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Using adaptive synaptogenesis to model the development of ocular dominance in kitten visual cortex.

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Introduction

Activity-dependent modification of synaptic weights is a hallmark of neural network computation. Activity-dependent synapse formation, on the other hand has been largely ignored. Synaptic connections in most neural network models are formed at random or with a particular spatial pattern before any modification of synaptic weight begins. However, in the experimental literature there exist anatomical studies of synapse formation that imply synaptogenesis may also depend on a neuron's history of activity. In fact, there seem to be both pre- and postsynaptic activity-dependent mechanisms affecting the probability that a synapse will be formed [e.g. 1,10,13]. Such mechanisms, which operate much slower than the modification of existing synaptic weights, seem useful for regulating the overall connectivity of a network by ensuring that individual neurons are neither overused or underused.

To demonstrate the effects of activity-dependent synaptogenesis on the development of a neural network, we simulated the development of ocular dominance in the kitten visual system [see also 8]. Ocular dominance is the relative ability of a stimulus to fire a neuron when presented to one eye versus the other. The plasticity of ocular dominance is well-studied experimentally [3,5,6,12] and theoretically [2,4,10]. Our work here differs by requiring the network to form all its synapses by activity-dependent rules and to reproduce the experimentally observed distribution of ocular dominance under different environmental manipulations. The dependent variable of interest in each simulation is ocular dominance, calculated as the ratio of the total synaptic weight that a cortical cell receives from each eye. As is traditional for ocular dominance, the results of the simulations are displayed as histograms [5,6], with equally binocular cells counted in the center bin and monocular cells counted in the outer bins.

The set of experiments that we successfully simulate here are (see Figure 1 for steady-state histograms),

1. Normal rearing. Both eyes open leads to binocularly responsive cortical cells[5].
2. Monocular deprivation. One eye open leads to cortical cells responsive only to the open eye[6].
3. Monocular deprivation and APV infusion into the cortex. APV is an NMDA receptor agonist that blocks the modification of synaptic weights. The distribution of ocular dominance remains much like the normal-rearing distribution[3].
4. Monocular deprivation and muscimol infusion into the cortex. Muscimol is a GABA-A agonist that selectively inhibits activity of the postsynaptic cells. The cortical cells become preferentially responsive to the closed eye[12].

The Network

The network is a highly simplified version of layer IVc of kitten visual cortex consisting of 32 cortical neurons that may receive input from 16 lateral geniculate (LGN) neurons. Each simulation begins with no synapses. Activity patterns of the LGN neurons are generated by a suitably biased random number generator. Each LGN neuron receives input from only one eye, and the pairwise correlations of LGN firings are specified within each eye and between the two eyes. In the normal environment there is good correlation of activity between the eyes. In the deprivation condition, the correlations of closed eye-associated neurons is greatly reduced. The activity of a cortical cell is calculated from the presynaptic activity by summing the products of each individual afferent's firing rate and synaptic weight.

Associative Modification and Synaptogenesis

In the model, existing synapses are modified according to

$$\Delta w_{i,j} = \epsilon f(y_j)(cx_{i,j} - w_{i,j})$$

where Δ is the change of the synaptic weight $w_{i,j}$, y_j is the rate of firing of the postsynaptic cell j , $f(\cdot)$ is a function of postsynaptic activity (here, $f(y) = y$), ϵ is a small positive constant, and c is a positive constant. See [7,9] for experimental and theoretical treatment of this synaptic modification rule. In the model APV directly blocks any modification by setting ϵ to zero. Note that no modification of synaptic weight can occur without some postsynaptic

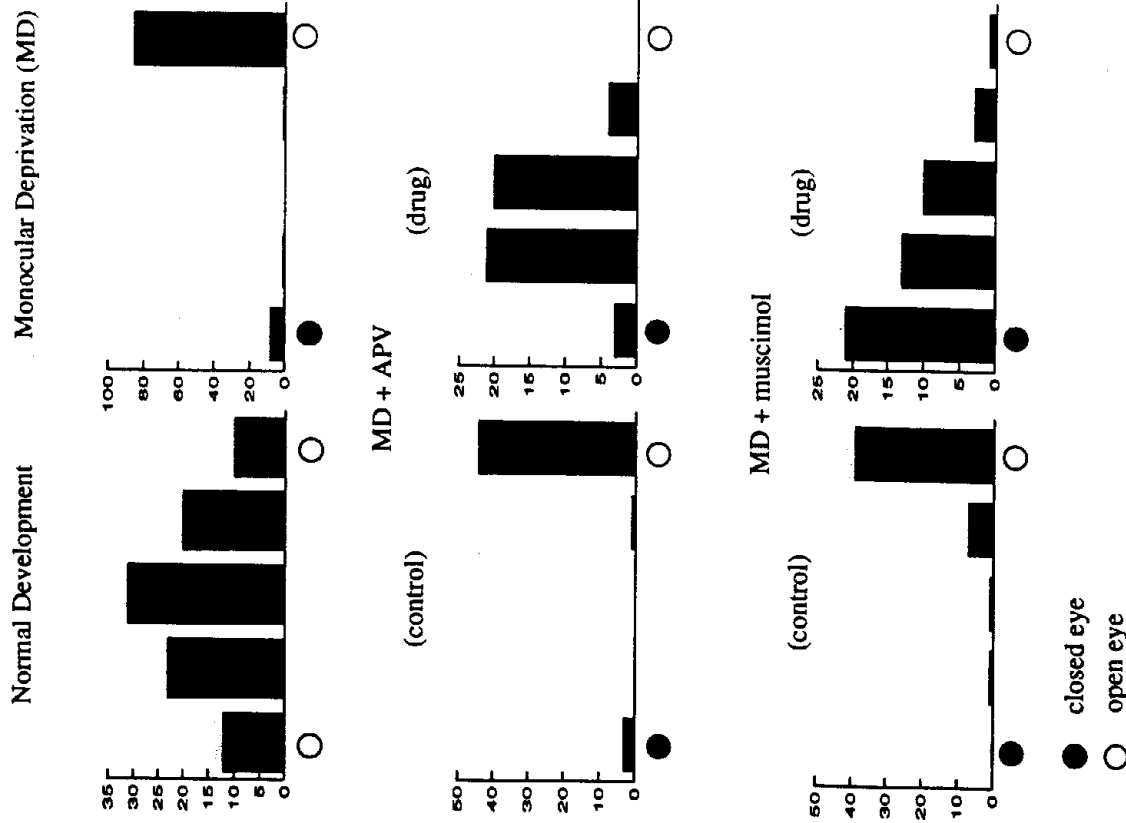


Figure 1: Simulations of Ocular Dominance Development in Different Environments

Ocular dominance distributions reproduced by the model network described in this paper. In simulations of drug effects, both control regions and drug-application regions are modeled.

activity. The drug muscimol also effectively blocks synaptic weight modification by reducing postsynaptic activity.

Synapses are formed between a pre- and a postsynaptic cell at a rate of

$$\Delta s = \gamma A_i R_j$$

where Δs is the probability of a new synapse being formed, γ is a small positive rate constant, A_i is the presynaptic cell i 's avidity for seeking new synaptic contacts, and R_j is the postsynaptic cell j 's receptivity for making new synapses. Avidity, A_i , is a decreasing function of the total weight of the synapses of the presynaptic cell i . Avidity is inspired by experimental results suggesting that a cell tries to maintain some maximum number (or weight) of synaptic contacts[13]. Receptivity, R_j , is a decreasing function of the average activity of the postsynaptic cell j . Receptivity is inspired by experimental results suggesting that postsynaptic cells are more likely to make new synapses if their activity is low [1,10]. Thus, in our model the rate of synapse formation depends on the activity history of both the pre- and postsynaptic cells forming the synapse. Synaptogenesis occurs at a rate much lower ($< 10^{-4}$) than synaptic modification of existing synapses.

Simulation of Monocular Deprivation and Muscimol

The dynamics of one simulation are summarized in Figure 2. To reproduce the distribution of ocular dominance observed experimentally with muscimol and monocular deprivation, synaptogenesis and associative modification must complement each other. *Top panel:* Early in the simulation, the network forms synapses. Later, after a stable state is achieved, the deprivation and muscimol manipulations begin and end (vertical dotted lines). *Postsynaptic activity panel:* Postsynaptic activity (average of control and muscimol groups) is initially zero, but increases as synapses are formed. At the start of the experimental manipulations, the average activity of each postsynaptic group drops because of the decreased correlations of the closed-eye cells, but the muscimol group is inhibited to a much greater degree. *Postsynaptic receptivity panel:* As average activity decreases, receptivity increases. This increase is much greater for the muscimol cells than for the controls. *Presynaptic avidity panel:* As the experimental manipulations begin, the closed-eye presynaptic cells begin to lose synaptic weight on the control postsynaptic cells, because of the activity-dependent modification rule for synaptic weight. Thus, the avidity increases for the closed-eye presynaptic cells. No synaptic weight is lost on the muscimol-treated postsynaptic cells because these cells have no activity and the synaptic modification rule is inactive. *Rate of synapse formation panel:* The open and closed-eye groups, presynaptically, and the control and muscimol groups, postsynaptically, yield four possible groups that can make synapses. Of these groups, only the closed-eye to muscimol group has a high probability of forming new synapses. Thus, there is a shift in dominance of the muscimol group toward the closed eye.

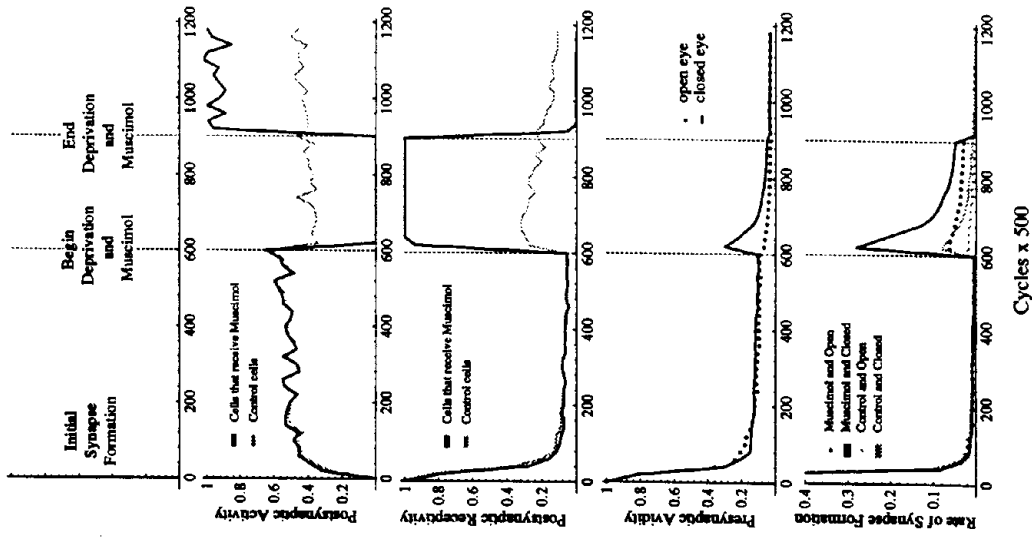


Figure 2: Detail of Muscimol Simulation

Values over time of the primary variables determining synaptogenesis. See text for details.

Discussion

This work demonstrates that activity-dependent synaptogenesis can complement associative synaptic modification to produce a simple, but biologically relevant, self-assembling neural network. As formulated, each of the equations depends on variables that are local to each neuron, and has some experimental justification [1,7,9,11,13]. Of relevance to both natural and artificial networks is that the synaptogenesis processes may help regulate the overall activity levels of individual neurons and may help distribute the representational information across the network.

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