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"BioFib" to Martin Lenz

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Periodic report

Martin Lenz

2 Publishable summary

Protein filaments and their geometrical organization are crucial for cell mechanics, and their failure is related to diseases ranging from sickle cell anemia to Alzheimer's to cancer. While such stakes would suggest a well-defined design to the engineer, sub-cellular filamentous structures are often surprisingly disordered, and very variable from one cell to the next. Physically, this disorder can be traced back to complicated random aggregation processes involving particles with intricate structures far from equilibrium. To help understand this paradoxical combination of reliability and randomness in the cell's architecture, we are theoretically characterizing robust, generic organizational principles for biofilaments on multiple, interrelated scales, from the whole cell to individual proteins.

The first system we consider is disordered assemblies of actin filaments and molecular motors that contract in vivo. These systems self-organize to induce cell motility according to different mechanisms than ordered structures, and we have compared these non-conventional mechanisms and determined which one dominates their activity. This problem crucially involves the mesoscopic structure of the filament assembly, which we are also considering. Going beyond existing naive equilibrium models, this second study focuses on the out-of-equilibrium competition between filament growth and aggregation, which experiments have recently shown to dominate actin gel structure. We have developed models of this process in the reaction-limited regime and are working towards complementing it with diffusion effects. Finally, we are questioning the foundations of these two first studies by asking why protein filaments are so abundant; indeed, they form even in situations where their presence harms the cell. Consistent with this we have shown that in a specific model protein-like particles have a natural tendency towards filament formation, which relieves the geometrical frustration resulting from their ill-fitting shapes.

The fellow has a permanent position at CNRS and has been successfully building his own research group since the beginning of the project, obtaining an ERC Starting Grant among others.