SAND2012-1533 C
SAND2012-1533C

Simulations and Theory of Model Microtubule Self-Assembly

Shengfeng Cheng and Mark Stevens

Sandia National Laboratories

Ankush Aggarwal

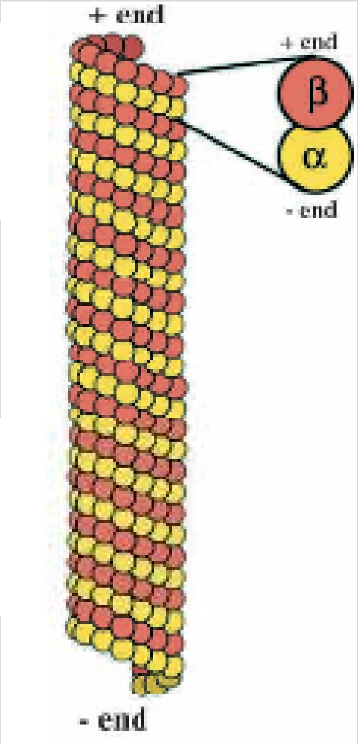
University of California Los Angeles

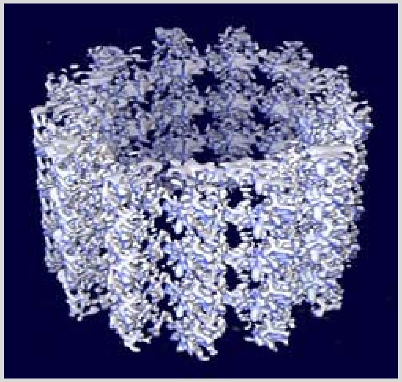
[arXiv:1201.2328: Self-assembly of artificial microtubules]

Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000

Microtubules and Tubular Structures

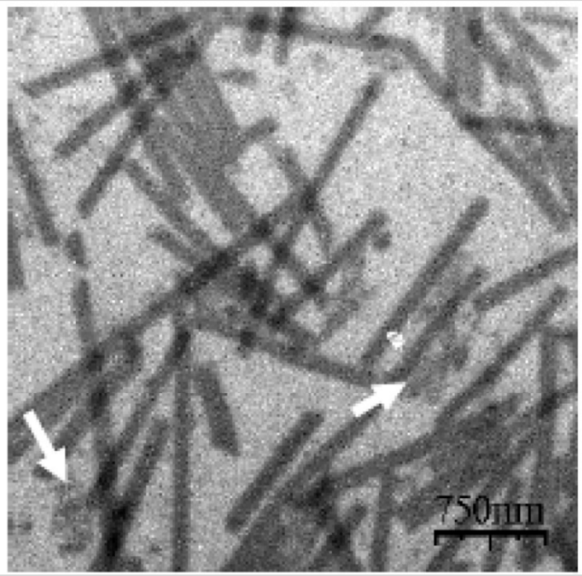
- monomer is α–β tubulin
- binding involves GTP/GDP
- tube contains 13 protofilaments
- polymerization/depolymerization
  - catastrophe
  - polarity
- γ-tubulin is a nucleation seed





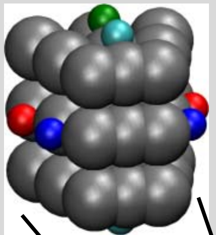
microtubule

- Tube-like structures of
  S-layer proteins
  amphiphilic macromolecules
  coiled nanofibers
  ...



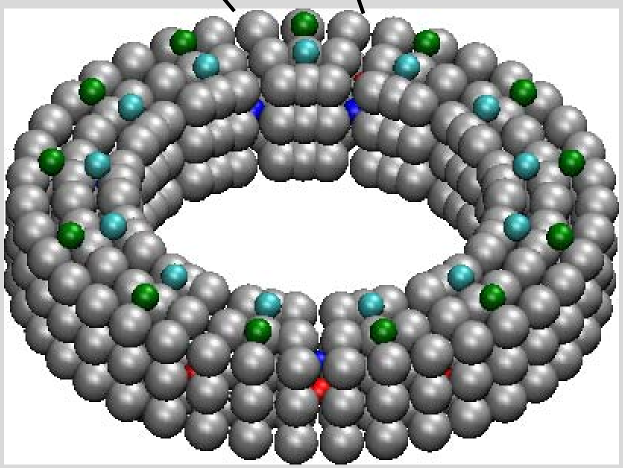
SEM of tubelike S-layer structures (Bobeth et al. 2011, Langmuir)

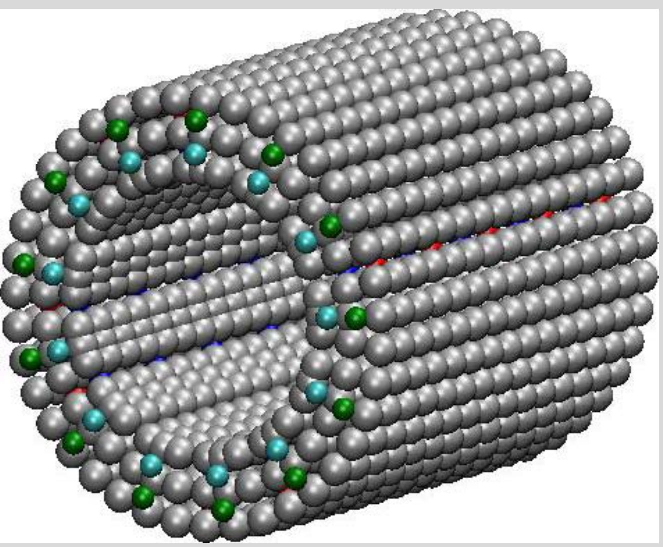
We use wedges as building blocks in MD simulations



rigid body

6 dof → 3 kT





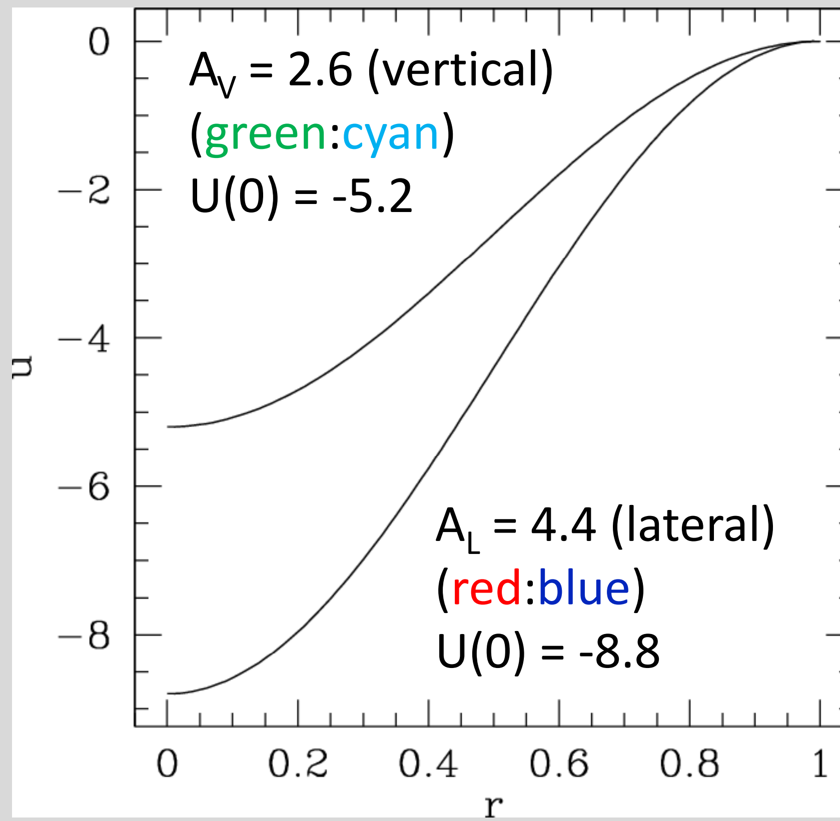
wedge particle

- similar to Rapaport for virus capsids
- designed to produce rings
- rings stack into tubes (13 wedges per ring)
- attraction only between specified sites
- gray particles interact purely repulsively

soft potential

$$U(r) = A\left[1+\cos\left(\frac{\pi r}{r_c}\right)\right]$$

$$U(0) = 2A$$

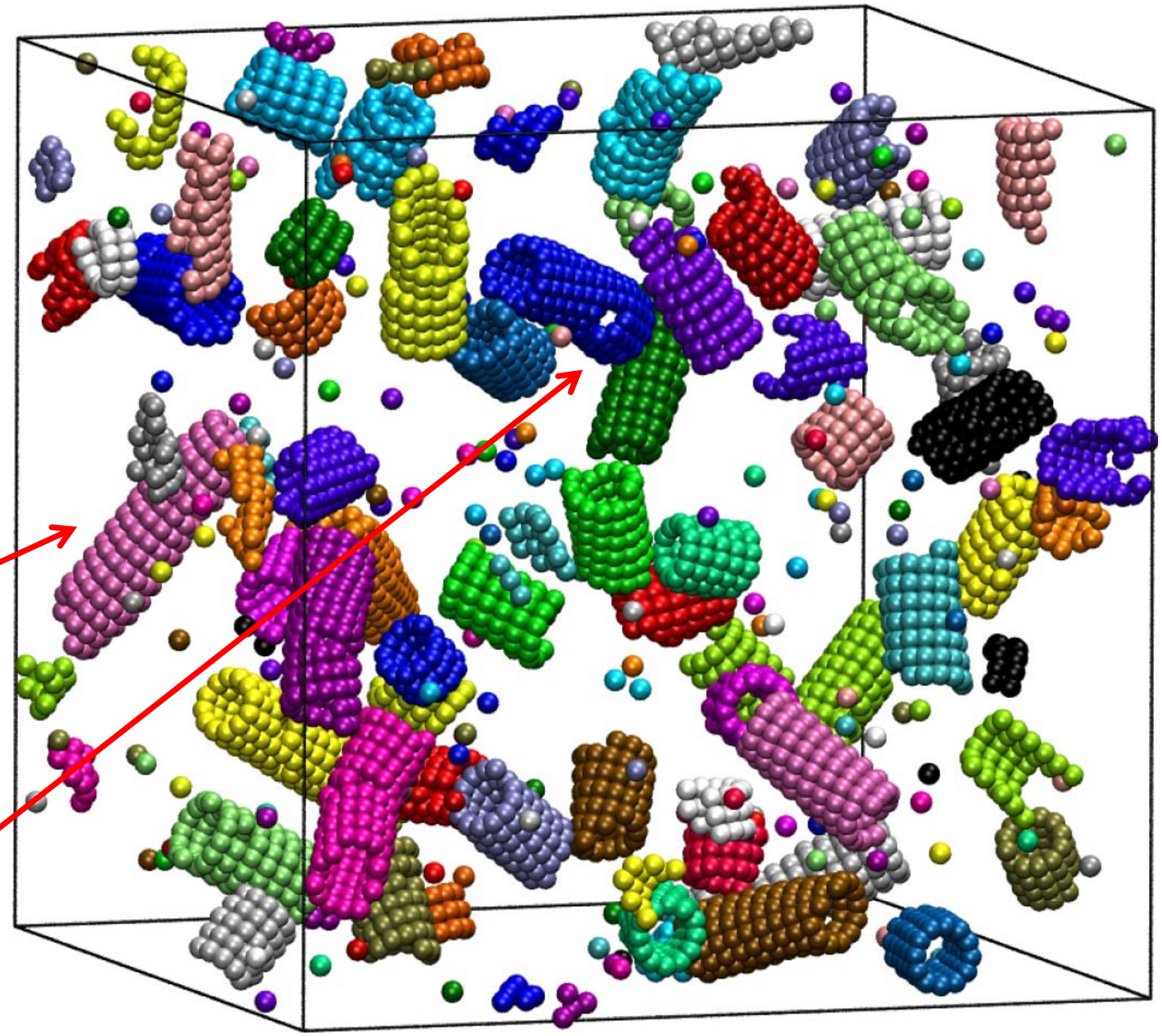


Self-Assembly of Wedges: An Example

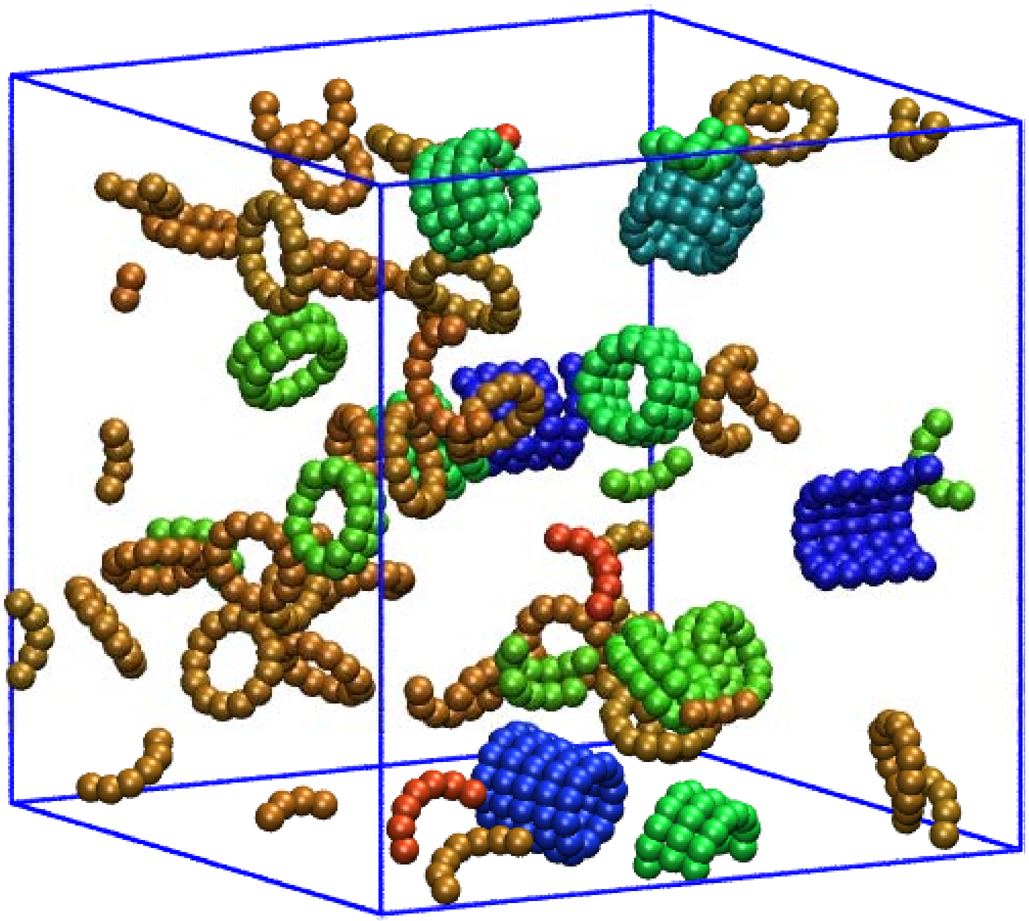
A_L =4.4 and A_V =2.6
monomer volume fraction ~ 4%
5000 wedge monomers
random distribution of monomers

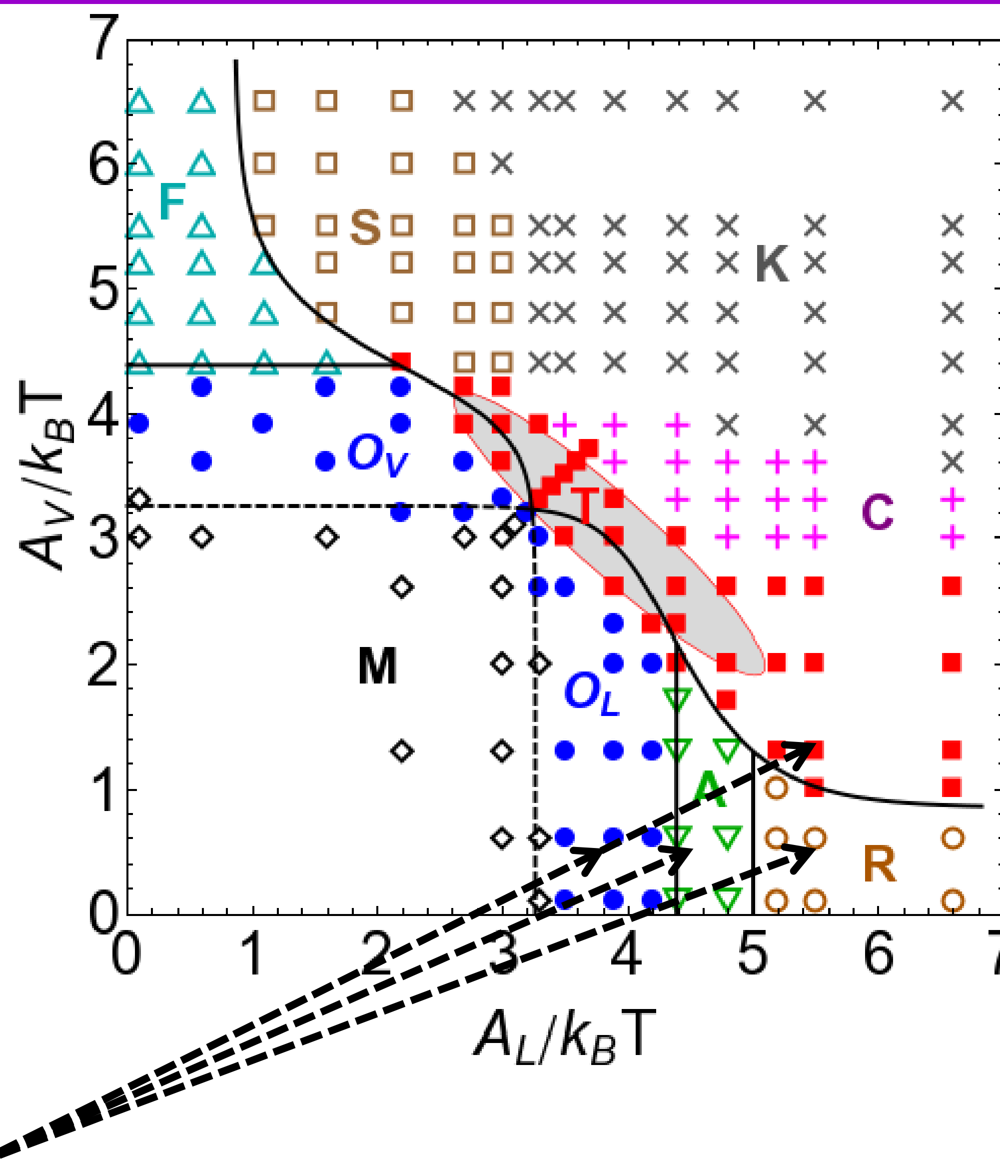
wedge shown as single particle
clusters size > 12 monomers

Many tubules & some fragments
with rings/tubes



Structure Diagram: Various structures can occur

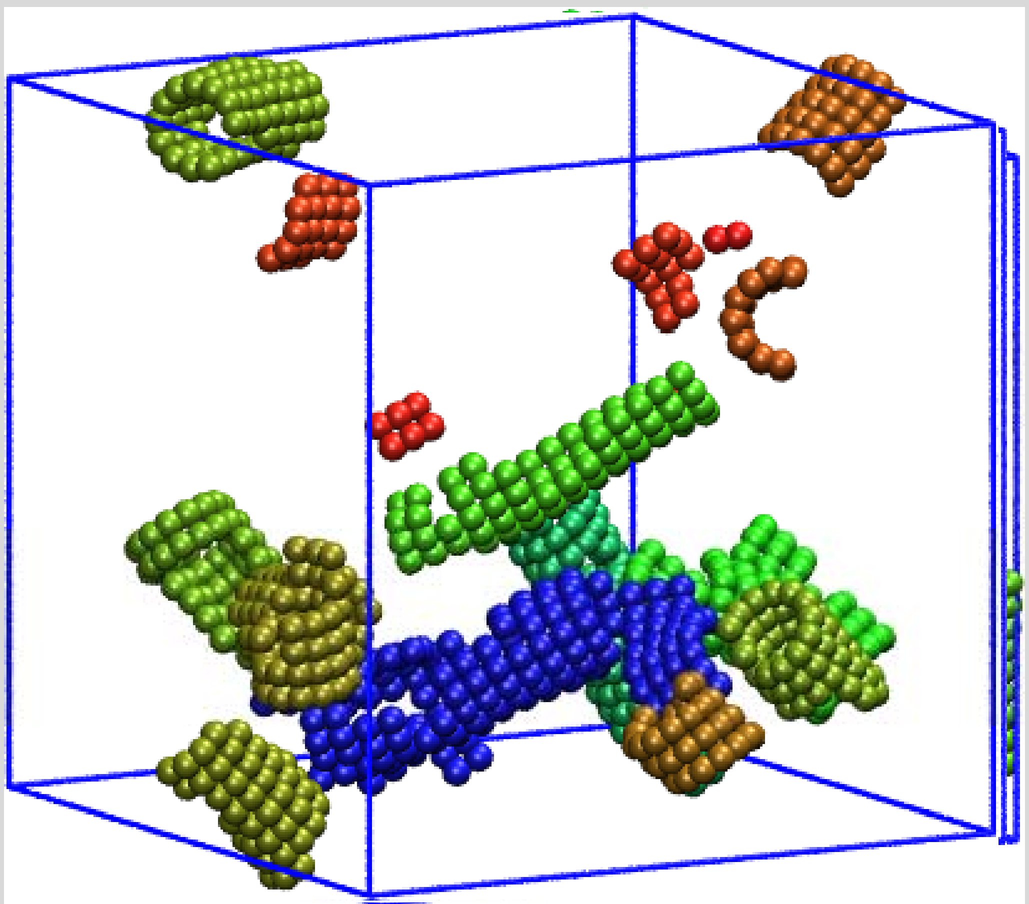


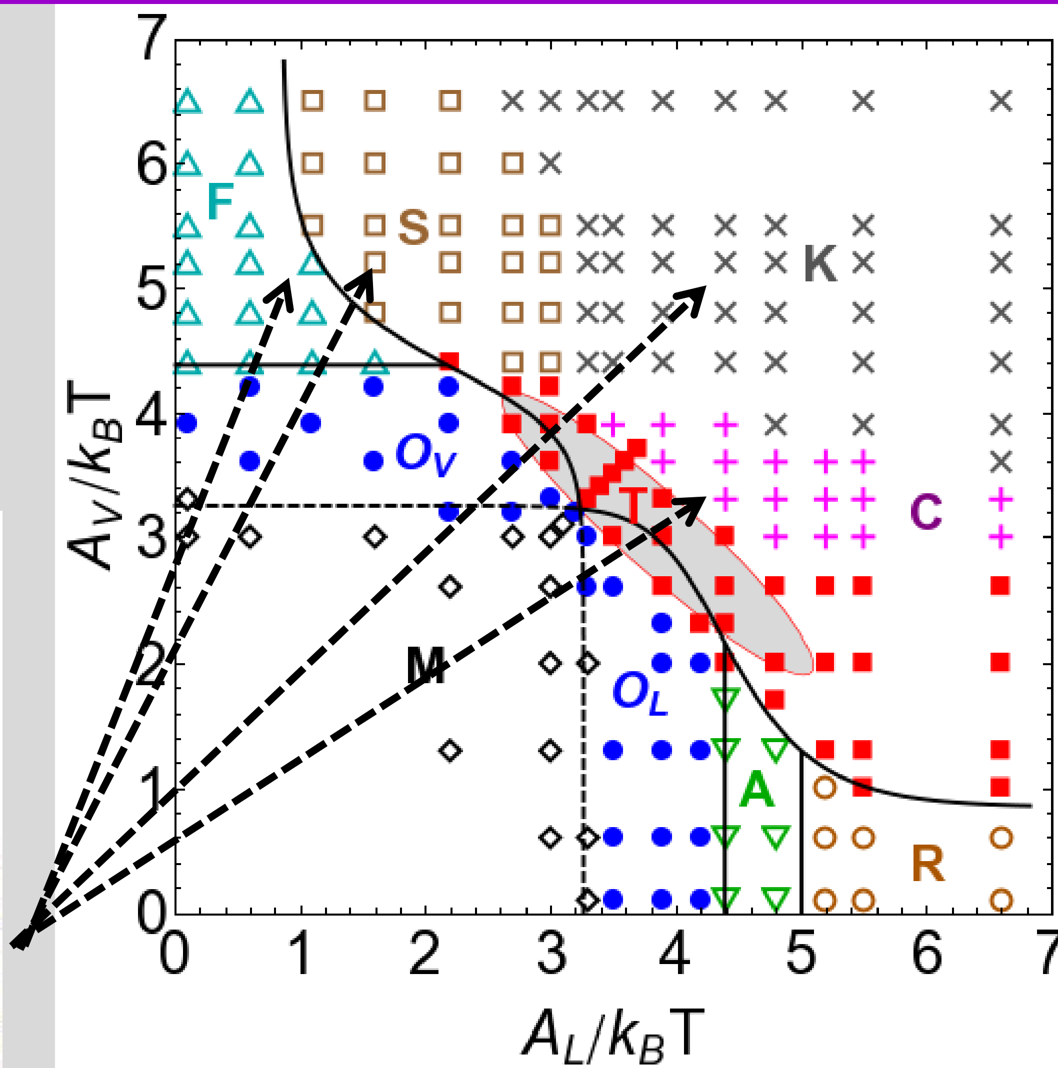


Structure Diagram (continued)

A_L=4.4 & A_V=5.2

percolated cluster

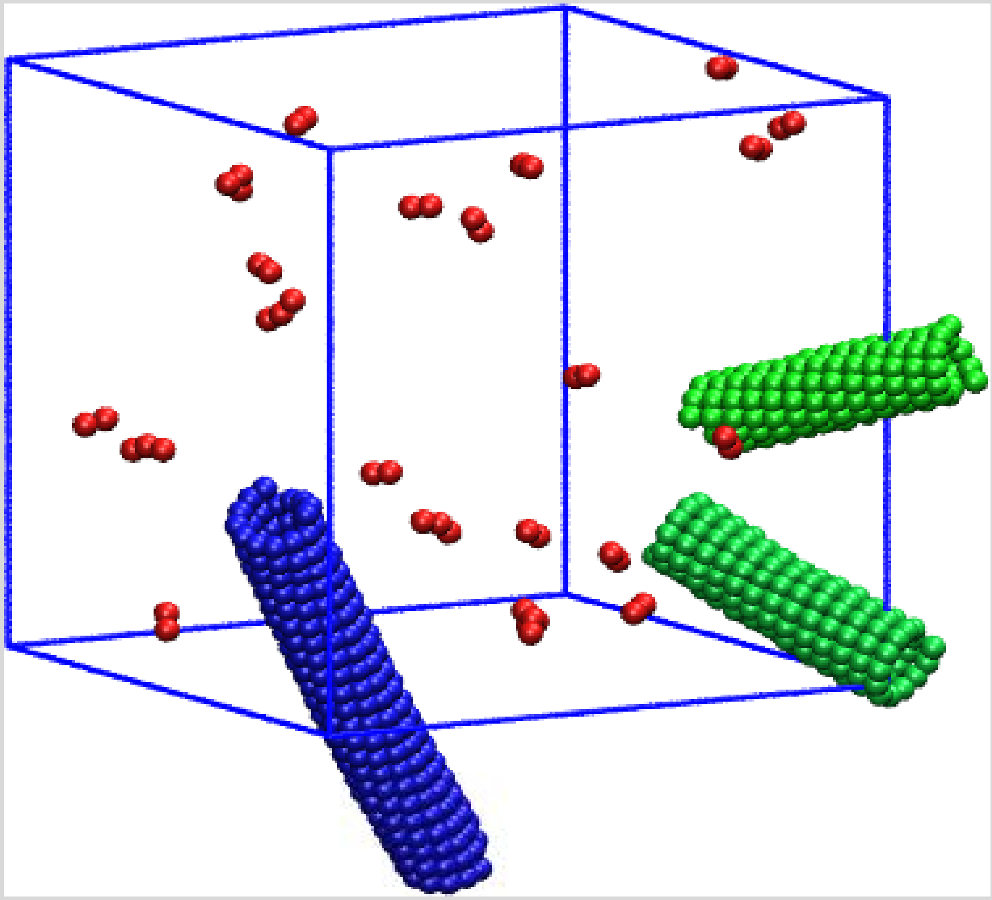


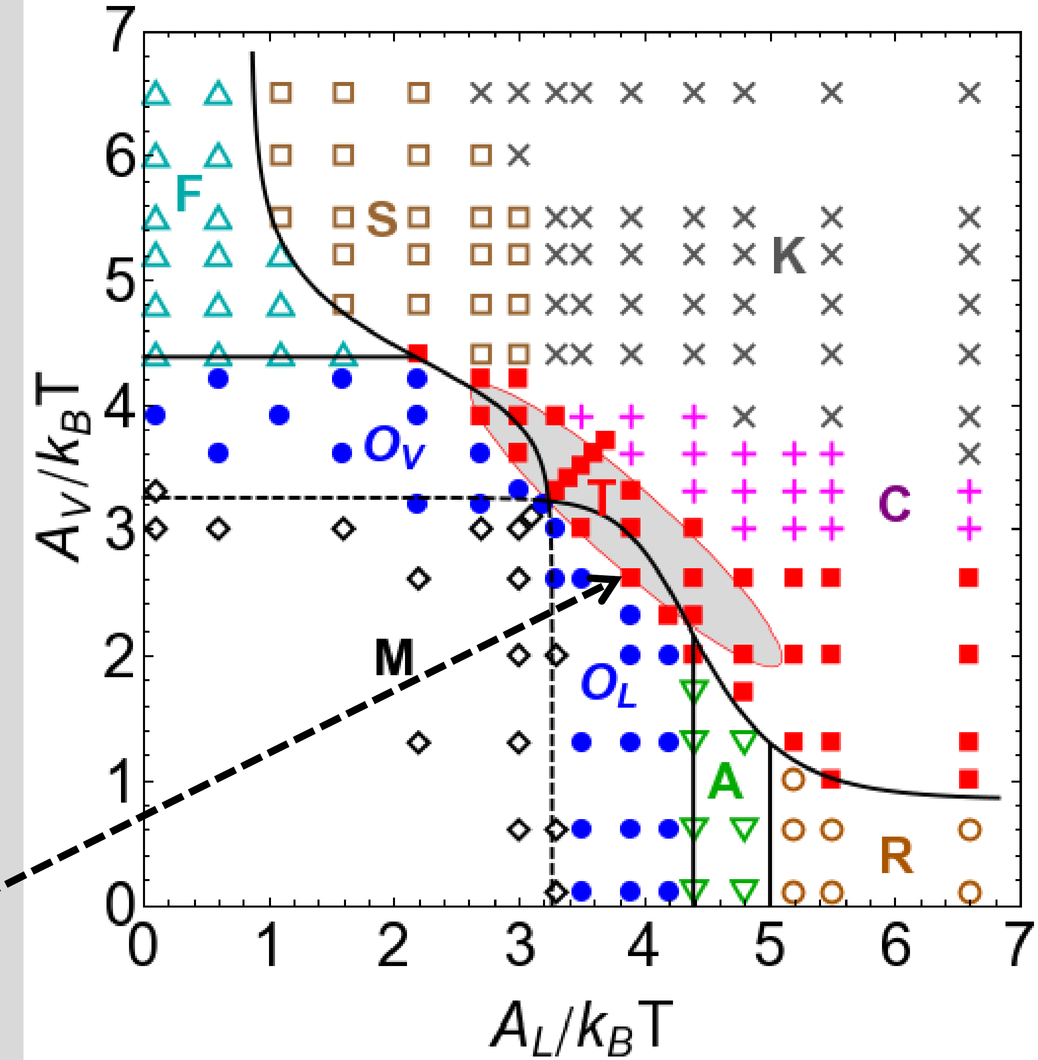


Tubes are only formed in a narrow range of A

A_L=3.9 & A_V=2.6

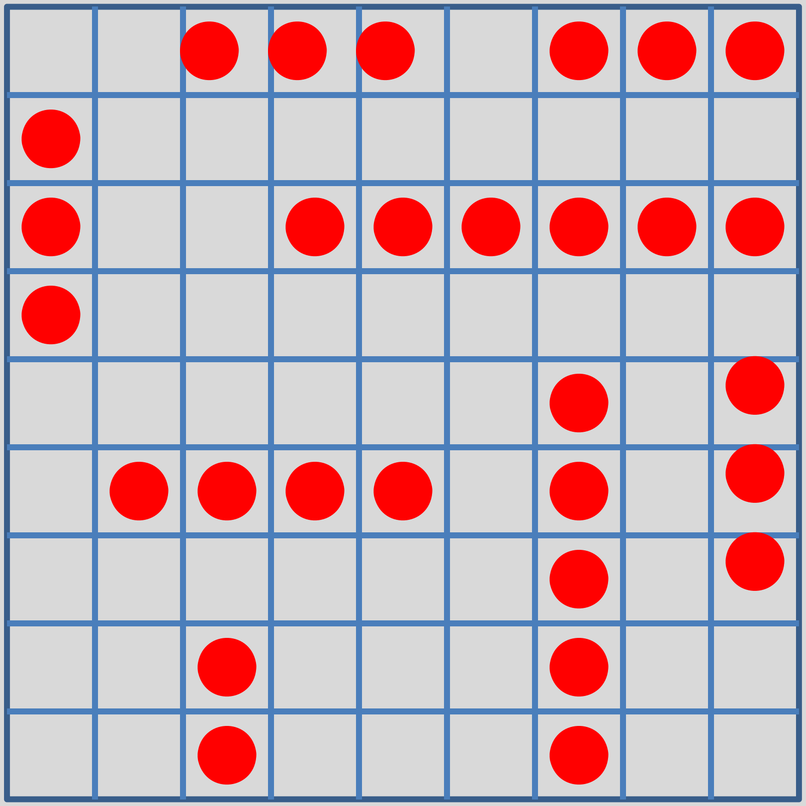
defect-free tubes (helical)





Reversibility of bonding is essential to remove defects by allowing structural rearrangements

A Flory-Huggins type lattice theory is developed to describe (straight) polymerization of wedges



When $A_L = 0$, wedges can only form straight chains through vertical bonding → straight polymerization

p : filament length

n_p: number of filaments with length p

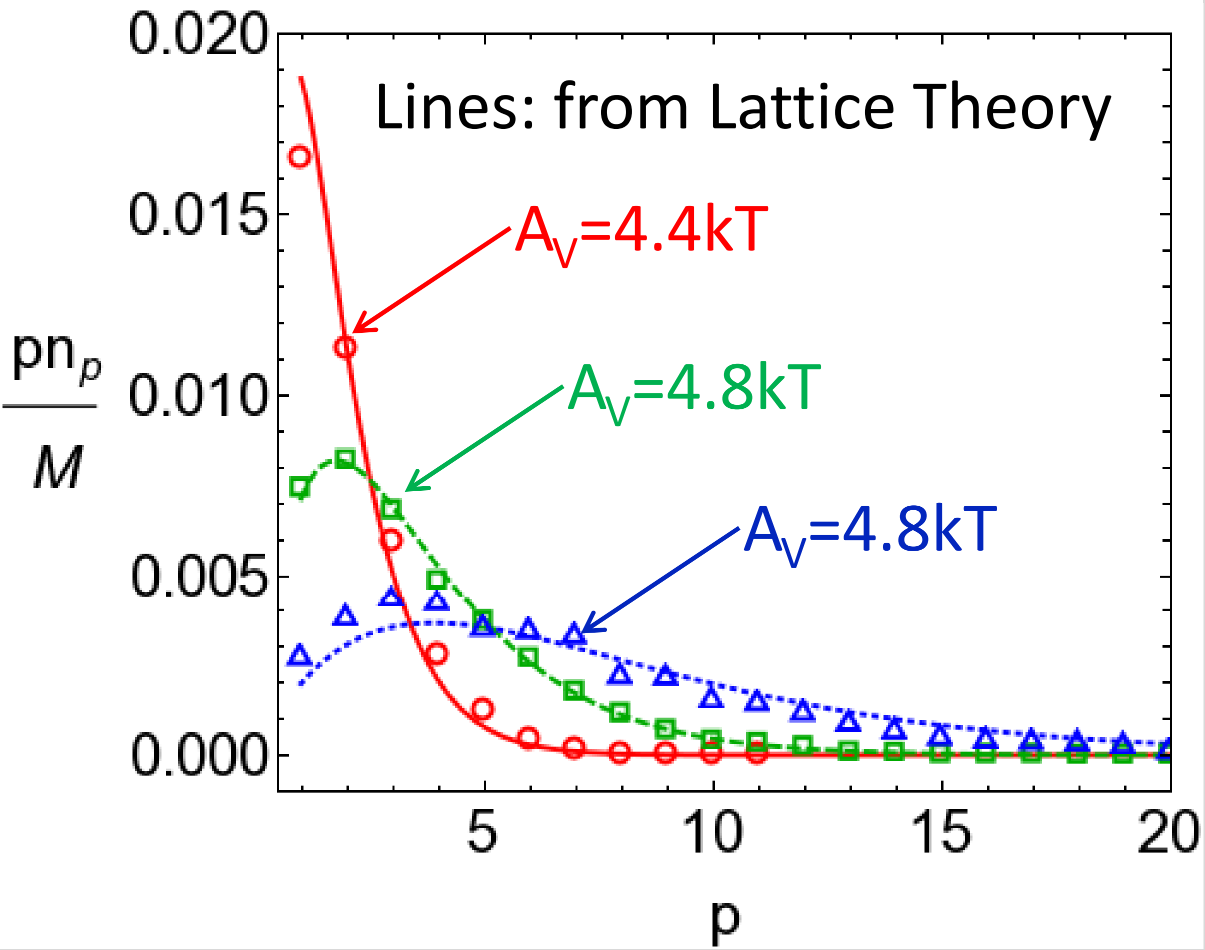
g : binding energy for each bond

$$F = \sum_{p=1}^{p_{max}} n_p \left((p-1)g - kT \ln z + kT \ln \frac{n_p}{M} - kT \right)$$

enthalpic contribution

entropic contribution

Mapping A in simulations to g in theory



$A_L = 0$
(straight polymerization)
p : filament length
n_p: number of filaments with length p

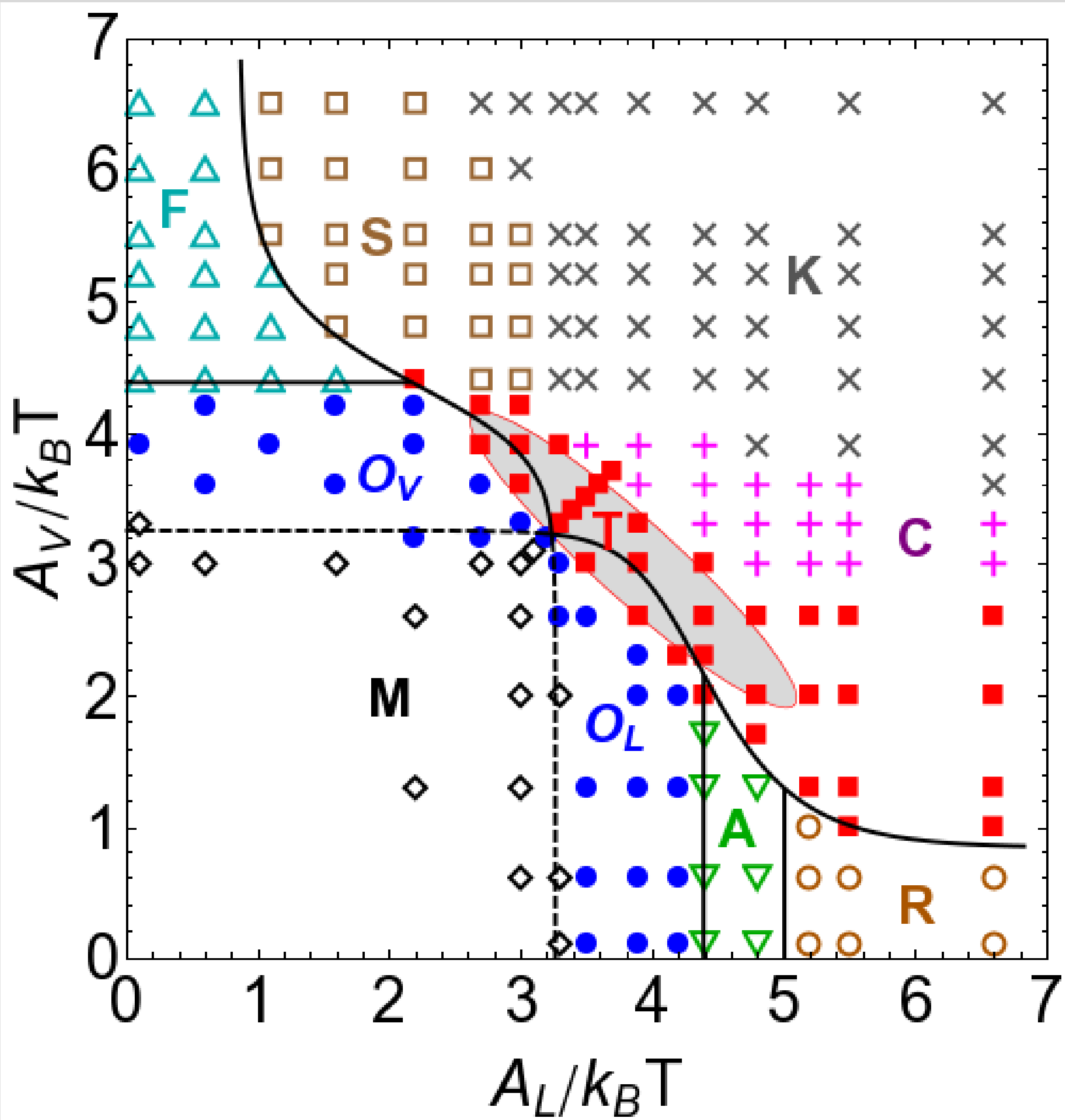
- Predictions of n_p from Lattice Theory depend on g
- Calculate n_p in simulations at various A_V

→ Mapping between A_V and g

$$g = 4A - 3.4 - 9.6$$

2 attractive sites × 2A — thermal fluctuations — energy barrier

Lattice theory explains structure diagram quite well



- Lattice theory for straight polymerization → formation of filaments/arcs/rings
- Two filaments/rings need to overcome energy barrier ~ 9.6kT to assemble → filaments join to form sheets or rings stack into tubes
- Sheet/cluster states are non-equilibrium structures and outside range of lattice theory

Conclusions

- wedges can self-assemble into tubules
  - model has basic level of features
- see helical structures more than nonhelical
- tubules only formed in a narrow range of interaction strengths → reversibility is crucial
- see rearrangement of monomers within clusters
  - important for defect removal
  - but not disassembly (need solvent?)
- lattice-type theory captures essential features of self-assembly

All simulations were done with LAMMPS developed at SNL