

Neural Plasticity with different time constants

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ABSTRACT

In lasting neural plasticity, certain morphological properties of the neurons are changed. The neuron achieves a slightly (or radically) different set of synaptic connections, its ability for dendritic integration changes due to a different distribution of ion channels, and its excitability or gain modulation becomes activated to a different degree by different neuromodulators. Accordingly, we may define a formal neuron by a set of three tuples describing functional locations, and a set of membrane proteins distributed to the locations for its *membrane parameters*, as well as a set of "plasticity factors" for different proteins, which relate membrane activity, general internal signals such as calcium, and specific signalling pathways in a location-specific way for its *internal parameters*. We may now feed this state description of a neuron into different patterns of ongoing activity, and observe the fluctuations of parameters on different time-scales. Specifically, we want to sketch out the occurrence of lasting changes in dopamine-related parameters (D1, D2-receptors and voltage-gated potassium channels) which translate into modulations of dendritic integration, dendritic transmission length, synaptic efficacy, and presynaptic glutamate release regulation as a function of both glutamatergic spike trains and dopaminergic spiking activity. For this we need to consider three different time-scales (100ms, 2 min, 20 min), each with its own description of activity. For Fig. 1, we relate

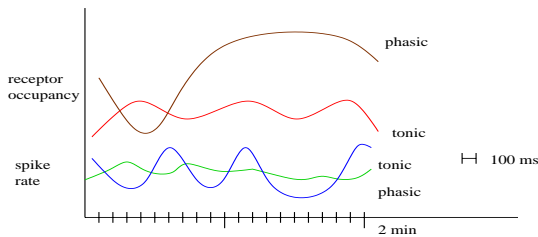


Figure 1: Physiological efficacy of DA depending on DA neuron dynamics

DA receptor occupancy at a patch of neuronal membrane to dopaminergic spikes, sampled at 100 ms.

$$e = s - dat \times \left(\sum_{i=1}^{d1} x_i \times a/d1 \right) \times \left(\sum_{i=1}^{d2} x_i \times b/d2 \right)$$

e (DA efficacy) is computed by the number of phasic DA releases (s) minus the current transporter activity (dat) divided by the number of receptors ($d1, d2$) currently in a sensitized state (x_i) factored by their intrinsic binding capacity

(a, b). Glutamatergic activity (spike trains) are reflected in x_i , dat may also be sampled at 2 min to provide an estimate with a different time resolution (cf. Fig. 2), and $d1, d2, a, b$ are constants at this level. We investigate two different conditions, (a) high fluctuation of spike counts following high glutamatergic activity ("phasic") and (b) low fluctuation with low glutamatergic activity ("tonic"). We can see that receptor occupancy is weakly oscillating in the tonic case, and has pronounced peaks and troughs in the phasic case. In this model, behaviorally correlated phasic bursts in DA neurons have increased physiological effectiveness even though overall dopaminergic activity may be homeostatically constrained and equal in both cases.

In Fig. 2, we depict both physiological DA efficacy at a cortical neuron, and relevant mRNA activation for 40 minutes including a 10-minute behavioral training regime. We suggest that the fluctuation in DA activity that leads to short-term neuronal plasticity needs specific favorable conditions to result in long-lasting change, conditions that may be more easily met during brain development. Different profiles of cell metabolism and genetic expression for different neuronal types (e.g. in primary sensory areas and higher associational areas) may also be used. Hence, most activity within the dynamic ranges between 100 ms and 20 min is short-term adaptivity that may be filtered out for long-term changes, rather than being added up as incremental change.

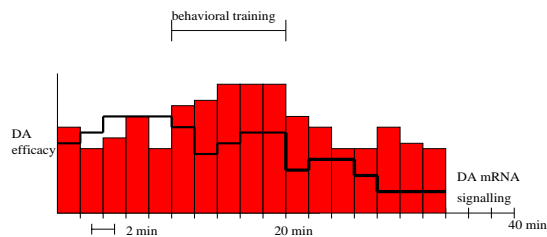


Figure 2: Lasting plasticity from behavioral training?

Naturally, with a framework like this we cannot answer any empirical questions. It requires experimentally obtained estimates for the relevant parameters as well as a mathematical analysis of error margins for them in order to achieve a theoretically sufficiently constrained model for empirical correspondence. But a discussion on a relevant theory that links the main physiological events seems very necessary in order to further guide experimental research.