News & views

Fluid dynamics

Microgravity makes mobility measurable

Michelle M. Driscoll

Experiments conducted in Earth's orbit have probed the complicated dynamics of moving droplets by circumventing the size limits imposed by gravity. The findings could lead to improved microchip fabrication techniques.

Understanding how a raindrop runs down a window pane seems like a simple task, but the physics involved is surprisingly complex. And testing models for the mechanics of sliding droplets is no mean feat either, because microscopic surface defects almost always get in the way, making it difficult to create conditions in which the liquid can move freely. In *Physical Review Letters*, McCraney *et al.*[1] report a clever way of overcoming this problem by conducting experiments on the International Space Station (ISS). Removing the limiting effects of gravity enabled the authors to create much larger droplets than would be possible on Earth, allowing them to validate existing models for freely moving droplets, and paving the way to extending these models to complex processes such as splashing.

The shape of a droplet of liquid at rest on a solid can be predicted using simple force-balance arguments. However, when the droplet is made to move (for example, when gravity pulls it down a windscreen) the contact line where liquid, gas and solid meet must advance, and the dynamics of this process is mathematically complicated[2]. Precisely at this contact line, the standard equations describing fluid motion in terms of macroscopic quantities, such as flow and pressure, cannot be used, because the stresses in the fluid increase uncontrollably at this point[3]. Instead, the motion of the contact line must be understood in terms of the microscopic details — the interactions of the atoms and molecules themselves — of both the surface and the liquid.

Investigating these phenomena experimentally is also challenging, because the droplets get pinned by surface defects, and because the contact line is micrometre-scale and thus difficult to resolve. This is especially true in the regime that is most relevant to many manufacturing processes, such as film coating, printing and the immersion fabrication of semiconductor microchips. Understanding the details of this contact-line motion is crucial for optimizing these processes. For example, instant-camera film is created by coating a solid substrate with a polymeric liquid, and the efficiency of this process is partially set by the coating speed. However, moving the solid at too high a velocity can cause the contact line of the liquid to become unstable, thereby trapping air in the coating and creating an undesirable final product that contains gaps and bubbles[4].

To work towards understanding these instabilities, and predicting the complex shape of the driven contact line, it is beneficial to first examine the simpler problem of how a droplet moves when shaken — and this is precisely the approach that McCraney and colleagues took. Applying a force of fixed amplitude and frequency to the plate on which a droplet sits causes the liquid to vibrate and change shape. These shape changes drive the contact line of the droplet back and forth on the plate, creating a convenient and relatively simple system with which to measure contact-line motion (Fig. 1).

This problem is a good starting point for understanding more complex processes, because it is simple enough to be described accurately by theories that can capture the precise shape of the shaken droplet. But although the experiments that are used to study this process are fairly straightforward, surface roughness still poses a challenge. The strength with which defects can pin the droplet is determined by the size of the defects relative to that of the droplet, and this ratio is difficult to alter, because the size of a droplet is set by the capillary length (a balance between surface tension and gravity). By working in the microgravity conditions on the ISS, McCraney *et al.* were able to enlarge the droplets so as to overcome the effects of defect pinning.

Crucially, this vibrating-droplet system makes it possible to observe large-scale changes in the shape of the droplet, which are controlled by the contact-line properties; this eliminates the need to resolve the microscopic contact-line motion directly. When the

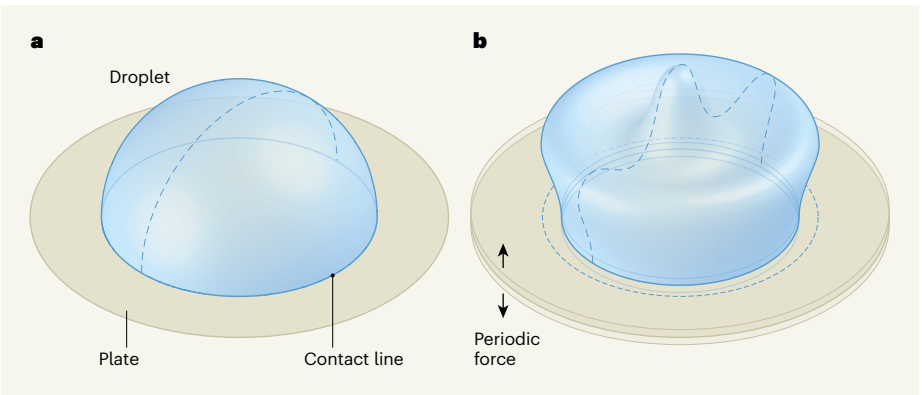

Figure 1 | Shape changes reveal the physics of moving droplets. a, The behaviour of a droplet moving on a plate is determined by the contact line between the droplet, plate and surrounding air, but the motion of this line is challenging to predict and measure. **b**, Applying a periodic force to the plate induces shape changes in the droplet, from which the properties of the contact line can be inferred, and this eliminates the need to resolve its motion directly. However, microscopic defects in the plate surface (not shown) can complicate such measurements by affecting the droplet's motion to a degree that is determined by the relative sizes of the droplet and defects. McCraney *et al.*[1] performed such experiments on the International Space Station, where the microgravity environment enabled the formation of larger droplets than are possible on Earth, allowing the authors to measure the properties of a fully mobile droplet.

vibration frequency is matched to the natural 'resonance' frequency of the droplet, the shape changes can be large, and they are well characterized by theoretical models. Thus, by identifying droplet resonance modes, McCraney *et al.* could use such models[5,6] to estimate a coefficient that parametrizes the mobility of the contact line. Although this parameter had been measured previously in droplets that were either completely or partially pinned[7–9], McCraney and colleagues succeeded in measuring it for a fully mobile droplet.

It remains an open question whether this mobility parameter can reveal the physics behind a given fluid–solid–gas system, or whether it is simply a parameter for fitting numerical work to experiments. The authors' measurements strengthen the argument that it is indeed a key material parameter, and pave the way towards confirming this hypothesis through careful measurements of pinned droplets.

Although it was necessary for McCraney *et al.* to conduct their experiments aboard the ISS, their results are likely to have immediate implications for droplet research on Earth. Materials science is advancing rapidly, and innovative fabrication methods are already giving rise to specialized surfaces[10,11] that could allow for fully mobile droplets, even at the millimetric scales set by the capillary length on Earth. Furthermore, the findings could also inform our understanding of wetting phenomena in microgravity — for example, how fluids flow in thermal-regulation or fuel systems that are far from Earth's surface.

McCraney and colleagues' study is limited to rather simple contact-line dynamics, but it offers a key step towards a full understanding of the physics of droplets by providing a valuable experimental validation of existing models. My hope is that the work will inspire researchers to delve into complex dynamic wetting problems, such as understanding the role that air has in governing splashing and coating processes.

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1. McCraney, J., Kern, V., Bostwick, J. B., Daniel, S. & Steen, P. H. *Phys. Rev. Lett.* **129**, 084501 (2022).
2. Snoeijer, J. H. & Andreotti, B. *Annu. Rev. Fluid Mech.* **45**, 269–292 (2013).
3. Huh, C. & Scriven, L. E. *J. Colloid. Interface Sci.* **35**, 85–101 (1971).
4. Blake, T. & Ruschak, K. *Nature* **282**, 489–491 (1979).
5. Davis, S. H. *J. Fluid Mech.* **98**, 225–242 (1980).
6. Hocking, L. M. *J. Fluid Mech.* **179**, 253–266 (1987).
7. Lyubimov, D. V., Lyubimova, T. P. & Shklyaev, S. V. *Phys. Fluids* **18**, 012101 (2006).
8. Vukasinovic, B., Smith, M. K. & Glezer, A. *J. Fluid Mech.* **587**, 395–423 (2007).
9. Xia, Y. & Steen, P. H. *J. Fluid Mech.* **841**, 767–783 (2018).
10. Li, Q., Wu, D. & Guo, Z. *Soft Matter* **15**, 6803–6810 (2019).
11. Fang, L. *et al. Adv. Funct. Mat.* **31**, 2100447 (2021).

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Molecular biology

Structural keys unlock RAS–MAPK signalling

Hugo Lavoie & Marc Therrien

Activation of the RAF protein is key to the RAS–MAPK signalling pathway, and involves the SMP protein complex. Structures for SMP shed light on the process, and suggest fresh targets for anticancer drug discovery. **See p.400, p.408 & p.416**

Unbridled activation of an intracellular signalling network called the RAS–MAPK pathway is the cause of several cancers and of developmental syndromes known as RASopathies[1]. This well-studied pathway (reviewed in ref. 2) starts with a membrane-bound RAS GTPase enzyme — HRAS, KRAS or NRAS — that, when activated by extracellular growth-factor proteins, binds to the nucleotide molecule GTP. RAS–GTP contacts physically and activates a kinase enzyme called RAF, triggering a signalling cascade that leads to activation of another kinase, MAPK. This enzyme, in turn, modulates the activity of proteins involved in many cellular processes. How RAS activates RAF has been the focus of much research. Writing in *Nature*, Liau *et al.*[3] (page 400), Kwon *et al.*[4] (page 408) and Hauseman *et al.*[5] (page 416) shed light on this crucial step by independently reporting the structure of a protein complex involved in RAF activation.

"The three current studies each resolve the structure of the SMP complex, and so offer answers to some lingering questions."

Multiple regulatory mechanisms act as locks on the RAS–MAPK pathway, reducing the likelihood that the cascade will be inadvertently activated. One such lock involves securing inactive RAF in the cytoplasm through interactions between the dimeric form of a protein called 14-3-3 and two phosphorylated serine amino-acid residues (dubbed the NTpS and the CTpS) in RAF's amino and carboxy termini, respectively[6]. RAS–GTP moves RAF from this secure position by interacting physically with a RAS-binding domain on RAF[7].

Our molecular understanding of what happens next remains largely speculative. The predominant view is that RAS–RAF binding displaces 14-3-3 from the NTpS. The exposed NTpS can then be dephosphorylated, preventing rebinding of 14-3-3. Concomitantly, the ability of RAS to form clusters at the cell membrane induces the dimerization of two RAF molecules — a key step towards RAF's catalytic activation (Fig. 1).

A protein complex known as SMP — composed of the scaffolding protein SHOC2, another RAS GTPase called MRAS and the catalytic subunit of the phosphatase enzyme PP1 (PP1C) — has been reported[8] to be involved in NTpS dephosphorylation. However, several aspects of how this SMP complex functions have remained poorly understood. The three current studies each resolve the structure of the SMP complex, and so offer answers to some lingering questions.

The groups reconstituted the SMP complex from individually purified proteins, and determined the order of assembly and the binding affinities of the interacting partners. The salient feature that emerged is that the binding of GTP to MRAS triggers the assembly of the complex. Consistent with previous observations[9,10], all three studies also showed that HRAS, KRAS or NRAS proteins could substitute for MRAS, albeit with a much reduced affinity. Although it remains to be demonstrated that such complexes exist naturally in cells, these results suggest that multiple RAS GTPases can support the formation of SMP-like complexes.

The teams then analysed the structure of the SMP complex — Liau *et al.* and Kwon *et al.* using cryo-electron microscopy, Hauseman *et al.* using X-ray diffraction. They converged on an identical topology, whereby PP1C and MRAS occupy the large concave surface area in the crescent-shaped SHOC2 (Fig. 1). The topology of the complex exposes PP1C's catalytic site and substrate-binding clefts. MRAS adopts a GTP-bound active conformation in which it can interact extensively with SHOC2 and PP1C, providing a structural explanation for why MRAS requires GTP. The C terminus of MRAS is not involved in these interactions and is therefore available for anchoring the complex to the cell membrane.