Survival of the aligned - how active polymers bundle

Self-organisation of mortal filaments: the role of FtsZ treadmilling in bacterial division ring formation
Authors: Christian Vanhille-Campos, Kevin D. Whitley, Philipp Radler, Martin Loose, Séamus Holden, and Anđela Šarić
bioRxiv 2023.05.08.539808

Recommended with a Commentary by Karsten Kruse, *Departments of Biochemistry and Theoretical Physics, Université de Genève*

The biologist Franqis Jacob famously stated that the dream of every cell is to become two cells. Many cells achieve this task by assembling a bundle of filamentous polymers – filaments for short – that wraps around the cell. Upon constriction of this ring, the mother cell is cleaved into two daughters. In the ring, filaments align along the circumference, an arrangement that is thought to be essential for ring contraction. Although alignment could be achieved through excluded-volume effects when increasing filament density, which leads to the transition from an isotropic to a nematic phase [1], the work by Vanhille-Campos *et al.* reveals a different mechanism to be operating in bacteria.

In many bacteria, the ring is built from filaments that nucleate and then grow on the inner surface of the membrane surrounding the cell interior. As a (poor) macroscopic analogy, you might think of mikado sticks distributed on a table. A random distribution of filaments does typically not exhibit long-range alignment. In the case of mikado sticks and for high enough densities, you could achieve such order by shaking the table. Cells could exploit the isotropic-nematic transition by having molecular motors induce contraction of the filament network, which would locally increase the filament density. This might indeed be the case in some species.

Bacteria, however, cannot use either of these strategies because they do not dispose of molecular motors. Instead, as shown by Vanhille-Campos *et al.*, they seem to exploit the non-equilibrium nature of filament assembly. Differently from polymers typically studied in physics, cellular filaments assemble from subunits that exist in two different states. These states are associated with different nucleotides being bound to a subunit: bound to a nucleotide triphosphate (NTP), a subunit has a high affinity for binding other subunits and assemble into filaments. In contrast, they disassemble when bound to a nucleotide diphosphate(NDP). NTP-bound subunits in a filament transit into the NDP-bound form by a process involving hydrolysis. Combined with structural differences displayed by the two

ends, this can lead to filament treadmilling [2], where one end grows at the same velocity as the other end shrinks, Fig. 1a. Note that the chemical energy continuously liberated by NTP hydrolysis is essential for localizing assembly and disassembly at the two opposite filament ends and makes treadmilling an active process.

To an external observer, the displacement of isolated treadmilling filaments appears similar to that of self-propelled filaments, but they behave very differently when encountering an obstacle: self-propelled filaments will be blocked. For many self-propelled particles, this mechanism can lead to motility induced phase separation (MIPS) [3]. Not so for treadmilling filaments: as their assembly is blocked by an obstacle, the opposite end continues to depolymerize and the filament eventually disappears, Fig. 1b.

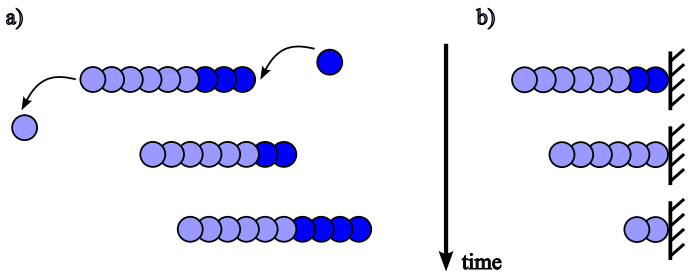

Figure 1: Illustration of filament treadmilling. a) Subunits with NTP bound (dark blue circles) are added at one end of a filament, subunits with NDP bound (light blue circles) are removed from the other end. Subunits in the filament change from NTP to NDP. b) At an obstacle, addition of subunits is blocked and the filament completely disassembles.

In a bacterium, other filaments naturally present obstacles to treadmilling filaments. Indeed, they cannot escape to the third dimension by detaching from the bacterial membrane. In this way, misaligned filaments are removed from the system, Fig. 2. Newly nucleated filaments will survive if aligned with previously present

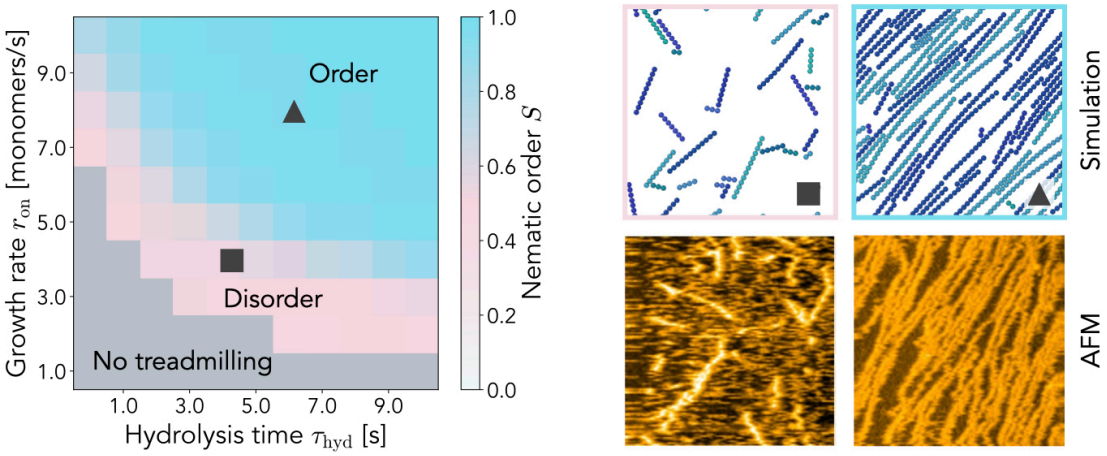

Figure 2: Alignment of treadmilling filaments. Left: Phase diagram as a function of the time needed for hydrolysis of a NTP bound to a subunit in a filament and of the filament growth rate (addition of NTP subunits. The nematic order parameter S is a measure of alignment. Right: Snapshots of representative simulations (top) and atomic force microscopy images of reconstituted FtsZ on supported lipid bilayers (bottom).

filaments. This is the mechanism reported in the study by Vanhille-Campos *et al.* In contrast to the isotropic-to-nematic transition of self-propelled or passive filaments, alignment of treadmilling filaments is controlled by their assembly kinetics.

The authors compare their theoretical results to *in vitro* experiments on the protein FtsZ, Fig. 2. In may bacteria, this protein forms filaments that assemble into a ring specifying the position of cell division. Its dynamics in the *in vitro* experiments closely resembles that studied theoretically. These findings suggest that the mechanism of filament alignment identified in this work is indeed underlying ring formation in bacteria. However, this is not the full story as the position of the FtsZ-ring is determined by external factors that affect filament assembly and nucleation. Furthermore, in simulations, ring orientation was only achieved after coupling the intrinsic curvature of FtsZ-filaments to the curvature of the bacterial cell wall. And, finally, the formation of tight rings required the presence of crosslinking proteins.

The work by Vanhille-Campos *et al.* nicely illustrates how a system that is intrinsically out of thermodynamic equilibrium can find alternative routes and use different control parameters to achieve state changes similar to known phase transitions in equilibrium systems. It is probably safe to assume that the active transition is much less prone to be trapped in a metastable state than its equilibrium counterpart and favorable for cells. From a biological point of view it will be interesting to see, whether this mechanism is employed in other than bacterial cells.

References

[1] L. Onsager, Ann. N. Y. Acad. Sci. **51**, 627 (1949).

[2] A. Wegner, J. Mol. Biol. **108**, 139 (1976).

[3] M. Cates and J. Tailleur, Annu. Rev. Condens. Matter Phys. **6**, 219 (2015).