Abstract

Brain functioning relies on the formation of specific connections that are established by a precisely guided axonal extension. A great effort in the past decades has led to the identification of “guidance” molecules critical for directing axons to their targets, which include netrins, slits, semaphorins, ephrins and neurotrophins. These molecules are acting at short-range by contact-mediated interactions or at long-range by diffusible gradient-mediated mechanisms. More recently it has been shown that combinations of two or more of these molecules can yield directional effects that none of them has alone. But how neurons convert combinations of guidance cues into a reproducible connectivity remains an exciting open question. Emerging technologies such as protein micro-patterning and microfluidics provide a unique advantage to address this challenge in an in-vitro context. Indeed, engineered microenvironment can now be tailored to investigate the response of growing axons to highly detailed spatial and temporal distributions of molecules with a high throughput approach. In collaboration with Sonia Garel (IBENS, Paris), we propose to use state of the art multi-protein patterning method that we have recently developed, in order to study the response of thalamic and hippocampal axons to combinations of gradients of multiple guidance cues such as slits or netrins. The combinatorial effect of this cues will be tested both as surface bound and diffusible signals. We will challenge our findings by performing ex vivo and in vivo experiments on various (slit, netrin-1) mutant mice. Together, these experiments will provide major and novel information on how axons integrate spatial information during brain wiring.

Qualification required

Cell biology, neuroscience (cell culture, dissection)
Optical Microscopy
For this interdisciplinary project, a taste for instrumentation is required
Computer science (instrument control, programming)