Sights on cone geometry

Rather than merely point-to-point dispatches, synaptic messengers also make wide-spread broadcasts, as evidenced by Steven DeVries, Wei Li, and Shannon Saszik (Northwestern University, Chicago, IL). Messages are received both near and far, they show, to create transient and sustained responses.

The cone presynaptic terminal is highly invaginated, with ribbons of glutamate-containing vesicles above each invagination. Cones respond to changes in light with graded changes in membrane potential. Decreases in light intensity depolarize cones and increase glutamate release, which then activates a class of cells known as Off bipolar cells.

In the new report, DeVries et al. show that Off bipolar cell dendrites contact cone terminals at two sites. Most subtypes of Off bipolar cells contact the base of the cone terminal, ~300 nm away from the vesicle fusion sites. The group found, however, that one Off cell subtype extended its dendrites up into each invagination to end close to fusion sites.

These contacts within invaginations experienced large, rapid fluctuations in glutamate levels when a cone was depolarized. Glutamate then spilled out of the invaginations to the basal contacts. In spite of their distance from release sites, even a single vesicle’s worth of glutamate was able to reach and activate these cells. Distance exacted a toll, however, as the glutamate concentrations sensed by these cells fluctuated more slowly and at much lower levels.

The invaginating cell senses glutamate via AMPA receptors, which recover rapidly from glutamate-induced desensitization and can thus decode rapid consecutive pulses. Basal cells instead use kainate receptors, which have much slower recovery times and produce responses that average over rapid fluctuations in glutamate concentration. The basally located Off bipolar cells thus generate more sustained responses.

The steady signal conveys the basic sight information of change magnitude and duration. The transient signal saying just that there was a change “is probably very important,” says DeVries, “because it can help an animal avoid predators or moving objects.”

Reference: DeVries, S.H., et al. 2006. Neuron. 50:735–748.

Alien sensing by GC content

A bacterial protein silences foreign DNA by recognizing low GC content, as shown by William Navarre, Ferric Fang (University of Washington, Seattle, WA), and colleagues. The silencing might allow the cell to experiment evolutionarily with intruding DNA.

The silencing protein is a Salmonella histone-like protein called H-NS. The group was searching for direct targets of this known repressor when they noticed that the H-NS binding sites were GC poor (~47%) compared with the rest of the chromosome (~52%). A GC-poor foreign gene that the group recombined into Salmonella was also repressed by H-NS.

Most bacteriophage and other bacteria are lower in GC content than Salmonella and its relatives, so invading DNA is an obvious target for H-NS. “It’s like a primitive immune system,” says Fang. “Reduce their expression, and the foreign genes can be tolerated.”

Useful newcomers might eventually be expressed, however, via mutations that increase their GC content or through the evolution of antisilencers. Many of Salmonella’s foreigner-derived virulence genes, for instance, are shut off by HNS but can be reactivated when needed by a transcription factor called SlyA.

Bacteriophage, of course, also evolved means to get around this defense system. Some encode their own HNS antagonists, whereas others maintain GC-neutral genomes.

Other GC-rich bacteria have related DNA-binding proteins that are possible analogues of H-NS. Bugs with AT-rich genomes might in turn have GC-binding repressors. If universal, this immune strategy would explain why each bacterial species maintains its distinctive GC/AT ratio.

H-NS seems to recognize short stretches of DNA, although how the protein reads GC content within just a couple hundred base pairs is not clear. Perhaps it recognizes the intrinsically curved or partially melted structure of AT-rich sequences.

Others have found that tandemly bound copies of H-NS form multimers. This probably blocks transcription by compacting the DNA in that vicinity. By locking many helical turns in place, it would also restrict changes in DNA superhelicity, thus explaining the known repressive effect H-NS has on heat- and salt-induced responses.

Reference: Navarre, W.W., et al. 2006. Science. doi:10.1126/science.1128794.