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Resolution of sub-element length scales in Brownian dynamics simulations of biopolymer networks with geometrically exact beam finite elements

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ABSTRACT

Networks of crosslinked biopolymer filaments such as the cytoskeleton are the subject of intense research. Oftentimes, mechanics on the scale of single monomers (∼5 nm) govern the mechanics of the entire network (∼10 μm). Until now, one either resolved the small scales and lost the big (network) picture or focused on mechanics above the single-filament scale and neglected the molecular architecture. Therefore, the study of network mechanics influenced by the entire spectrum of relevant length scales has been infeasible so far. We propose a method that reconciles both small and large length scales without the otherwise inevitable loss in either numerical efficiency or geometrical (molecular) detail. Both explicitly modeled species, filaments and their crosslinkers, are discretized with geometrically exact beam finite elements of Simo–Reissner type. Through specific coupling conditions between the elements of the two species, mechanical joints can be established anywhere along a beam's centerline, enabling arbitrary densities of chemical binding sites. These binding sites can be oriented to model the monomeric architecture of polymers. First, we carefully discuss the method and then demonstrate its capabilities by means of a series of numerical examples.

1. Introduction

Vast and highly dynamic protein filament networks such as the cytoskeleton of eukaryotic cells provide key properties of life such as movement, sensory functions, and biological progeny [1]. The constituents of such networks are macromolecules, that are polymerized from monomer base units when required and are depolymerized when their task is fulfilled. The three structurally most important fibrous proteins of the eukaryotic cytoskeleton – actin microfilaments (F-actin), intermediate filaments, and microtubules – consist of a large number of these monomers. In principle, all monomers of a filament (depicted as spheres in Fig. 1(a)) are eligible for chemical interaction. With a diverse arsenal of small crosslinking proteins (henceforth called *linkers*) and molecular motors, cells connect filaments transiently and are able to create and apply forces to complex networks with highly tunable mechanical properties [2,3].

The simulation of such large biopolymer networks is a thriving scientific field due to its vast predictive and analytical potential. However, two interdependent aspects present a major dilemma towards the development of an efficient computational method that can precisely model the mechanical behavior of large polymer networks. In general, numerical methods

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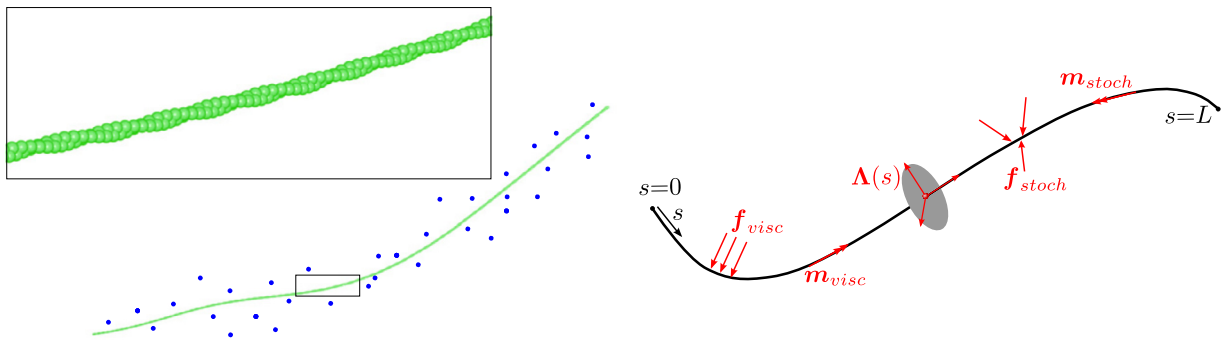

(a) Actin filament and fluid molecules (b) Cosserat continuum

Fig. 1. From the molecular representation to a continuum description using the example of F-actin. (a) Monomers arranged into a left-handed helix surrounded by fluid molecules. (b) Coarse-grained, one-dimensional *Cosserat continuum* with a circular cross section. Effective forces and moments model the interaction between filament and fluid.

modeling monomers explicitly fall short of reaching lengths scales beyond ∼500 nm and observable times beyond 1 s [4–6]. By contrast, Brownian dynamics finite element simulations of networks with hundreds of filaments and implicit time integration reach physical system sizes of ∼5 µm and $\sim 10^3$ s of simulated time [7]. Their computational efficiency is up to three orders of magnitude higher than high-end bead-spring approaches with explicit time integration [4,8]. However, in this case, chemical interaction only takes place at nodes of the elements, i.e., the chemical resolution scales with the degree of mechanical coarse-graining. This inevitably leads to a loss of detail: balancing numerical efficiency and mechanical resolution, common micromechanical filament models (e.g. [9–12]) trade the resolution of short length scales for long time scales. If problems involve a broad range of length scales from single monomers to filament agglomerates, this trade-off corrupts the validity of the model and cannot be applied.

In this paper, we propose the retrieval of the short length scales without compromising computational efficiency. To this end, we describe a coupling condition between beam elements representing linkers and beam elements discretizing filaments. This condition allows for the creation of mechanical joints between the nodes of the linker elements and an arbitrary material point along the filament. Previously, the numerical treatment of joints between beam finite elements has been discussed in [13,14]. We stress the fact that the material points do not necessarily coincide with the element nodes of the filament. This decoupling of the chemical binding site distribution and the finite element discretization allows for much coarser discretizations, leading to a significant increase in numerical efficiency without decreasing the resolution of chemical binding sites.

The methodic efforts can be motivated both generally and with respect to our specific biophysical application. The approach is universal and can be applied in principle to any set of jointed bodies (cf. [13]), including many types of networks or meshes of fibrous constituents (e.g., synthetic polymers, textile meshes, or carbon fiber composites). Our focus on applications in biophysics may be understood as a showcase, which can be generalized to applications with other kinds of fiber networks. The methodic approach can be of interest to material scientists and engineers, who wish to understand the mechanics of fabrics or, e.g., need to pre-evaluate the mechanical properties of novel fiber composite designs.

To the authors' knowledge, all approaches modeling intracellular networks in literature so far suffer from the congruence of the chemical topology and the mechanical discretization of the filament. In many cases, this constraint is the essential driver of computational cost as it leads to an unnecessarily fine mechanical discretization just to capture the chemical kinetics of a problem. With our new approach, we present a remedy to this fundamental shortcoming, granting a boost in numerical efficiency and enabling the simulation of systems the size of cells. We enable the resolution of sub-element length scales (e.g., single monomers) without a further refinement of the mechanical discretization, providing the necessary chemical resolution without diminishing the numerical performance. While resolving the filaments' molecular architecture was not required for our work on the self-assembly [15] and the rheology [16,17] of, and Casimir interactions within semiflexible polymer networks [18], it is explicitly required for many fascinating biophysical problems, e.g., how cells control the size of cytoskeletal protrusions (see Section 3). Hence, based on our original approach outlined in Section 2, this publication will present extensions for the models of filaments and linkers. First, we will enrich the filament model with information on its monomeric architecture, allowing for an arbitrary chemical binding site density along the filament center line (Section 4). Second, we will enable the linker to bind to any of these binding site positions (Section 5). Finally, in Section 6, a series of numerical examples will demonstrate the capabilities of the approach.

2. Introduction into Brownian dynamics finite element simulations

We consider the three major constituents of biopolymer networks: *filaments*, *linkers*, and a *fluid* phase, in which the former two are suspended. This section compactly introduces how these constituents are modeled by the Brownian dynamics finite element method providing the basis for the model extensions. Since the method has been thoroughly discussed in [7,19,20,9], we only provide a very compact description that puts the subsequent sections into context.