Equilibrium and non-equilibrium processes and internal friction in dynamics of single biopolymer

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Folding/unfolding dynamics of single biopolymer occupies essential part of biological functions. Even more macroscopic biological phenomenon like molecule-membrane interaction or cell adhesion also can be attributed to this kind of microscopic dynamics. It is well known that thermodynamical or equilibrium processes classified into enthalpic and entropic responses contribute macroscopic elasticity of the single molecule. On the other hand, mechanical response of the molecule also includes various types of non-equilibrium processes like relaxation or denaturing due to external forces. While the classical thermodynamics can only deal with a phenomenon simply as a difference between two equilibrium states, non-equilibrium approaches may provide detailed understanding of the transition itself. A key to the dynamic process is energy dissipation or internal friction. In the present study, force spectroscopy technique based on atomic force microscopy (AFM) is intensified by introducing the idea of viscoelasticity measurement. An AFM cantilever is magnetically excited at a particular frequency well below its resonance and the resultant responses in its amplitude and phase are analyzed to extract elastic and viscous properties of the molecule during the course of its forced unfolding. As a model system for the present study, a titin (or connectin) single molecule, which exists in each sarcomere in muscle was chosen. It has a characteristic modular structure of immunoglobulin (Ig) and fibronectin-3 (Fn3) domains. While the stiffness during unfolding of each domain proved to approximate a derivative of the DC force profile relatively well, it did not reflect the characteristic transition to an unfolding intermediate that was observed in the DC force. This means that the transition can be, at least in the time-scale of the present modulation frequency, can be regarded as a non-equilibrium process. In addition, a particular domain was observed to exhibit a characteristic slow unfolding process in contrast to the others that were mostly denatured in ca. 10 msec. or faster. The process had 2 stages of relaxation prior to ordinary random-coil-like extension profile, and in the latter of the two a peaking in the drag coefficient was observed as shown in Fig. 1. This characteristic viscosity is discussed from a viewpoint of internal friction in a polymer chain.

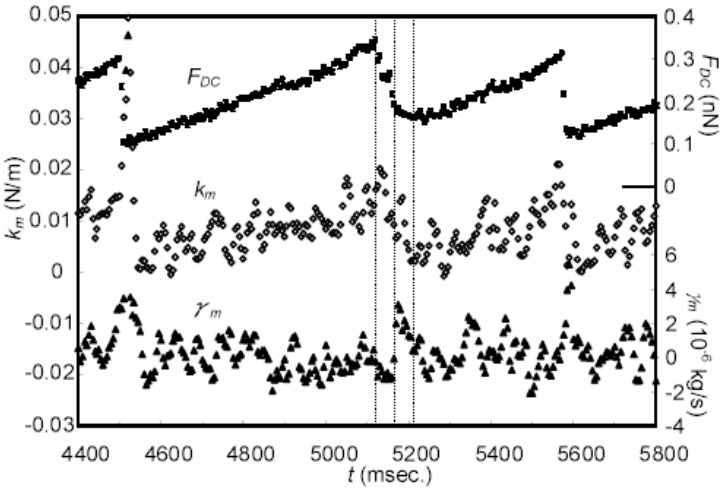

Fig. 1 Simultaneously measured force (F_{DC}), molecular stiffness (k_m) and drag coefficient (γ_m) of a titin single molecule showing characteristic slow decay process from t=5120 to 5210 msec.