Aim: Match the size of evoked EPSC amplitude in Sargeant et al (mean -48pA) and Rothman 2009 to the granule cells in the granule layer simulation.

The overall method is to match the electrophysiological results as closely as possible to those in these papers. This was done using a compartment model but the same process should work for an I.F. model. The match will not be exact, but the gross features such as the size of EPSCs should be altered to be close (by changing weight factors in neuroConstruct).

I loaded the granule cell simulation and removed cells so that there is simply one mossy fibre connected to a granule cell with a current clamp in the mossy fibre. I set the current clamp to inject a small spike of current (2nA for 2ms) which causes a depolarisation of the granule cell (EPSC).

I set a voltage clamp in neuron, holding at -70mV (as in Sargeant).
This gave a voltage clamp current of -43pA with neuroconstruct weight values of: 5.24 AMPA and 4.51 NMDA. (quite close)
[Actual peak conductances in neuron and in the xml file: AMPA: 1.12e-7, NMDA: 1.19e-7.]

Took Jasons data. Found that there is a 4.7:1 observed AMPA:NMDA ratio. When the single unit conductance is taken into account this translates into a 7.85 AMPA multiplication factor. Setting the NMDA factor to **0.775 and the AMPA factor to 6.08** preserves this and gives a peak voltage clamp current of 49pA (-1.7pA) holding when briefly depolarising the mossy fibre input.

In simulations set a Gaussian distribution having this as its mean. Truncate the distribution at 0. Variance is given in terms of the multiplication factor. As a beginning estimate let us constrain 64.2% of the EPSPs to be within the range 27.3pA-67.3pA. This seems a reasonable dispersion looking at Sargent.

Network set-up

I first set the weights from mossy fibres to granule cells to values retrieved from data from Jason. Initially want the network to easily comparable to the theory so we shall consider the case that we have 30 inputs. In this case at realistic densities we should have 84 granule cells. (This is not quite true but will do for now).

Want to investigate info. transmission of binarised activity patterns under two threshold setting regimes:

A) Fixed input frequencies (associated with ‘on’ or ‘off’) and variable threshold (bias current)
B) Fixed bias current and variable input frequencies: i.e. the frequency encodes the threshold, the spatial pattern carries information.

A) Need the input firing frequency to be strong enough that at 0 bias current, a single input fires the cell (low frequency 5-10Hz, but clearly above granule cell spontaneous rate - which is nearly 0).

Previously the match to synaptic conductances produced from Jasons data using SynapseTest.nml did not match the fit from Sargeants data using the granule cell model in the Granule layer model (Maex & DeSchutter 98). Upon inspection, the reason for this is that the peak conductance for these mechanisms is different in each file. Furthermore the AMPA mechanism in the Synapse test file is a double exponential synapse with time constants that differ markedly from the MF_AMPA model.

Fit to Jasons Data:
(SynapseTest)

(AMPA 1e-8S), factor 0.11, conductance 1.1e-9S
(NMDA 2e-8S), factor 0.082, conductance 1.64e-9S

Fit to Sargeant data:
(GranCellLayer)

(AMPA 1.12e-10S), factor 1.1, conductance 1.123e-10
(NMDA 1.87e-10), factor 8.6, conductance 1.61e-9S

Here the Sargeant fit is consistent with the fit to Jasons data. Furthermore the inconsistency in the AMPA fit should be disregarded due to the differing mechamisms. Therefore we shall take the Sargeant fit here.

Under these conditions the mf firing frequency sufficient to fire a granule cell having one active mf input is: Mf 100Hz, giving granule rate of 33Hz

Now, let us agree that we shall set a threshold for a cell to be considered active as that it should fire at a rate greater than 20Hz. (Really this should be 7Hz on average)

Determine constant bias currents such that 1 - 10 inputs active are required to fire the cell.

Number inputs active to fire	Bias current (nA) [Single trial Grc frequency on testing bias]
1	0 (33Hz)
2	-0.007 (29Hz)
3	-0.012 (28Hz)
4	-0.015 (31Hz)
5	-0.0177 (21Hz)
6	-0.0195 (28Hz)
7	-0.022 (21Hz)
8	-0.0235 (28Hz)
9	-0.0255 (29Hz)
10	-0.026 (44Hz)

(The above granule cell firing rates are too high, should be around 7Hz on average)