Hebbian Learning by a Simple Gene Circuit

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The single celled ciliate, Paramecium caudatum, can be classically conditioned therefore it must contain an intracellular circuit capable of associative learning. Hebbian learning was proposed as a mechanism for associative learning in neurons whereby synaptic weights would increase as a product of the correlated firing of pre and post synaptic neurons. Hebbian type learning by single cells could allow unsupervised self-organization of genetic receptive fields, or supervised training of gene expression patterns. One implementation of the circuit is shown in figure 1. Although the paramecium is used to illustrate the circuit we propose, the actual mechanism of classical conditioning in paramecia is more likely to use a variant of the adenylyl cyclase, cAMP, Ca^{2+} channel system involved in associative learning in Aplysia.

Let V represent the conditioned stimulus (vibration) and S represent the unconditioned stimulus (shock). Assume they activate transcription factors $u_1$ and $u_2$ which do not bind to the promotor unless modified (e.g. phosphorylated) into the $U_1^{*}$ and $U_2^{*}$ forms respectively. Upon binding of the transcription factor, the cilia beat to produce the avoiding response, but in addition produce a re-entrant signal kinase oPKK, which is an internal representation of the extent of cilia beating. This kinase oPKK is activated specifically by binding rapidly to either $U_1$ or $U_2$. If it binds to $U_1$ then it activates another kinase $mPK_1$ and if it binds to $U_2$ it activates the kinase $mPK_2$. These second level kinases are in a slow equilibrium and so effectively integrate the concentration of activated oPKK over time. They specifically phosphorylate the transcription factors and allow them to bind the promotor. In analogy with Hebbian learning, the transcription factor concentrations represent the pre-synaptic activities, the cilia activity and the oPKK concentration represents the post-synaptic activity, and the concentrations of $mPK_i$ represent the synaptic weights. Figure 2 shows a simulation of the classical conditioning training procedure.

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