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COARSE-GRAINED MODELING AND SIMULATION OF ACTIN FILAMENT DYNAMICS: POLYMERIZATION, DEPOLYMERIZATION AND SEVERING

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ABSTRACT

The actin filament, which is the most abundant component of the cytoskeleton with a double-helical polymeric structure consisting of actin monomers, plays important roles in fundamental cellular activities such as shape determination, cell motility, and mechanosensing [1-3]. In each activity, the actin filament dynamically reorganizes its structure by polymerization, depolymerization, and severing [4, 5]. In this study, to develop a multiscale modeling and simulation method for such actin filament dynamics, a coarse-grained modeling was applied based on the Brownian dynamics [6], which can describe phenomena in the scale ranging from the dynamics of one molecule to the filament structural changes, as showin in Fig.1.

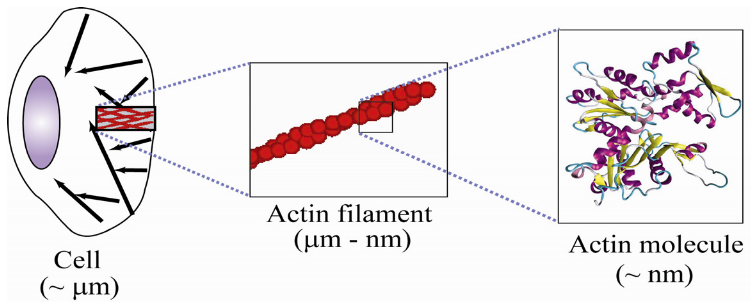

Figure 1: Hierarcy in actin filament structure from molecular to cellular levels.

In the model, the actin monomers and the solvent were considered as globular particles and a continuum, respectively, in which the motion of the actin molecules was assumed to follow the Langevin equation. Three fundamental processes at the molecular level were modeled as shown in Fig.2. The polymerization, which increases the filament length, was determined by the distance between the center of the actin particle at the barbed end and actin particles in the solvent. The depolymerization, which decreases the length, was modeled such that the number of dissociation particles from the pointed end per unit time was constant. In addition, the filament severing, in which one filament divides into two, was modeled to occur at an equal rate along the filament.

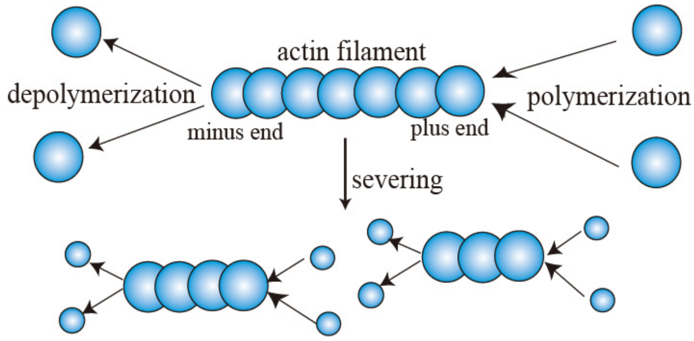

Figure 2: Schematic of coarse-grained actin filament dynamics model, assuming that polymerization occurs only at barbed end, depolymerization at pointed end, and severing at interparticles resulting in an increase in number of filaments.

We simulated the actin filament dynamics to analyze filament elongation rate, filament turnover, and the effects of severing on polymerization/depolymerization. The results indicated that the model reproduced the linear dependence of filament elongation on time, filament turnover process by polymerization/depolymerization, and acceleration of polymerization/depolymerization by filament severing. Our results qualitatively agreed with those obtained in the experiments. Thus, the developed model could be the basis of the model that describes the actin filament dynamics from the molecular-level behavior.

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