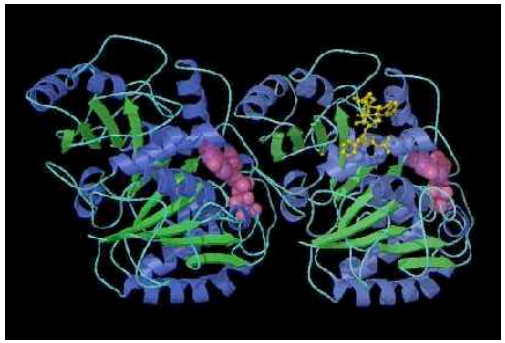
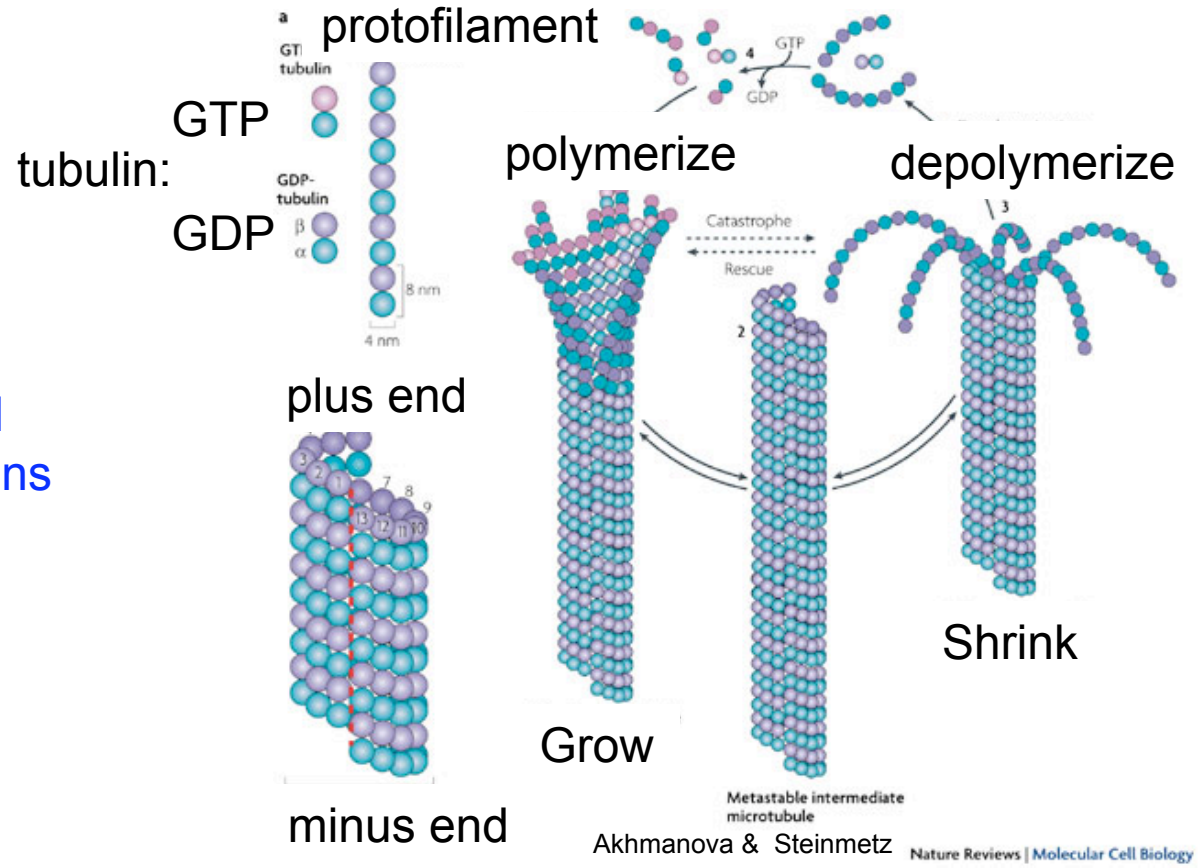
Basic Energy Sciences

Highlight: Artificial Microtubules

tubulin dimer = monomer

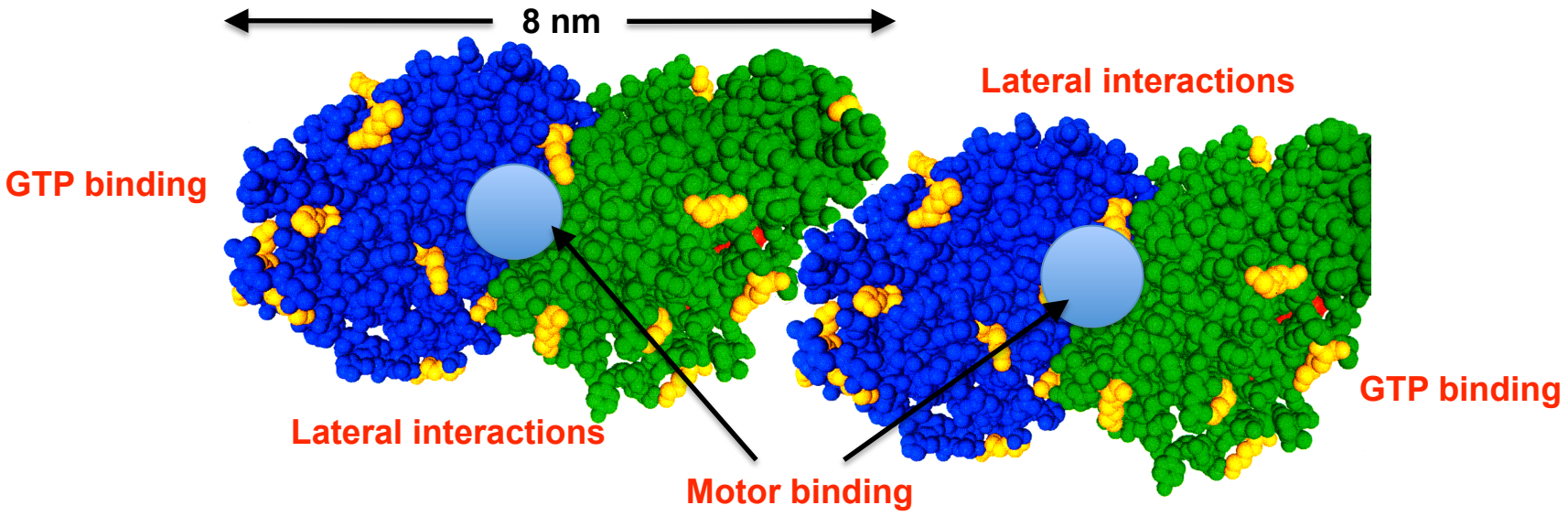


Monomer is a nanoparticle and is capable of multiple interactions



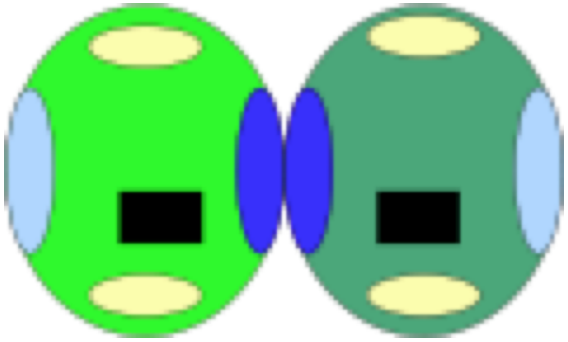
Task Goal: Duplicate the functions of programmable energy-consuming proteins using artificial analogues.

Attributes of Microtubules to be Reproduced



- Nano-scale “monomer” (or dimer).
- Monomer geometry that dictates assembled architecture.
- Polymerization/Depolymerization (nature of the bond)
- Programmable sites and “glue” (~GTP).
- Energy source to program glue.
- Active sites for artificial motors

tubulin analog

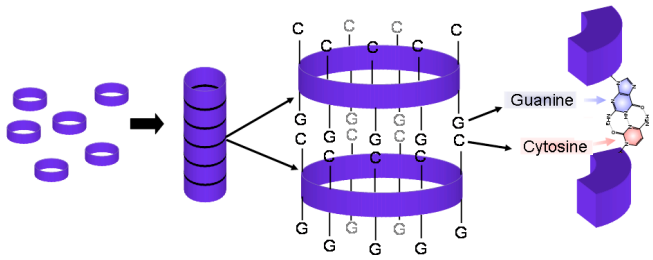


Basic Energy Sciences

Task Components: Artificial Microtubules

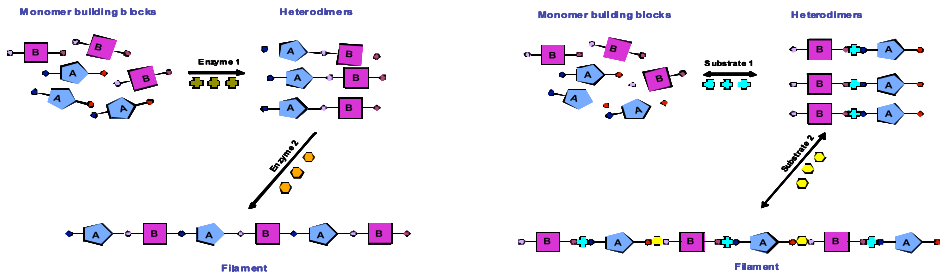
Task Lead: Erik Spoerke

Polypeptide scaffolds



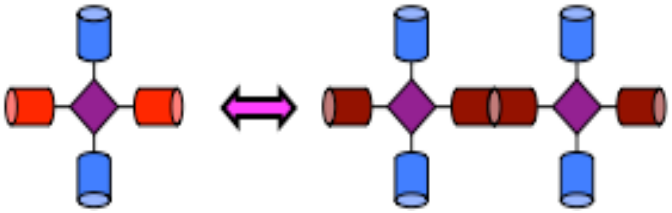
Erik Spoerke

Programmable Elements



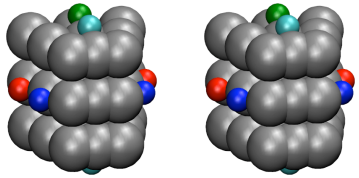
George Bachand, Bruce Bunker

Dendrimers and Particles



Jim McElhanon

Theory/Modeling



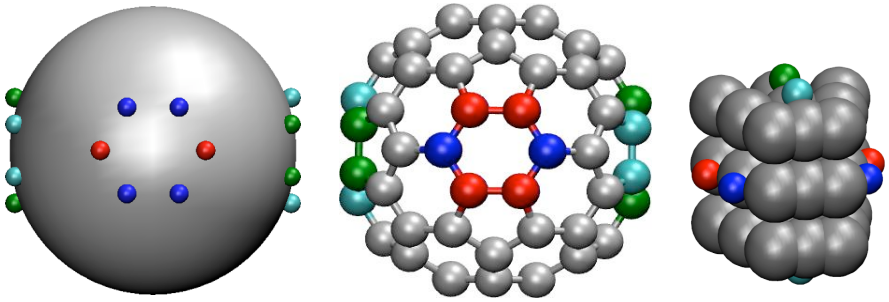
Mark Stevens

To date, research in the new task has focused on Modeling and Dendrimers.

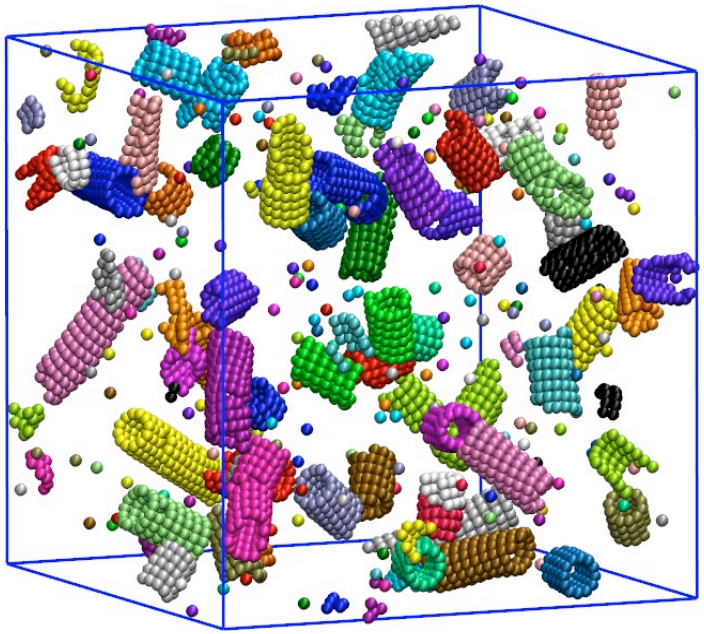
Developing Design Rules for Artificial Tubulin

Step 1: Create Monomer Model

Adjustable parameters:
- **Bonding sites & strengths**
- **Shape**



Step 2: Polymerization Dynamics



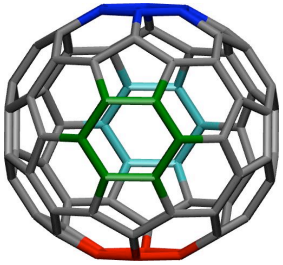
Simulations are used to guide the design of monomers to achieve end-states: e.g. filaments, sheets, tubes

Simulations: Sheet Formation

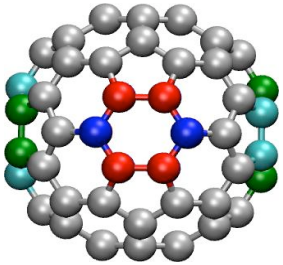
Monomer Attributes

gray sites are repulsive
    make particles impenetrable
red:blue and green:cyan are attractive
    polarity (future)
like colored sites are repulsive

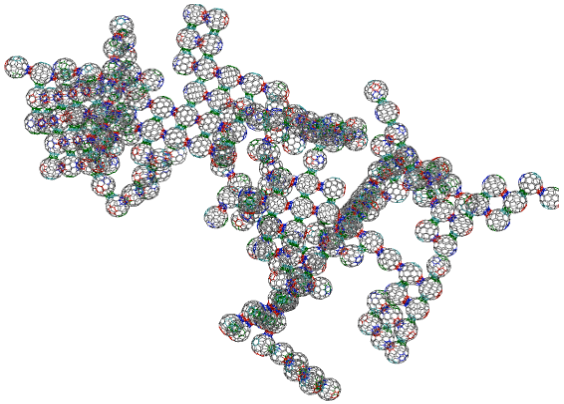
should produce sheets

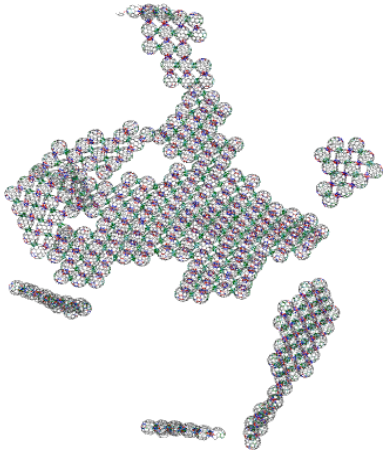


broken symmetry



Polymerized Structure



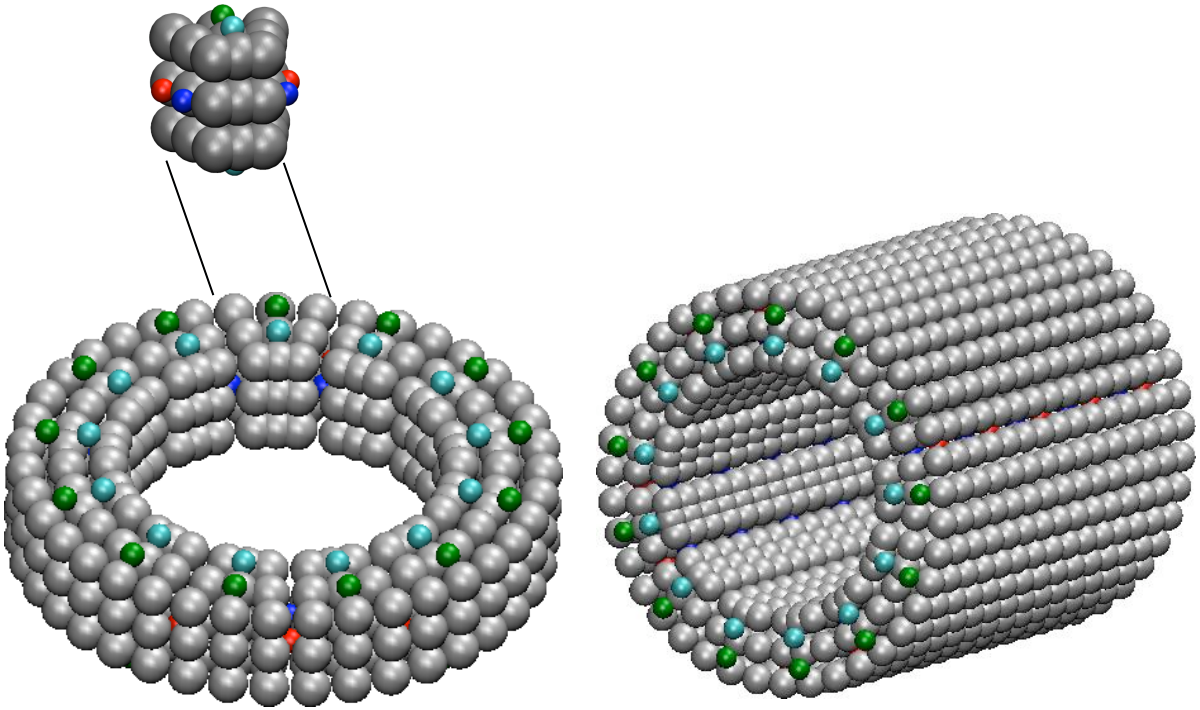


Conclusion: Must control symmetry of attractive binding sites

Tubular Assembly

wedge monomer

- similar to Rapaport (PRL 08) for capsids
- designed to produce rings that **stack** into cylinders (13 wedges per ring)
- attraction only between specified sites (no size)
    - include broken symmetry
- gray particles interact purely repulsively

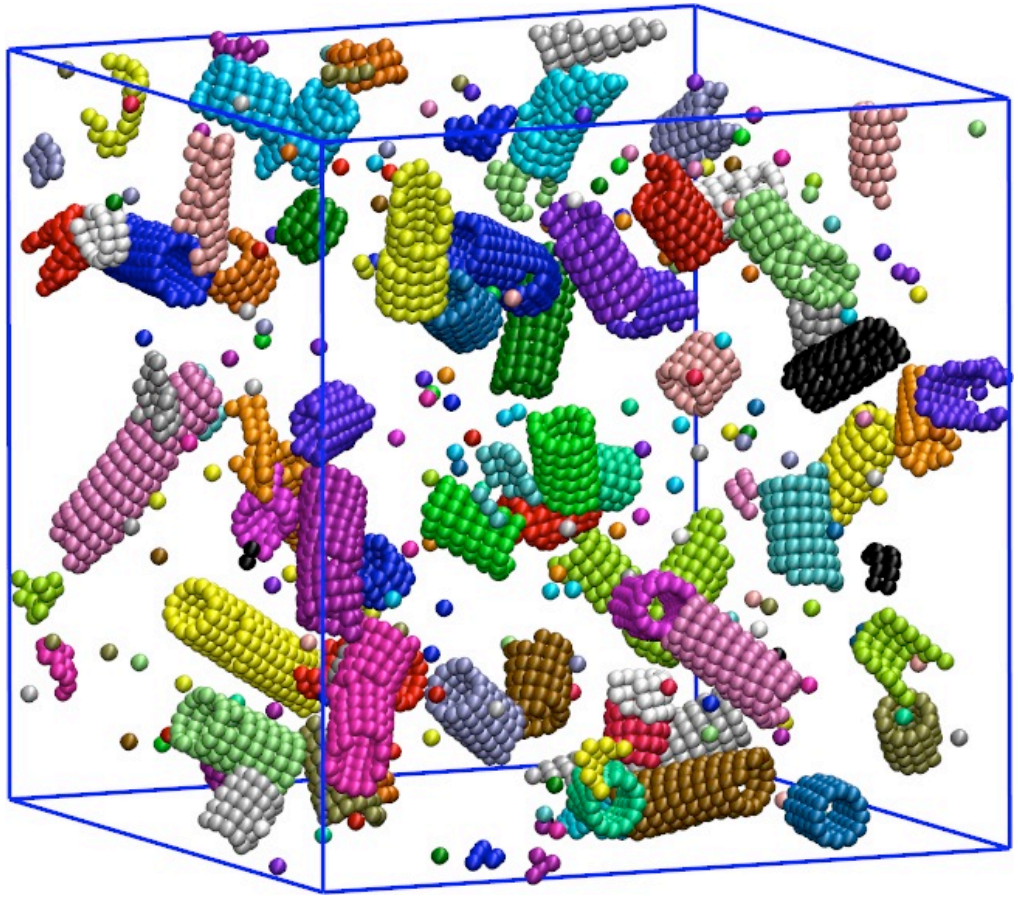


Self-Assembly of Wedge Monomers

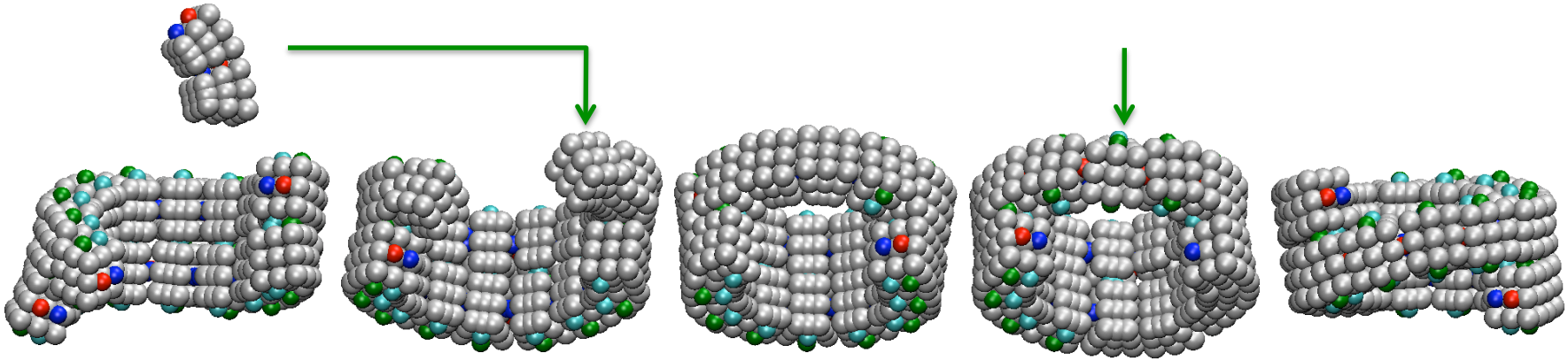
5000 wedge monomers
random distribution of monomers
0.2 monomer number density

Force field: 8.8 / 5.2 (kT)
ring vs. filament strength
(POST-IT note strength)

Many tubules form.



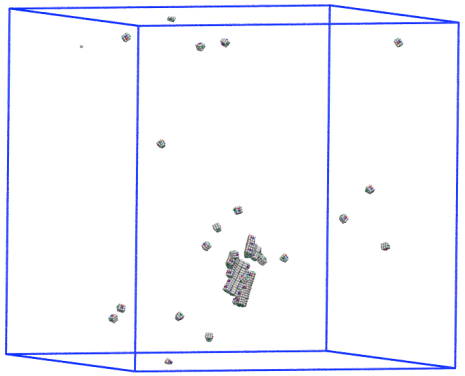
(Helical) Ring Formation



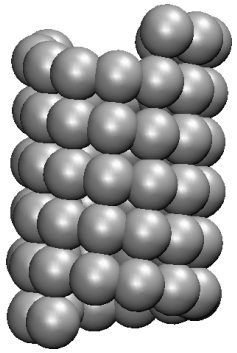
frame 52 53 54 73 74

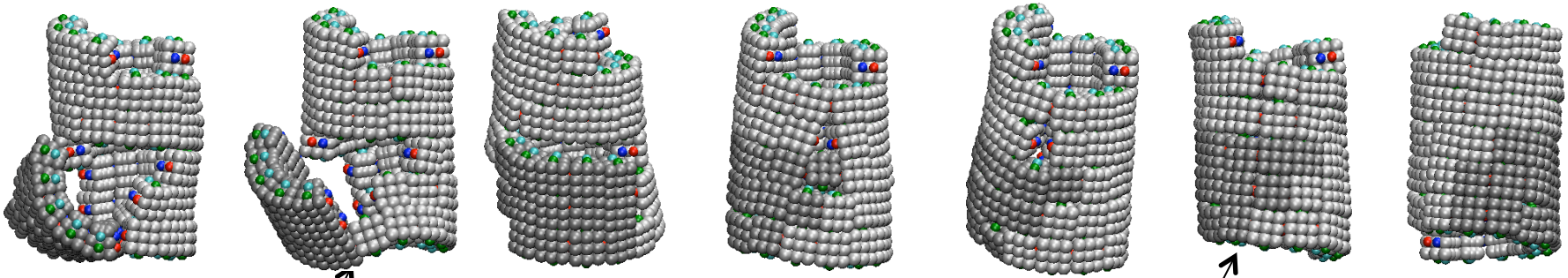
Ring forms first. Then transitions to helix.
Interaction strength allows reconfiguration.

Tubule Formation



All the parts that make this helical tubule



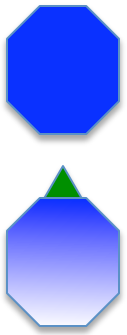


monomers diffuse within cluster

Future Work: Design Rules for Artificial Tubulin

Demonstrated can achieve some of the basic assembly properties
Now doing *statistical* analysis
Next:

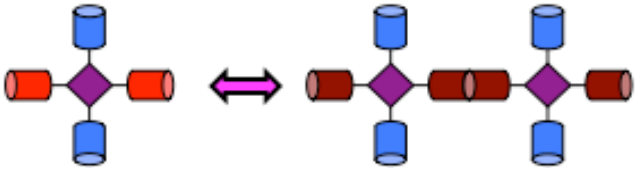
- Assembly-Disassembly:
  - explicit solvent (Rappaport) [much more CPU time]
- Modeling energy driven dynamics
  - ~GTP/GDP in microtubules?
  - nonlocal dynamics
  - two state monomer
  - how do within MD?
    - time dependent potentials
- Electrostatics
  - long range
  - push/pull



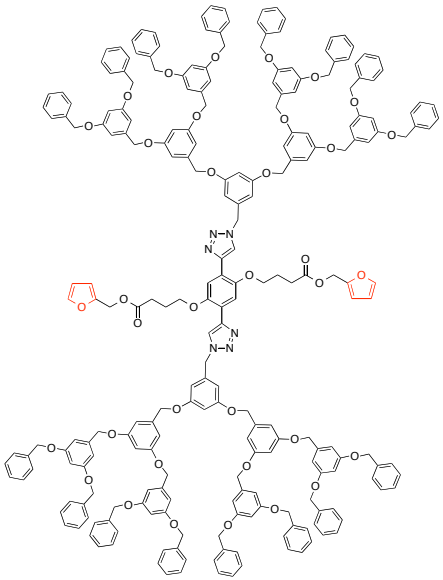
Specific modeling of experimental systems
Atomistic simulations to model monomer-monomer interactions (peptide).

Artificial Microtubules: Dendrimeric Monomers

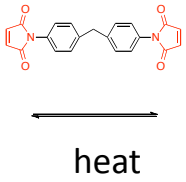
Structures of Programmable Dendrimers*

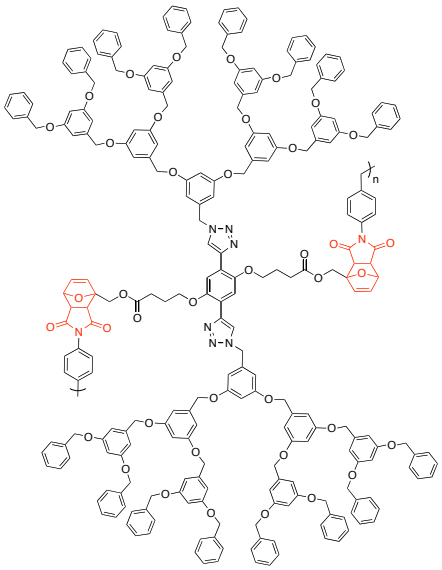


Dendrimer Attributes:
Asymmetric core.
"Programmable" axial groups.
"Non-interacting" side chains.



Monomer





Polymer

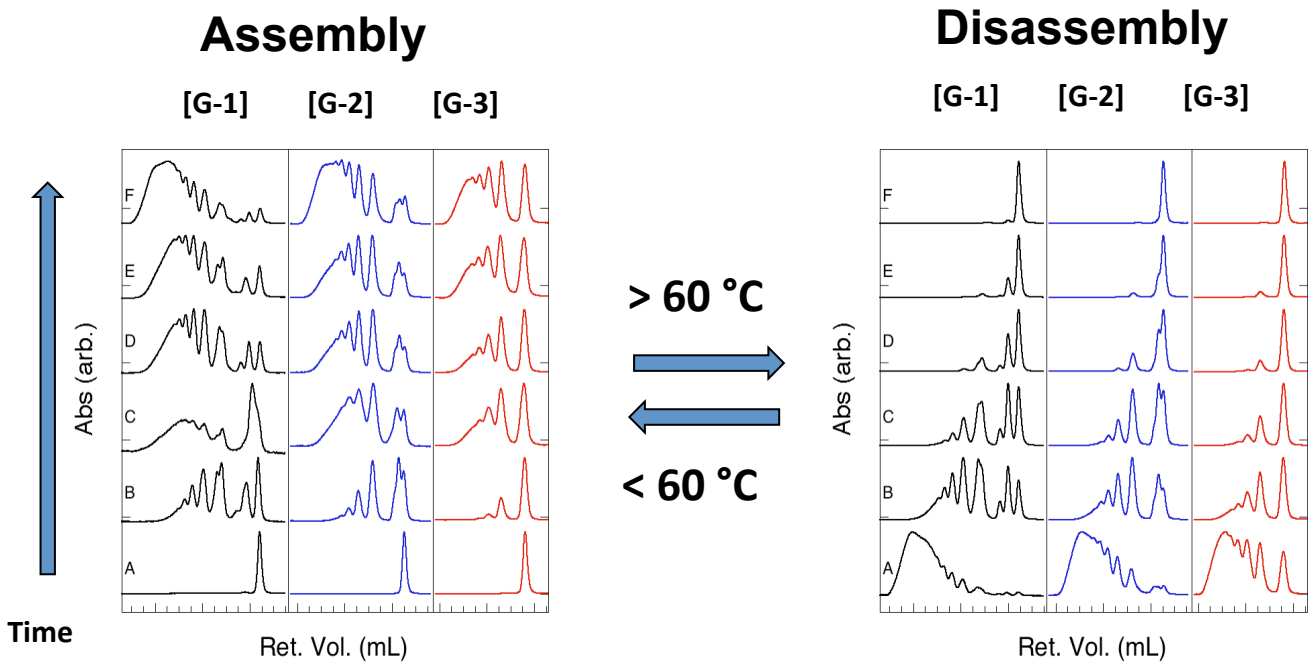
Initial dendrimers are designed to promote reversible polymerization of protofilaments.

*Polaske, McGrath, and McElhanon, Macromolecules (2010)

*See Poster by Jim McElhanon.

Reversible Dendrimer Polymerization

*See Poster by Jim McElhanon.



Monomer → Polymer

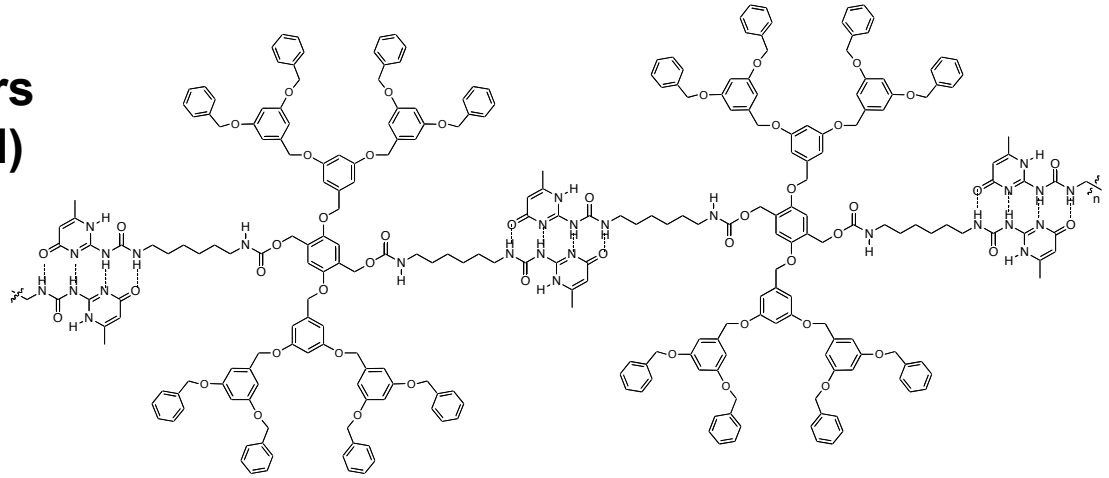
Polymer → Monomer

Polaske, McGrath, McElhanon, Macromolecules (2010)

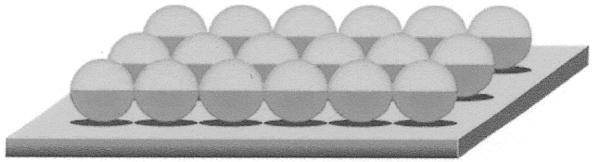
Gel permeation chromatography reveals the kinetics and extent of both polymerization and depolymerization processes.

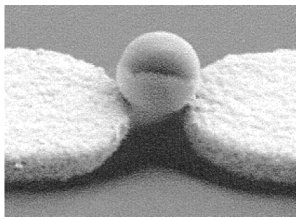
Future Work: Dendrimer/Particle Constructs

Dendrimers (H-bonded)



Janus Particles

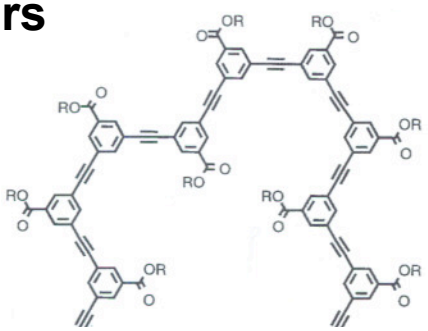


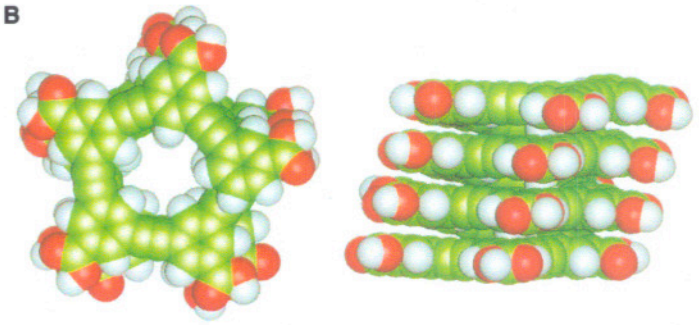


- Investigate other programmable linkers.
- Modify both longitudinal and lateral interactions.
- Explore constructs that function in water.
- Explore particulate constructs (Janus particles).

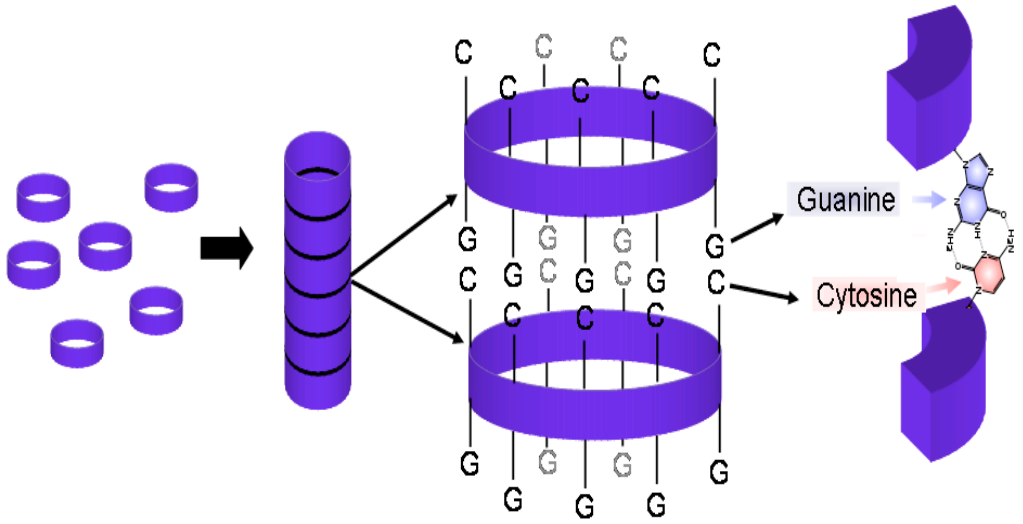
Future Research: Polypeptide Templates

Foldamers





Polypeptides + Oligonucleotides

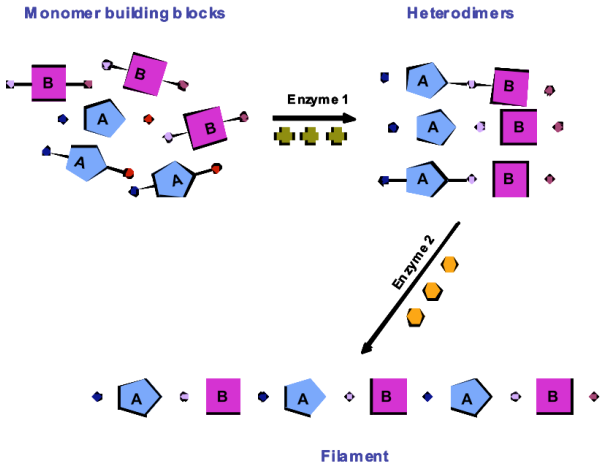


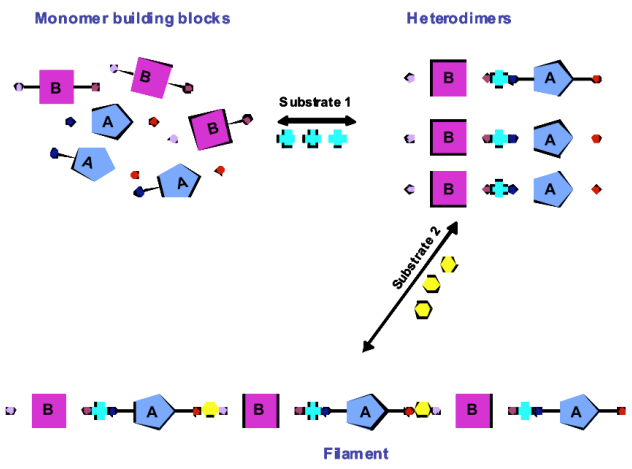
Goal: Exploit folding motifs in polypeptides/proteins to direct the formation of both "monomers" and extended architectures.

Future Research: Programmable "Glues"

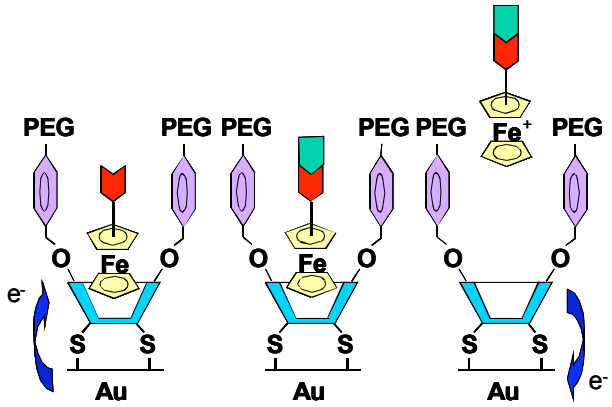
– A – B –

Enzymes:
- Phosphatases
- Kinases
- Chymotrypsin
- Oxidoreductase





Molecular Switches:
- Ferrocene/Cyclodextrin
- Elastin
- Redox-active switches
- Azobenzene



Goal: Exploit both enzymes and other programmable molecules to mediate polymerization and/or reconfiguration processes involving designer monomers.

Summary

- Dendrimer system that thermally polymerization/depolymerization
    - hydrogen bonded version underway
- Found need symmetry broken interaction regions
- Model produces tubular structures
    - helical structures
    - monomer diffusion within clusters occurs
    - have interaction strengths in regime for dynamic formation/reformation

We have multiple strategies to create artificial microtubules

- different mechanisms to turn on/off the molecular glue
- will be examining what works and what advantages/disadvantages exist

Our initial success gives us confidence that at least some of these systems will work. We expect that there is a broad set of systems that will produce exciting new materials.