Regulation of Pom cluster dynamics in Myxococcus xanthus

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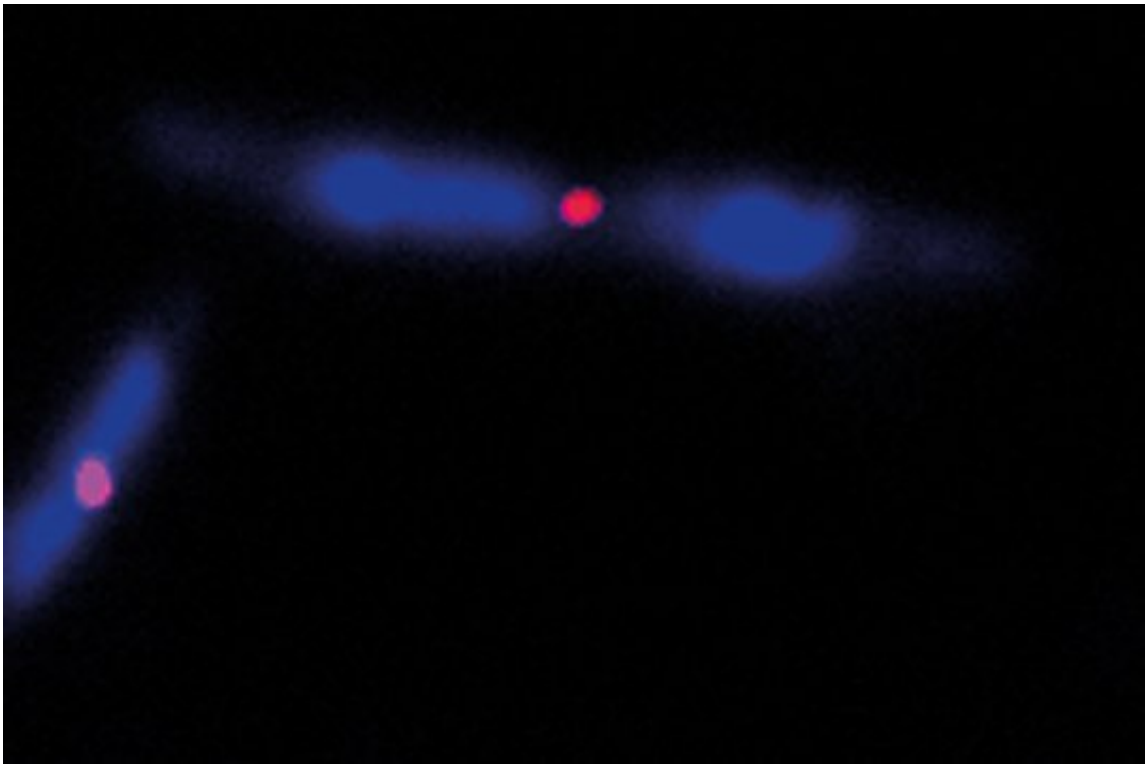

The Pom cluster locates in the middle of the nucleoid and thus determines the plane of division. Fluorescence microscope image of a M. xanthus cell with the nucleoid in blue and the Pom cluster in red. Credit: L. Søgaard-Andersen, MPIterMic

Rod-shaped bacterial cells normally divide by constriction midway along their long axis. LMU physicists have developed a theoretical model to explain how Myxococcus xanthus localizes the plane of division to mid-

cell.

Essential biological processes, such as cell division, must be tightly regulated. For example, correct localization of the plane of cell division is vital for correct segregation of the duplicated genomes, and hence for the survival of both daughter cells. Bacterial cells generally divide symmetrically by forming a contractile ring, which is progressively constricted to form two daughter cells of equal size. In a new study, LMU doctoral student Silke Bergeler and her supervisor Professor Erwin Frey have developed a model that explains how the plane of division is specified in the rod-shaped bacterium Myxococcus xanthus. The model, which is based on experimental work done by Professor Lotte Søgaard-Andersen and her group at the Max Planck Institute for Terrestrial Microbiology in Marburg, is described in the online journal *PLoS Computational Biology*.

Prior to cell division, the bacterial genome is replicated. The region occupied by the bacterial chromosome (or 'nucleoid') is functionally equivalent to the nucleus in the cells of higher organisms. When the cell divides, the nucleoid must be centered, so that the duplicated nucleoids are equally divided between the two daughter cells. Three proteins have been identified which are required for the proper localization of the plane of cleavage at mid-cell in M. xanthus. Experiments by the research group in Marburg have shown that two of these, named PomX and PomY, assemble to form a large cluster, which will ultimately mark the position of mid-cell. The third, PomZ, is an ATPase – an enzyme that binds the nucleotide ATP and can convert it into ADP. Dimer molecules made of two ATP-bound PomZ proteins can attach to the chromosomal DNA and diffuse along it, and can also bind to the PomXY cluster and diffuse at a lower rate. The action of this system ensures that the cluster is localized to the midpoint of the nucleoid, which coincides with mid-cell, where the contractile ring will form.

"We have developed a mathematical model and used it to study the detailed dynamics of the process that leads to the positioning of the cluster in the center of the nucleoid," says Bergeler. The analysis revealed that the PomZ proteins are the crucial components in this operation. They first bind to the chromosomal DNA and subsequently recruit the cluster, thus tethering it to the nucleoid. Simultaneous binding of PomZ to the cluster and the chromosomal DNA, however, eventually activates the ATPase activity of PomZ, which causes it to detach from both the cluster and the DNA. It then diffuses in the cytosol and finally binds randomly to the nucleoid again. In addition to this delay, one other factor plays an important role in shuttling the cluster to midnucleoid: The chromosome exhibits a certain degree of elasticity, such that a specific position on the chromosome can explore the region around its equilibrium position as a result of thermal fluctuations. "Thanks to this elasticity, PomZ proteins that are bound to both the chromosome and the PomXY cluster can exert a net force on the cluster." Moreover, simulations show that the velocity of the cluster depends on the difference between the fluxes of PomZ into the cluster from either side. "The crucial point is that, if the cluster is asymmetrically placed, more PomZ proteins will be fed into it from the direction of the longer segment of the nucleoid than from the opposite side," Bergeler explains. This imbalance in the flux of PomZ serves to push the cluster toward, rather than away from, mid-cell. When the cluster's location coincides with the center of the chromosome, it remains in place because the number of PomZ molecules impinging on it from each side is essentially the same.

According to its authors, the model is also of interest in the context of other intracellular positioning systems, such as the Min system used to center the contractile ring in E. coli, plasmid segregation, or the mechanisms that are responsible for the localization of flagella. "By studying the similarities and differences between the various systems, one can identify the general mechanisms on which they are based," says

Frey. This view is supported by the finding that the proposed mechanism can in principle lead to two distinct dynamic behaviors. If the dynamics of PomZ's movement along the nucleoid is slow relative to the diffusion of the cluster, the latter does not stably maintain its position at midnucleoid. Instead, it oscillates back and forth about the center of the nucleoid.

More information: Silke Bergeler et al. Regulation of Pom cluster dynamics in Myxococcus xanthus, *PLOS Computational Biology* (2018). DOI: 10.1371/journal.pcbi.1006358