

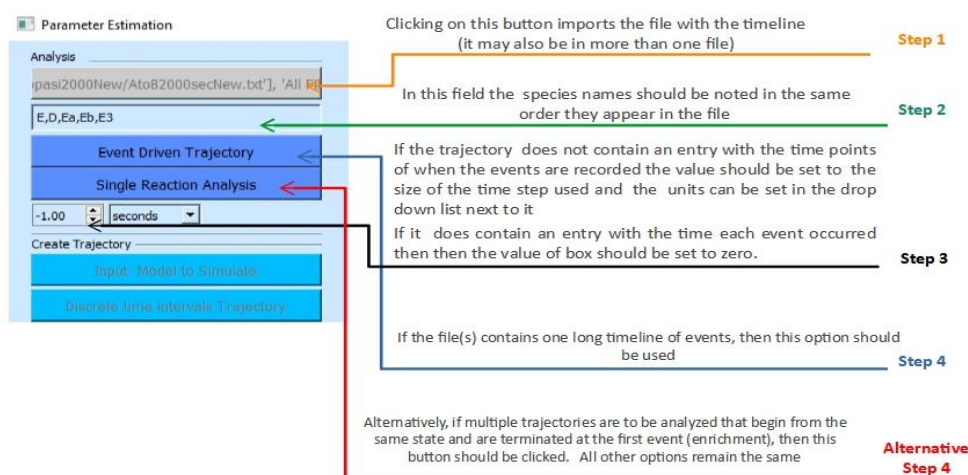
The tool Interface consists of three areas:

- On the left is the area with the blue buttons that analyze a timeline of events created using other external tools and underneath are
- The cyan buttons that are used to create a timeline of events using Tellurium by just uploading the reacting system written in the scripting language Antimony and then analyzing it.
- The remaining area is for visualizing the results.

By placing the mouse over a button without clicking, a tip for the button's function appears.

To begin analyzing a timeline created externally it should be in the following format, each line should contain the number of each species as it was recorded at that time point separated by a comma, a tab or a semicolon. It could also contain, but not necessarily, the time points the events occurred as the first entry of each line.

The steps needed to analyze a trajectory of events are shown in the following picture:



A similar pattern is followed when utilizing a simulation using the embedded features of Tellurium. It must be noted that the output of this section has the time intervals between events calculated exactly, contrary to the calculation on the previous step that it may also calculate the time intervals between events as the sum of the time points between two subsequent events.

The screenshot shows the 'Create Trajectory' window with the following steps and annotations:

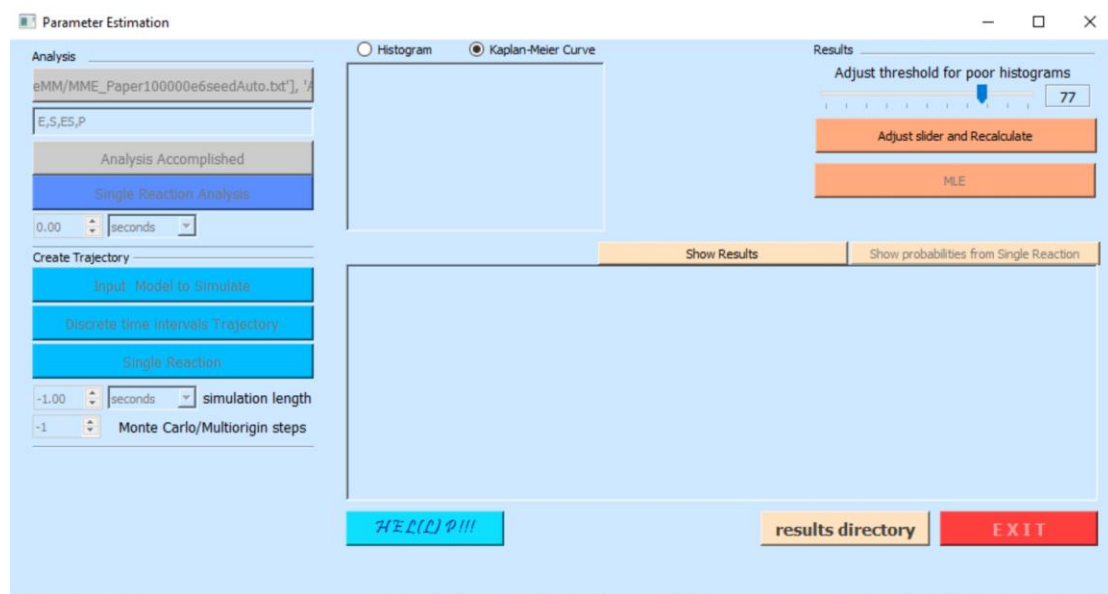
- Step 1:** Clicking on this button imports the kinetic model (scripted in Antimony). An arrow points to the 'Model Loaded' button.
- Step 2:** In this box the simulation length should be set for a full length trajectory or for each of the multiple trajectories of the enrichment simulation. An arrow points to the 'Discrete time intervals Trajectory' button.
- Step 3:** This is set to the number of different trajectories are needed to be generated for the enrichment simulation. An arrow points to the 'Single Reaction' button.
- Step 4:** Clicking on this button starts the simulation, the time between events is exact and not the sum of evenly spaced intervals. An arrow points to the 'Monte Carlo/Multirigin steps' input field.
- Alternative Step 4:** Alternatively, if multiple trajectories are to be analyzed that begin from the same state and are terminated at the first event (enrichment), then this button should be clicked. All other options remain the same. An arrow points to the 'simulation length' input field.

At some point this popup window appears and to continue the compartment volume of the simulation should be filled in Liters. A second action that should be taken is to check the lamda button if it is not already checked, this selects the method of calculation of the mean time the systems spend in each state. The other optios are only for debugging purposes and the results they render are not to be taken under account.

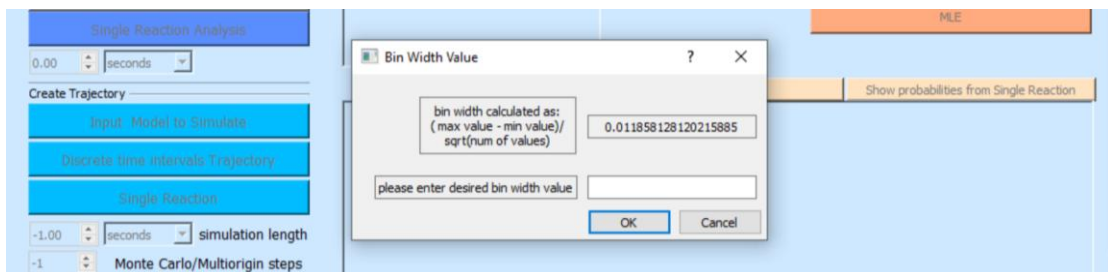
The screenshot shows the 'Parameter Estimation' window with the following features:

- Analysis:** eMM/MME_Paper100000e6seedAuto.bt, E,S,ES,P. Analysis Accomplished.
- Create Trajectory:** Input: Model to Simulate, Discrete time intervals Trajectory, Single Reaction.
- Simulation length:** 0.00 seconds.
- Monte Carlo/Multirigin steps:** -1.00.
- Results:** Adjust threshold for poor histograms (77), Least Squares, MLE, Show probabilities from Single Reaction.
- Dialog Box: Select method for mean calculation**
 - Compartment Volume: 1e-12 in Liters e.g. 4.574645e-12
 - Mean Survival Time:
 - ☐ Kaplan Meier for Survival Analysis
 - ☐ Trapezoid Rule for Histogram (for debug purposes only)
 - ☒ lamda
 - ☐ Arithmetic mean of survival times (for debug purposes only)
 - Buttons: OK, Cancel
- Footer:** HELL[?]!!!, results directory, EXIT

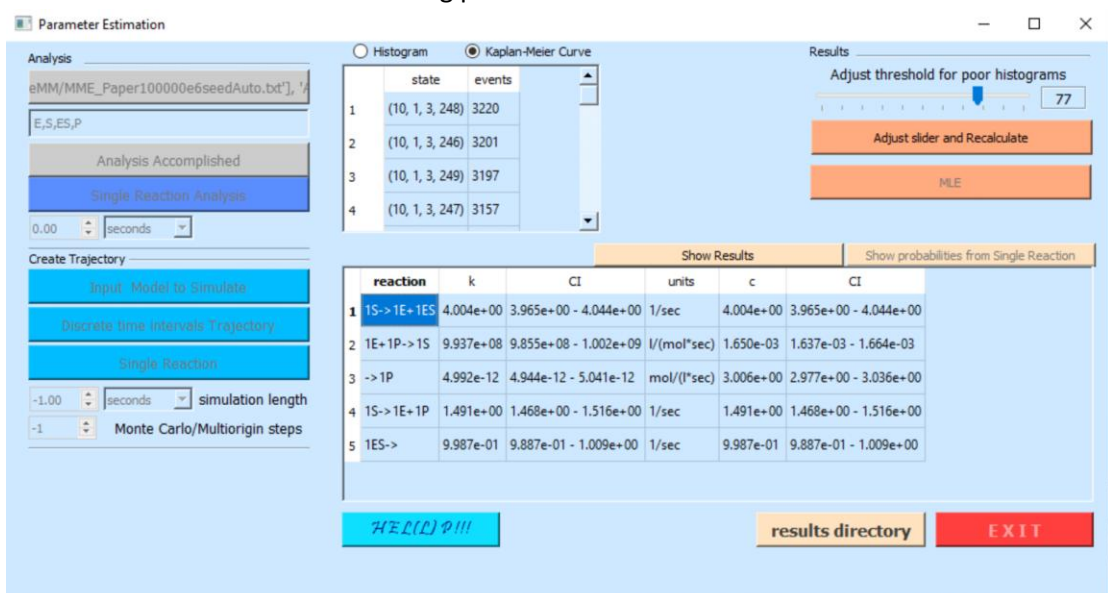
The third part which dispalys the results has the following features:



When the timeline analysis is finished the button changes to grey colour and the orange button on the right is activated. To proceed, the slider that sets the threshold cut off should be adjusted (preferably to 20). Then the button Adjust slider should be clicked. This popup window will appear, no action is required because its function is related to debugging purposes. Clicking OK is all that is needed to proceed.



After that the “show results” button is active and by clicking it the results are displayed in the box as it is shown in the following picture



On the top appears a table with the states the system has visited on the first column and the number of times the system was in that state on the second column. One final feature that is available only in the options for the enrichment simulations is available. It is accessed through the yellow button “*Show probabilities from Single Reaction*” and after the enrichment simulation is analyzed it displays the probability to go to each state after one reaction from the state it originates.

