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Mechanics of Model Microtubules

MARK J. STEVENS

Sandia National Laboratories

Center for Integrated Nanotechnologies(CINT)
msteve@sandia.gov

Shengfeng Cheng → Virginia Tech

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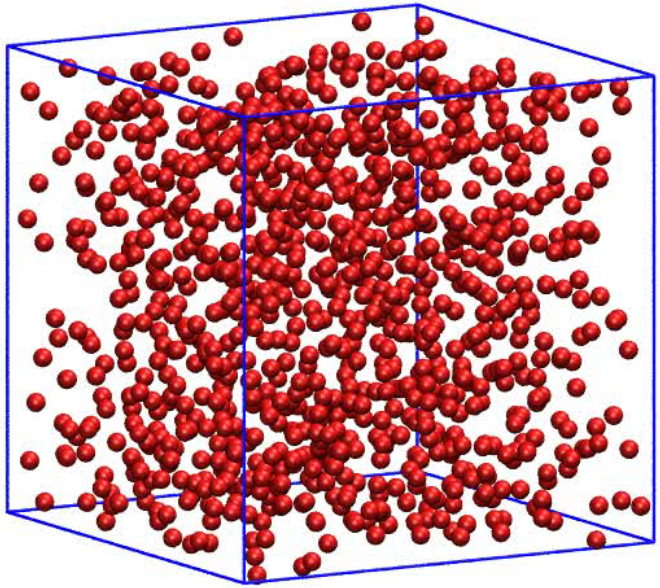
MD Simulations

- standard NVT MD, ~ 1 billion time steps
- 1000 achiral wedge monomers

- Starting state: with A_L =4.2 kT and A_V =3.0 kT
- Wedge shown as single sphere
- Monomers to tubules



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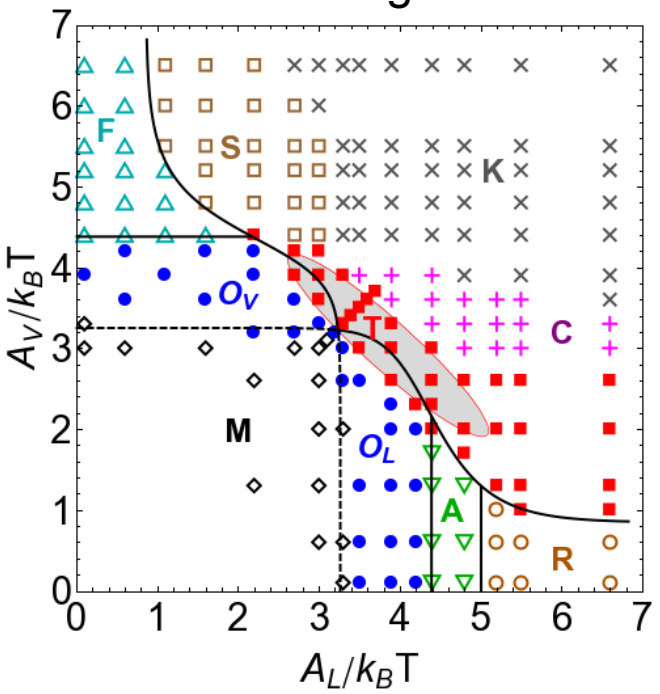
vary lateral A_L and vertical A_V interaction strengths

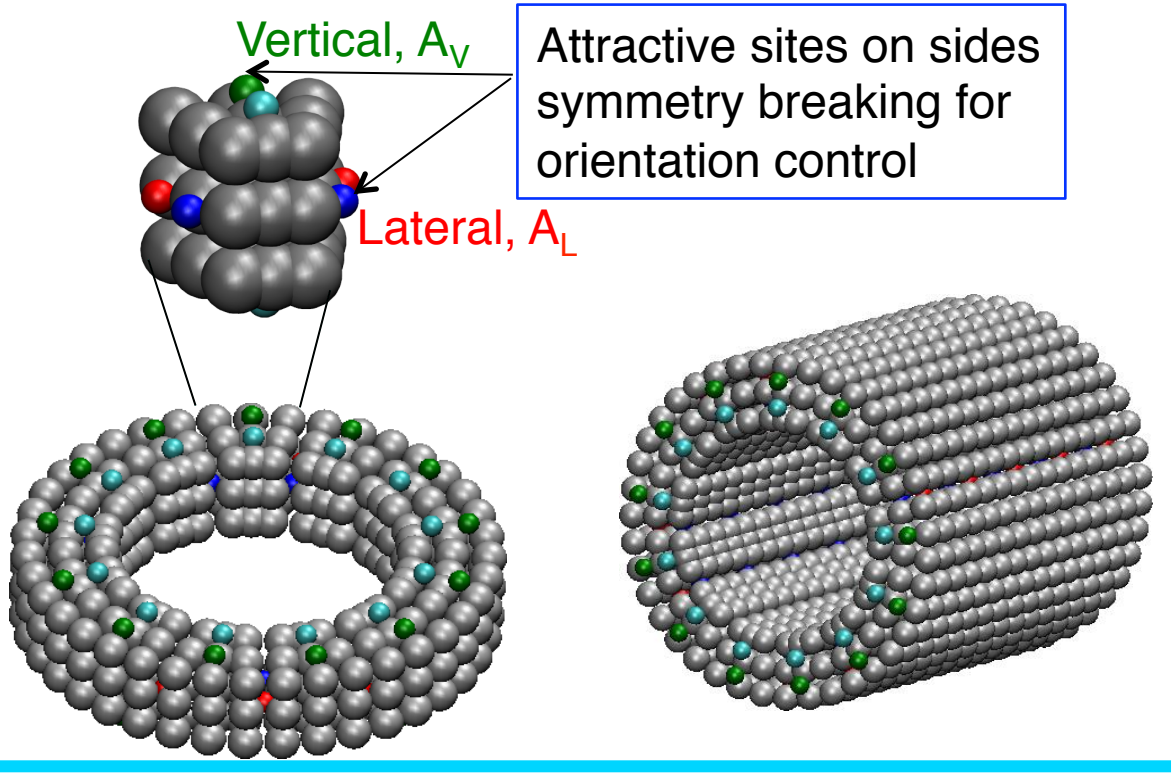


Mark Stevens
msteve@sandia.gov

Monomer Model

Wedge monomer
- shape designed to produce rings that stack into cylinders
  - 13 wedges/ring
  - gray particles define shape
  - rigid body
- gray particles interact purely repulsively
- attraction only between sites of same 'color'
- implicit good solvent

monomer
- (rigid) body
- shape (not spherical)
- surface-surface interactions

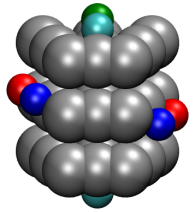


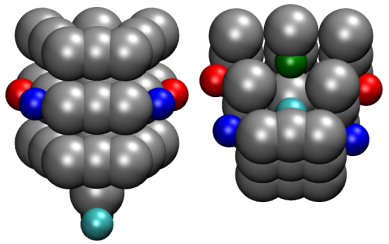
Mark Stevens
msteve@sandia.gov

Tubule Pitch

- How control pitch?
  - chiral monomer
  - reduce variation in pitch
- Twist misaligns vertical placement
  - increase A_v ?
  - lock & key

Chirality *c*
Shift positions of lateral site up/down to produce chirality





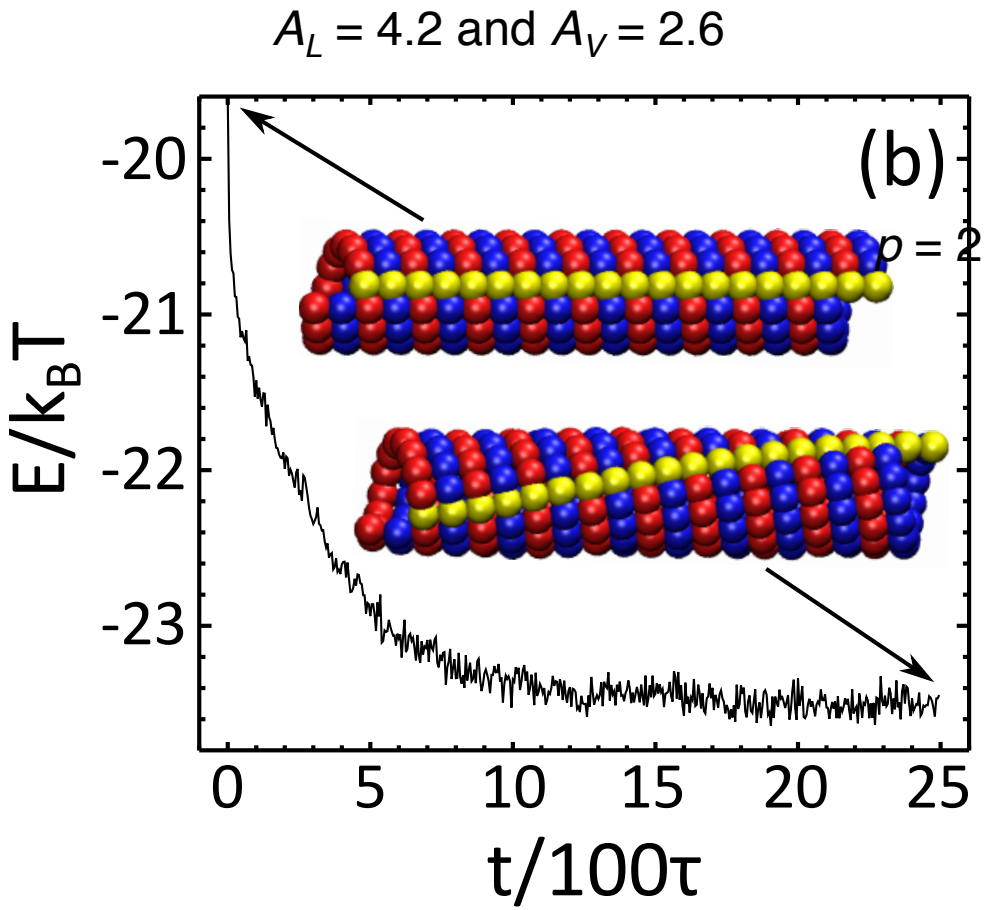
Lock & Key *LK*
Push central column down

Mark Stevens
msteve@sandia.gov

Twist & Energy

- Build tubule with pitch *p*
- Do MD
- Calculate energy distribution

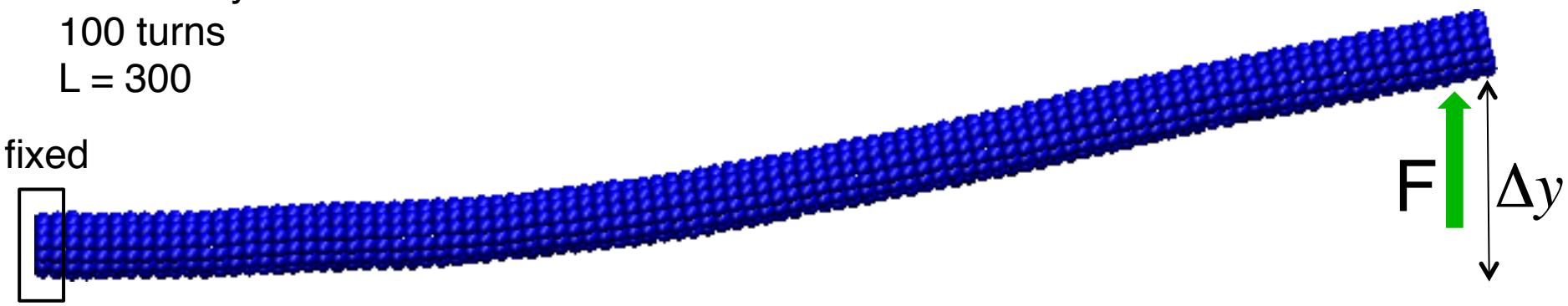
- Tubule twists
- Energy drops
- Stabilizes structure with pitch



Mark Stevens
msteve@sandia.gov

Schematic of Beam Bend

A_V=4.2 A_L=2.6
no chirality
100 turns
L = 300

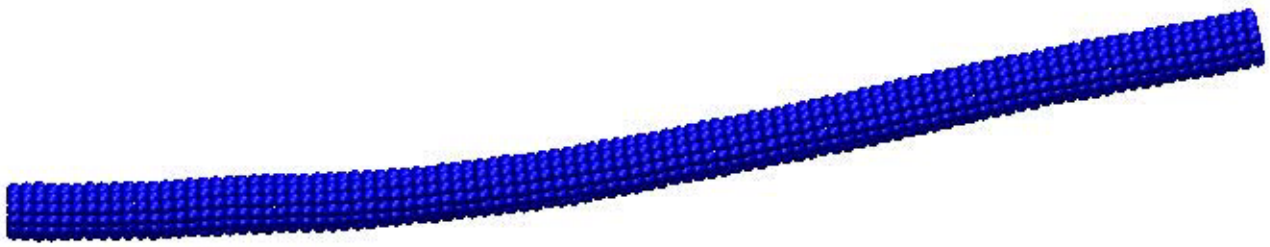


$$\Delta y = F\frac{L^3}{3EI}$$

$$E = F\frac{L^3}{3I\Delta y}$$

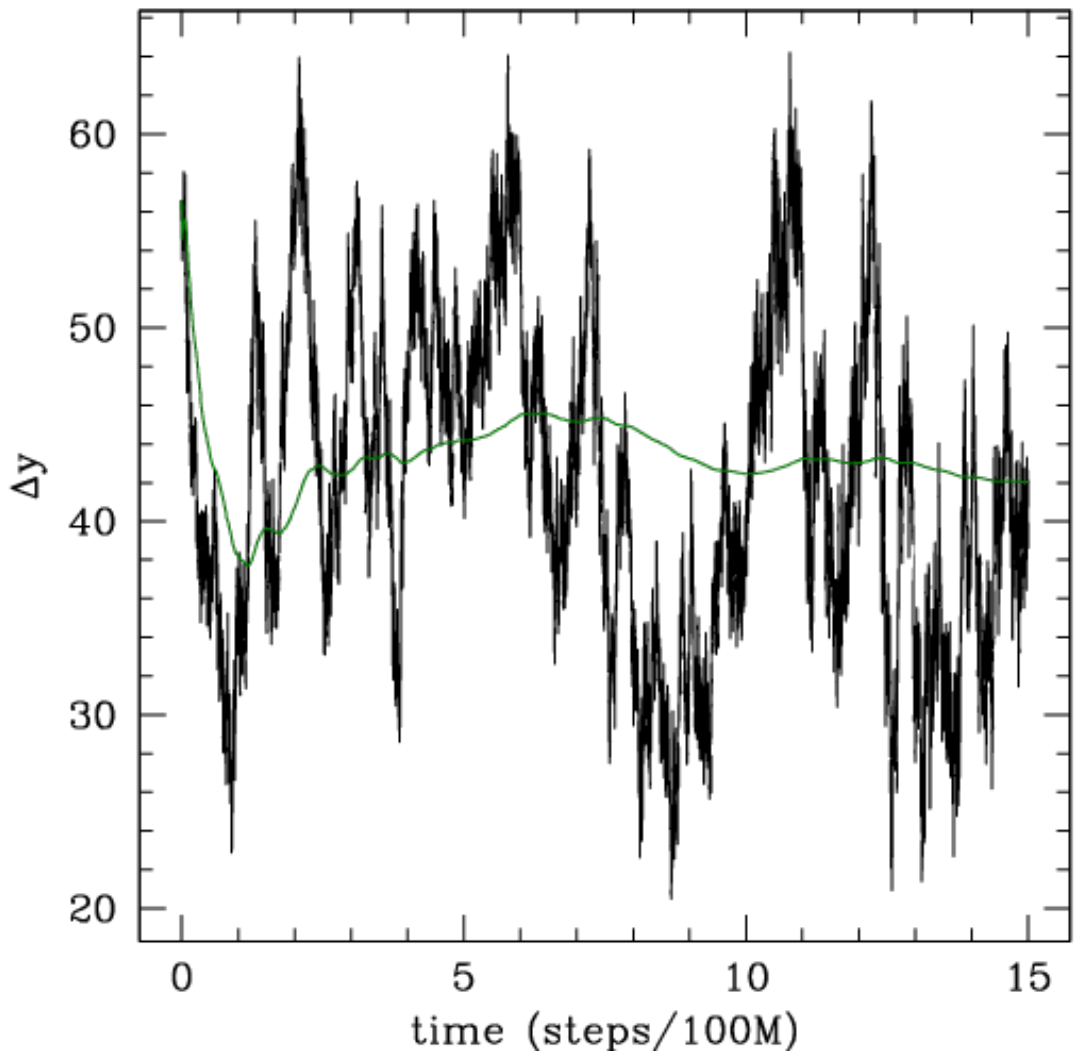
Mark Stevens
msteve@sandia.gov

Dynamics



Time dynamics

100 turns
chirality = 0
F = 0.003

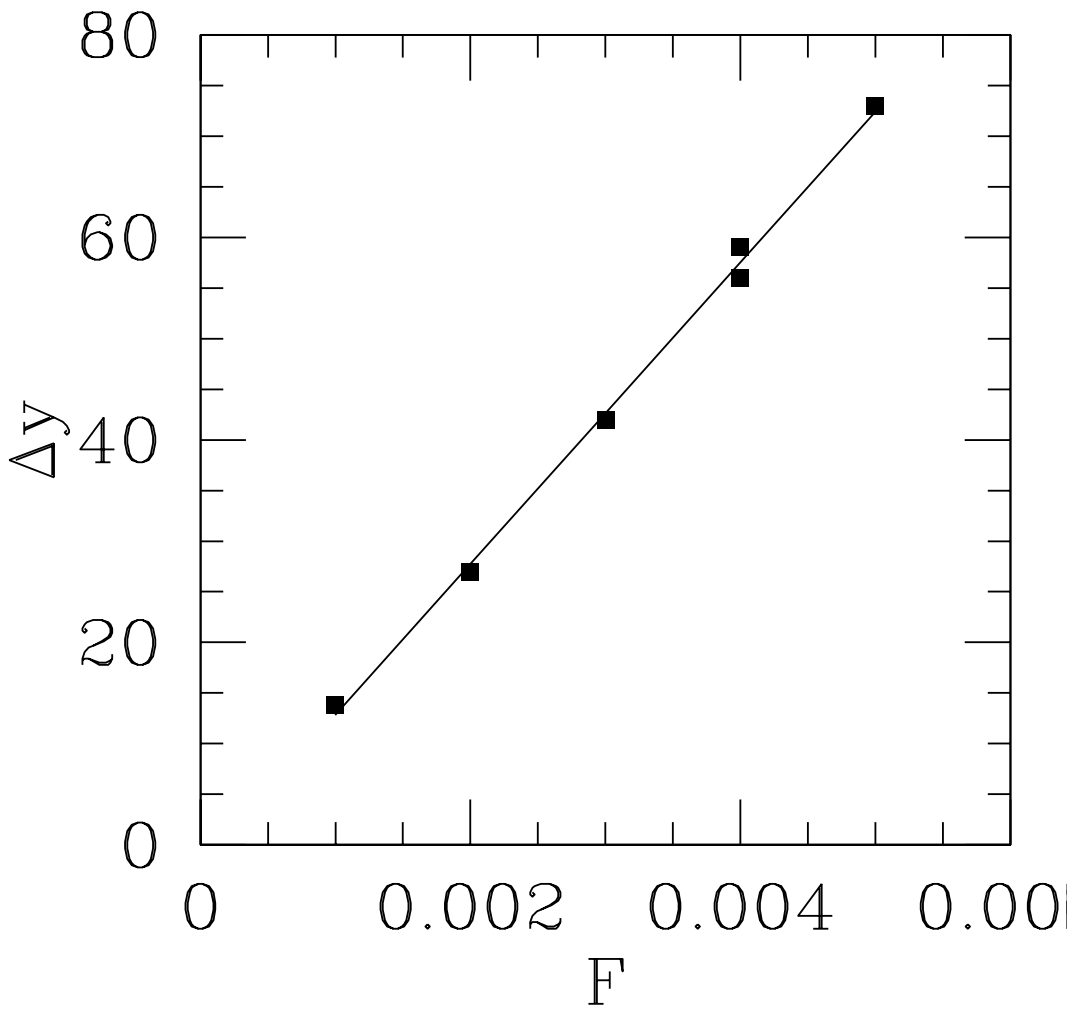


Mark Stevens
msteve@sandia.gov

Bend vs. Force

A_V=4.2 A_L=2.6
no chirality
100 turns
L = 300

E = 0.4



Mark Stevens
msteve@sandia.gov

N = 1000

A_V=4.2 A_L=2.6
no chirality
1000 turns
L = 3000d

Take 3d = 4 nm
Then have 4 μ long tube.

Mark Stevens
msteve@sandia.gov

Summary

Doing micron long tubules within experimental range.
Tubules could be stiffer.
Stiffness is related to ‘rigid’ body interaction + binding interaction.

Effect of chirality, lock & key … TBD

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msteve@sandia.gov

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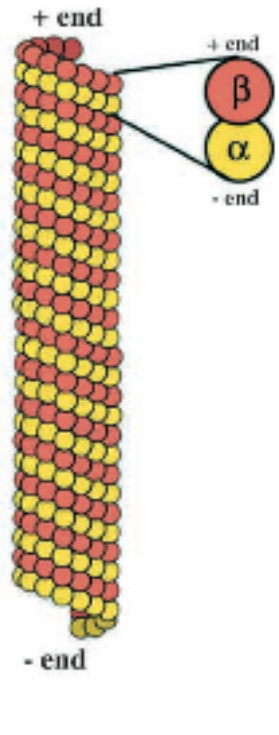
Microtubules

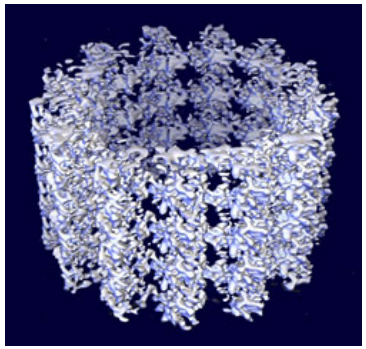
monomer is α-β tubulin
13 monomers per turn
24 nm diameter
polymerization/depolymerization
- protofilaments→sheets→tubules
- catastrophe
- polarity
- binding involves GTP/GDP

motor proteins walk on MT

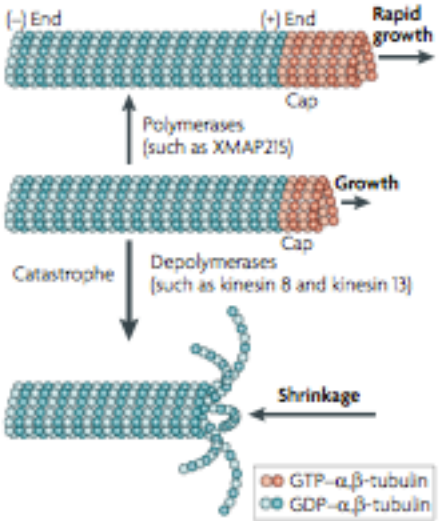
tubulin polymers
- straight: protofilaments, GTP bound
- curved: depolymerizing protofilaments/GDP bound

Microtubules are an example of heirarchically assembled structure with many interesting features.





GTP cap



GDP filaments bend

Mark Stevens
msteve@sandia.gov

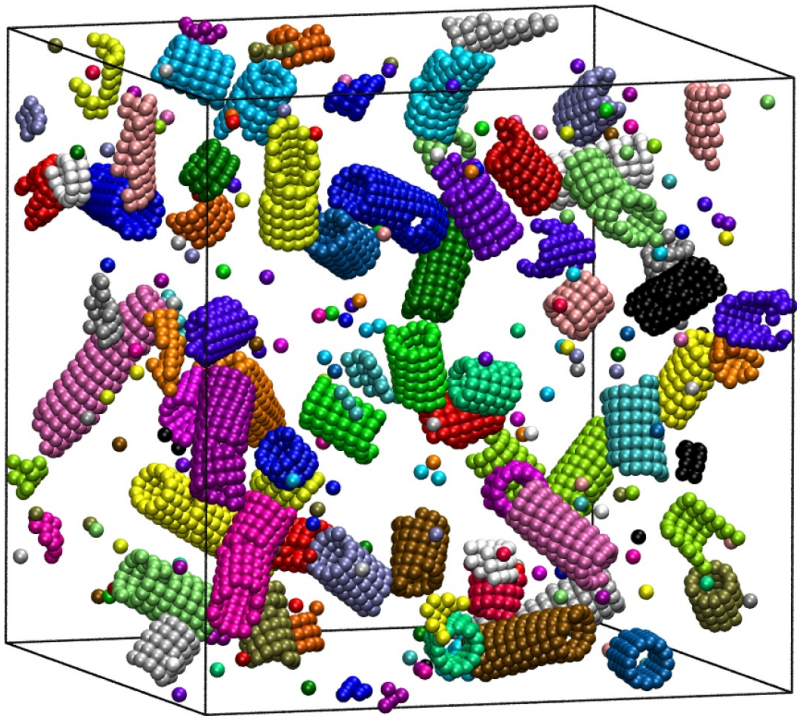
What are the factors that control assembly?

What features are necessary in the monomer?

The monomer is going to be a nanoparticle or a macromolecule (e.g. dendrimer) with large surface area.

- How do monomer shape and structure influence polymer structure (i.e. tubule).
- Where are interaction sites placed?
- How strong should they be?

Proteins as monomers possess a complex set of interactions.



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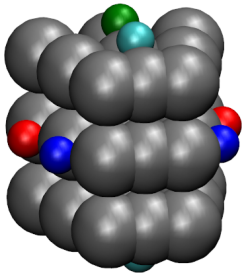
Theoretical Structure Diagram

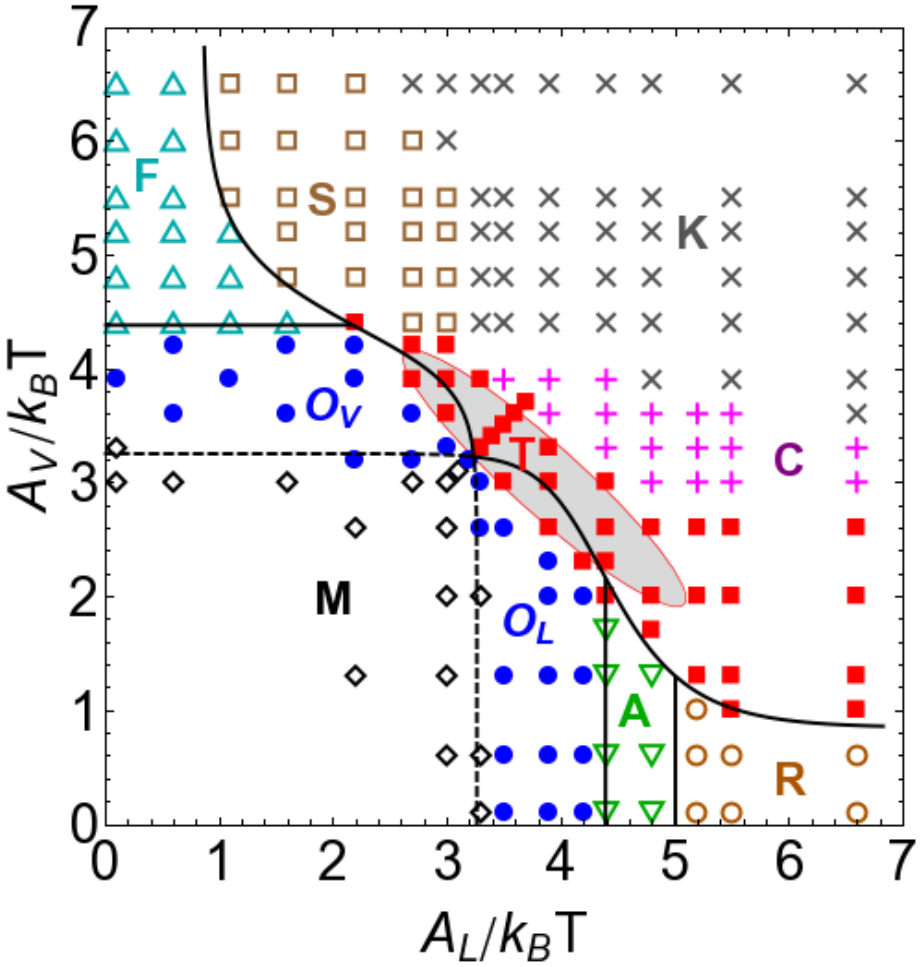
Each wedge is represented by a sphere.
Color represents cluster size.

M) no assembly
O) oligomers
F) filaments
A) arcs
R) rings
S) sheets
K) kinetically trapped (gunk)
C) clusters
T) Tubes

vertical, A_v



Lateral, A_L



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