Neurons are translationally smart

Apparently, neurons, themselves the tools of learning, smartly synthesize proteins where they are needed. Two recent publications demonstrate that neurons are capable of localized translation in dendrites and in axons.

The first article, by Linnea Ostroff, Kristen Harris, and colleagues (Boston University, Boston, MA), demonstrates that polyribosomes get redistributed to dendritic spines during long-term potentiation (LTP). LTP enhances synaptic responses and is currently thought to promote forms of learning and memory. Although the first phase of LTP is translation independent, sustained LTP is known to require new protein synthesis.

Harris’s results indicate that the newly made proteins may not have to travel far. Using Star Wars-quality three-dimensional reconstructions of serial sections of neuronal tissue, the authors showed that synapse-containing dendritic protrusions known as spines accumulated polyribosomes when given an LTP-inducing stimulus. This gain was accompanied by a loss of polyribosomes in the nearby main body of the dendrite.

Larger synapses were found on the spines that had gained polyribosomes, indicating that increased local protein synthesis enhances synaptic activity. “The next phase is unraveling which proteins are synthesized there,” says Harris. Candidates include scaffolding proteins, which could stabilize the synapse-enhancing glutamate receptors inserted into the plasma membrane during the translation-independent phase of LTP.

In the second paper, axons were also shown to have translation ability. Perry Brittis, Qiang Lu, and John Flanagan (Harvard Medical School, Boston, MA) isolated axons and growth cones and found these were able not only to translate RNAs that they were fed, but also to transport the newly synthesized proteins to the cell surface. Their results also showed that axons were capable of localized translational up-regulation of receptor mRNAs, possibly to change responsiveness to guidance cues during pathfinding.

References:
Ostroff, L.E., et al. 2002. Neuron. 35:535–545.
Brittis, P.A., et al. 2002. Cell. 110:223–235.

Lipids tell channel to open wide

Structural studies of a bacterial ion channel in a new article by Eduardo Perozo (University of Virginia, Charlottesville, VA), Boris Martinac (University of Western Australia, Crawley, Australia), and colleagues reveal how the channel senses when to open through interactions with membrane lipids.

Mechanosensitive channels, such as bacterial MscL studied by Perozo, open when the pressure inside a cell increases, thus allowing the passage of ions and other solutes. MscL needs only a lipid environment to respond to pressure, indicating that interactions between lipids and channel proteins are sufficient to regulate channel structure.

The new study reveals that a change in intramembrane pressure rather than membrane thinning is the key determinant for channel opening.

As tension grows in the cell, the bilayer thins, possibly exposing hydrophobic amino acids of the channel to the aqueous environment. Perozo et al. mimicked this effect using lipids of various acyl chain lengths. Shorter chains (i.e., thinner membranes) primed the channel for opening by smaller pressures, but did not open the channel.

Increasing pressure within the cell may also place more pressure on the outer head-groups of membrane lipids and less pressure in the acyl chain regions. Sure enough, the channel did open upon mixing cone-shaped lipids into the bilayer, which should mimic the effect of pressurized cytosol on lipid heads.

Another paper, by Monica Betanzos, Shergei Sukharev (University of Maryland, College Park, MD), and colleagues, examined how the proteins of the channel rearrange upon opening. Each of the four subunits of one MscL channel contains two transmembrane (TM) domains, TM1 lining the pore and TM2 on the periphery. Sukharev’s group found that the TM domains together tilt outward in response to osmotic shock, widening the pore like the opening of an iris. This model is consistent with that recently demonstrated in a second paper by Perozo and colleagues.

References: Perozo, E., et al. 2002. Nat. Struct. Biol. 10.1038/nsb827.
Betanzos, M., et al. 2002. Nat. Struct. Biol. 10.1038/nsb828.
Perozo, E., et al. 2002 Nature. 10.1038/nature00992.