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Specificity of synaptic connections formed during development of a functioning neuronal network

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When neuronal circuits develop, do cellular recognition processes ensure that only specific, "correct" synaptic connections form? To assess this question we have examined synaptic connections between neurons in the developing spinal cord of the hatchling frog tadpole when neuronal circuits for reflexes and swimming are functioning. We made electrical recordings from 500 pairs of neurons to determine synaptic contact probabilities between 7 different neuron types. Overall, the results from paired recordings reveal very widespread connectivity. Where evidence is available, neurons with dendrites receive synapses from all other neuron classes.

We then examined the anatomical distributions of the axons and dendrites of these 7 types of neuron, more precisely their dorsoventral positions. This allowed us to calculate the probabilities that axons would contact dendrites and therefore be able to form synaptic connections. When contact probabilities determined from anatomy were compared to synapse probabilities determined directly by electrical recording, the two were significantly correlated.

These results suggested that synapse formation may not depend on specific recognition between axons and "correct" dendrites. To test if rules based simply on contact probabilities could lead to functioning spinal networks, we made physiological models of spinal neurons, based on the Hodgkin-Huxley neuron model, and connected them using the contact probabilities we had determined. Networks created in this fashion turned out to be quite reliable: the majority produced swimming. Purely random networks, with the same overall degree of connectivity, were much less successful in producing swimming, even when preserving the sensory pathway from the probabilistic rules.

Simple rules controlling axon growth may determine the initial connections made as the nervous system develops. Our detailed analysis implies that cellular recognition to specify correct connections may be unnecessary for the formation of pioneer functional networks.