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Effect of tensile force on the mechanical behavior of actin filaments

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ABSTRACT

Actin filaments are the most abundant components of the cellular cytoskeleton, and play critical roles in various cellular functions such as migration, division and shape control. In these activities, mechanical tension causes structural changes in the double-helical structure of the actin filament, which is a key modulator of cytoskeletal reorganization. This study performed large-scale molecular dynamics (MD) and steered MD simulations to quantitatively analyze the effects of tensile force on the mechanical behavior of actin filaments. The results revealed that when a tensile force of 200 pN was applied to a filament consisting of 14 actin subunits, the twist angle of the filament decreased by approximately 20°, corresponding to a rotation of approximately −2° per subunit, representing a critical structural change in actin filaments. Based on these structural changes, the variance in filament length and twist angle was found to decrease, leading to increases in extensional and torsional stiffness. Torsional stiffness increased significantly under the tensile condition, and the ratio of filament stiffness under tensile force to that under no external force increased significantly on longer temporal scales. The results obtained from this study contribute to the understanding of mechano-chemical interactions concerning actin dynamics, showing that increased tensile force in the filament prevents actin regulatory proteins from binding to the filament.

1. Introduction

The major components of the actin cytoskeleton, actin filaments, play critical roles in various cellular functions, such as migration, division and shape control (Svitkina et al., 1997; Watanabe and Mitchison, 2002; Pollard and Berro, 2009; Pollard and Borisy, 2003; Adachi et al., 2009). In these activities, the actin cytoskeleton undergoes dynamic rearrangements governed by mechanical and biochemical factors (Arber et al., 1998; Isenberg et al., 1980; Pollard and Cooper, 1986; Theriot and Mitchison, 1991). In particular, changes in mechanical conditions within the cells and in their surrounding environment are key regulatory factors affecting the global reorganization of the actin cytoskeleton (Naruse and Sokabe, 1993; Neidlinger-Wilke et al., 2001; Sato et al., 2000, 2005;Yamamoto et al., 2006).

In this reorganization process, microscopic mechanical stretching, twisting and bending cause structural changes at the molecular level in single actin filaments having a double-helical structure (Holmes et al., 1990; Oda et al., 2009). This structural modulation is critical for inducing local cytoskeletal reorganization by interacting with a variety of biochemical factors and triggering the binding of actin regulatory proteins to the filaments (Hayakawa et al., 2008; McGough et al., 1997; Prochniewicz et al., 2005). Investigation of the molecular mechanisms underlying how mechanical forces such as tension (Ishijima et al., 1991; Shimozawa and Ishiwata, 2009) and torsional moment modulate the mechanical behaviors of a single actin filament is thus important (Tsuda et al., 1996).

Analysis of the mechanical behaviors of actin filaments at the molecular structural level is performed using numerical simulations based on the molecular dynamics (MD) method (Chu and Voth, 2005, 2006; Pfaendtner et al., 2010). The steered MD (SMD) method (Isralewitz et al., 2001) enables control of the positions and/or velocities of some specific atoms by applying external steering forces in the appropriate direction. The SMD method is widely used to investigate the mechanical behaviors of proteins, such as stretching of the extracellular matrix (Krammer et al., 1999) and muscle proteins (Craig et al., 2002), binding/unbinding of protein–substrate complexes (Isralewitz et al., 1997; Lu et al., 1998) and adhesion

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