4th GACM Colloqium on Computational Mechanics

Modeling the Cytoskeleton with three-dimensional, nonlinear Beam Elements

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Biopolymer networks

Biopolymers such as *actin*, *cellulose* or *chitin* are macromolecules synthesized by living organisms in order to carry out various essential tasks. In many cases, those molecules establish networks. The most versatile among these networks is the protein backbone of the cell , the *cytoskeleton* (**Fig. 1a**, green) :

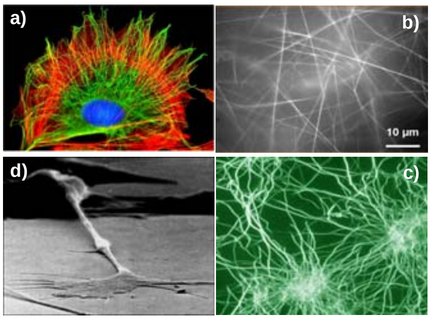


Fig. 1a-d: fluorescent cell [1]; actin bundles [2]; clusters [3]; neuron with filopodia [6]

Components:
- *Actin, intermediate filaments, microtubules*

Functions / tasks:
- maintain *Mechanical stability*
- support/initiate *Cell division/migration/motility*
- *mechanotransduction, etc.*

→Very little knowledge about network mechanics

→*Experiments have limits that simulations do not:* capturing events on subcellular length and time scales very demanding, often impossible

Finite Element Approach

- Filaments → **Beam Elements,** excellent match to experiments and theory [7]
- Stochastic forces and moments (molecule collisions): **Space-time white noise**

$$f_{stoch} = \sqrt{2k_BT s_{trans}} \frac{\partial^2 W_f(\xi,t)}{\partial\xi\partial t} \qquad m_{stoch} = \sqrt{2k_BT s_{rot}} \frac{\partial^2 W_m(\xi,t)}{\partial\xi\partial t}$$

- Dynamics modeled by *stochastic partial differential equations* (SPDEs)

$$f_{el}(x,\theta,\xi,t) + f_{visc}(x,\theta,\xi,t) = f_{ext}(x,\xi,t) + \underline{f_{stoch}(x,\theta,\xi,t)}$$
$$m_{el}(x,\theta,\xi,t) + m_{visc}(x,\theta,\xi,t) = m_{ext}(x,\xi,t) + \underline{m_{stoch}(x,\theta,\xi,t)} + x'(\xi,t) \times q_{el}(x,\theta,\xi,t)$$

- Mathematical intricacies of SPDEs require care with discretization / integration

→Finite element discretization in space, backward Euler scheme in time [7,8].

→Discrete, piecewise constant stochastic forces and moments

Simulation of cytoskeletal polymorphism

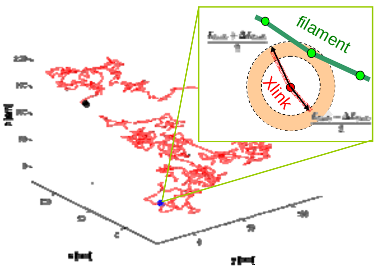


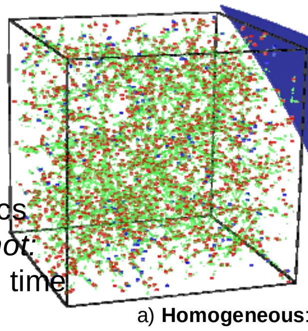
Fig. 2: Random walk of a free Crosslinker (point-like particle); linker search for binding spots on filaments

Investigate the cytoskeleton's ability to shift shapes

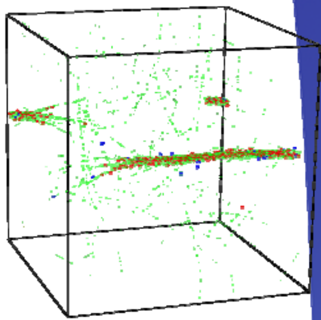
Setup:
- Periodic boundary conditions
- *Point-like crosslinkers*, subject to diffusion (**Fig. 2**)
- Links establish by evaluating binding potentials
- Constraints for Linkers connecting two filaments:
  - *proximity* and *inter-filament orientation*

    → if constraints met, *add element*

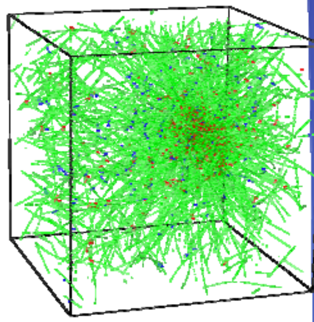
Result: Vary linker species/conc. → different network types (**Fig. 4**); observed in experiments (Fig 1b,c) [2-5].



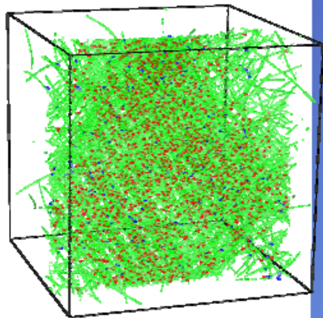
a) **Homogeneous**: no transient links



b) **Bundle**: parallel / no orientational constraint



c) **Cluster**: orthogonal orientational constraint



d) **Layer**: orthogonal orientational constraint

Fig. 4: different network archetypes

Future work

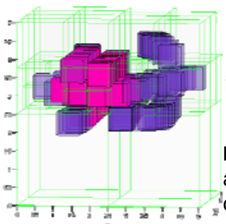


Fig. 3: beam contact and octree-based contact detection

- include contact for very slender structures
- efficient contact detection: Octree & OBBs
- modeling binding spot geometry: actin double-helix
- modeling of crosslinker power stroke

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