

Clearly the precise role of the parahippocampal gyrus in navigation is still unclear. We also still have much to learn about how it interacts with the hippocampus, thought to be the storehouse of the flexible 'cognitive map' of the large-scale spaces that we frequent<sup>14</sup>. The current study suggests a plausible basis on which we might start to reconsider that relationship. It may be that navigation, ubiquitous and of high survival value, is subserved by an efficient and coop-

erative brain system in which the parahippocampal gyrus selects information that maximally benefits the functioning of the hippocampus.

1. Burgess, N. *et al. Neuron* **35**, 625–641 (2002).
2. Aguirre, G.K. & D'Esposito, M. *Brain* **122**, 1613–1628 (1999).
3. Maguire, E.A. *et al. J. Cogn. Neurosci.* **10**, 61–76 (1998).
4. Aguirre, G.K. *et al. Cereb. Cortex.* **6**, 823–829 (1996).
5. Kohler, S. *et al. Hippocampus* **12**, 718–723 (2002).
6. Bar, M. & Aminoff, E. *Neuron* **38**, 347–358 (2003).
7. Epstein, R. & Kanwisher, N. *Nature* **392**, 598–601 (1998).
8. Blades, M. & Medlicott, L. *J. Environ. Psychol.* **12**, 175–185 (1992).
9. Janzen, G. & van Turenout, M. *Nat. Neurosci.* **7**, 676–680 (2004).
10. Dolan, R.J. & Vuilleumier, P. *Ann. NY Acad. Sci.* **985**, 348–355 (2003).
11. Passoa, L. & Ungerleider, L.G. *Prog. Brain Res.* **144**, 171–182 (2004).
12. Squire, L.R. *Psychol. Rev.* **99**, 195–231 (1992).
13. Hartley, T. *et al. Neuron* **37**, 877–888 (2003).
14. O'Keefe, J. & Nadel, L. *The Hippocampus as a Cognitive Map* (Oxford Univ. Press, New York, 1978).

## Assaying axon sensitivity

Molecular gradients are thought to guide axons to their proper targets. However, to properly understand both the function of graded axon guidance cues *in vivo*, as well as their downstream signaling mechanisms, we need to know just how sensitive axons are to these gradient cues. Better still, to study this guidance precisely, we also need to be able to quantitatively control molecular gradients. Now, on pages 678–682, Geoffrey Goodhill and colleagues report a new technique that allows for the efficient generation of precise and reproducible gradients of diffusible molecules. They use this technique to show that growth cones of developing axons are capable of detecting a concentration difference as small as about one molecule across their spatial extent, but that this sensitivity exists only across a small range of ligand concentrations.

The authors established molecular gradients by 'printing' drops of solution onto the surface of a thin collagen gel. Based on the mechanics of diffusion, the shape and steepness of the gradient can be controlled, and the actual concentration gradients produced by this method can be measured quantitatively with fluorescence imaging. Their gradient generation method allows for the generation of large numbers of identical gradients that require only limited quantities of chemotropic molecules. Moreover, the gradients were stable for at least a day after generation. This technique could also be used to generate gradients of multiple factors with different shapes and arbitrary spatial relationships.

The authors then used this technique to study the response of rat dorsal root ganglion axons by culturing explants (see image) in a three-dimensional collagen gel with an exponential concentration gradient of nerve growth factor. They found that developing axons are more sensitive to guidance factors than previously thought, and that a concentration difference as small as 0.1% across the growth cone can direct neurite outgrowth, making neuronal growth cones among the most sensitive concentration-sensing devices known. The paper provides a powerful new technology that can be applied to quantitative studies of other biological processes controlled by molecular gradients, such as cell migration. It may also be useful for designing guidance factor-based therapies for axonal regeneration following injury.

This paper also inaugurates the Technical Report format for *Nature Neuroscience*. This new section is meant for primary reports of new techniques that are likely to be influential in neuroscience research. These reports are formatted like Articles, but do not require a new biological discovery to prove the usefulness of the technique, and they are reviewed primarily on the strength of the method and its broad applicability.

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