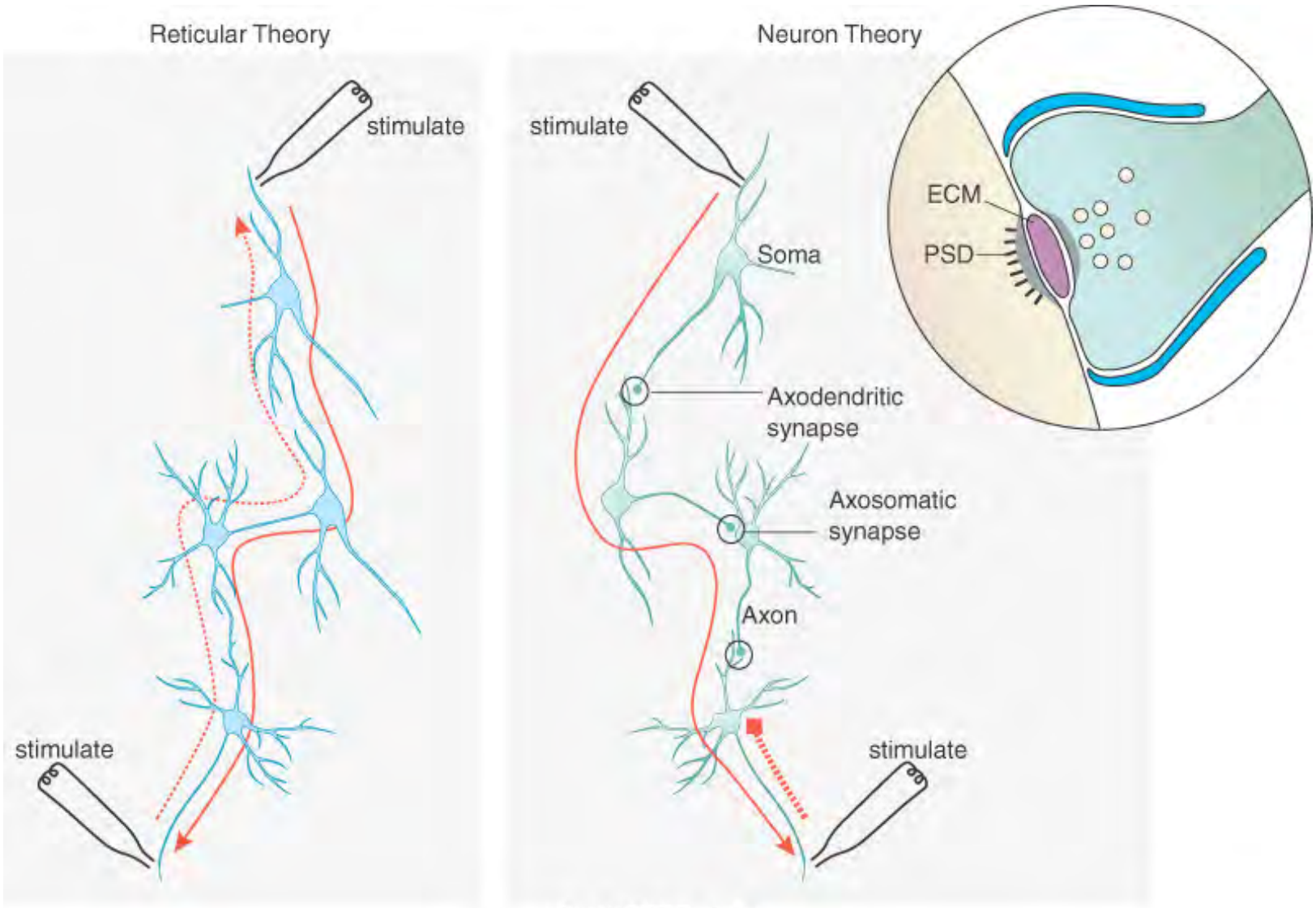
MCDB 153

Neural Development

Synaptogenesis
Lecture Set 7



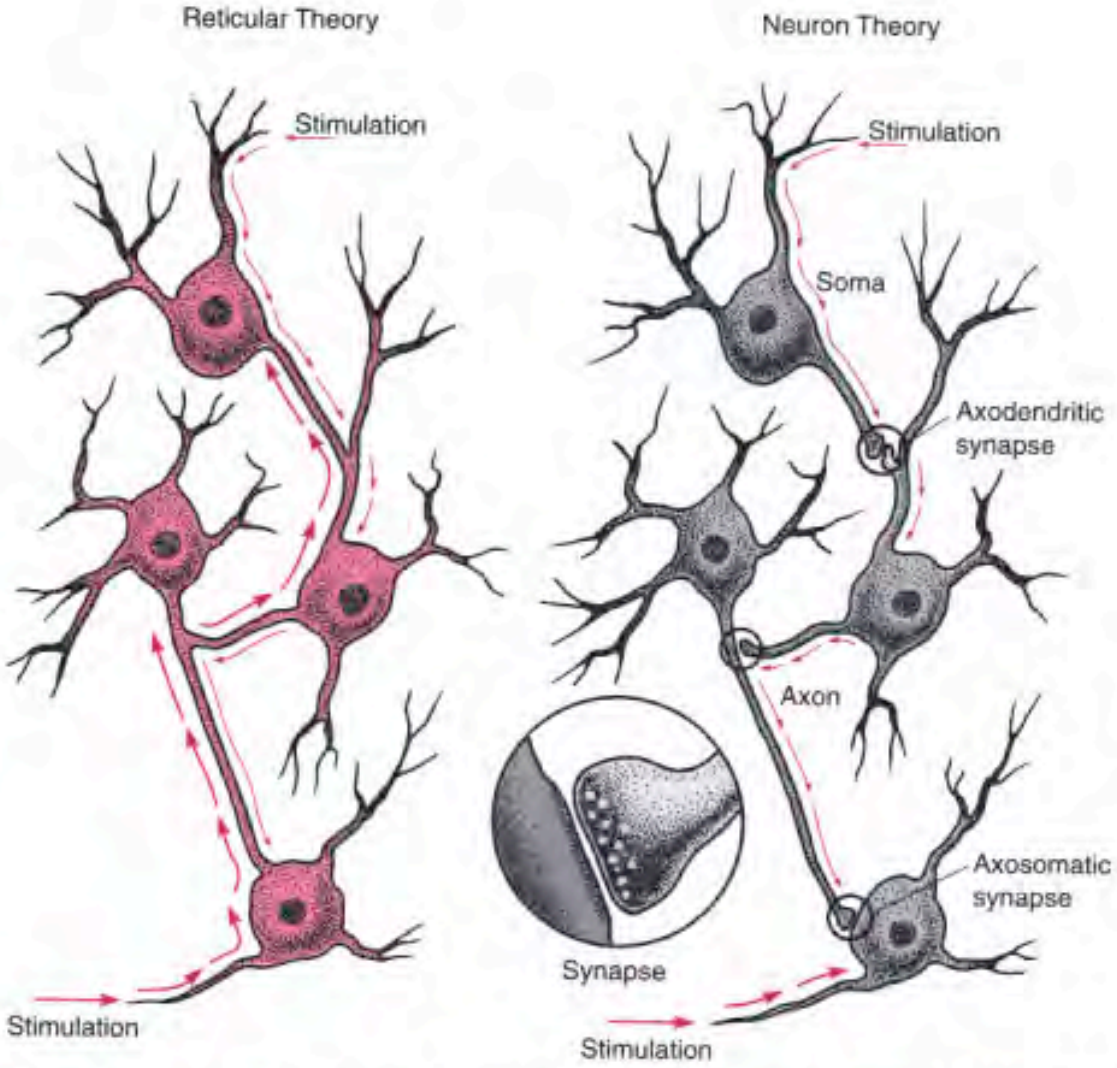
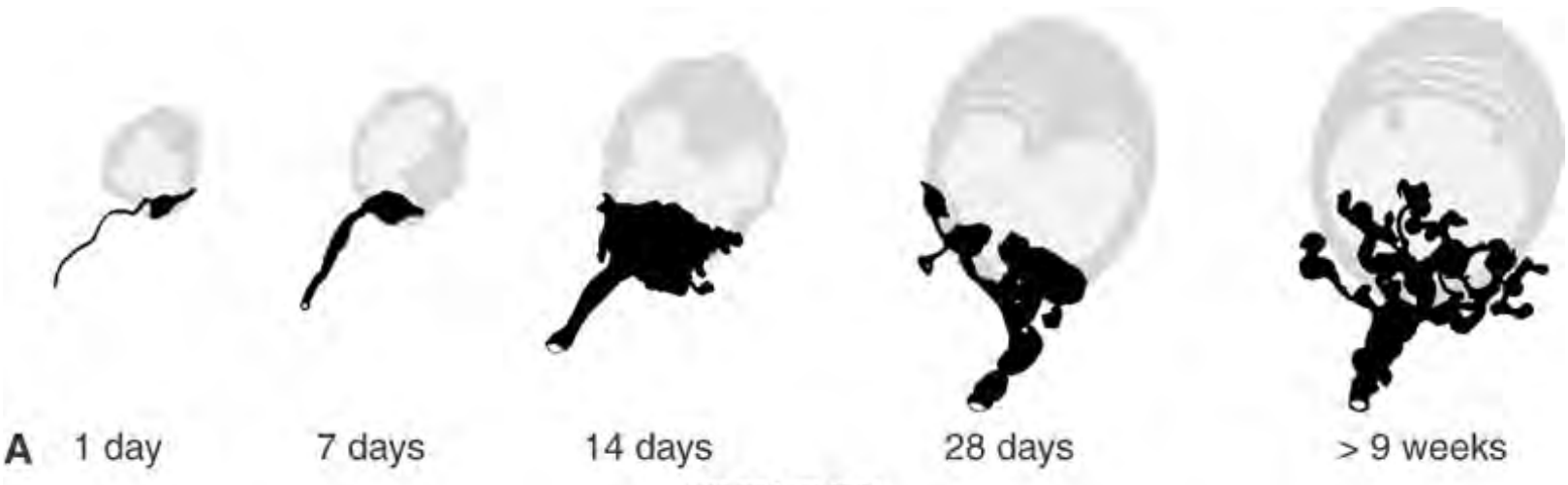
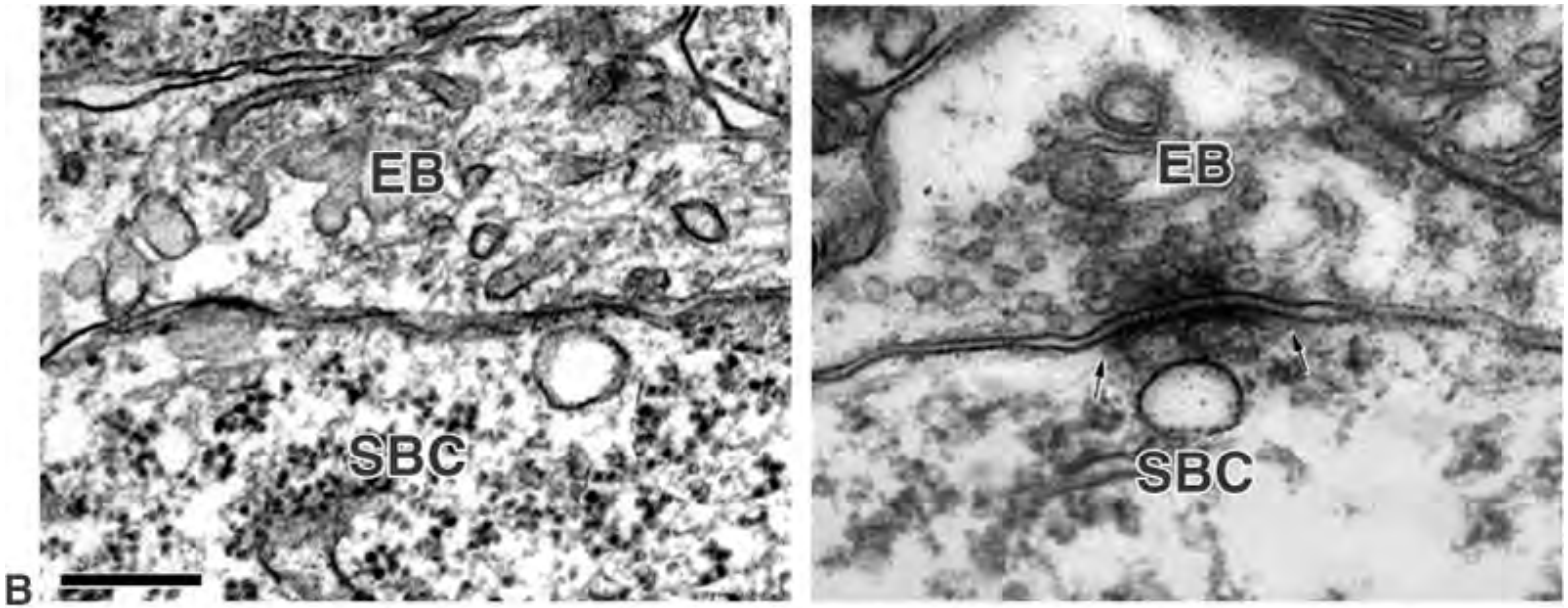


Figure 8.1 Reticular versus neuron theory. Over a century ago, the nervous sytem was thought to be a syncytium (left) of cells that were joined together by their processes. This arrangement would permit electrical activity to travel through the syncytium in either direction (thin and thick arrows) upon stimulation. As evidence mounted that neurons were separate cells (right), it was recognized that a chemical synapse (inset) would permit electrical activity to travel in only one direction (thin arrows).



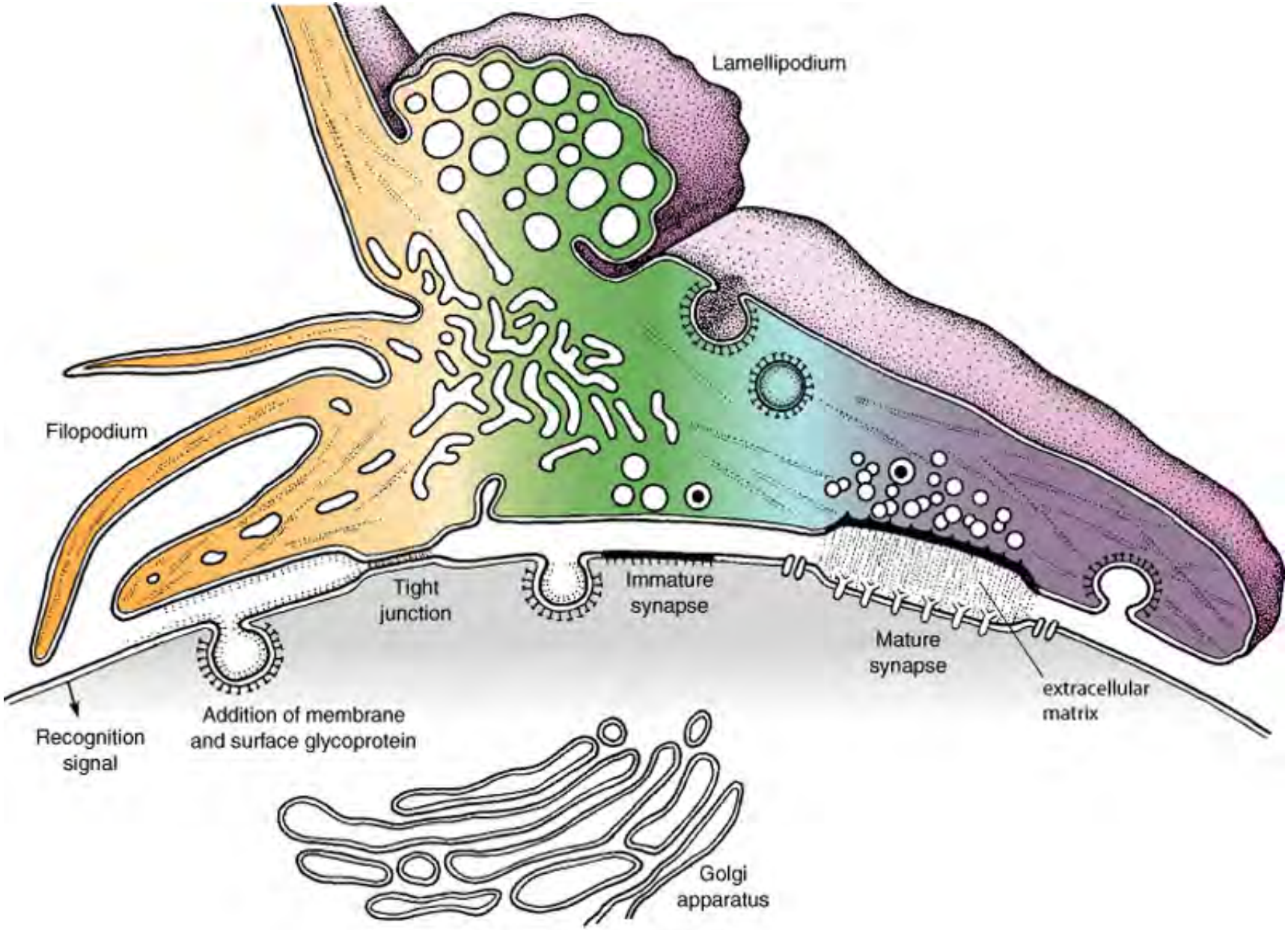
(Limb and Ryugo, 2000.)



(Limb and Ryugo, 2000.)

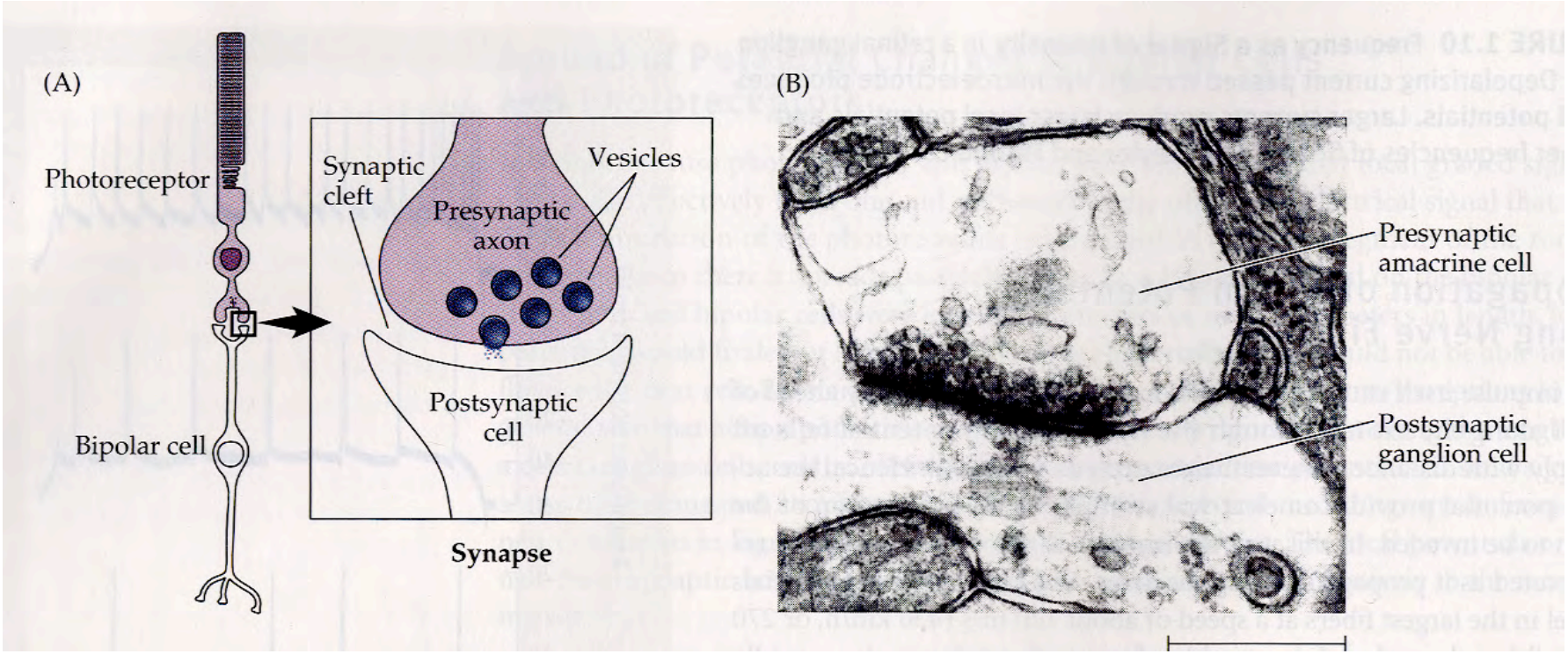
early in development

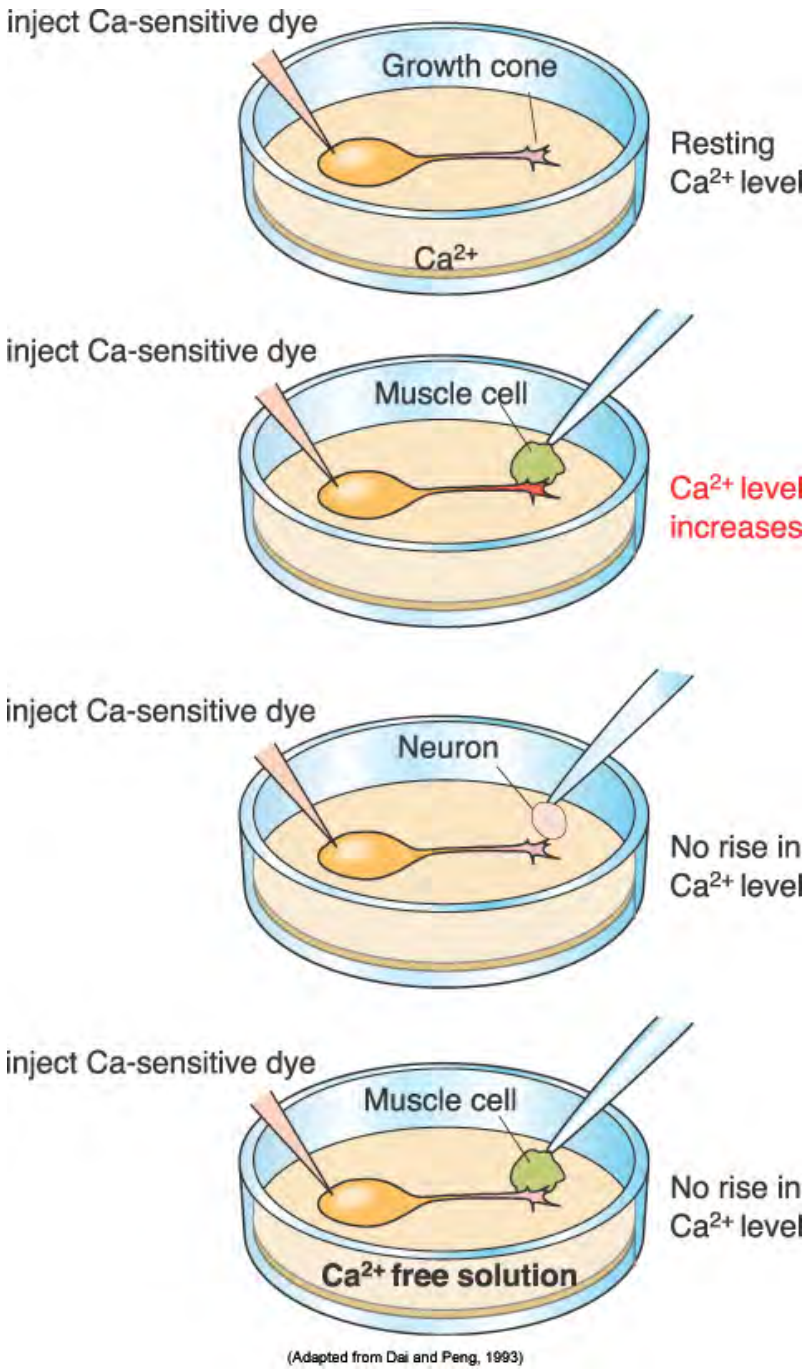
later in development



(Adapted from Rees, 1978)

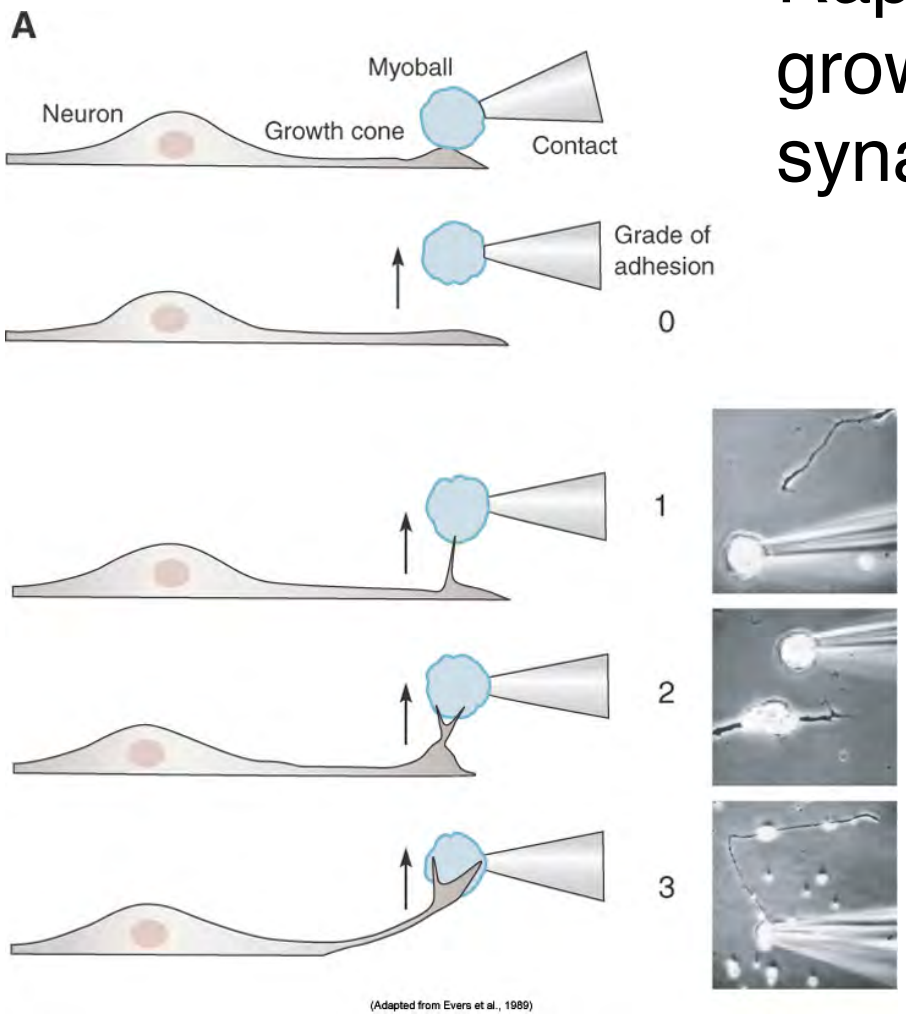
The synapse

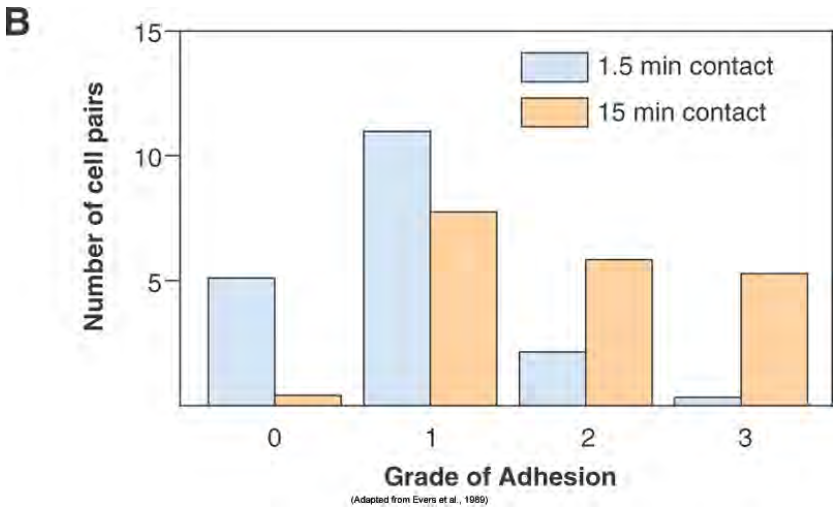

(A)
Photoreceptor
Bipolar cell
Synaptic cleft
Vesicles
Presynaptic axon
Postsynaptic cell
Synapse
(B)
Presynaptic amacrine cell
Postsynaptic ganglion cell

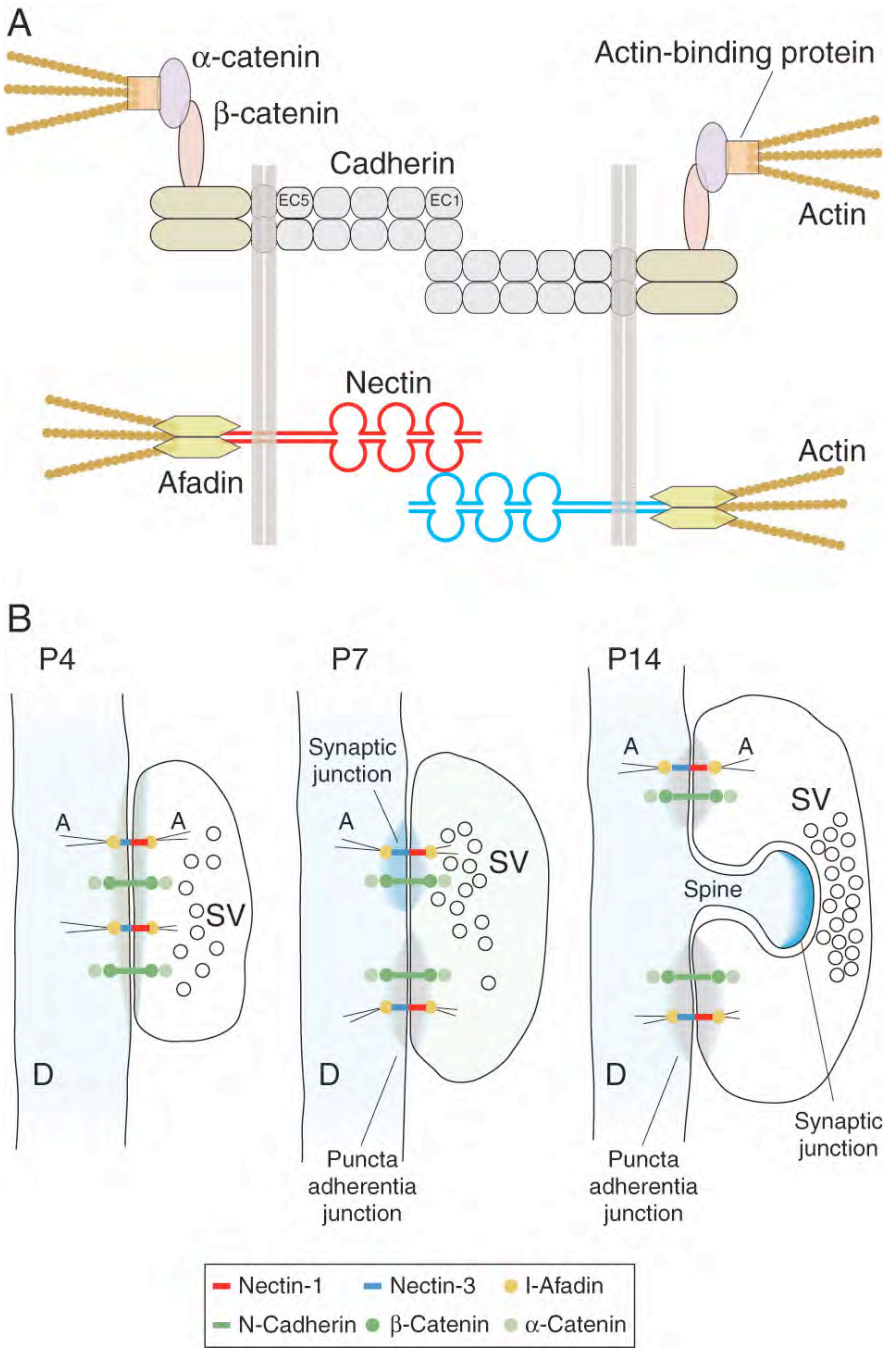


(Adapted from Dai and Peng, 1993)

Rapid adhesion between growth cone and post-synaptic muscle cell

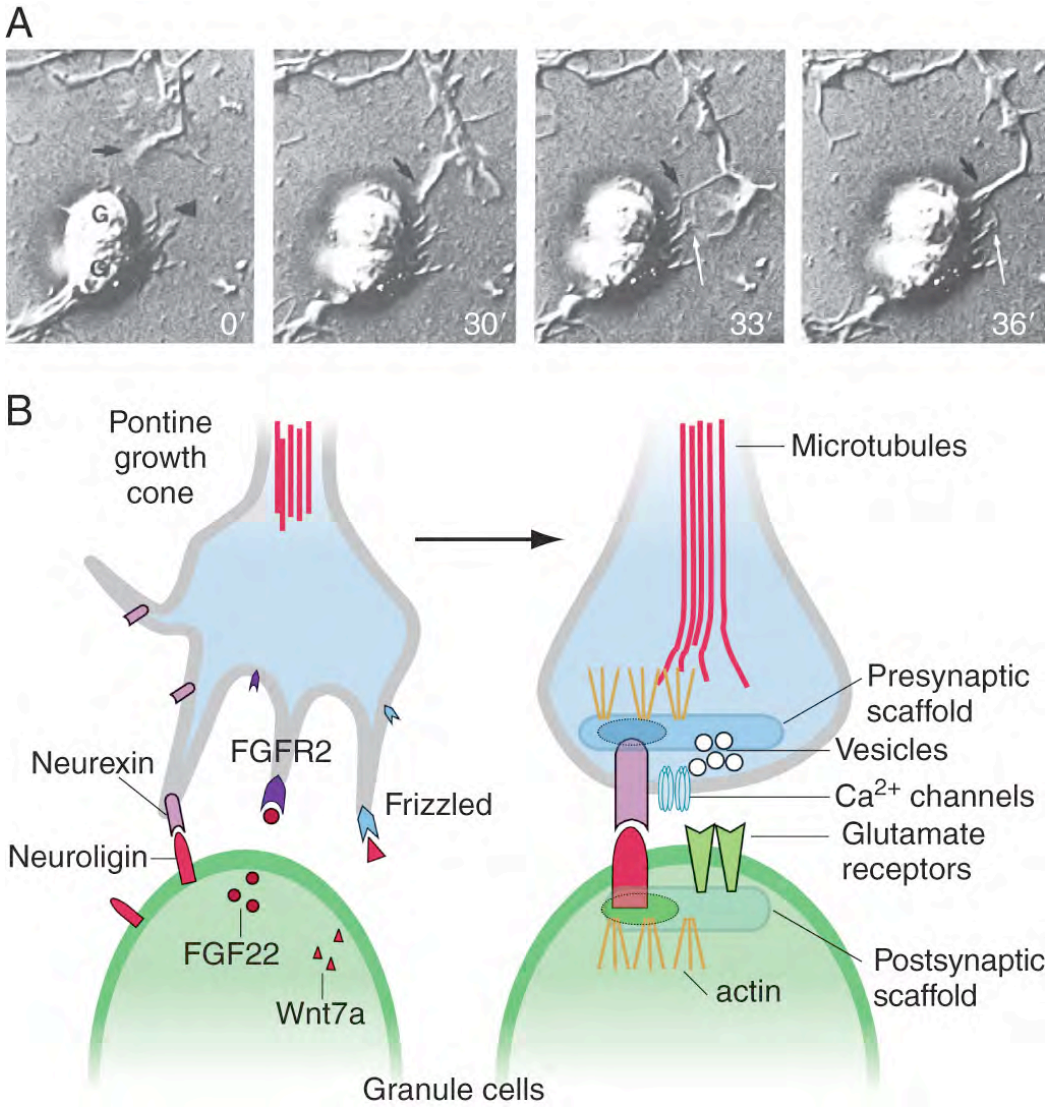


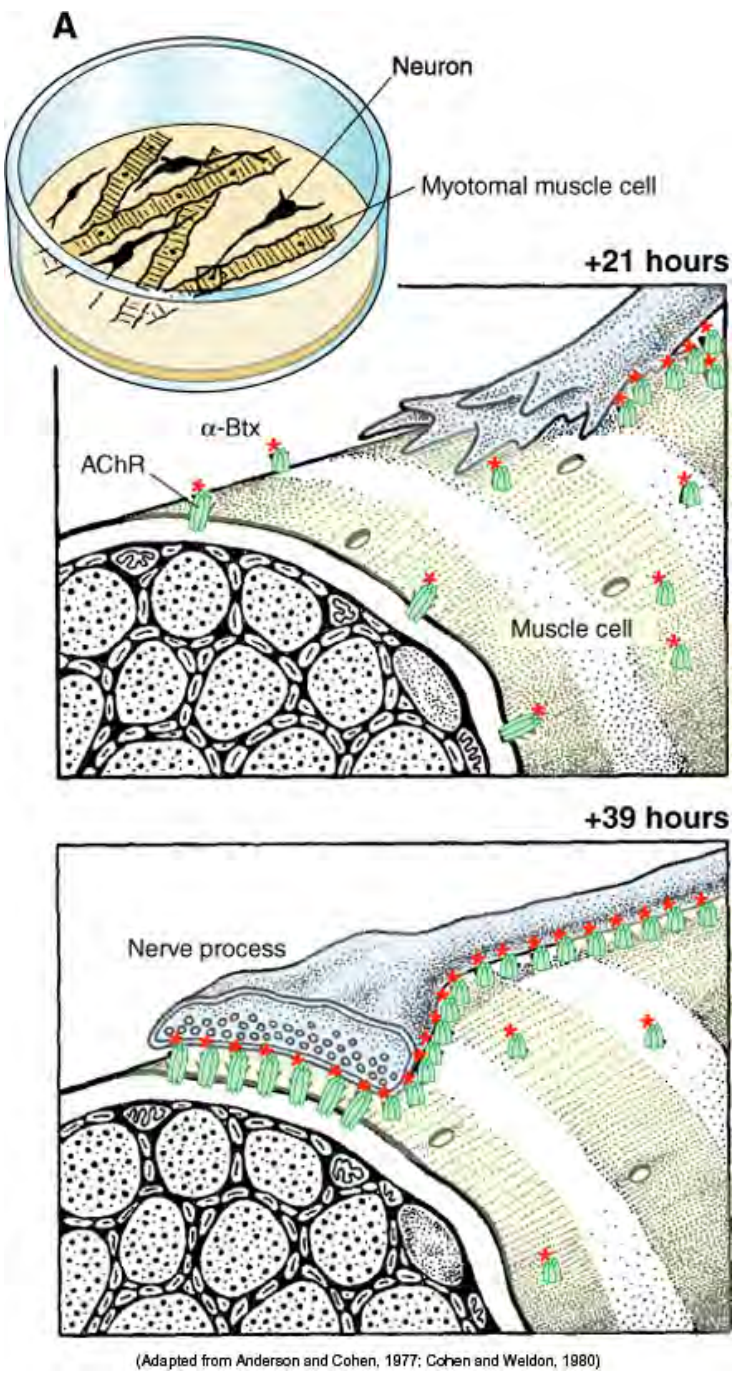




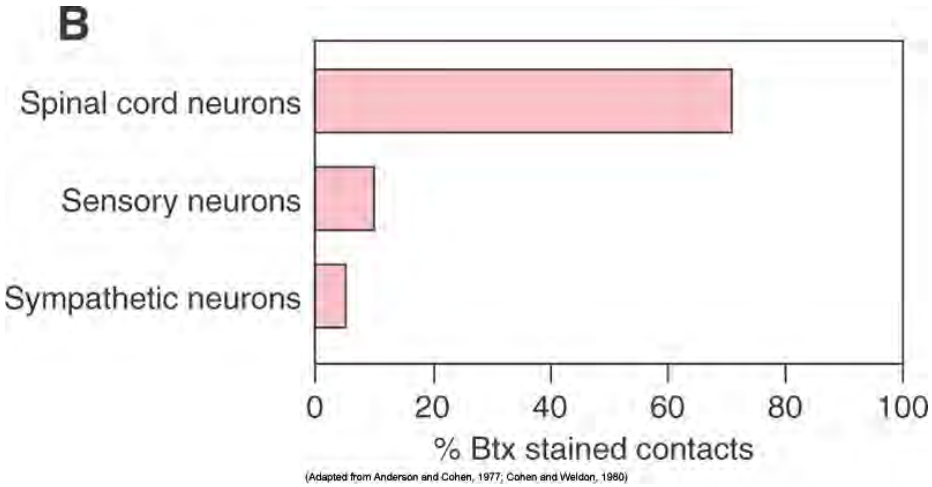
Cell adhesion molecules and synapse formation

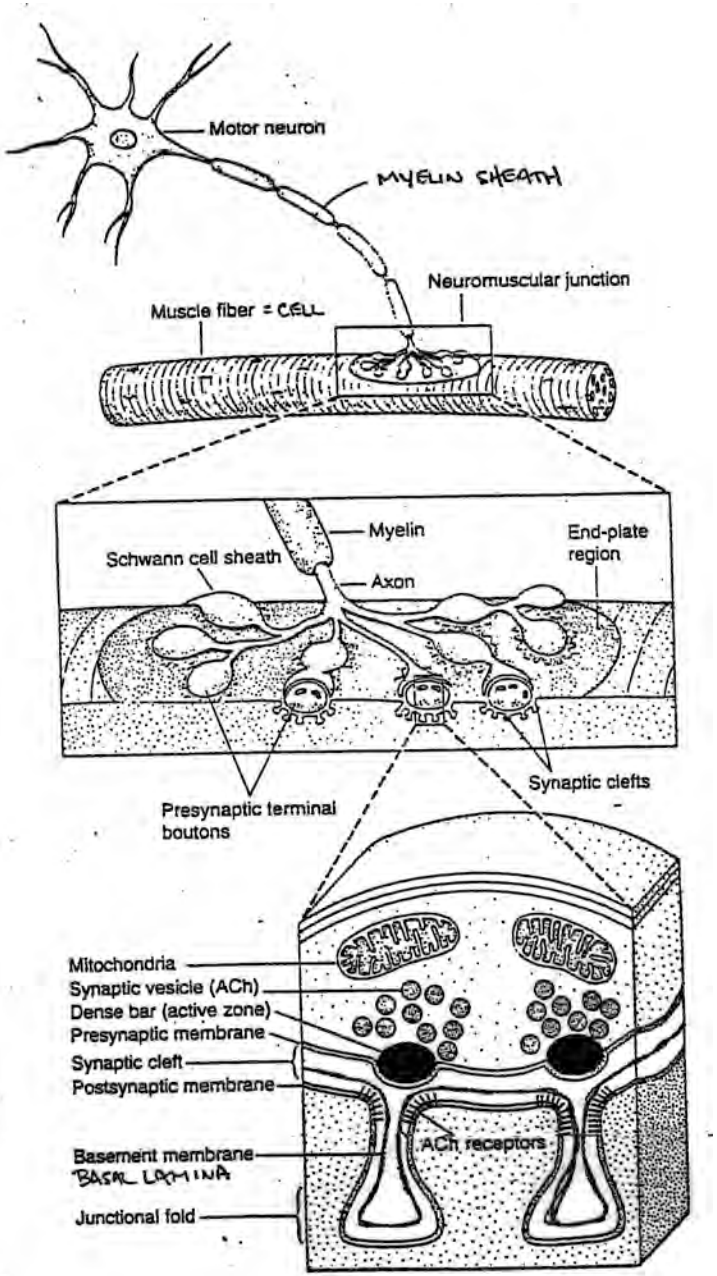
Signals that promote growth cone differentitation. A. Pontine growth cones (arrow) stop when they contact granule cell targets (arrowhead). B. receptors are Frizzled, FGFR2 and β-neurexin; ligands are Wnt-7a, FGF2 and Neuroligin-1. These pathways promote differentiation of the growth cone into a pre-synaptic terminal.





AChReceptor clustering on muscle fibers is induced by contact with spinal neurons. A: co-culture of neurons and muscle cells labelled with fluorescent α-btx at 21 or 39 hours. Soon after the spinal neurite/ growth cone grows across the muscle surface, fluorescent α-btx appears at the contact site, indicating that AChR aggregations is induced. B: cell type specificity



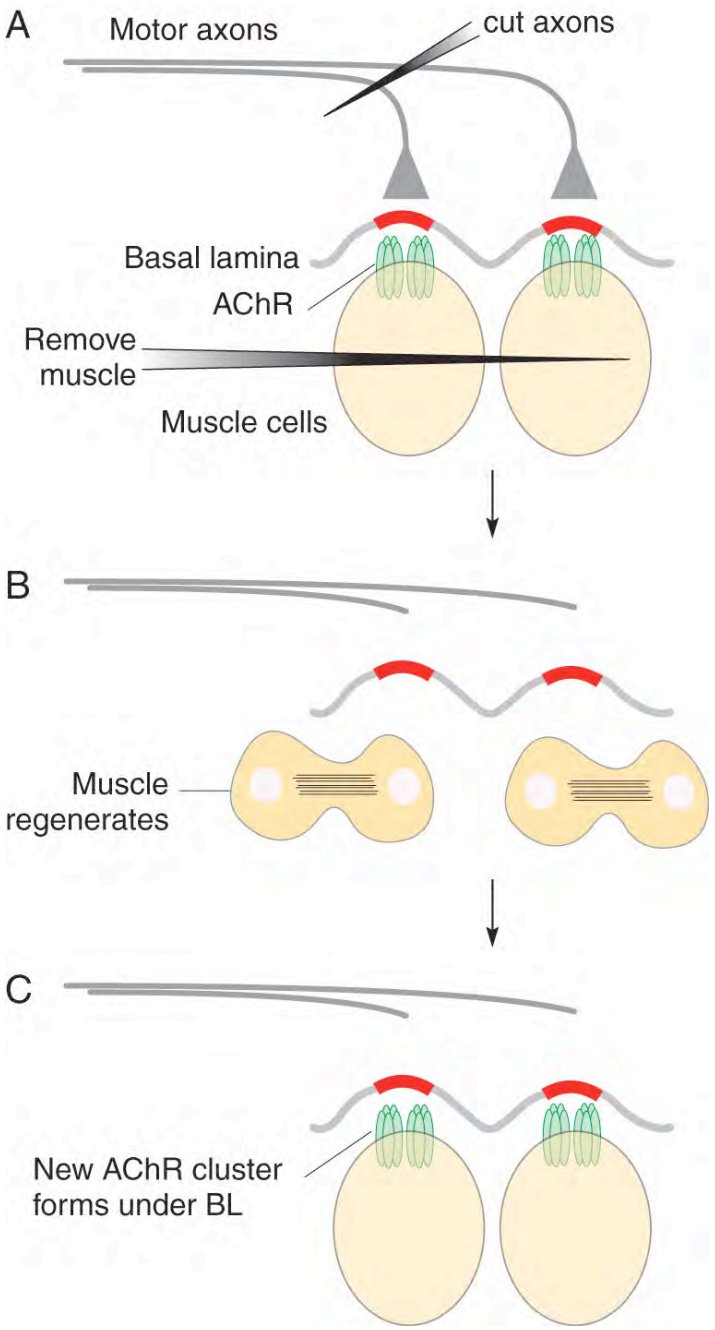


The mature neuromuscular junction

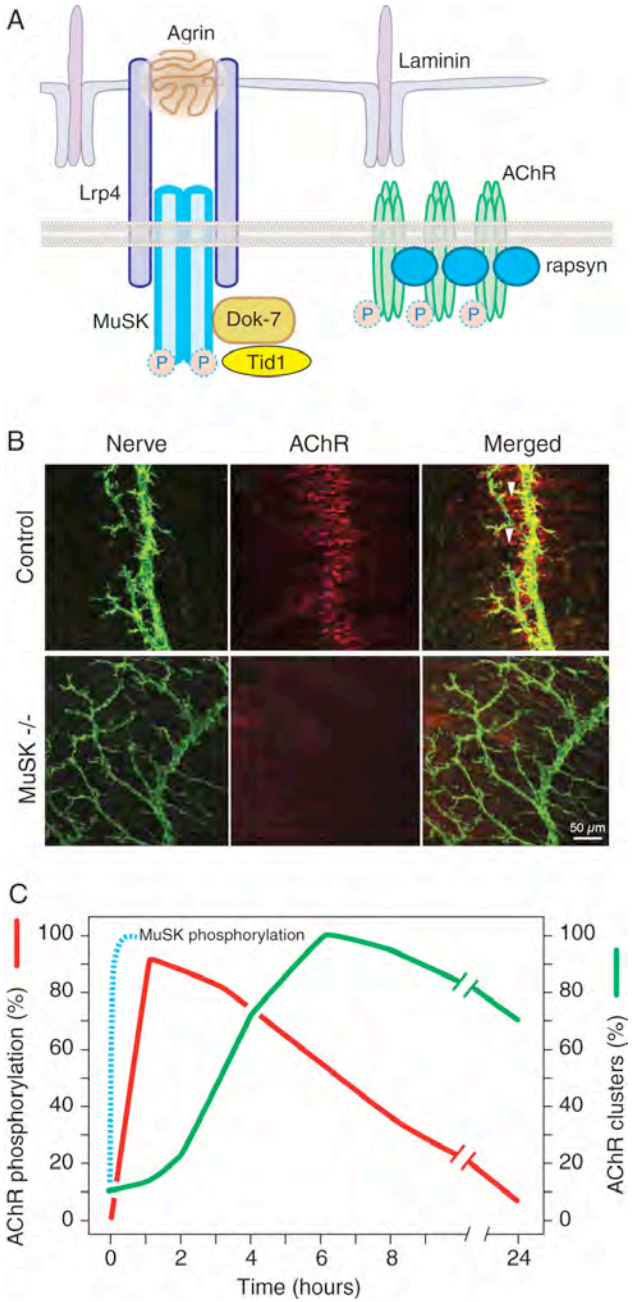
A. In adult from NMJ, the motor axons are cut and the muscle cells destroyed, leaving only the basal lamina (aka, ECM).
B. New myofibers are generated as a result of new cell division.
C. AChR clusters form on the regenerated muscle fibers, directly beneath the synaptic portion of the basal lamina.

Converse experiment also works:

A. Cut neurons and destroy muscle cells, leaving basal lamina
B. X-ray muscle cells so that they can not divide
C. Neurons re-grow and set up pre-synaptic cells at same locations as before.

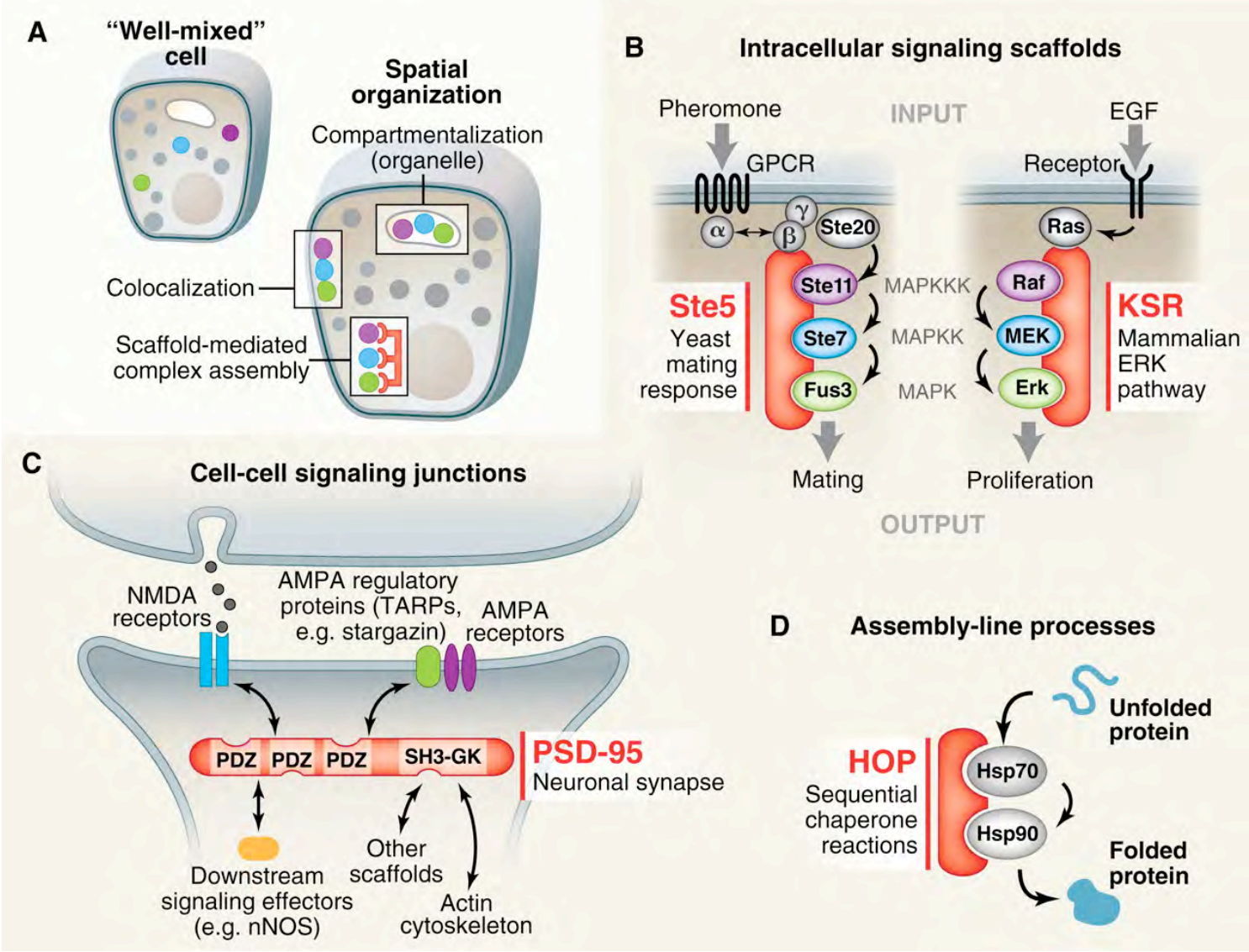


MuSK Gene Knockout (MuSK -/-)



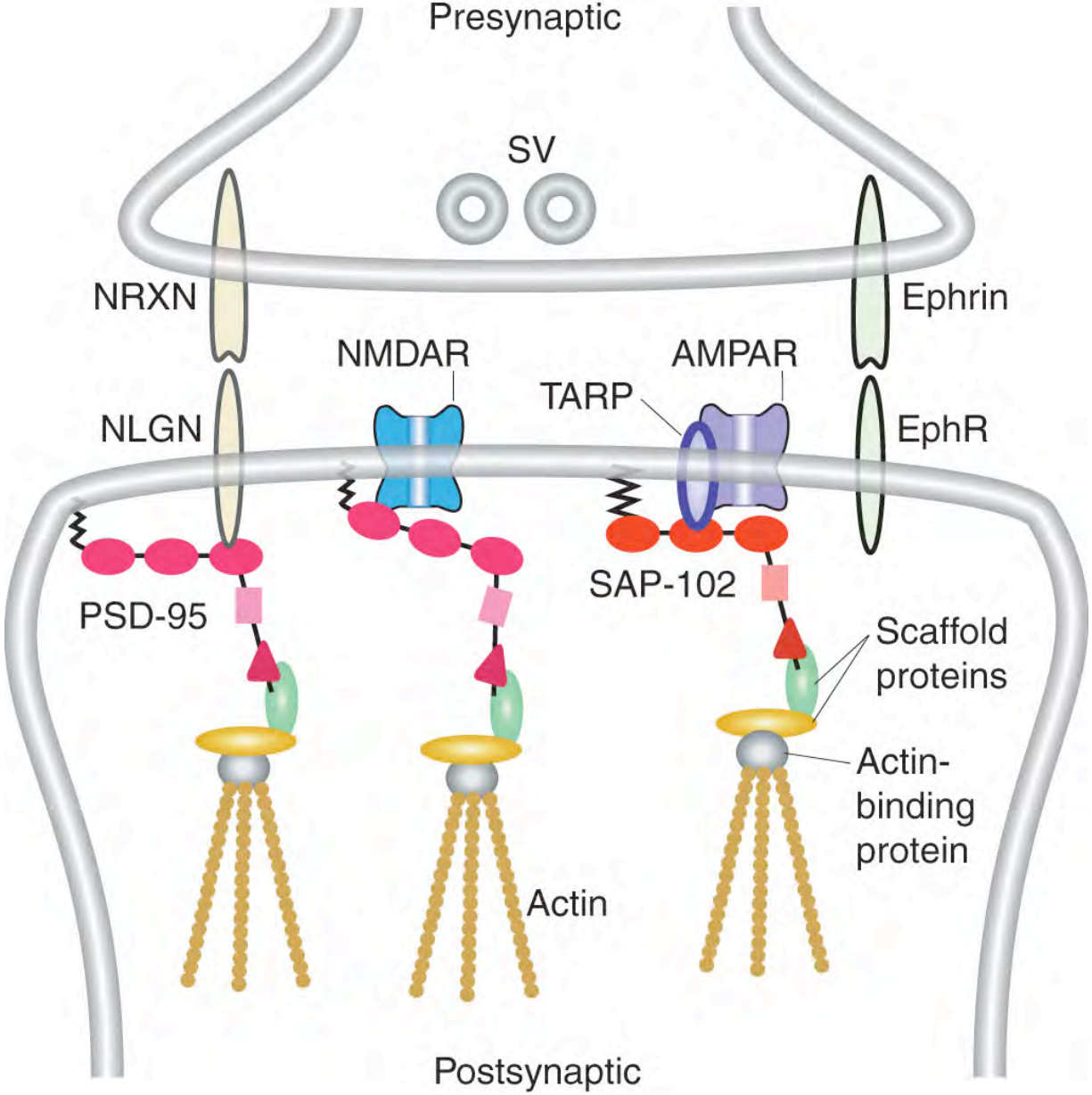
No ACh receptor clustering

Fig. 1 Scaffold proteins organize cellular information flow.

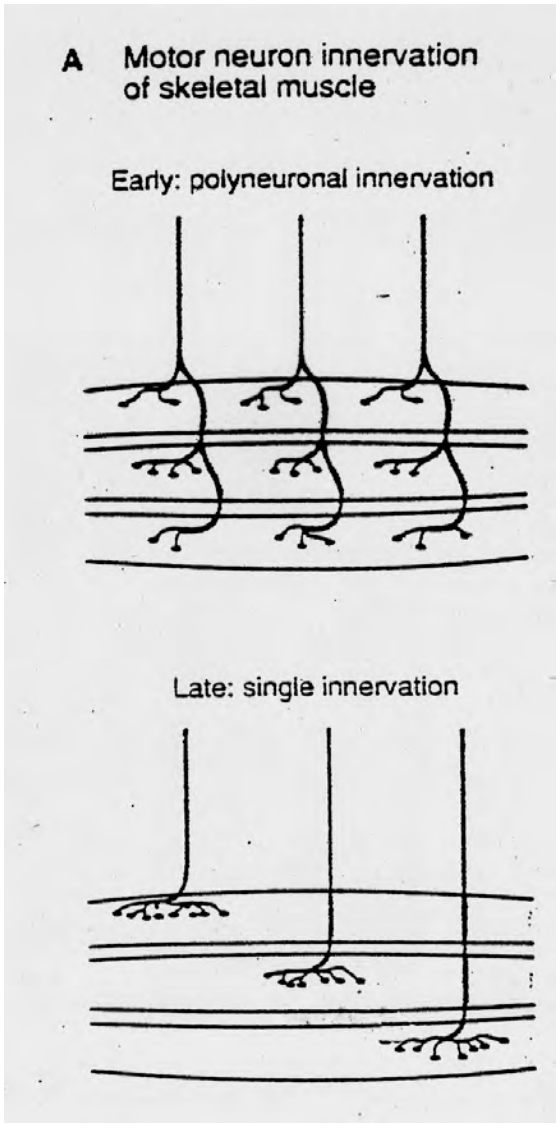


M C Good et al. Science 2011;332:680-686

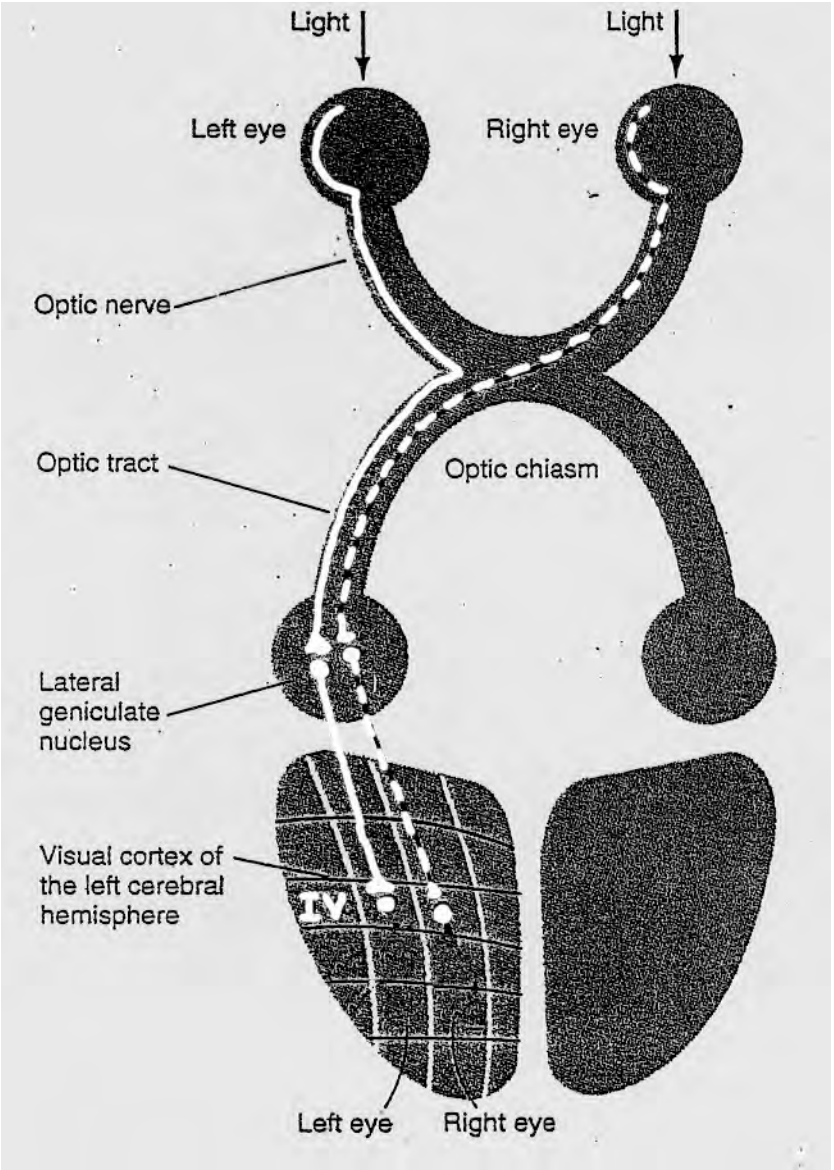
Post-synaptic scaffold of glutaminergic synapses



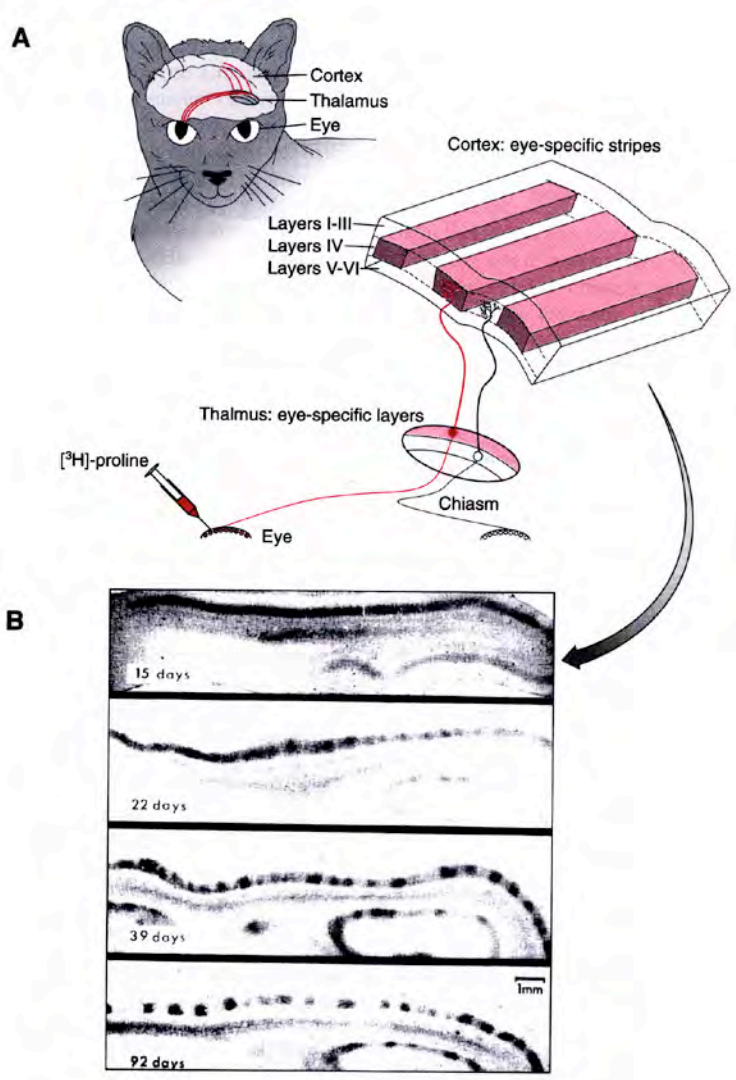
Motor neuronal innervation of muscle fibers; An example of synapse elimination and fine tuning



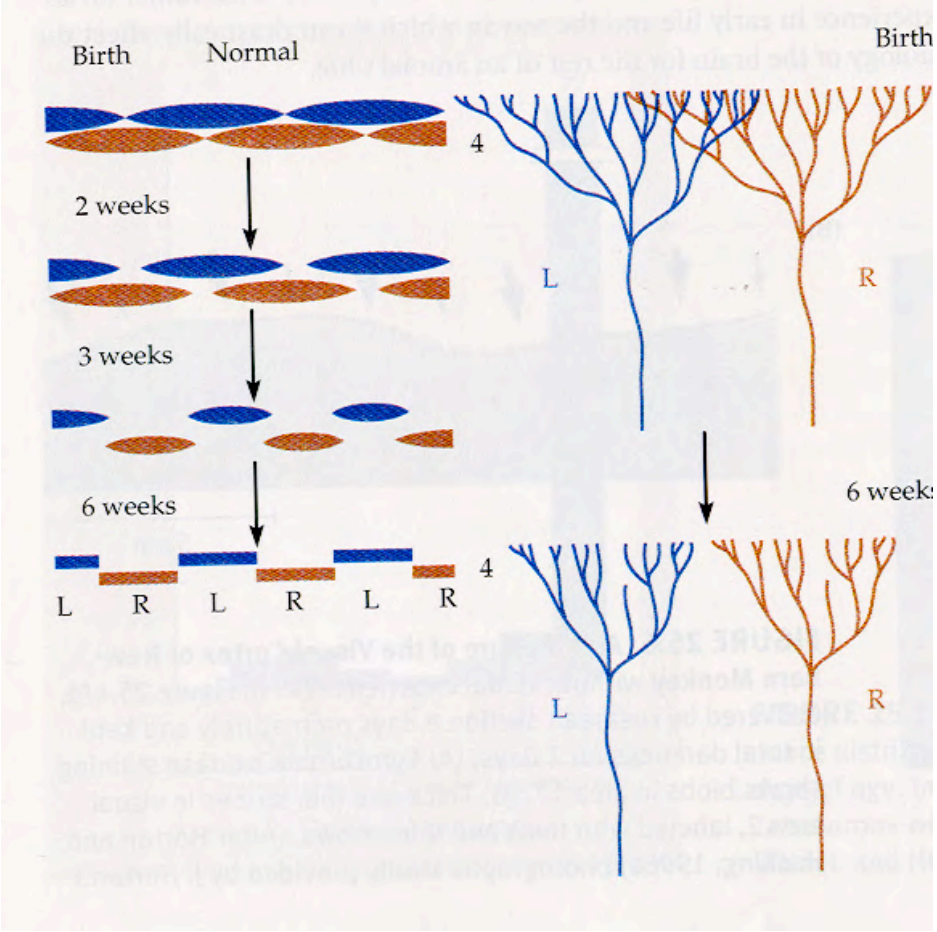
Visual system organization (mammals)

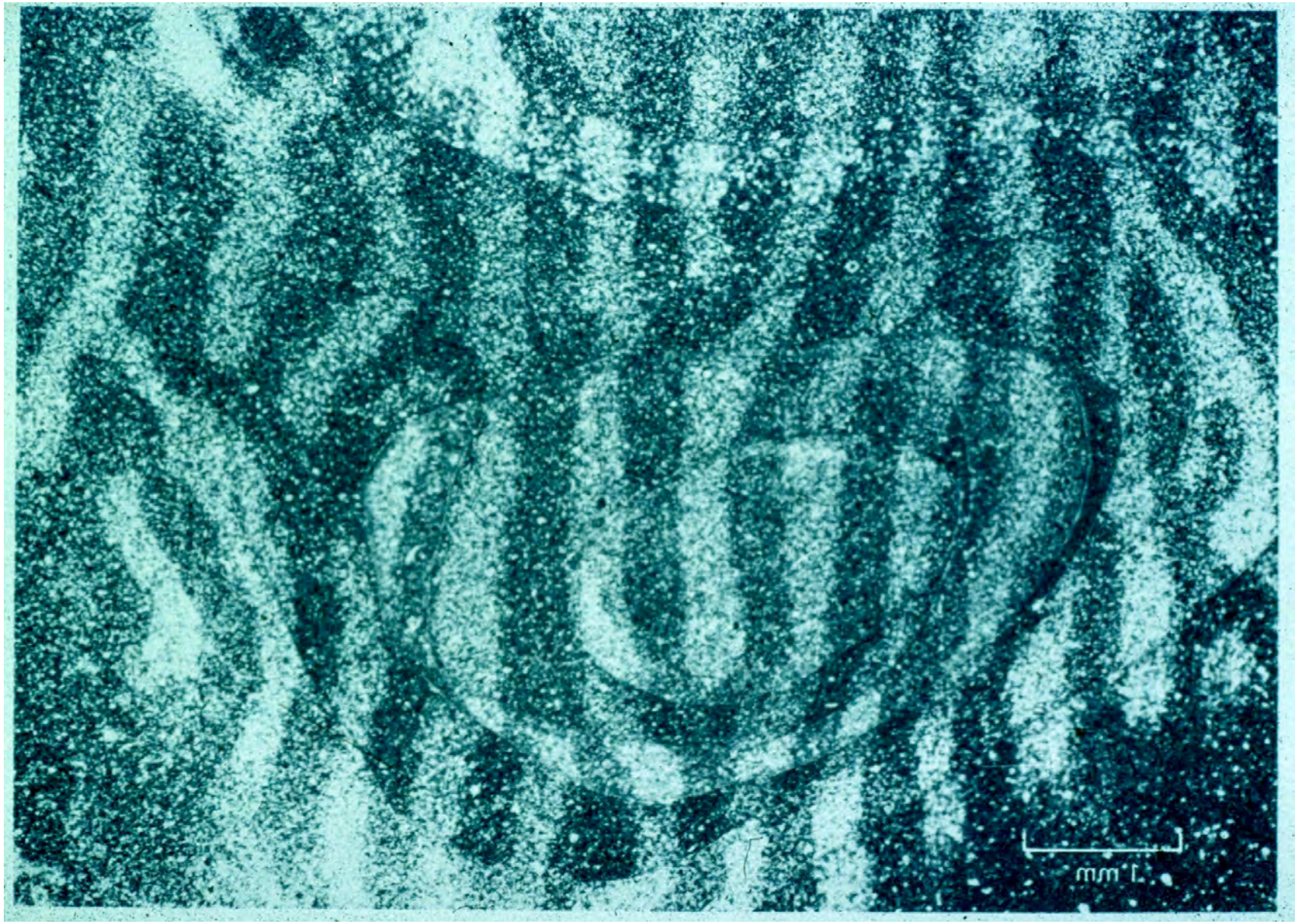


Occular dominance columns can be visualized using radioactivity

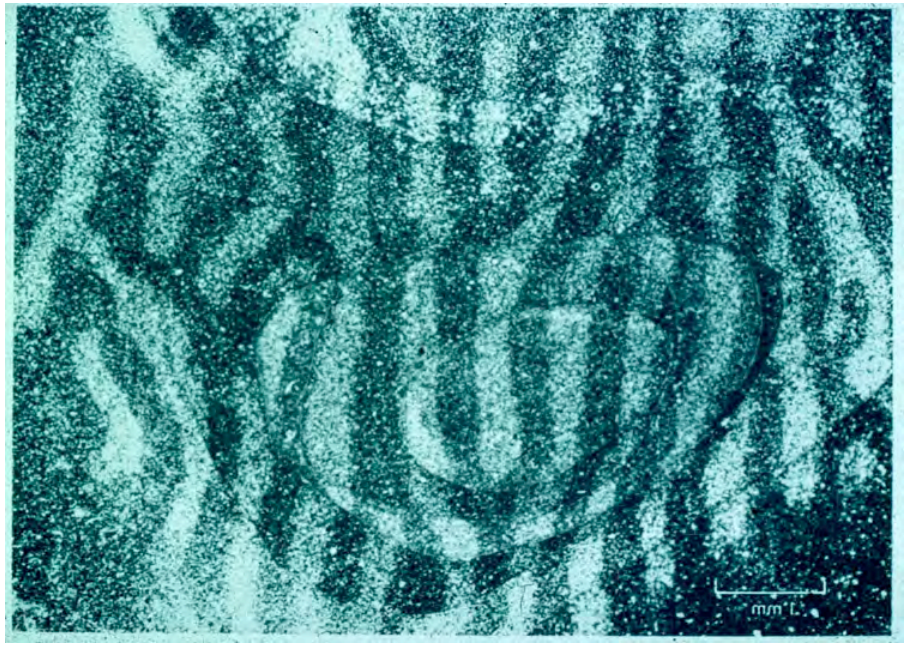


Formation of Occular Dominance Columns

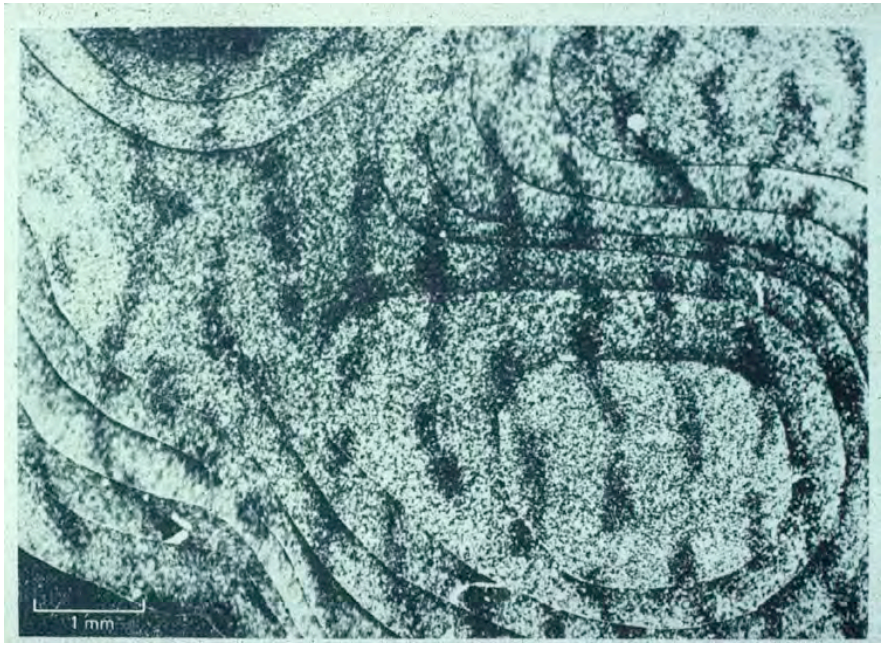



1 mm

Monocular input deprivation



Normal



One-eye closed during development

Summary

1) Synaptogenesis exhibits cell type specificity
2) Pre- and post-synaptic cells release proteins that influence synapse formation (ex. Agrin)
3) Activity of a neuron is involved in synapse refinement/elimination
    -active synapses are strengthened/maintained
    -inactive synapses are weakened/eliminated

6) Competition between terminals determines organization
    -active neurons will occupy more space than inactive neurons
    -competition for neurotrophic factors??

Waltz through the neuropil; Kirsten Harris, University of Texas at Austin
http://www.youtube.com/watch?v=FZT6c0V8fW4