# Closing the ring

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Above a certain threshold particle density (subunit concentration), the rotational movement of, and collisions between, the curved polymers lead to the formation of clustered ring-like structures. Source: C. Hohmann (Nanosystems Initiative Munich).

How bacterial cells divide in two is not fully understood. LMU physicists now show that, at high concentrations, a crucial protein can assemble into ring-shaped filaments that constrict the cell, giving rise to two daughter cells.

In the final step in bacterial cell division, constriction of the so-called Z-ring, an annular structure that forms on the plasma membrane near the midpoint of the cell, gives rise to the two daughter cells: A research team led by Erwin Frey, who holds the Chair of Statistical and Biological Physics at LMU, has now used mathematical modelling to understand the mechanism that drives formation of the Z-ring, and in so doing have uncovered a novel class of pattern-forming mechanism in biological systems. Simulations based on the model show that the major constituent of the Z-ring can self-organize into ring-like structures once its local subunit concentration exceeds a certain threshold value. "From a biological standpoint, this is a very interesting observation, because it sheds new light on the previously mysterious protein dynamics that underlies bacterial cell division," says Frey. The results of the new study appear in *Physical Review Letters*.

The Z-ring is made up of the protein FtsZ, which polymerizes in the form of filaments that have an intrinsic curvature, as confirmed by experiments carried out with artificial membranes. Moreover, the rings form vortex patterns on the membrane as a result of active subunit exchange: This phenomenon arises because FtsZ polymers are polarized: Subunits can be added to only one end of the filament and are lost from the other. This so-called tread-milling makes it appear as if the filaments are actively crawling along the membrane. "Under certain conditions, the polymers begin to form closed ring-shaped clusters that rotate," says Jonas Denk. "And strikingly, the diameter of these rings is equivalent to that of the average bacterial cell."

That FtsZ polymers self-organize has been known for some time, but Frey's group has also developed a mathematical model which takes the intrinsic curvature of the polymers and their swirling, tread-milling behavior into account. In addition, the model includes the stipulation that filament arcs repel one another, which ensures that filaments do not overlap. Numerical simulations based on this model recapitulate the non-linear dynamics observed in experimental model systems. "What we really wanted to know was the underlying mechanism responsible for the formation of the vortex patterns," says Huber. The simulations demonstrated that the critical factor is particle density – in other words, the total concentration of subunits in the system: In a system in which the particle density is low, opportunities for interaction are few, and individual filaments are widely separated. As the total number of particles is increased, the polymers become increasingly likely to collide with each other. As a consequence of such collisions and the rotary motion of each of the curved filaments, the polymers begin to cluster together, forming densely nested arcs.

According to the Munich researchers, these results imply that formation of the Z-ring is a direct consequence of the dynamics of FtsZ self-organization – and the concentration of FtsZ in the cell is the controlling variable that regulates where and when it forms in the cell. Such an autocatalytic system also provides an entirely novel mechanism for the growth of ring-shaped structures, which differs fundamentally from that used for daughter cell segregation in eukaryotic cell division: In eukaryotes, specific motor proteins which attach to the cell membrane and undergo active contraction are essential for this process, Denk points out. Moreover, quite apart from their biological significance, the new findings are of considerable physical and mathematical interest, Huber adds: The underlying phenomenology of our model differs fundamentally from that conventionally used in modelling the behavior of powered or active particle systems. Its mathematical description turns out to lead to a generalized version of a complex equation that plays a role in the context of phenomena such as bacterial turbulence and pattern formation in more general, non-linear systems.

**More information:** Jonas Denk et al. Active Curved Polymers Form Vortex Patterns on Membranes, *Physical Review Letters* (2016). DOI: 10.1103/PhysRevLett.116.178301

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