Soft Matter Physics Approaches to Biology

A novel approach to the simulation of cytoskeletal polymorphism

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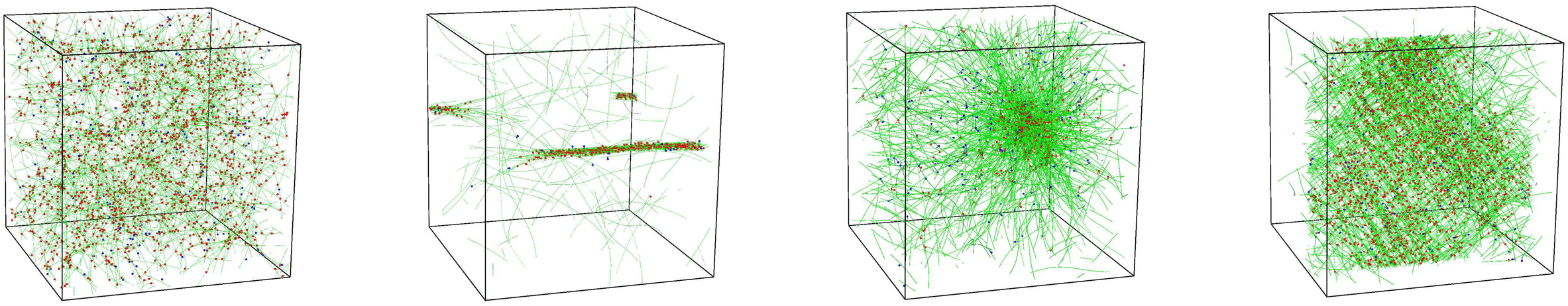
Simulation of large biopolymer networks



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

Figure 1: Depending on the crosslinker species, our simulations show 4 different equilibrium states: homogeneous, bundle, cluster, and layer networks, which have also 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 is also of crucial importance in many mechanically or biochemically triggered processes throughout the cell. It is well-known that the polymorphism of the cytoskeleton, i.e. the reorganization into different network architectures, plays a pivotal role in these processes.

Only little is known about the equilibrium and non-equilibrium structures in biopolymer networks. Here we present a highly efficient finite element approach for the investigation into the polymorphism of cytoskeletal networks. Results show excellent agreement between the architectures in simulation (Figure 1) and experiments (Figure 2).

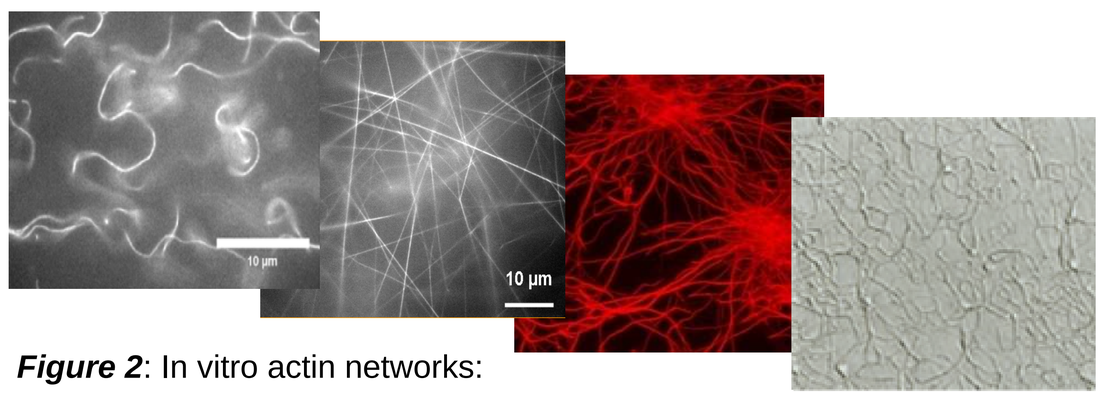


Figure 2: In vitro actin networks:

homogeneous [5], bundles [6], cluster [7], layer [8]

Finite Elements and Stochastic Forces

Single filaments in biopolymer networks are modeled as rod-like continua. Stochastic forces and moments are modeled as space-time white noise excitations which can be written as the generalized derivatives of a multidimensional Standard Wiener processes:

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

Polymer dynamics is modeled by the equations of linear and angular momentum which are stochastic partial differential equations (SPDEs)

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

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

Owing to the mathematical intricacies of SPDEs, a new method has been developed to discretize them. 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).

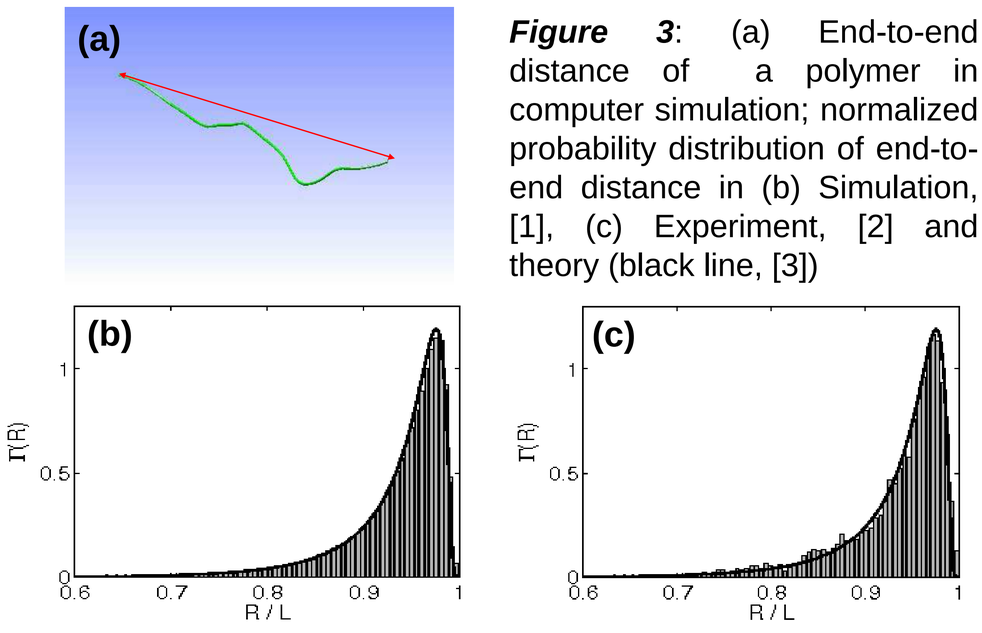


Figure 3: (a) End-to-end distance of a polymer in computer simulation; normalized probability distribution of end-to-end distance in (b) Simulation, [1], (c) Experiment, [2] and theory (black line, [3])

Equilibrium Network Phases

Filaments and crosslinkers are simulated within a volume with periodic boundary conditions. Free crosslinker molecules and those 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. Simulations lead to the phases shown above in Figure 1.

Our current interest lies in the study of thermodynamically equilibrated states but our approach is also capable of dealing with non-equilibrium structures in a highly efficient manner and the respective algorithms have already been implemented, see e.g. Figure 4.

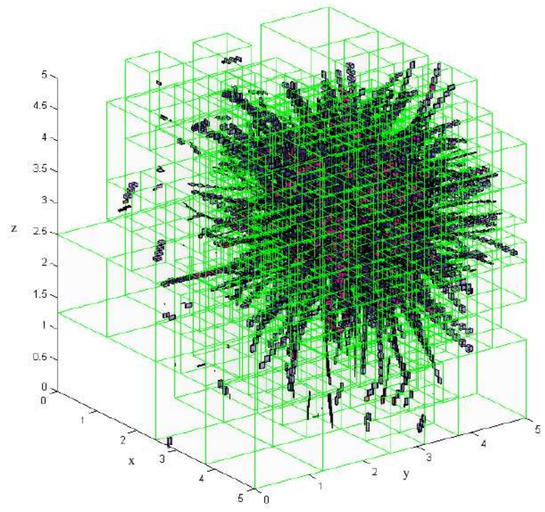


Figure 4: Octree with bounding boxes around finite elements for quick contact detection.

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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