Soft Matter Physics Approaches to Biology

A novel approach to the simulation of cytoskeletal polymorphism

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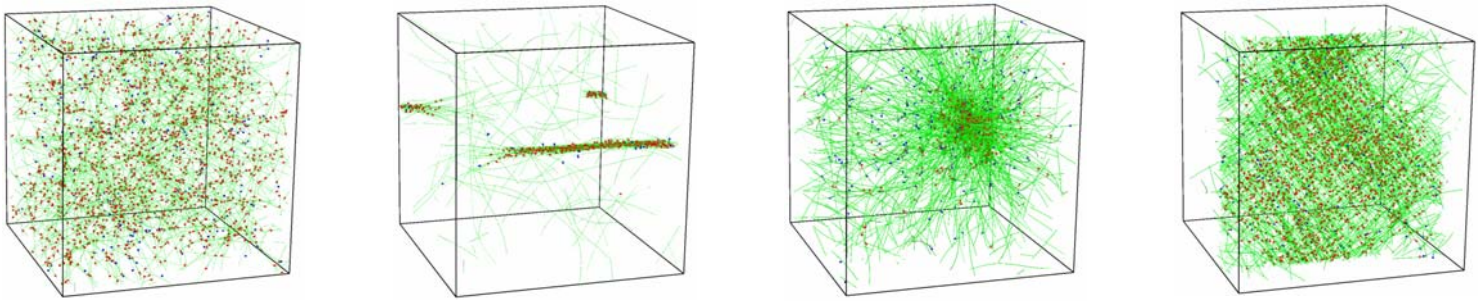
Simulation of large biopolymer networks



(a) Homogeneous network **(b) Bundle network** **(c) Cluster network** **(d) Layer network**

Figure 1: Depending on the crosslinker species, our simulations show an initially linker-free entangled filament solution developing into different equilibrium states such as homogeneous, bundle, cluster, and layer networks. These structures have already been observed in experiments (see figure 2).

The cytoskeleton of biological cells is a complex biopolymer network. It is not only the provider of the structural integrity of the cell but also plays a pivotal role in many mechanically or biochemically triggered processes throughout the cell. Being subjected to massive structural changes which is met by quick reorganization, the cytoskeleton displays properties which in many cases may only be investigated in depth by the means of simulations.

We have conducted the first simulations of biopolymer networks this large (up to c_{fil}=16μM) developing into thermodynamically equilibrated states, see Figure 1. For the first time, the well-known and highly efficient Finite Element Method (FEM) is enhanced by accounting for thermally induced Brownian motion of actin-like filaments and crosslinker molecules. First Results show network morphologies often observed both *in vivo* and *in vitro* (Figure 2).

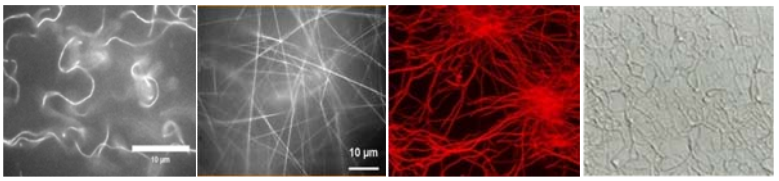


Figure 2: In vitro actin networks: homogeneous [5], bundles [6], cluster [7], layer [8]

Finite Elements and Stochastic Forces

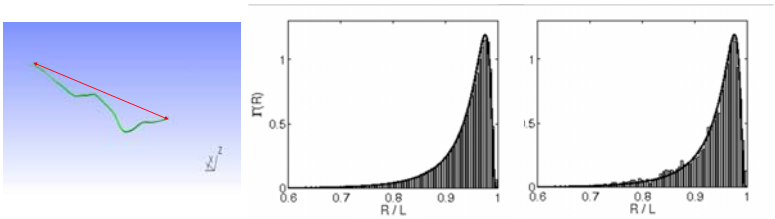
We model biopolymer networks by coarse-graining single filaments, which leads to a rod-like continuum description. Stochastic forces and moments are modeled as a space-time white noise excitations which can be written as the generalized derivative of a multidimensional Standard Wiener Process:

$$\boldsymbol{f}_{stoch} = \sqrt{2k_BT}\boldsymbol{s}_{trans}\frac{\partial^2 \boldsymbol{W}_f(\xi,t)}{\partial\xi\partial t} \qquad \boldsymbol{m}_{stoch} = \sqrt{2k_BT}\boldsymbol{s}_{rot}\frac{\partial^2 \boldsymbol{W}_m(\xi,t)}{\partial\xi\partial t}$$

Polymer dynamics are modeled by the equations of linear and angular momentum which turn into stochastic partial differential equations (SPDE)

$$\boldsymbol{f}_{el}(\boldsymbol{x},\boldsymbol{\theta},\xi,t) + \boldsymbol{f}_{visc}(\boldsymbol{x},\boldsymbol{\theta},\xi,t) = \boldsymbol{f}_{ext}(\boldsymbol{x},\xi,t) + \boldsymbol{f}_{stoch}(\boldsymbol{x},\boldsymbol{\theta},\xi,t)$$

$$\boldsymbol{m}_{el}(\boldsymbol{x},\boldsymbol{\theta},\xi,t) + \boldsymbol{m}_{visc}(\boldsymbol{x},\boldsymbol{\theta},\xi,t) = \boldsymbol{m}_{ext}(\boldsymbol{x},\xi,t) + \boldsymbol{m}_{stoch}(\boldsymbol{x},\boldsymbol{\theta},\xi,t) + \boldsymbol{x}'(\xi,t)\times\boldsymbol{q}_{el}(\boldsymbol{x},\boldsymbol{\theta},\xi,t)$$



(a) **(b)** **(c)**

Figure 3: (a) End-to-end distance of polymer in computer simulation; normalized probability distribution of end-to-end distance in (b) Simulation, [1], (c) Experiment, [2] and theory (continued black line, [3])

Due to specific rules applied when integrating SPDE, a new method has been developed to discretize the SPDE . A finite element discretization in space and a backward Euler scheme in time allow for highly efficient simulations of biopolymers on a sound mathematical basis [1,4]. The employed algorithms have already been validated and verified carefully by comparison with experimental data and analytical predictions (see e.g. Figure 3).

Equilibrium Network Phases

Filaments and crosslinkers are simulated within a boundary volume subject to periodic boundary conditions. Free crosslinker and molecules attached to a filament are modeled as point-like particles. A free molecule may occupy a binding spot of a filament if it is within binding distance and has passed a probability test. Attached molecules may link two filaments if, additionally, orientational constraints are met. The linker is now modeled as a beam element.

Our interest lies in the study of thermodynamically equilibrated states. Thus, we for now abstain from modeling excluded volume effects. However, our approach is capable of addressing excluded volume effects in a highly efficient manner and the respective algorithms have already been implemented, see e.g. Figure 4.

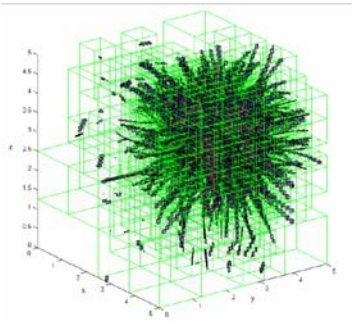


Figure 4: Octree with bounding boxes around finite elements for quick contact detection.

Future work

Our current and future work aims for a deeper understanding of the mechanical properties of biopolymer networks. To this end, microrheological experiments were conducted in vitro with several different types of biopolymer networks. The viscoelastic properties will be compared to simulation results. Furthermore, issues such as finite filament bundle diameters, trapped states and a more detailed model of a filament's binding spot geometry will be addressed.

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