Journal of the Mechanics and Physics of Solids 59 (2011) 2044–2069

Contents lists available at ScienceDirect

Journal of the Mechanics and Physics of Solids

journal homepage: www.elsevier.com/locate/jmps

Phase boundaries as agents of structural change in macromolecules

Ritwik Raj, Prashant K. Purohit *

Department of Mechanical Engineering and Applied Mechanics, University of Pennsylvania, Philadelphia, PA 19104, USA

ARTICLE INFO

Article history:
Received 3 February 2011
Received in revised form
24 June 2011
Accepted 10 July 2011
Available online 20 July 2011

Keywords:
Phase transformation
Biological material
Rod-like molecules
Finite differences
Polymeric material

ABSTRACT

We model long rod-like molecules, such as DNA and coiled-coil proteins, as one-dimensional continua with a multi-well stored energy function. These molecules suffer a structural change in response to large forces, characterized by highly typical force-extension behavior. We assume that the structural change proceeds via a moving folded/unfolded interface, or phase boundary, that represents a jump in strain and is governed by the Abeyaratne–Knowles theory of phase transitions. We solve the governing equations using a finite difference method with moving nodes to represent phase boundaries. Our model can reproduce the experimental observations on the overstretching transition in DNA and coiled-coils and makes predictions for the speed at which the interface moves. We employ different types of kinetic relations to describe the mobility of the interface and show that this leads to different classes of experimentally observed force-extension curves. We make connections with several existing theories, experiments and simulation studies, thus demonstrating the effectiveness of the phase transitions-based approach in a biological setting.

1. Introduction

The schematically simple Molecular Force Probe experiments have shed a great deal of light on the behavior of the macromolecules under the application of a point force. Single molecule mechanics experiments are performed in an AFM, magnetic tweezers or optical tweezers (Fig. 1). A molecule is held between rigid and semi-rigid supports in a fluid flow. The molecule is then stretched out by moving one of the supports, maintaining either a constant pulling velocity or a constant force. The result of these experiments is a force-extension curve of the individual molecule. The high degree of reproducibility of these curves makes them a suitable window to interpret how these molecules behave under simple tension.

Several macromolecules exhibit evidence of structural change at high forces. In the work presented in this paper, we have focused on the behavior of DNA under axial stretching. At 65 pN, the molecule undergoes a structural transition, the mechanism of which has still not been resolved completely. However, certain facts about this transition are indubitable. Around 65 pN, the force-extension curve changes suddenly from a sharply rising curve to a nearly flat plateau. The extension continues to increase for a very little increase in the force until the molecule has reached about 1.7 times its original contour length (Cluzel et al., 1996; Smith et al., 1996). At this point, the curve switches to another sharply rising curve, and further stretching eventually breaks the molecule. This transition is called an overstretching transition. It is accompanied by absorption of energy as the bonds holding the DNA in its native state are broken. There may also be a subsequent re-forming of bonds different from the ones just broken as is the case when α-helical intermediate filaments are stretched leading to the formation of β-sheets after the unraveling of the α-helices (Qin et al., 2009). We will not address the exact details of these changes in this paper.

* Corresponding author. Tel.: +1 215 898 3870.
E-mail address: purohit@seas.upenn.edu (P.K. Purohit).

0022-5096/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jmps.2011.07.003

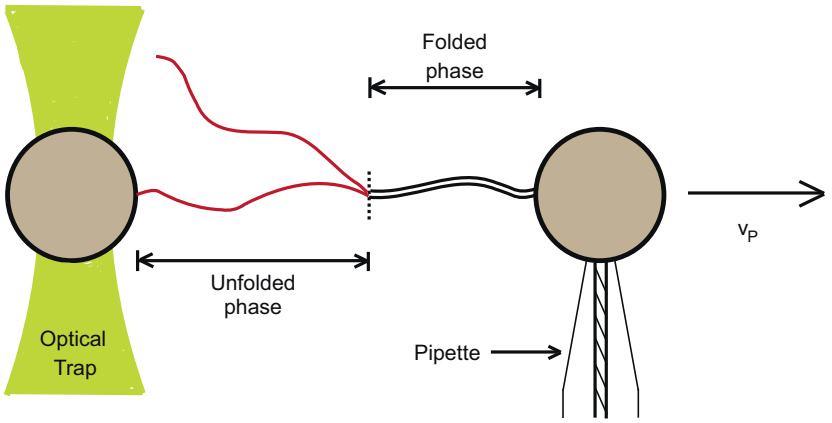

Fig. 1. Schematic diagram of the experimental apparatus.

It has been demonstrated that the rising parts of this curve can be fitted well with worm-like chain relations and two pairs of contour and persistence lengths. Both the mechanisms of the transition, as well as the intermediate states involved, have been vigorously debated over the past decade. At the center of the debate is the nature of the bonding between the two strands as the molecule gradually unfolds under the applied force. Various theories have claimed that this is due to the conversion of B-DNA to a unique intermediate state called S-DNA. Other studies have attempted to characterize the transition as a force-induced melting of double stranded DNA to single stranded DNA. These theories have their respective merits and there is experimental evidence in support of each (Rief et al., 1999; Rouzina and Bloomfield, 2001; Williams et al., 2002; Williams and Rouzina, 2002).

It is important to point out here that this type of plateau unfolding behavior is not unique to DNA. Many coiled-coil proteins are not only similar to DNA in structure (in that they are double helical), but also extremely similar in their response to forces. Plateaus like those seen in DNA have been observed in proteins like myosin II (Schwaiger et al., 2002) and desmin (Kreplak et al., 2008). This common feature of the response to tensile force in structures separated by two orders of magnitude in length and force is intriguing. Intermediate filaments, which are a category of structural proteins, share structural features of coiled-coils. Their importance is great in the study of mechanical properties of cells as they are capable of large, reversible deformations which have similar mechanisms to those in smaller proteins such as the myosin coiled-coil. Therefore, any results for smaller proteins hold considerable value in understanding structural properties of cells and their underlying intermediate filament networks.

1.1. *Significance and approach of this work*

In the body of literature devoted to this subject, there have been theories that incorporate the three distinct parts of the force-extension curve for DNA (Storm and Nelson, 2003; Chakrabarti and Levine, 2005). However, the rate dependence of the transition has not been fully addressed. There have been models proposed, that have shed light on the cooperative nature of the transition. These models have employed the concept of this structural change as being a phase transition and yielded results about the thermodynamics of the process. There have also been models that build upon the Arrhenius rate of reaction model. However, they involve fitting parameters which are largely arbitrary and do not yield further insights (Best et al., 2008; Rief et al., 1998). Also, until very recently, there was no visual evidence regarding how this transition progresses through the molecule. However, recently van Mameren et al. (2009) have demonstrated for the first time that interfaces exist in an unfolding DNA molecule during overstretching. Prior to this, Qin et al. (2009) had also demonstrated the existence of interfaces between folded and unfolded regions during atomistic level simulations for unfolding of a vimentin (a type of intermediate filament) dimer. In the work presented herewith, we have proposed a mechanism for this structural transition based on the motion of the interfaces through the molecule.

We have modeled the unfolding transition in DNA as a phase transition between two metastable phases, namely, the folded and the unfolded configurations. The DNA molecule in its native or folded state, also called B-DNA, has been modeled as a one-dimensional continuum with a constitutive law given by the worm-like chain relation (Marko and Siggia, 1995; Odijk, 1995). The unfolding has been assumed to proceed via a folded/unfolded front that moves along the molecule. The motion of this front or interface is governed by the Abeyaratne–Knowles theory of phase transitions (Abeyaratne and Knowles, 1993, 2006). This theory has been used with great success in studying phase transitions in bulk materials. In particular, the theory builds upon earlier work by Eshelby (1956, 1970) and Truskinovsky (1982, 1985), among others. In such cases, the motion of the interface is three-dimensional. However, we work with the advantage that the experiments under consideration are one-dimensional.