Models of VOR learning in MHC knockout mice

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Abstract

We see if we can model VOR gain increase and decrease learning in mice with a knockout in MHC as well as wild type.

Contents

1 The setup

sec:setup

1.1 Models of synapses

sec:synapse

We make the following assumptions:

- There are N identical synapses with M internal functional states.
- The states of different synapses are independent of each other.
- The synapses that are eligible for plasticity are chosen randomly.
- The potentiating/depressing plasticity event timings are distributed as Poisson processes with rates $rf^{\text{pot/dep}}$, where $f^{\text{pot}} + f^{\text{dep}} = 1$.
- Potentiation and depression are described by Markov processes with transition probabilities $\mathbf{M}^{\text{pot/dep}}$.
- The synaptic weights of the internal states are given by the column vector $\mathbf{w}$. This can only take two values that we can call ± 1.

The independence and identicalness of synapses means that the state of the system can be completely described by the probability distribution of the internal states, the row vector $\mathbf{p}(t)$.

The evolution of this probability is described by a forgetting matrix, $\mathbf{W}^{\mathrm{F}}$:

$$\frac{\mathrm{d}\mathbf{p}(t)}{\mathrm{d}t} = r\mathbf{p}(t)\mathbf{W}^{\mathrm{F}}, \qquad \mathbf{W}^{\mathrm{F}} = f^{\mathrm{pot}}\mathbf{M}^{\mathrm{pot}} + f^{\mathrm{dep}}\mathbf{M}^{\mathrm{dep}} - \mathbf{I}. \tag{1}$$

eq:evolve

Eventually, this will settle into the equilibrium distribution:

$$\mathbf{p}^{\infty}\mathbf{W}^{\mathrm{F}} = 0. \tag{2}$$

eq:eqprob

With only two possible synaptic weights, the distribution of synaptic weights is completely described by the mean, $\mathbf{p}(t)\mathbf{w}$.

1.2 Model of VOR learning experiment

c:learning

Training the animal will not change the internal dynamics of a synapse under potentiation or depression. It will change the environment, will lead to a change in how often potentiation and depression occur. It could be manifested in a change in which synapses are potentiated/depressed, but this could not be captured in this type of model. We will model this by changing $f^{\mathrm{pot/dep}}$, leaving r and $\mathbf{M}^{\mathrm{pot/dep}}$ unchanged.

The untrained case will be described by $f^{\mathrm{pot}} = f_0^{\mathrm{pot}}$. Gain increase training will be described by $f^{\mathrm{pot}} = f_{\mathrm{inc}}^{\mathrm{pot}} < f_0^{\mathrm{pot}}$, and gain decrease training will be described by $f^{\mathrm{pot}} = f_{\mathrm{dec}}^{\mathrm{pot}} < f_0^{\mathrm{pot}}$. Note that the forgetting matrix (1) and the equilibrium distribution (2) depends on f^{pot}, which we will indicate with subscripts.

Before training, the synaptic distribution will in equilibrium with f_0^{pot}. During gain increase training, it will evolve according to (1) with $f_{\mathrm{inc}}^{\mathrm{pot}}$:

$$\mathbf{p}(t) = \mathbf{p}_0^{\infty} \exp\left(rt\mathbf{W}_{\mathrm{inc}}^{\mathrm{F}}\right). \tag{3}$$

eq:nopre

On the other hand, if the gain increase training follows gain decrease pre-training for some time period, t_{pre}:

$$\mathbf{p}(t) = \mathbf{p}_0^{\infty} \exp\left(rt_{\mathrm{pre}}\mathbf{W}_{\mathrm{dec}}^{\mathrm{F}}\right) \exp\left(r(t-t_{\mathrm{pre}})\mathbf{W}_{\mathrm{inc}}^{\mathrm{F}}\right). \tag{4}$$

eq:withpre

We will describe the effect of training by the decrease in mean synaptic weight:

$$L(t) = \left(\mathbf{p}(0) - \mathbf{p}(t)\right)\mathbf{w}. \tag{5}$$

eq:learning

The behavioural output (VOR gain) will be some non-linear function of the synaptic weights, so the best we can hope for is to reproduce qualitative features of the experiment.

The MHC knockout has a lower threshold for depression. We can model this by changing $\mathbf{W}_{\mathrm{WT}}^{\mathrm{dep}}$ to $\mathbf{W}_{\mathrm{D^bK^b}}^{\mathrm{dep}}$, which should have larger matrix elements.

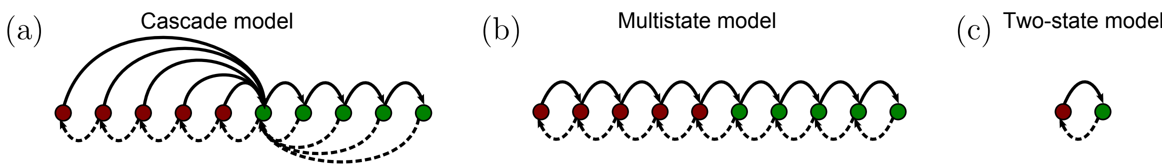

Figure 1: Transition probabilities for different models. (a) In the cascade model, the transition probabilities decay geometrically with a parameter x (see [1]). (b) In the multistate model the transition probabilities for potentiation/depression are all equal and it is parameterised by these two values. (c) The two-state model is parameterised by the two transition probailities. fig:models

QUESTION: Should $f^{\mathrm{pot}}_{\mathrm{WT}} = f^{\mathrm{pot}}_{\mathrm{D^bK^b}}$?

If they are equal, this would change the mean synaptic weight in equilibrium. This seems like it would affect the ability of the network to perform its function, and one might expect adaptation to the environment to produce an equilibrium state that has the same performance. In any case, if the synaptic weights are different, the electrical activity will be different, and there will be no reason to expect the same statistics for potentiation or depression.

On the other hand, one could imagine adjusting $f^{\mathrm{pot}}_{\mathrm{WT}}$ and $f^{\mathrm{pot}}_{\mathrm{D^bK^b}}$ so that $\mathbf{p}^{\infty}_{\mathrm{WT}}\mathbf{w} = \mathbf{p}^{\infty}_{\mathrm{D^bK^b}}\mathbf{w}$. But, now that the synaptic weights are the same, the electrical activity will be the same, and there will be no reason to expect different statistics for potentiation or depression.

2 Simulations

sec:sims

2.1 Models and parameters

We will look at three different models, the cascade model (see [1] and Figure 1a), the multistate model (see [2, 3] and Figure 1b) and the two-state model (which can be thought of as a special case of the previous two, see Figure 1c).

For the cascade model, we will use the same value for the parameter x (which controls the decay of transition rates, see [1]) for potentiation and depression in the wild-type as well as potentiation in the $\mathrm{D^bK^b}$-/- mutant. We will use a larger value for x for depression in the $\mathrm{D^bK^b}$-/- mutant.

For the multistate and two state models, we will use the same value for the transition probabilities, q for potentiation and depression in the wild-type as well as potentiation in the $\mathrm{D^bK^b}$-/- mutant. We will use a larger value for q for depression in the $\mathrm{D^bK^b}$-/- mutant.

In each case, we set $f^{\mathrm{pot}}_0 = \frac{1}{2}$, $f^{\mathrm{pot}}_{\mathrm{inc}} = f^{\mathrm{pot}}_0 + \Delta f$ and $f^{\mathrm{pot}}_{\mathrm{dec}} = f^{\mathrm{pot}}_0 - \Delta f$. The values of all these parameters are listed in Table 1.

Model	# states	pot,WT dep	$\mathrm{D^bK^b}$-/- dep	Δf
Cascade	10	$x = 0.25$	$x = 0.3$	-0.1
Multistate	10	$q = 0.6$	$q = 0.8$	-0.1
Two-state	2	$q = 0.6$	$q = 0.8$	-0.1

Table 1: Parameters used in simulations. `tab:params`

References

`2005cascade` [1] S. Fusi, P. J. Drew, and L. F. Abbott, "Cascade models of synaptically stored memories," *Neuron* **45** (Feb, 2005) 599–611, `PubMed:15721245`.

`94learning` [2] D. J. Amit and S. Fusi, "Learning in neural networks with material synapses," *Neural Computation* **6** (1994) no. 5, 957–982.

`multistate` [3] S. Fusi and L. F. Abbott, "Limits on the memory storage capacity of bounded synapses," *Nat. Neurosci.* **10** (Apr, 2007) 485–493, `PubMed:17351638`.