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Mechanisms of Axonal Gradient Detection

(NINDS R01-NS046059 FY 02)

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The goal of this project was to develop a mechanistic understanding of axonal behavior in gradients of guidance factors by building computational models of gradient detection and directed movement for axons, directly constrained by data from a novel quantitative chemotaxis assay. This assay allows relatively stable molecular gradients of precisely controlled shape to be established in a collagen gel. Using this approach we have shown that axons can detect a concentration of only about 1 molecule across their spatial extent, making them some of the most sensitive devices for detecting gradients yet known. Our modeling work has shown that the inevitable stochastic noise in the receptor binding process can be overcome by spatial and temporal averaging of receptor binding. I will review these results and describe our current efforts to directly measure the dynamics of extending growth cones through live cell imaging in collagen gels. Our preliminary results show that the morphology and dynamics of the growth cone in a three-dimensional environment is dramatically different than the same cell type growing on a flat, stiff surface.

Publications

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2. Goodhill, G.J., Gu, M. & Urbach, J.S. (2004). Predicting axonal response to molecular gradients with a computational model of filopodial dynamics. Neural Computation, 16, 2221-2243.

3. Rosoff, W.J, McAllister, R.G., Esrick, M.A., Goodhill, G.J. & Urbach, J.S. (2004). Generating controlled molecular gradients in 3D gels. Biotechnology and Bioengineering 91, 754-9. (2005).

4. Xu, J., Rosoff, W.J., Urbach, J,S. & Goodhill, G.J. (2005). Adaptation is not required to explain the long-term response of axons to molecular gradients. Development 132, 4545-52 (2005).