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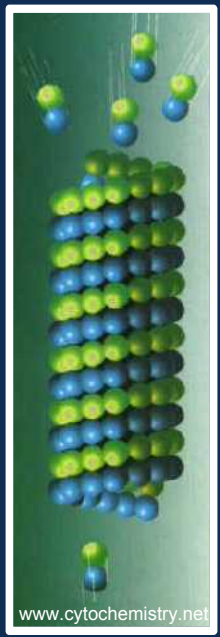

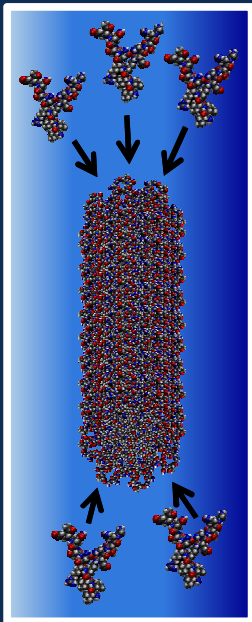

Engineered Peptides for Controlled Nanofiber Assembly

Dara Van Gough

Jill S. Wheeler, Shengfeng Cheng, Mark Stevens, and Erik D. Spoerke

Sandia National Laboratories

Exceptional service in the national interest

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Microtubules as inspiration

Exploring microtubules and motor proteins as tools for nanomaterials assembly is motivated by their ability to dynamically organize nanomaterials precisely and scalably in nature

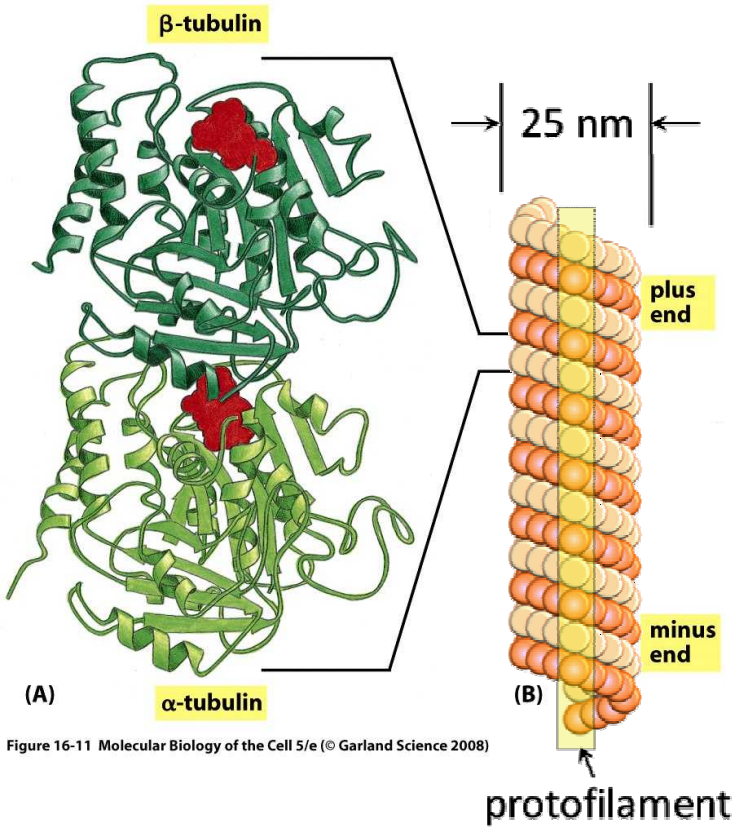
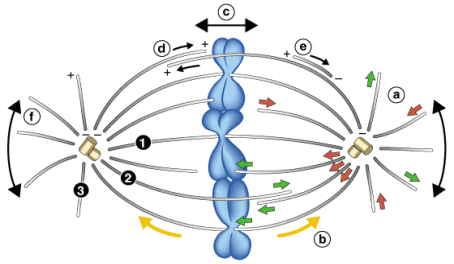
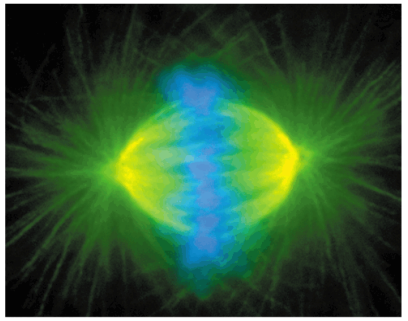


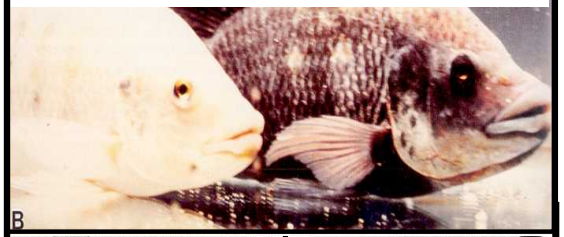
Figure 16-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

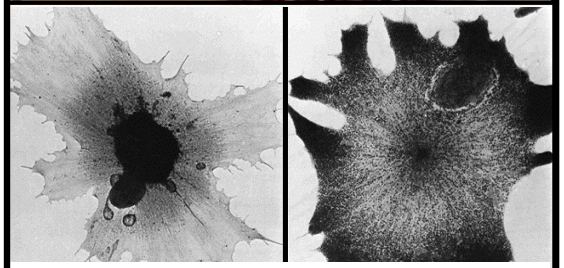




Chromosome positioning/separation during cell division

*L. Haimo and C. Thaler, BioEssays 16, 727-733 (1994).





Adapted from: http://wilkes-fs1.wilkes.edu/~terzaghi/BIO-226/lectures/24.html

Adaptive reorganization of pigment granules in melanocytes

Design Targets for Artificial Microtubules

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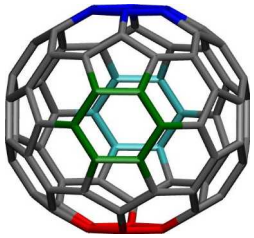
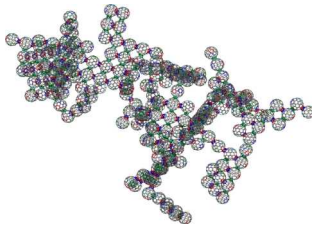
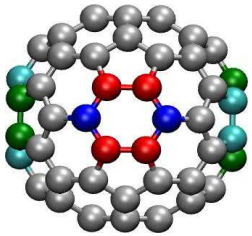
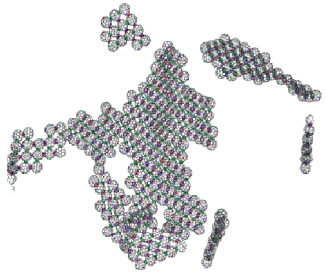
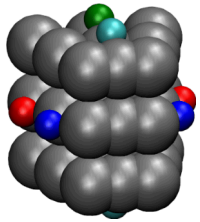
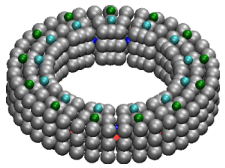
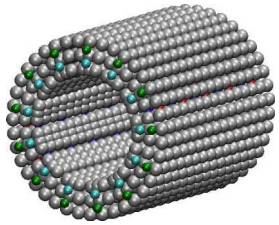
Key Characteristics of Microtubules:

- Polymerized from nanoscale building blocks
  - α-tubulin/β-tubulin dimers
  - Balance of Lateral and Vertical interactions
- 1-Dimensional Nanostructures
- Biomolecular Polarity (α-β asymmetry)
- Building Block Chemistry and Form Direct Assembled Architecture
- Programmable Assembly/Disassembly (chemical and thermal)
- Secondary Assembly (MT organization)
- Motor Protein Interactions

Simulation Established Design Rules

Symmetry of shape and interactions is key to determining self-assembled morphology

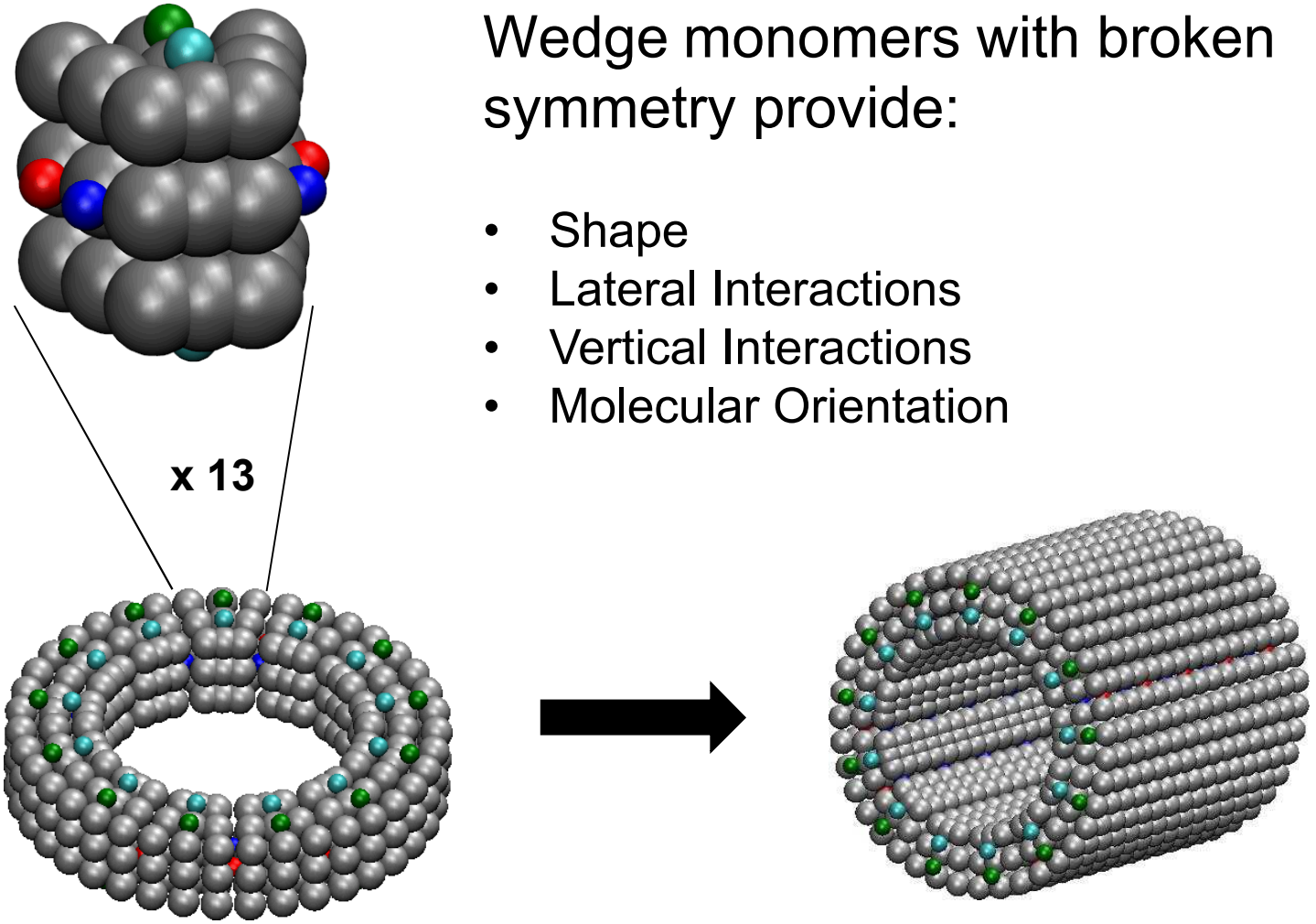
	Monomer Building blocks	Polymerized Structures
Sphere with symmetric attractive sites		
Sphere with broken symmetry		
Wedge with broken symmetry		 

Assembly Parameters

- Gray sites are repulsive
- Red:blue and green:cyan are attractive
- Like colored sites are repulsive

Monomer shapes as well as strength and geometric distribution of interaction potentials on each monomer are critical

Asymmetric Wedge Building Blocks

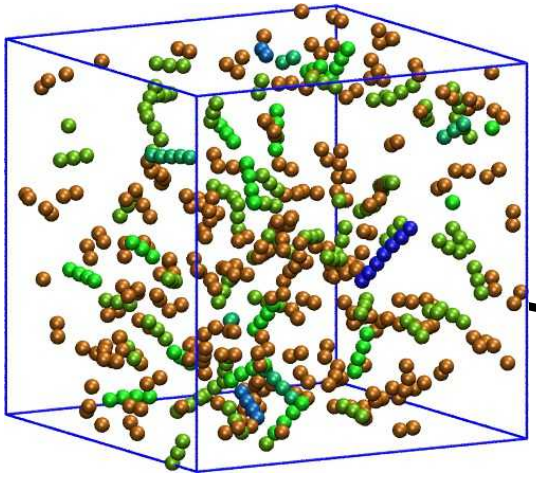


Wedge monomers with broken symmetry provide:

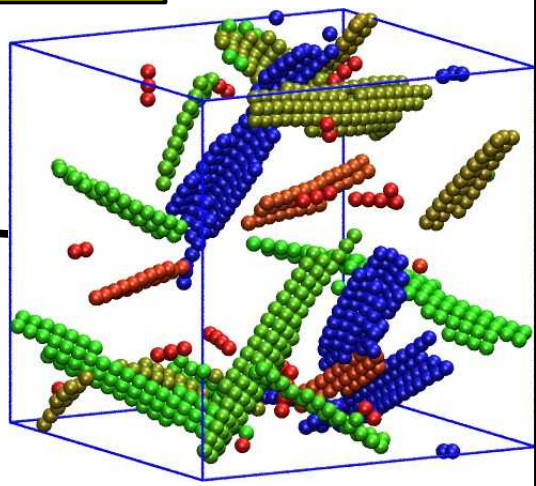
- Shape
- Lateral Interactions
- Vertical Interactions
- Molecular Orientation

Wedge assembly behavior

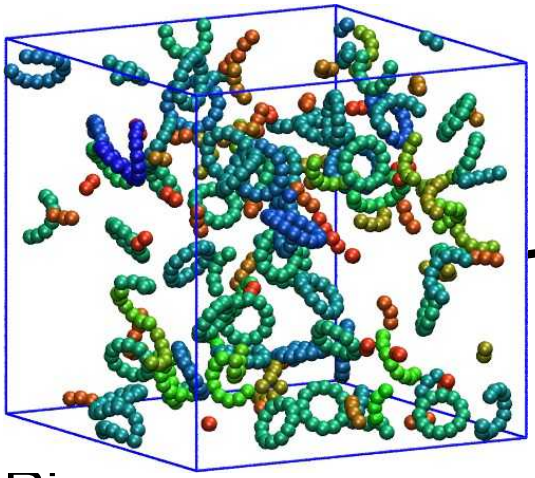
Tuning the lateral and vertical interaction parameters drives the assembly of filaments, rings, sheets, and tubes



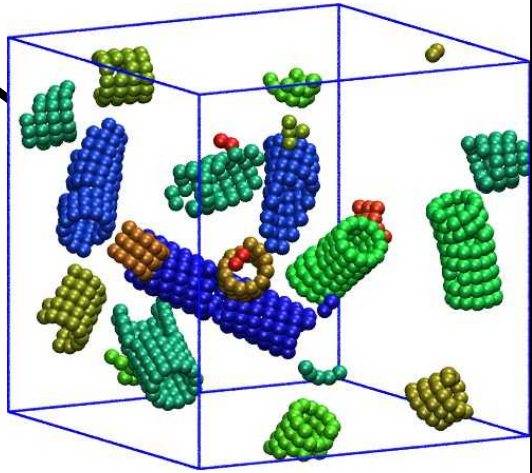
Filaments



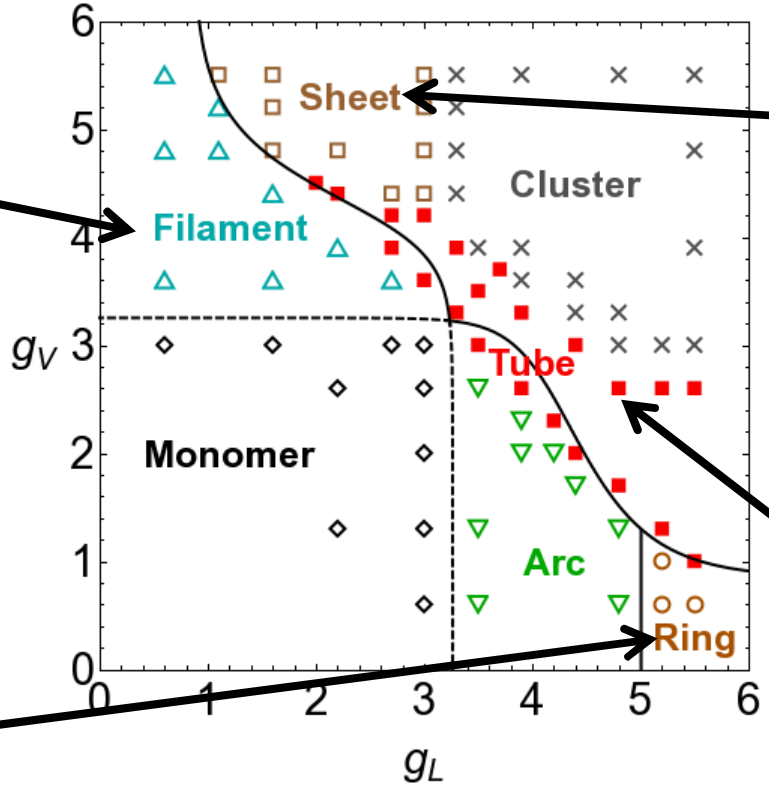
Curved sheets



Rings



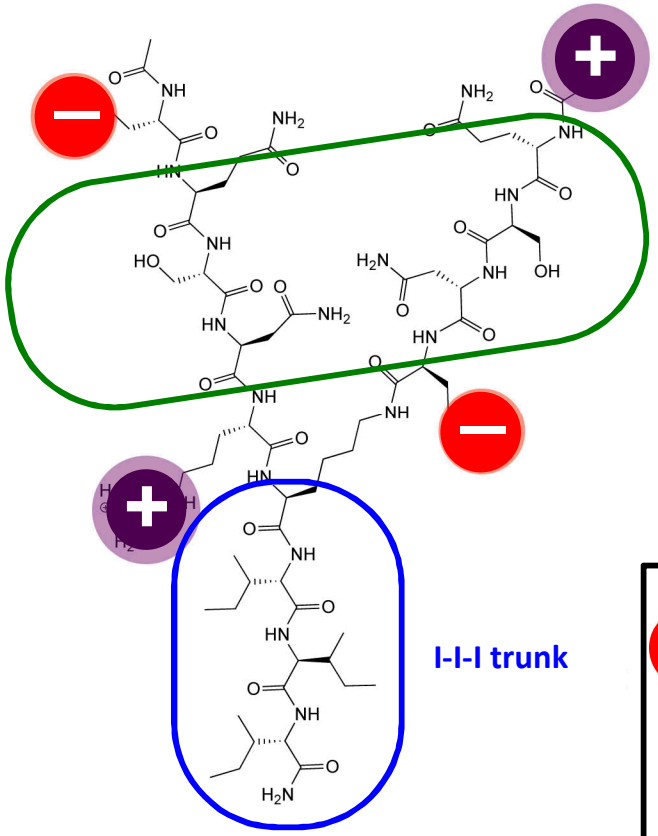
Hollow tubes



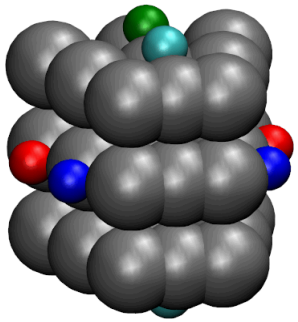
Soft Matter (2012) 8, 5666-5678

Peptide building blocks

Peptide wedges provide a unique experimental platform for probing the effects of monomer design on supramolecular assembly.



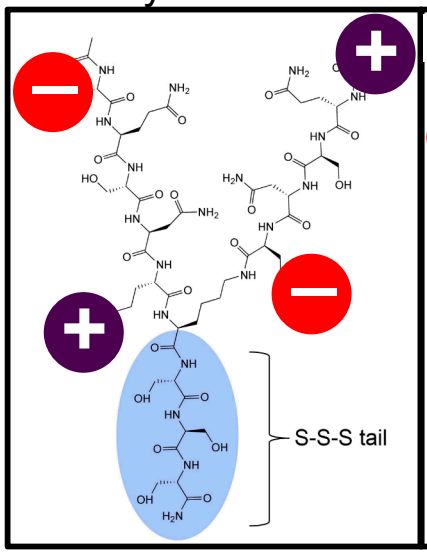
Asymm-Wedge



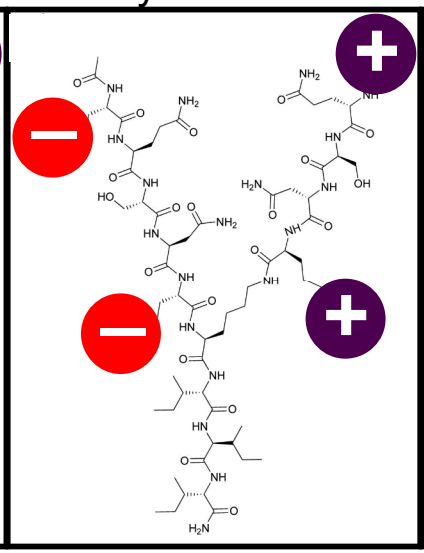
Variable Parameters:

- Peptide size, shape
- Electrostatic charge
- Amphiphilicity
- Hydrogen Bonding
- Molecular Asymmetry

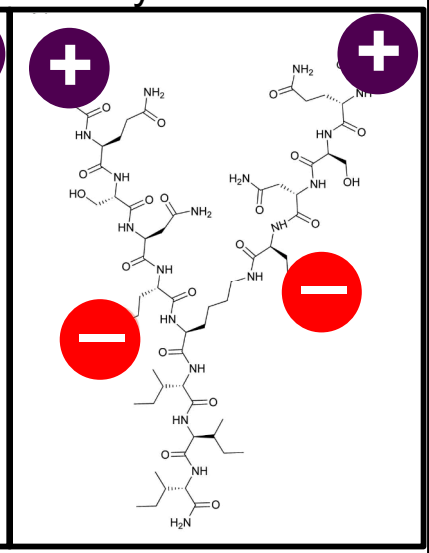
Asymm-SSS



Symm-Vert



Symm-Horiz



Asymm-Wedge self-assembles into nanofibers

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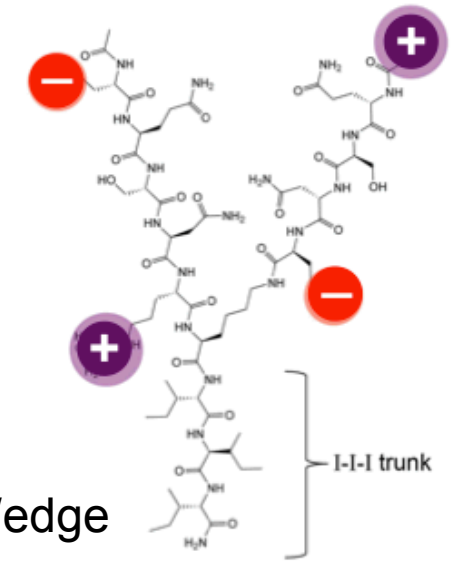
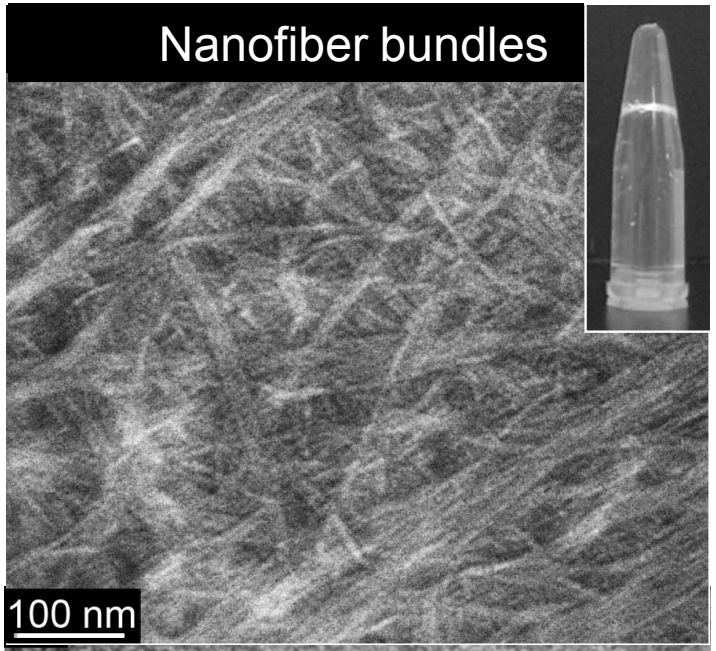
Asymmetry of charge and hydrophilicity promote nanofiber formation

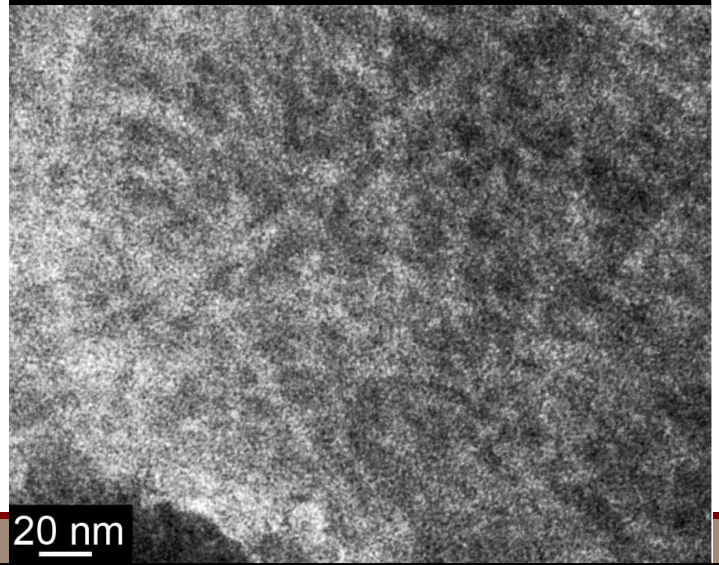


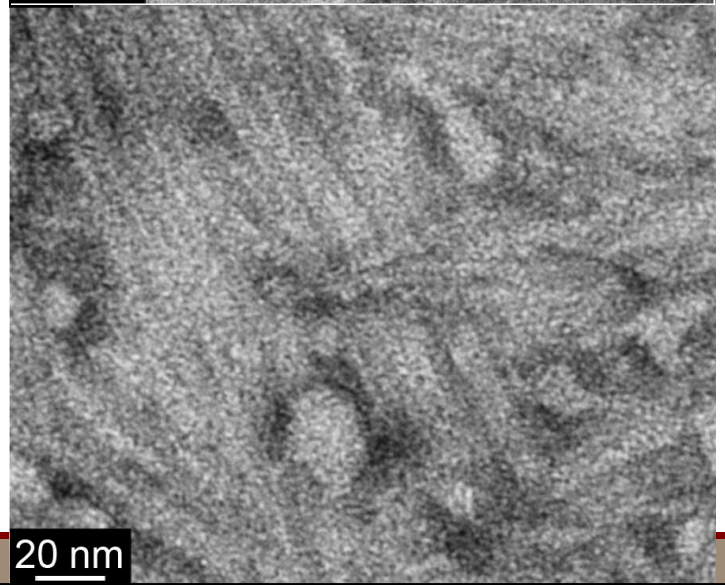
Asymm-Wedge

Nanofiber bundles



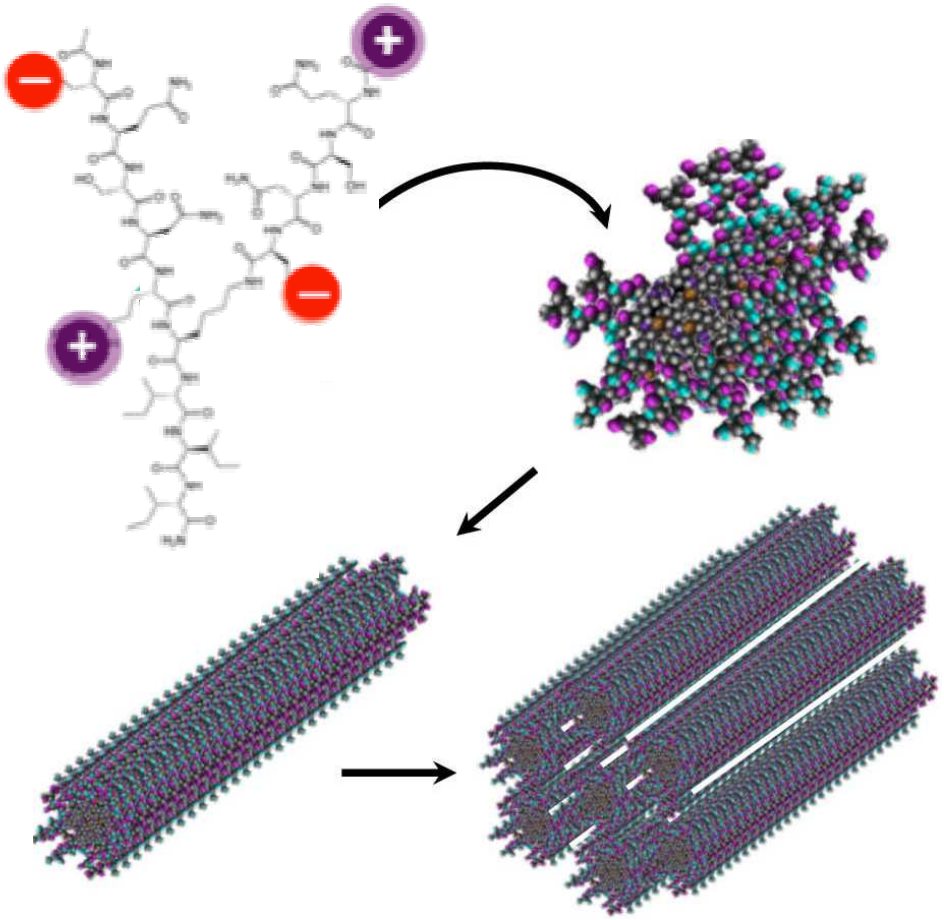
Individual nanofibers

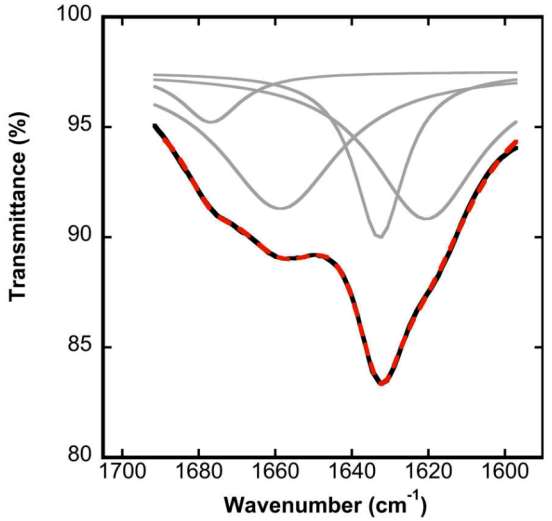


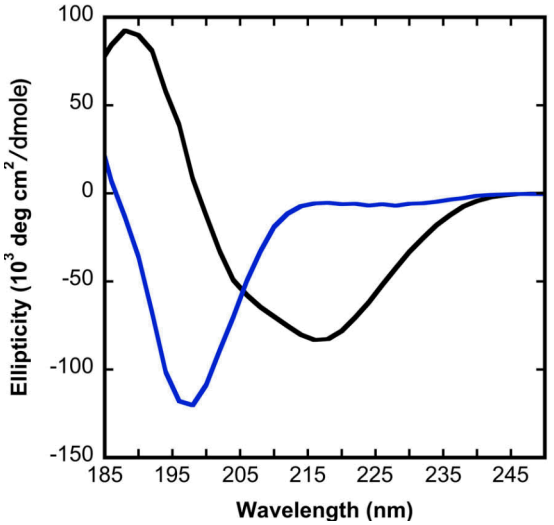


Peptide ordering within nanofibers

β-sheet formation is expected in cylindrical peptide assemblies and is observed spectroscopically



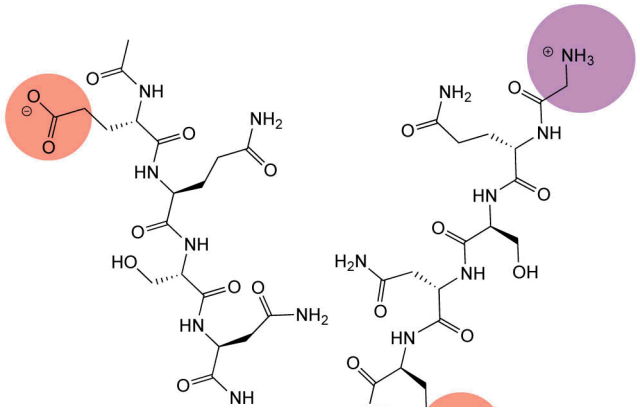


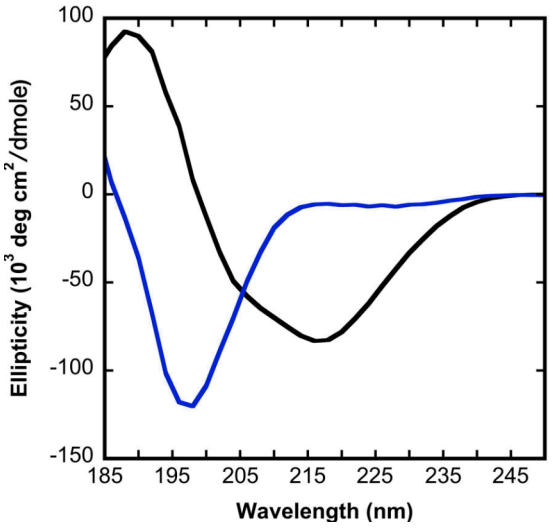


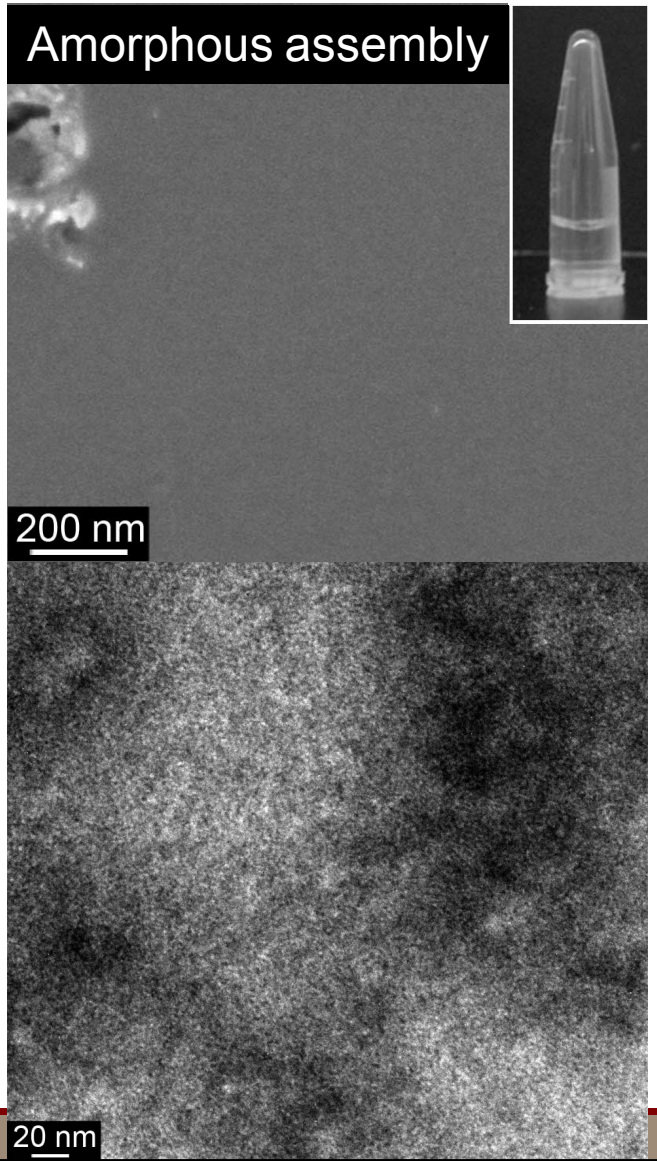
Observe nanofibers assemble into bundles

Probing hydrophilic asymmetry

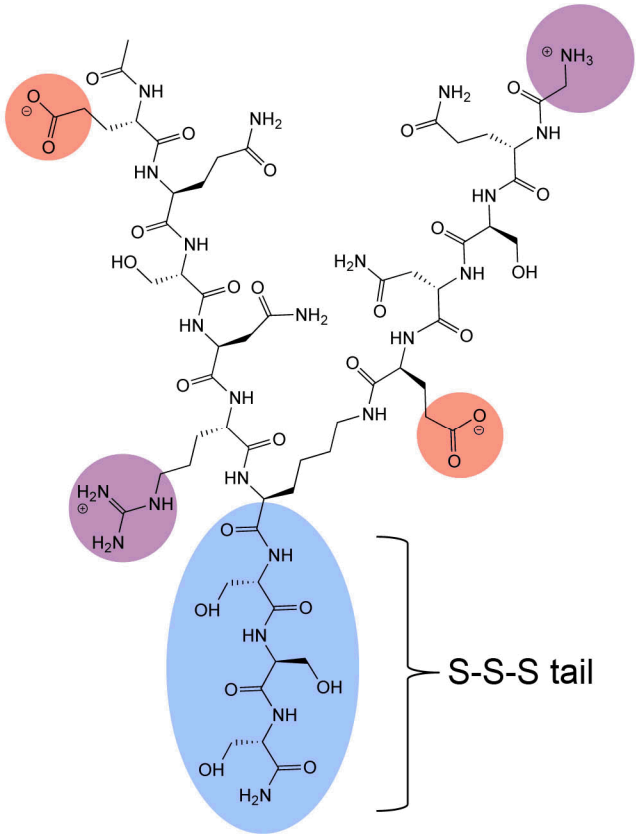
β-sheet promoting amino acid sequences do not ensure nanofiber formation. Hydrophilic asymmetry is key.



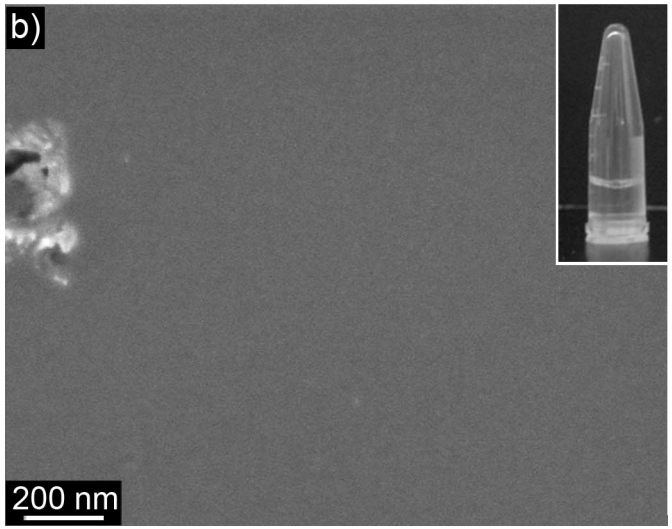


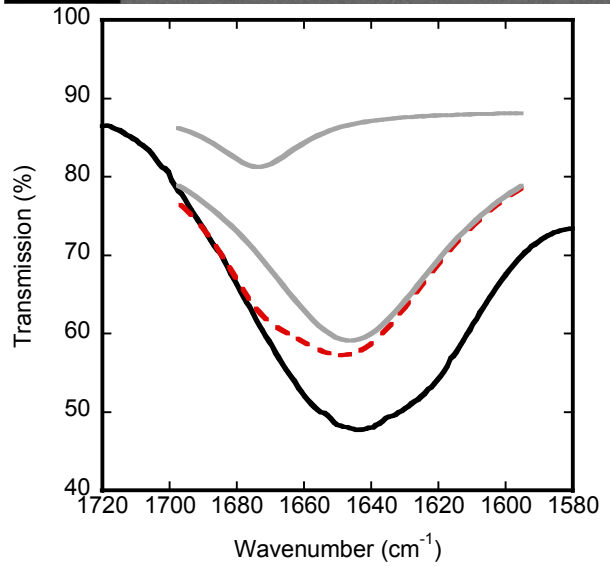


Hydrophilic asymmetry

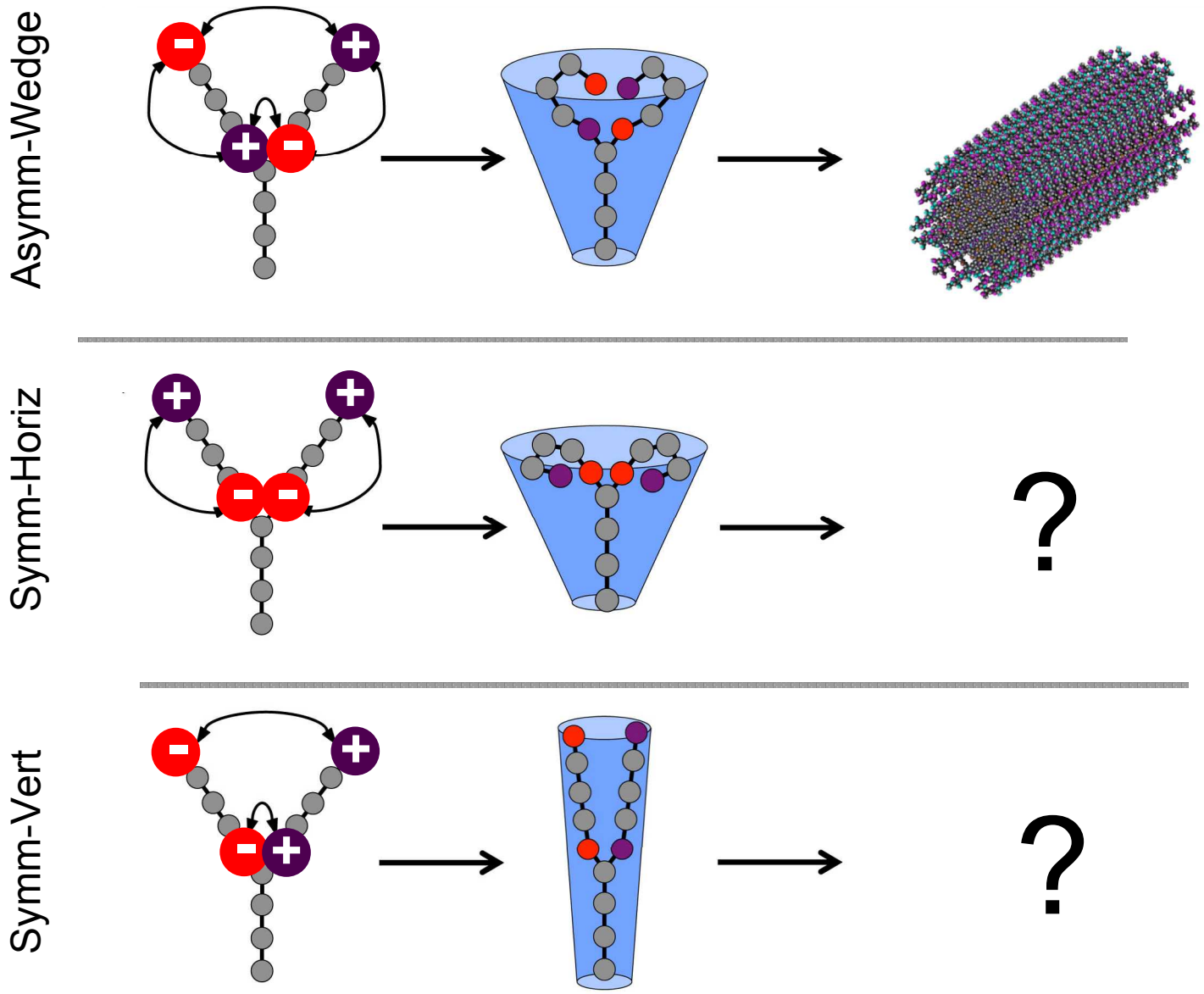


Asymm-SSS





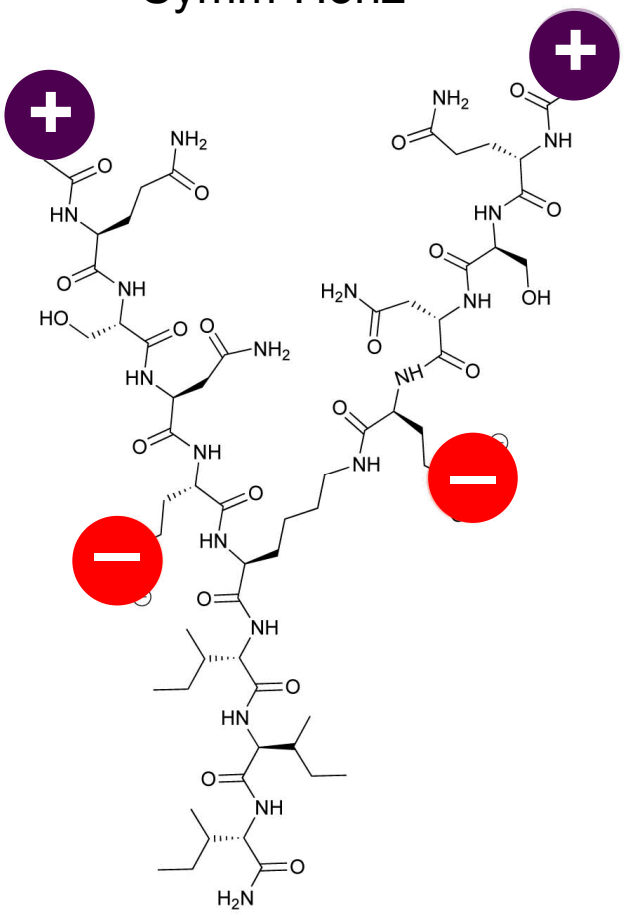
Morphology of self-assembled peptides



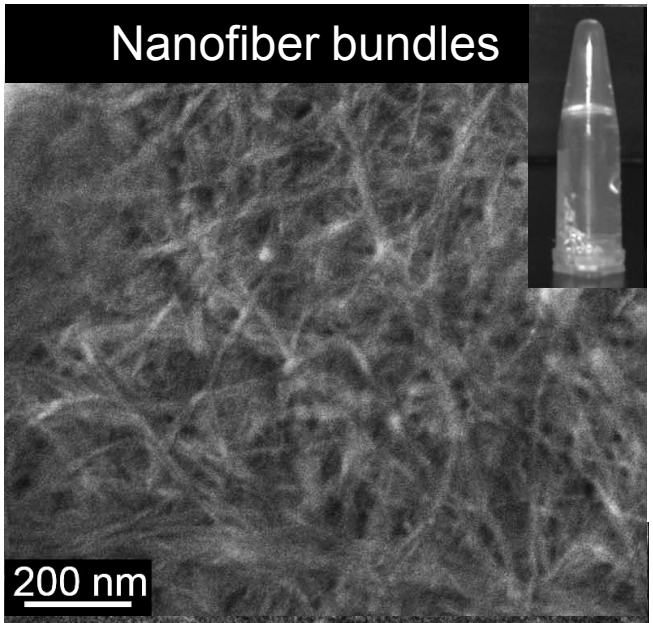
Lateral charge symmetry

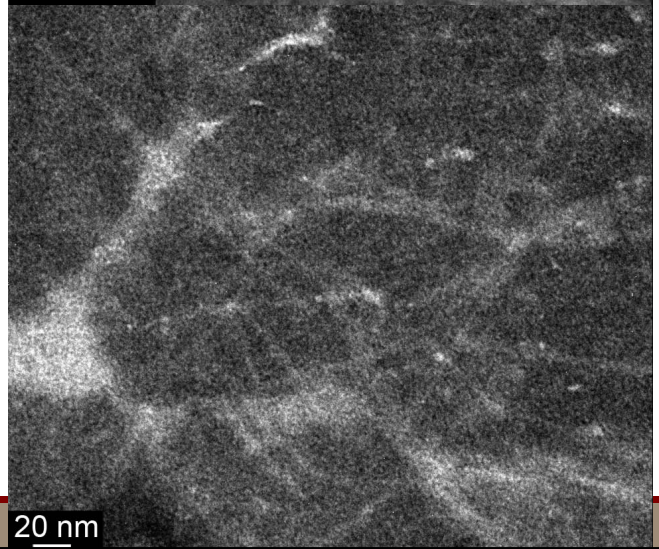
Hydrophilic asymmetry combined with lateral charge symmetry promotes β-sheet and nanofiber formation

Symm-Horiz



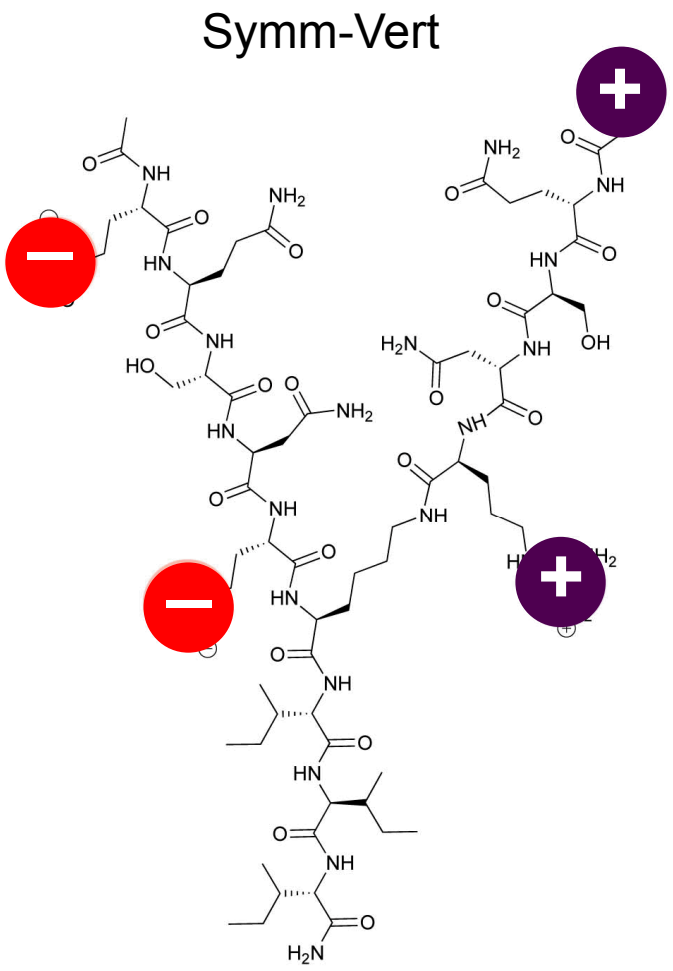
Nanofiber bundles

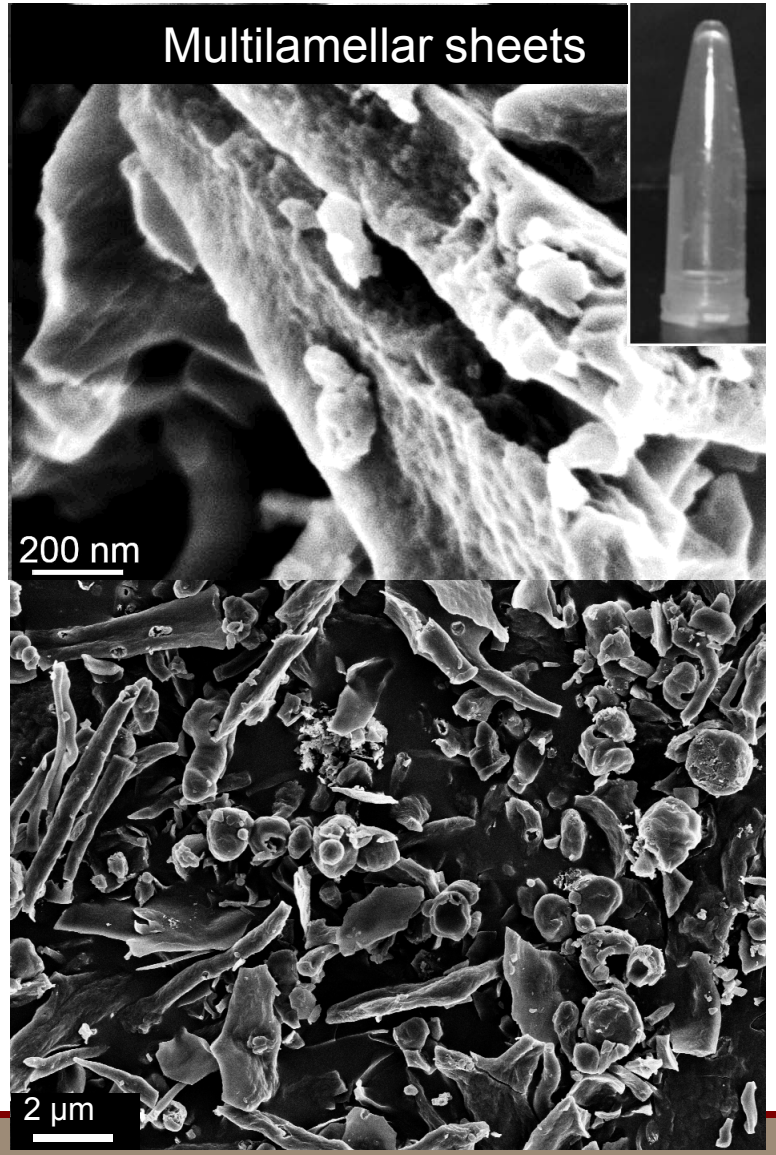




Lateral charge asymmetry

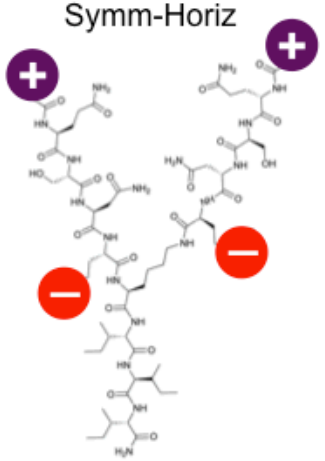
Hydrophilic asymmetry combined with lateral charge symmetry promotes β-sheet and multi-lamellar sheet formation

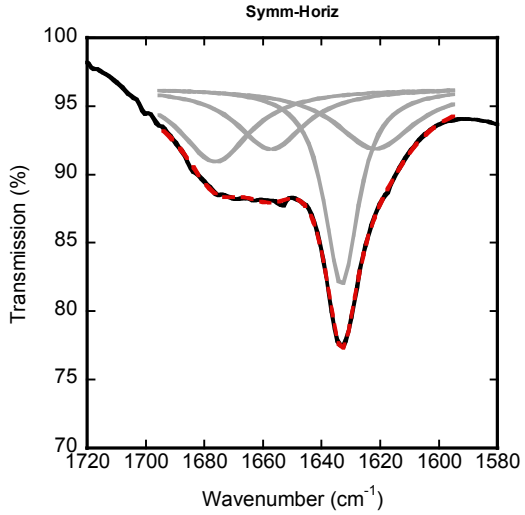




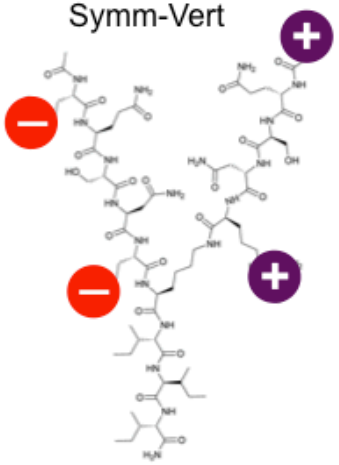
β-sheet formation is observed spectroscopically

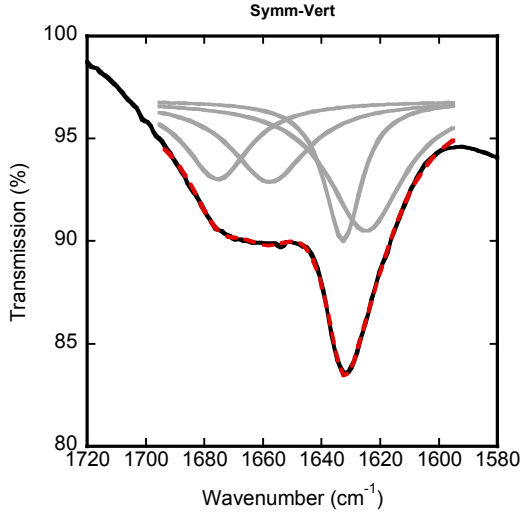
Symm-Horiz



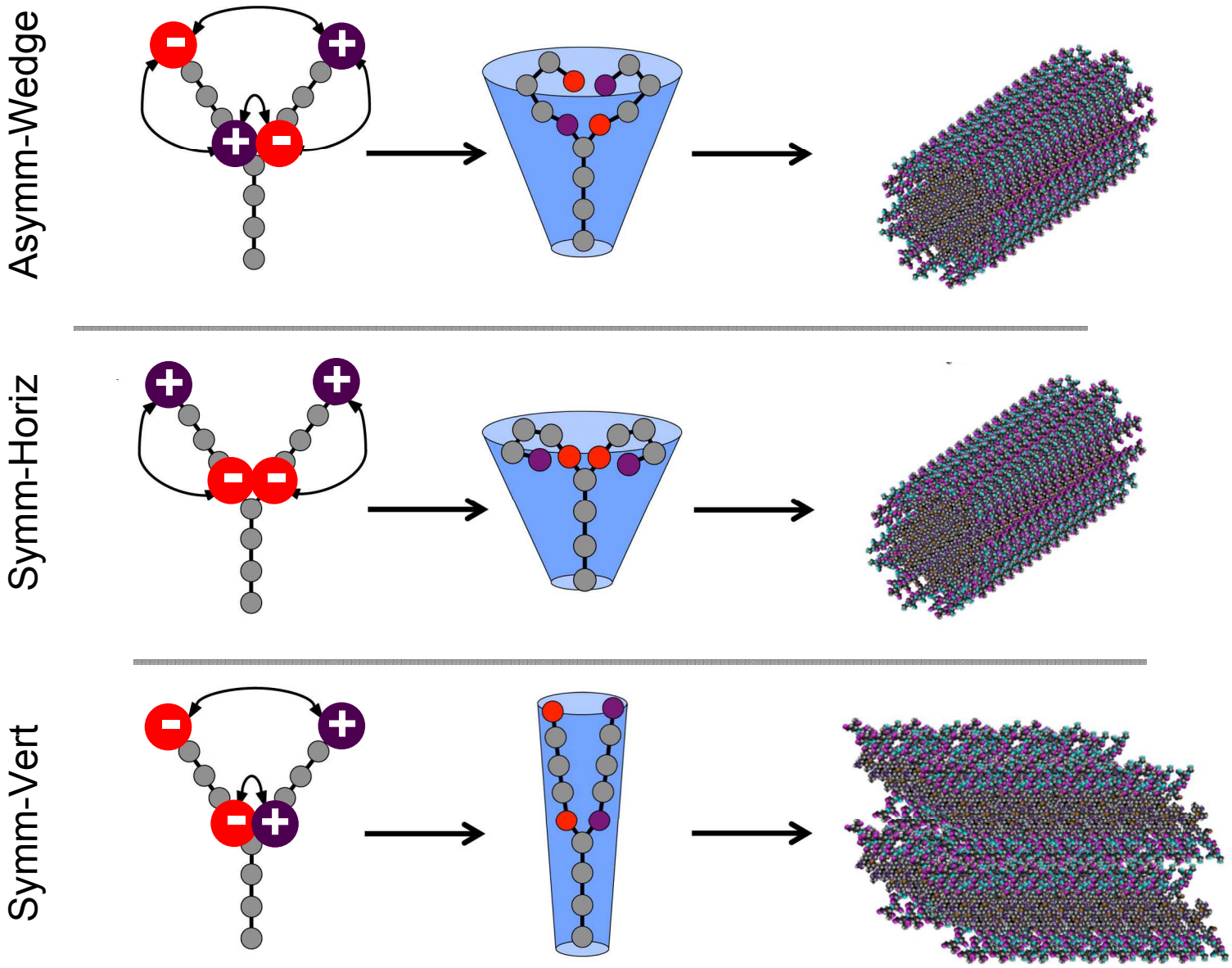


Symm-Vert



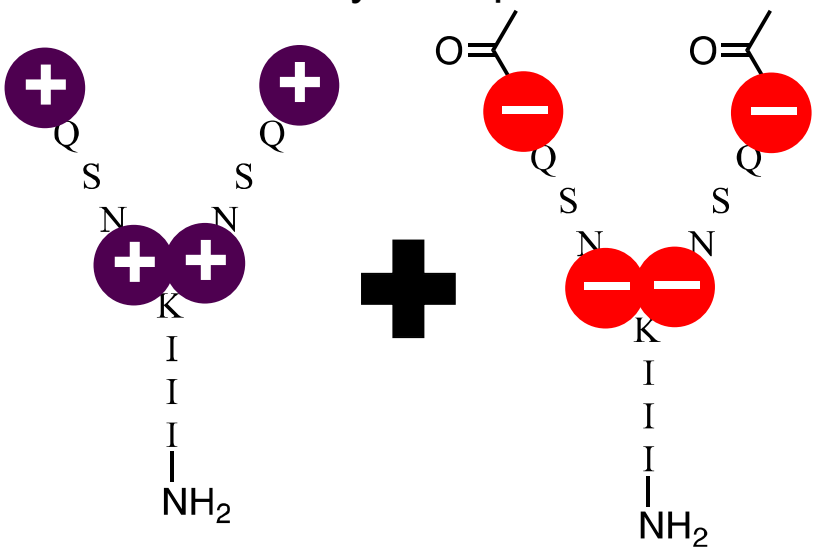


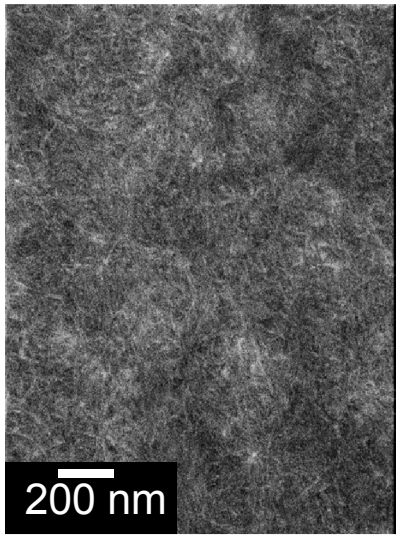
Model for morphologies observed



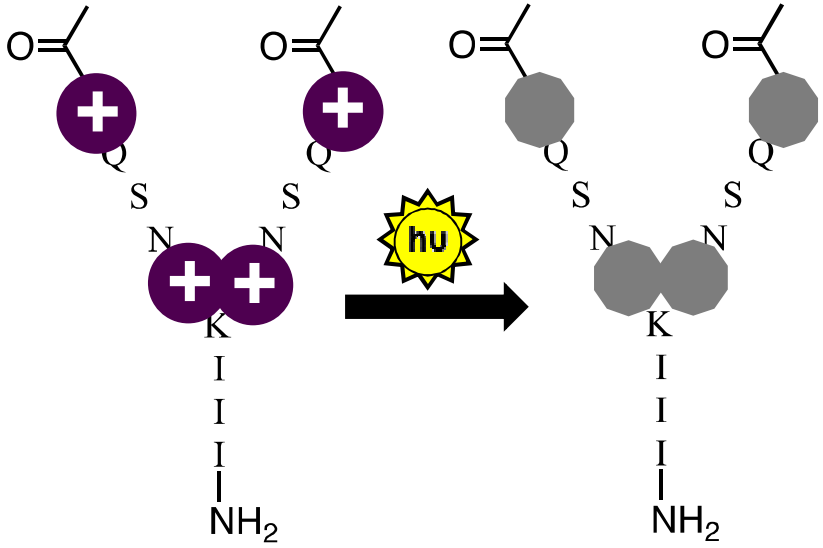
Ongoing work

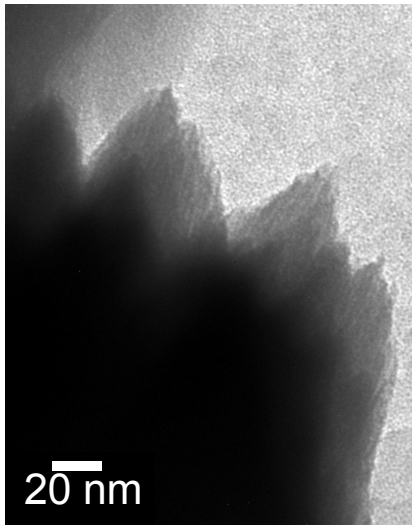
Assembly of α, β-dimers





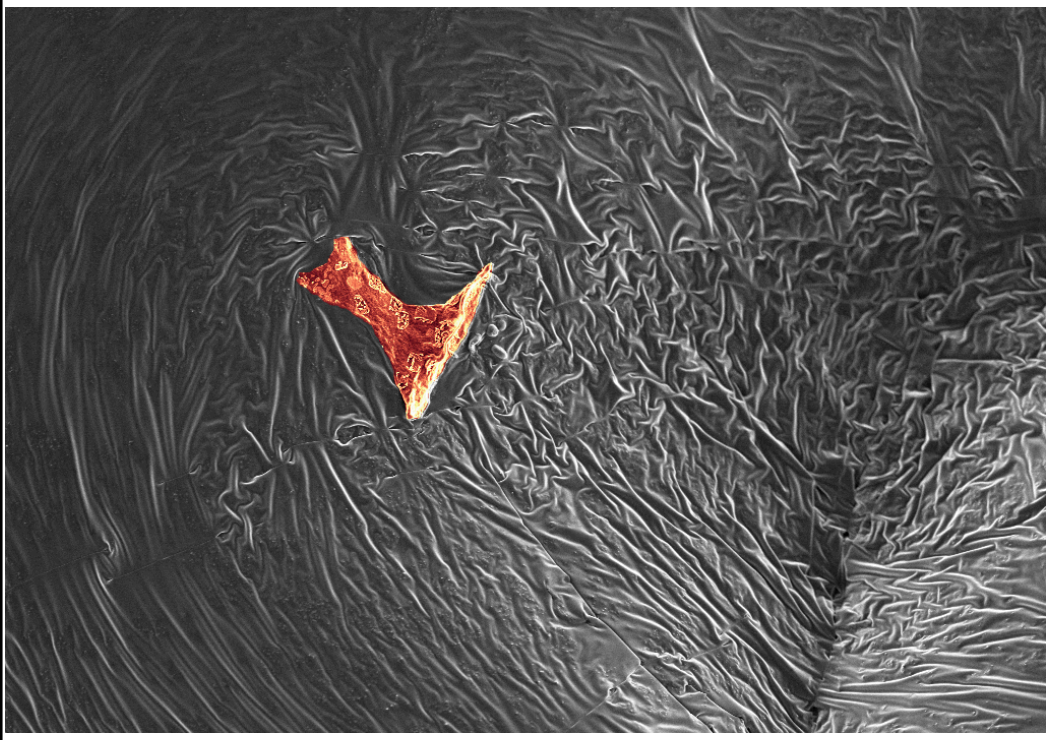
Light activated self-assembly





With D. Wheeler

We would like to gratefully acknowledge funding support from the U.S. Department of Energy, Office of Basic Energy Sciences, Division of Materials Sciences and Engineering.



"Summer dress" made from wedge-nanofiber fabric in a micro-whirlpool

Acknowledgements:

Jill Wheeler
Erik Spoerke
Mark Stevens
Shengfeng Cheng
Bruce Bunker
George Bachand
David Wheeler
Bonnie McKenzie

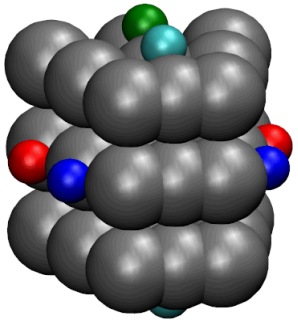
U.S. DEPARTMENT OF ENERGY

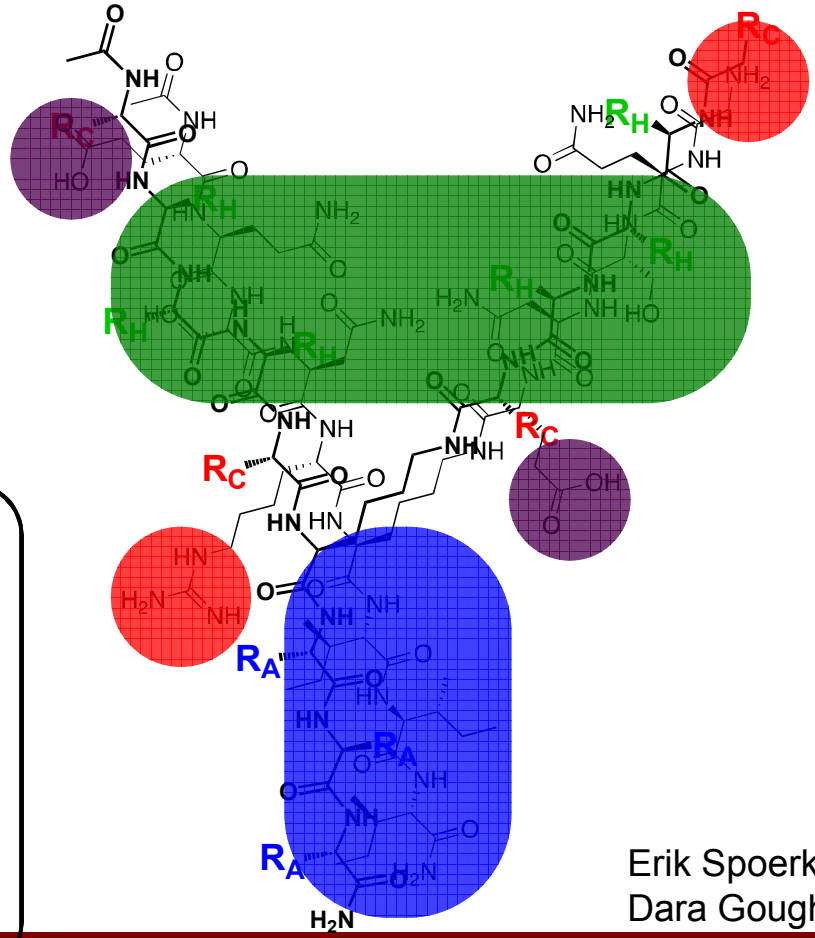
Simulation-Inspired Peptide Wedges

Peptide Wedges provide a unique experimental platform for probing the effects of monomer design on supramolecular assembly.

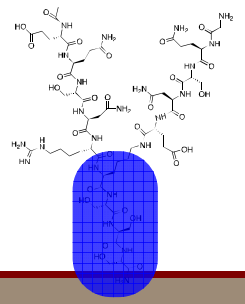
Variable Parameters:

- Peptide size, shape
- Electrostatic charge
- Amphiphilicity
- Hydrogen Bonding
- Molecular Asymmetry

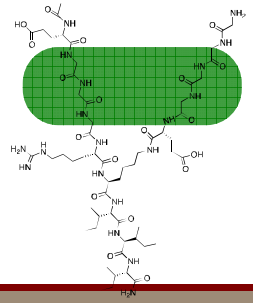




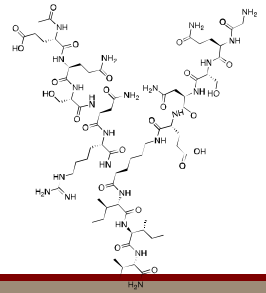
Hydrophilic



Reduced H-Bonding



No Modifications

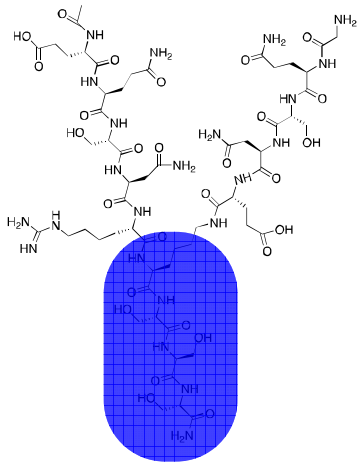


Erik Spoerke
Dara Gough
Jill Wheeler

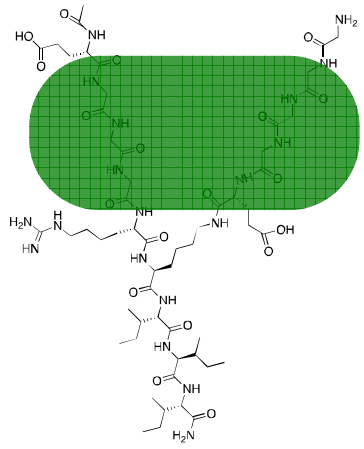
Varying Peptide Composition Affects Molecular Self-Assembly

Modifying either the amphiphilic or hydrogen bonding portions of the wedges prevents nanofiber formation!

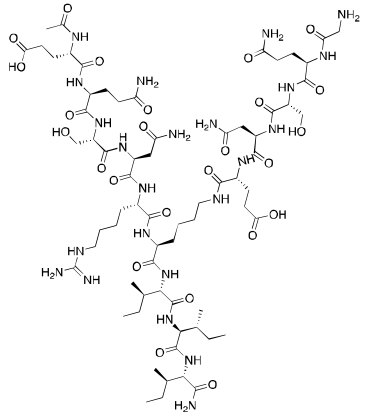
Hydrophilic

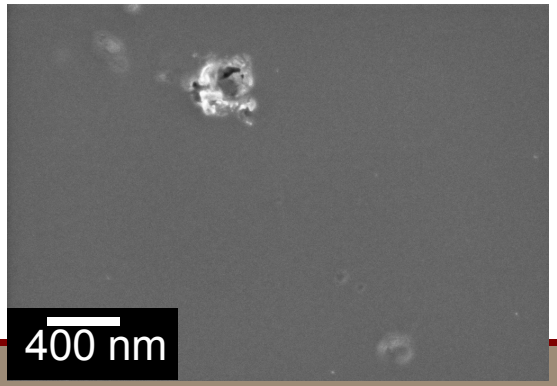


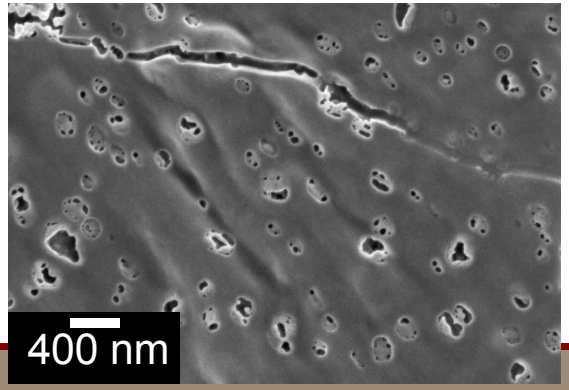
Reduced H-Bonding

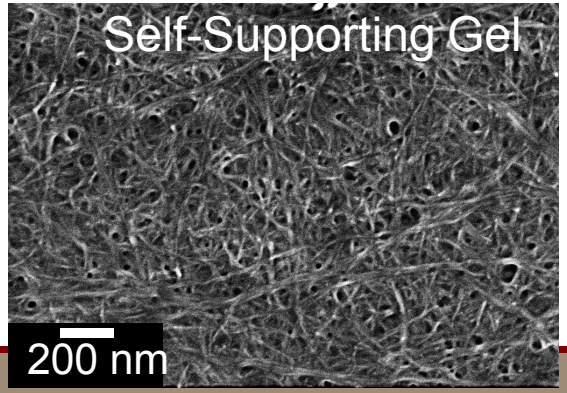


Wedge 1

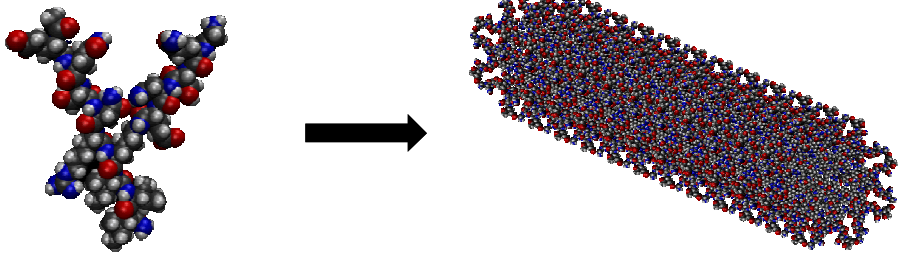


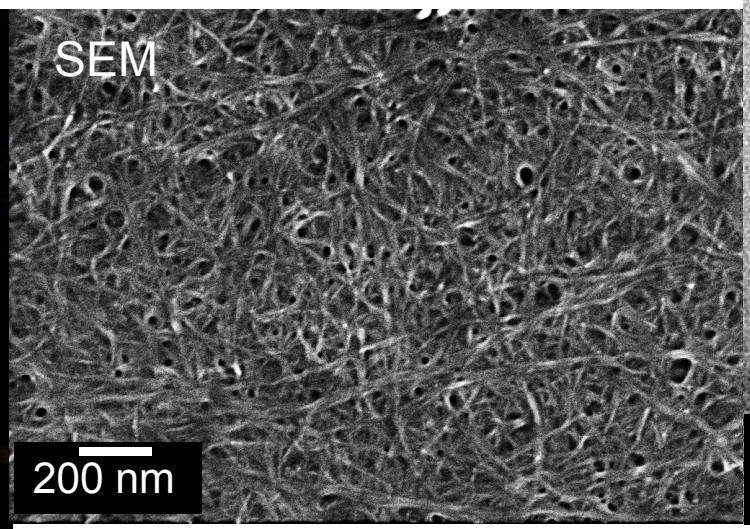


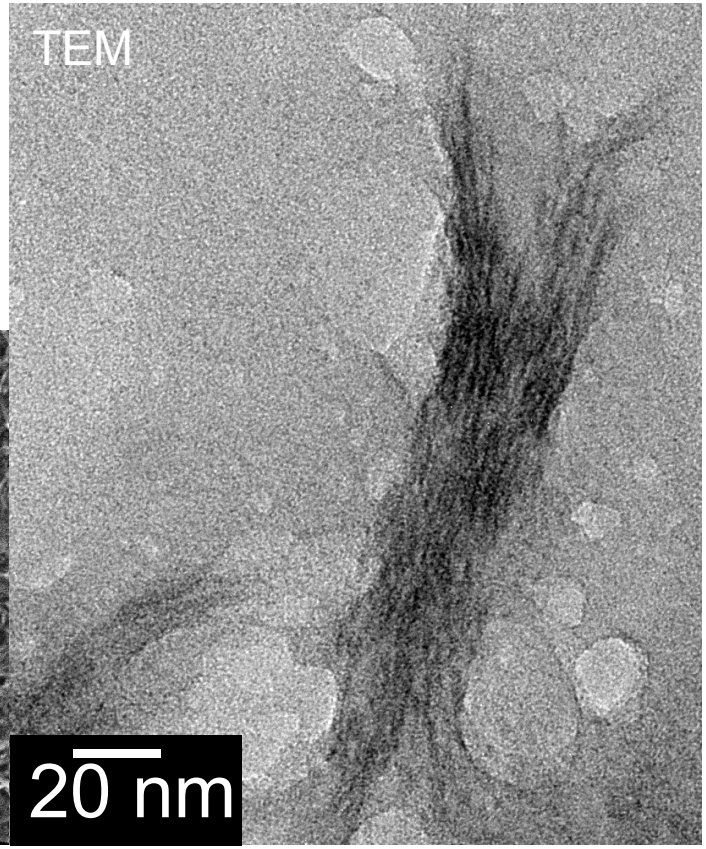




Asymmetric Wedge Assembly into Nanofiber Gels



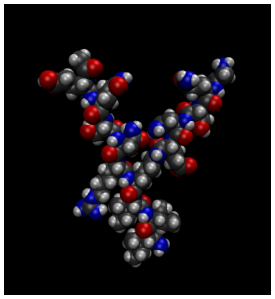




Peptide Wedges with 1) Hydrogen Bonding, 2) Electrostatic Charge, and 3) Amphiphilic Character form self-supporting gels comprising uniform nanofibers

~3.7nm across

Variable Assembly of Peptide Wedges



Variations in Wedge structure and chemistry could produce dramatically varied assemblies.