Instructions for using the synapse model

1. To download the STELLA software needed to run the model, go to:

   http://www.hps-inc.com/redirect.asp?topic=stella7sdr

2. Choose an option for installing the software.

3. Launch: STELLADemoKit.exe

4. Launch: Save-disabled version of STELLA

5. Click File, then Open, then click on the file Brager.STM which you downloaded with this document.

6. Select OK to translate model to version 7.

7. The model consists of several modules, which are indicated by the pink boxes. To get a feel for the components of each module and how the various variables interact during the running of the model, click the small black inverted triangle near the upper left corner. Click the small black upright triangle near the upper left corner to return to the front page.

8. In the blue boxes there are several variables that may be adjusted by either typing new values into the text box or by rotating the knob with the mouse. The preset values are the ones we used in the manuscript. You can change any of these variables and run the model, but they will be returned to the preset values when the model is closed. The variables are:

Total # of HF stimuli:	# of high frequency stimuli delivered during the tetanus at the specified interstimulus interval.
ISI:	interstimulus interval (in msec) during tetanus.
Kd lower limit:	Maximum decrease in the Kd (arbitrary units) of the calcium binding sites on the sensor for exocytosis. During paired pulse stimulation, calcium influx causes the Kd to drop from 125 to this lower limit, and this increase in affinity underlies the facilitation in release.
Kd tau:	time constant (in msec) with which Kd recovers (underlies the recovery of PPF).
Prob of Ca channel:	mean probability that calcium channels open in response to a stimulus (SD = 10% of mean).
PSI max:	maximum inhibition of calcium channel opening probability by presynaptic inhibition.
Magnitude of Ca:	calcium influx (arbitrary units).
Replenish time:	time (in msec) for single released vesicle to be replaced in RRP.
Ca microdom tau:	time constant (in msec) with which calcium concentration in the microdomain recovers.
Residual Ca tau:	time constant (in msec) with which bulk cytoplasmic calcium concentration recovers.
Delay to recov:	time interval (in msec) between end of tetanus and first recovery stimulus.
Recovery ISI:	interval between stimuli during the recovery period (in msec).

9. The front page has a small pink graph labeled release. Double clicking on this will open a plot of release (in quanta) as a function of time in the experiment (in ms). The graph will be updated as the experiment runs.

10. The front page also has three green boxes. Double clicking on these will open spreadsheets in which the results of the experiments will be written. Total Release reports the number of quanta released in 25 msec bins; the main output of the model. For multiple runs (see below), each column will contain the results of one run. Mean status consists of 5 overlaid spreadsheets. Page 1 reports the mean number of vesicles remaining in the RRP of the 5 nerve terminals (in 25 msec bins). Clicking on the small white triangle in the lower left corner of the spreadsheet will reveal the mean hindrance (pg. 2), the mean probability of a vesicle being released from a given terminal (i.e. p_{term})(pg. 3), the mean microdomain calcium influx (pg. 4), and the mean probability of release for each RRP vesicle (i.e. p_{ves})(pg. 5), the mean bulk calcium concentration (= residual + microdomain influx)(pg. 6), and the mean residual cytoplasmic calcium concentration (pg. 6) of the 5 nerve terminals modeled. Data can be copied out of the graphs and pasted into an Excel spreadsheet by clicking in the top left cell ('ms'), then holding down the shift key and clicking in the top right cell (e.g. '#:mean'). While the data are highlighted, click Edit and Copy, change to Excel and paste into a blank spreadsheet. After you have extracted the data from a series of model runs, you will need to click Interface, Restore, Graphs & Tables to erase the old data before beginning a new run.

11. There is also a green box labeled sorting. A value of 1 is placed in this spreadsheet at every 25 msec bin in which there has been a stimulus delivered. Copy the sorter column into Excel, then sort the data by your 'sorter' column and eliminate any data for time bins in which there was no stimulus. You will now have a spreadsheet with a time column (one bin for each ISI of your tetanus) and columns containing the corresponding data. You can average across the rows of this data to compute the mean value at each time point for however many runs of the model you have performed.

12. After you have set the variables, set the duration of each experimental run by clicking the menu item Run, and selecting Run time. The duration of the run (in ms) is from from: to to: (DT should be 1.0 and sim speed should be 0). The duration of the run must be 25 msec longer than the length of the experiment. There is a delay of one ISI before the first stimulus. The number of runs that will be performed sequentially is set by clicking Run and Sensi Specs, and then setting # of runs (the sensitivity on box should be checked and the selected value should be For_Multiple_Runs).

13. To run the model, either click Run and S-run, or the little running person icon in the lower left. You can watch the run in progress with either the graph or one of the spreadsheets open, which is useful to be sure that it is working the way you expect, but this slows down the speed of the run enormously. Once you are sure the model is running, you can hit Run and Pause, close the graphs or spreadsheets, and then hit Run and Resume.