Therefore, a sensitive and high-throughput measure of viral latency is clearly needed.

Third, how much of the viral reservoir might be eliminated by HDAC inhibition? In the current study, the cells isolated from 5 of the 16 tested subjects failed to show any response to vorinostat and therefore these patients were not eligible for the clinical trial. Although those who eventually received the drug exhibited an increase in HIV RNA production, the overall clinical effect was probably marginal, as the concentration of viral particles in plasma did not increase and there was no apparent decrease in the size of the HIV reservoir.

Fourth, which assays will we use in the future to screen potential drug candidates for anti-latency activity? Vorinostat has demonstrated activity in most tests[5,6], but not all[7]. Finally, what is the fate of the virus-producing cells after HDAC inhibition? Although many investigators have assumed that either the virus or the host immune system would destroy such cells and would therefore clear the virus, recent data suggest that this might not be true[8]. If the ultimate goal is to shock and kill infected cells, then more work is needed on how to eliminate them[9,10].

Despite these uncertainties, the importance of Archin and colleagues' study cannot be overstated, as it provides a rationale for an entirely new approach to the management of HIV infection. In many ways, their results are comparable to the initial finding that the anti-HIV drug zidovudine (also known as AZT) reduced viral replication in people. Even though zidovudine proved to have limited benefit on its own, the result showed that HIV could be inhibited, and the drug eventually became the basis for the first generation of drug combination regimens. I hope that HDAC inhibitors could ultimately become part of a combination approach to curing HIV infection. ■

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MATERIALS SCIENCE

The abilities of instabilities

A method has been developed for preparing a variety of potentially useful spherical particles, ranging from several nanometres to millimetres in diameter. It relies on the same fluid instability that causes taps to drip. **SEE LETTER P.463**

ALI PASSIAN & THOMAS THUNDAT

Despite the many advantages offered by nanoparticles as materials for a wide variety of applications, their use is currently limited by the lack of scalable, high-throughput techniques for synthesizing multifunctional particles of uniform size. Nanoparticles that are made from multiple materials are especially interesting, because they have potential applications in many devices, such as biological and chemical sensors. On page 463 of this issue, Kaufman *et al.*[1] report a scalable fabrication technique that uses the dynamic instabilities of a fluid column to make particles of complex architecture*. Using this approach, they have prepared same-sized particles from combinations of vastly different materials, and with an unprecedented range of particle sizes.

Instabilities in fluid systems often produce undesirable effects — for example, standing up in a canoe can induce buoyancy instabilities that capsize the boat. However, instabilities can prove highly useful if they are harnessed properly, as Kaufman *et al.* demonstrate. Their fabrication technique depends on 'Plateau–Rayleigh instabilities' (PRIs), which are often manifested as remarkable flow patterns when a fluid is perturbed by heat.

Although the effects of PRIs can be quite subtle, these instabilities can grow exponentially, spatially and temporally modifying the motion or the flow pattern of a continuous body of fluid until it breaks up into 'pieces'. This is what happens when droplets form from dripping taps. The resulting fluid domains tend to form as spheres, as demonstrated in the microgravity environments of space laboratories[2]. When small sinusoidal perturbations are engendered along a fluid column composed of different liquids, the wavelengths and growth rates of the perturbations depend on the fluid viscosities and on the diameters of the participating fluid columns — an effect exploited by Kaufman *et al.* in their technique.

The authors' process for making particles begins with a 'preform' — a centimetre-scale rod in which a core of the materials to be made into particles is clad by a shell of scaffold material. This rod is heated and drawn into a fibre, until the diameter of the core matches the desired diameter of the particles. The fibre is then heated in such a way as to induce PRIs, which cause the core to split into spherical droplets (Fig. 1). These droplets are frozen *in situ*, forming particles encased within the scaffold material.

Microstructure-fabrication techniques in which PRIs break up multilayer, coaxial fluidic columns have been explored previously. For example, microspheres[3] have been prepared using a microfluidic device in which droplets of a gel flowing at the core of a column of oil are polymerized by exposure to ultraviolet light. A similar approach[4] has been used to fabricate microcapsules and strips of connected microcapsules. However, Kaufman and colleagues' method differs by virtue of having achieved PRIs in prefabricated core–shell fibres. Most impressively, their technique is scalable, allows a variety of particle morphologies to be made (including 'beach ball' particles that contain six segments made of alternating materials), and works for particle sizes ranging from 20 nanometres to 2 millimetres — a whopping five orders of magnitude.

Other methods for making particles — based either on chemical synthesis[5] or on physical methods such as laser ablation in liquids[6] — have been used to generate suspensions of a variety of highly pure nanoparticles. However, a great advantage of Kaufman and colleagues' technique is its ability to create multilayered nanoparticles.

Understanding and controlling fluid behaviour at a small scale is of tremendous technological importance. The Navier–Stokes equation is used to describe the motion of fluids, but this must often be modified to take into account the constraints of specific flow systems. For example, a study[7] of the de-wetting of thin polymer films has shown that thermal noise — random forces in a fluid caused by molecular motion that is induced by thermal agitation — can strongly influence the time- and length-scales of the films' flow. Given that Kaufman *et al.* use thermal perturbation as a means to induce instabilities, and that thermal noise increases with temperature, one would expect the break-up of the thin liquid columns in their technique to be influenced by such

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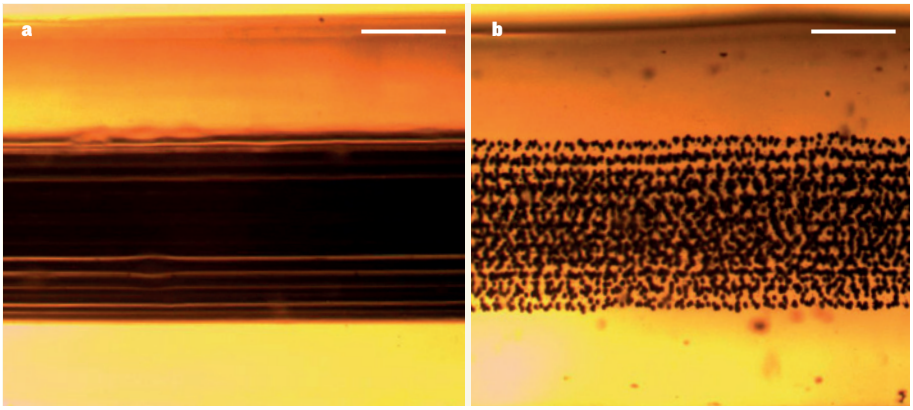

Figure 1 | An orderly break-up. Kaufman *et al.*[1] report a technique for making particles from fibres of material clad by a polymeric scaffold. **a**, In this image, black fibres of a glass (arsenic triselenide) are visible at the centre of an amber-coloured column of polymer (polyethersulphone). **b**, When heated in such a way as to generate fluid instabilities in the glass, the fibres break up into equally sized, spherical particles. Scale bar, 200 micrometres.

noise. The authors' theoretical description[1] of fluid flow in their system might therefore benefit from the inclusion of prevailing stochastic processes, as this would enable them to obtain better design parameters.

Furthermore, given that the surface tension of fluids generally decreases with increasing temperature, and that fluids move from regions of low surface tension to regions of high surface tension, it is worth considering whether the flow in Kaufman and colleagues' system receives additional contributions from temperature gradients generated in their experiments. Instabilities and flow systems driven by surface-tension gradients find applications in processes that involve the self-assembly of nanoparticles[8], and in the optical translation of droplets[9]. They also give rise to fascinating phenomena such as 'tears of wine' — the clear ring of liquid that forms on the inside of a filled wine glass above the drink, from which droplets constantly form and trickle back into the wine. In the case of PRIs, when a droplet breaks away from a column of fluid, the newly formed meniscus undergoes oscillations. This effect is important, for example in the operation of inkjet printers[10].

A potential limitation of Kaufman and colleagues' method is the nature of the materials that can be used in the nanoparticle fabrication. Chemically reactive and/or thermally incompatible materials (those that become incompatible when heated, for example because one of the materials degrades or changes its physical state) might not be able to sustain sufficient columnar or interfacial integrity for the PRIs to cause the desired break-up. This could also make it difficult to remove particles from the surrounding polymer, unless they can be dissolved in another chemical — although this runs the risk of the nanoparticle population being contaminated by chemical residues. Such contamination can affect the surface reactivity of nanoparticles, which, in turn, can adversely affect their functions in applications, for example when used in sensors.

Although not applicable to every material, Kaufman and colleagues' technique is ideal for making composite spherical particles from selected materials, such as the beach ball particles mentioned earlier. The authors also synthesized particles consisting of a core of one material covered with a shell of another, and 'Janus' particles, which have hemispheres made of different materials. Indeed, the authors' technique overcomes the limitations of present methods for making Janus particles, which modify only the particles' surfaces. Such particles are especially interesting because they can be used in sensors, actuators and energy-conversion devices, and as building blocks for self-assembling structures. The ability to make them reliably therefore opens up new vistas in the development of these applications. ■

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VISION

Looking to develop sight

Producing a single image from two eyes requires complex brain circuitry. A comparison of neural responses in babies shows that early visual stimulation following premature birth leads to accelerated development of the visual system.

EILEEN BIRCH

Our eyes look at the world from two different positions, yet we see one unified three-dimensional environment. The brain extracts information from the two-dimensional images formed on the two retinas by matching corresponding points, and then reconstructs the third dimension using residual disparities between the monocular images. When and how the brain develops the capacity for this complex binocular task has long been a focus of research for neuroscientists and vision researchers. Infants of both humans and non-human primates exhibit a sudden post-natal onset of binocular vision that corresponds to the start of the 'critical period', during which binocular function can be severely and permanently disrupted by abnormal visual experience. This maturational time course led to a consensus view that visual development during the pre-critical period is guided by genetically programmed molecular and neuronal signals, whereas environmental signals maintain and refine the neuronal circuitry for binocular vision during the critical period. Writing in *Proceedings of the National Academy of Sciences*, Jandó *et al.*[1] challenge this consensus and offer the first evidence in human infants that visual experience also guides development during the pre-critical period.

Interest in using visual-system development as a model for studying the role of experience in guiding brain development was stimulated by Hubel and Wiesel's elegant descriptions[2,3] in the early 1960s of the organization of neural circuits in the primary visual cortex — the first visual area of the cortex where information from the retinas is processed. A seminal contribution from these researchers was the identification of a feature of neural organization that is crucial for combining information

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