Single Cell Biology

Letort and Burute, Single Cell Biol 2017, 6:1
DOI: 10.4172/2168-9431.1000158

Commentary OMICS International

Centrosome Centering and Decentering by Microtubule Network Rearrangement

Gaëlle Letort[1*] **and Mithila Burute**[2]

[1]*Institut Curie, Mines Paris Tech, Inserm, U900, PSL Research University, F-75005, Paris, France*

[2]*Cell Biology, Faculty of Science, Utrecht University, 3584 CH, Utrecht, The Netherlands*

[*]**Corresponding author:** Gaëlle Letort, Institut Curie, Mines Paris Tech, Inserm, U900, PSL Research University, F-75005, Paris, France, Tel: +33 1 40 51 90 00; E-mail: gaelle.letort@curie.fr

Rec date: Feb 15, 2017; **Acc date:** Feb 27, 2017; **Pub date:** Mar 01, 2017

Commentary

Seeing is believing but not necessarily understanding. Advances in microscopy techniques have allowed us to watch cellular machinery at work. For example, sequence of events imaged during cell division revealed important cytoskeletal and shape transformation of cell. Understanding how forces that bring about spindle pole movement are balanced during cell division requires additional tweaking to the system than mere observations. Elegant experimental setup such as laser microsurgery or optical tweezers can be used to identify components of force balance. However, it remains experimentally challenging to precisely perturb only one parameter of the system without disturbing the rest of its components. Therefore, after more than hundred years after knowing that the centrosome is located at the center of the cell, exact contribution of forces that maintain centrosome at the geometric cell center are still not identified. Moreover, changes in force components necessary for centrosome off-centering during morphogenetic processes such as ciliogenesis and cytotoxic T cell activity are poorly understood. Theoretical approaches provide a way to test and understand physiologically relevant configurations of cytoskeleton organization.

In the work of Letort et al., we used the power of numerical simulations, using Cytosim, to study the main parameters controlling pushing and pulling forces transmitted to the centrosome through microtubules and their effect on its positioning [1]. Cytosim is highly flexible software with agent-based approach (each microtubule is treated as a separate individual) to simulate large systems of cytoskeletal filaments with associated proteins and molecular motors [2] to understand genesis of different cytoskeleton organizations. By using this software, we identified, in conditions like *in-vitro* experiment, different regimes in which centrosome is robustly centered, off-centered or in an unstable equilibrium where a shift from centering to off-centering did not require large perturbations. Importantly, these considerations revealed a major feature of microtubule network property: when the network is in a reactive conformation e.g., if individual microtubules have a certain freedom of motion such as gliding or pivoting, only small perturbations whether external or internal, are sufficient to trigger centrosome repositioning. Morphogenetic events involve dramatic changes in internal organization and cell shape and it seems very plausible that the cell attains the reactive conformation of microtubule network to efficiently respond to the environmental cues and accordingly transit to different states.

Epithelial to mesenchymal transition (EMT) is one such important morphogenetic process of embryo development, where cells transit from cohesive to single cell migratory state. In an experimental scenario of EMT, centrosome off-centering was observed to correlate with a change of tubulin density [3]. Cytosim simulations confirmed that a reactive microtubule network conformation was indeed sensitive to microtubule density and caused centrosome off-centering. Moreover, the simulations predicted the main contribution of pushing forces of microtubules in the centrosome off-centering process. The experimental validation of this prediction indeed showed that by globally altering the microtubule properties such as microtubule stabilization, final cell phenotype could be controlled through centrosome repositioning during EMT.

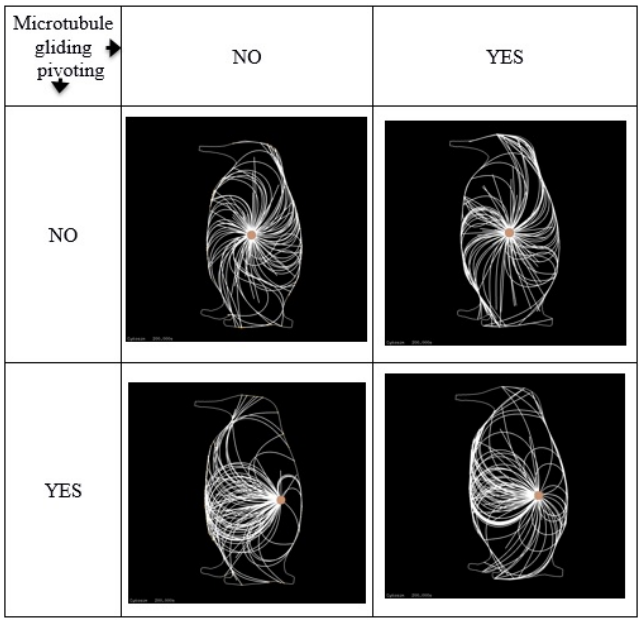

Figure 1: Where is the centrosome in a penguin-shaped cell?

The power of numerical simulations lies within their ability to identify a minimal set of parameters that governs the behaviour of a biological system and to test their precise contribution. This is often very challenging to assess from the experimental work because of the limitations with the degree of manipulation of the biological system. The real strength of mathematical modelling and numerical simulations can be exploited when combined with in-depth knowledge of biophysical properties of the system. A good mathematical model will not only explain the experimental observation but also predict behaviours of the system ahead of our experimental capabilities.

For example, let's say, while contemplating different cellular configurations, you wonder where the centrosome would be if the cell takes the shape of a penguin. Then you can just ask Cytosim, where is the centrosome in a penguin-shaped cell? And you will have the answer… (Figure 1).

References

1. Letort G, Nedelec F, Blanchoin L, Théry M (2016) Centrosome centering and decentering by microtubule network rearrangement. Mol Biol Cell 27: 2833–2843.
2. Nedelec F, Foethke D (2007) Collective Langevin dynamics of flexible cytoskeletal fibers. New J Phys 9: 427.
3. Burute M, Prioux M, Blin G, Truchet S, Letort G (2017) Polarity Reversal by Centrosome Repositioning Primes Cell Scattering during Epithelial-to-Mesenchymal Transition. Dev cell 40: 168-184.