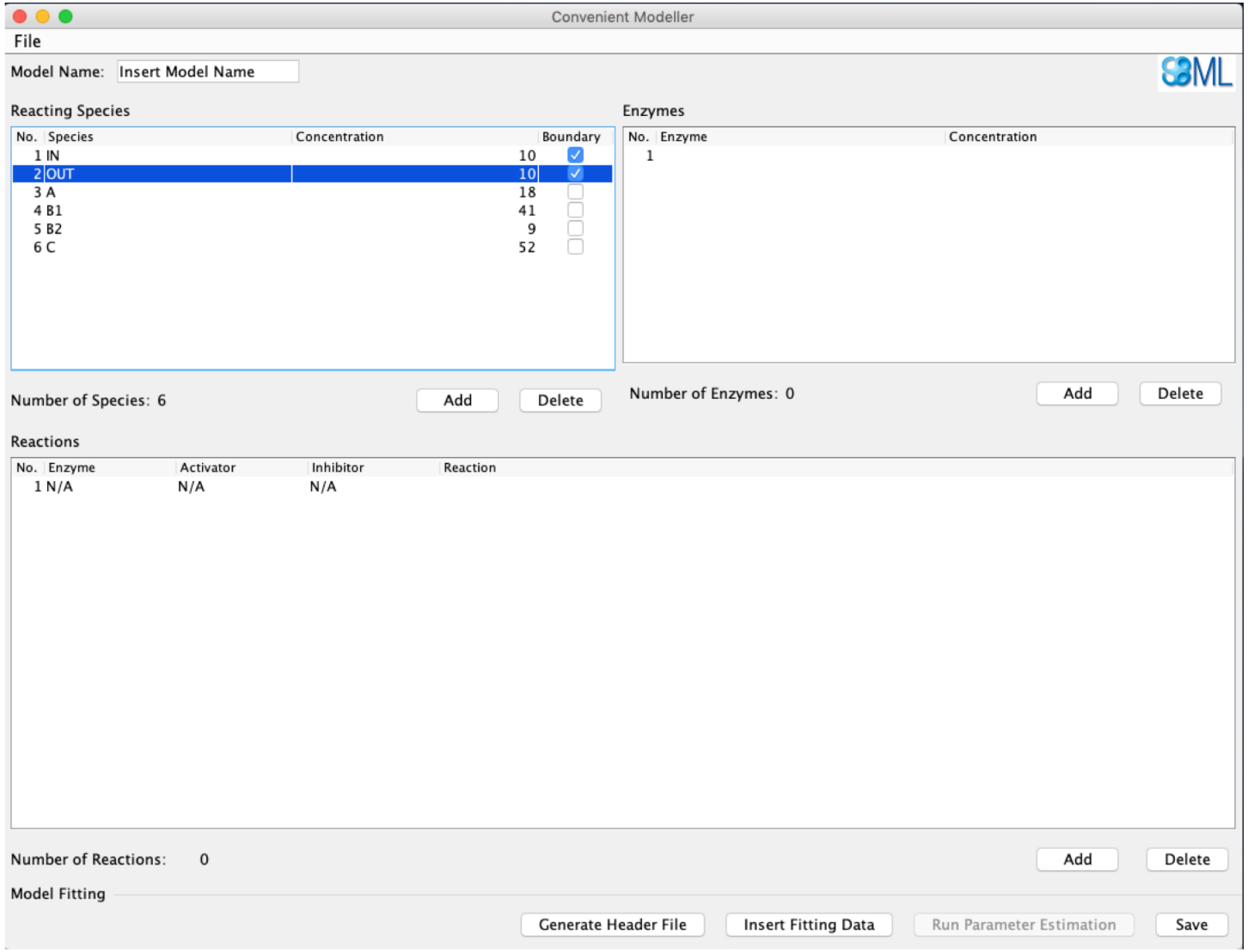
*if enzyme involved are unknown, pseudo name and concentration of 1 can be used.
**to add product and substrates users need to double click on the reaction cell for a different interface to appear.

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

Example use of Convenient Modeller

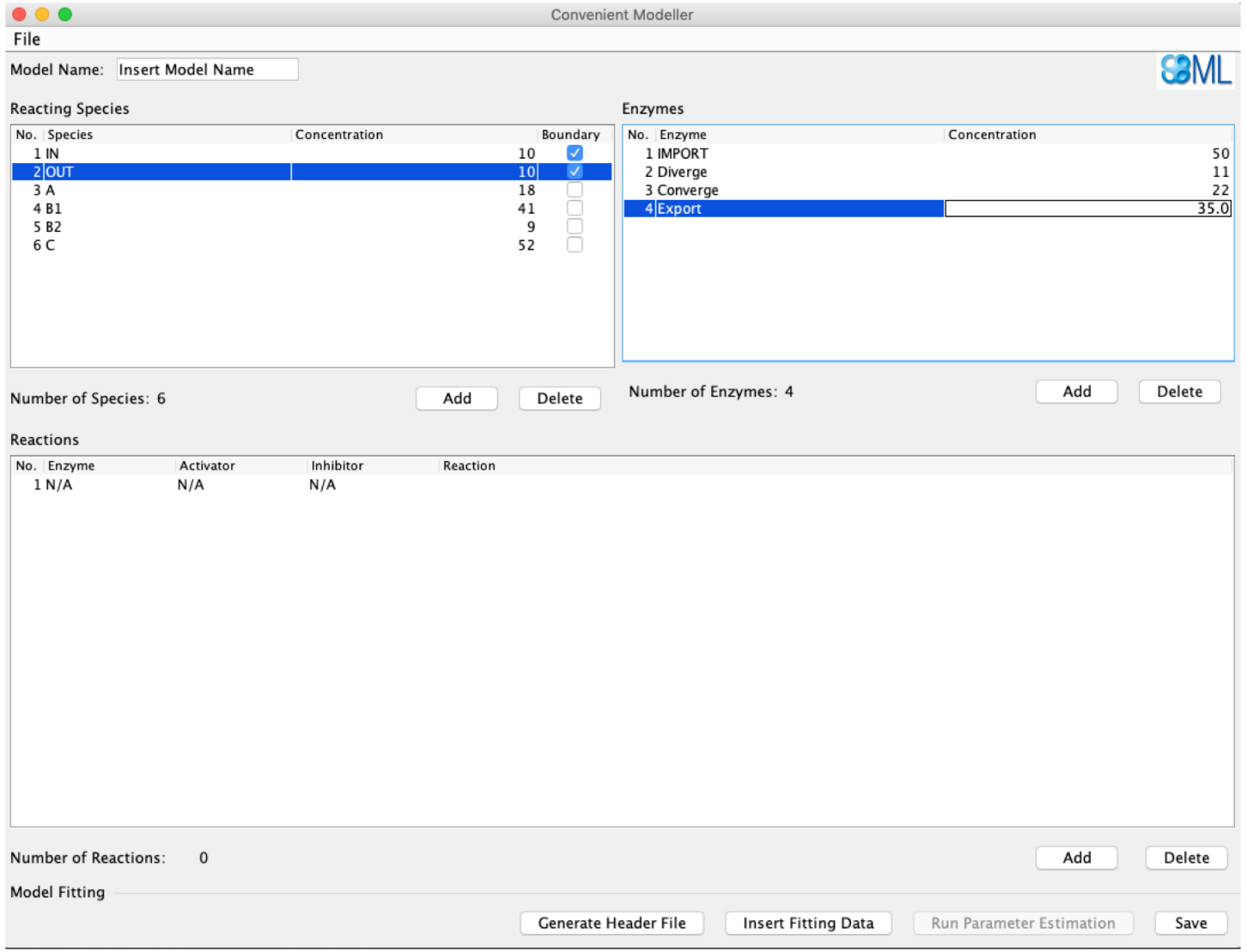
Step 1: Add all known metabolites and its initial concentration (if they are unknown, concentration of 0.1 is suggested)

*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.



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

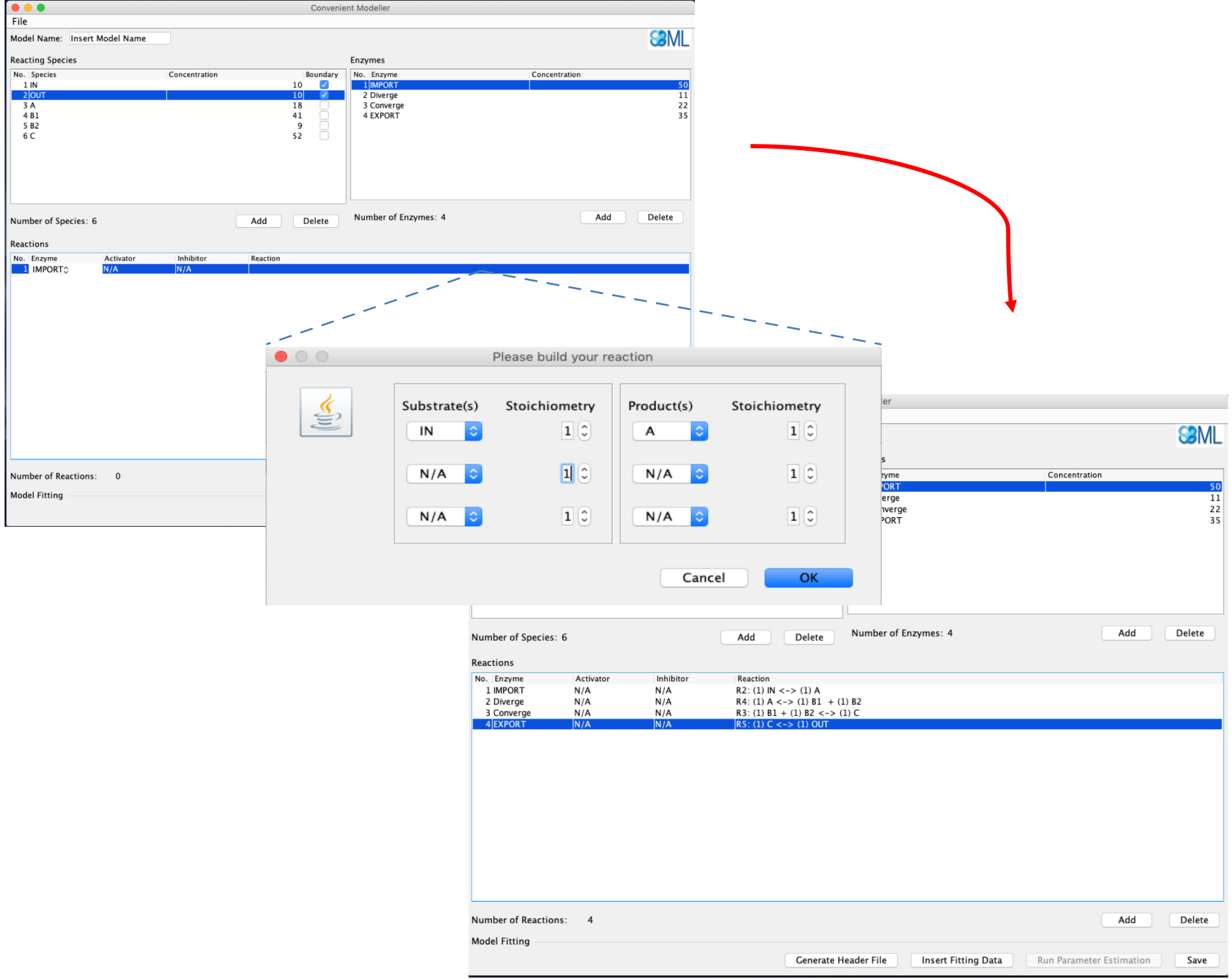
*if enzyme for an reaction is unknown OR if it is a pseudo reaction, a pseudo name can be used.



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



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)

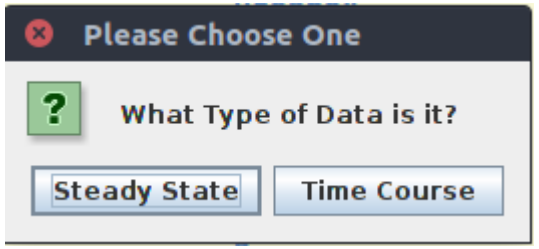
4a: click on generate header file for fitting data.

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.

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.

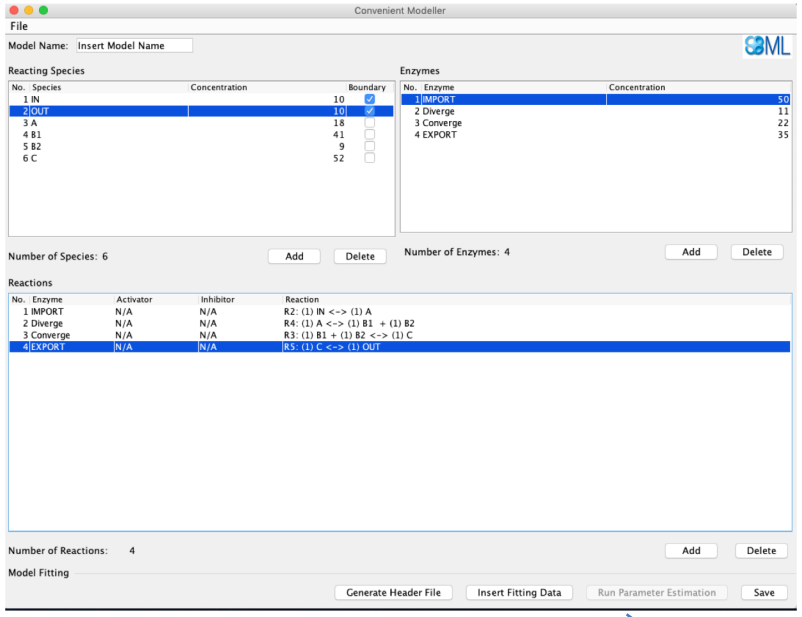
Population: Number of models to be solved (high values would lead to longer parameter estimation time)

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)

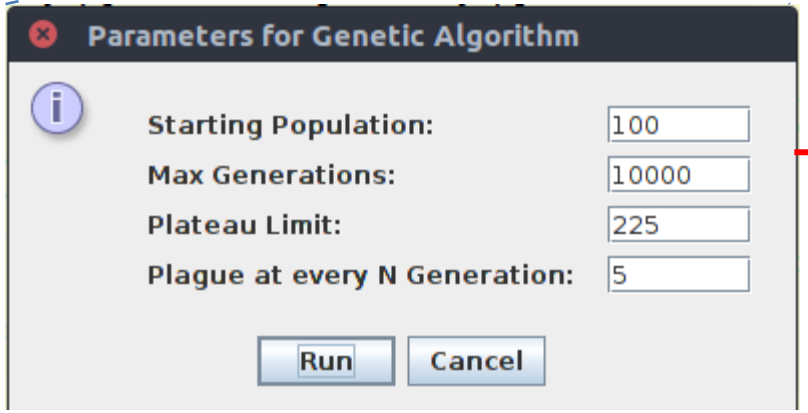
Plateau limit: Number of generations where there is no further increase in fitness score. After reaching the given number, the process would stop.

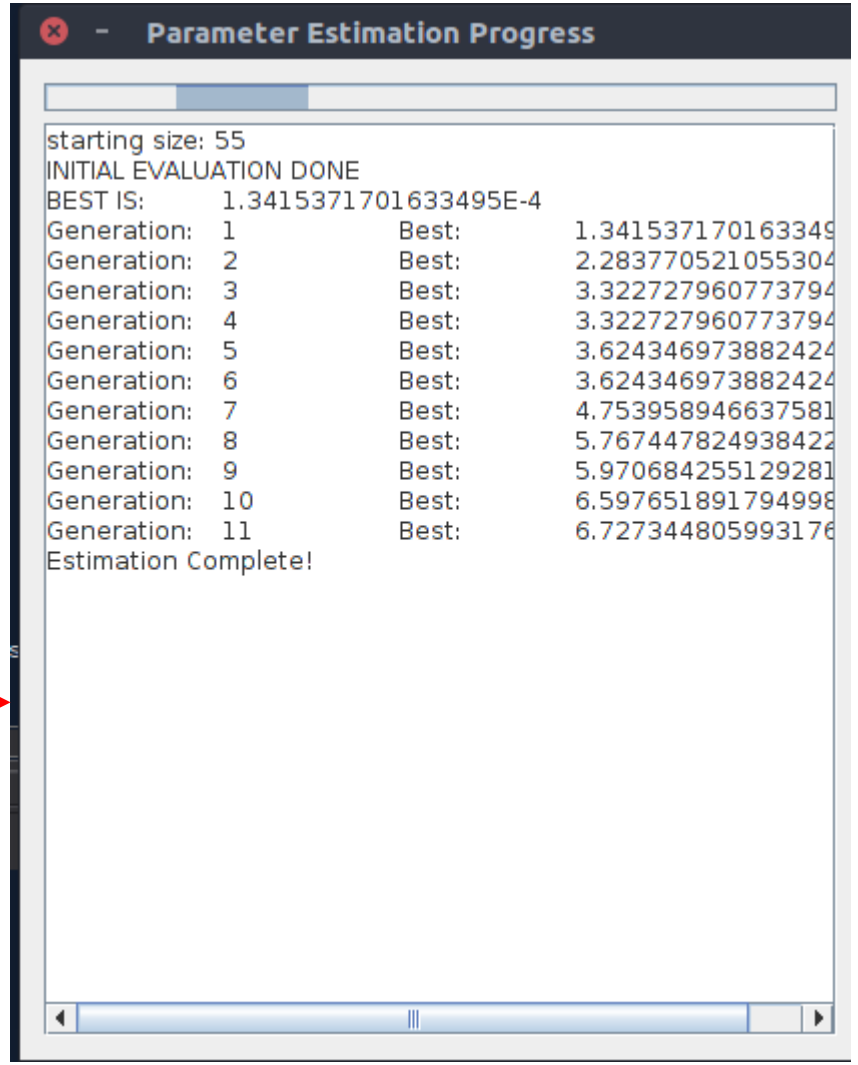
Plague: Process of removing unfit individuals and maintaining only the initial population size at given number of generation.

*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.



5a:





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	ACTIVATOI	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