Supporting Material

Monte Carlo Simulation of Buffered Diffusion Into and Out of a Model Synapse

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6 supplementary figures

3 supplementary movies (captions in this document)

Movie S1

The onset phase of ligand diffusion into the model synapse (Figure 1) containing a high density of receptors. The movie runs in real time. The parameters listed in Table 1 were used for the simulation; Fig. 2 is a graphical display of the same simulation. Green and red dots represent unliganded and liganded receptors respectively.

Movie S2

The recovery phase of ligand diffusion out of the model synapse (Fig. 1) containing a high density of receptors. The movie is a continuation of Supplementary Movie 1. It begins at t = 5 s when the external ligand concentration is clamped to zero. The movie runs in real time between t=5-20 s and is speeded up 30x between t=20-100 s. Fig. 3 is a graphical display of the same simulation. Green and red dots represent unliganded and liganded receptors respectively.

Movie S3

The diffusion of an irreversible ligand into the model synapse (Fig. 1) containing a high density of receptors. The movie runs in real time. The parameters listed in Table 1 were used for the simulation except that $l_- = 0$; Fig. 8 is a graphical display of the same simulation. Green and red dots represent unliganded and liganded receptors respectively.
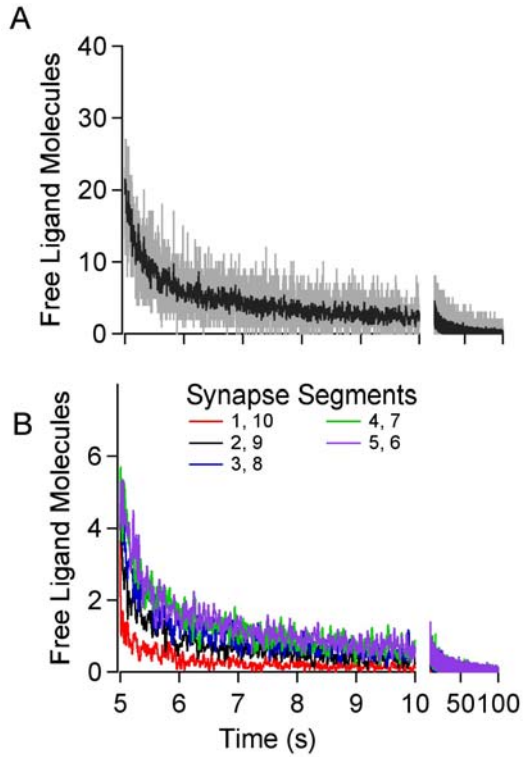
Fig. S1
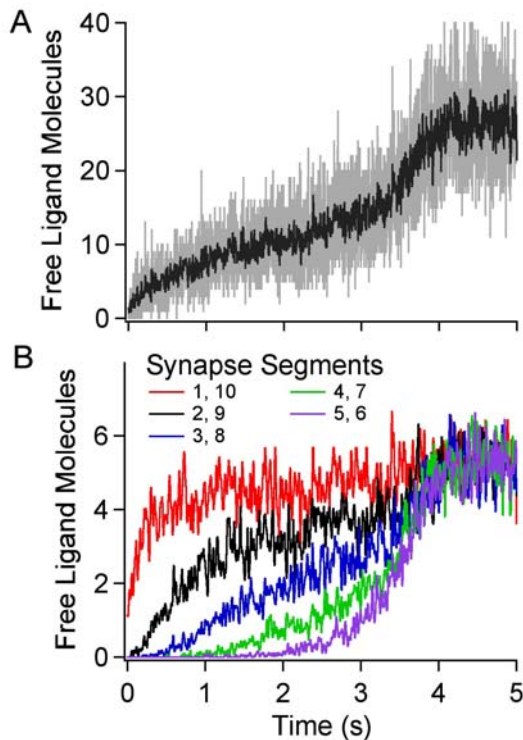
Free ligands during the onset phase of buffered diffusion. The Simulation parameters are given in Table 1. Fig. 2 in the paper shows the corresponding receptor occupancy graphs.

A. Free ligands within synapse as a function of time. The gray trace shows the actual number, the black trace has been smoothed for purpose of display with a sliding average of 100 points.

B. Free ligands (smoothed with a sliding average of 100 points) as a function of time within the different segments of the box synapse.

Fig. S2

Free ligands during the recovery phase of buffered diffusion. The Simulation parameters are given in Table 1. Fig. 3 in the paper shows the corresponding receptor occupancy graphs.

A. Free ligands within synapse as a function of time. The gray trace shows the actual number, the black trace has been smoothed for purpose of display with a sliding average of 100 points.

B. Free ligands (smoothed with a sliding average of 100 points) as a function of time within the different segments of the box synapse.

Fig. S3
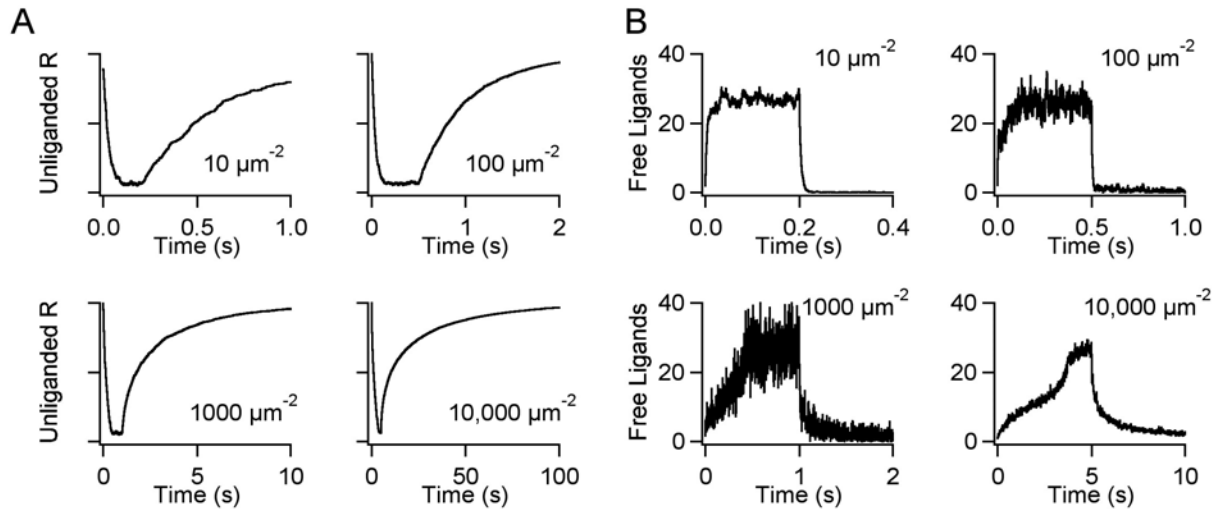
The effect of receptor density on receptor occupancy and free ligand concentration. Parameters are the same as shown in Table 1 except for receptor density. For low receptor density, the simulations were repeated with different random number seeds and the results averaged: 10 μm^{-2} (20 simulations), 30 μm^{-2} (10 simulations), 100 μm^{-2} (5 simulations). After receptors were equilibrated with $15xL_{eq}$ ligand, the external concentration was clamped to zero ligand at t=0.2, 0.5, 1.0 and 5.0 s for densities of 10, 100, 1000 and $10^4 \mu m^{-2}$ respectively. The time interval between displayed data points ranges from 10 μs to 1 ms depending on the time scale. Fig. 4 in the paper shows the corresponding graphs of $t_{0.5}$ vs density.

A. Unliganded receptors (R) as a function of time for different densities. Note the differences in time scales. The maximum number of unliganded receptors is 20, 200, 2000 and 20,000 respectively.

B. Free ligands as a function of time for different densities. The predicted number of free ligands in the synapse at equilibrium is 27. Traces show the smoothed average of 10 individual data points.

Fig. S4
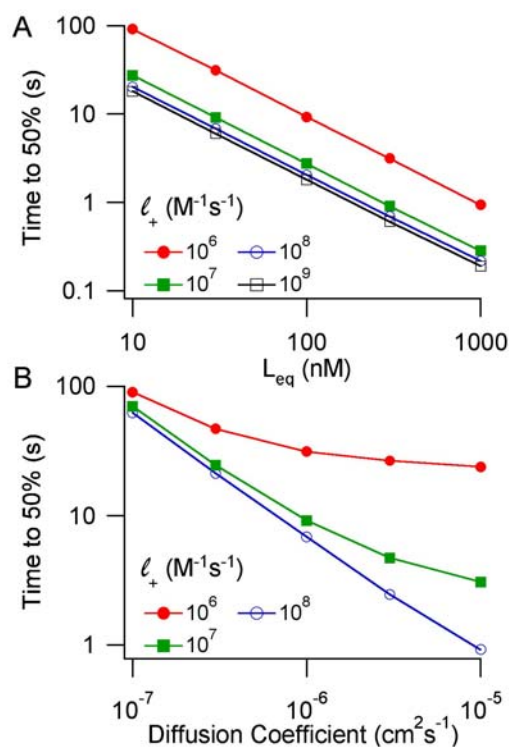
Effect of ligand affinity and diffusion coefficient on the recovery kinetics of receptor occupancy during buffered diffusion. Onset is shown in Fig. 5 of the paper.

Fig. S5
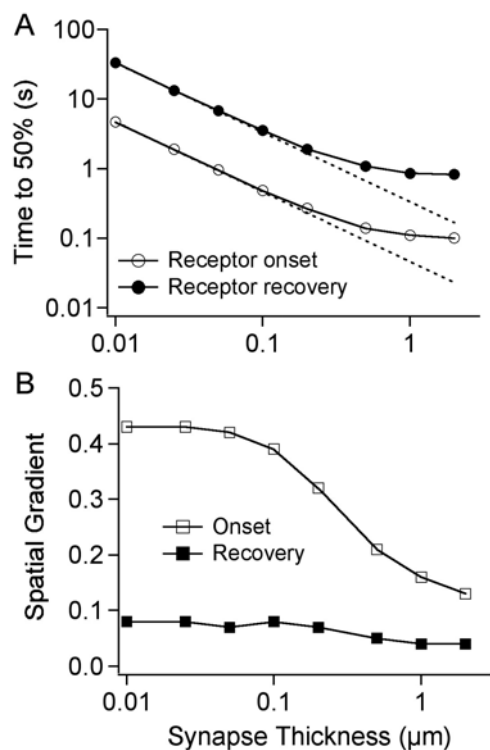
The effect of synapse dimensions on diffusion of ligands into and out of the box synapse. Conditions are the same as shown in Table 1 except for the synapse cleft thickness, t_{cleft}. Because the x-dimension of the synapse is 1 µm, the synapse thickness /width ratio is equal to the gap size in µm.

A. The time needed to reach 50% of maximum receptor occupancy for onset and recovery simulations with different synapse thicknesses. Dashed lines correspond to a linear correlation for $t_{cleft} \leq 0.2$ µm between $\log(t_{50})$ and $\log(thickness)$; the slopes are -1.0.

B. The spatial gradient during onset and recovery for different synapse thicknesses.

Fig. S6
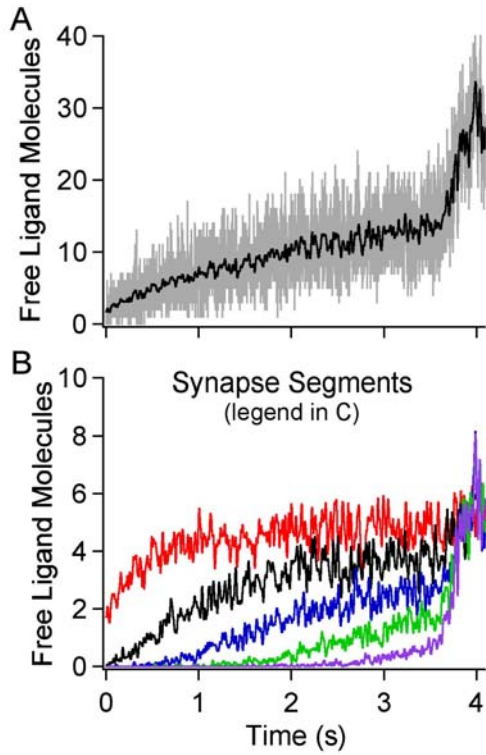
Diffusion of irreversible ligands into the box synapse. This simulation used the parameters from Table 1, except that l_- is set to 0 so that bound ligands do not dissociate. Fig. 8 in the paper shows the corresponding receptor occupancy graphs.

A. Free ligands within synapse as a function of time. The gray trace shows the actual number, the black trace has been smoothed for purpose of display with a sliding average of 100 points.

B. Free ligands (smoothed with a sliding average of 100 points) as a function of time within the different segments of the box synapse.