to the base types. Hence, the sequence of colours observed in real-time identifies the DNA sequence. The team reported sequencing at a rate of approximately three bases per second per molecule (that is, per zero-mode waveguide).

To increase the sequencing speed, the researchers simply run the process in parallel, simultaneously observing activity in 3,000 zero-mode waveguides. Each waveguide effectively acts as a tiny processor sequencing pieces of DNA.

To be practical, the approach requires a convenient scheme to illuminate all the waveguides simultaneously. The researchers use a holographic optical element, a confocal pinhole array and a dispersive optical component. This approach allows acquisition of spectroscopic information from each of the sample locations in real time[5].

The data from each of the waveguides are assembled into complete sequences. As with any 'shotgun' technique, in which random smaller pieces of a larger DNA puzzle are pieced together, some over-sequencing is required to ensure satisfactory overlap for accurate assembly. However, according to Turner, the long read lengths of the technique here will not only increase speed, but also accuracy. "The puzzle pieces will be larger, so you have an easier job putting it together. The bigger the pieces are, the more likely you are to get it right", he told *Nature Photonics.*

Whereas the recently reported work involved 3,000 waveguides, the level of multiplexing in a commercial device — expected to be ready in 2010 — is likely to be much greater. "Although the exact number of waveguides in the final design is not yet known, the instrument we ship in 2010 will have a much higher multiplex than the experimental platform used in the *Science* paper. We are pushing the limits on every aspect," Turner said.

According to Turner there were many challenges in moving from the earlier zero-mode waveguide work on single-molecule dynamics[3] to actual DNA sequencing. He said that the multidisiciplinary nature of what they were doing required the coming together of researchers from a wide range of fields. These included surface chemists, optical engineers, protein engineers, computer scientists, physicists, electrical engineers and nanotechnologists, who all speak different scientific languages.

According to Pacific Biosciences' website, the ultimate goal of the company is "to translate nature's ability to replicate an entire genome in under an hour to an instrument that will sequence a human genome in minutes for under a hundred dollars". Such a level of performance doesn't seem out of the question given the scalability of the optical multiplexing technique. ❐

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OPTOFLUIDS

# Arbitrary flow

The idea of using laser beams as 'optical tweezers' to pick up and move solid microparticles is well known, especially in the fields of physics and biology, but researchers have now shown that laser beams can direct and control the flow of fluids as well.

A team of researchers from Ludwig-Maximilians University Munich in Germany has recently reported optically driven fluid flow along user-defined paths as narrow as 2 μm in a film of water (*J. Appl. Phys.* **104,** 104701; 2008).

Dieter Braun and Franz Weinert used an infrared laser scanning microscope to trace a light path over a film of water. The laser beam locally heats the water reducing its viscosity. When combined, the effects of thermal expansion and a viscosity gradient cause the water to flow along the light path in the opposing direction to that of the moving focal spot.

Put simply, the laser beam creates a moving hot spot around 10 K higher in temperature than its surroundings. Near the laser spot, in the region of increasing temperature, the fluid expands; in the cooling volume already passed by the laser beam, the fluid contracts. If nothing else enters into the equation, the expansion and contraction are equal and opposite — no net flow results. However, as the viscosity of the fluid (water in this case) is temperature-dependent, this process can become asymmetric resulting in a net fluid flow.

An advantage of the laser-induced fluid flow is that it negates the need for physical, micromachined channels, enabling the prospect of user-defined channels that can be reconfigured and could transport nanoparticles and dissolved molecules.

To investigate the process, Braun and Weinert used 20 nm fluorescent beads that were guided by the flow on a millimetre length scale without significant diffusion into the surrounding fluid. The researchers also show mixing of 'DNA hairpins' in dynamically created gel pockets, demonstrating controlled molecule mixing capabilities.

The fluid velocities of 150 μm $s^{-1}$ achieved are an order of magnitude slower than those possible using conventional microfluidics; however, the optically driven technique used here removes the need for bulky, physical connections and external pumps. Although the team shows the effect in two-dimensional fluids, the researchers noted that the method — a valveless, contactless and pumpless one — could be applied to three-dimensional fluids in the future.

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