

margins achieved by snakes<sup>10</sup> and robots<sup>11</sup>, and is greater than the safety margins used by humans to grasp small objects<sup>12</sup>. Once stabilized on the perch, birds relax their grip, avoiding the unnecessary continued energy cost of muscle activation.

A limitation of Roderick and colleagues' work is that it did not investigate the role of the nervous system in controlling how gripping establishes a stable landing. The authors report superfast (1–2 milliseconds) initial anchoring movements of the claws, which suggests that these might be rapid, intrinsic, elastic mechanisms that do not involve neural control. However, these superfast movements are followed by longer-lasting adjustments in toe and claw movements that probably help to establish the stable grasp allowing birds to then relax their grip. These slower adjustments probably require proprioceptive feedback through the nervous system. Such feedback control could be evaluated by recording muscle activation and force patterns over the course of landing and perching. Inhibiting the activity of the

mechanosensory receptors in a bird's toe pads with an anaesthetic would offer a way to determine whether the loss of sensory feedback from toe pads affects these foot movements and the bird's landing ability.

The landing flights in this study were short and were made between perches on the same horizontal level. However, Pacific parrotlets probably fly to perches above or below the animal's current location when foraging. It would therefore be interesting to examine whether body orientation and landing forces vary depending on the trajectory of landing flights. Perhaps such flights might show less consistent patterns in the early stages of the landing process than were found by the authors. Nevertheless, Roderick and colleagues' detailed biomechanical analysis provides an important road map for future work on how feet, toes and claws enable animals to grip surfaces stably. ■

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## MICROFLUIDICS

# Dissolving without mixing

Microfluidic devices have revolutionized biological assays, but complex set-ups are required to prevent the unwanted mixing of reagents in the liquid samples being analysed. A simpler solution has just been found. [SEE LETTER P.228](#)

ROBERT HOŁYST & PIOTR GARSTECKI

On page 228, Gökçe *et al.*<sup>1</sup> report a clever solution to a fundamental problem in microfluidics: a simple and inexpensive method for delivering a liquid to multiple dried reagents that doesn't mix all the reagents together. By considering diffusion, convection (the flow along a channel) and capillary forces, the authors designed a microfluidic structure that produces a complicated, yet highly reproducible, liquid flow that first passes around dried spots of reagents and then back over them. This dissolves the dried reagents, but minimizes unwanted dispersal within the flow.

The 1990s saw an explosion of interest in microfluidics, driven by a vision of liquid-handling systems that were faster, simpler and smaller than existing devices being used in chemistry and biology. The fluid dynamics of liquids in microfluidic channels is fascinating: streams of distinct liquids typically flow side by side without turbulence or mixing<sup>2</sup>, unlike liquid flows at larger scales. Convection in these systems can be tuned to rates similar to those of diffusion, which opens up a way to control the concentration gradients

of chemical reagents across parallel streams. Surprisingly, it was also found that the flow of immiscible liquids, which involves highly complex surface-tension forces, produces regular patterns of equally sized microdroplets in microchannels<sup>3</sup>.

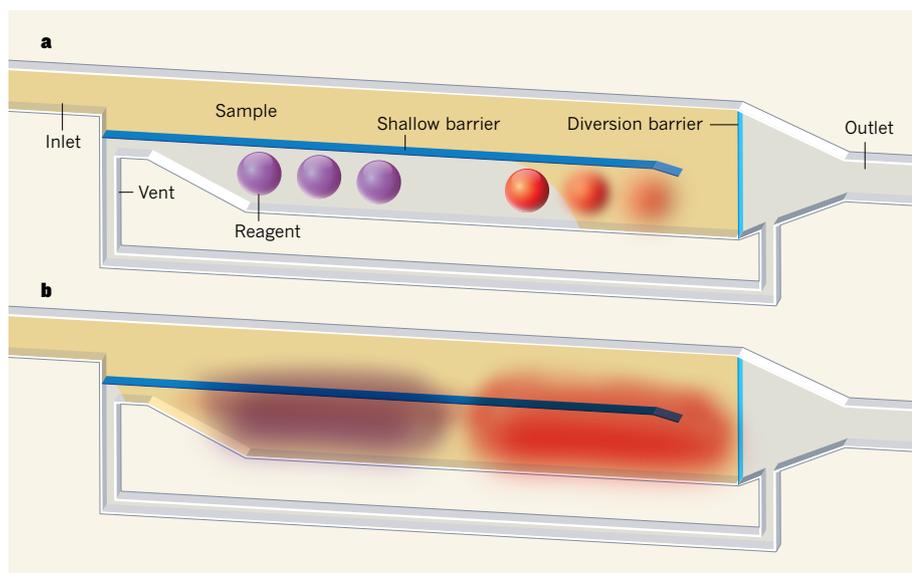
The ratio of the surface area of a microchannel-confined liquid (that is, the surface area bounded by the channel walls) to its volume is large, allowing heat and mass to be rapidly transferred to such liquids. Moreover, the flow of the liquid can be tightly controlled. Taken together, these features make microfluidics devices a useful platform for studying chemical reactions and biological processes. For example, miniature water droplets suspended in an oily continuous phase in microchannels can be used as reactors for chemical or biological processes.

The advent of microfluidics and droplet technologies led to breakthroughs in the life sciences. For example, these technologies have enabled digital assays<sup>4</sup> that can measure the concentration of specific genes in a sample without calibration. They are also key to the single-cell genetic-sequencing techniques<sup>5</sup> currently used in the Human Cell Atlas, a

project that aims to characterize every cell type in the human body<sup>6</sup>. Furthermore, microfluidics technologies are powering a wave of new point-of-care systems that bring diagnostic assays closer to the patient's bedside<sup>7</sup>.

But a fundamental problem remains. In most applications, the microfluidic assay must run multiple analytical reactions on the same liquid sample. Each reaction requires a different reagent, which is dried and pre-stored on the cartridge before the sample is added. These reagents should not mix with each other, because this would ruin the assay. But mixing is hard to avoid once the sample has been added, because of dispersion effects in the liquid. Several solutions to this problem have been proposed, always involving two steps — one to deliver the sample to the reagents, and the other to isolate the microchambers in which the reagents are stored from each other. The second step typically either uses an immiscible liquid as a barrier, or the microchambers are enclosed by solid walls, but either option complicates the design, manufacturing and use of these systems.

Gökçe *et al.* have tackled the problem in a much simpler way. They prepared a straight section of channel that is divided into two along its length by a shallow barrier, and deposited dried spots of reagents in one of the resulting halves (Fig. 1). They then introduced a sample liquid so that it filled the other half of the channel, before changing direction to bend around the end of the barrier and fill the portion of the channel containing the dried spots. Once the whole channel has been filled, the resulting solution of reagents is released through a valve so that it can enter the next section of the microfluidic system. This produces a solution that has an approximately uniform concentration of reagents throughout



**Figure 1 | A module for microfluidics.** **a**, In Gökçe and colleagues' microfluidic architecture<sup>1</sup>, a straight microchannel is divided by a shallow barrier, and dried reagents are spotted along one half. A liquid sample entering from the inlet first passes down one side, and then fills the side containing the reagents. Air pushed ahead of the moving front of the liquid escapes through a vent. **b**, The dried reagents dissolve, and the resulting solution spills over the shallow barrier to fill the whole channel. The capillary forces generated in the system prevent the reagents from being dispersed so that they become concentrated at the moving front, as they would have been in a simple channel. Once the channel is full, the liquid is released through the diversion barrier to the outlet. The system allows multiple reagents to be dissolved in a liquid sample without being mixed together by dispersion.

its volume. By contrast, when dried reagents are dissolved by a liquid in a simple, unstructured microchannel, dispersion processes cause the reagents to become concentrated at the moving front of the liquid.

The authors went on to demonstrate how their system could be used to precisely control the concentration and the timing of addition of reagents in complex biochemical reactions, in two assays: one that detected DNA sequences of the human papilloma virus, and the other that quantified the activity of an enzyme. In both cases, the assays involved the use of several reagents (enzymes and their substrates, cofactors, fluorescent reporter molecules, and so on).

The key to Gökçe and co-workers' invention is the shallow barrier in the channel, which acts as a capillary pinning line — an interface with the liquid that constrains the liquid's motion through capillary forces. The phenomenon of capillary pinning is common in nature; for example, it holds water droplets to minuscule specks of dirt on glass. Capillary-pinning lines underlie such diverse effects as the formation of coffee rings from droplets spilt on a table<sup>8</sup>, or the unidirectional flow of water in the carnivorous pitcher plant *Nepenthes alata*<sup>9</sup>.

Capillary pinning has been used in microfluidics systems before, for example in capillary valves<sup>10</sup>, which control liquid flow without using mechanical parts. They have also been used in phaseguides, which form barriers to flow perpendicular to the direction of motion of the liquid–air meniscus — these barriers hold the meniscus until enough

pressure has built up for liquid to flow over the barrier<sup>11</sup>. Gökçe *et al.* have used capillary pinning in a new way: to enable liquids to flow over dried spots of reagents without causing the reagents to disperse uncontrollably within the liquid, thus allowing the concentration profile of the reagents in the resulting

solution to be controlled by the positioning of the original spots.

The authors' use of small-scale capillary forces allowed them to segregate reactions without using solid walls. This opens up a simple approach for preprogramming and implementing large numbers of biochemical reactions in straight microchannels, removing the need for complex microfluidic chips that have large numbers of compartments and valves. The authors also show that the geometries of their microchannel systems can be made using inexpensive mass-production methods. These systems could therefore help to bring increasingly sophisticated biochemical assays closer to patients in point-of-care devices. ■

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## ARCHAEOLOGY

## Early European babies bottle-fed animal milk

**The foods used to supplement or replace breast milk in infants' diets in prehistoric times aren't fully understood. The finding that ancient feeding vessels from Europe had residues of animal milk offers a clue. SEE LETTER P.246**

SIÂN E. HALCROW

Small pottery vessels, sometimes with animal-like forms (Fig. 1), containing a spout through which liquid could be poured, have been found at prehistoric archaeological sites in Europe. One idea put forward is that they were used as feeding vessels for sick adults and the elderly. However, on page 246, Dunne *et al.*<sup>1</sup> describe an analysis of spouted vessels found in ancient graves of infants in Germany that indicates that these artefacts contained animal milk. This evidence suggests

that such vessels were used to feed animal milk to children, providing crucial insight into the diet of developing infants in prehistoric human populations.

For years, many archaeologists ignored children when studying ancient populations, but researchers now increasingly recognize the importance of children when trying to understand the factors affecting earlier societies<sup>2,3</sup>. One such example concerns a major societal turning point in human prehistory, known as the Neolithic demographic transition, when there is evidence of a substantial increase