

## Practical 4: AMPA synapse. Note to Answers

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1. Check in matlab that the transition matrix has the properties stated in the lecture notes. Make sure you understand the script. The only open state in the diagram is the sixth entry in the state vector.

*Answer: to check that this is a proper transition matrix the columns sum to zero. in Matlab `sum(m)` will show that this is the case. For diagrams with loops, not the case here, it will be necessary to check detailed balance is fulfilled. For diagrams without loops this is automatically the case.*

2. What is the steady state when the transmitter  $T$  is absent, i.e.  $T = 0$ . Guess how long it will take to reach it. What is the formal expression for the steady state for any given, fixed amount of  $T$ ?

*A quick estimate for how long it takes goes as follows. The inverse of the (non-zero) eigenvalue closest to zero will correspond to the slowest time scale. Matlab: `1./sort(eig(m))` will give 2.5 sec. This would be the time to reach fraction  $(1 - e)$  of the final state.*

*The formal expression is given by  $ds(t)/dt = 0$ , or, equivalently, it is the eigenvector corresponding to the zero eigenvalue; it will get very complicated when written out.*

3. What happens when you give two pulses (of neurotransmitter) close after each other?

*As you can see from the script, a second impulse will increase the open probability further. But is the second increase as big as the first one? You will find it is not. Still, this could be due to saturation. But if you space the two pulses further apart so that the first has decayed, e.g. one pulse between 384 ms and one at 43 and 43 ms (adjust ntime), you will find that the second pulse still leads to a smaller effect. Indeed, inspection of the state occupations, shows that channel get stuck in the d1 state (blue) and the occupancy of which only decays very slowly. This effect is called de-sensitization of the receptor. For much smaller concentrations (e.g.  $1\mu M$ ), if given quickly after each other you can also get facilitation: then the response to the second pulse is bigger than that to the first one. Such effects are already present in the state-diagram of the lecture notes where the open probability goes as  $T^2$ .*