ACTIVE MATTER

Spontaneous flows and self-propelled drops

The construction of *in vitro* assemblies of biological components that exhibit properties of living matter may shed light on the physical aspects of the dynamic reorganization that continuously occurs inside cells. SEE LETTER P.431

M. CRISTINA MARCHETTI

Liquids and gels can be made to flow by applying external forces at their boundaries. In this issue, Sanchez *et al.*[1] report the observation of self-sustained flows that occur in the absence of external forces — a hallmark of living systems — in a model gel. When this 'active' gel is confined to the interior of water droplets in a water–oil emulsion, the flows resemble the streaming used by cells to circulate their fluid content. Even more remarkable is the fact that, when one of these gel-filled droplets comes into contact with a hard surface, the self-driven flows of the confined gel drive the droplet along the surface*.

To build their gel, Sanchez *et al.* sequentially assembled ingredients extracted from cells (Fig. 1). The first — and key — components are microtubules. These stiff, cylindrical filaments are one of the constituents of the cytoskeleton, the polymer network that mediates force transmission and motility in cells. Microtubule dynamics in cells is regulated by several proteins. Among these is kinesin, a motor protein capable of 'walking' on individual microtubules by converting chemical energy from ATP fuel molecules into mechanical work. To construct the active units of their gel, the authors used a protein called streptavidin as a scaffold to assemble clusters of kinesins that could simultaneously bind to multiple microtubules.

Finally, Sanchez *et al.* added nanometre-sized polymer coils to the solution. This step was essential to promote the formation of microtubule bundles that, in the presence of ATP, are continuously remodelled by the action of the crosslinking motor proteins. The coils induce attractive forces between the microtubules through a mechanism known as depletion interaction. This interaction arises when two filaments come near to each other, because the narrow gap between them is no longer accessible to the polymer coils. This creates an osmotic pressure difference that effectively acts as an attractive force between the filaments[2]. Sanchez and colleagues' overall hierarchical assembly process was recently used by the same group to build artificial cilia that beat periodically and, when densely packed on a substrate, spontaneously synchronize their beating pattern to create travelling waves[3].

At a moderate density, the microtubule bundles form a polymer network that is internally driven by the action of kinesins. The network flows spontaneously and exhibits mixing and enhanced transport, compared with its non-active counterpart (which is obtained when the ATP fuel runs out); this was demonstrated by the authors by tracking small particles suspended in the gel.

At scales much larger than the typical bundle length (tens of micrometres), the rich dynamics of the system resembles that of complex fluids such as liquid crystals driven by externally applied fields, but differs from them in that it occurs spontaneously as a result of the internal drive. This is the key property of active materials that are driven out of equilibrium not by forces applied at their boundaries, but rather by an input of energy on each unit, as in a suspension of swimming bacteria. Energy uptake at the microscopic scale is crucial for driving emergent phenomena and self-organization in disparate systems[4] — from naturally occurring ones, such as bacterial suspensions and flocks of birds, to chemical and mechanical analogues, such as self-propelled Janus colloids (microscopic particles that have two faces with distinct properties).

When Sanchez *et al.* confined the microtubule network to a water–oil interface, the resulting dense, two-dimensional film again exhibited self-sustained streaming flows that seemed to be associated with bundle fracturing and healing. The complex dynamics yielded patterns resembling topological defects — structures that can be generated in liquid crystals at equilibrium by confinement or external drive.

Finally, when the researchers confined the active gel to droplets of at least 30 micrometres in diameter, the gel was spontaneously adsorbed to the inner surface of the droplets, turning into a two-dimensional active film on a curved substrate. Remarkably, the self-sustained active flows of the trapped gel drove autonomous movement of the droplet on a substrate. Although the motile droplets moved along somewhat circular trajectories, rather than travelling in a straight line, they covered about 250 micrometres in 33 minutes. These moving drops bring to mind recent theoretical work[5] showing that active drops in a fluid spontaneously acquire directed motility. For drops in which the active constituents — the microtubule bundles in Sanchez and colleagues' work — form large domains and have, on average, a common orientation but no preferred direction, the theory indeed predicts rotational motion of the drops.

Reconstituted microtubule–kinesin systems have been explored before as models for active self-assembly, not least in the remarkable experiments[6,7] that led the way to current studies of pattern formation in active systems. In those experiments, kinesin complexes driven by ATP organized microtubules into

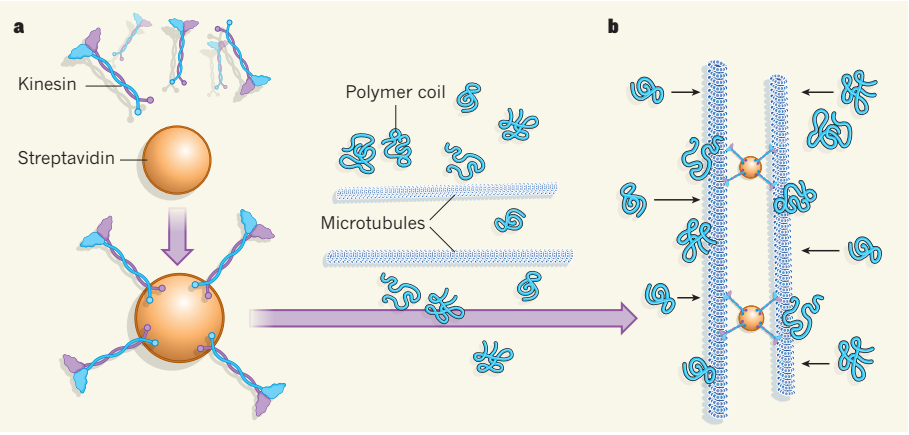

Figure 1 | Assembly of microtubule bundles. **a**, Sanchez *et al.*[1] combined the protein streptavidin with kinesin motor proteins that had been modified to bind to streptavidin (modification not shown). The proteins self-assembled to form clusters of several kinesin molecules in complex with streptavidin. **b**, The authors then added microtubule filaments and polymer coils to the mix. The polymer coils generated 'depletion' forces that pushed the microtubules together, promoting the formation of microtubule bundles mediated by the kinesin clusters. The bundles formed the basis of an 'active' gel — a material that generated self-sustained, internal flows of fluid in the absence of external forces.

*This article and the paper under discussion[1] were published online on 7 November 2012.

spirals and asters reminiscent of a cell's mitotic spindle, a star-like microtubule assembly that mediates cell division. One important difference is that the structures seen in the earlier work[6,7] were essentially static, whereas Sanchez and colleagues' microtubule gel generates continuously evolving, spontaneous flows that persist as long as ATP is present — not unlike what happens in living cells. Furthermore, Sanchez *et al.* report that the internally generated flows in their active gel can be tuned by varying the ATP concentration, confirming the self-sustained, non-equilibrium nature of the dynamics. The fact that microtubules are assembled into bundles seems to be essential for yielding self-sustained motion (see Movie S2 in the Supplementary Information to the paper[1]), but the reason for this remains an open question. Also unexplained is why the behaviour of the active microtubule network is so different from that of gels composed of actin filaments and myosin motor proteins, in which activity yields spontaneous contraction[8].

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Sanchez and colleagues' work is a beautiful example of a growing class of experiment in biomimetic assembly, aimed at building systems that exhibit some of the features of living matter. Will it be possible to control and direct the motility of the active droplets? And can the flow-induced structures be harnessed and used as guides for the transport of particles through fluid, as those in cells are? This remains to be seen. Meanwhile, experiments of this type are beginning to shed light on the physical aspects of the complex dynamical reorganization that occurs continuously inside cells. When combined with studies of the biochemical machinery and signalling that drive such reorganization, they may ultimately lead to a quantitative understanding of the mechanics of living matter. ■

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ANIMAL BEHAVIOUR

Personality in the wild

Behavioural traits can influence an individual animal's fitness, and trait combinations can change over its lifetime, according to a study of wild trout during a key period in their development.

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Life is hard for a young brown trout in a cold Swedish stream. There are so many dangers to watch out for, such as a hungry mink lurking around the bend, and so many things to do, such as competing for food. Indeed, a young brown trout has only around a 10% chance of surviving to adulthood[1]. If a fish can beat the odds and survive this dangerous period, it emerges different from before — not just bigger, but also behaviourally changed. A recent paper by Adriaenssens and Johnsson in *Ecology Letters*[2] reports that the individuals that make it through this bottleneck behave more predictably across contexts than they did before. Is this because of those harrowing early experiences? Or are these fish the ones that were better adapted in the first place? Adriaenssens and Johnsson's findings suggest that the answer is an intriguing combination of both factors.

Animal personalities are interesting to researchers because behaviour is notoriously flexible — unlike most morphological traits, behaviour can change almost instantaneously. Within seconds, a fish might go from aggressively attacking an intruder to foraging alone in the middle of the stream. But there is growing evidence that behaviour does not always change at a moment's notice, and that animals have distinctive personalities that they retain over time. One view[3] is that animal personalities may result from constraints: limiting mechanisms that prevent an individual from being able to change, such as a genetic propensity. An alternative interpretation[4] is that consistent differences in behaviour between individuals might be the result of adaptation through natural selection. There is evidence for both the constraint[5] and the adaptive[6] models, and strong support for the latter comes from research showing that behavioural consistency arises from both behavioural plasticity (when individuals change their behaviour in response to environmental conditions) and non-random survival of individuals[7]. However, that study was carried out in the lab, where life is relatively simple. The significance of Adriaenssens and Johnsson's work is that it starts to show us how adaptive personalities can emerge in the wild.

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Figure 1 | Fishy activity. Adriaenssens and Johnsson's study[2] of the behaviour of wild brown trout (*Salmo trutta*) shows that individuals with consistently high activity levels are more likely to survive the early months of life.

The authors captured young (around two and half months old) brown trout (*Salmo trutta*; Fig. 1) in a stream in western Sweden and gave each individual a unique colour mark. The trout were then put through a series of behavioural assays in the lab. One of these was an 'open-field test', in which trout were individually placed in an open arena and observed to determine whether they were the kind of fish that explores everything, or the type that moves little and hunkers down in one spot. Another assay involved a confrontation with an opponent — in this case, the trout's own reflection in a mirror. Here, the researchers were looking to see whether the individual attacked the intruder or if it was relatively non-aggressive. After assessing each fish in all of the assays, the researchers released them back into the stream.

Two months later, Adriaenssens and Johnsson returned to the stream. Of the 81 individuals that were tested, they recaptured 28. On the basis of the assumption that those fish that were not recaptured had died, the authors' analyses showed that an individual's behaviour predicted its survival: trout that had been very active in the open-field test were more likely to survive to 4.5 months of age than those that had moved around less. An alternative explanation would be that the inactive individuals did not die, but rather were