MOTOR SYSTEMS

Predict and control

According to work by Flanagan *et al.*, described in *Current Biology*, we learn to predict the consequences of our actions before we learn to control them — under certain circumstances, at least. These experimental results were predicted by several recent theoretical models of motor learning, and should help us to understand more about motor learning and motor control.

Motor control can be considered in two parts: control, or the process of generating motor commands to produce a desired outcome; and prediction, which is the internal generation of expected sensory consequences from a set of motor commands. Flanagan and colleagues used a task in which subjects had to manipulate an object along a straight line, while the load on the object was varied during the trial. Over repeated trials, the subjects learned to compensate for the load so that they could produce a straight trajectory.

To compare prediction with control, the authors looked at two measures of performance. The hand trajectory was used to measure how quickly subjects learned to control the movement, whereas prediction was measured by looking at changes in grip force. In early trials, grip force was changed reflexively as the hand path (and therefore the load force) was perturbed, but subjects quickly learned to alter their grip force predictively. By contrast, it took many trials for them to learn to control the load.

Recent theoretical models of motor control have included separate components for prediction and control, and some have proposed that the 'predictor' is used to train the 'controller'. The experimental finding that subjects learn to predict the behaviour of a manipulated object before they learn to control it is consistent with this idea.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Flanagan, J. R. *et al.* Prediction precedes control in motor learning. *Curr. Biol.* **13**, 146–150 (2003)

WEB SITES

Flanagan laboratory: http://pavlov.psyc.queensu.ca/~flanagan/cal/index.html

Wolpert laboratory: http://hera.ucl.ac.uk/

NEUROTECHNIQUES

Quantum leap for quantum dots

Quantum dots (QDs) are nanoparticles of one semiconductor surrounded by a second semiconductor. There has been considerable interest in their use as inorganic fluorophores, owing to the fact that they offer significant advantages over conventionally used fluorescent markers. For example, QDs have fairly broad excitation spectra — from ultraviolet to red — that can be tuned depending on their size and composition. At the same time, QDs have narrow emission spectra, making it possible to resolve the emissions of different nanoparticles simultaneously and with minimal overlap. Last, QDs are highly resistant to degradation, and their fluorescence is remarkably stable.

But despite their promise, the feasibility of using QDs in biological preparations has been questioned. If the semiconductors are not perfectly coated, the fluorescent signal is quenched, making it imperative to develop appropriate coats for QDs. It is also necessary to establish ways for QDs to interact specifically with the biomolecule of interest and to reduce nonspecific binding. Last, to be used *in vivo*, QDs should not be toxic or interfere with cellular function. Two recent papers in *Nature Biotechnology* give a strong push to the use of QDs as tools for cellular imaging by reporting ways to circumvent these problems.

In the first paper, Wu *et al.* coated QDs with a polyacrylate cap and covalently linked them to antibodies or to streptavidin. They then used these nanoparticles to label surface, cytoskeletal and nuclear proteins in fixed cells and tissue sections. Labelling was highly specific, and was brighter and more stable than that of other fluorescent markers. Moreover, they simultaneously used two QDs of different emission spectra and managed to detect two different targets with a single excitation wavelength.

Wu *et al.* also succeeded in labelling live cells with their QDs, but in the second paper, Jaiswal *et al.* provide compelling evidence for the use of QDs *in vivo*. They coated the nanoparticles with dihydrolipoic acid, and electrostatically conjugated them to avidin or to antibodies through an intermediate, positively charged protein. The authors allowed cells to incorporate the QDs by endocytosis and followed their fate for more than a week. The cells continued to grow, differentiate and respond to cellular signals in a normal way. Similarly, the label was stable throughout the experiment and there was minimal nonspecific binding. Last, Jaiswal *et al.* also used QDs with different emission properties to show the feasibility of simultaneously detecting more than one fluorophore.

As the use of quantum dots is still in its early days, these two papers and their demonstration that QDs are viable imaging tools should stimulate their use in neurobiology, a field in which their potential has not begun to be explored yet.

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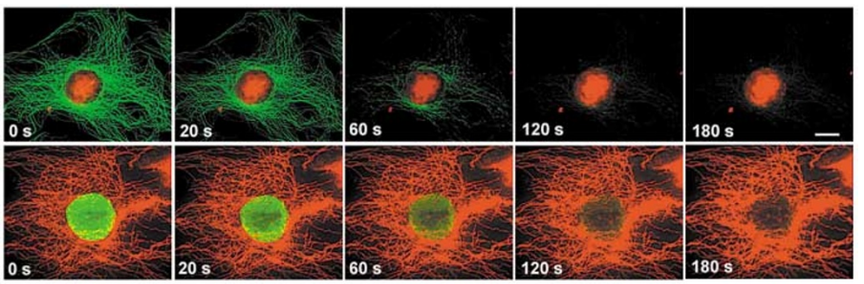
References and links

ORIGINAL RESEARCH PAPERS Wu, X. *et al.* Immunofluorescent labeling of cancer marker Her2 and other cellular targets with semiconductor quantum dots. *Nature Biotechnol.* **21**, 41–46 (2003) | Jaiswal, J. K. *et al.* Long-term multiple color imaging of live cells using quantum dot bioconjugates. *Nature Biotechnol.* **21**, 47–51 (2003)

FURTHER READING Jovin, T. M. Quantum dots finally come of age. *Nature Biotechnol.* **21**, 32–33 (2003)



In the top row, nuclear antigens and microtubules were labelled with QDs and the fluorescent dye Alexa 488, respectively. The bottom row shows the reverse combination. Continuous illumination for three minutes caused the Alexa signal to fade completely, whereas QDs remained stable. Reproduced, with permission, from Wu *et al.*, *Nature Biotechnology* © (2003) Macmillan Magazines Ltd.