e-mail: harvey_cantor@dfci.harvard.edu

1. Saligrama, N. *et al. Nature* **572**, 481–487 (2019).
2. Han, A. *et al. Proc. Natl Acad. Sci. USA* **110**, 13073–13078 (2013).
3. Gee, M. H. *et al. Cell* **172**, 549–563 (2018).
4. Daniel, C., Weigmann, B., Bronson, R. & von Boehmer, H. *J. Exp. Med.* **208**, 1501–1510 (2011).
5. Nakagawa, H., Wang, L., Cantor, H. & Kim, H.-J. *Adv. Immunol.* **140**, 1–20 (2018).
6. Anfossi, N. *et al. J. Immunol.* **173**, 3773–3782 (2004).

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ENGINEERING

Droplet motion electrically controlled

The movement of small droplets on a substrate is governed by surface-tension forces. A technique that can tune the surface tension of robust oxide substrates for droplet manipulation could open up many applications. SEE LETTER P.507

FRIEDER MUGELE

Many plants and insects control their interactions with raindrops and other forms of ambient humidity using surface patterns of hydrophobic and hydrophilic regions[1]. In artificial devices, the ability to switch between such patterns enables the complex manipulation of droplets for applications including biomedical lab-on-a-chip systems[2,3], optofluidic lenses[4] and displays[5], and energy-harvesting systems[6]. A method called electrowetting-on-dielectric (EWOD) is arguably the most mature and versatile tool for achieving such functionality[7]. However, its commercial success has been limited, because the required hydrophobic dielectric (electrically insulating) surfaces gradually degrade. On page 507, Li *et al.*[8] report an approach to tune the wettability of chemically robust hydrophilic surfaces by electrically controlling the adsorption and desorption of molecules called surfactants. If this technology is successful, it might help to turn some previous EWOD-based systems into reliable devices.

The wettability of a solid surface for a particular liquid is determined by the chemical properties of the materials involved. If molecules of the liquid and the solid strongly attract each other, the liquid will cover as much of the solid surface as possible. As a result, there will be a small contact angle — the angle between the liquid surface and the solid surface at the point at which these surfaces meet. In the case of water, such a solid (for example, clean glass or silicon oxide) is hydrophilic. By contrast, if the attraction between water and the solid is weak (for instance, in the case of the non-stick pan coating polytetrafluoroethylene), the surface is hydrophobic and water will bead off.

For hydrophobic surfaces, the tension (force per unit length) at the interface between the solid and the liquid is larger than that at the interface between the solid and the surrounding gas (Fig. 1). For hydrophilic surfaces, the opposite applies. At equilibrium, the contact angle adjusts itself in such a way that the difference between the solid–liquid and solid–gas interfacial tensions is balanced by the horizontal component of the liquid–gas interfacial tension.

Tuning the wettability requires the balance between these surface-tension forces to be manipulated. In EWOD, this is achieved by applying a voltage between a droplet on a thick, hydrophobic dielectric layer and an electrode that is positioned underneath the layer. This voltage generates an electric force that, along with the solid–gas interfacial tension, pulls on the droplet and thereby reduces the contact angle (Fig. 1a). The combination of EWOD and patterned electrodes allows for complex droplet operations such as transport, splitting, merging and mixing[2,3].

The success of EWOD crucially depends on the stability and the chemical inertness of the dielectric layer. Almost two decades of applied research have focused on optimizing these layers, based on the principle that they should be hydrophobic and as thin as possible, but also should block any voltage-induced electric current that would degrade performance. This has led to layers of polytetrafluoroethylene-like fluoropolymers being a gold standard in the field. Notwithstanding impressive successes, the intrinsically high tension of any interface between a hydrophobic layer and water makes such surfaces prone to adsorption of solutes and to other degradation processes on continued exposure to water. This limitation has become the main bottleneck for the commercialization of the technology.

Li and colleagues avoid this inherent problem of EWOD by using a hydrophilic silicon oxide surface that has an intrinsically small solid–liquid interfacial tension. They tune the wettability of this surface using electrically controlled, reversible adsorption of surfactants (Fig. 1b). These molecules consist of a hydrophobic tail and a hydrophilic head. Their adsorption on the hydrophilic surface reduces the solid–gas interfacial tension and thereby increases the contact angle. For this reason, the authors refer to their approach as

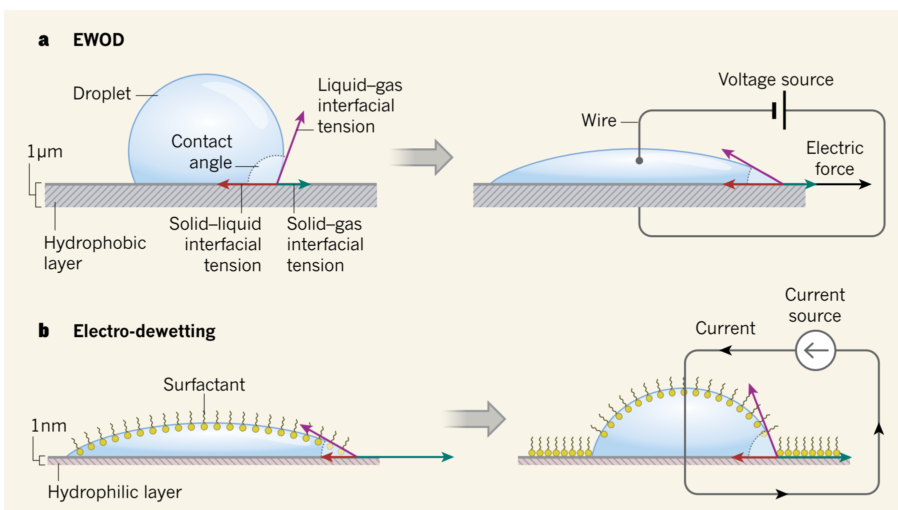

Figure 1 | Droplet manipulation. a, In a method called electrowetting-on-dielectric[7] (EWOD), a droplet is placed on a micrometre-thick hydrophobic layer. The solid–liquid interfacial tension (force per unit length) is larger than the solid–gas interfacial tension. The difference between these tensions is balanced by the horizontal component of the liquid–gas interfacial tension. As a result, the contact angle between the solid and the liquid is large. An applied voltage generates an electric force that causes this angle to decrease. **b,** Li *et al.*[8] report a technique dubbed electro-dewetting, in which a droplet is placed on a nanometre-thick hydrophilic layer. The solid–liquid interfacial tension is smaller than the solid–gas interfacial tension and the contact angle is small. The droplet contains charged molecules called surfactants that have a hydrophobic tail and a hydrophilic head. Under an electric current, surfactants are adsorbed on the hydrophilic layer. These regions are rendered hydrophobic, which causes the contact angle to increase.

electro-dewetting, in contrast to electrowetting and, therefore, EWOD.

Unlike EWOD, in which the dielectric layer blocks any electric current, electro-dewetting relies on passing a current through the liquid and a nanometre-thin silicon oxide layer to an underlying electrode. Depending on the direction of the current, charged surfactants are transported either towards or away from the solid surface, inducing surfactant adsorption or desorption, respectively. The authors demonstrate that this technique can be applied to a remarkably wide range of liquids and surfactants, as long as the concentration of these molecules is within a specific range of conveniently low values. Efficient droplet manipulation is also shown for some highly saline buffer solutions that are commonly used in biotechnology.

Li and colleagues use electro-dewetting in conjunction with patterned electrodes, and demonstrate lateral movement of droplets and the basic droplet operations of lab-on-a-chip systems. They find that these manipulations can be carried out even more easily than when using EWOD, despite somewhat slower response times for the droplets and a smaller range of accessible contact-angle variations.

The main promise of the authors' approach is to deliver a robust and versatile droplet-manipulation platform. Although the results presented show a remarkable degree of versatility, challenges remain. For instance, the surfactants tend to adsorb to the solid surface and increase the contact angle even without an applied electric current. But Li *et al.* show that this adverse effect can be suppressed by adjusting the liquid's composition (for example, its pH) depending on the type of surfactant that is used. Given the wide range of surfactants that are available, it seems plausible that suitable material combinations can be found that maximize the electro-dewetting efficiency and that minimize possible interference from other solutes such as proteins, for many applications.

Another challenge is that the required electric current will drive electrochemical reactions that could gradually degrade the droplet-manipulation platform and the associated liquids. Stringent tests will need to be carried out after hundreds, thousands or even millions of adsorption–desorption cycles to fully evaluate the robustness and versatility of electro-dewetting.

Li and colleagues' work might also have implications for fundamental research. Standard wetting theories[9] are equilibrium theories that are based on energy minimization. However, the need for a permanent electric current in electro-dewetting demonstrates that the microscopic origin of this mechanism requires some intrinsically non-equilibrium processes that remain to be identified. This concept could therefore offer opportunities for controlling interfacial adsorption even beyond wettability alteration. ■

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1. Yao, X., Song, Y. & Jiang, L. *Adv. Mater.* **23**, 719–734 (2011).
2. Cho, S. K., Moon, H. & Kim, C.-J. *J. Microelectromech. Syst.* **12**, 70–80 (2003).
3. Pollack, M. G., Fair, R. B. & Shenderov, A. D. *Appl. Phys. Lett.* **77**, 1725–1726 (2000).
4. Berge, B. & Peseux, J. *Eur. Phys. J. E* **3**, 159–163 (2000).
5. Hayes, R. A. & Feenstra, B. J. *Nature* **425**, 383–385 (2003).
6. Krupenkin, T. & Taylor, J. A. *Nature Commun.* **2**, 448 (2011).
7. Mugele, F. & Heikenfeld, J. *Electrowetting: Fundamental Principles and Practical Applications* (Wiley, 2018).
8. Li, J., Ha, N. S., Liu, T., van Dam, R. M. & Kim, C.-J. *Nature* **572**, 507–510 (2019).
9. De Gennes, P. G. *Rev. Mod. Phys.* **57**, 827–863 (1985).

DEVELOPMENTAL BIOLOGY

Genetics and mechanics guide gut formation

An analysis of gut formation in the fruit fly has revealed how gene expression and mechanical forces are coordinated in adjacent populations of cells. The findings highlight the tissue-level control of embryonic development. SEE ARTICLE P.467

KRISTEN A. PANFILIO

During embryonic development, generating the correct 3D body form, a process called morphogenesis, requires extensive tissue remodelling. Sheets of cells fold and alter their geometry, undergoing changes equivalent to the paper-folding intricacies of origami. In an early embryo, the cells that will form muscle tissue (termed the mesoderm) and gut tissue (the endoderm) move inwards, and the cells of the outer layer form the skin. On page 467, Bailles *et al.*[1] report a previously unknown aspect of how cells internalize, as revealed by studies of the fruit fly *Drosophila melanogaster*.

Investigations into mesoderm internalization in *D. melanogaster* have established molecular links between cell identity and the physical changes that cells undergo during development. The protein Twist regulates gene expression to confer muscle cell identity, and cells that express Twist constrict their outer (apical) surfaces while maintaining contact with neighbouring cells[2]. The tissue buckling that results from this apical constriction drives cell internalization. Internalization is thus hardwired in the mesoderm, but it also generates forces that affect neighbouring, non-mesodermal tissues[3]. How does mesoderm internalization compare with other examples of cell internalization during development, particularly when many events of morphogenesis occur simultaneously? Bailles and colleagues studied endoderm internalization to investigate this.

Endodermal cells internalize as the entire endoderm tissue — a circular patch of about 15 rows of cells — migrates towards the head region of the early embryo. Using a live-cell imaging microscopy approach and experimental methods supported by mathematical modelling, the authors reveal that there are two distinct regions of the endoderm that differ in their internalization mechanism.

The part of the endoderm that the authors call the primordium region is the first to internalize. Like mesoderm internalization[2], this occurs through a process that is directly regulated by gene expression. The expression and activity of the protein Fog results in an increase in the proteins non-muscle myosin II (MyoII) and Rho1 in the apical region of cells, leading to apical constriction by remodelling of the cells' cytoskeleton (a filament-like internal scaffold in the cytoplasm)[4]. Bailles and colleagues observed that this local Fog activity led to the simultaneous contraction and internalization of all cells of the primordium region (Fig. 1).

In the other part of the endoderm, which the authors term the propagation region, internalization occurred progressively, one row of cells at a time. Bailles and colleagues made the surprising discovery that if transcription was suppressed or the local source of Fog protein was lost, internalization of the propagation region still occurred if the primordium region had already started to contract. Modelling the rate of internalization of the propagation region compared with the maximum estimated speed of Fog diffusion allowed the authors to rule out Fog diffusion as an explanation for how this internalization process is controlled.

Bailles and colleagues then examined whether mechanical influences might have a role. For this, they physically impeded tissue movement, used genetic approaches to alter embryo geometry or used a drug that inhibited MyoII. Their experiments revealed that internalization of the propagation region proceeds by a mechanical positive-feedback