Shape - Static and Dynamic

“Form ever follows function, and this is the law”
(Louis H. Sullivan - 1896)

to the SSSC (NRC)

Medical Laboratories

In City and Country

By G. Martin Moeller, Jr.

2007 Award for Excellence in Architecture
2007 Presidential Citation for Sustainable Design

Howard Hughes Medical Institute
Janelia Farm Research Campus
Ashburn, VA

Rafael Viñoly Architects, PC
Contractor: Turner Construction Company

First-time visitors to the main building of the Howard Hughes Medical Institute's Janelia Farm Research Campus may wonder if they have happened upon the fantastical lair of an evil genius from a James Bond movie. Nestled almost clandestinely into its gently rolling site, lined with an orderly array of sleek laboratories and serene courtyards, and exuding an understated sophistication that is rarely seen in structures of such scale and complexity, the building is both breathtaking and more than a little mysterious.

Fortunately, nothing nefarious is afoot here. In fact, the elegant structure—known simply as the Landscape Building—is the centerpiece of one of the nation's most advanced biomedical research facilities. The main building's moniker derives, of course, from its terraced design, which obscures its true scale—it is nearly 1,000 feet long and more than 200 feet deep—while preserving views across the site. This arrangement also yielded the second-largest green roof in the United States.

Even spaces deep within the Landscape Building's semi-underground floors enjoy clear views to the outside and abundant natural light, due in large part to the copious use of structural glass along the outer perimeter. Each floor was laid out so as to maximize opportunities for informal interaction among the scientists in residence, while also allowing for easy, rapid reconfiguration of laboratory spaces to respond to changing program needs and opportunities. The building's gently curving plan creates dynamic vistas along circulation corridors, avoiding what otherwise could have become a monotonous phalanx of laboratory benches and offices.

Just to the northeast of the main building is an even more sinuous structure that provides accommodations for conference participants and other short-term guests of the Institute. With its refined glass façade overlooking a calm lake—one of two on the campus that serve as retention ponds for stormwater—the 96-room facility could easily be mistaken for an expensive resort hotel, especially at night when the tastefully restrained interiors of the rooms are visible from the outside. Nearby, a separate group of structures provides longer-term housing for visiting scientists and their families.

The Janelia Farm Research Campus received both an Award for Excellence in Architecture and a Presidential Citation for Sustainable Design. From an environmental standpoint, in addition to its vast green roof, daylighting strategies, and water retention systems, the project is notable for its incorporation of materials obtained from the very site on which it was built. All of the oak trees that were removed during construction, for example, were processed for use in flooring, furnishings, and other finishes, while extracted rock was recycled into roadways and under-structure fill.

For architect Rafael Viñoly, FAIA the environmental aspects of the design were a logical complement to the building program. As he said in his remarks at the groundbreaking ceremony in 2003, “It is a building about nature. Nature is the centerpiece of research and Janelia Farm, and the building follows that idea.”

Janelia Farm HHMI

Rafael Viñoly

Mark Bowick (Syracuse University) April 2, 2009

Outline

1. Big intellectual questions
2. Active research: Shape - Static and Dynamic
3. Funding & Public Relations

Part I: Open Questions

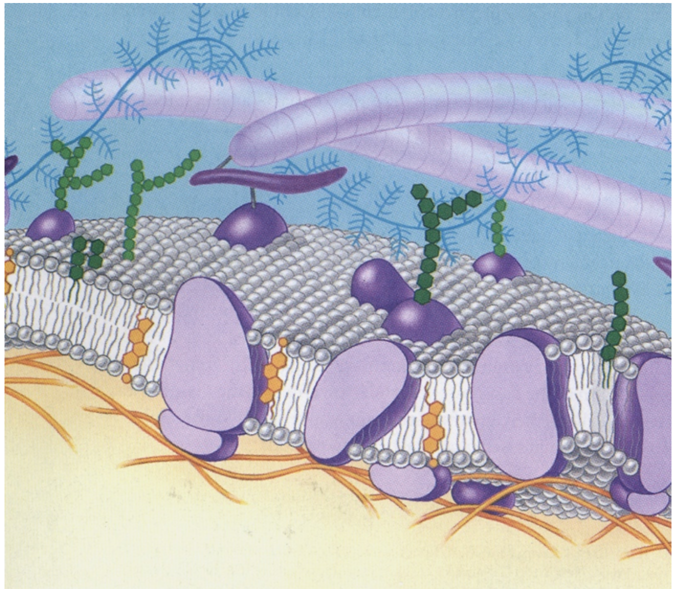
1. How important are physical processes in biological systems? (Very)
2. Do we have the techniques/formalism to treat active (non-equilibrium) systems with structure on many time and length scales (Not yet).
3. How can we bridge the atomistic (single molecule)-collective divide (moving from component descriptions to system descriptions)?
4. How tight is the structure-function connection?
5. What are the minimal functional modules for biological systems?
6. What are the universality classes (types of common behavior) and how do we uncover them experimentally and theoretically?
7. What are the dominant constraints (spatial, temporal, energetic) and what is being optimized to perform specific functions?
8. Physics of disordered solids and glasses- hard!
9. Catalog library of "superatoms" available for self or engineered assembly into supermolecules and bulk materials (replacing quantum mechanical atoms at the nano to meso-scale).
10. Inverse problem - what potentials give rise to specified structures?

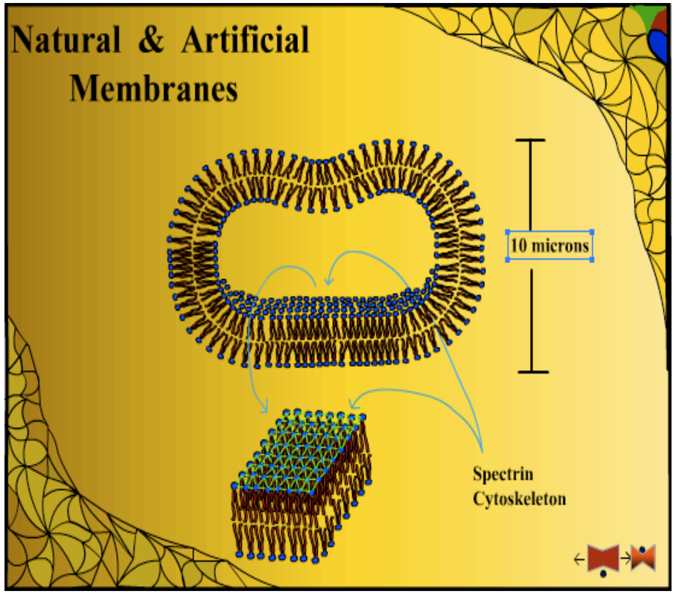
Part II: Research Problems

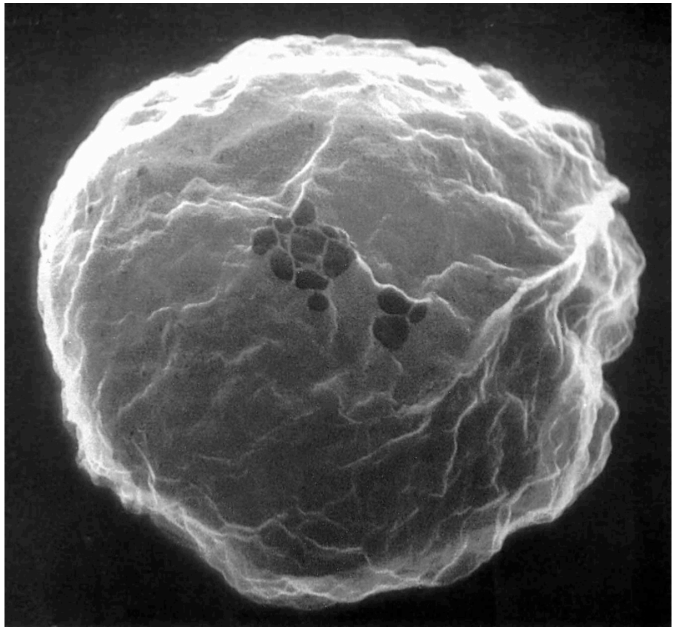
Bio-inspired Soft Matter & Materials Science

- Auxetic Membranes
- Tunable Robust Artificial Structured Vesicles
- Viruses
- Self-Propelled Particles (Myxo-Bacteria)
- Cell as a Material - Soft Active Matter

Membranes

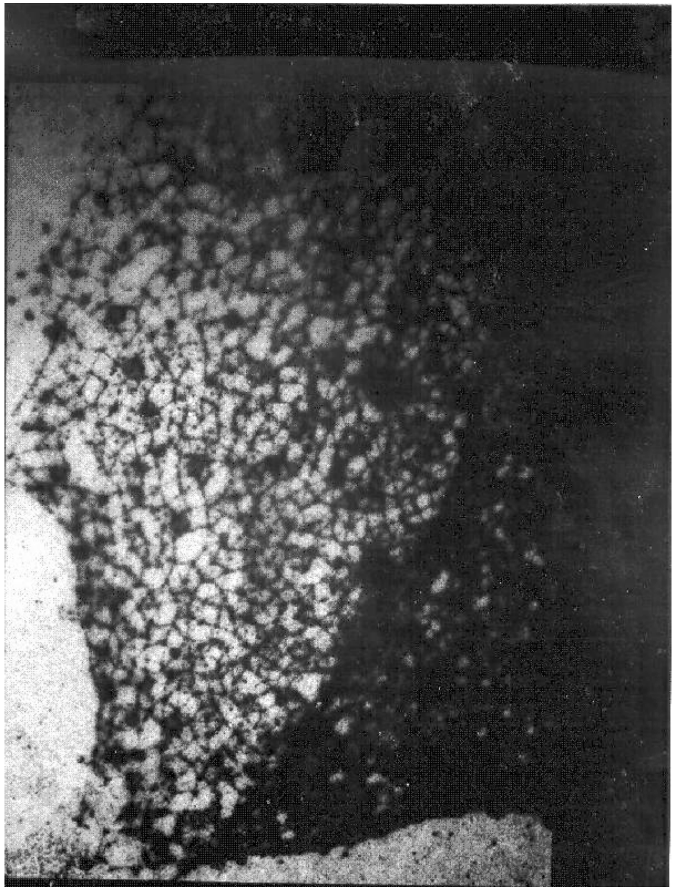




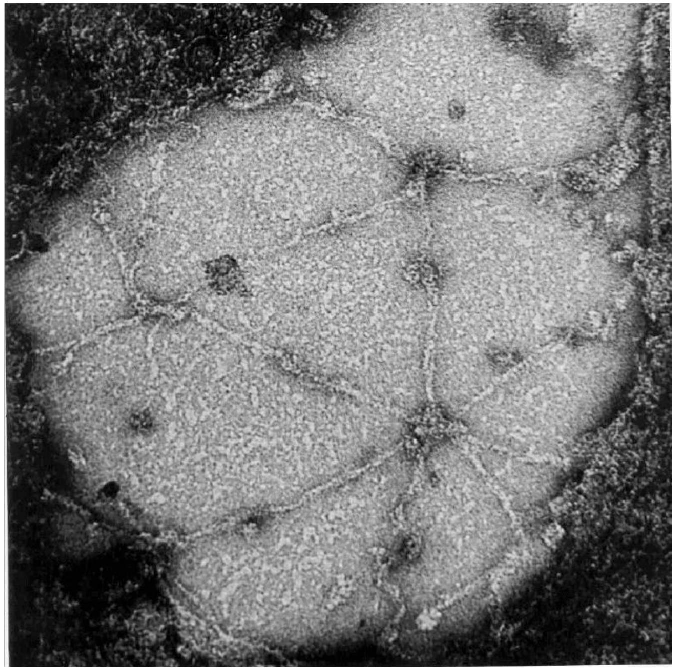


Hainfeld & Steck (1977) 10,000X

MJB

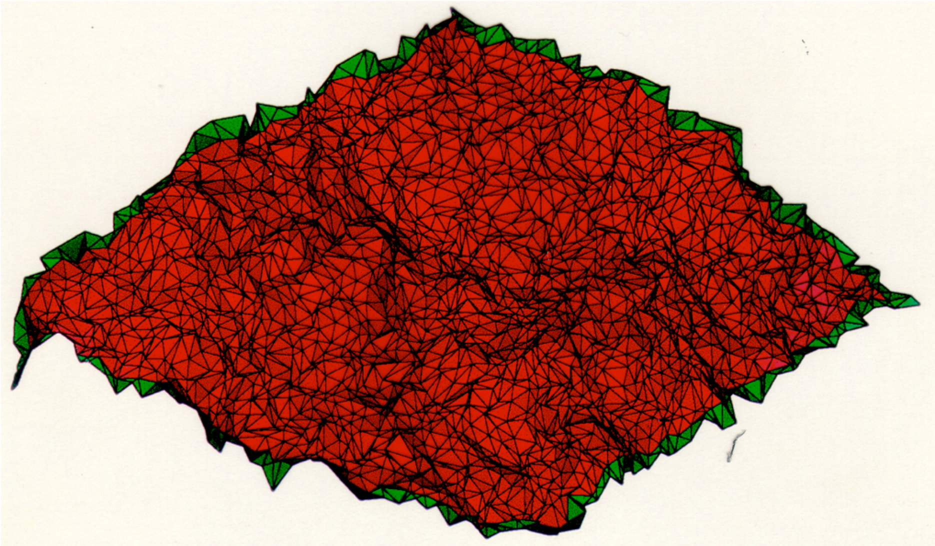


Branton



Branton

MJB

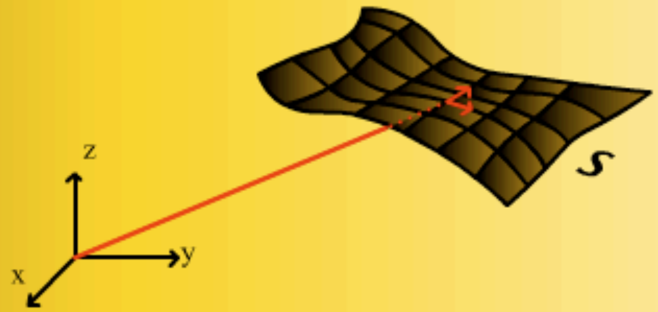


2D Elastic Flexible Membrane

$$F = F_{EL} + F_{B} + F_{SA}$$

Elasticity | Bending | Self-Avoidance

$$r: S^{(2)} \longrightarrow \mathbb{R}^{(3)}$$



Elastic Moduli

$$\text{ShearModulus } \mu(q) \qquad \text{Bulk Modulus } K(q)$$

$$\text{Bending Modulus } \kappa(q)$$

Thermal fluctuations drive

$$\kappa \text{ to } \infty \text{ at long length scales } (q \to 0)$$

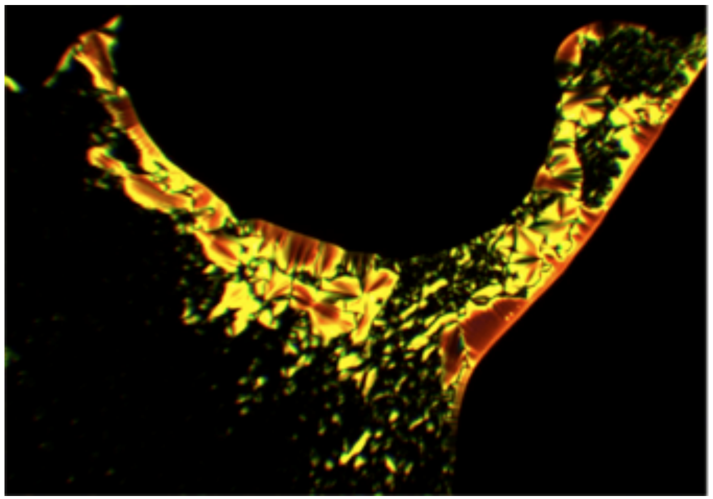
$$\mu \text{ and } K \text{ to } 0 \text{ with } K = \tfrac{1}{2}\mu$$

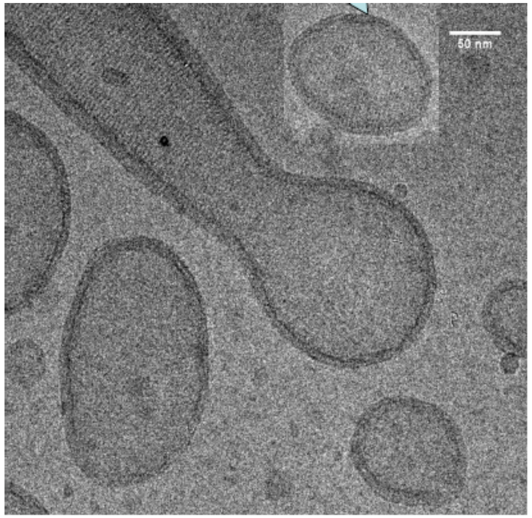
Stiff to bend but soft to squeeze with universal negative Poisson ratio

$$\sigma = \frac{K-\mu}{K+\mu} = -\frac{1}{3}$$ (Anti-rubber)

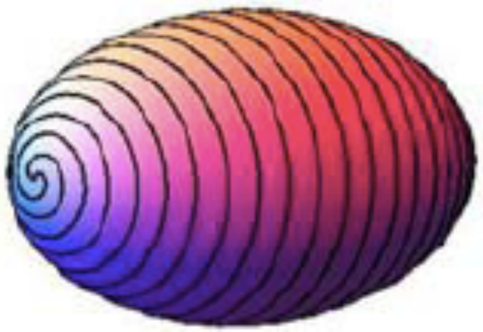
Artificial Cells
Structured (CoPolymer) Vesicles

with Min-Hui Li (Institut Curie, Paris) and X. Xing (Syracuse)





PEG2000-*b*-PAChol (28/72)



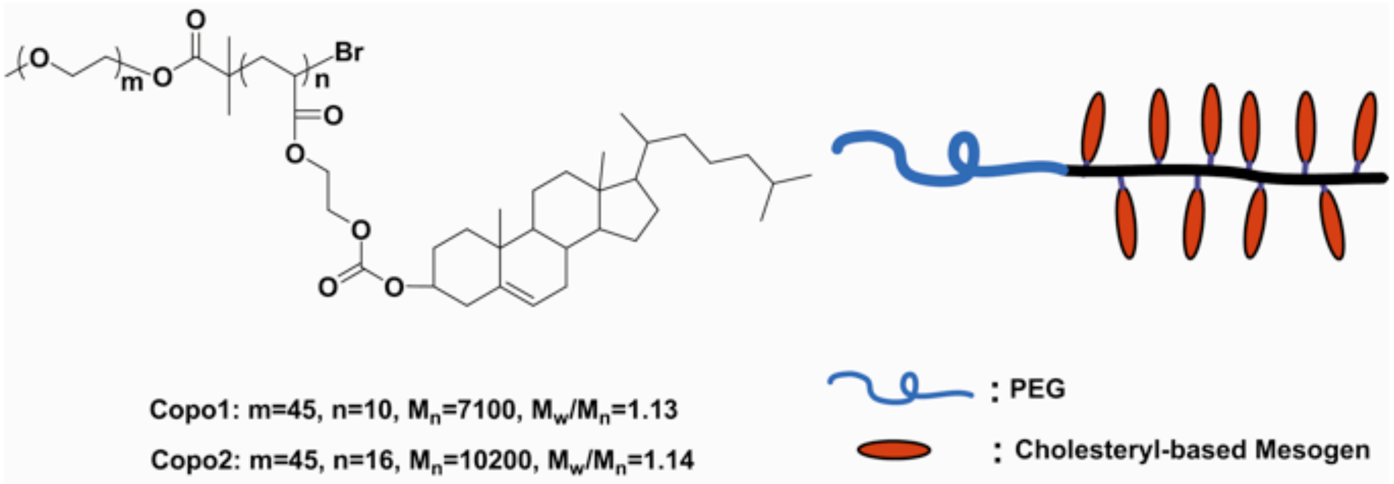
2D Order

Phase	**Order**
Crystalline	Quasi-Long Range Translational Truly Long-Range Bond-Orientational
LC Nematic	Orientational
LC Smectic	One-Dim Translational
Hexatic	Quasi-Long Range Bond-Orientational

Vesicles

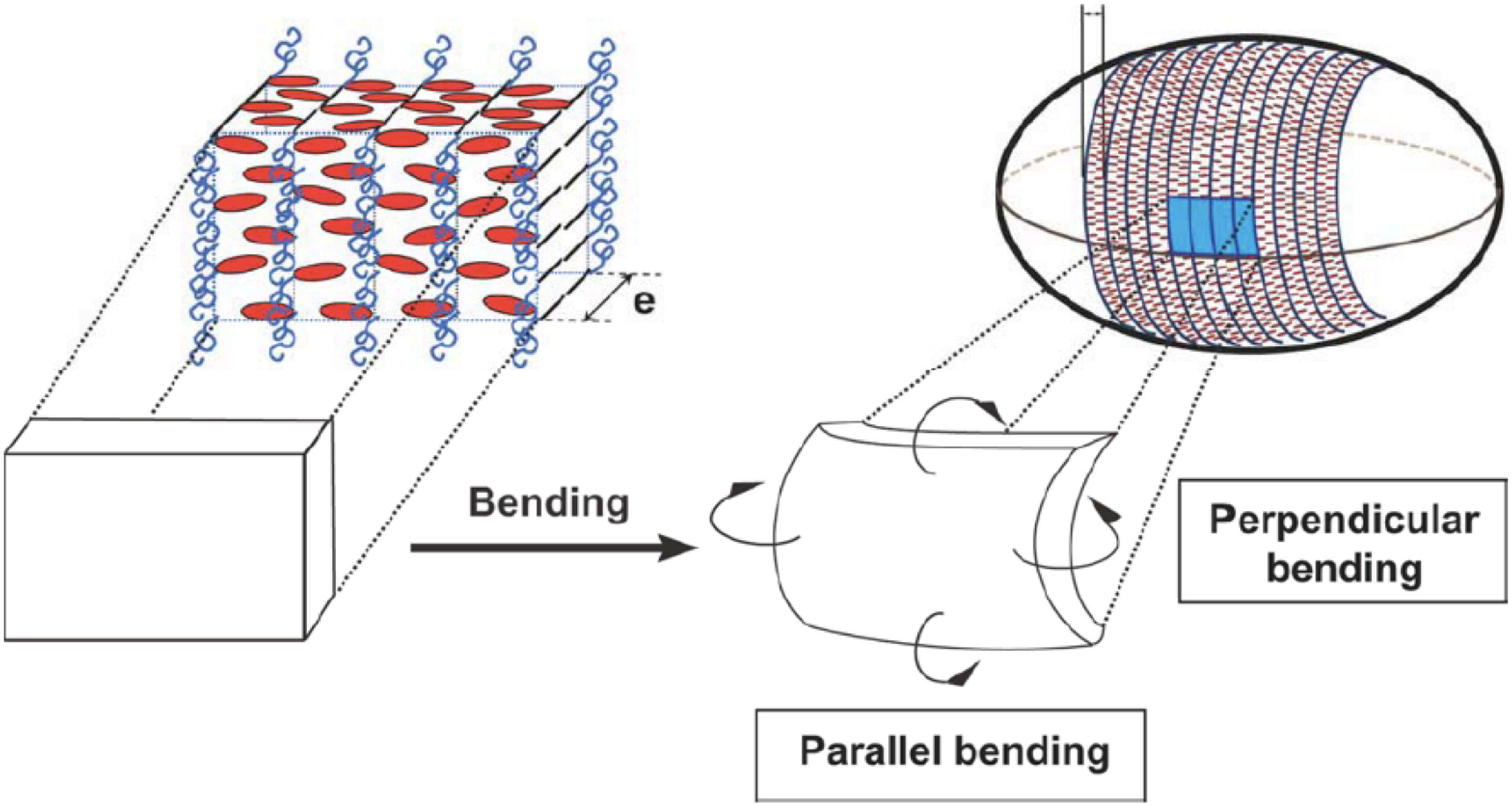
Amphiphilic Bilayers → Lipid Bilayers

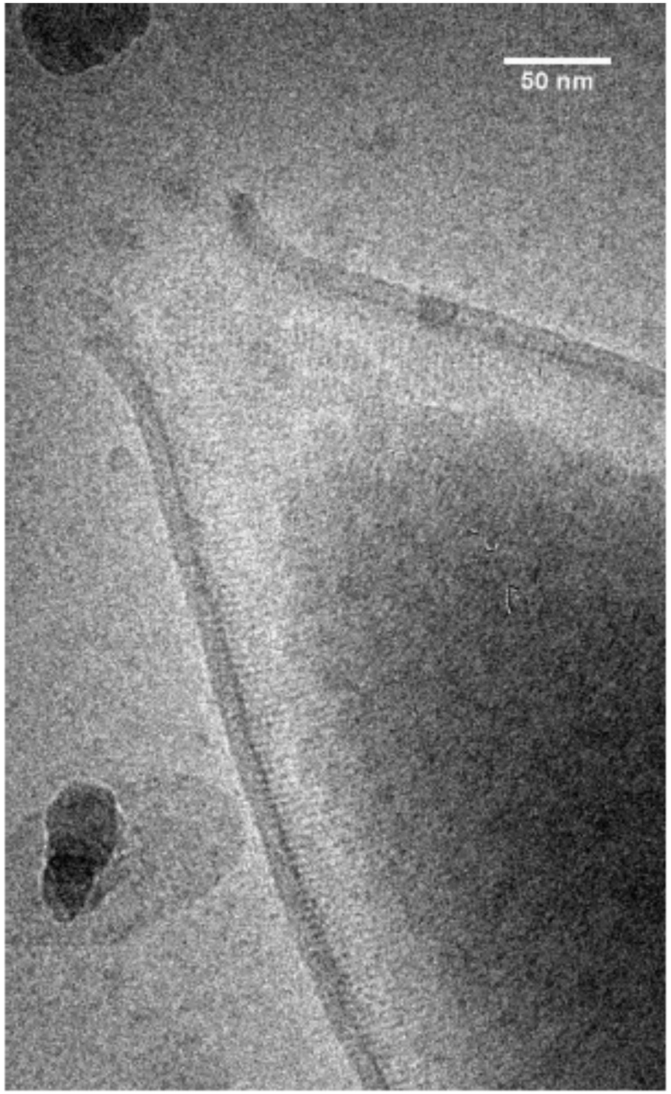
Amphiphilic Bilayers → Block Copolymer Bilayers



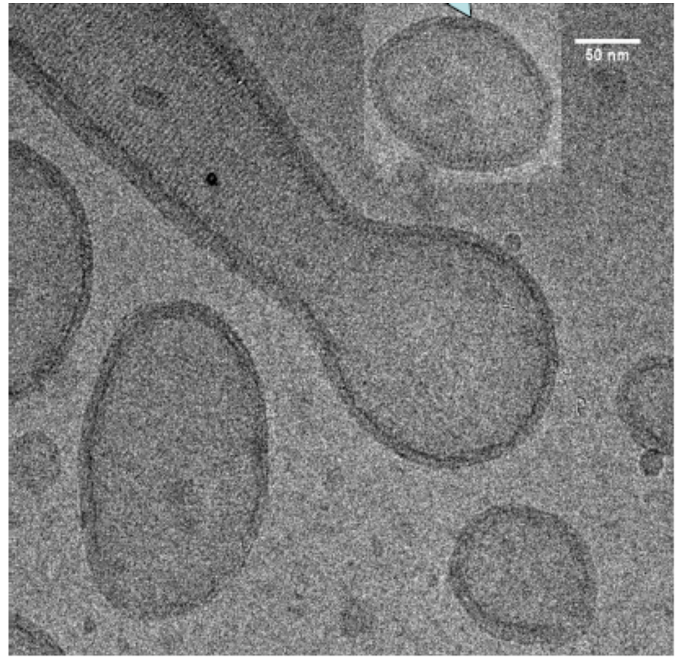
(PAChol)

Smectic Vesicles

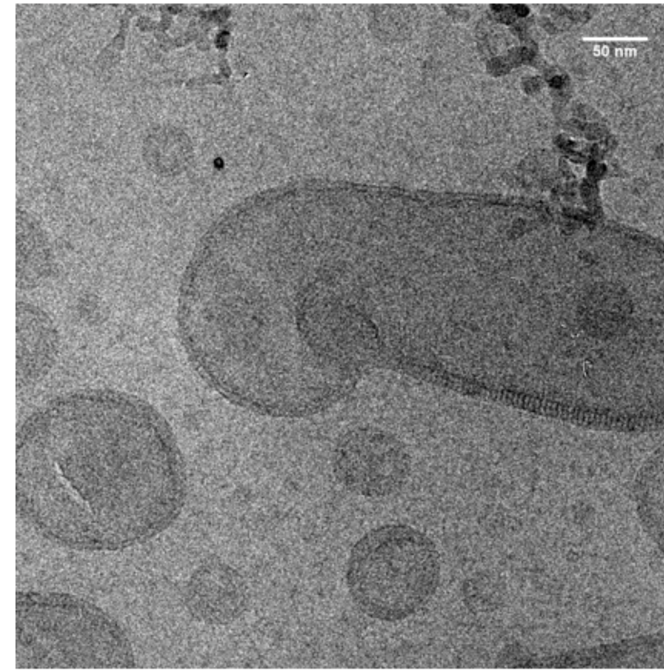




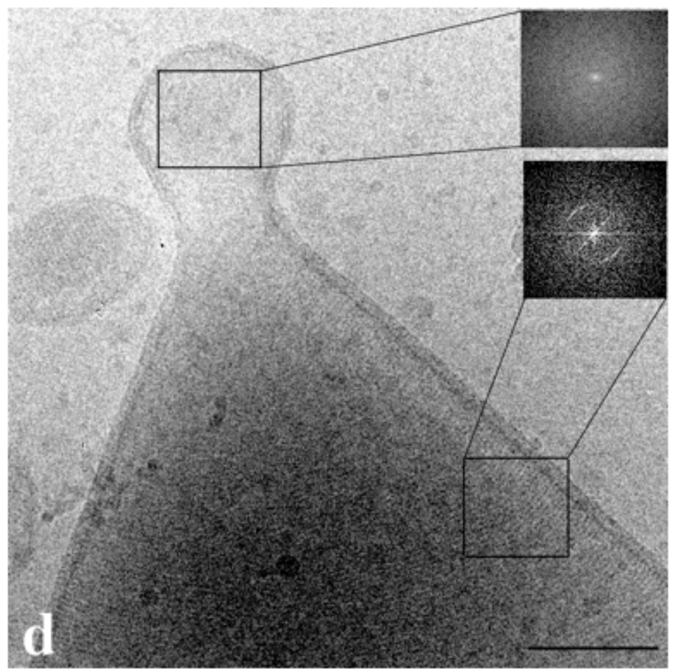
PEG2000-*b*-PAChol (20/80)



PEG2000-*b*-PAChol (28/72)

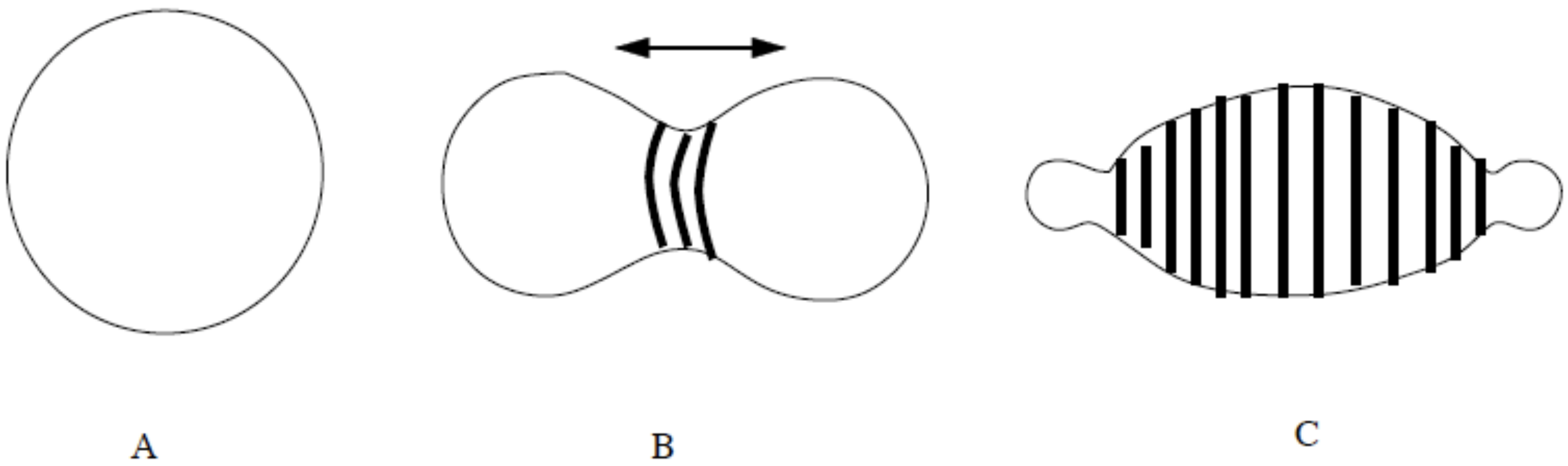


PEG-b-PAChol (28/72)

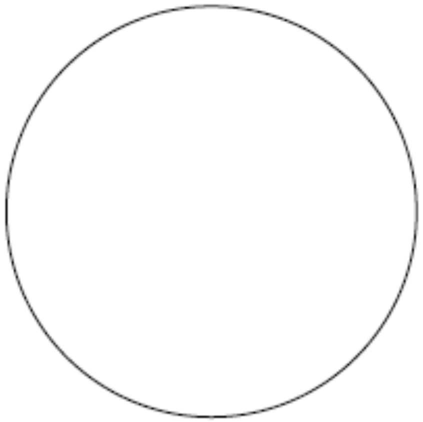


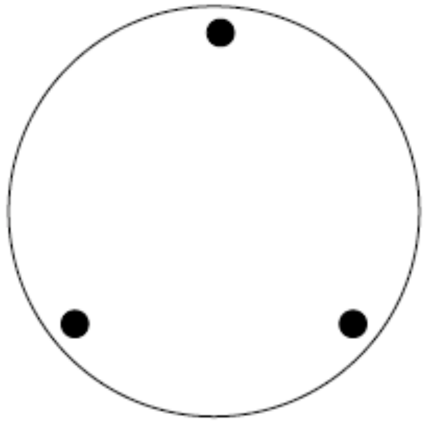
Shape Evolution

Isotropic ⟷ Smectic

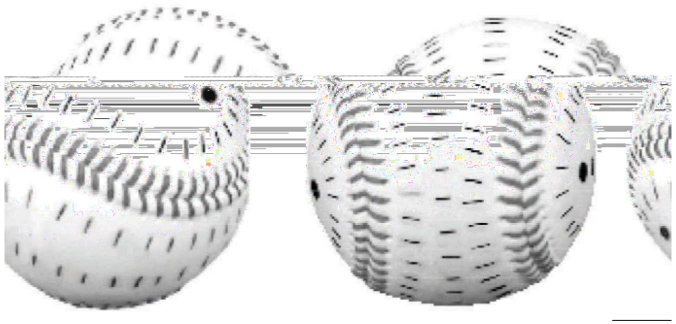


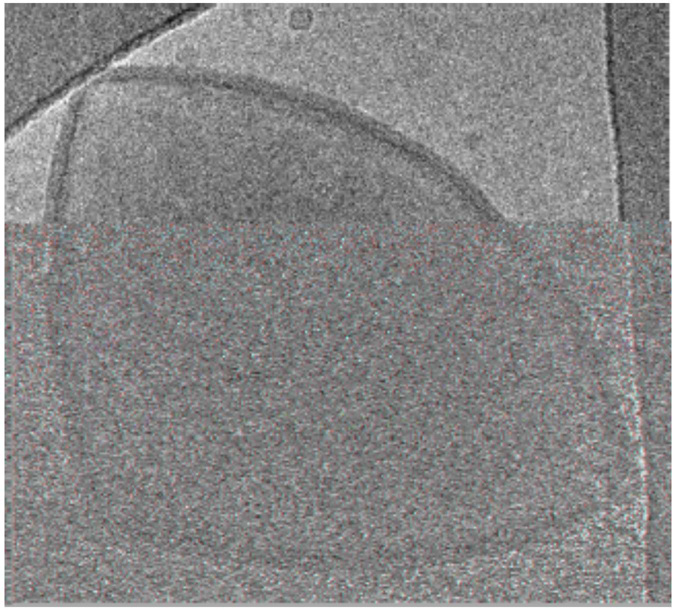
Isotropic → Nematic → Smectic





"Faceted" liquid droplets

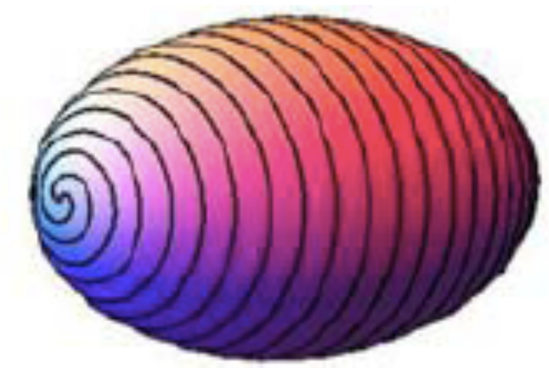




PEG2000-*b*-PAendon1 (20/80)

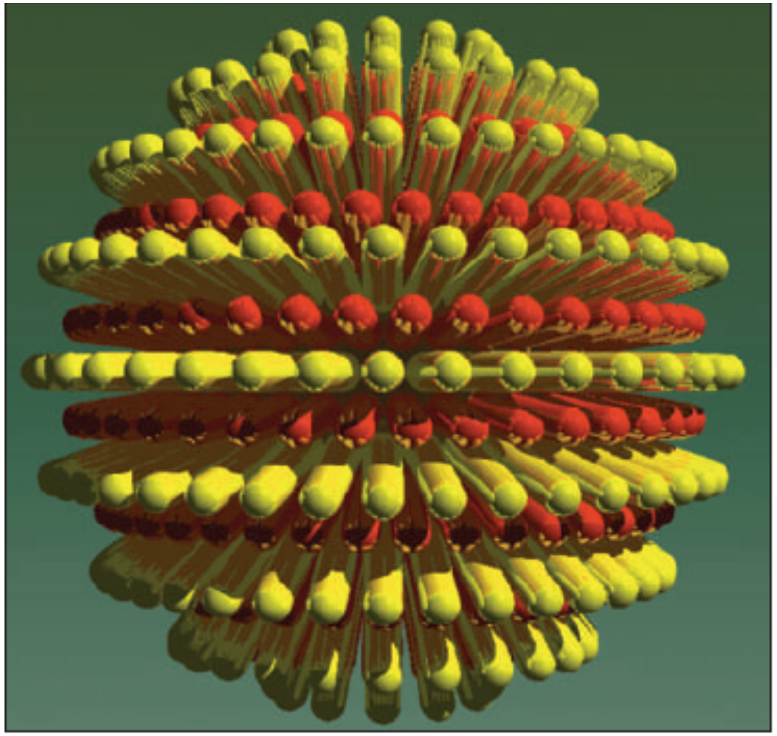
Supramolecular Assembly via Defects

2 disclinations (vortices)

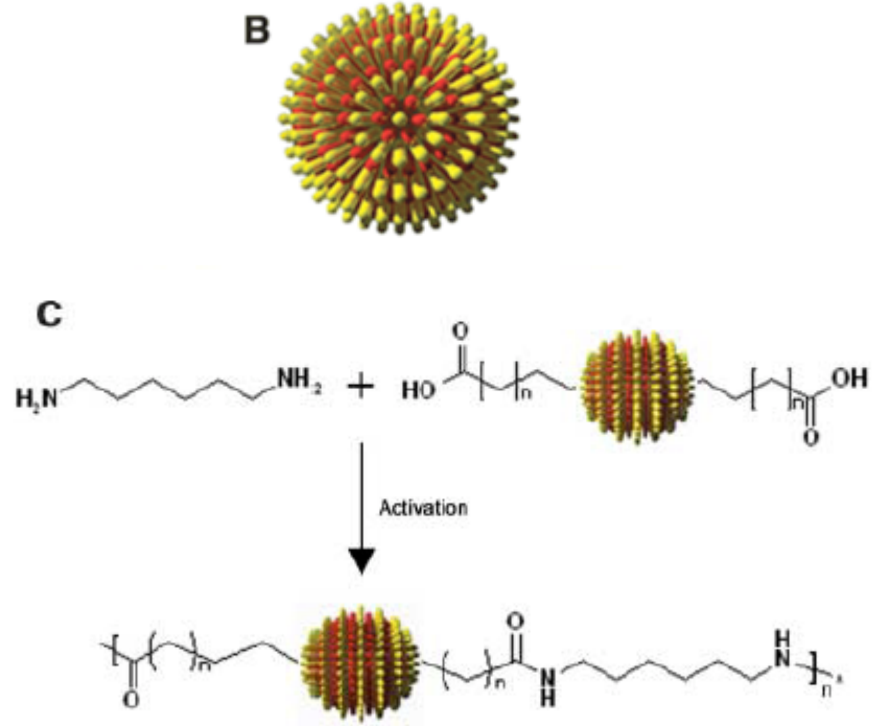


Functionalize defects with streptavidin and biotinylated DNA?

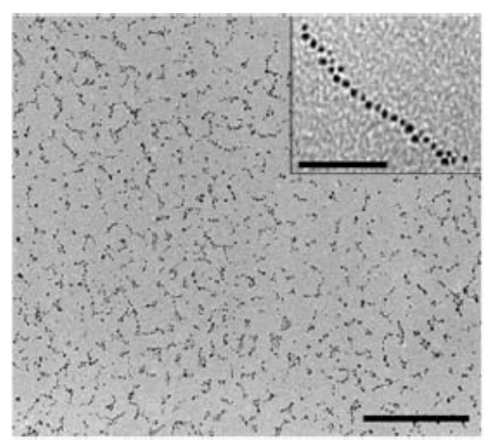
cf. Stellacci group (MIT) - divalent Gold Nanoparticles



SAM consisting of 2 types of thiol-terminated ligands (1-nonanethiol and 4-methybenzenethiol) on Gold



Functionalization by MUA

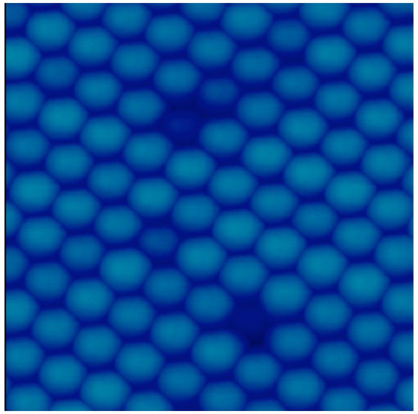


NP Polymer

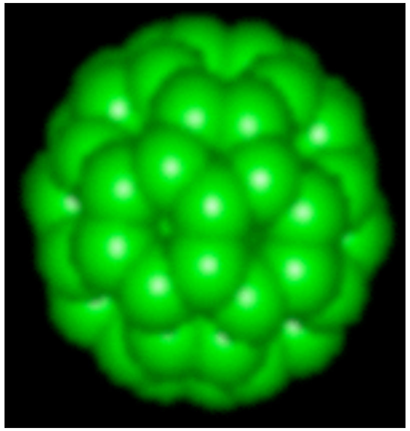
Spherical Crystals

DMR-0219292 (ITR): A. Bausch, MJB et al., Science 299 (2003) 1716

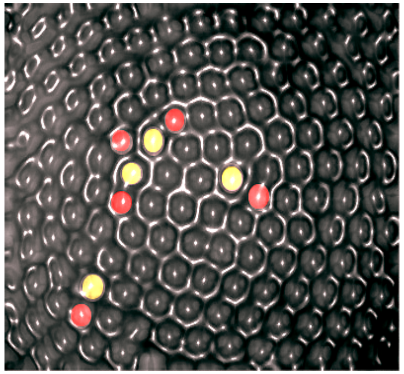
Flat space hexagonal close packing of colloidal beads with no defects – all beads are 6-fold coordinated.



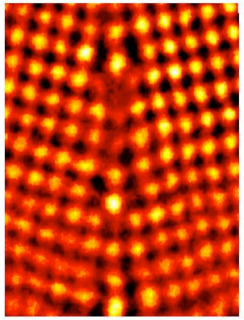
Packing on a sphere in the C60 buckyball. There are 12 5-fold coordinated vertices at the center of the 12 pentagonal carbon rings.

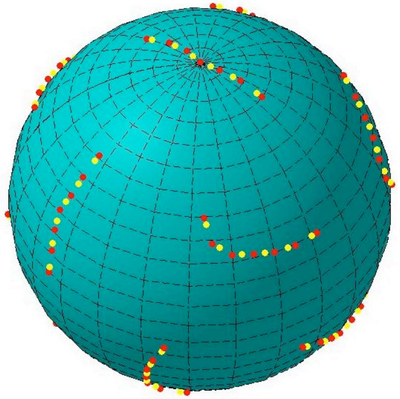


The packing of more than 500 colloidal beads on the surface of a ball leads to the proliferation of scars – these are linear arrays of dislocations (5-7 pairs) with one excess disclination (5).

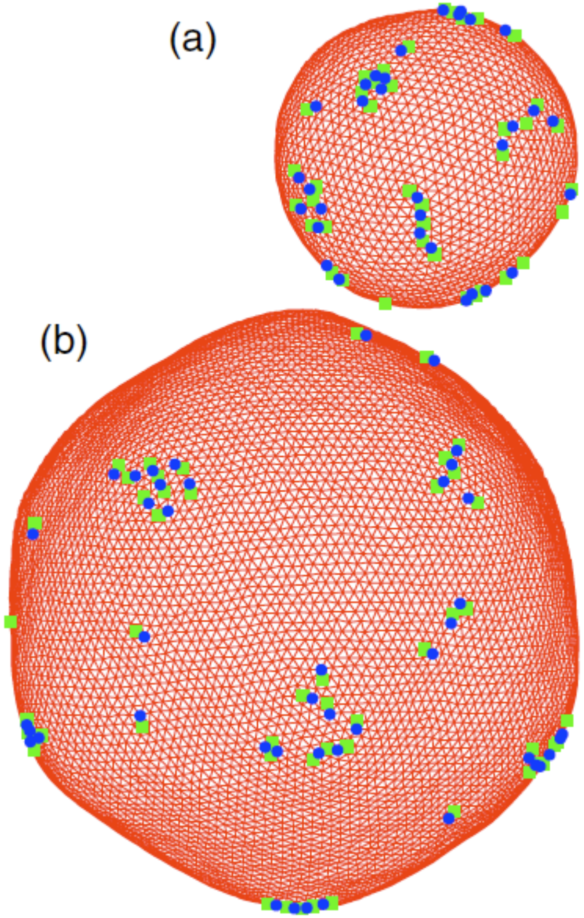


Grain boundaries in the flat space image on the right extend all the way across the sample whereas the scars to the left (experiment) and below (simulation) are freely terminating.

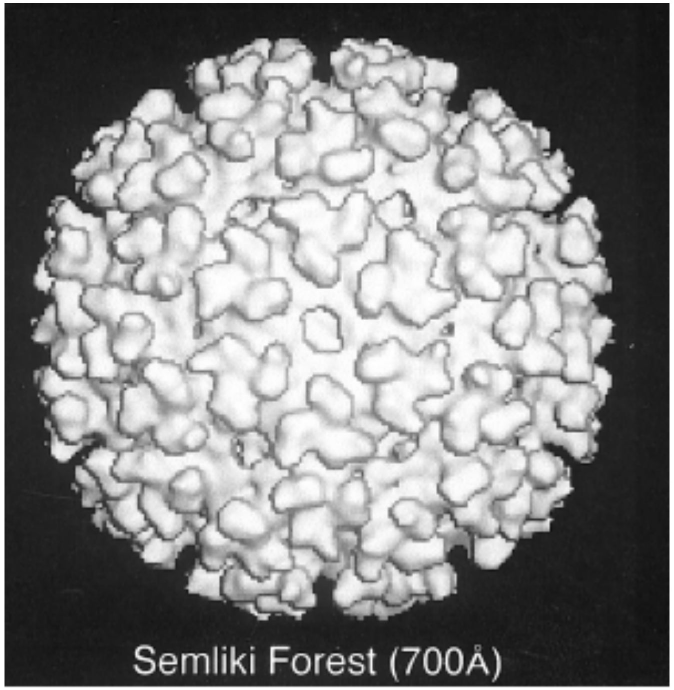




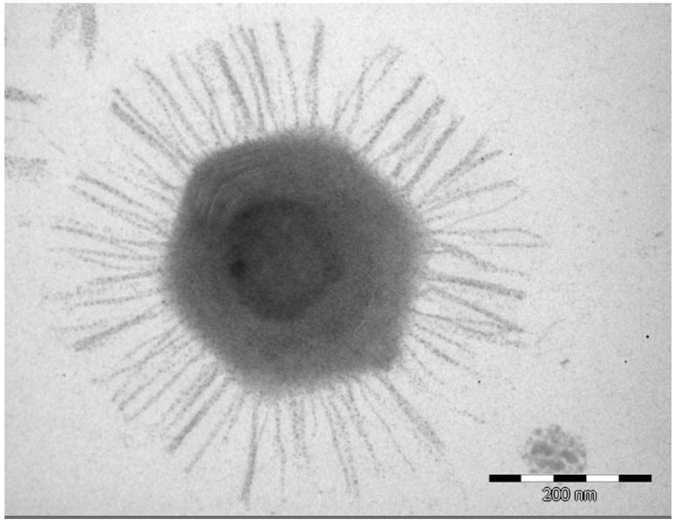
MJB, D.R. Nelson and A. Travesset (2000)



Kohyama & Gompper, PRL (2007)

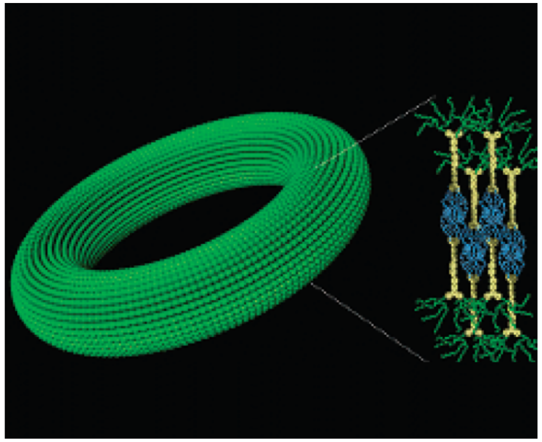


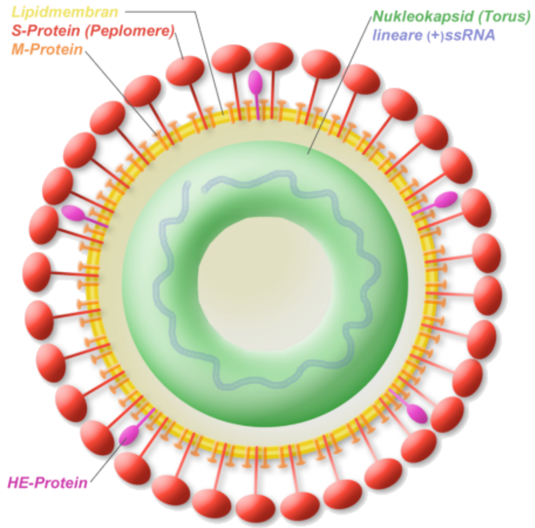
13kb RNA

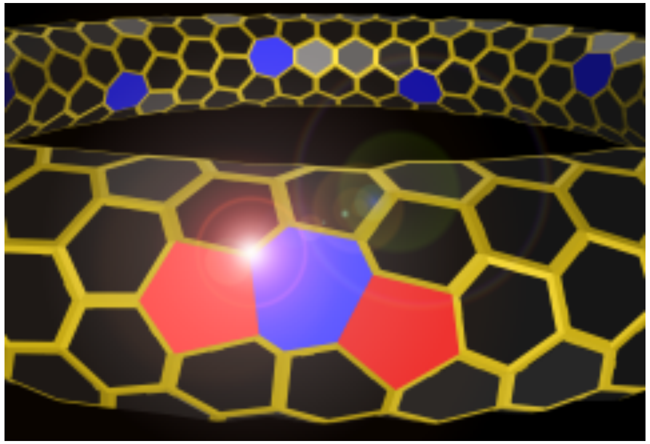


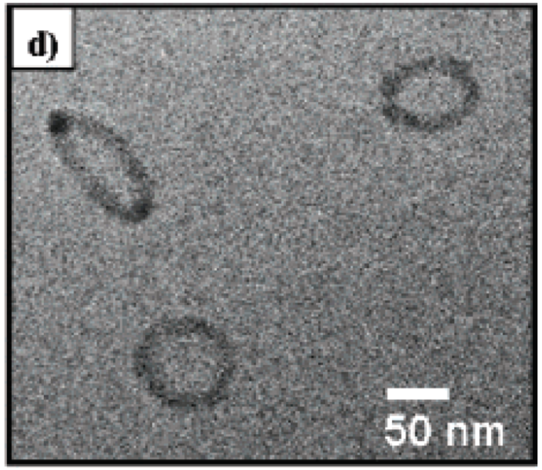
Mimivirus 1.2-Mb (dsDNA)
GiantVirus.org

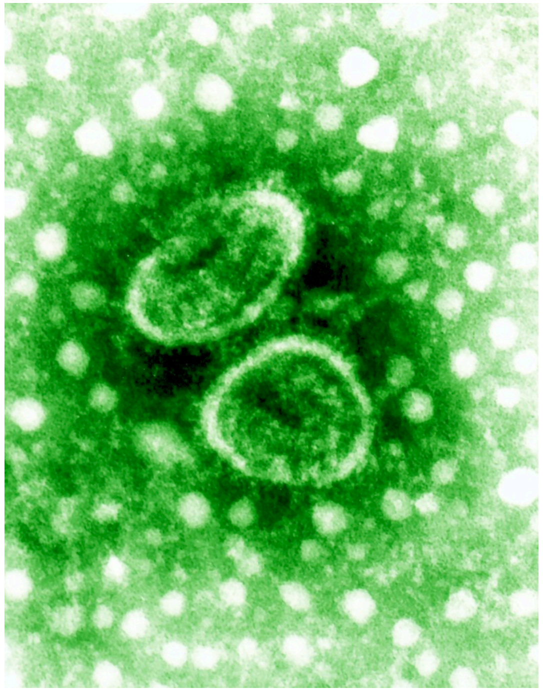
Tori







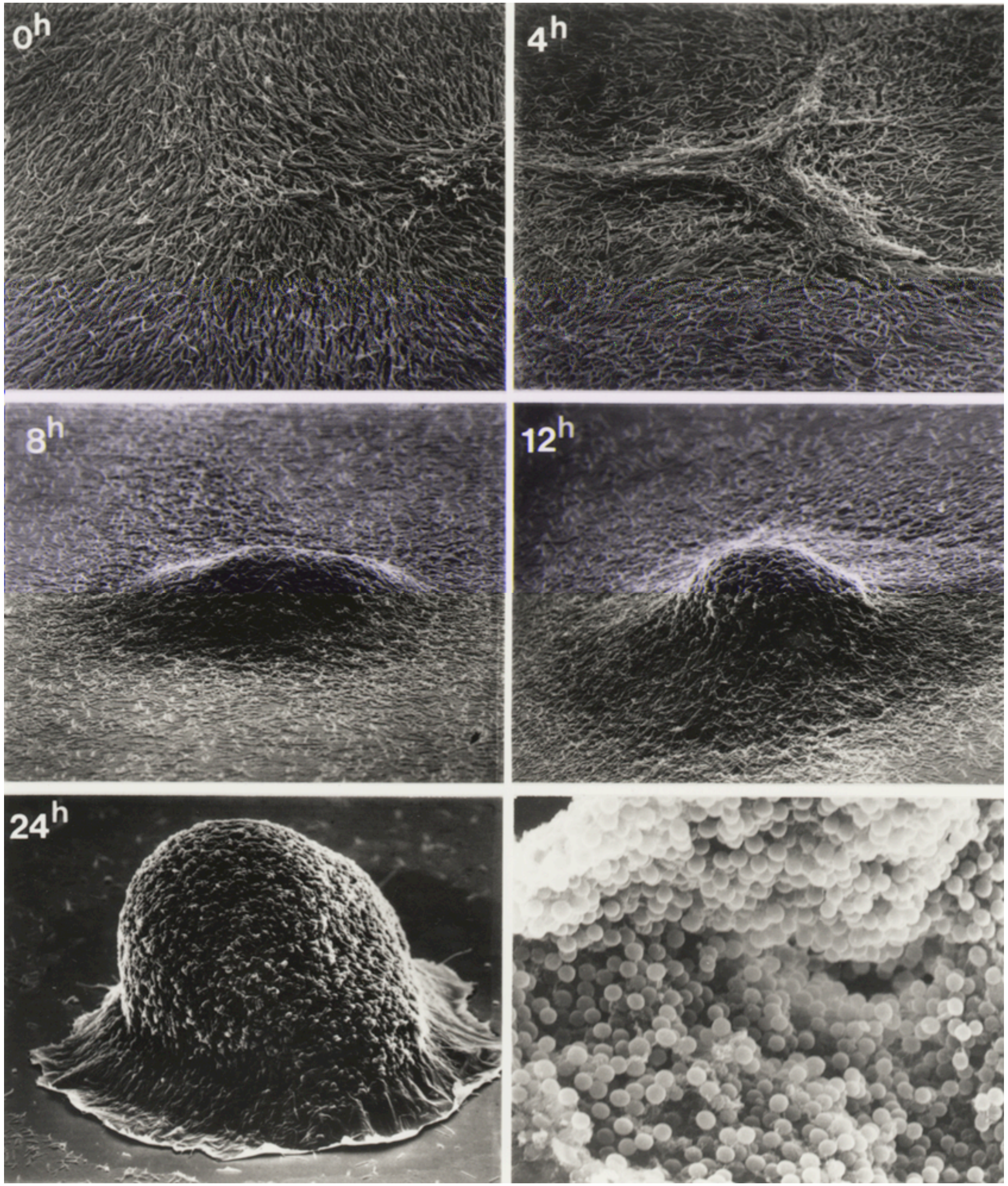




MJB, L. Giomi (2008)

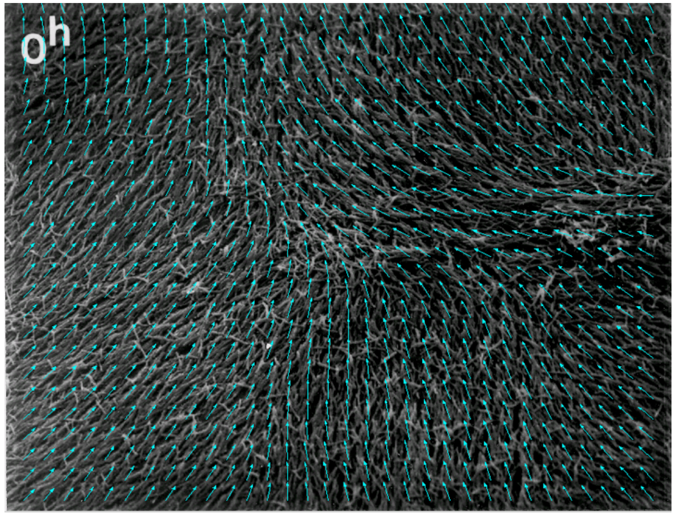
Myxobacteria

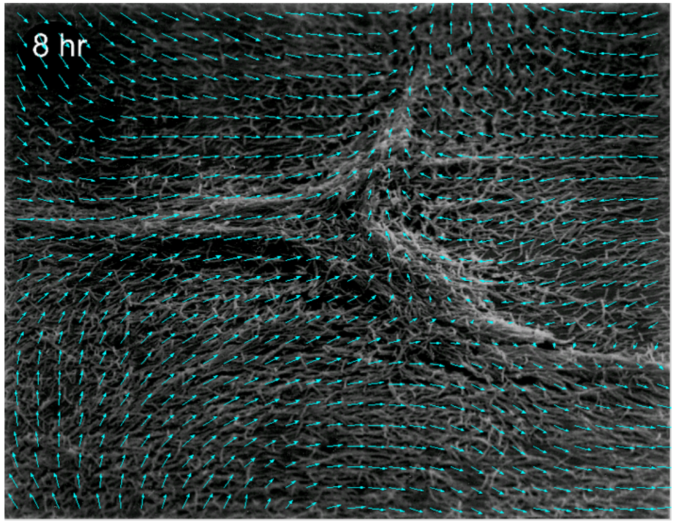
Non-chemotactic self-propelled particles



Living Liquid Crystals

Kaiser (Stanford)
Welch (Syracuse)





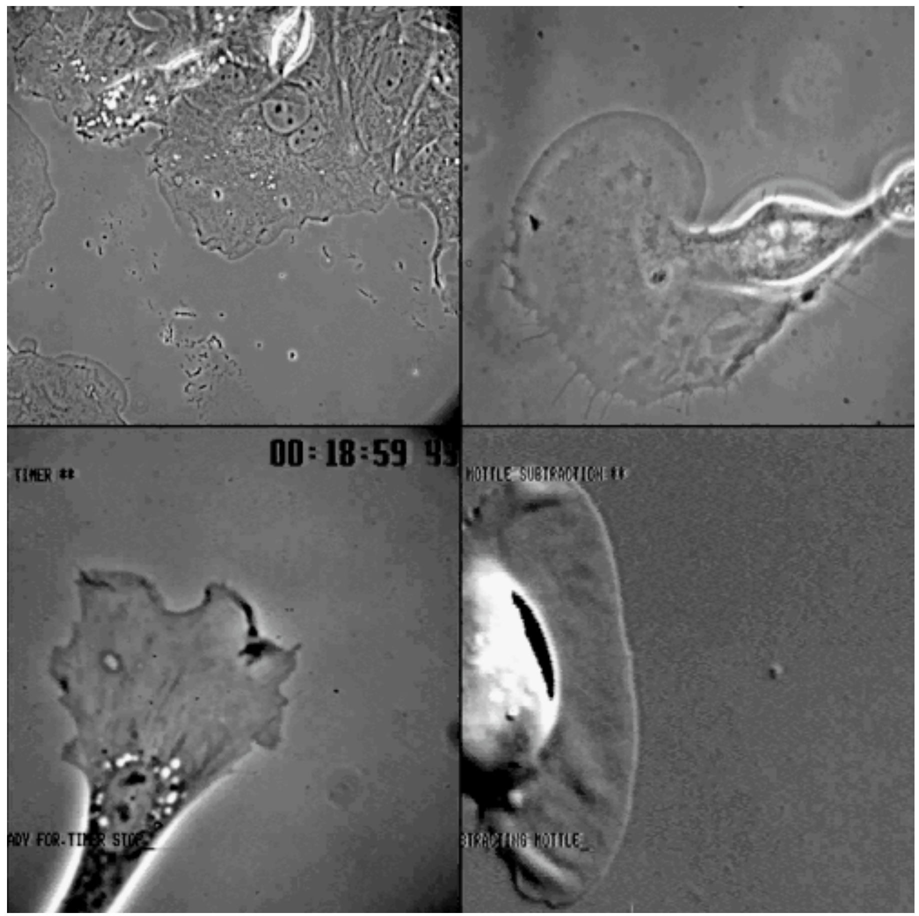
Disclination defect as nucleation site of structure formation

Cell as a material

(K. Kasza et al., Current Opinion in Cell Biology 2007, 19:101-107)

mouse
fibroblasts
(3h)

mouse
melanoma
(20min)



chick
fibroblasts
(2h)

trout
keratocyte
(4min)
v=15μm/min

V. Small, IMBA, Vienna.

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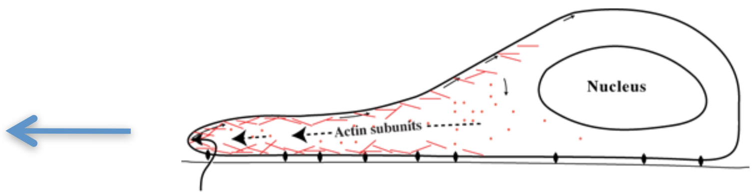
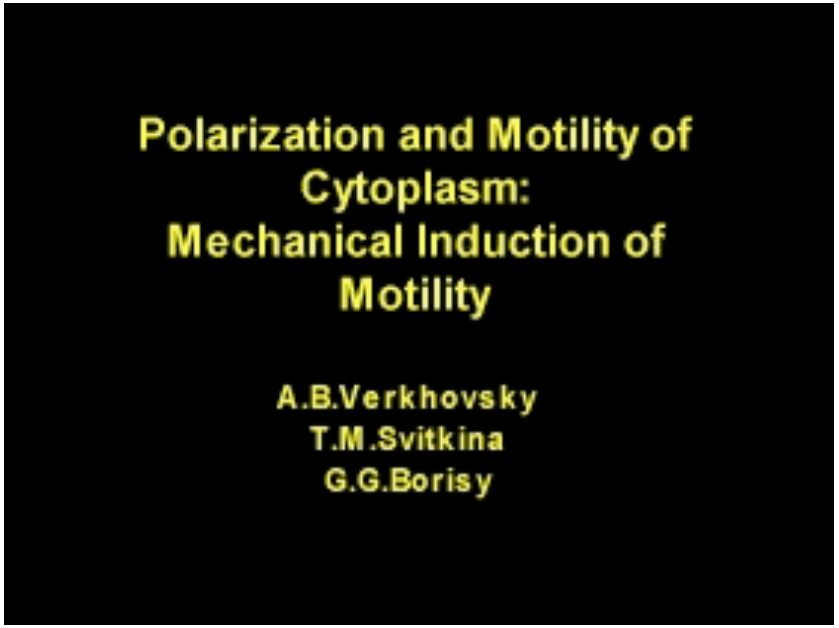
A fragment of a keratocyte lamellipodium can be set into motion
→ motility as a material property of the actin lamellipodium?





Lamellipodium: crosslinked actin network, with mechanical properties controlled by various crucial nonequilibrium effects:

- Contractile role of myosin motor proteins
- Polymerization of actin filaments
- Force transduction at adhering focal points

Actin lamellipodium as an active polarizable viscoleastic medium with intriguing materials properties → continuum theory of active gels

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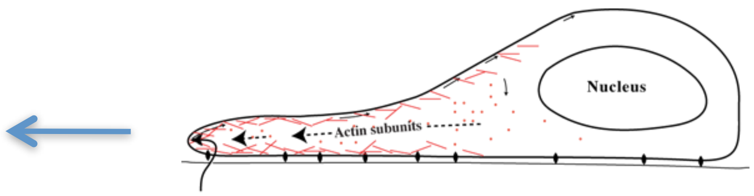

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Actin lamellipodium as an active polarizable viscoleastic medium with intriguing materials properties → continuum theory of active gels

Example: spontaneous flow of active polar films

Voituriez, Joanny, Prost, EPL (2005); Giomi, Marchetti, Liverpool PRL (2008)

Equilibrium nematic film anchored to a substrate: no applied forces → no flow

Active nematic film anchored to a substrate: no applied forces → **spontaneous flow**

Contractile effect of myosin generates active stresses that strain the local orientation and induce flow $(\partial_y v_x \neq 0)$ to maintain net zero stress in the system.

$$\overleftrightarrow{\sigma}_{net} = \overleftrightarrow{\sigma}_{flow} + \overleftrightarrow{\sigma}_{active} = 0$$

$$\overleftrightarrow{\sigma}_{flow} = \eta \vec{\nabla} \vec{v}$$

$$\overleftrightarrow{\sigma}_{active} \sim \alpha \, \hat{n} \, \hat{n}$$

Part III: Why support Quantitative Biology & Some Structural Problems

1. New data driven era of "quantitative biology" to which condensed matter physicists can and will make seminal contributions.
2. Students very much interested in working in this area with their acquired physics skills.
3. Support for interdisciplinary research is often spoken of as desirable and even crucial but the funding realities are brutal because of "territorial imperative".
4. People who change field are often thought of as washed up in their original field and dilettantes in their new field. Mostly BARRIERS to changing directions not INCENTIVES.
5. New grants still favor fresh PhDs.
6. Programs required that fund strong proposals from outsiders with good track records.
7. Fund long term (5 year) RISKY projects (Janelia Farm model). We are writing proposals full-time.

Public Relations

1. Condensed Matter/Materials Scientists do a poor job in communicating the excitement and intellectual content of our field to the public as compared to the cosmologists and the high-energy/particle/string community.
2. The public is excited by the novel, the exotic and the unimaginable more than the everyday which they feel they understand.
3. Emphasize the truly surprising over the pragmatic.
4. "Quantitative Biology" better name than Biophysics to highlight the current data-driven era.

Soft Active Matter

- Assembly of interacting self-driven units with collective behavior on large scales
- Energy input that maintains the system out of equilibrium is on each unit, not from boundaries (unlike shear flow or 3d granular)
- Orientable units (rod-like)$\rightarrow$ polar & nematic order

Living or active liquid crystals:

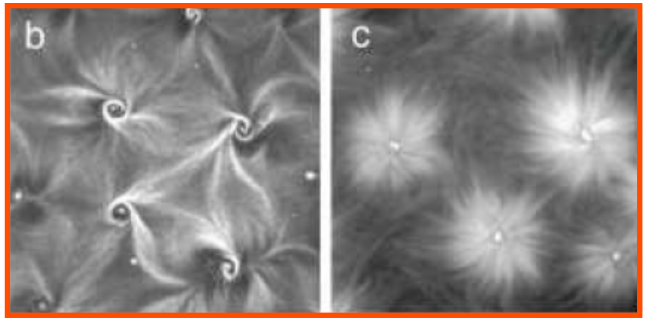
- Bacterial suspensions
- Extracts of cytoskeletal filaments and motor proteins (microtubules & kinesins, actin and myosins)
- Sperm cells, melanocytes, …

Active gels:

Cell cytoskeleton

In vitro acto-myosin systems

Active Liquid Crystals I



Suspension of microtubules and kinesins, T. Surrey, F. Nédélec, S. Leibler, E Karsenti, Science **292**, 1167 (2001).

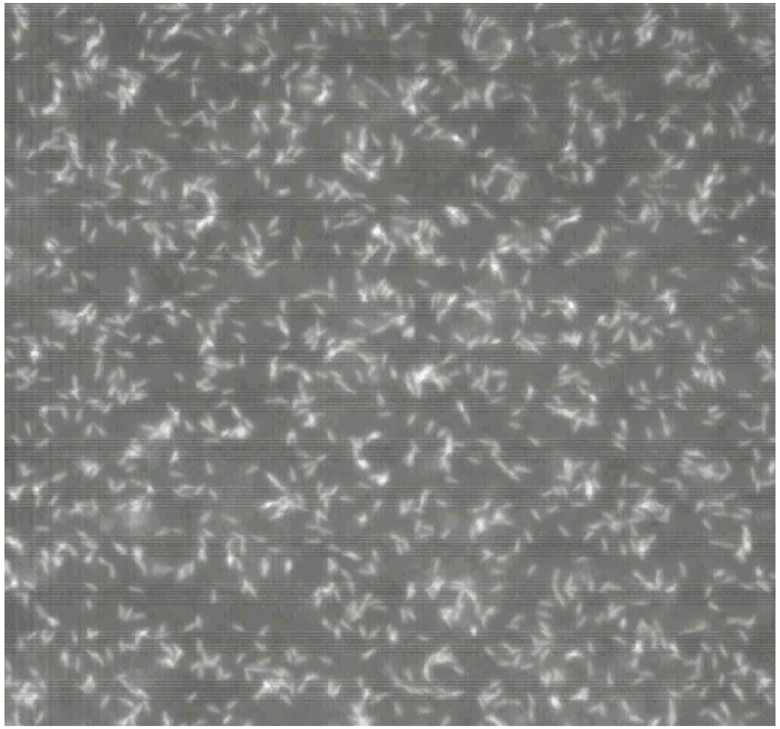
- Pattern formation on various scales
- Spontaneous flow in ordered active films: R. Voituriez, J.-F. Joanny and J. Prost, EPL 70 404 (2005); L. Giomi, M. C. Marchetti and T. B. Liverpool, PRL 101, 198101 (2008)
- Giant number fluctuations in living nematic: V. Narayan, S. Ramaswamy, N. Menon, Science 317 (2007) 105

Active Liquid Crystals II: swarming and vorticity in supensions of bacteria and other unicellular organisms

Circulating spermatozoa form a 2D array of vortices.

A Self-Organized Vortex Array of Hydrodynamically Entrained Sperm Cells, I. H. Riedel, K. Kruse and J. Howard, Science **309**, 300 (2005)

Active Liquid Crystals II: swarming and vorticity in supensions of bacteria and other unicellular organisms



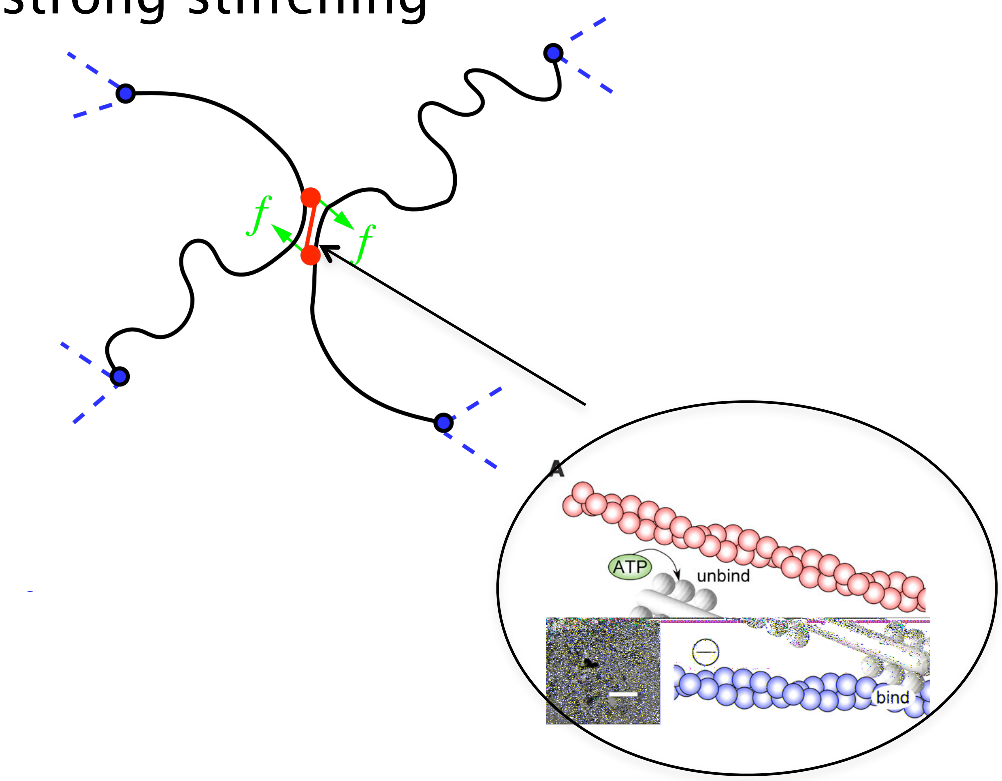
Circulating spermatozoa form a 2D array of vortices.

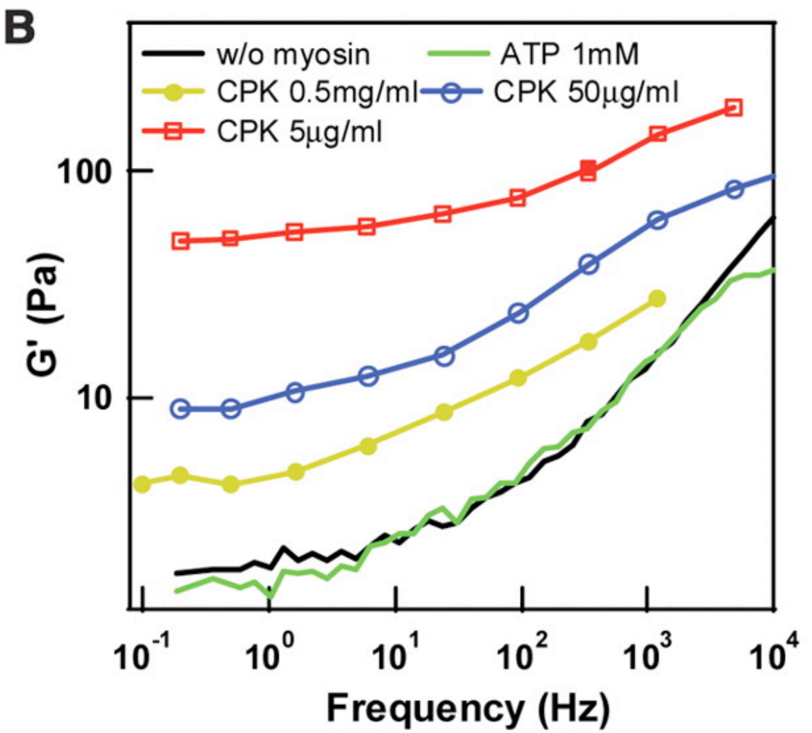
A Self-Organized Vortex Array of Hydrodynamically Entrained Sperm Cells, I. H. Riedel, K. Kruse and J. Howard, Science **309**, 300 (2005)

Active Gels

Myosin II motors alter the mechanics of a gel of cross-linked actin filaments in vitro, mimicking the mechanical properties of the cell cytoskeleton:

- spontaneous contractility
- strong stiffening





Nonequilibrium Mechanics of Active Cytoskeletal Networks, D. Mizuno et al., Science 315, 370 (2007)