SPECTROSCOPY

Proteins: caught in the trap

Two independent groups have recently devised innovative methods using light to trap and manipulate particles as small as proteins.

Though it may conjure up a vision from 'Star Trek' of the Enterprise caught in a larger ship's 'tractor beam', since the mid-1980s scientists have harnessed beams of light to trap and transport small biological particles such as cells and viruses, a technology known as optical tweezers.

But trapping smaller particles such as a protein or strand of DNA is notoriously more difficult because trapping energy scales with particle volume. Consequently, very high-powered lasers are required to manipulate small particles because optical tweezers cannot transport objects smaller than the wavelength of light. Small particles can be attached to larger handles, such as a bead, to facilitate transportation, but this limits the technique's practical use.

Recently, two independent groups devised alternative methods to trap biomolecules. David Klenerman and colleagues at the University of Cambridge describe resonance optical trapping of fluorophore-labeled antibodies (Li *et al.*, 2006), and Dean Hafeman of Protein Discovery, Inc. and his colleagues at Oak Ridge National Laboratory and California Institute of Technology demonstrate protein transportation via a process called photoelectrophoretic localization and transport (PELT; Hafeman *et al.*, 2006).

Fluorescence bursts are recorded as fluorophore-labeled single molecules pass through a focused laser beam under conditions of resonance excitation. While using this technique, Klenerman and his colleagues noticed that DNA labeled with a fluorophore lingered slightly longer in the laser beam than unlabeled DNA. They hypothesized and confirmed that labeling with multiple fluorophores increased the trapping time. "Unlike normal optical trapping where the particle is excited off-resonance, we excite the fluorophores at resonance so as to get a much larger response from the incident light, and hence observe some biomolecules to be trapped at much lower laser power," explains Klenerman.

The method has potential to be used for sorting single biomolecules, analogous to flow cytometry for cell sorting. "Fluorescence is widely used as a detection method; if you could sort the molecules you can produce a pure concentrated population of molecules of interest, and then use the enriched sample in further experiments," suggests Klenerman. However, unavoidable fluorophore photobleaching could ultimately limit the practical application of this technology.

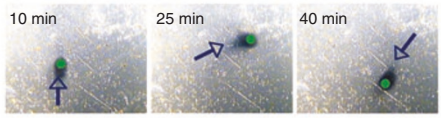

Figure 1 | PELT-mediated protein transportation over 40 min. A 1-mW 543 nm helium-neon laser beam (position shown as a green dot) was used to steer a mixture of 7 stained proteins. Copyright 2006 National Academy of Sciences, U.S.A.

In a very different methodological approach, Hafeman and his colleagues created electrical-field molecular traps by shining light onto a photoconductive semiconductor surface. "Wherever you shine the light is where you will get a current," explains Hafeman. "Like a black hole, it sucks in the charged molecules that are nearby." They used PELT to demonstrate that aliquots of proteins could be steered (**Fig. 1**) or even divided by using multiple light beams.

Hafeman foresees important future practical applications of the technology. "It is a rapid and easy method to focus proteins to a small spot," he says. "The main application that we are working on as a company right now is to use mass spectrometry for proteomics studies." They envision that the technique could be instrumental in generating a highly sensitive technology for biomarker discovery.

Though much further work is needed before either technology will be incorporated into a useful tool for biologists, it just goes to show that sometimes science fiction has some basis in reality.

Allison Doerr

RESEARCH PAPERS

Li, H. *et al.* Evidence for resonance optical trapping of individual fluorophore-labeled antibodies using single molecule fluorescence spectroscopy. *J. Am. Chem. Soc.* **128**, 5711–5717 (2006).

Hafeman, D.G. *et al.* Optically directed molecular transport and 3D isoelectric positioning of amphoteric biomolecules. *Proc. Natl. Acad. Sci. USA* **103**, 6436–6441 (2006).