

permutations of source materials could also be programmed to self-assemble.

Several challenges lie ahead. The method requires a lot of effort to generate new dT staples, which may limit adoption. The DNA-protein hybrid shapes are genetically encoded but have not yet been shown to work in living organisms, unlike alternative RNA-based methods (9) and protein scaffolds (10) that have been used to control metabolic flux in vivo. It may be difficult in general to translate complex self-assembly methods to work in vivo, even though simple DNA nanostructures have been expressed and folded in bacteria (11).

On a positive note, the hybrid DNA-protein structures reported by Praetorius and Dietz do not rely on any ssDNA components, which might be a major advantage because custom ssDNA is typically difficult to produce in cells. It will be interesting to see what kinds of functionalization can be

added to dT staples, especially because applications in cells may require careful regulation of expression and folding conditions. Fortunately, there will be no shortage of options to explore as molecular engineers get ever closer to biological-level sophistication and complexity. ■

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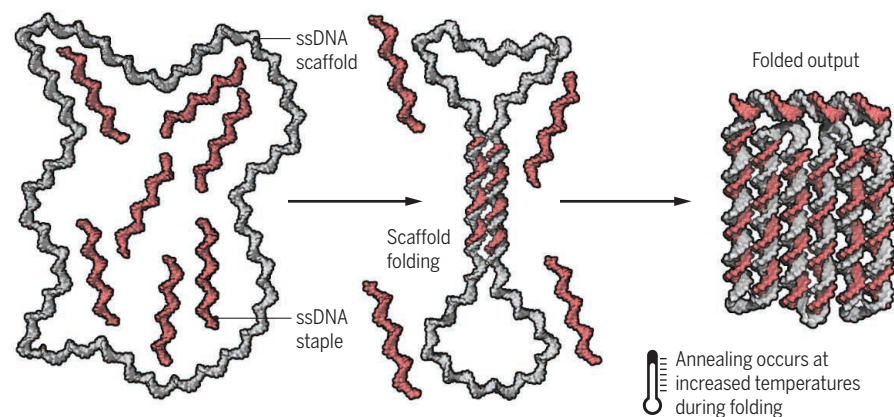
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Bringing proteins into the fold

Biomolecular nanostructures can be built using a powerful approach—staple-directed folding of scaffold templates. This strategy has been extended to work with genetically encoded building blocks.

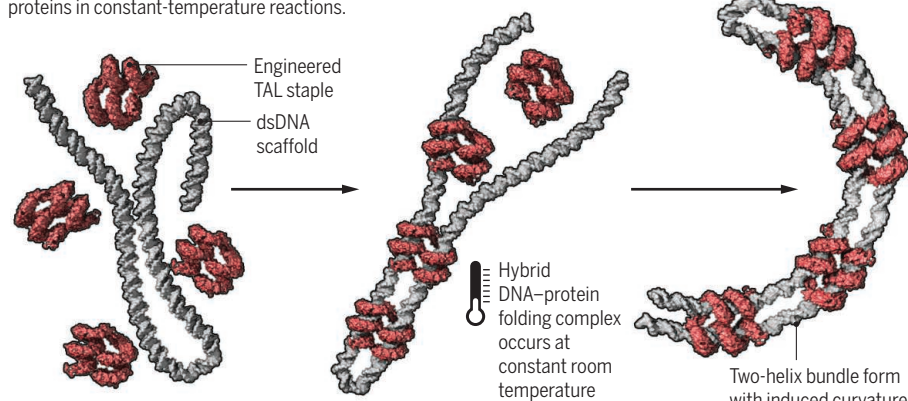
Traditional single-stranded DNA (ssDNA) origami folding

Long strands of ssDNA are folded together with ssDNA staples using thermal annealing ramps.



Double-stranded DNA (dsDNA) folding with protein staples

Custom shapes can be folded from dsDNA scaffolds and double-TAL staple proteins in constant-temperature reactions.



ACTIVE MATTER

From chaos to order in active fluids

Random flows in an active fluid become directional under confinement

By Alexander Morozov

There are few sights more spectacular than the swarming of a school of fish or a flock of birds that suddenly gives way to a directional motion. Arguably, our admiration is rooted in the surprise that individual organisms, capable of self-propulsion on their own, organize to move en masse in a coherent fashion. Coherent motion is common in a large class of biological and synthetic materials that are often referred to as active matter. Such materials consist of particles immersed in a fluid that can extract energy from their surroundings (or internal fuel) and convert it into directed motion. Living organisms, biological tissues, rods on a vibrated plate, and self-phoretic colloids are just a few examples (1). Similar to schools of fish and flocks of birds, active matter often exhibits random swarming motion (2–5) that until now was impossible to control or use. On page 1284 of this issue, Wu *et al.* (6) demonstrate that an active fluid can be manipulated to flow in a particular direction without any external stimuli by confining it in microchannels.

Active systems can display unusual properties that develop from the motion of their individual components. Enhanced diffusion of passive tracers added to active fluids (7), superfluid-like behavior of bacterial suspensions (8), and an ongoing debate about how to define the pressure inside an active fluid (9, 10) add to recent fascination with active matter across many disciplines. In physics, active systems act as a playground for developing new nonequilibrium methods applicable in situations in which usual statistical mechanics breaks down. In biology, it poses a fundamental question of what traits can be considered truly biological and what is emergent and caused by the activity of its constituents. In materials science, these fluids might be manipulated to per-

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form useful work by transporting payloads over large distances, as in targeted drug delivery or assembly of materials.

The work of Wu *et al.* (6) makes an important contribution to all of these areas. They used an active system pioneered previously by their group (4) that consists of a mixture of tubulin microtubule filaments, synthetic clusters of kinesin molecular motors, adenosine 3'-triphosphate (ATP, the fuel that drives the kinesin motors), and a depletion agent, all suspended in a liquid. These ingredients are abundant in eukaryotic cells and are implicated in intercellular transport, spatial organization of cells' organelles, and their propulsion. Molecular motor clusters can bind to two microtubules simultaneously and cause mutual sliding of microtubule bundles, the formation of which is promoted by the depletion agent, and drive fluid flow (see the figure). At sufficiently large concentrations of microtubules and ATP, local motor activity leads to spontaneous formation of large-scale chaotic vortices, with a characteristic size of 100 μm —much larger than individual filaments (4).

It was previously believed that in order to induce a transition from chaotic to unidirectional flow, active matter would have to be confined to sizes smaller than the typical vortex size (11). The surprising discovery of Wu *et al.* is that spontaneous unidirectional flows can be produced by confining their active fluid in cylindrical or torus-like microchannels with linear dimensions orders of magnitude larger than the typical vortex size. Provided that either the channel's width or height was not more than about three times larger than the other dimension, the fluid spontaneously flowed along the channel, around the axis of the cylinder, or along the periodic direction of the torus. The maximum flow velocity reached values of about 10 $\mu\text{m}/\text{s}$, which is comparable with the velocities of pump-driven flows routinely used in microfluidics. The observed velocity profiles were similar to that of water in the same geometry, but this should not distract from the fundamental distinction. The active fluid was not driven from the outside, but self-organized the random motion of its individual microtubular bundles into coherent, unidirectional flow.

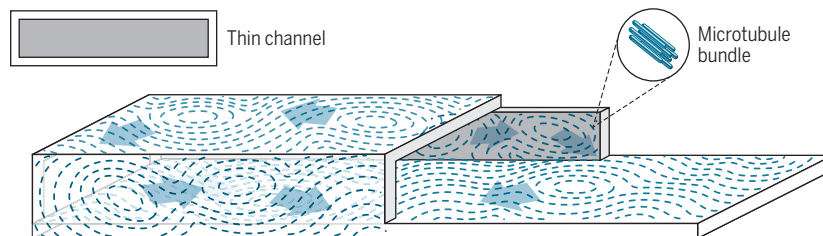
The direction of the flow emerged through a spontaneous symmetry-breaking, with equal probabilities of observing clockwise and counterclockwise motion. To bias the flow, Wu *et al.* introduced periodic notches to the outer edge of the channel and observed that even a single defect was sufficient to control the flow direction. Additionally, experiments in complementary pairs of tall and narrow and short and wide channels demonstrated the same unidi-

Squared up and on the move

A fluid driven by biological motors moves in random directions when spread as a thin film, but flows in one direction when confined in a channel with a square cross section.

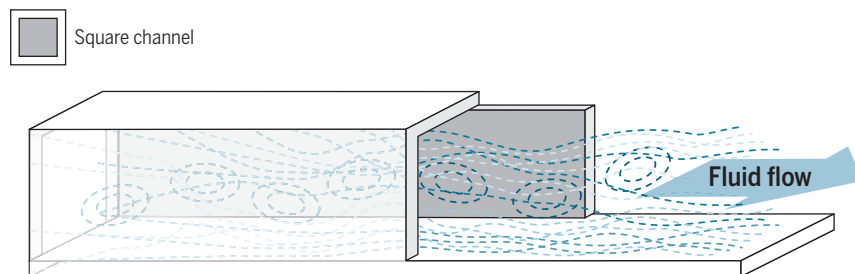
Chaos in nonsquare channels

A microtubules–molecular motors mixture in a thin channel (much wider than it is thick) sets up vortices (about 0.1 mm in diameter) that move in random directions.



Directed flow in square-like channels

Wu *et al.* show that when confined in a channel with a square cross section, microtubule bundles form a nematic layer at the surface and push the fluid in one direction.



rectional flow, implying that the channel's curvature does not play a role in sustaining coherent motion. Last, the practical potential of such flows was demonstrated in a straight geometry in which the active fluid pumped itself along a pipe 1 m in length.

Currently, the mechanism of this transition is unknown. The peculiar constraint on the channel's shape and the observation that the flow velocity is larger in wider and taller channels hint at an intriguing interplay between the fluid's activity and confining geometry. These particular constraints might also explain why this phenomenon was not observed earlier. Previous studies often focused on quasi-two-dimensional layers of active fluids next to boundaries, whereas the work by Wu *et al.* shows that unidirectional flows can only be supported in channels with almost-square cross sections and are essentially three-dimensional phenomena.

Another implication of their study is the irrelevance of the internal length scale of the fluid, be it the size of a bundle or the typical size of chaotic vortices, for the transition to directed motion. The origin of this behavior may lie in the formation of nematic-like layers at the boundaries of the channel that drive the bulk fluid irrespective of its thickness, similar to the surface layers of bacteria observed in confined bacterial turbulence (11).

In the field largely dominated by theory and numerical simulations, Wu *et al.* deliver a new set of observations that change our understanding of active matter and pave the way to its practical application. Do these observations apply to other active matter systems, or are they specific to the microtubule–molecular motor mixtures? Do living organisms control cytoskeleton motion by changing their geometry? More experiments are required to answer these questions, but the results of Wu *et al.* already have the potential to create self-sustaining flows and transport cargo in microfluidic devices. ■

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From chaos to order in active fluids

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