MODELING HOW CHEMICAL ENERGY IS CONVERTED INTO ACTIN-BASED MOTILITY

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The chemo-mechanical motor of several physiological and pathological processes in biological systems is a polymerization process, which converts chemical energy into mechanical work. The chief component in this activity is actin, a multi-functional protein forming filament in the cell cytoskeleton. External impulses of a chemical or mechanical nature trigger a chemical reaction, which converts the monomeric form of actin, G-actin, into a polymerized branched-filamentous form, F-actin. Upon polymerization, the cross-linked network acts against the plasma membrane, a pathogenic bacterium, or an endosome, pushing them forward and promoting directional motility.

At the leading edge of cells, actin is organized in an almost bidimensional dendritic array of branched filaments [1]. Binding proteins control actin turnover and filament elongation, mediate the initiation of new filaments as branches on pre-existing filaments and promote (de)branching and (de)polymerization, thus regulating the mechanical response of moving cells.

In a recent publication [2], a thermodynamically consistent continuum-mechanics formulation was proposed, stemming from continuity equations that account for actin chemical kinetics [3]. We have suggested that the volumetric expansion exerted after the phase change from monomeric to a cross-linked network of actin filament ultimately converts chemical energy into motion.

In this note, the formulation in [2] will be extended and unpublished results presented for the first time. The main novelty is the application of Helmholtz free energies with no entropic contributions. Numerical simulations of Listeria pathogens, see Fig. 1, with data taken from biological literature, show that the main features of actin-based motility are captured with remarkable accuracy.

The model manifests itself in macroscopic descriptors of biochemical and biological details of the relevant processes, thereby resulting in sufficient generality to be appropriate for several biological systems, targeting cellular motility as a whole.

Fluorescent imaging and quantitative analysis describing the cellular force transducer elements, like the cytoskeleton, will validate our computational models.

Actin fibers and focal adhesion in live cells cultured in different conditions will be stained, to characterize their organization and the dynamic turnover, with the aim to extract quantities of interest (such as number, size, lifetime).

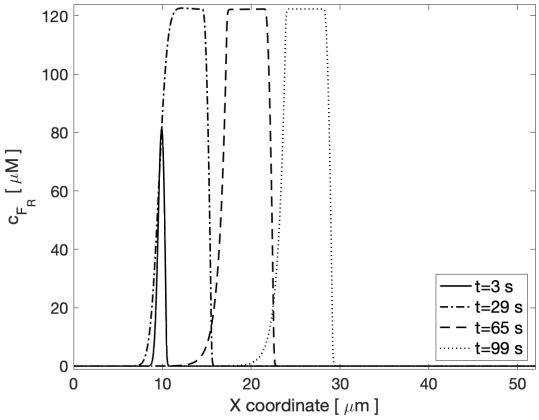

Figure 1: Concentration of F-actin network in Listeria pathogens comet tail.

References

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