

SAXS/SAXRD: Unraveling Supramolecular Assemblies

Youli Li

Materials Research Laboratory
University of California, Santa Barbara

In Collaboration with (at UCSB)

The Safinya Group: Uri Raviv, Dan Needleman, Linda Hirst,
Cyrus Safinya, ...

The Wilson Group: Hurbert Miller, Les Wilson

The MacDonald Group: Emily Parker, Noel MacDonald

Funding Support: NIH GM-59288, NSF DMR- 0203755, CTS-0404444, DOE W-7405-ENG-36 (BES)

NNI Workshop 2005 – X-rays and Neutrons: Essential Tools for Nanoscience Research

Outline

- Outstanding problems
- Application of x-rays and neutrons techniques
- Example: Lipid/DNA and Lipid/Protein Complexes: multi-faceted puzzles solved by using more than x-rays
- Summary & looking forward

Outstanding Problems

General Properties

- Occur in wide range of materials (polymers, proteins/nucleic acids, colloids, nanoparticles)
- Structures formed by weak, non-specific interactions
- Lengthscale from nanometers to microns
- Disordered and partially ordered structures
- Information on Structure & interactions

Relevance and Applications

- Theoretical understanding & control
- Gene and drug delivery
- Hierarchical assembly in biological systems
- Protein Interactions & Complexes
- Material with controlled nanostructures

Key Questions

1. What are the structures that can be formed by self-assembly? (Structure and phase diagram)
2. How to control these structures? (Interactions and theoretical understanding)

X-rays and neutrons can provide information on both structure and interaction

Structural Probes for Self-Assemblies

X-rays and Neutrons – View from Reciprocal Space

- SAXS – Single Particles
- SAXRD – Ordered or partially ordered structures
- Light Scattering – Larger lengthscales

Imaging Techniques – Real Space Methods

- Electron Microscopy (1 nm resolution, directly complements x-ray and neutron data)
- Optical Microscopy (>200 nm)
- Scanning Probe (AFM and variants)
- X-ray Imaging – ~30 nm resolution, limited by low contrast

Real problems require applying multiple techniques

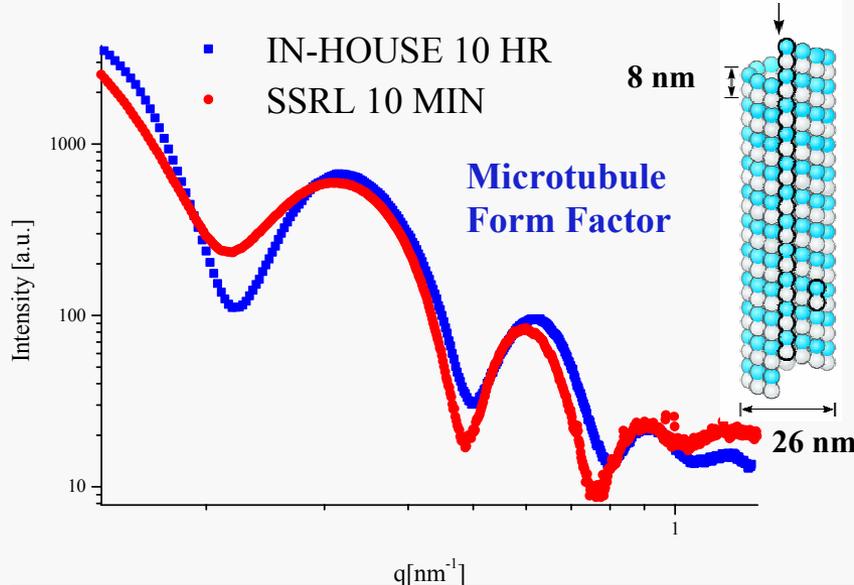
SAXS/SAXRD Primer

SAXS – Single Particles

Scattering dominated by form factor
(particle shape and size)

$$I \propto \left| \int \rho(r) e^{iqr} dr \right|^2$$

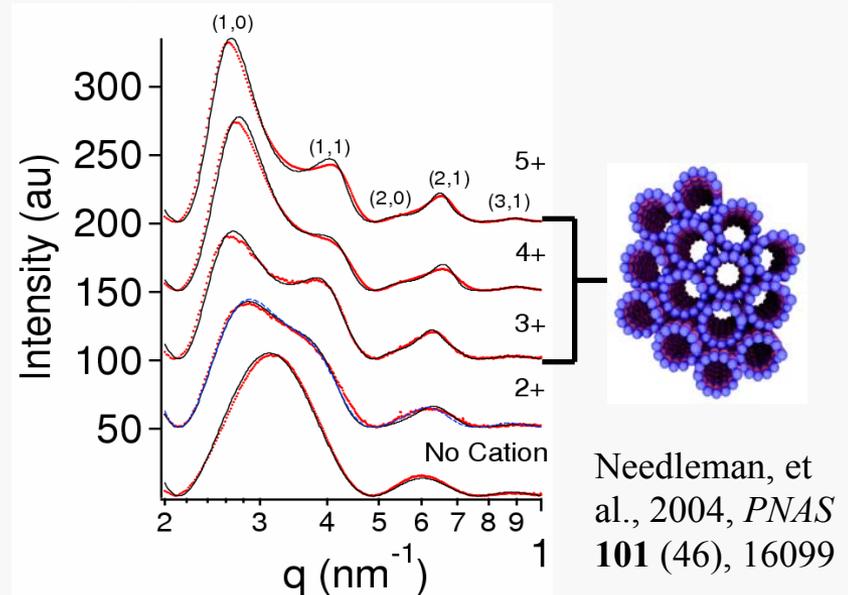
$$I = I_0 e^{-\frac{q^2 R_g^2}{3}} \quad (qr < 1, \text{Guinier})$$



SAXRD – Partially Ordered Systems

Scattering determined by structure factor (single particle + inter-particle interference)

$$I = \left| \sum_j \left(\int \rho(r) e^{iqr} dr \right) e^{iqx_j} \right|^2$$



Lipid-DNA and Lipid-Protein Complexes

- Complexing cationic lipids with negative charged bio-polymers
- Applications: drug & gene delivery, biologically inspired nanostructures, model systems for investigating poly-electrolyte physics

PGA

DNA

F-Actin

Microtubule

$$\sigma = 1e/0.63 \text{ nm}^2$$

$$1e/1.06 \text{ nm}^2$$

$$1e/6.3 \text{ nm}^2$$

$$1e/1.15 \text{ nm}^2$$

$$l_p = 2 \text{ nm}$$

$$50 \text{ nm}$$

$$10 \mu\text{m}$$

$$1 \text{ mm}$$

$$D = 1.3 \text{ nm}$$

$$2 \text{ nm}$$

$$8 \text{ nm}$$

$$26 \text{ nm}$$

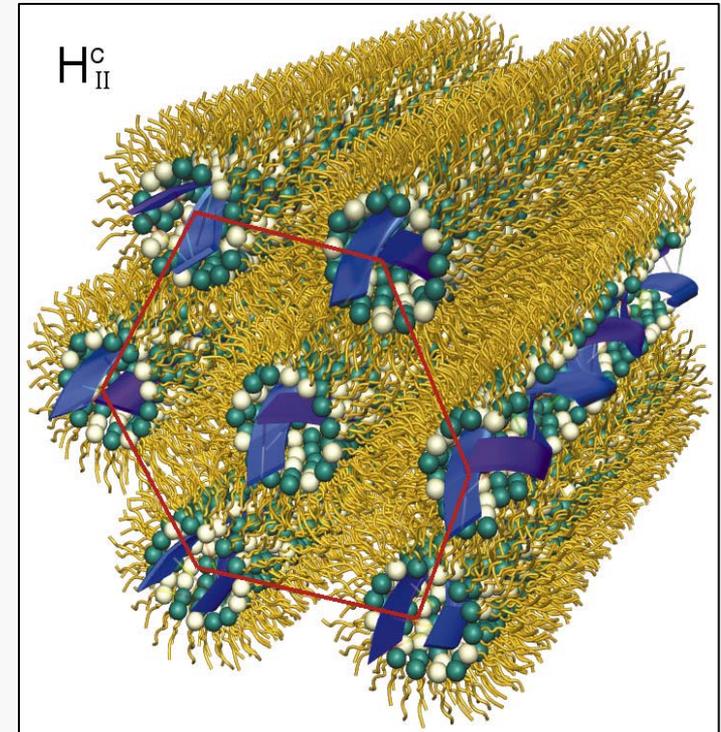
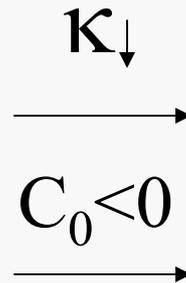
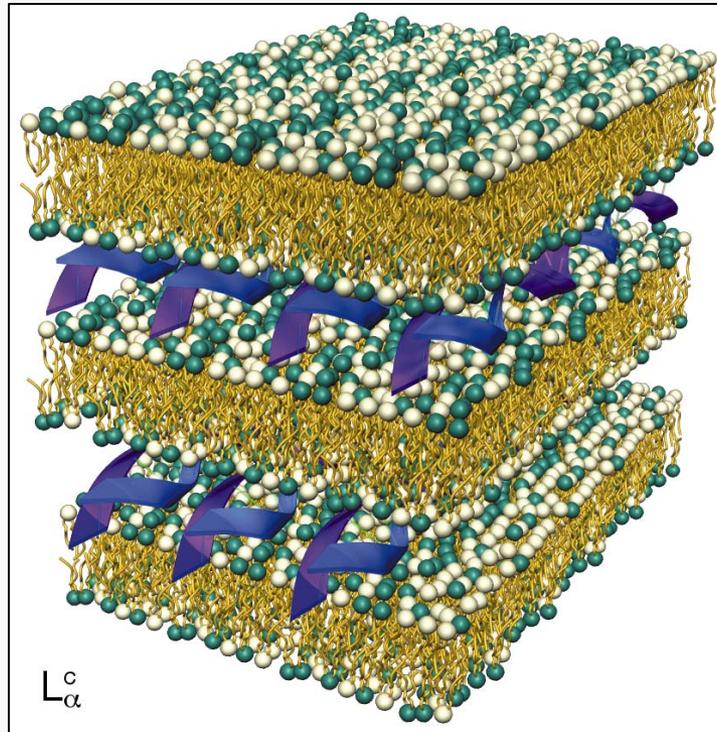
$$C_p = 2/D = 1.5 \text{ nm}^{-1}$$

$$1 \text{ nm}^{-1}$$

$$0.25 \text{ nm}^{-1}$$

$$0.076 \text{ nm}^{-1}$$

Cationic Lipids as Carriers of Genes



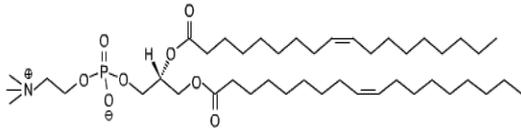
Science 275, 810-813 (1997)

Science 281, 78-81 (1998)

J. Medicinal Chemistry, 45 (23) 5023-5029 (2002)

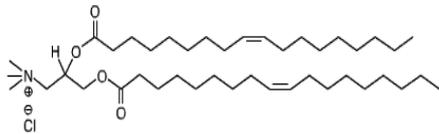
Interplay between charge density and natural curvature of membrane and polymer leads to very different structures

L_α Lipid-DNA Complex



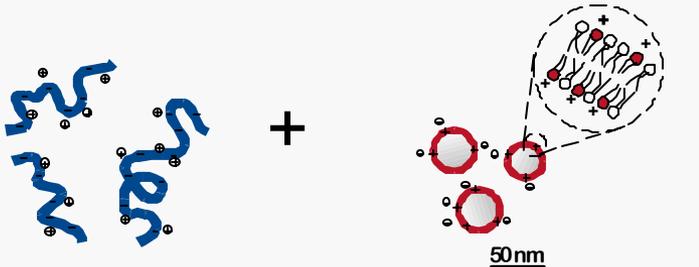
1,2-Dioleoyl-*sn*-Glycerophosphocholine (DOPC)

©Avanti Polar Lipids

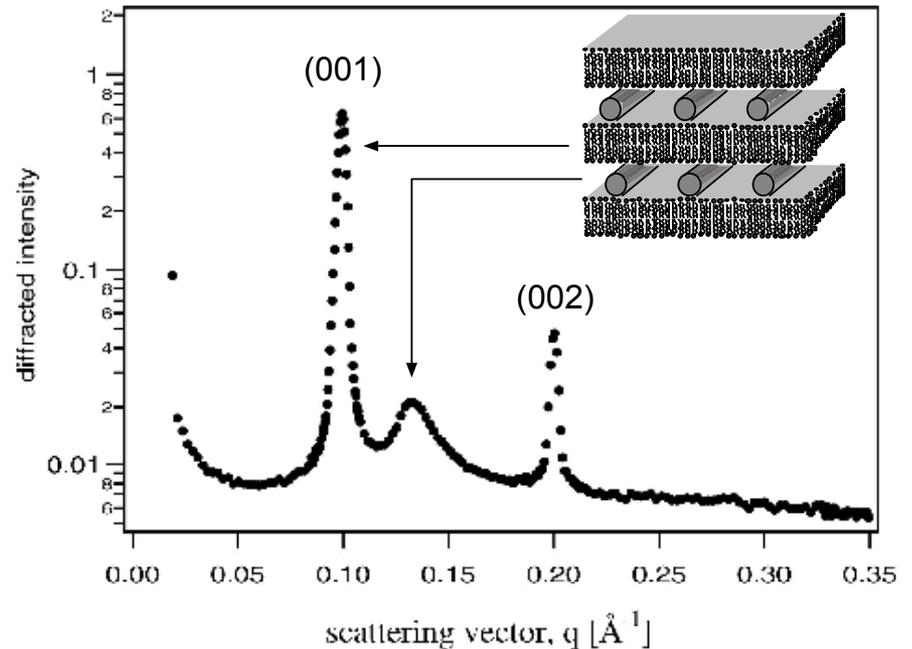
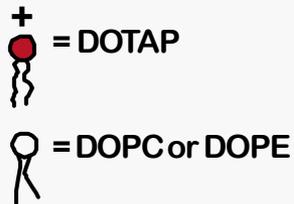


1,2-Dioleoyl-3-Trimethylammonium-Propane (DOTAP)

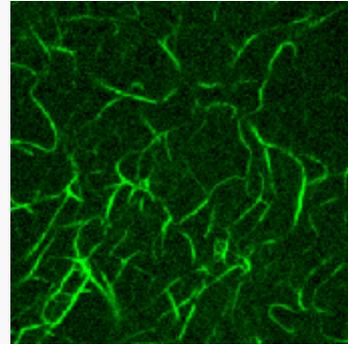
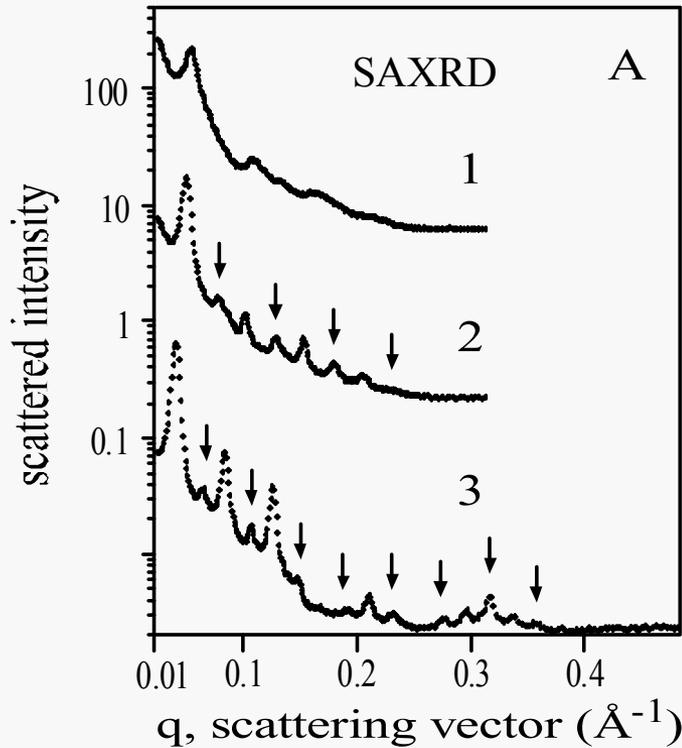
©Avanti Polar Lipids



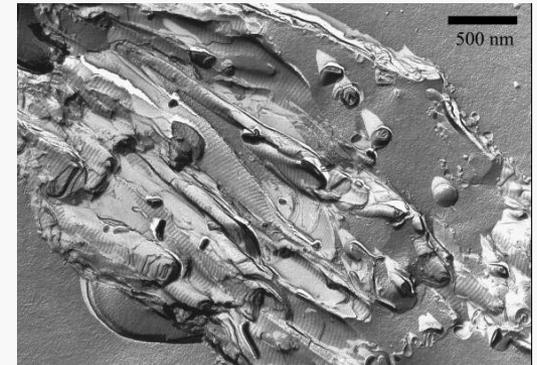
λ-phage DNA
 contour length ~17 μm
 48 kbp
 ξ ~ 500 Å



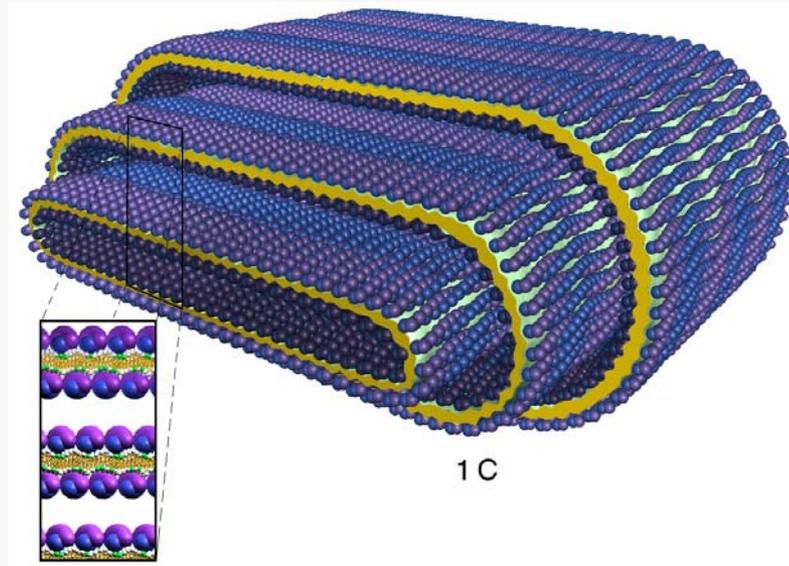
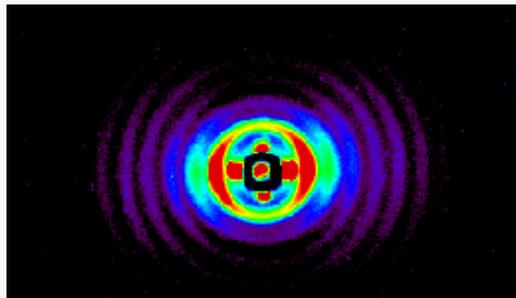
Lipid-Actin Complex



Confocal Microscopy

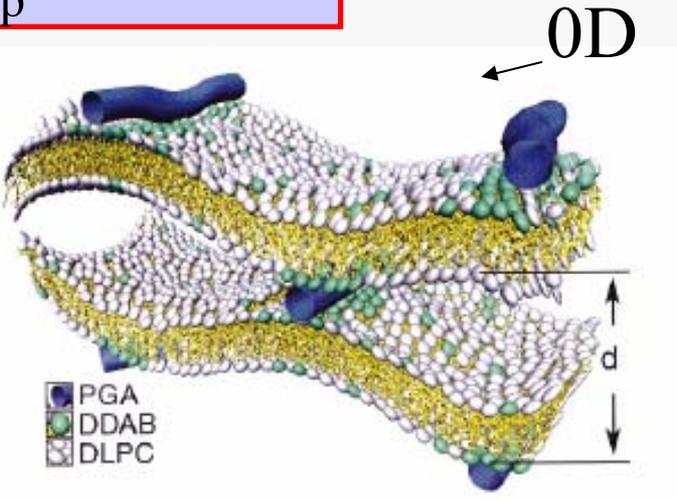


Freeze-Fracture EM



Wong, et. al, *Science* 288, 2035-2039 (2000)

$C_p = 1.5 \text{ nm}^{-1}$

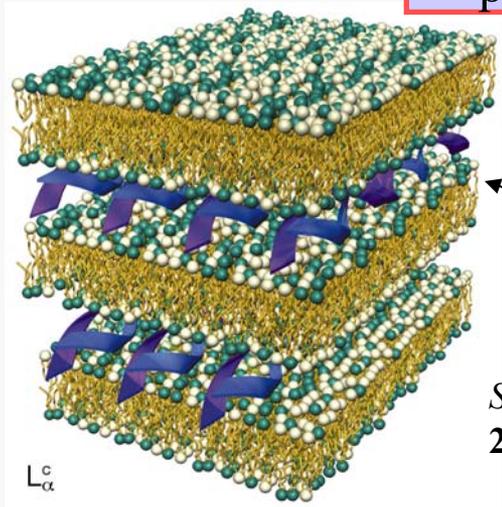


JACS,
122, 26 (2000)

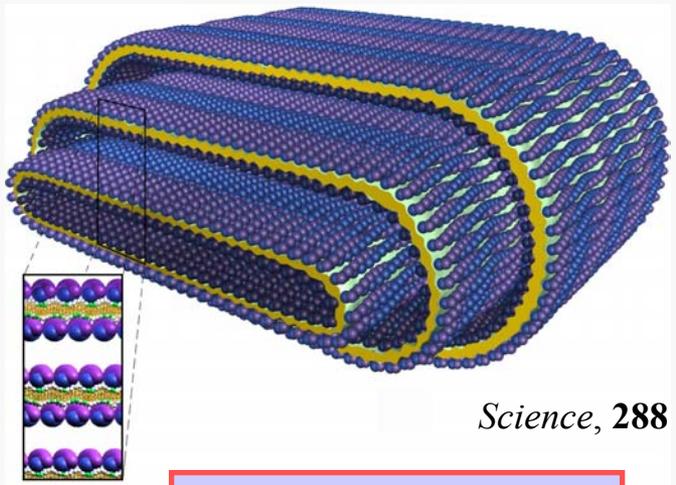
Lipid/MT
?

$C_p = 0.076 \text{ nm}^{-1} \rightarrow C_0$

$C_p = 1 \text{ nm}^{-1}$



Science,
275, 810 (1997)



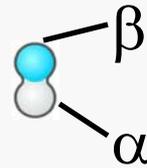
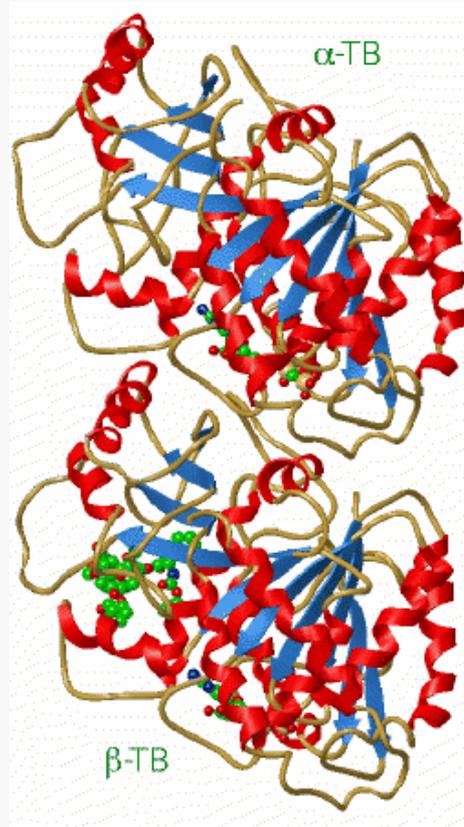
Science, 288 2035 (2000)

$C_p = 0.25 \text{ nm}^{-1}$

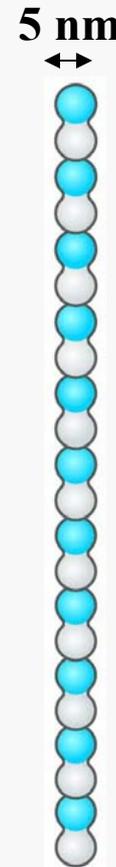
Structures of tubulin, a protofilament, & a microtubule

Adapted/redrawn from Cell Movements by Dennis Bray

Nogales *et al.*, Nature **391**, 199 (1998)



Tubulin dimer



protofilament

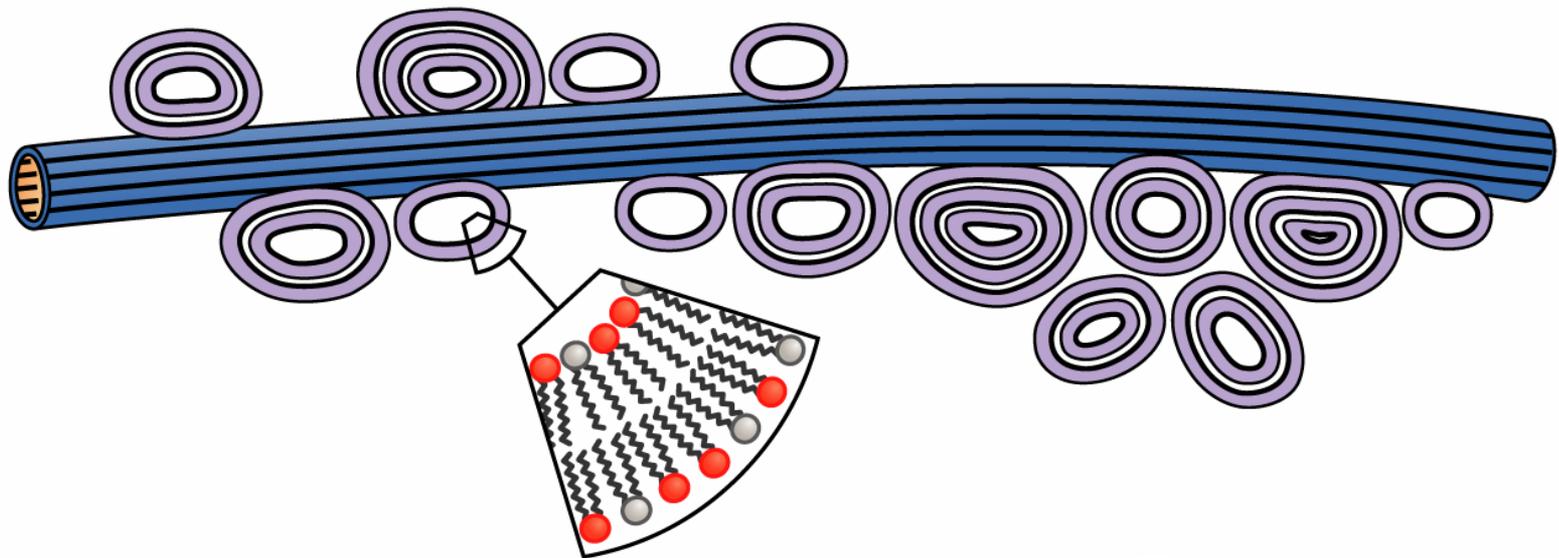


microtubule

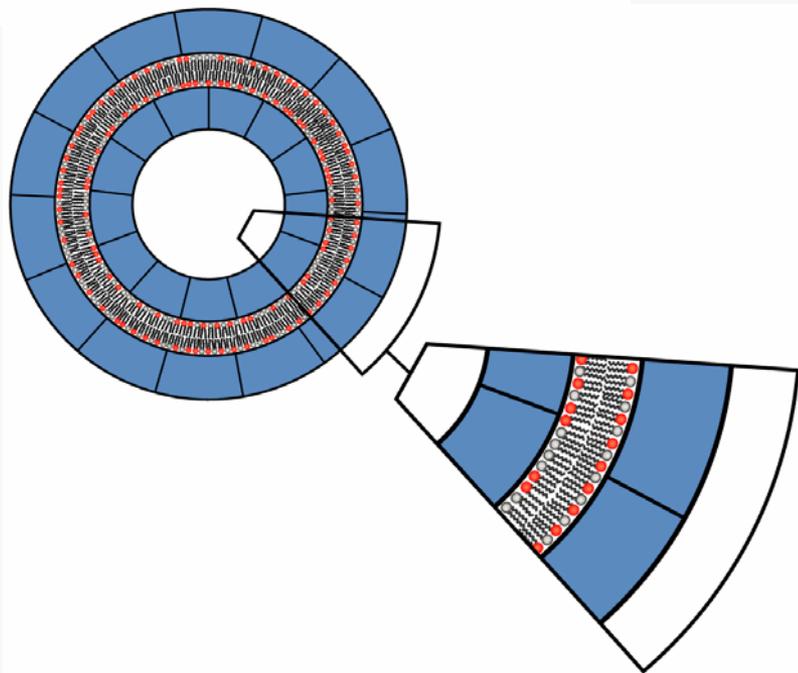
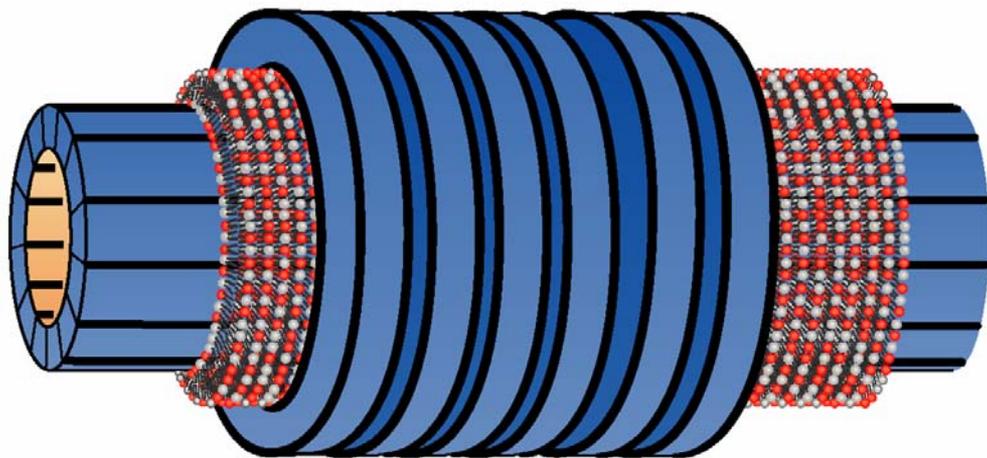
Microtubule = Rigid,

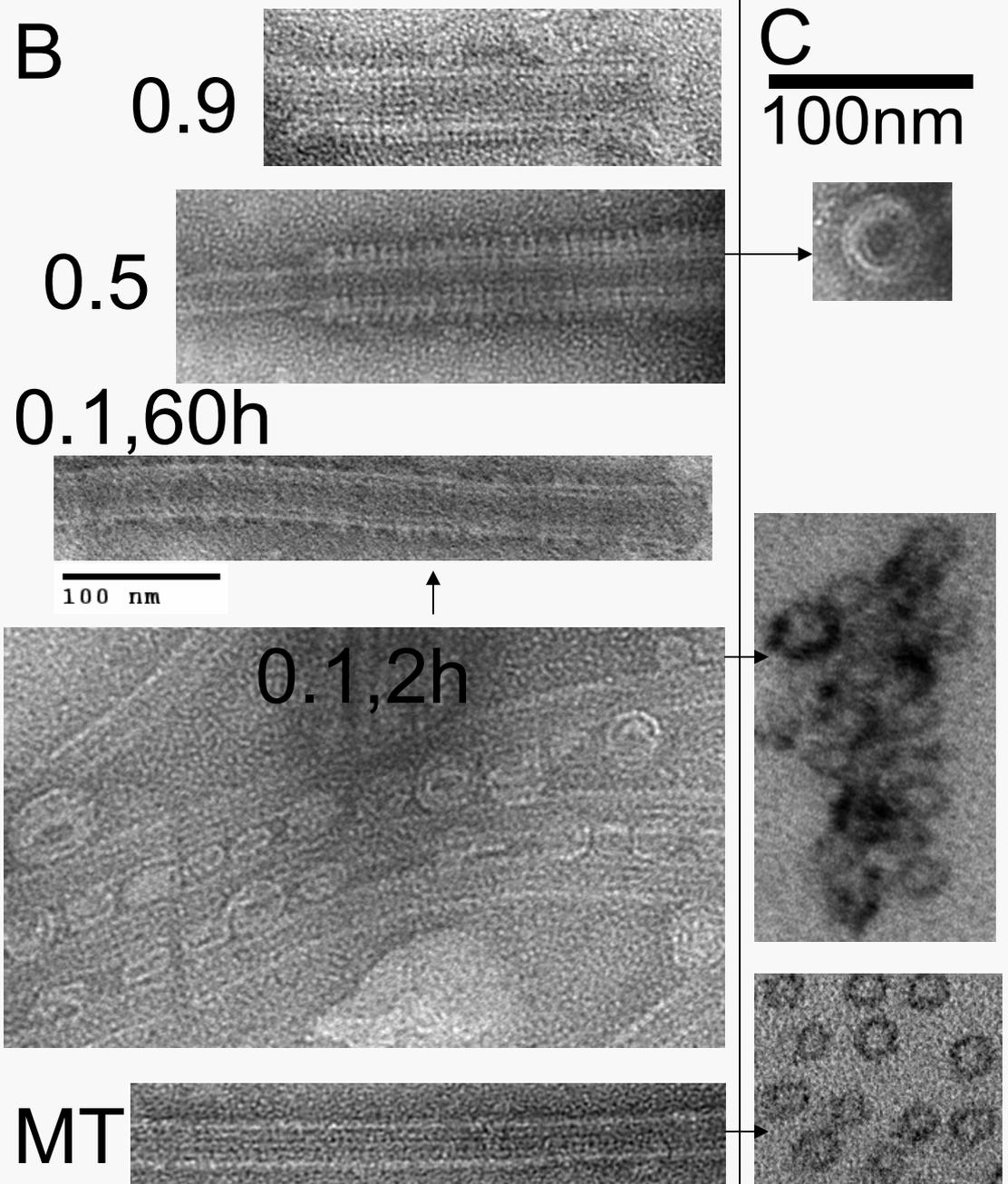
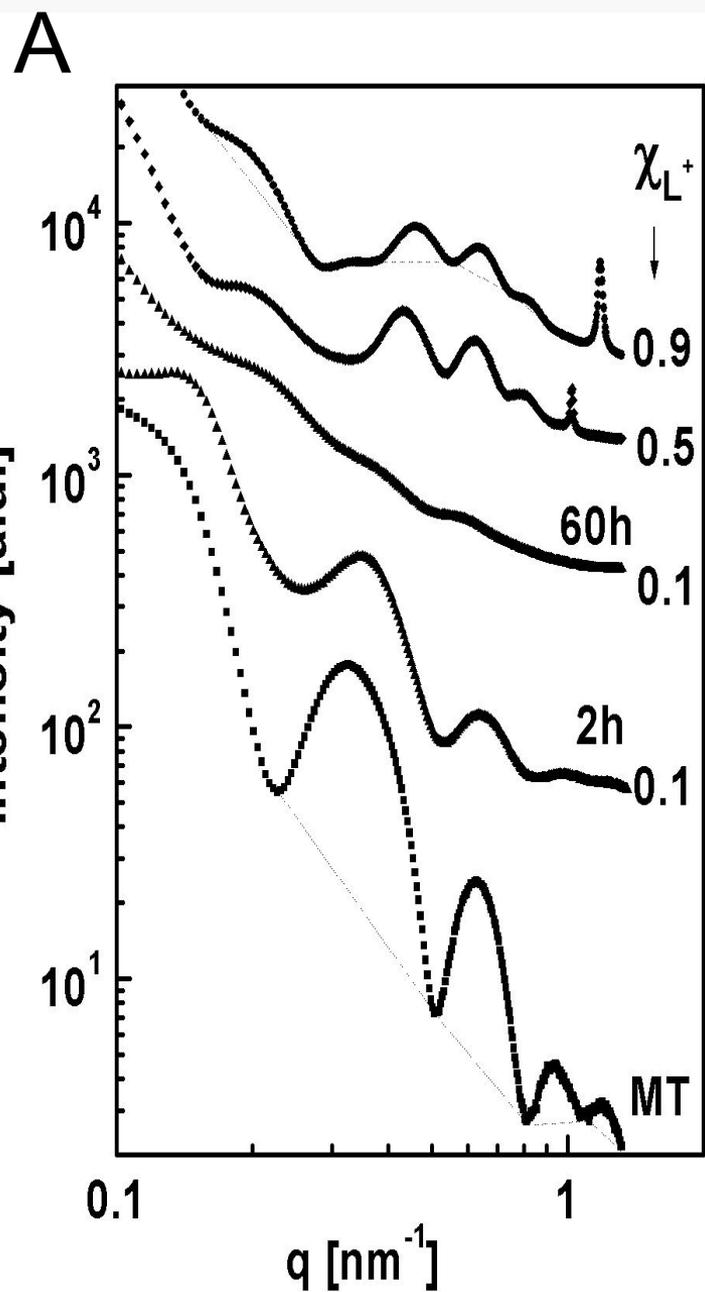
$\xi_p = 2-6 \text{ mm}$

$-41 \text{ e/tubulin dimer}, \sigma = 0.87 \text{ e/nm}^2$

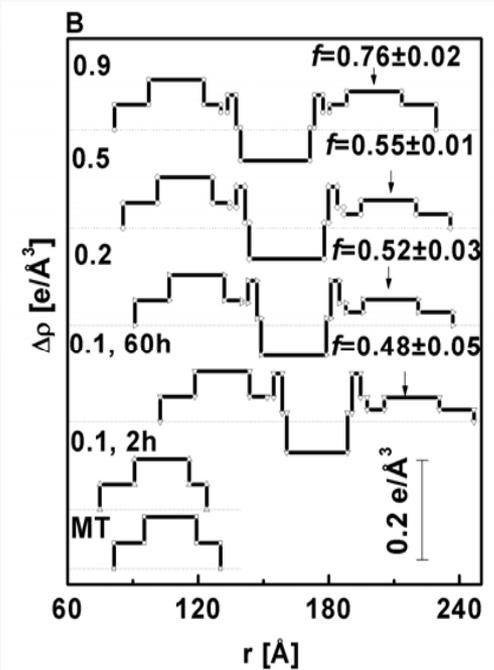
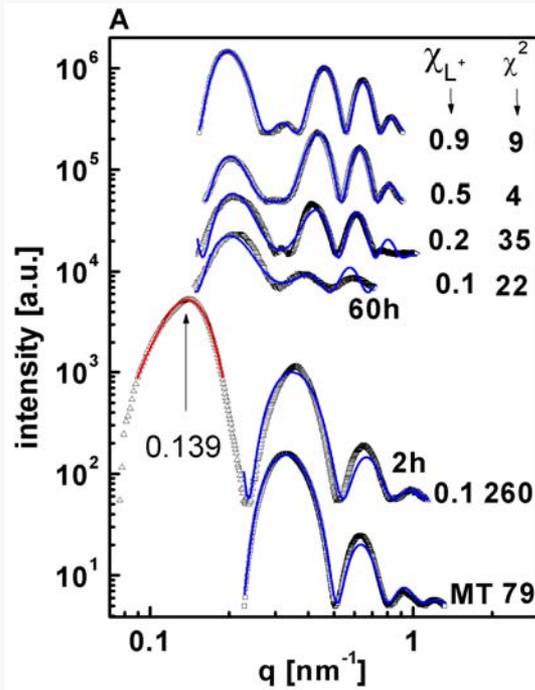
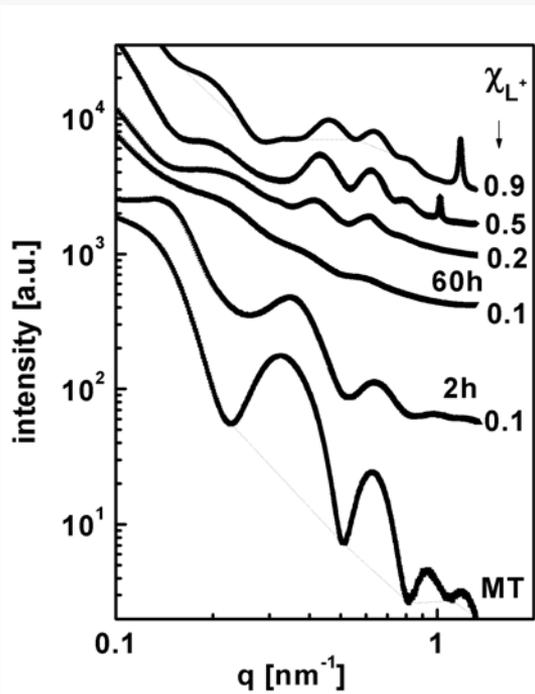
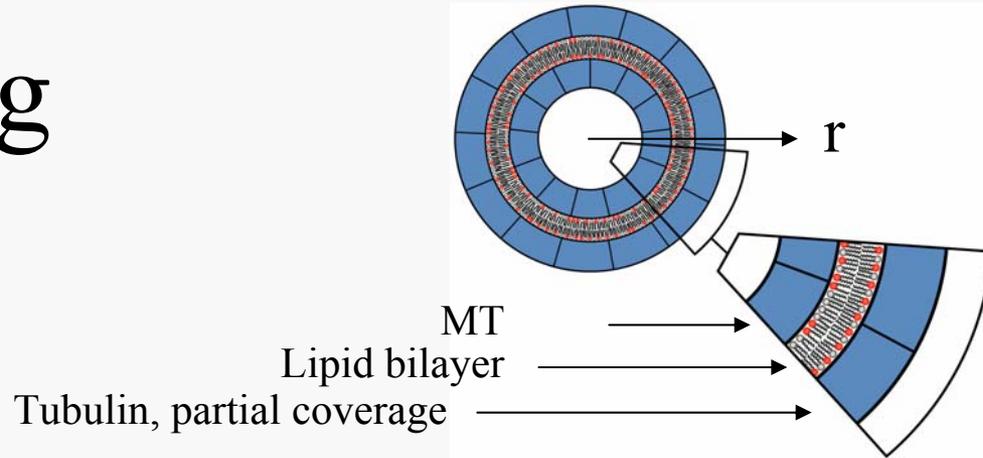


$\downarrow \sigma \uparrow \kappa \downarrow$





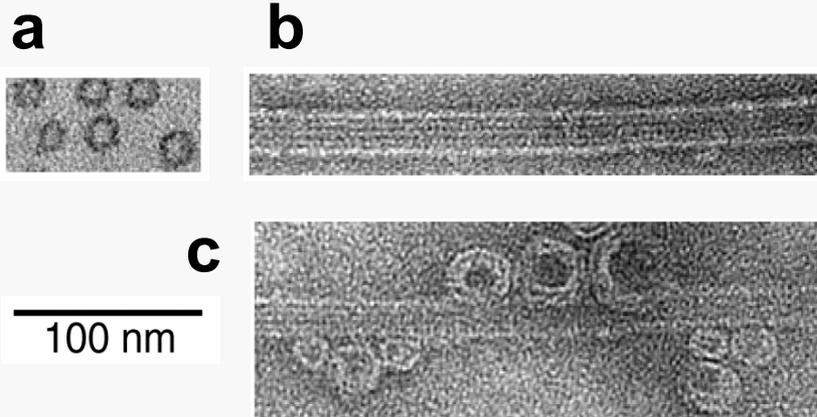
Modeling



(Uri Raviv et al, *PNAS*, in press, 2005)

Cationic Liposome (DOTAP/DOPC)-Microtubule Complexes

(Uri Raviv et al, submitted)



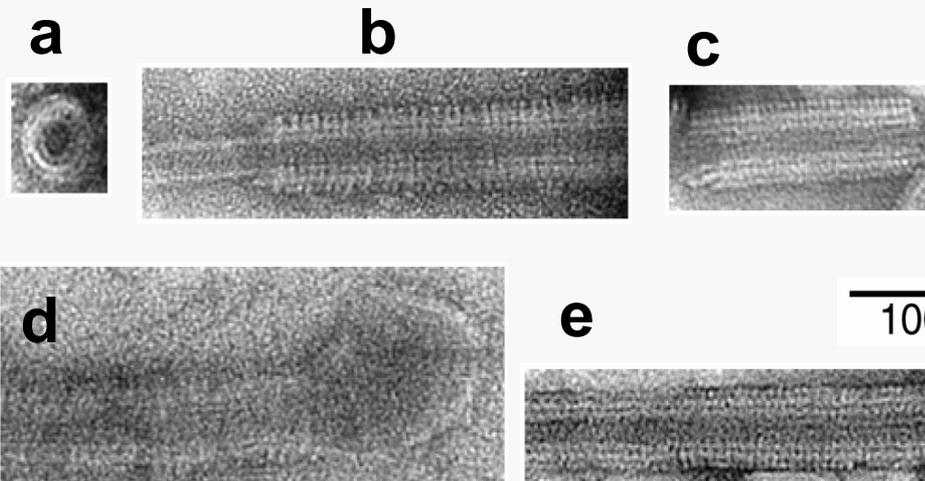
$$(c) \chi_L = N_{L+} / (N_{L0} + N_{L+}) = 0.1$$

$$R_{+/-} = 120$$

$$R_{+/-} = N_{L+} / N_t, \text{ isoelectric} = 40$$

Two State (open/closed) Lipid Protein Nanotubes

(for $M^+ > 0.1$)



$$(b) \chi_L = 0.5 \text{ and } R_{+/-} = 40,$$

$$(c) \chi_L = 0.5 \text{ and } R_{+/-} = 80$$

$$(d) \chi_L = 0.5 \text{ and } R_{+/-} = 120,$$

$$(e) \chi_L = 0.8 \text{ and } R_{+/-} = 80$$

Summary and Looking Forward

- Supramolecular assemblies present a rich library of templates for nanostructured materials
- No clear understanding yet of interactions leading to complex structures, especially with biological macromolecules – nature continues to surprise us with richness and exquisite control
- X-rays and Neutrons are powerful tools for studying self-assembled nanostructures; even more powerful when combined with optical and electron microscopy (instruments integrating multiple probes would be very useful)
- An easy to use, comprehensive SAXS/SAXRD analysis package for partially ordered structures is very much needed (learn from successful story in protein crystallography)
- New technique development will bring new opportunities (e.g. μ SAXS) – increased support and collaborative efforts are needed