Untangling the Mechanics of Entangled Biopolymers

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Soft Squishy Matter is amazing, complex & all around us

Fascinating, multifunctional *viscoelastic* properties

Comprised of *polymers*

What’s happening on a **molecular level** to give rise to such dynamic, complex behavior?

Macroscopic Viscoelasticity

10^{23} Entangled Polymers

Molecular-level Dynamics & Interactions
Biopolymers are highly versatile and tunable

Random Coil Conformation
Persistence Length: $l_p = 50$ nm
Typical lengths: 5 – 20 µm

Extended Contour
Persistence Length: $l_p = 17$ µm
Typical length: 5 – 20 µm

Enzymes control topology

Replication controls length

Polymerization controls length

Crosslinking proteins control actin network architecture

Fig 4: One field of view of actin from the same sample, but where the slide was prepared using actin from the bottom of the eppindorf tube, instead of from the middle. While this is much less dense than 10 µM actin, it is still far too dense to measure single filament lengths.

Fig 5: A separate field of view from the same slide as in Fig 4. Note the large change in density even on a single slide. Here several filaments longer than 40 µm are visible.
Biological cells are crowded with a wide variety of biopolymers

**Nucleic Acids**

Biopolymers make up ~20-40% of cell volume

**Cytoskeleton filaments**

Crowding plays important roles in:

**Small Folded Proteins**

Persistence Length: ~5 nm

Typical length: 0.1 - 1 μm

**diffusion**

**Binding rates**

**Folding**
We can track single biopolymers & measure intermolecular forces

Fluorescence Microscopy & Particle Tracking

Optical Tweezers Microrheology
We investigate molecular mechanics of crowded and entangled DNA and Actin

Diffusion & Conformation of Crowded Linear & Ring DNA

Mapping Deformations of Entangled Actin Filaments


Falzone, et al; Soft Matter (2015);
We investigate molecular mechanics of crowded and entangled DNA and Actin

Diffusion & Conformation of Crowded Linear & Ring DNA

We track single DNA molecules to directly measure molecular dynamics.

Track Center of Mass of DNA
Calculate **Diffusion Coefficient**

Track Axes lengths of diffusing DNA

Quantify conformational **shape** and **size**

\[ \langle (\Delta x)^2 \rangle = 2Dt \]
We track linear & ring DNA in dextran solutions that mimic cellular crowding.

- **Track** Center of Mass of DNA
- **Calculate** Diffusion Coefficient
- **Track Axes lengths** of diffusing DNA
- **Quantify** conformational shape and size

Slope = 2D

\[ \langle (\Delta x)^2 \rangle = 2Dt \]
Crowded DNA universally diffuses faster than classically expected

DNA diffusion in dextran solutions

Crowders hinder linear and ring DNA mobility equally

Crowder size plays principle role in diffusion reduction

Classical Stokes-Einstein diffusion: $D = \frac{k_B T}{6\pi \eta R}$

DNA mobility reduction is independent of DNA topology

Mobility decreases less than classically expected from increased viscosity

Universal scaling of DNA mobility is driven solely by reduced solution volume

DNA diffusion in dextran solutions

DNA mobility reduction is independent of DNA topology

Mobility decreases less than classically expected from increased viscosity

Universal mobility reduction scales exponentially with crowder volume fraction
Crowding induces topology-dependent changes in DNA conformation

Distribution of DNA Conformations

Ring DNA compacts
Linear DNA $R_{\text{max}}$ increases

Compacted ring DNA is ~47% of random coil volume

Do linear chains swell or elongate?

Crowded Ring DNA compacts while linear DNA elongates

Distribution of DNA Conformations

Compacted ring DNA is ~47% of random coil volume

Do linear chains swell or elongate?

Elongated and compacted conformations are smaller than random coils

Distribution of DNA Conformations

Compacted ring DNA is ~47% of random coil volume

Elongated linear DNA is ~66% of random coil volume

Elongated and compacted conformations are smaller than random coils

Dilute Linear DNA
Random Coil

Crowded Linear DNA
Coil Elongation

Compacted ring DNA is
~47% of random coil volume

Elongated linear DNA is
~66% of random coil volume

Crowder entropy maximization drives DNA to elongate or compact to facilitate diffusion.

Crowding forces DNA into lower entropy state to maximize entropy of crowders. Smaller volume DNA states can diffuse faster through viscous crowded environment.
We investigate molecular mechanics of crowded and entangled DNA and Actin

Mapping Deformations of Entangled Actin Filaments

Falzone, et al; *Soft Matter* (2015);

Optical tweezers microrheology measures molecular-level viscoelastic response

Bulk Rheology

Macroscopic Strain ($\gamma$) exerted
Resultant Stress ($\sigma$) on material measured

Solid: Elastic

Fluid: Viscous

Viscoelastic

Microrheology

Molecular-level Strain ($\gamma$) exerted
Resultant Stress ($\sigma$) measured
The response of entangled polymers to large deformations is complex and not well understood.

Small strain amplitudes = linear viscoelastic response

Large strain amplitudes & rates = nonlinear viscoelastic response

No disruption of entanglements
No chain stretching

Classical tube theory cannot explain bulk experimental data
New proposed theories remain untested

Classical tube theory describes data well
We track actin filament deformations induced by microscale strains

Discretely label segments along entangled actin filaments

Track segment displacements during and following microscale strain

We track actin filament deformations induced by microscale strains

Discretely label segments along entangled actin filaments

Track segment displacements during and following microscale strain
We map filament deformations throughout the network out to mesoscopic length scales.

Quantify displacement dependence on distance from strain path.

Track segment displacements during and following microscale strain.
We couple microscale stress response to induced deformations of actin filaments

Quantify displacement dependence on distance from strain path

Measure force filaments exert to resist strain
We link discrete filament displacements and microscale forces to mesoscale network deformations.

What macromolecular deformations lead to the resistive network force response?

How do induced deformations & stress propagate through the network?
Elastic force response yields to dissipation at rate-dependent distances

Relative resistive force actin exerts

Elastic response yielding point increases with strain rate

The disentanglement time controls dissipative yielding of entangled actin

Relative resistive force actin exerts

Elastic response yielding point increases with strain rate

slower than $\tau_{\text{ent}}^{-1}$

faster than $\tau_{\text{ent}}^{-1}$

Yield time $\approx$ theoretical

Disentanglement time $\tau_{\text{ent}}$

Entangled actin elasticity yields to dissipation when individual entanglements can relax

Unexpected stress-stiffening of entanglements suggests strain-induced crosslinking

Relative actin response stiffness

How do entanglements deform to produce stiffening response?

Faster than $\tau_{\text{ent}}^{-1}$

Slower than $\tau_{\text{ent}}^{-1}$

Can microscale stiffening lead to macroscopic softening?

nonlinear stress-stiffening only predicted/measured for crosslinked actin networks

We map the propagation of filament deformations throughout the network

Stress-stiffening is coupled with long-range strain propagation & effective crosslinking

Fluid-like deformations exponentially die out 
\( \sim \) persistence length from bead path

Rigid entanglement deformations propagate out to several persistence lengths

Long-range linear dissipation of deformations: macroscale signature of crosslinked networks

Fractional recovery of entanglement deformations quantifies elasticity of response

Fluid-like deformations exponentially die out ~persistence length from bead path

Rigid entanglement deformations propagate out to several persistence lengths

Long-range linear dissipation of deformations: macroscale signature of crosslinked networks

Actin persistence length controls spatial crossover to continuum network mechanics

All deformations beyond persistence length from strain display self-averaging behavior

Discrete entanglement segments are mechanically linked by the persistence length of semiflexible actin filaments

Mesoscale spatial crossover to continuum mechanics unique to semiflexible polymers

Recovery mechanics display nonclassical tube dilation near strain path

Mechanics following strain

Force and deformation recovery display entanglement tube dilation near strain

Dilated entanglements exponentially contract to classical size far from strain

Mesoscale continuum mechanics suppress microscale nonlinearity

Mechanics following strain

Force and deformation recovery display entanglement tube dilation near strain

Dilated entanglements exponentially contract to classical size far from strain

Microscale nonlinearity suppressed to linear response beyond persistence length

Deformation recovery

Exponential deformation recovery rates
Molecular-level experiments reveal complex biopolymer dynamics in entangled & crowded systems

Diffusion & Conformation of Crowded Linear & Ring DNA

Crowding-induced compaction & elongation facilitates DNA diffusion

Mapping Deformations of Entangled Actin Filaments

Persistence length controls crossover to continuum network mechanics

Nonlinear strains induce crosslinking of entanglements


Falzone, et al; Soft Matter (2015);
Undergraduate Women can do amazing things!

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