Breakout Report on **Biomaterials**

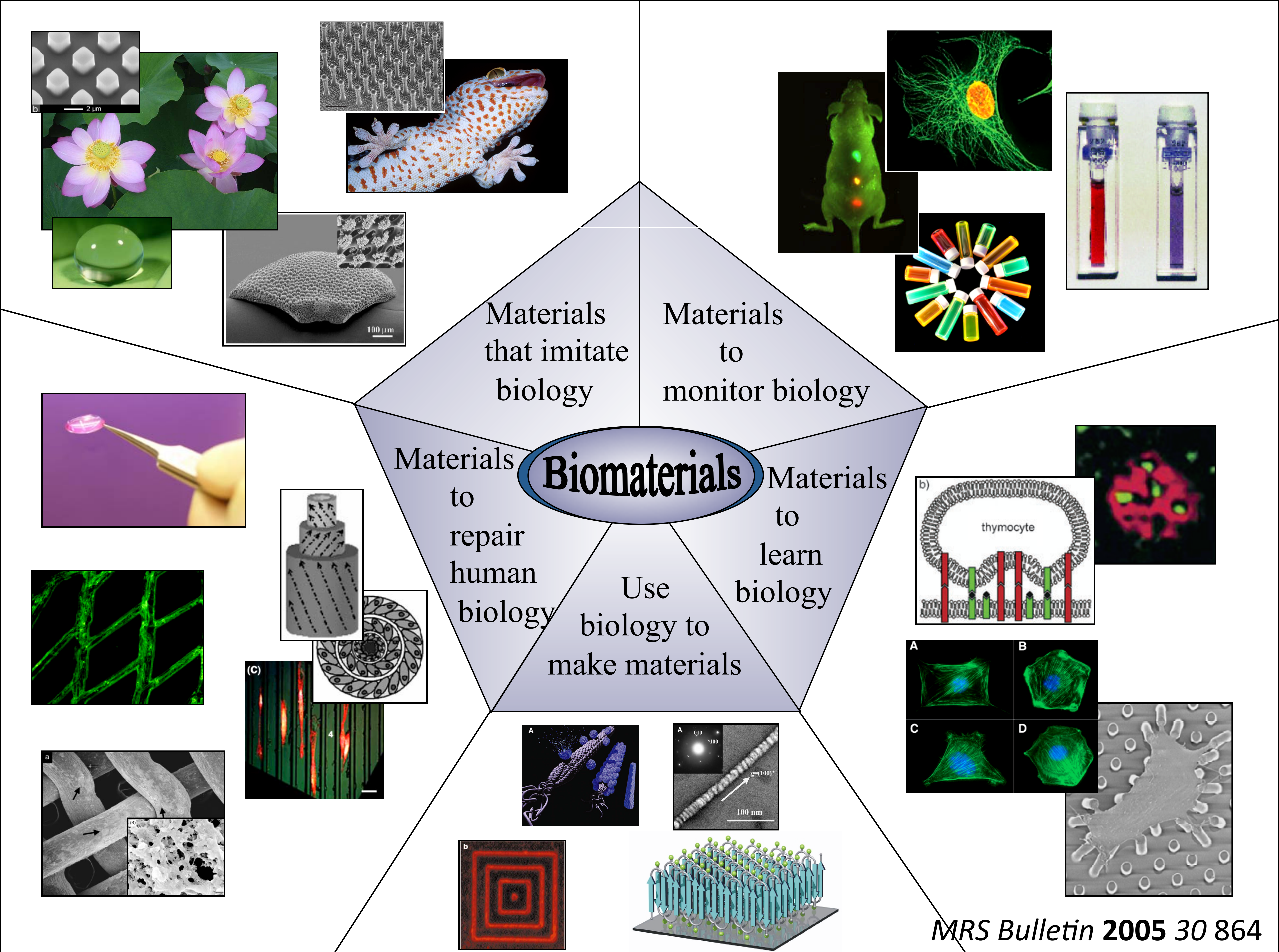
Identification of Grand Challenges

Breakout Biomaterials

- Chair: Sam Stupp
- Co-Chair: Rajesh Naik

- Speakers: Sam Stupp, Rajesh Naik

- Invited Participants: T.Douglas, I. Aronson, M. Olvera, A. Balasz, I. Szleifer, S. Forry, B. Ratner, P. Messersmith, P. Yin, W. Shih, D. Irvine



Biomaterials

Materials that imitate biology

Materials to monitor biology

Materials to learn biology

Use biology to make materials

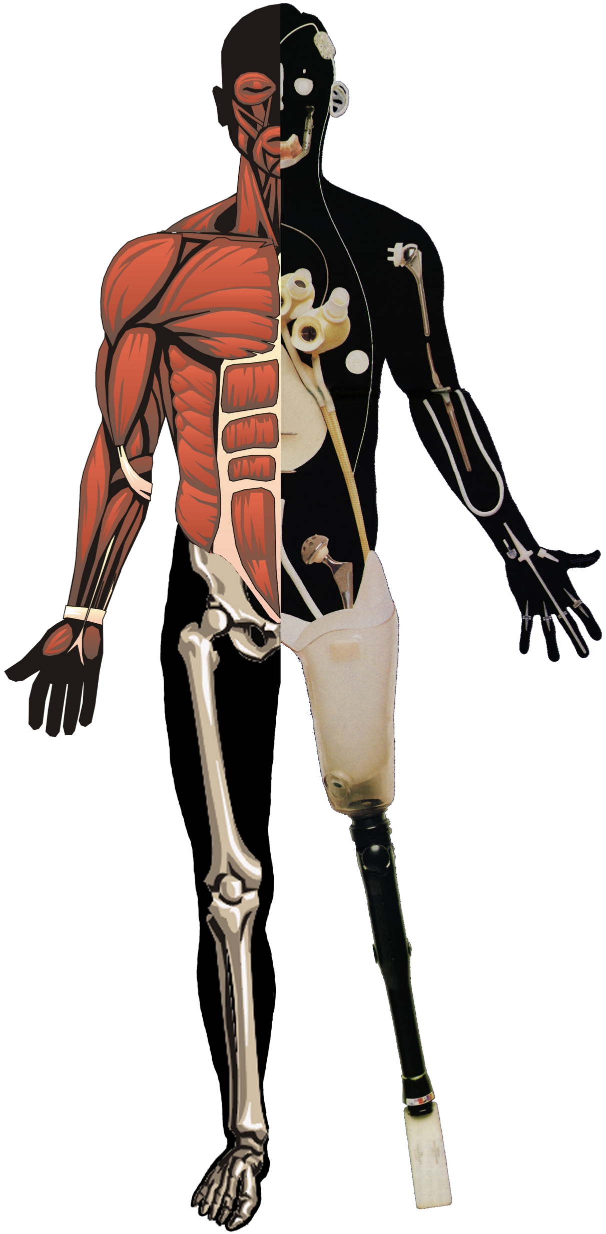
Materials to repair human biology

MRS Bulletin **2005** *30* 864

Scope of Biomaterials

- **Biomedical Materials for the Repair of Human Tissues and Organs**
- **Bio-inspired Synthetic Materials**: *hierarchical structures, self-assembling, structurally self-correcting, active materials with engineered spatio-temporal responses, energy-transducing materials*
- **Bio-Fabricated Materials**: *harnessing biology to make materials (non-canonical amino acids for artificial proteins, engineering viruses as molecular components of materials, genetic manipulation for designed materials properties)*
- **Materials to Interface with Biology**: *synthetic materials that modulate biological functions or interrogate biological systems (stem cells, bacteria)*

Regeneration of Body Parts

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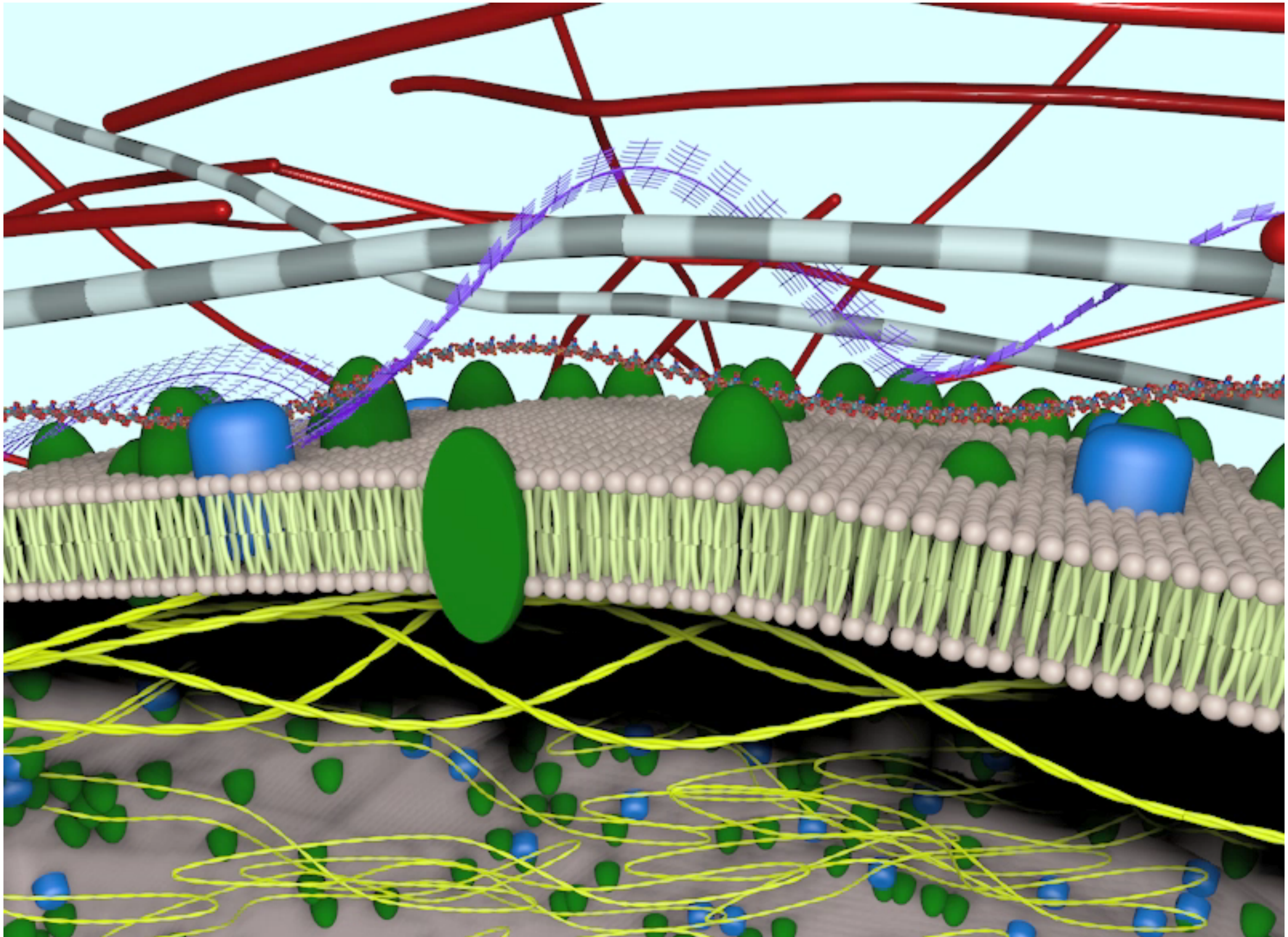
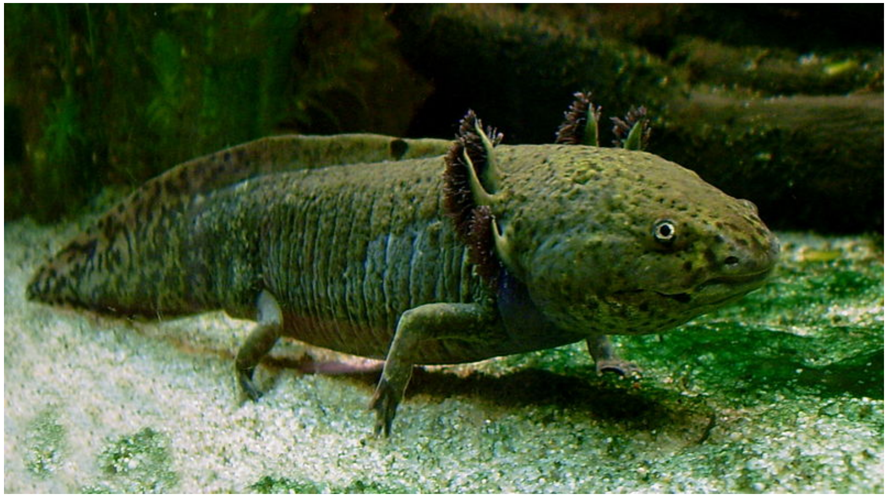
Emulate Shape Persistence and Structural Precision of Fibers in Extracellular Matrices Using Supramolecular Structures

Artificial Biomimetic Matrices for Cell-Signaling



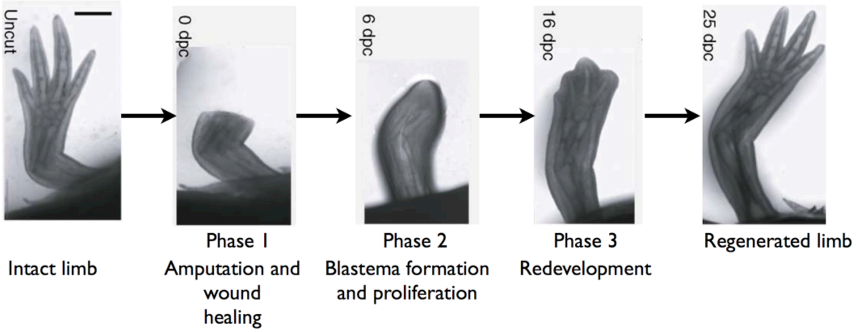
Amphibian Envy: Can Chemistry Help Us Mammals?

the axolotl: from lake in central Mexico, means “water monster” in Uto-Aztecan language

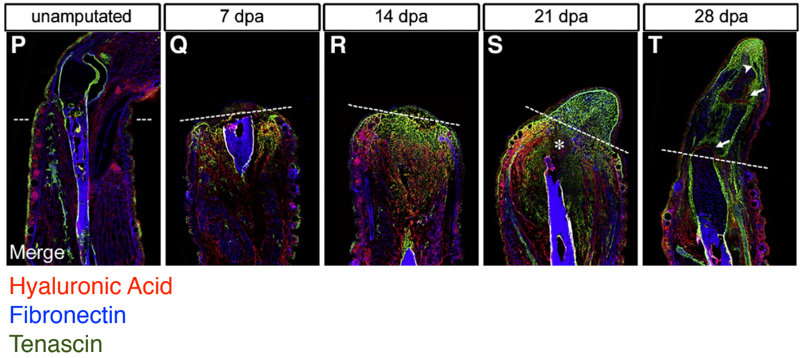


http://en.wikipedia.org/wiki/Axolotl

http://animals.nationalgeographic.com/animals/amphibians/axolotl/



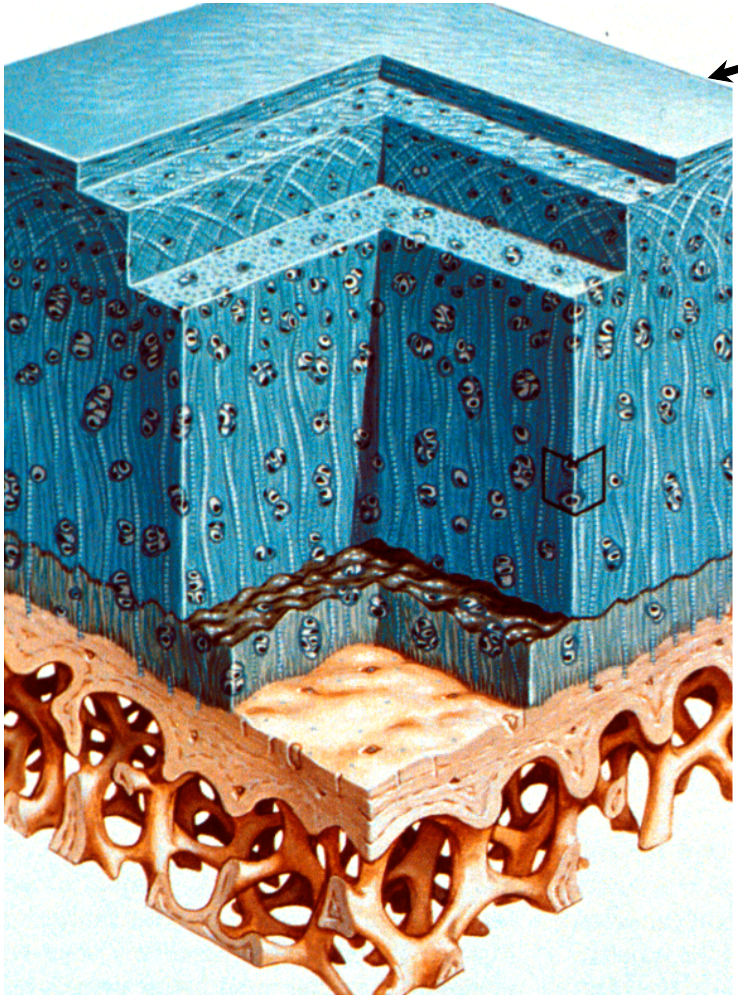
axolotl limb regeneration



Chemistry Changes in Space and Time

can we mimic such spatiotemporal control over bioactivity?

Bio-Inspired Materials: Hierarchical Structures such as Cartilage Function of Articular Cartilage



Superficial Zone (parallel fibrils)

Provides low friction articulating surface

Transition Zone (random fibrils)

Deep Zone (radial fibrils)

Distributes loads-minimizes stresses

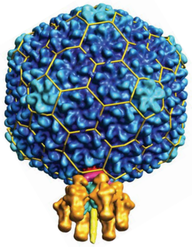
Calcified Cartilage

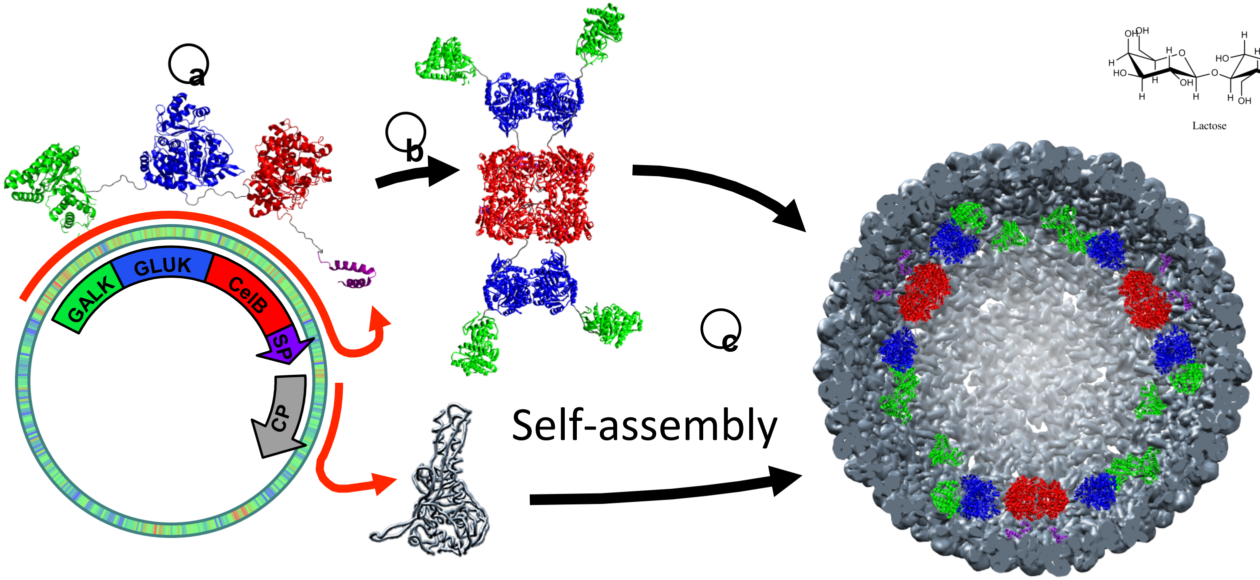
Subchondral bone

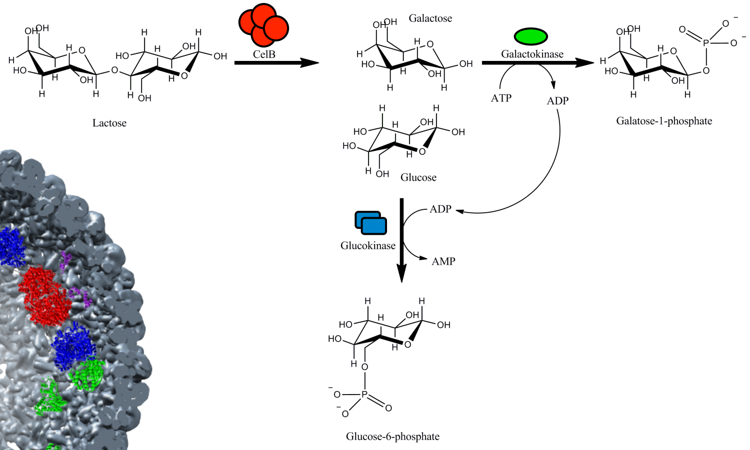
Cancellous bone

Complex Catalytic Materials

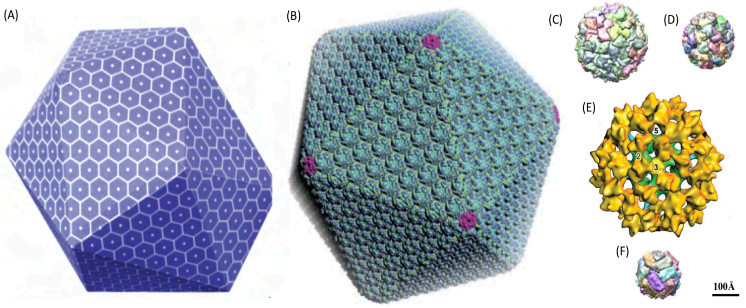
– multi-enzyme encapsulation (genetic level synthesis, self-assembly)







Mimicking Subcellular Protein-Based Enzyme Compartments



T. Douglas (Indiana University)

MGI State-of-the-art in the Biomaterials Industry

- Biomedical Biomaterials is a well established multi-billion dollar industry but lacks innovation due to regulatory concerns
- Development of non-biomedical biomaterials is nascent and limited to start up companies for the most part: optimal time for MGI activities and new industrial opportunities
- MGI-relevant strategies only exist at the level of simple combinatorial and drug discovery strategies
- The limited data available reside in individual companies and do not benefit the community at large
- NCBI is a good model for open access data sharing for the biomaterials community

Opportunities and Usefulness

The field of bioactive materials for regeneration of tissues and organs is of high technical and market risk but with enormous potential to generate revenue and huge impact on human welfare—*the MGI strategies could accelerate development of the structures that are highly bioactive—cure neuro-degenerative diseases now that humans are living up to 100 years!!*

Hierarchical materials—with varying structures and compositions across multiple scales--using biological principles are a great opportunity for new properties: we do not know how to synthesize them or characterize them with high precision; we lack methods to synthesize them with high fidelity and scale

Use biology to make commodity materials or new materials: e.g. artificial proteins, artificial polysaccharides

Technical Challenges and Gaps

- Theory and Modeling Tools: we do not know how to go across many length and time scales; requires better algorithms, faster processors, new modeling approaches, numerical methods

- Synthetic tools for hierarchical materials require deeper knowledge of supramolecular chemistry and self-assembly

- We need non-destructive tools to characterize and interpret order in non-crystalline soft materials

- How do we program hierarchical assembly of materials?

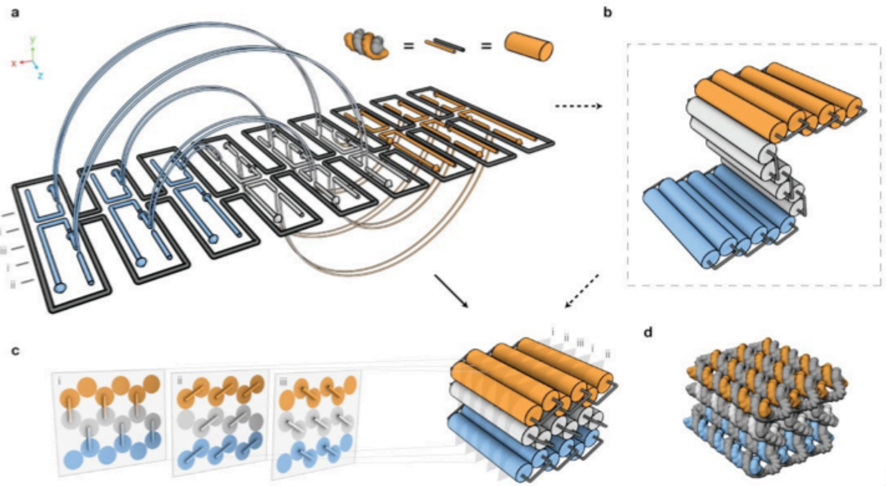
- It is critical for new generation experimental scientists to understand the computational/theory side of MGI and for theoreticians to appreciate experimental challenges and interpret robustness of experimental outcomes

- Defining a common language and metrology (ontology) for biomaterials data sharing

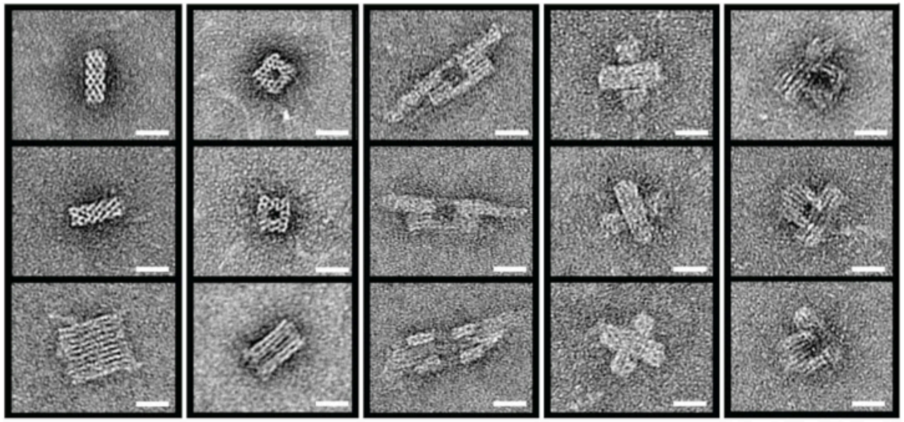
A New Field Has Emerged in Biomaterials that has Captured the Imagination of Many Scientists

DNA Nanotechnology

Self-assembly of DNA into nanoscale three-dimensional shapes

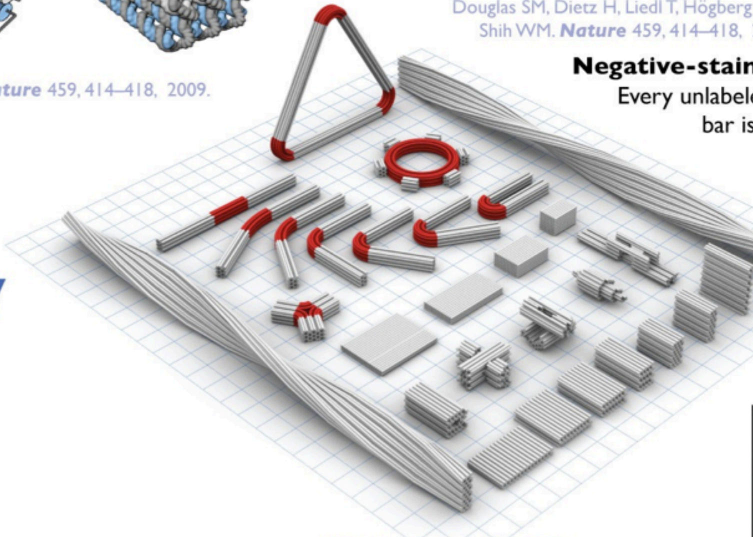


Douglas SM, Dietz H, Liedl T, Högberg B, Graf F, Shih WM. ***Nature*** 459, 414–418, 2009.



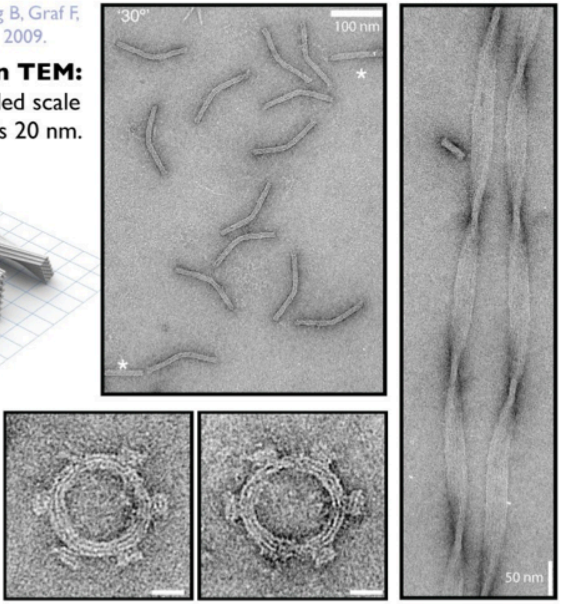
Douglas SM, Dietz H, Liedl T, Högberg B, Graf F, Shih WM. ***Nature*** 459, 414–418, 2009.

Negative-stain TEM:
Every unlabeled scale bar is 20 nm.



Shih WM, Lin CX, ***Curr. Opin. Struct. Biol.*** 20, 276–282, 2010.

Every grid square is 20 nm x 20 nm.



Dietz H, Douglas SM, Shih WM, ***Science*** 325, 725–730, 2009.

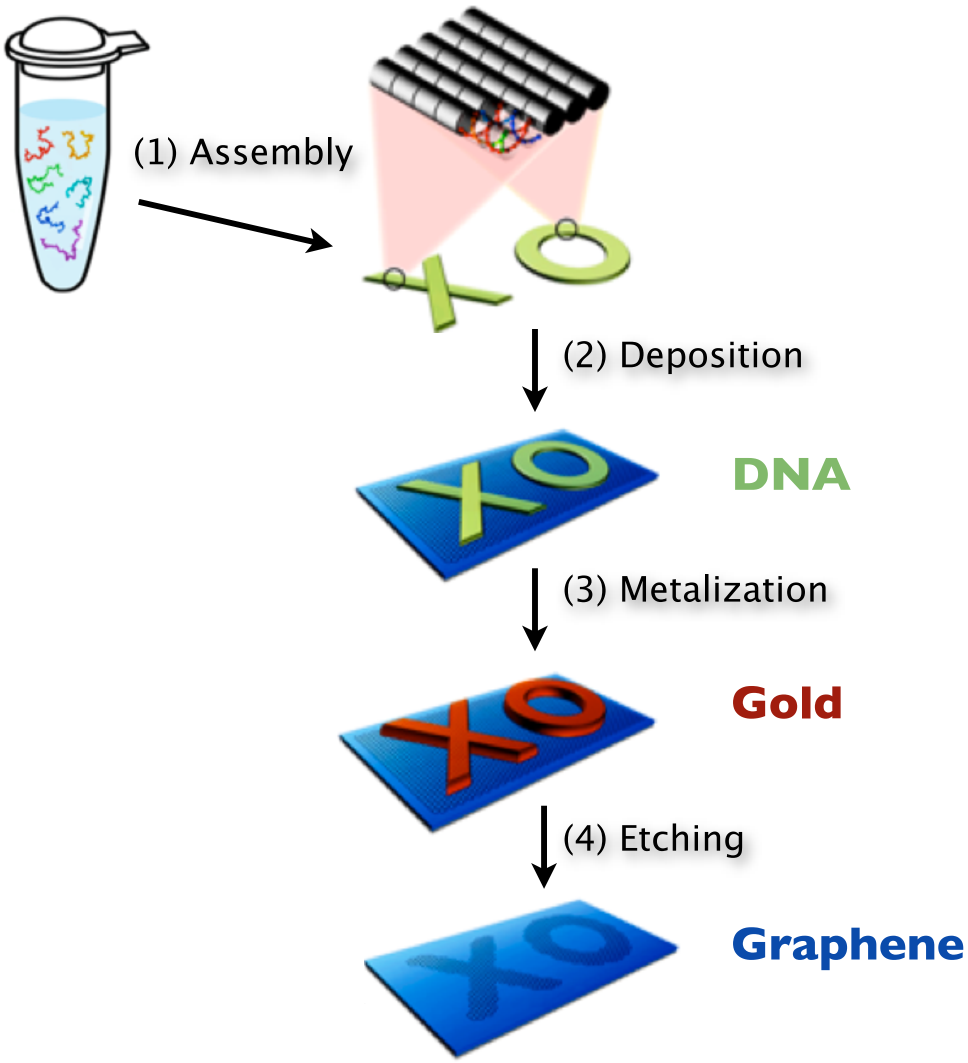
Shih Laboratory

DANA-FARBER
CANCER INSTITUTE

WYSS INSTITUTE

HARVARD MEDICAL SCHOOL

Etching graphene with metalized DNA masks



(1) Assembly

(2) Deposition

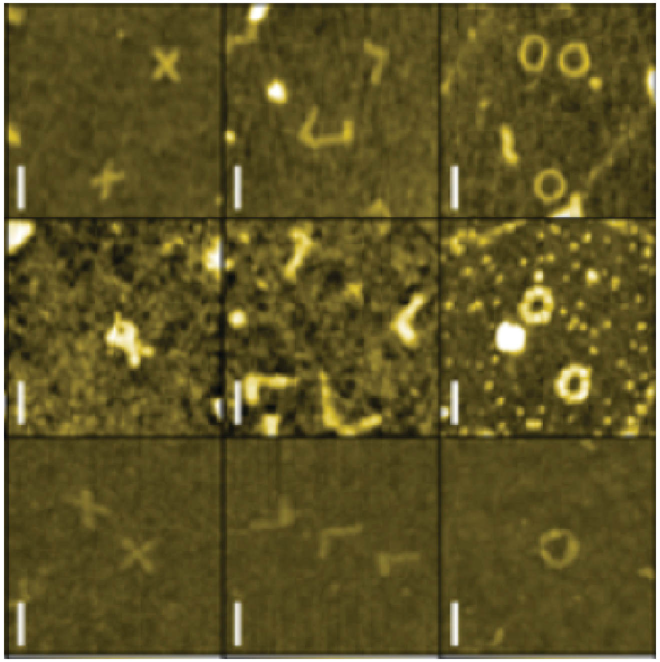
DNA

(3) Metalization

Gold

(4) Etching

Graphene



Scale bars: 100 nm

Jin, Sun, Ke, Shih, Paulus, Wang, Mu, Yin* & Strano*. **Nature Communications**. 4:1663 (2013)

Grand Challenges Summary

- Theoretical and Modeling Tools Across Length and Time Scales
- Engage MGI to accelerate the development of dynamic self-assembly of materials and the harnessing of biology for synthesis and fabrication
- Design materials that will form 3D self-assembling functional objects with chemistry that mimics the fidelity of Watson-Crick pairing: *a non-DNA DNA*
- Develop bioactive materials for regenerative medicine: multifunctional self-assembling stents, hierarchical structures that reverse cardiovascular disease, materials that empower cells to cure neurodegenerative diseases and stroke
- Materials that control functions of living systems or viceversa
- Develop strategies to obtain chemically sequenced polymers
- Develop strategies to create emergent properties in materials: self-replication of structures to evolve optimized functions, e.g., strategies for positive and negative feedback loops
- Development of tools for non-destructive structural characterization of biomaterials at varying scales to discover links to function
- Could MGI help with "D" strategies in R&D of Biomaterials given the weakness of true innovation in large industries: the dark ages of science and innovation by industry at the beginning of the 21st century