Physical properties of F-actin and filamentous phages: phase transitions, networks and motions

Jay X. Tang

Department of Physics & Institute of Molecular Biology
Indiana University, Bloomington, IN
Email: jxtang@indiana.edu
http://physics.indiana.edu/~jxtang/

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Outline

• Introduction: filamentous viruses and F-actin as model semiflexible polymers
  • Isotropic-nematic phase transition and filament dynamics
  • Rheology and mechanical manipulations
  • Cell motility: molecular mechanism of force generation and movement
Physical properties of F-actin and filamentous phages: ...

filament length ≈ 0.9 μm
diameter ≈ 7 nm
molecular mass ≈ 16.4 × 10^6 Da
linear charge density ≈ −10e/nm

Atomic Model of F-actin

**Physical properties of F-actin and filamentous phages:**

**Polymerization of Actin**

- MW = 42,000 Dalton
- G-F transition
- Condensation model (F. Oosawa, 1960s)
- Binding energy ~14 kT
- Critical concentration < 1 µM, or 0.04 mg/ml
- ATP hydrolysis

**Thermodynamics of Actin Polymerization**

- **Exercise:**
  a. The critical concentration of actin is 3 µM at 10°C, which decreases to 0.5 µM at 25°C. Calculate changes of both enthalpy & entropy?
  b. Is the actin polymerization an endothermal or exothermal process?  
  F. Oosawa, 1975, Thermodynamics of the Polymerization of Proteins

- **Solution:**
  a. \[ K_d = c_c \Rightarrow \ln c_c = G/RT \Rightarrow \]
     \[ \ln c_c = \Delta H/RT - \Delta S/R \Rightarrow \]
     \[ \Delta H = 20 \text{ Kcal/mol}, \]
     \[ \Delta S = 28 \text{ Kcal/mol} \]
  b. Actin polymerization is an endothermal process. The process absorbs heat and gains entropy, via changes in interactions among protein, ions & water (hydration).
Physical properties of F-actin and filamentous phages: ...

Actin in Cells

* Alberts *et al*., Molecular Biology of the Cell

http://expmed.bwh.harvard.edu/projects/motility/neutrophil.html

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Physical properties of F-actin and filamentous phages: ...

Mechanistic model for cell motility

- Protrusion
- Attachment
- Retraction
- Repeat Protrusion

• Alberts et al., Molecular Biology of the Cell

Topic 1: Isotropic-nematic transition of F-actin

Isotropic | Anisotropic
Physical properties of F-actin and filamentous phages: ...

Labeled F-actin imbedded in a nematic network

Domain alignment of nematic F-actin following shear
Physical properties of F-actin and filamentous phages: ...
Physical properties of F-actin and filamentous phages: ...

I-N transition of F-actin is continuous in both concentration and orientational order parameter

![Graph showing birefringence and fluorescence as functions of position.]

Preferential longitudinal diffusion in the nematic state

![Images showing preferential diffusion.]

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Topic 2: Viscoelasticity of filamentous networks

• Biological motivation
• Semiflexible filaments in network
• Particle tracking microrheology
• Mechanical manipulation by AFM
• Nanoelectronics and mineralization
Physical properties of F-actin and filamentous phages: ...

**Biological Motivation**

- Filamentous networks occur in many physiological settings
- Cell is not just a bag of enzymes, but instead has a filamentous skeleton
- Cytoskeletal structure is essential for scaffolding, transport, signaling, force transmission, motility, etc.

Svitkina & Borisy, JCB, 1999

**Viscoelasticity of semiflexible polymer network**

Theory of polymer dynamics

de Gennes, 1970s
TUBE MODEL & REPTATION

Recent treatments for network of semiflexible polymers

A. Maggs, 1994, PRE
F. MacKintosh et al, 1995, PRL
R. Granek, 1997, J. Phys
E. Frey et al, PRE & PRL, 1998
D. Morse, Phys. Rev. E; Macro., 1998

The stress tensor and response times
Measurement of Viscoelasticity

- Macrorheology
  - Parallel plates (cone-plate) mechanical rheometer
  - Magnet driven rotating disk rheometer (Sackmann)

- Microrheology (beads rheology)
  - Magnetic tweezers (Sackmann)
  - Diffusing wave spectroscopy (Weitz)
  - Particle tracking microrheology (PTM) (Schmidt, Kuo)

- Mechanical manipulation using AFM

Viscoelastic moduli of fd network

Theory Curves
D. Morse

Exp. Data
Schmidt, Hinner
Sackmann & Tang
PRE 2000
Physical properties of F-actin and filamentous phages: ...
Physical properties of F-actin and filamentous phages: ...

Force measurements and mechanical manipulation of actin network by AFM

- Alberts et al., Molecular Biology of the Cell

Typical force distance curves for AFM
Physical properties of F-actin and filamentous phages: ...
Other projects using solution AFM

- Single filament conductivity
- Nano-fabrication by mineralization

Is F-actin a conducting nanowire in solution?

- Interest and controversy of DNA conductivity (Fink, Nature, 1999; de Pablo, PRL, 2000)
- Importance of protein filaments in scaffolding and transport in cells
- Ionic flux and physiological functions

- Cable-like properties of F-actin in solution will be measured using conducting AFM tips in combination with the micro-patterning technique
Physical properties of F-actin and filamentous phages: ...

Topic 3: Physics behind cell motility

• Video segments on cell motility
• Understanding the listerial head rotation by extending a symmetry breaking concept
• Current effort towards understanding the helical tail growth

Listeria monocytogenes moving in PtK2 cells (150x)

http://cmgm.stanford.edu/theriot/movies.htm
Physical properties of F-actin and filamentous phages: ...

Concept of spontaneous symmetry breaking to explain the initiation of directed motion


Rotatory motion of a bacterium while propelled by its own tail

http://cmgm.stanford.edu/theriot/movies.htm
Physical properties of F-actin and filamentous phages: ...

Summary & Future Directions

- Features of I-N phase transitions for F-actin
- Polyelectrolyte properties of viruses and protein filaments
- Viscoelasticity of biopolymer network
- Actin network dynamics and force generation

- Self-assembly of bio-complexes (protein filaments, lipids, DNA, viruses, etc.)
- Rheological properties of semiflexible filament network
- Protein filament nano-electronics and transport properties
- Understanding physical mechanisms of cell motility
- Applying physics of protein-assembly and networks to cell biology and disease intervention

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