Beta-Hairpin Peptide Self-assembly: Construction of Advanced Materials from Injectable Gels to Nanoparticle Arrays

Bottom-Up Construction of Nanostructures and Materials

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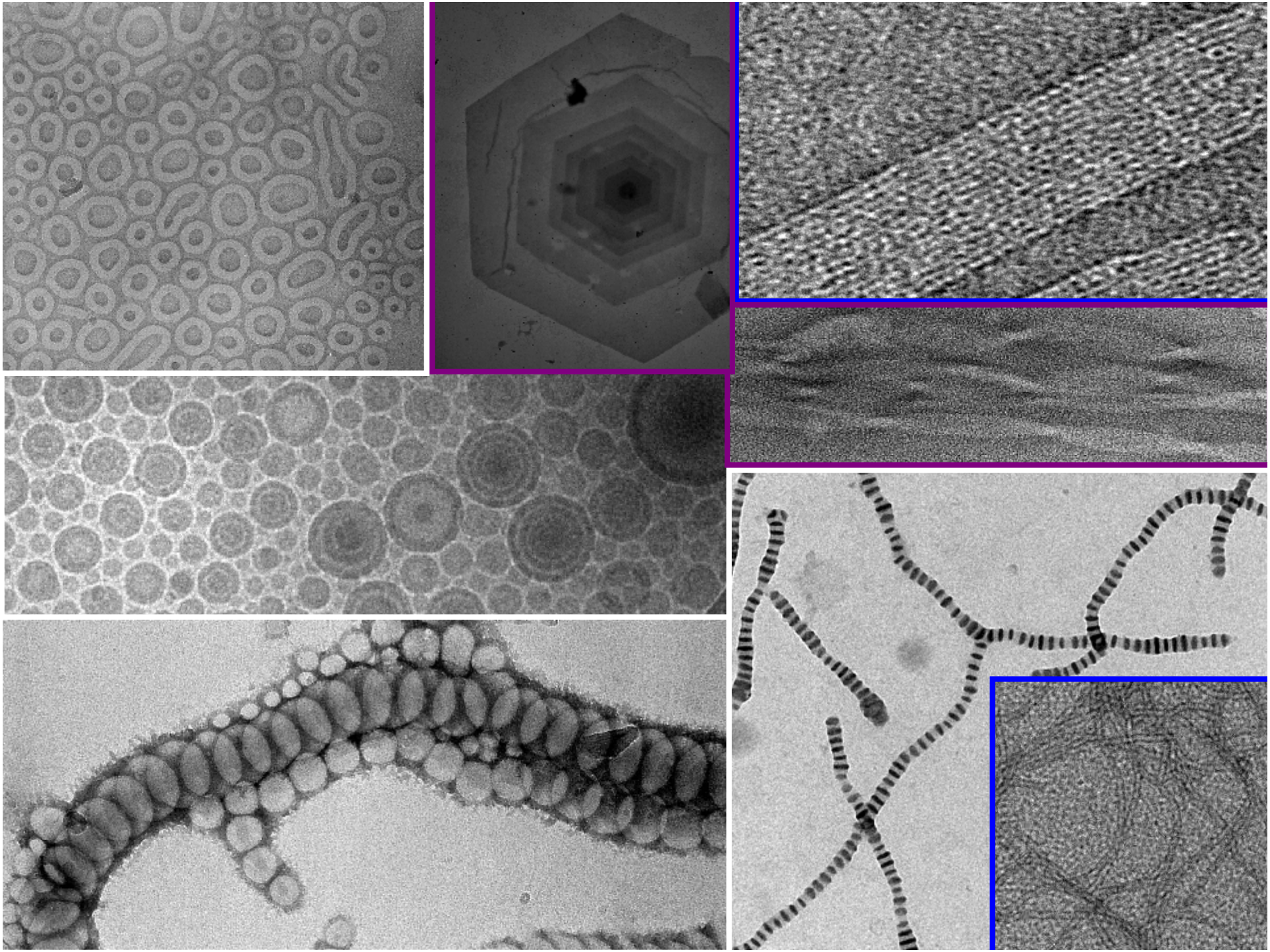


Outline of Important Points of Talk:

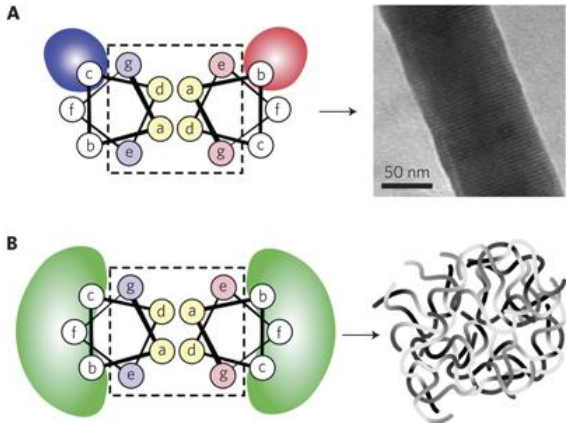
-Why use peptides for materials construction?

-**Hydrogel material properties** (example: self-assembly, shear-thinning and rehealing, initial biological properties)

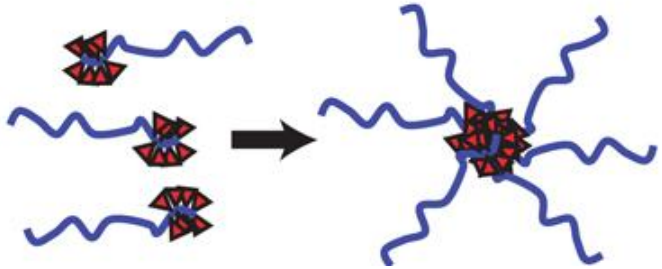
-**Effects of peptide changes on self-assembly behavior and structure**

- **Peptide materials for non-biological applications** (example: inorganic nanoparticle templating)

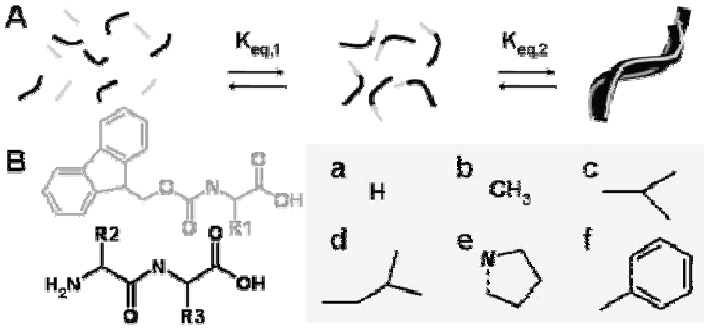
- Future opportunities



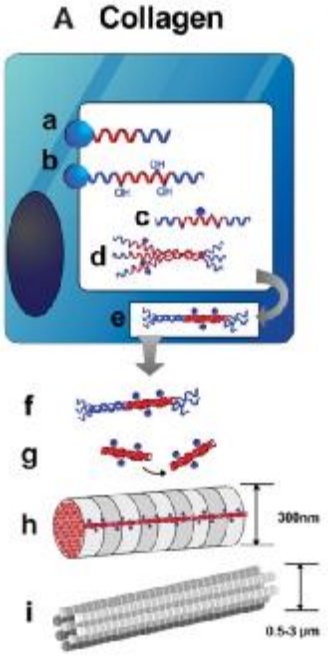
E. F. Banwell, E. S. Abelardo, D. J. Adams, M. A. Birchall, A. Corrigan, A. M. Donald, M. Kirkland, L. C. Serpell, M. F. Butler and D. N. Woolfson, *Nat. Mater.*, 2009, 8, 596



JA MacKay, M Chen, JR McDaniel, W Liu, AJ Simnick and A Chilkoti. *Nature Materials* 2009 8 993-999.



S. Toledano, R. J. Williams, V. Jayawarna and R. V. Ulijn, *J. Am. Chem. Soc.*, 2006, 128, 1070



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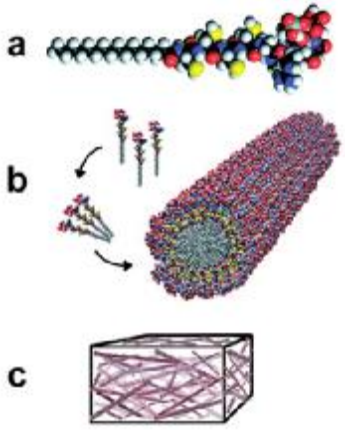
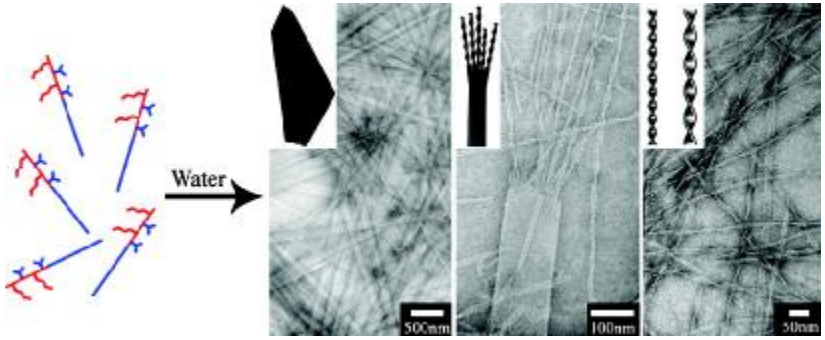
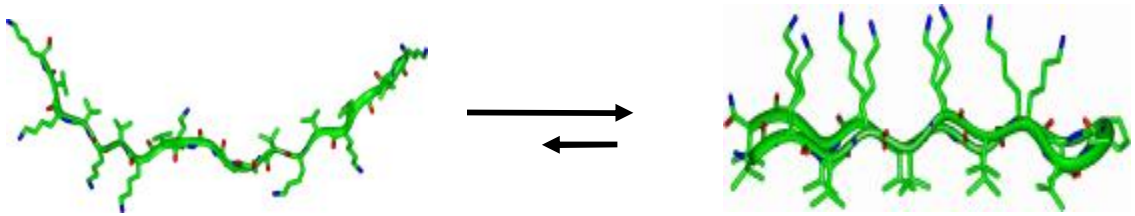


J. D. Hartgerink, E. Beniash and S. I. Stupp, *Science*, 2001, 294, 1684



H. Cui, T. Muraoka, A. G. Cheetham and Samuel I. Stupp, *Nano Lett.*, 2009, 9, 945

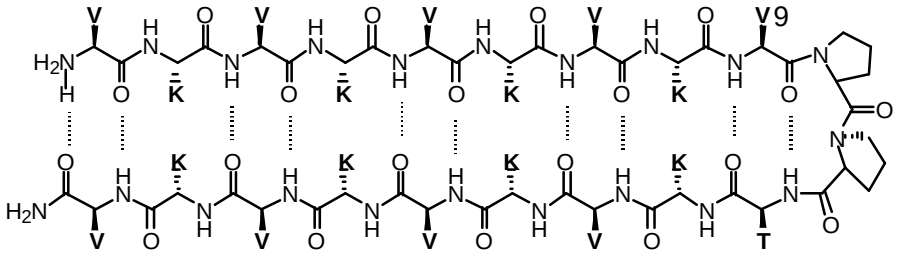


Why use peptides for Materials Construction?

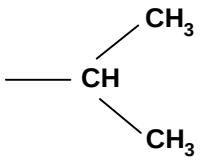
- Adopt triggered secondary, tertiary and quaternary conformations in solution that assemble into hierarchical nano-scale architectures
- Nanostructure, gelation kinetics and elastic modulus depends on primary sequence and can thus be conveniently changed by changing the primary sequence
- Chemical/biological functionality may be engineered at specific sites due to ease and versatility of the solid phase or recombinant DNA synthesis process
- Simple aqueous solution self-assembly construction methods for reliably producing a diversity of nanostructures and materials

Why use peptides for self-assembly?
Design for **folding** and **consequent self-assembly**

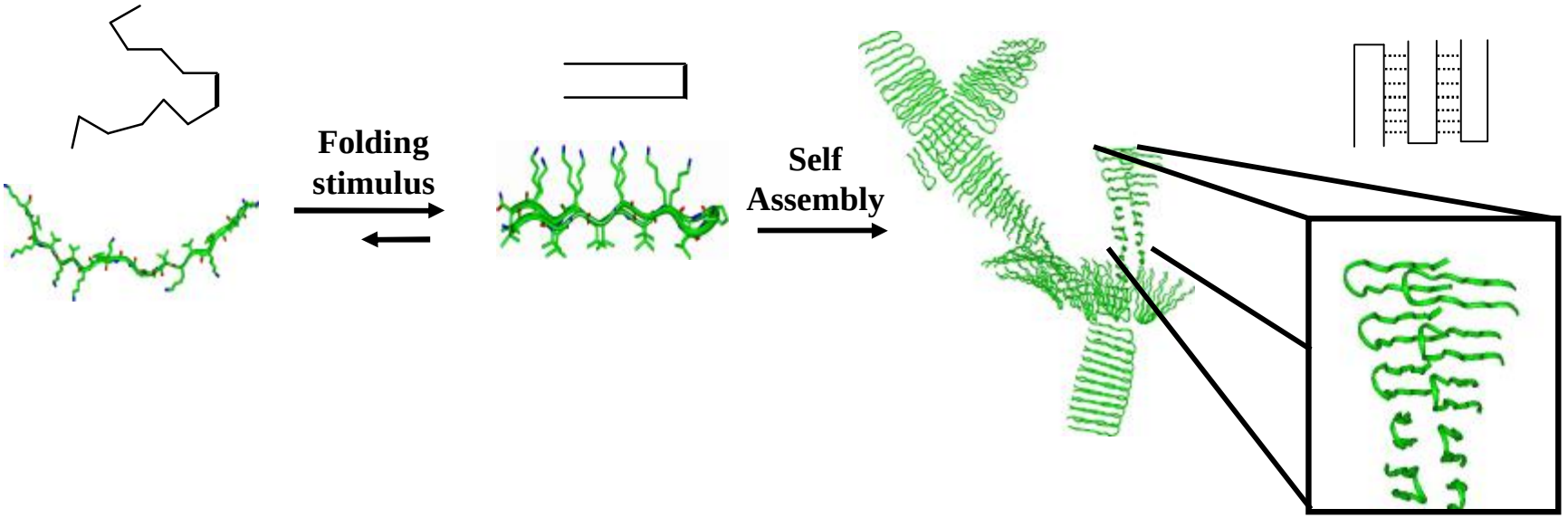
MAX1: VKVKVKVKV^{D}PPTKVKVKVKV-NH_2



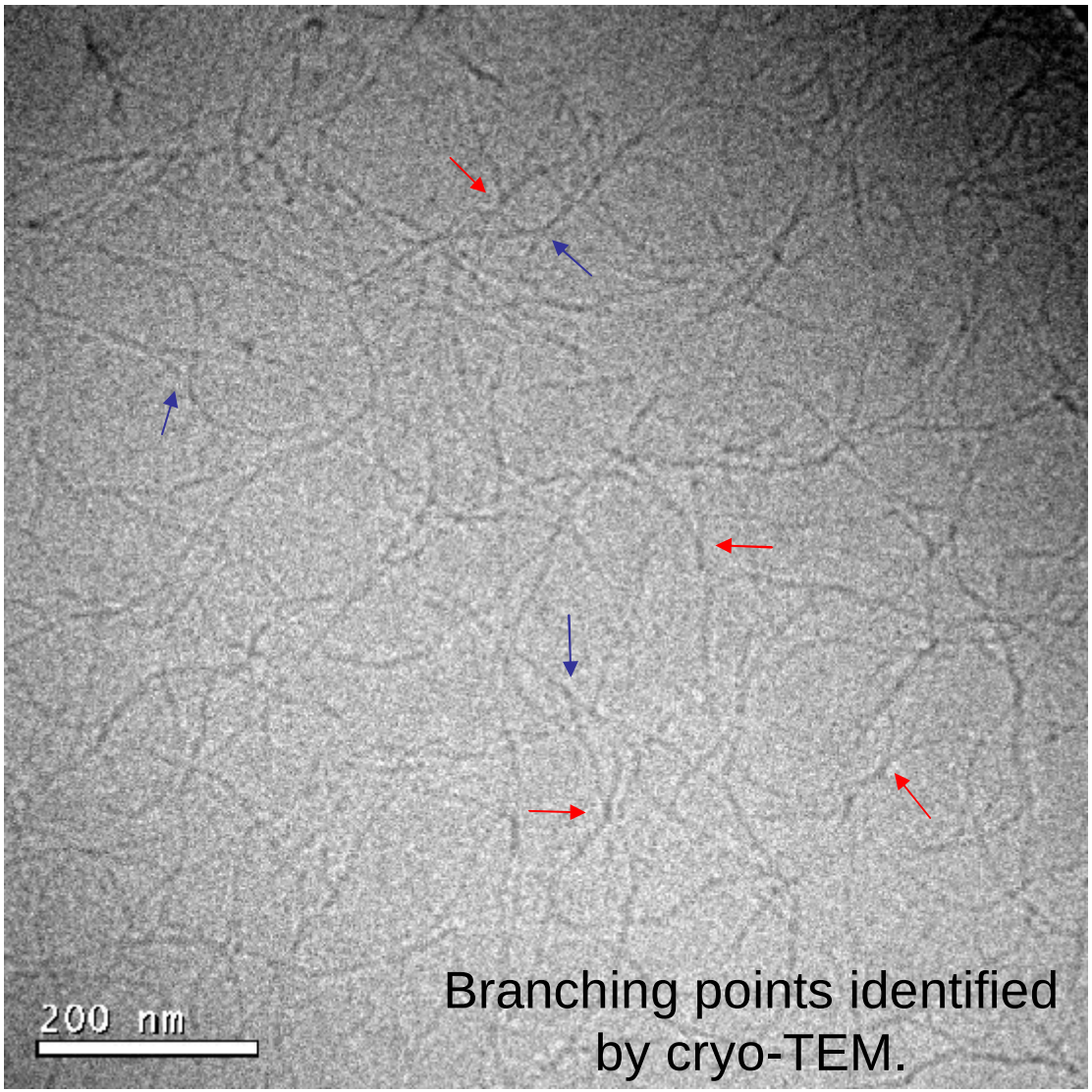
V (valine)



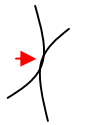
K (lysine)

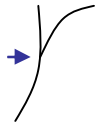


Nature of Inter-Fibrillar Interactions



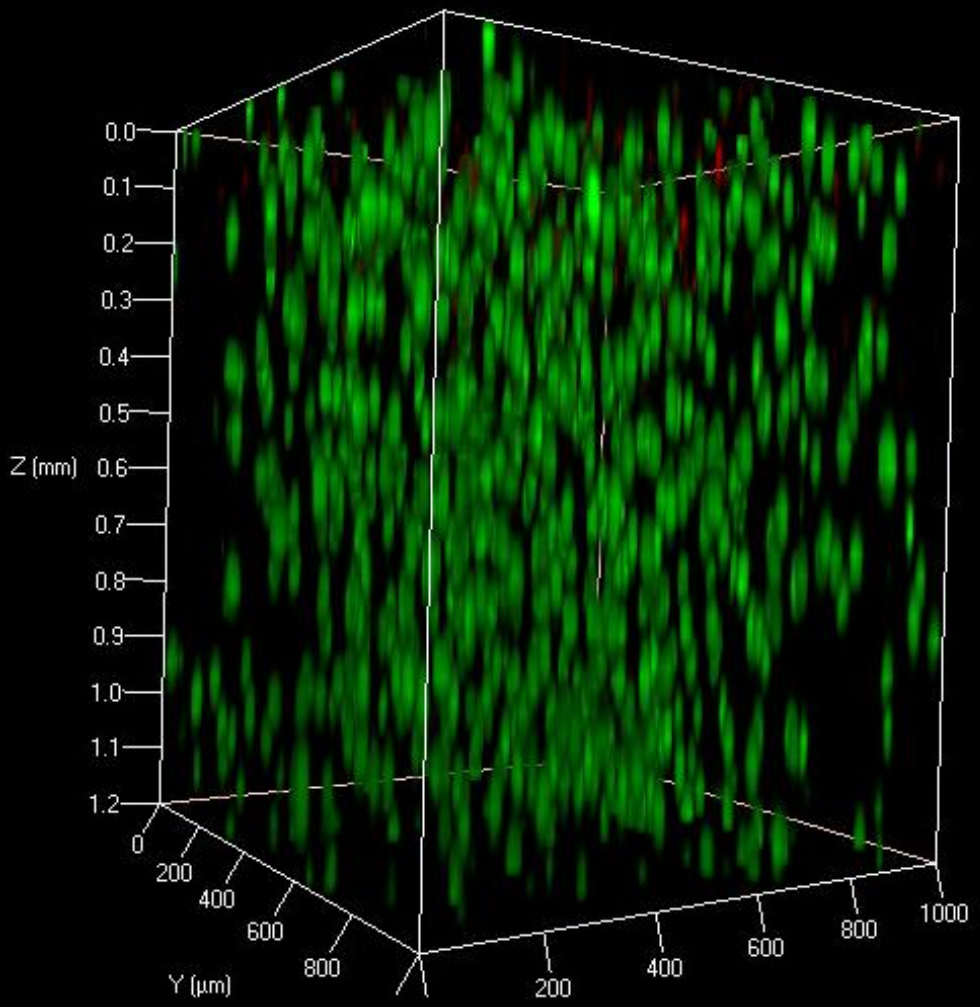
Branching points identified by cryo-TEM.

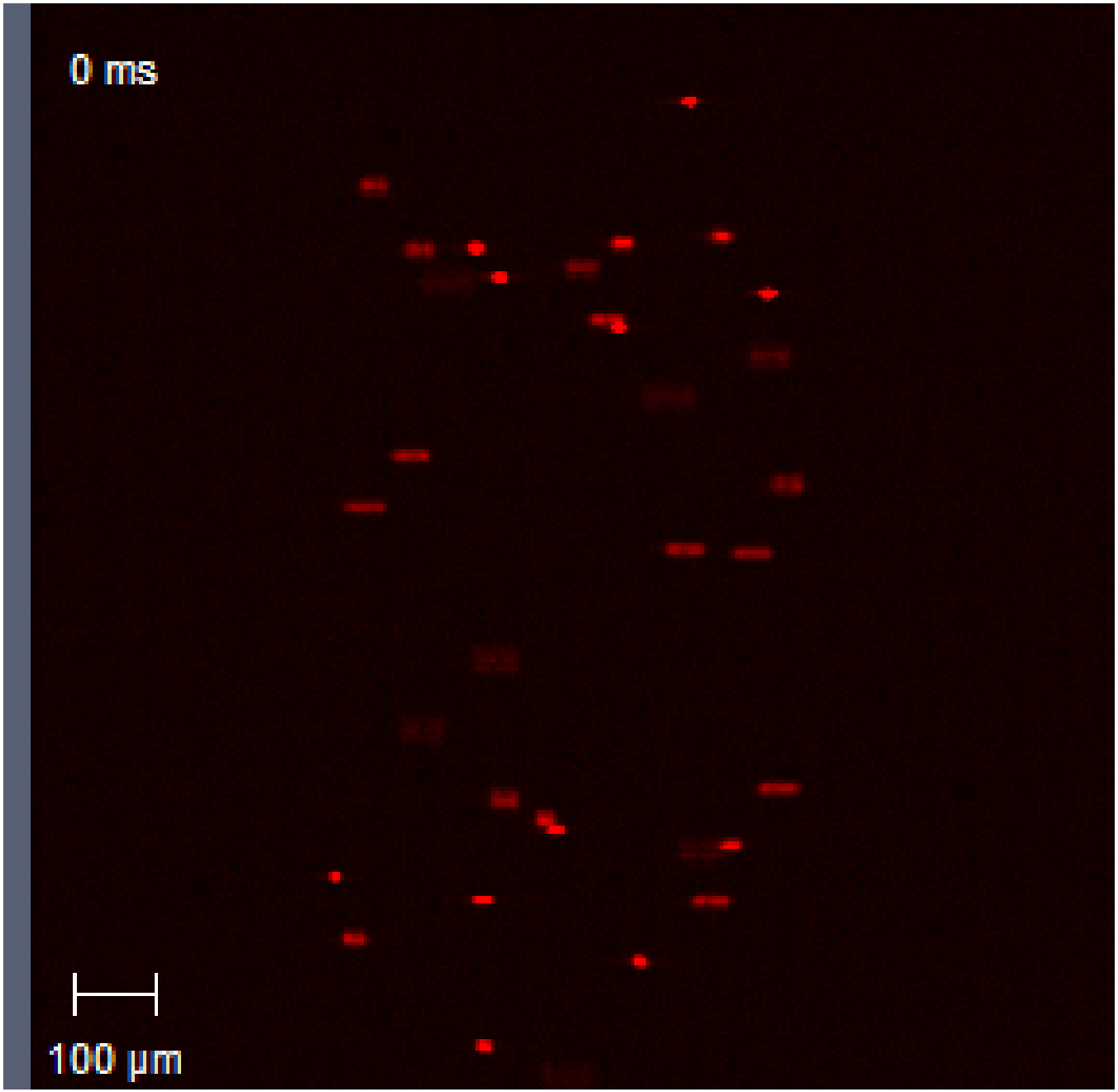




Cui, Pochan, *et al.*, Soft Matter, 2007, *3*, 945-955.
Yucel, Pochan, *et al.* Macromolecules, 2008, 41, 5763–5772.

MG63 cells 3D encapsulated in 0.75wt% MAX8 hydrogel:
3hrs after being injected at 8mL/hr respectively.




0 ms
100 µm

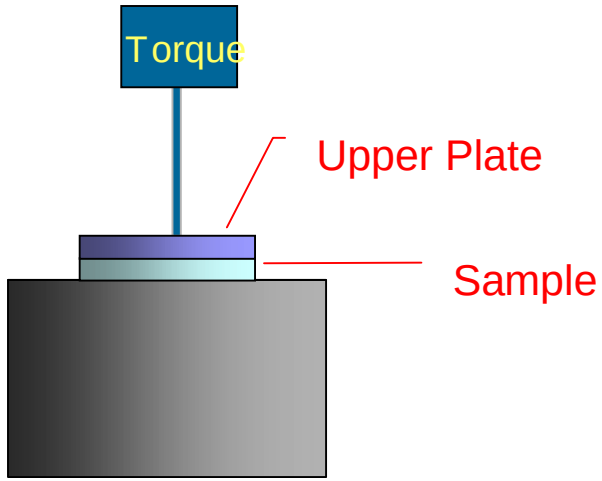
Shear-thinning and self-healing of gels

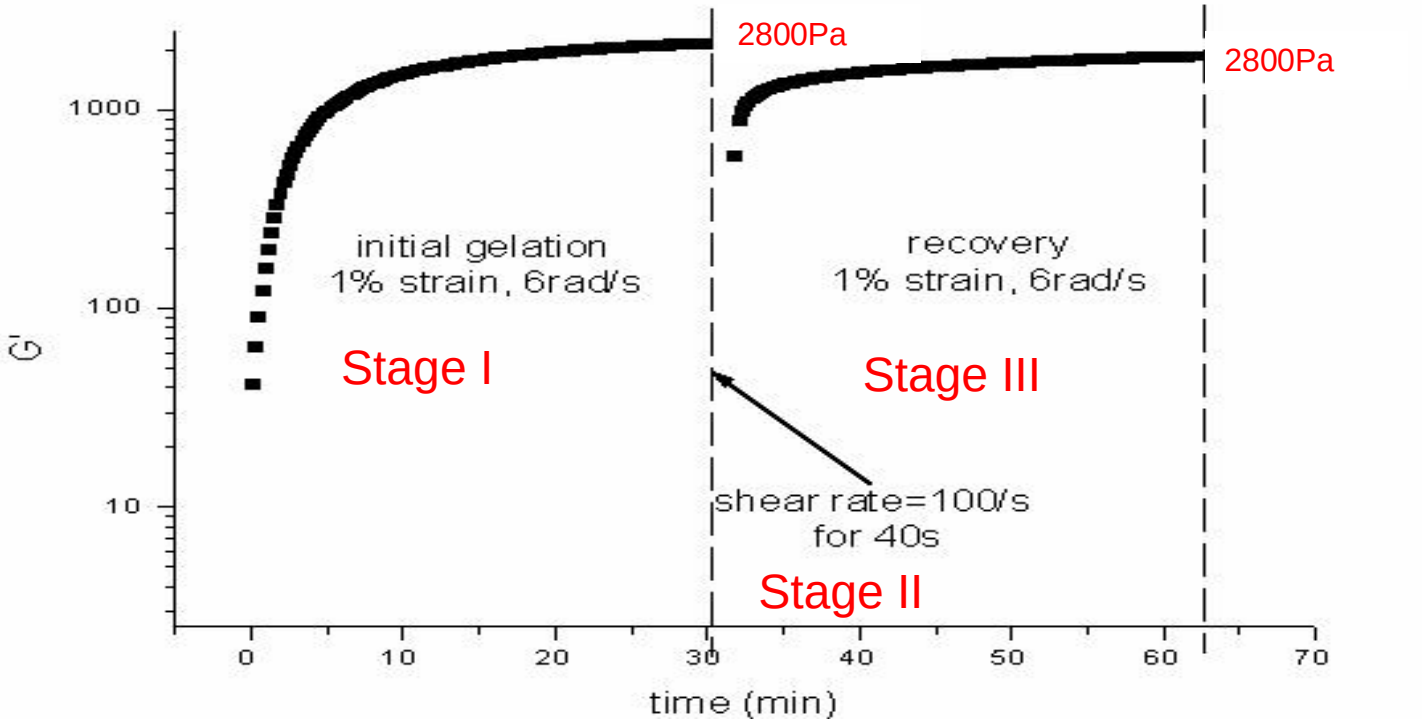
Procedure of rheometric measurement

Stage I: Gelation

Stage II: Shear disruption

Stage III: Restoration

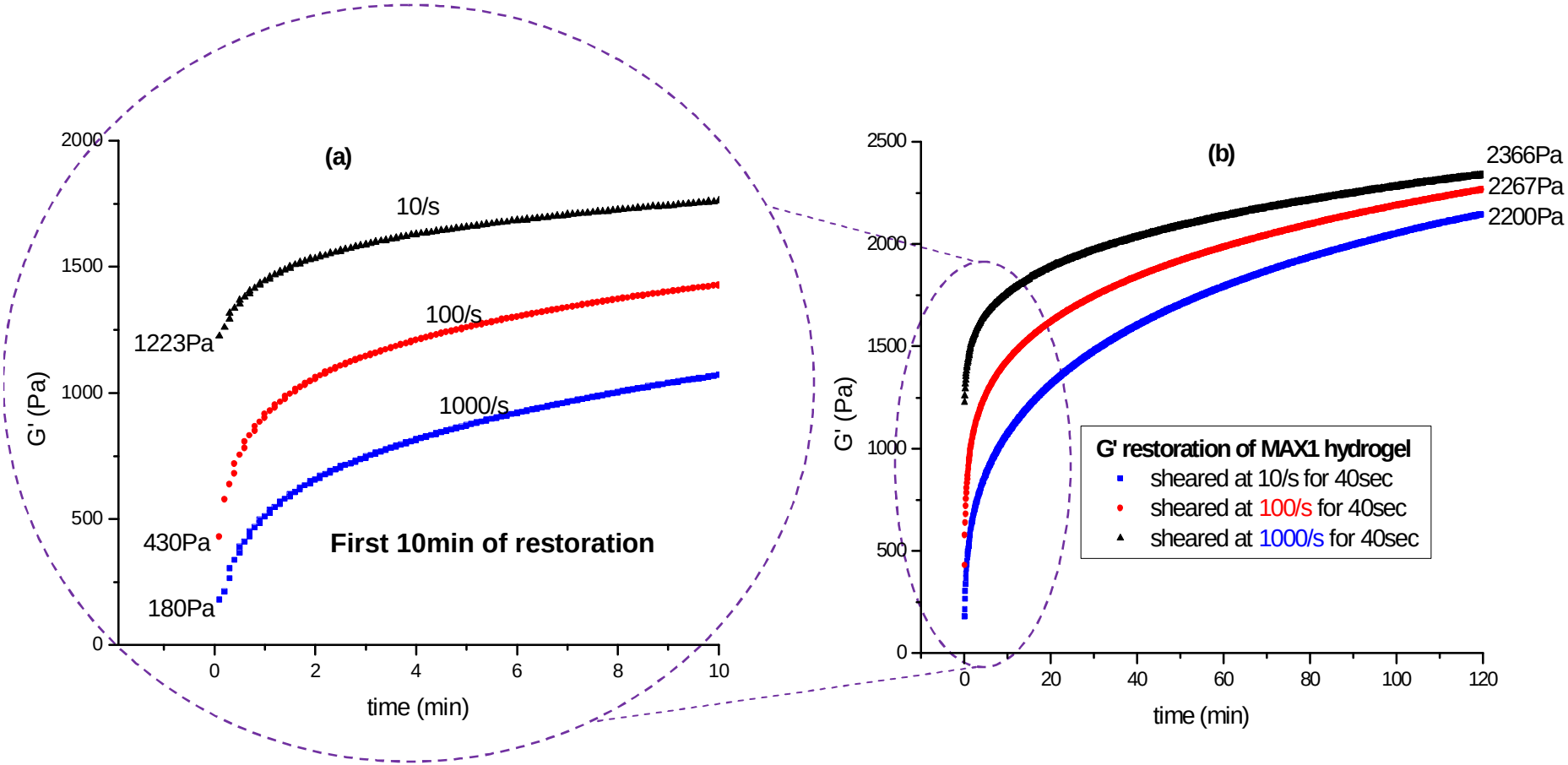




2wt% MAX1 with 50mM BTP and 400mM NaCl at pH7.4, 20℃

Same shear duration, different shear rate

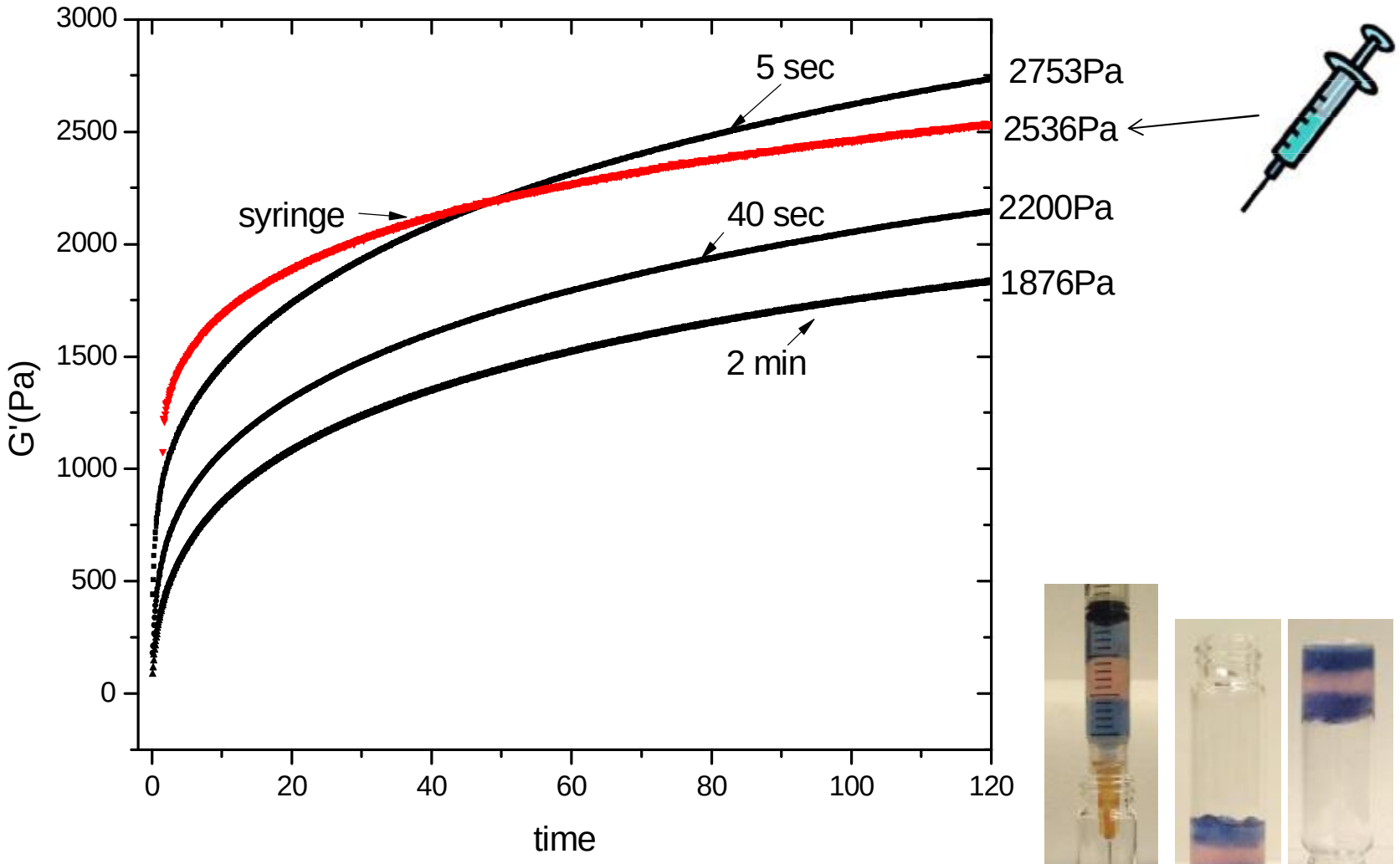
At 20℃ , equilibrated 2wt% MAX 1 hydrogels



Yan, et al. Soft Matter, 2011, asap

Restoring gel stiffness: injection shear vs. rheometer-induced shear.

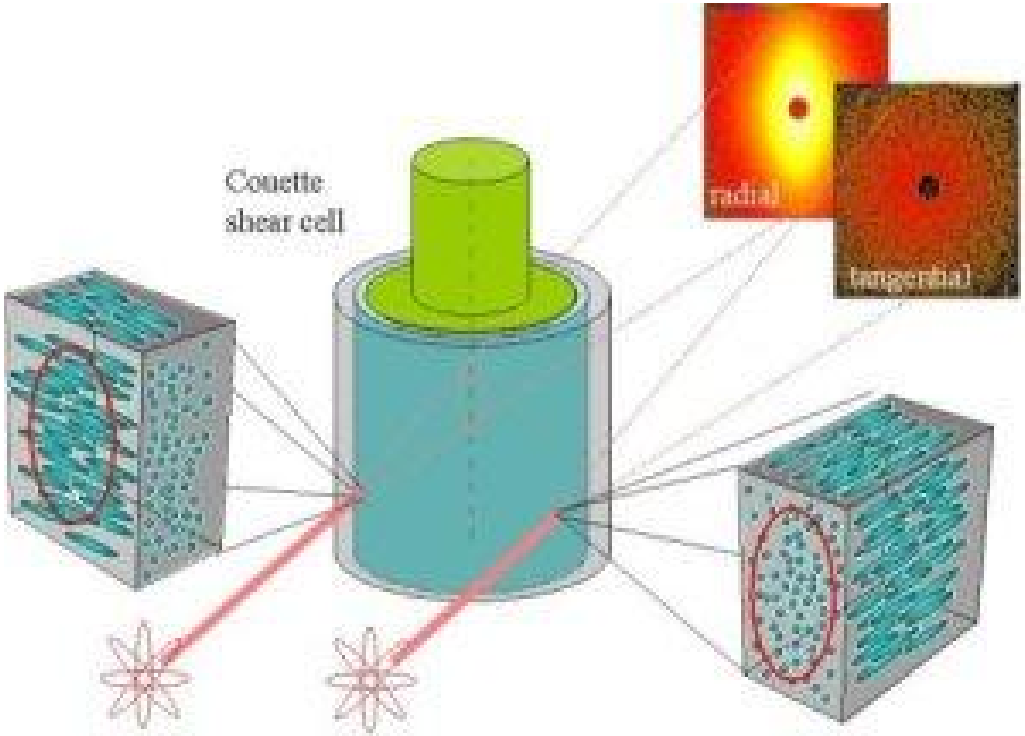
At 20℃ , equilibrated 2wt% MAX1 hydrogels (Plateau G'=2900±200Pa)



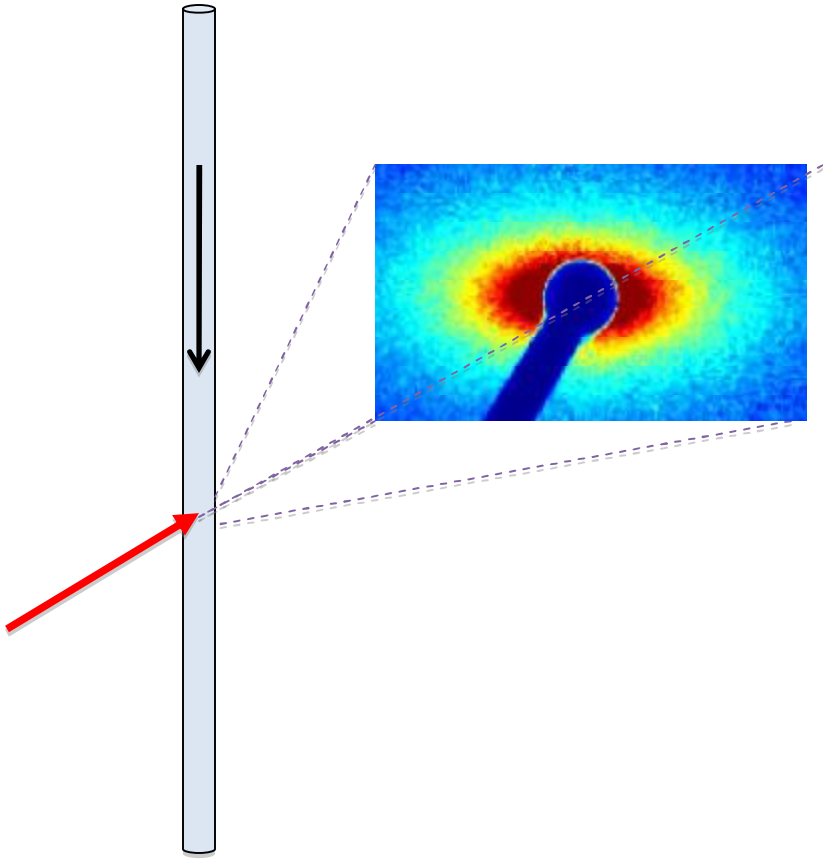
Yan, et al. Soft Matter, 2011, asap

Dynamic network morphology during flow.

Objective: any anisotropic features under flow—fibril alignment



Rheo-SANS (NCNR, NIST)

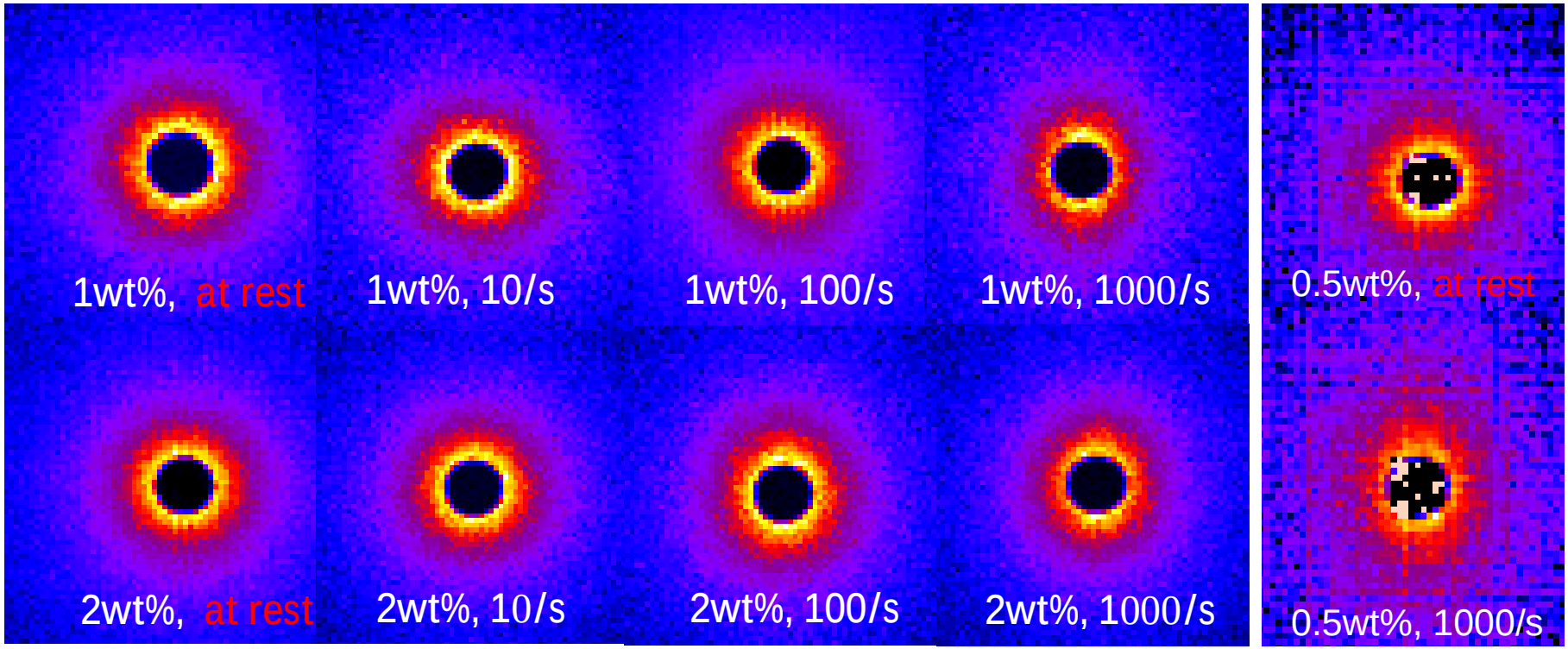


Flow cell-SAXS (BioCAT, Argonne)

http://www.ncnr.nist.gov/equipment/Publications/Greenwald.pdf

Rheo-SANS: 2D radial scattering patterns

Objective: any anisotropic features under shear flow—fibril alignment

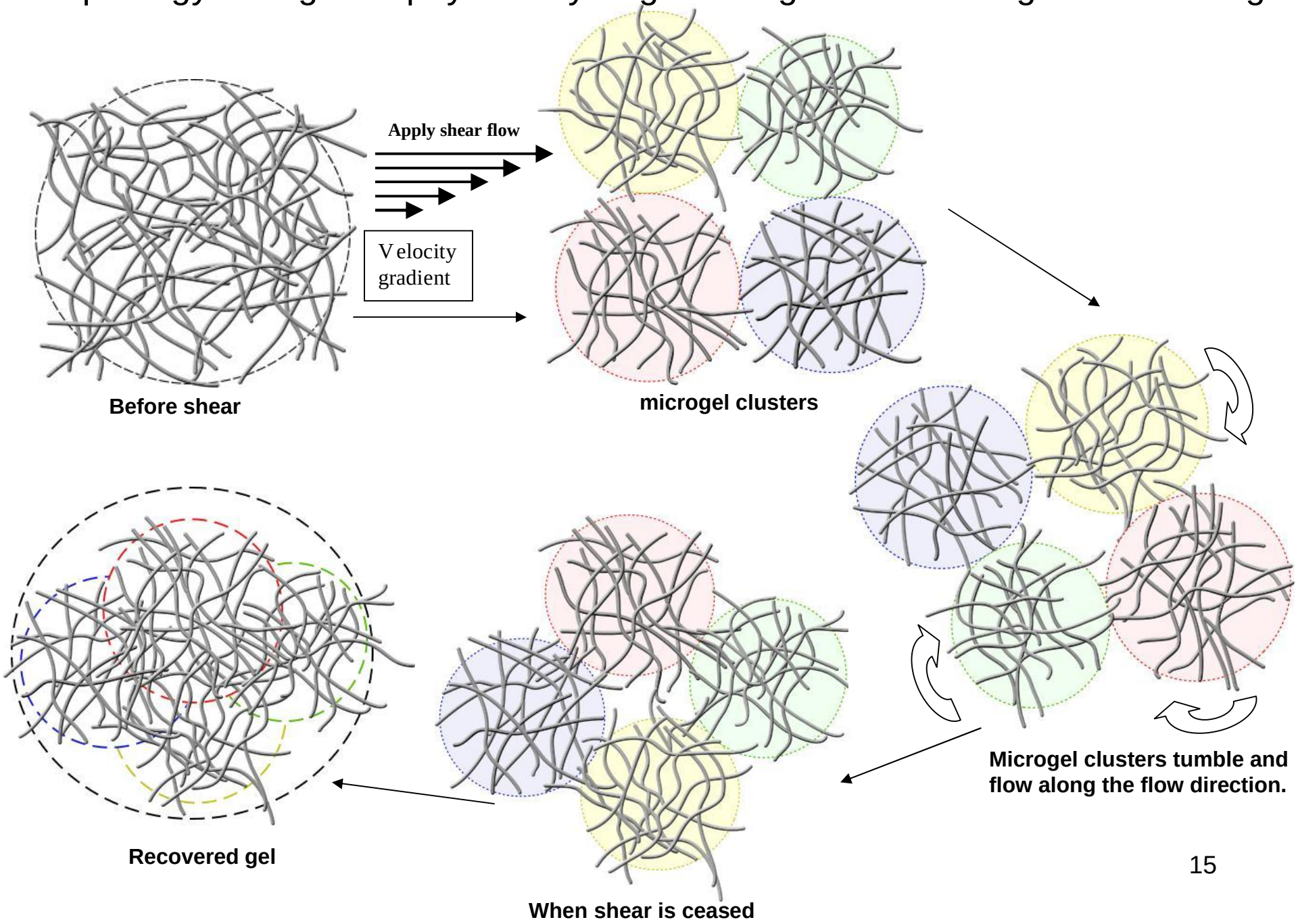


1wt% and 2wt% MAX1 gels

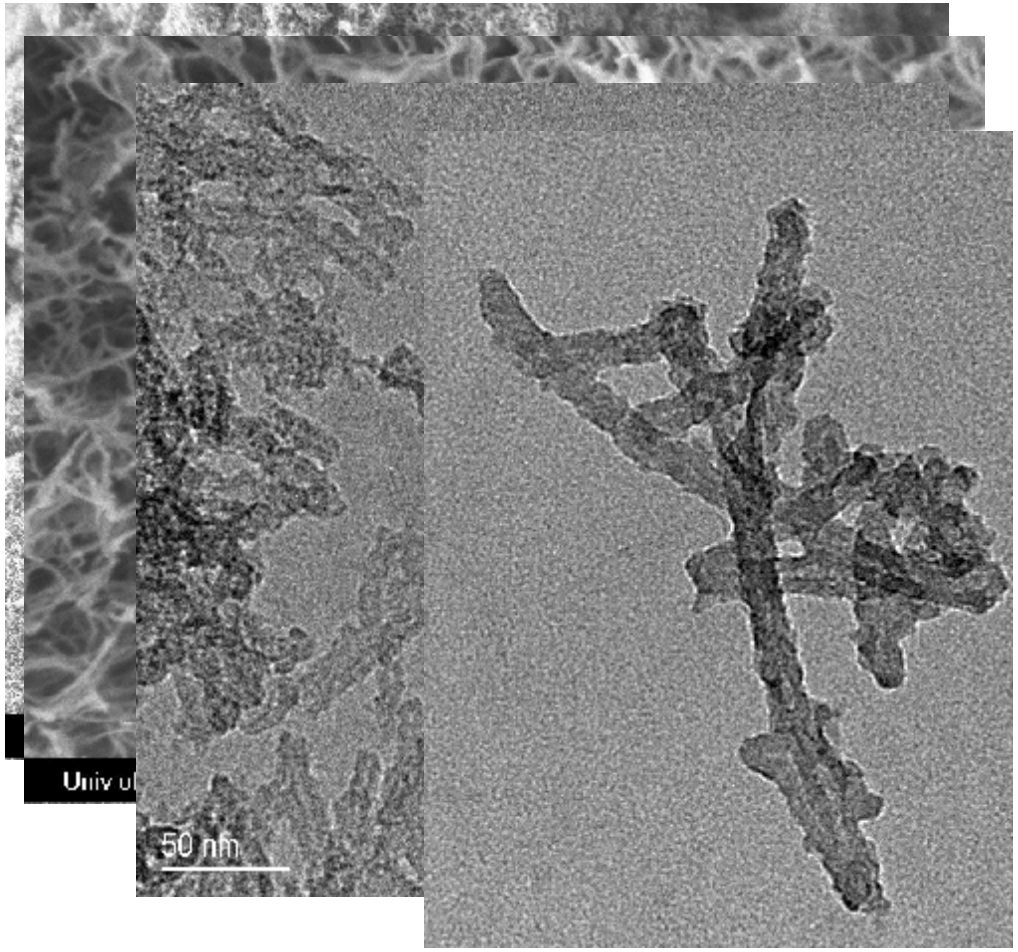
0.5wt% MAX8 gels

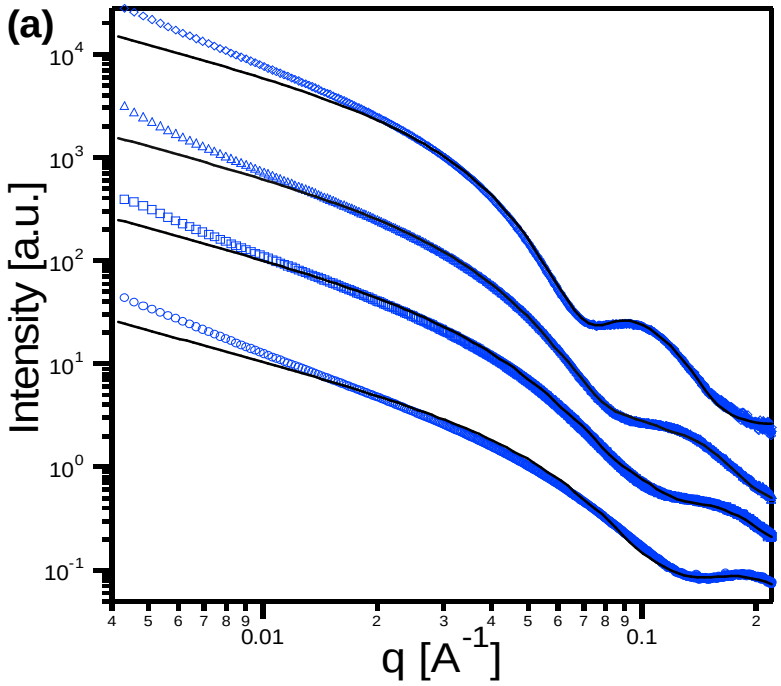
Yan, et al. Soft Matter, 2011, asap

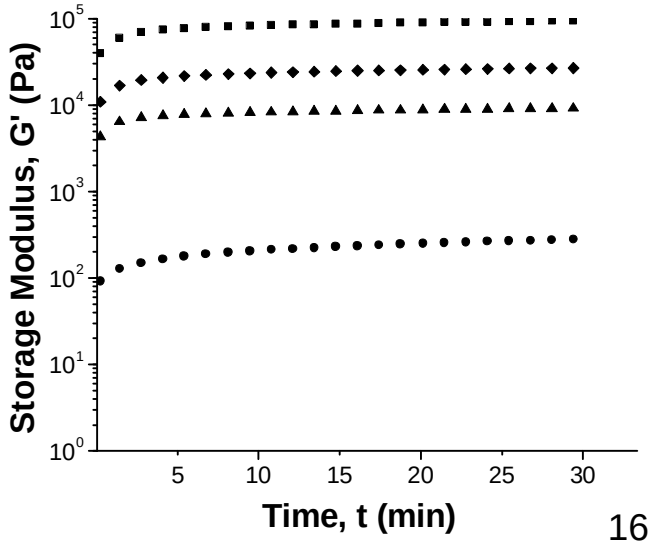
Morphology changes of physical hydrogel during shear-thinning and rehealing



Hybrid composite materials through sol-gel chemistry:

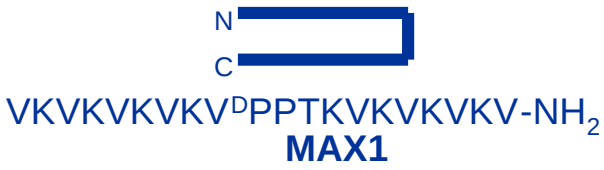






Altunbas, et al. *ACS Nano*, 2009, *4*, pp 181-188.

Peptide design to alter nanostructure



VKVKVKVKV^{D}PPTKVKVKVKV-NH_2

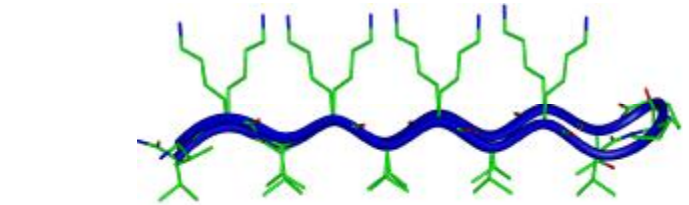
MAX1

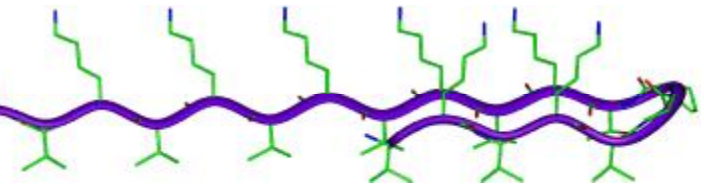
VKVKVKV^{D}PPTKVKVKVKVKV-NH_2

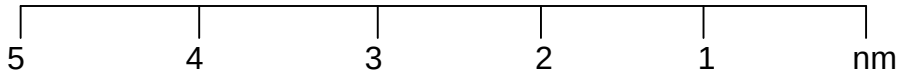
SS1

VKVKV^{D}PPTKVKVKVKVKV-NH_2

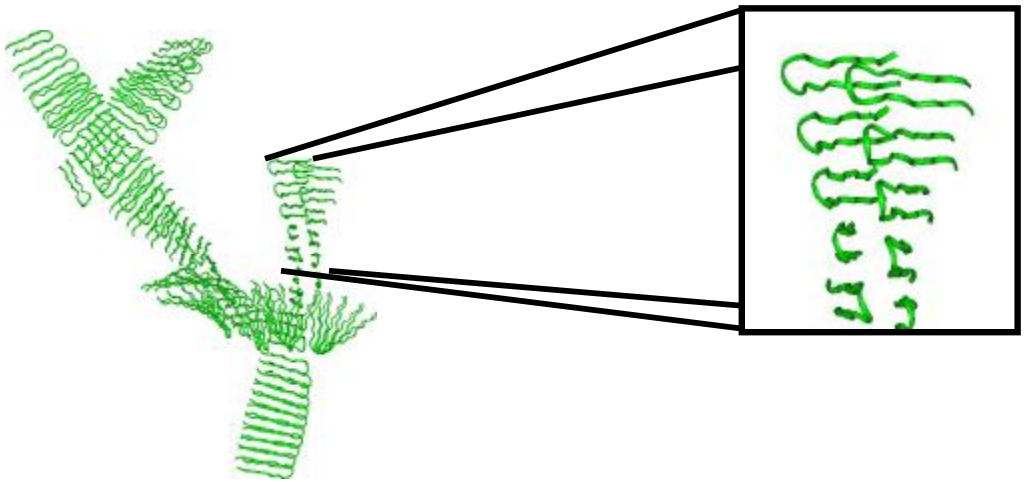
TIN







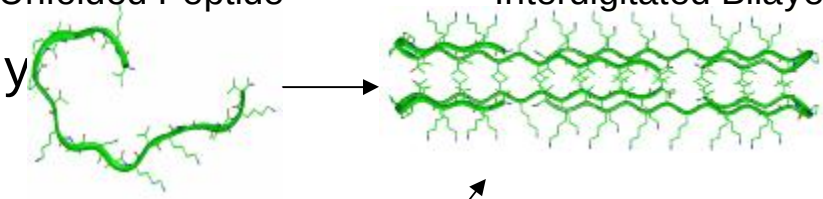
Nagarkar, Hule, et al. *J. Am. Chem. Soc.* **2008,** 130, 4466-4474

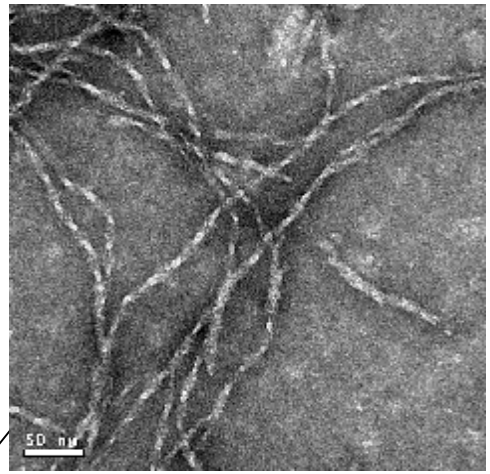


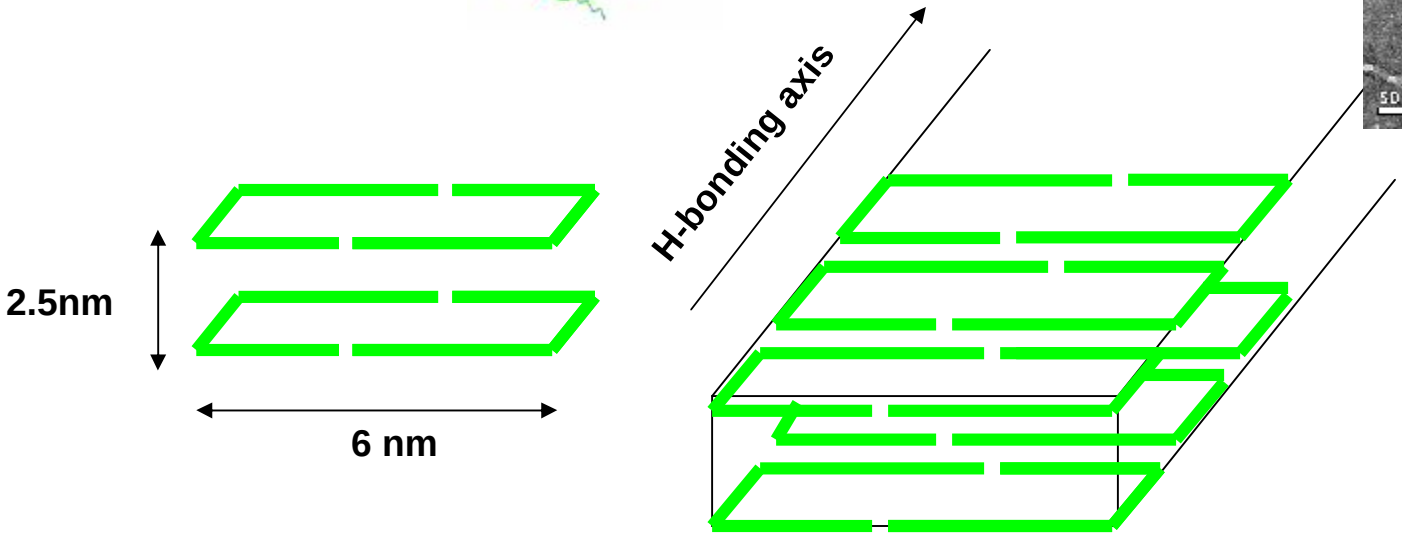
Asymmetry Assembly Mechanism:

Unfolded Peptide

Interdigitated Bilayer



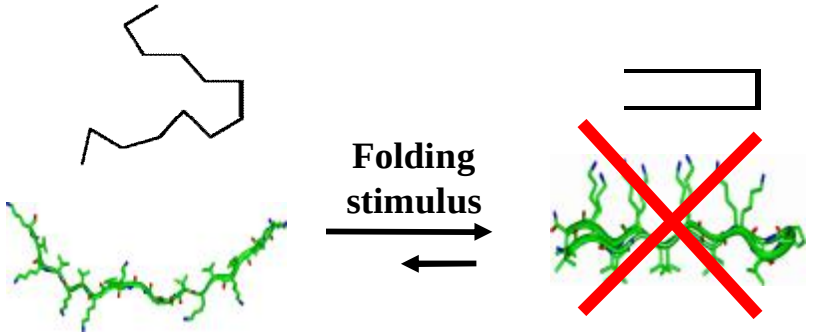


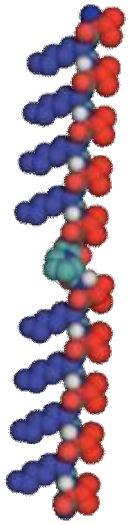


Nagarkar, Hule, et al. *J. Am. Chem. Soc.* **2008,** 130, 4466-4474

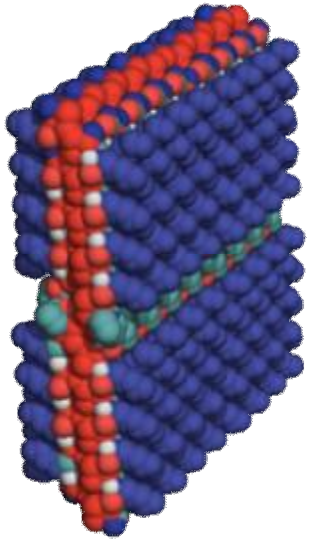
MAX1: VKVKVKVKV^{D}PPTKVKVKVKV-NH_2

VKVKVKVKV**P**PTKVKVKVKV-NH_2

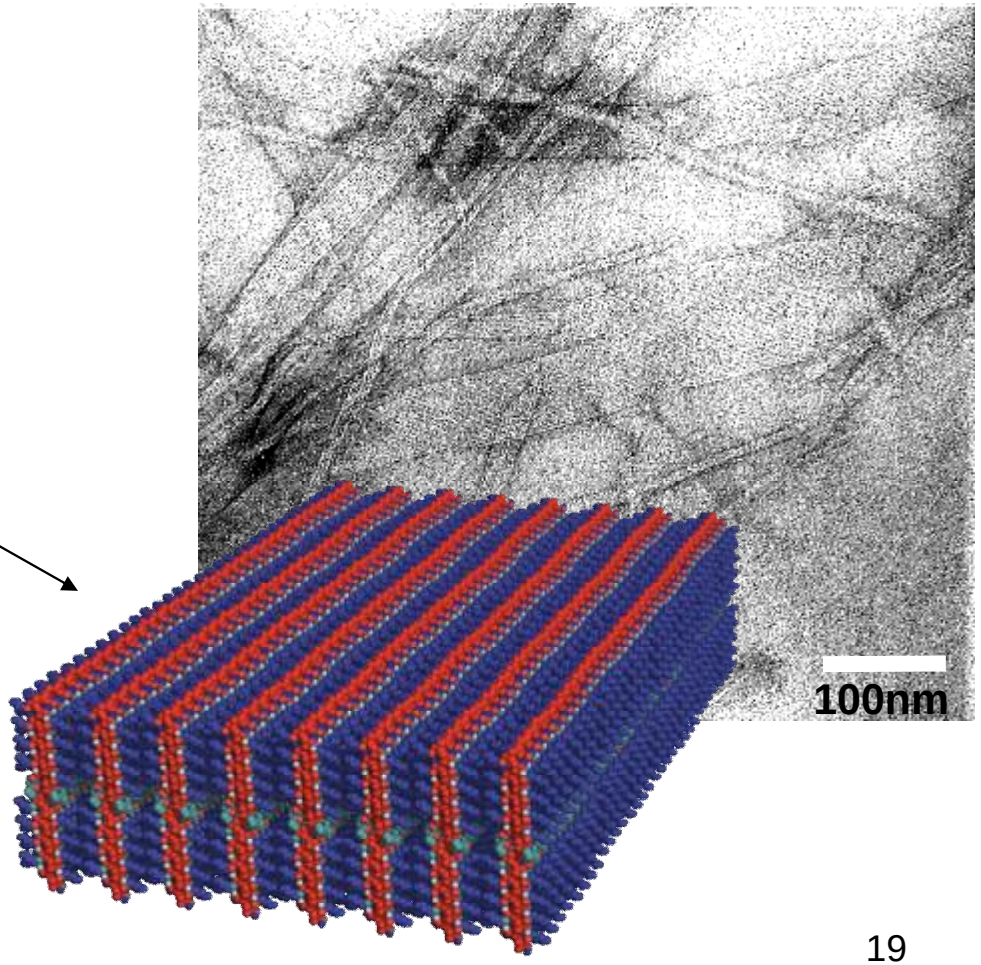




Extended
β-Strand



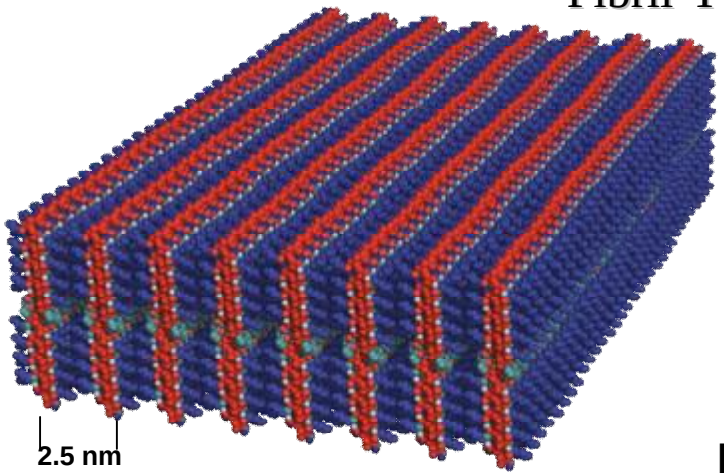
β-Sheet Bilayer



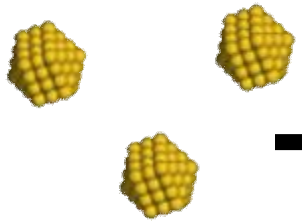
Laminated β-Sheet Fibril

Lamm et al, JACS, 2005, 127, 16692

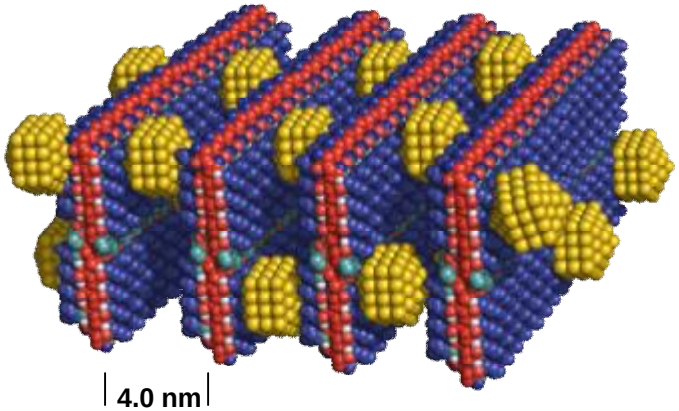
Fibril-Templated Nanoparticle Arrays



Laminated b-Sheet Fibril

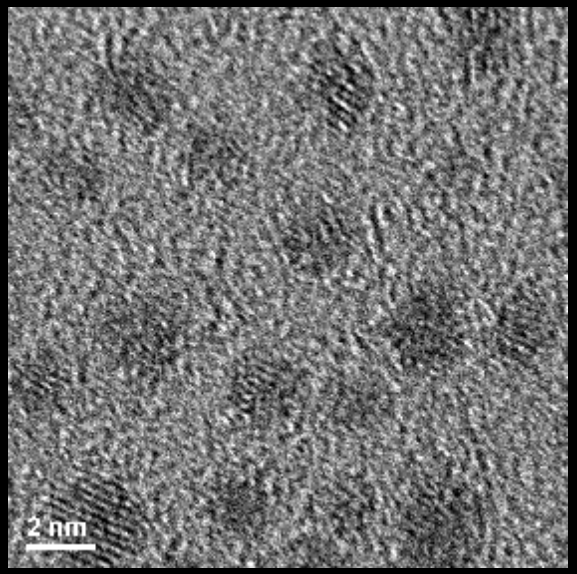


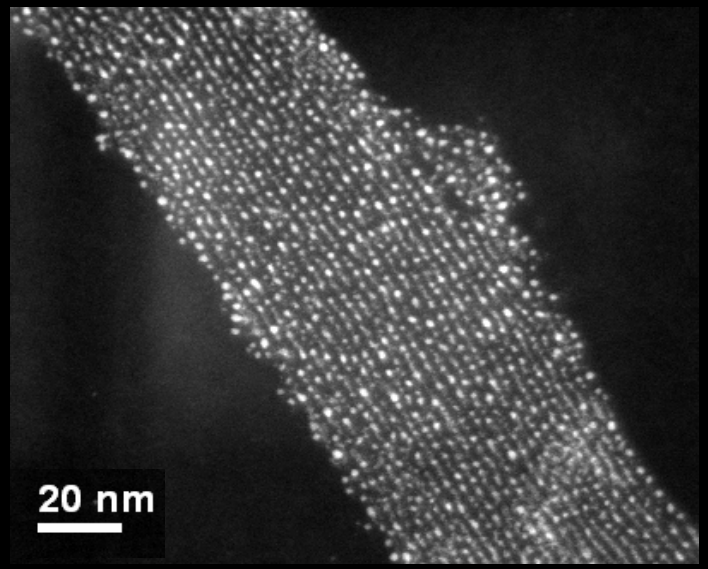
Negatively charged Gold Nanoparticles

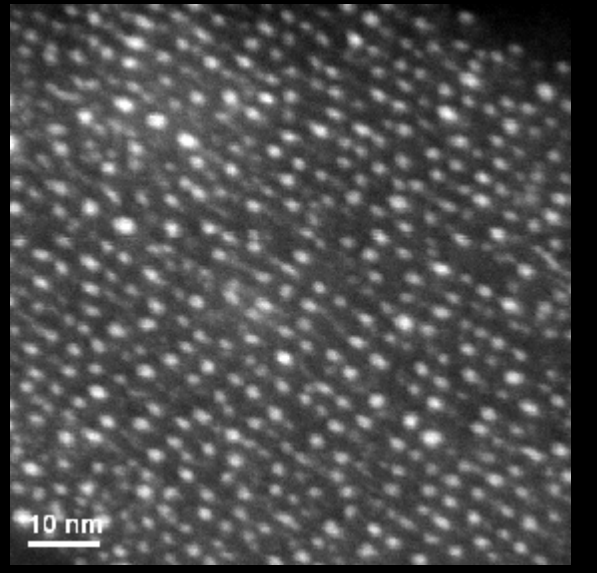


Templated Nanoparticle Array

HAADF-STEM



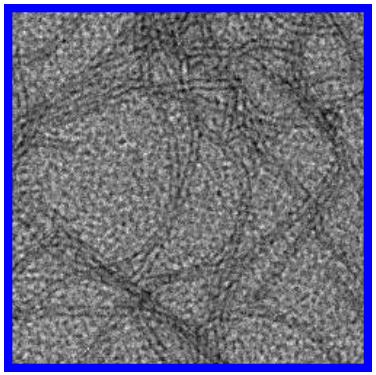




Lamm, et al., Advanced Materials, 2008, vol 20 pg. 447.

Peptides: Biomaterials and Nanotechnology of the Future!(?)

-More functionality in molecules
  -e.g. Degradability, drugs, natural proteins

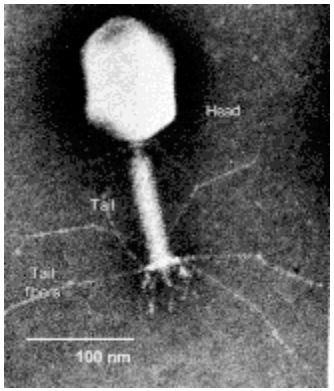


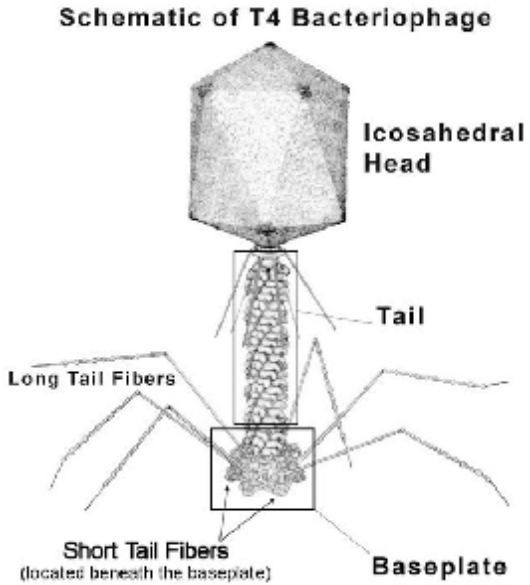
-Local construct delivery
  -Multiple drug, sustained and defined profile, then degrade

  -Multi-cell delivery

-Model system to discover new cell biology

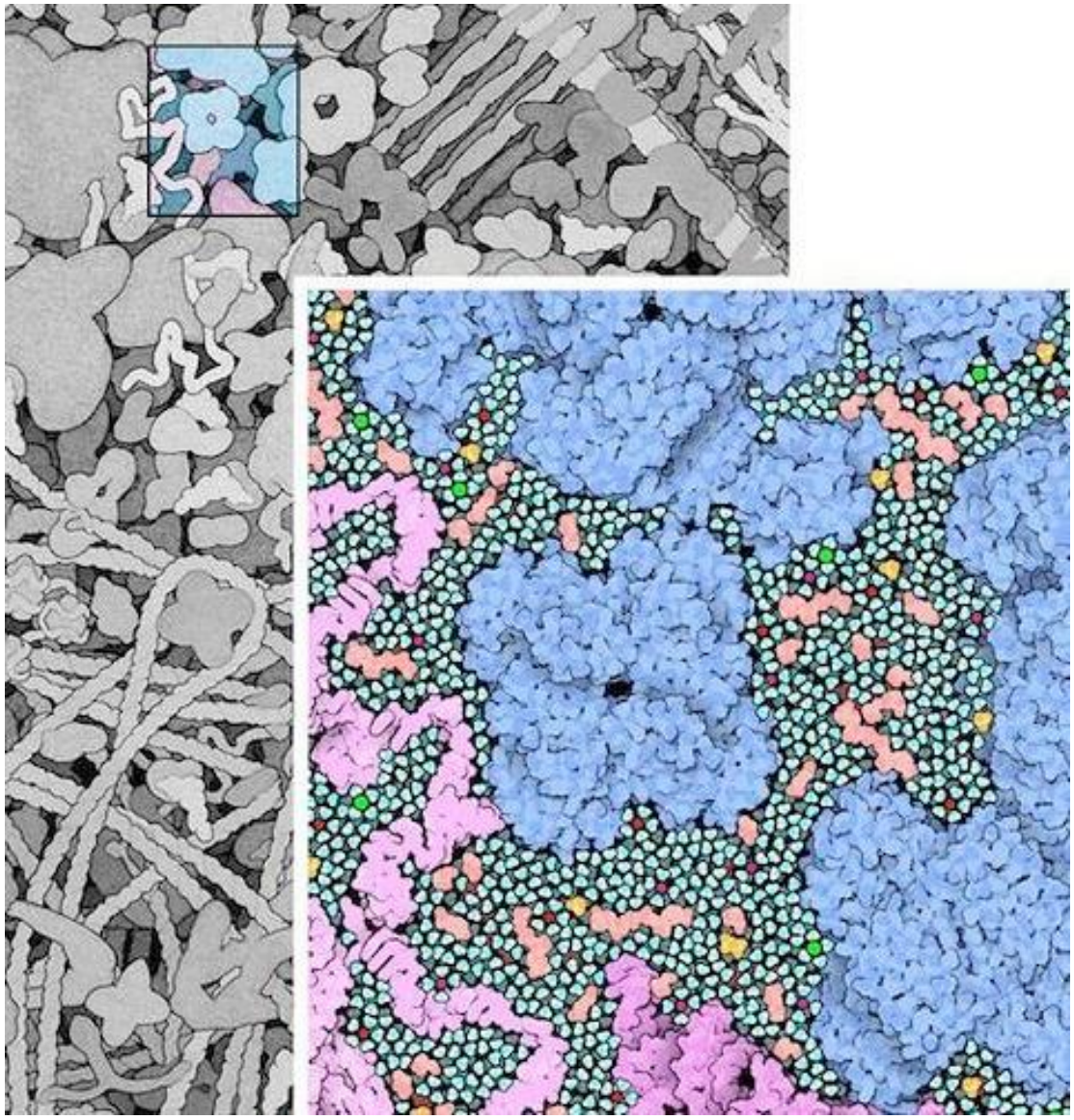
-2 and 3-dimensional assembly !!!!!!!!

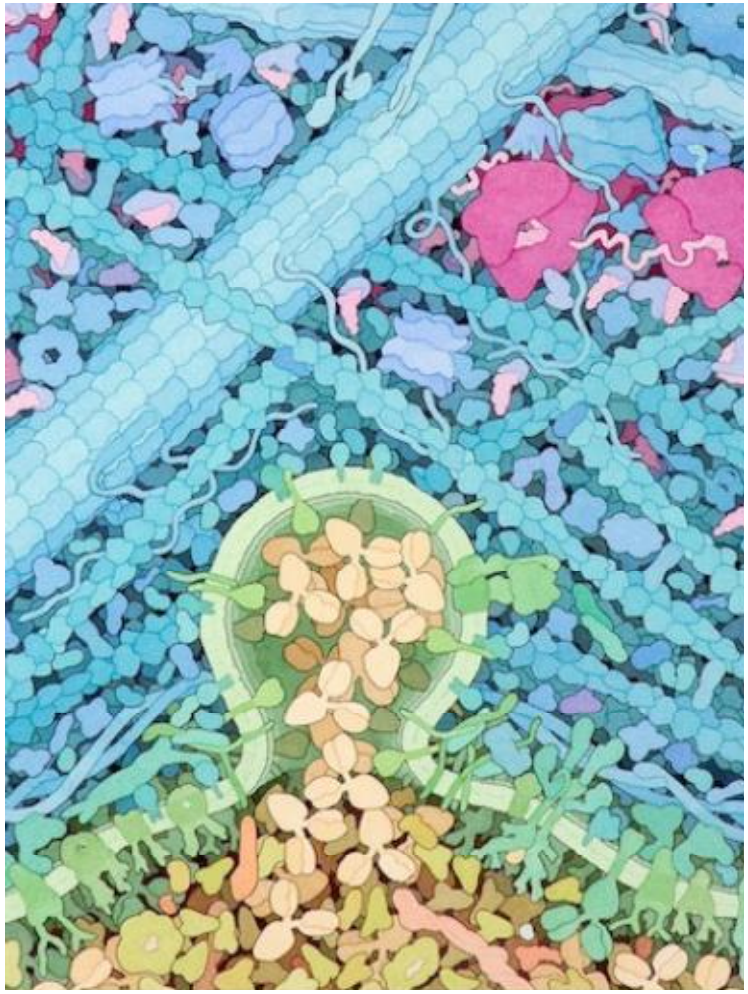




Gizmodo.jp

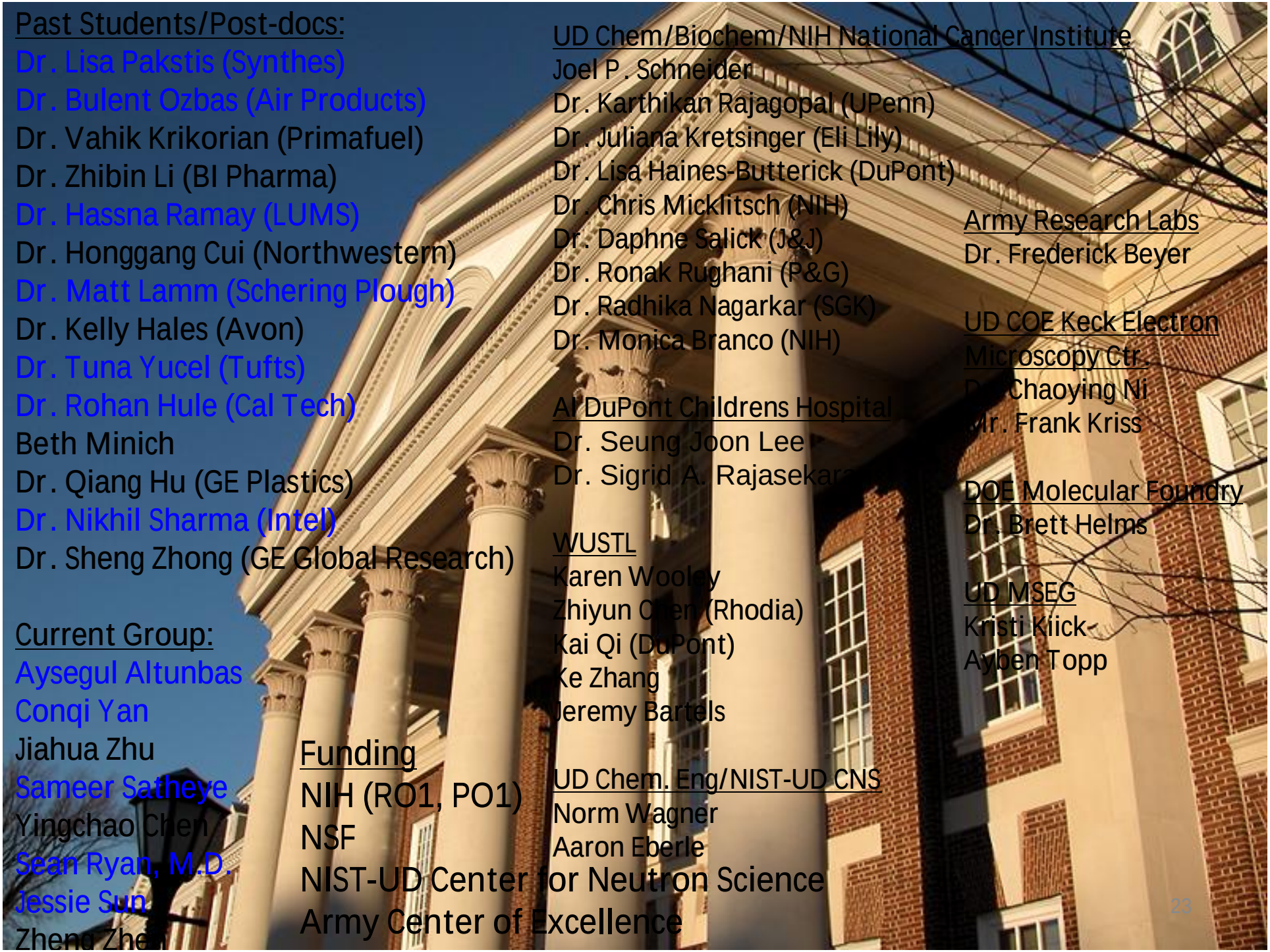
We say “bioinspired”…
but biology is COMPLEX!





David Goodsell's "The Machinery of Life”, Springer, 2009

and TIME!!!!!



Past Students/Post-docs:
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Dr. Matt Lamm (Schering Plough)
Dr. Kelly Hales (Avon)
Dr. Tuna Yucel (Tufts)
Dr. Rohan Hule (Cal Tech)
Beth Minich
Dr. Qiang Hu (GE Plastics)
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NIST-UD Center for Neutron Science
Army Center of Excellence

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UD MSEG
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Ayben Topp

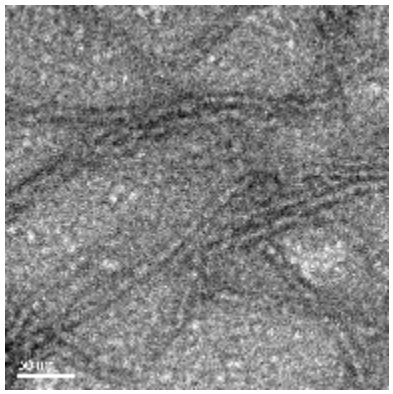
Polypepetide design and self-assembly

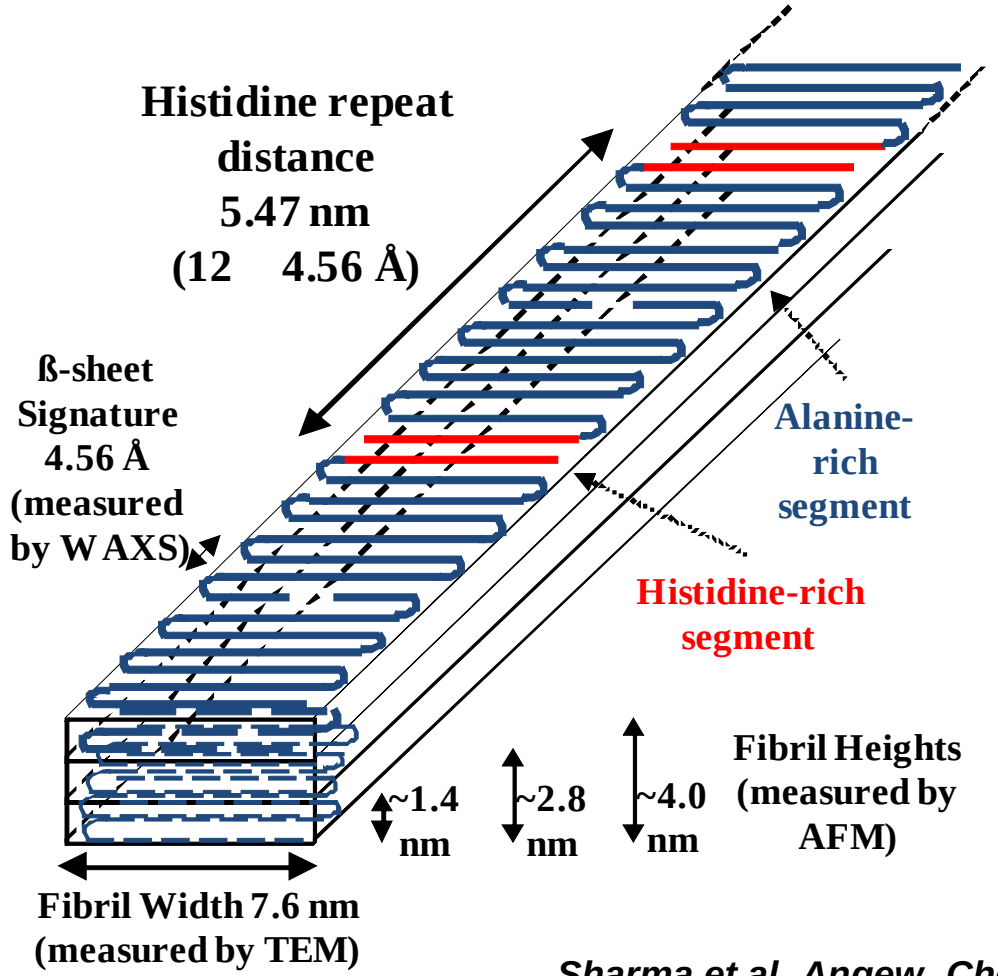
MG**H$_{10}$**SSGHIHM [AAAQEAAAAQAAAQAEAAQAAQ]$_6$ AGGYGGMG

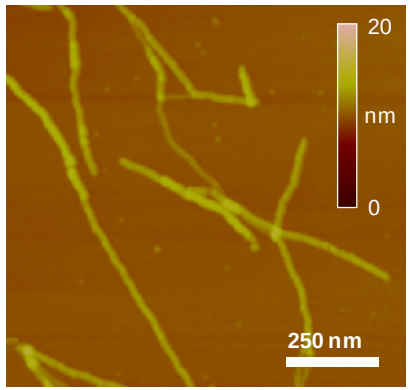
19 residues
Positively charged Histidine block

22 residues
Hydrophobic Alanine rich segment

8 residues
Hydrophobic Glycine rich segment



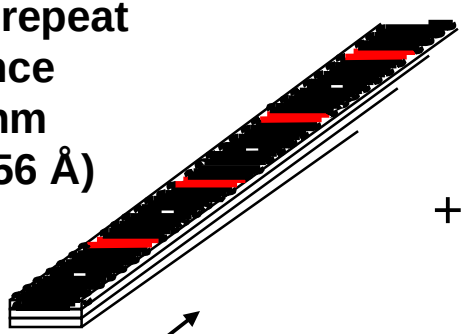




***Sharma et al. Angew. Chem. Int. Ed* 2009, 48, 7078**

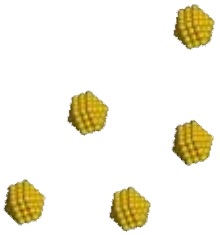
Electrostatically Directed Assembly

Histidine repeat distance 5.47 nm (12 × 4.56 Å)

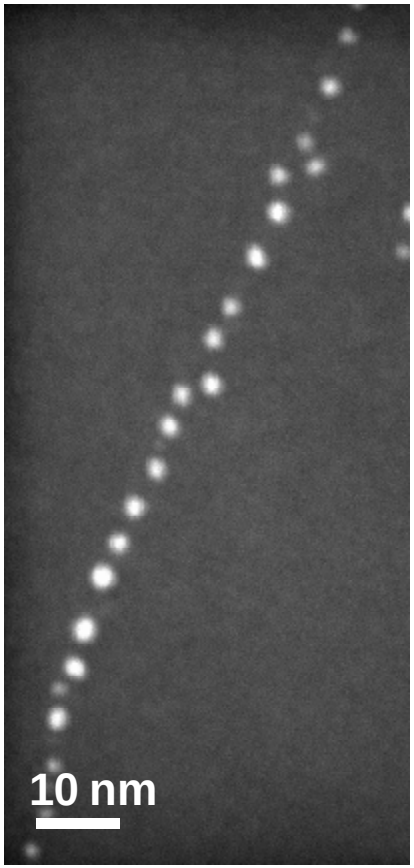


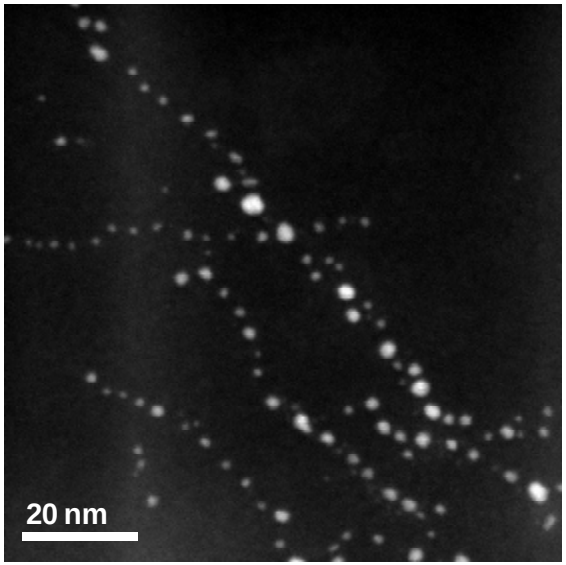
17H6 fibrils bearing positive charge

+

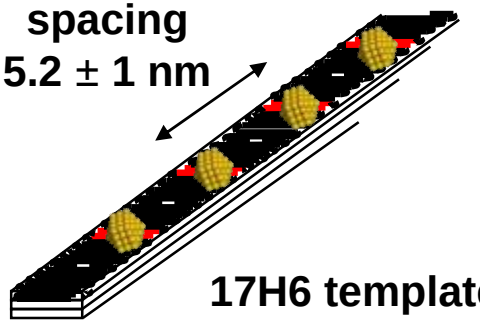


Negatively charged gold nanoparticles





Inter-NP spacing 5.2 ± 1 nm

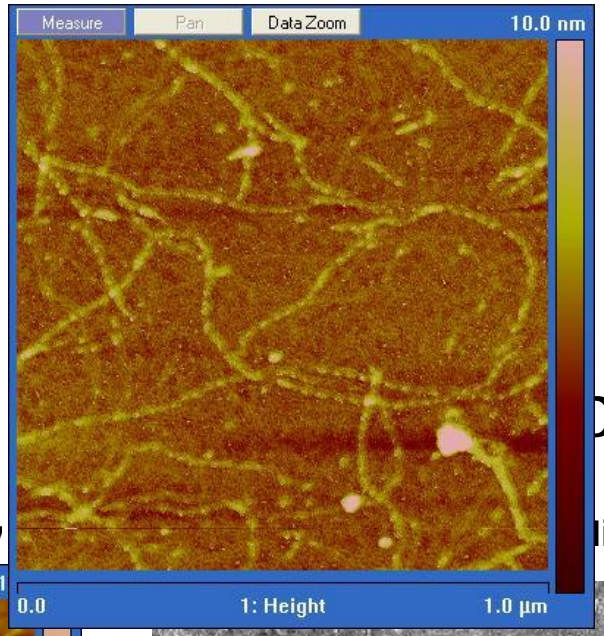


17H6 templated 1D nanoparticle arrays

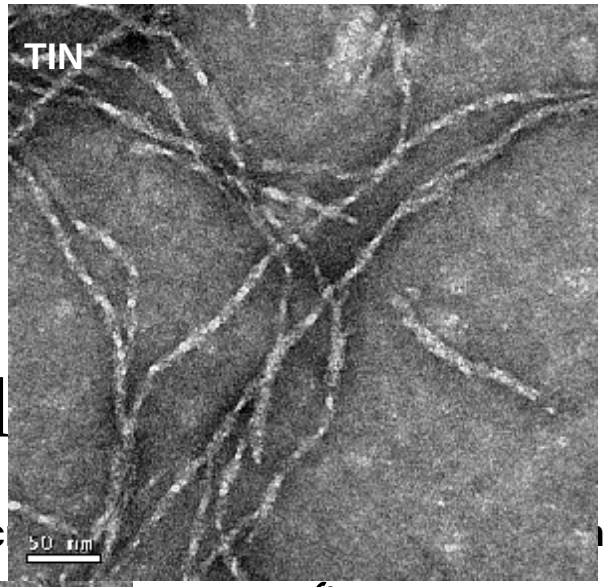
***Sharma et al. Angew. Chem. Int. Ed* 2009, 48, 7078**

TIN Self Assembly

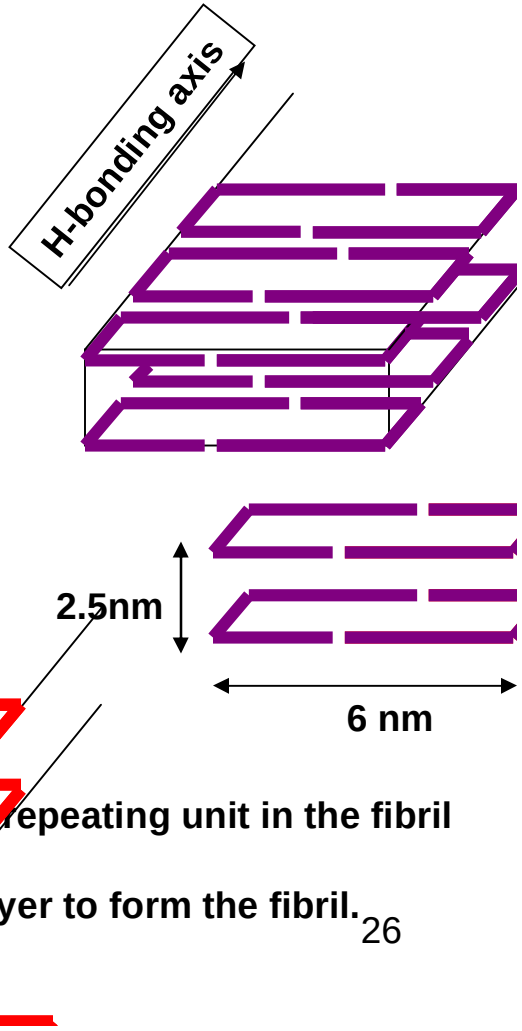
Atomic Force Microscopy



Transmission Electron Microscopy

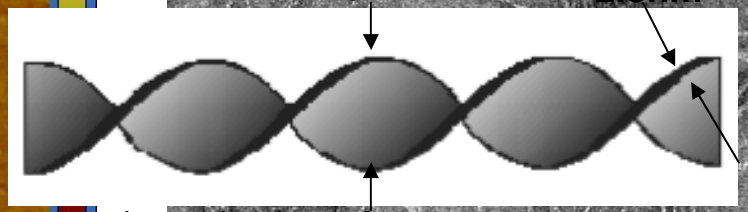


Fibril Cartoon



Fibril height ~ 6nm

Fibril width ~ 6nm



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atures:

nterdigitated bilayer as the repeating unit in the fibril

ater bilayer to form the fibril.

Nagarkar, Hule, et al. *J. Am. Chem. Soc.* **2008**, 130, 4466-4474