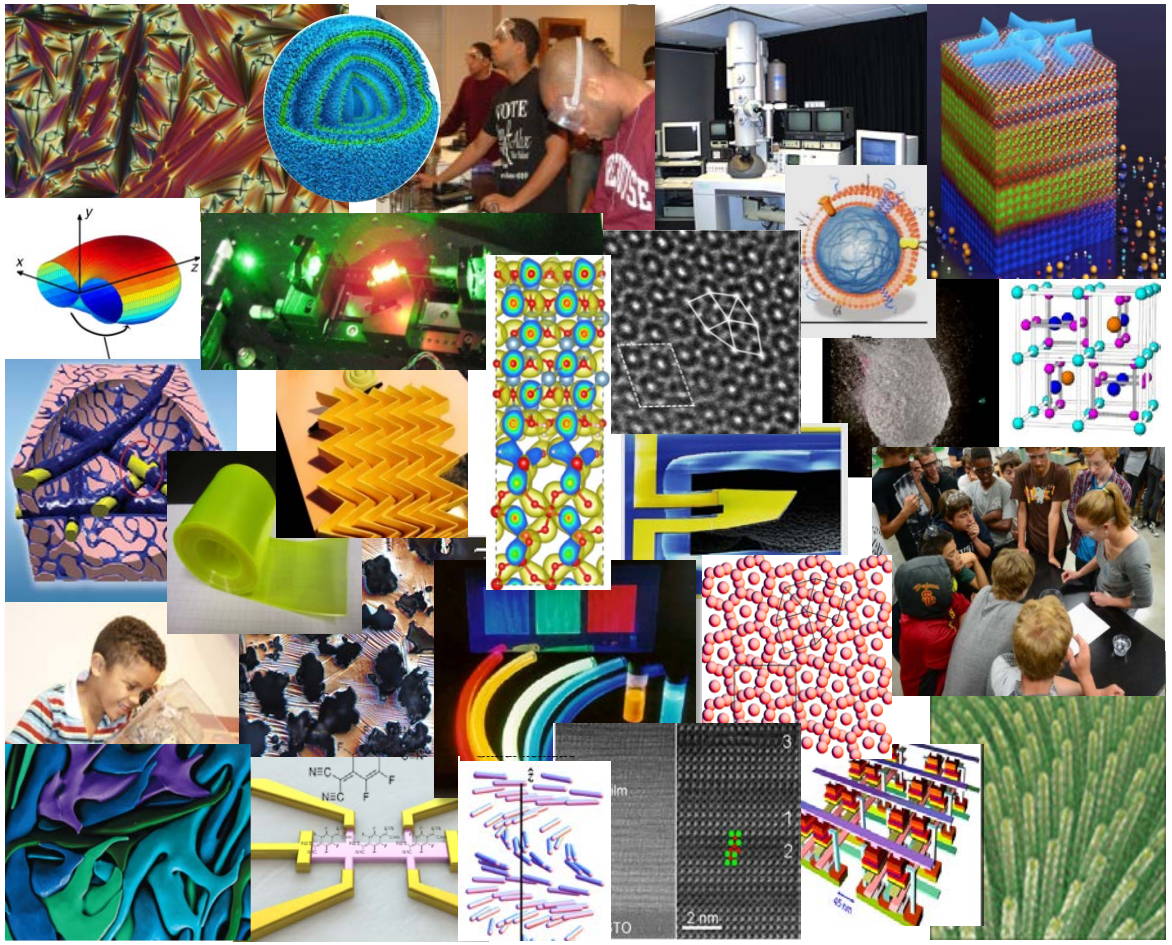
National Science Foundation-CMP/DMR

MPS-AC May 2019 Meeting
Synthetic Biology & BioMaterials



Germano Iannacchione

Division of Materials Research, National Science Foundation

Synthetic Biology: Brief History

Term first coined by Stéphane Leduc (*Théorie physico-chimique de la vie et générations spontanées* - 1910 and *La Biologie Synthétique* - 1912)

1970s-80s: Discovery of DNA structure – genetic engineering (1st synthetic human insulin in 1978: *Humulin*)

1990s: advances in microscopy and microfluidics = visualization and control

2000s: advent of synthetic biological circuits (E.coli)

Elowitz MB, Leibler S (January 2000). "A synthetic oscillatory network of transcriptional regulators". Nature. 403 (6767): 335–8. doi:10.1038/35002125.
Gardner TS, Cantor CR, Collins JJ (January 2000). "Construction of a genetic toggle switch in Escherichia coli". Nature. 403 (6767): 339–42. doi:10.1038/35002131

2019: 1st artificial bacterial genome (Caulobacter ethensis-2.0)

Venetz, Jonathan E.; et al. (1 April 2019). "Chemical synthesis rewriting of a bacterial genome to achieve design flexibility and biological functionality". Proceedings of the National Academy of Sciences of the United States of America. doi:10.1073/pnas.1818259116

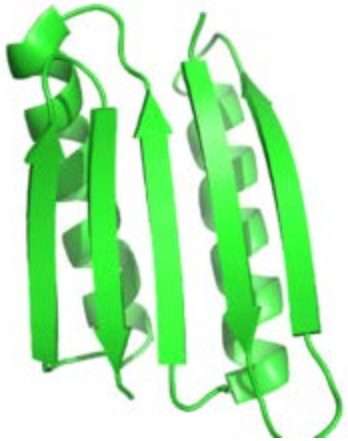
Synthetic Biology: Current

Enabling Technologies:

- DNA and gene synthesis
- Sequencing
- Microfluidics
- Modularity
- **Modeling (DATA)**
- Synthetic transcription factors
- Microscopy

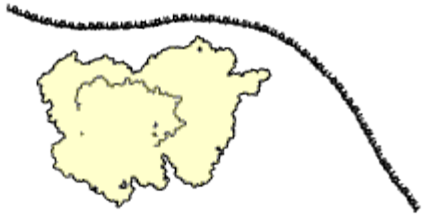
Applications:

- Biological computers
- Biosensors
- Cell transformation
- Designed biomolecules
- **Space exploration / Astrobiology**
- Synthetic life
- Drug delivery platforms



Top7 protein was one of the first proteins designed for a fold not seen in nature

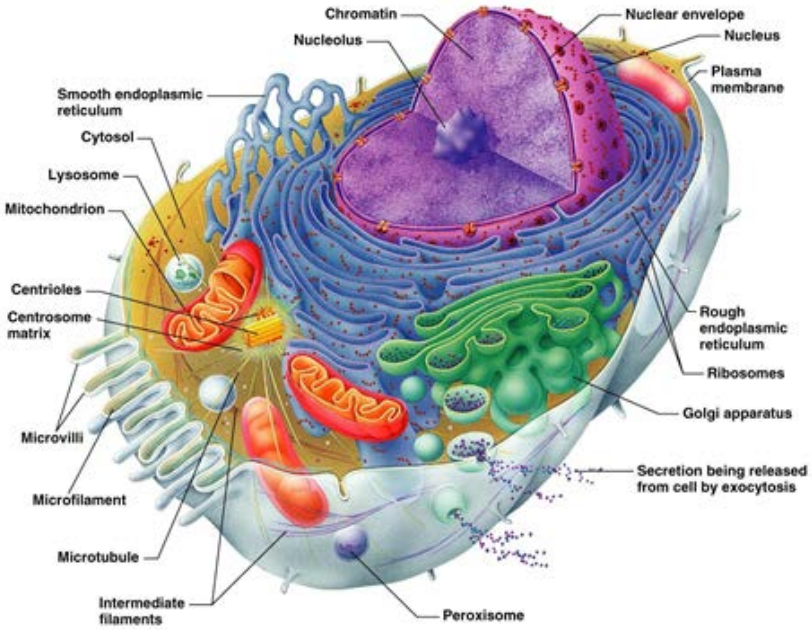
Kuhlman B, Dantas G, Ireton GC, Varani G, Stoddard BL, Baker D (November 2003). "Design of a novel globular protein fold with atomic-level accuracy". Science. 302 (5649): 1364–8.



Ribosome = bio-machine

https://en.wikipedia.org/wiki/Synthetic_biology

Synthetic Biology: Frontier



The problem of **chirality**

Everything right-handed:

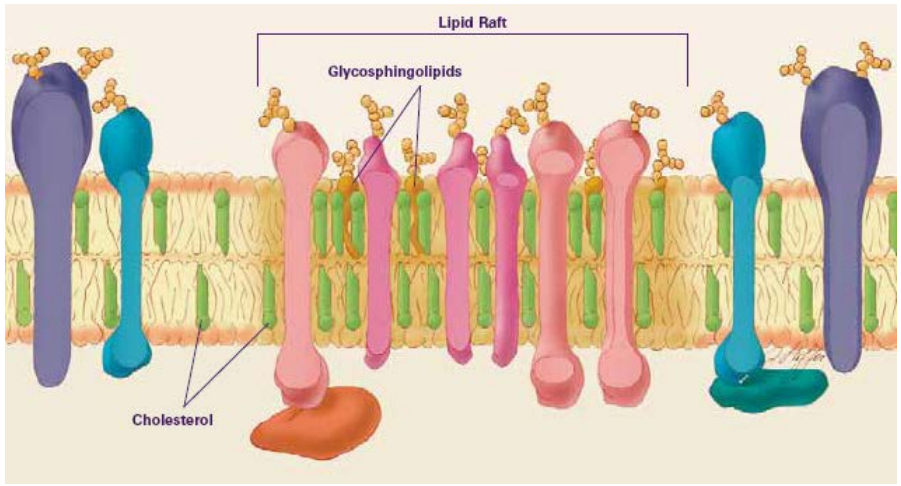
- Why?
- Origin?

Everything has a mirror:
Boot-up a left-handed cell?

~35,000 lipids (fats)

- Why so many?
- Role at interfaces?

Artificial lipids?



Biomaterials: Classical

Traditional research on materials that are
from biology or **for biology**

Multidisciplinary (polymers, ceramics, metals, composites, etc.
(a sub-area of Soft-Condensed Matter Physics)

As a science ~ 50 years old.

FEATURES:
- Bioactivity / Compatibility – inorganic materials
- Self-assembly
- Structural Hierarchy
- Applications Driven
- Biopolymers (keratin - protein, chitin/cellulose - polysaccharide)
- Biomotors (kinesin)

Problem / Application Driven

National Science Foundation-CMP/DMR

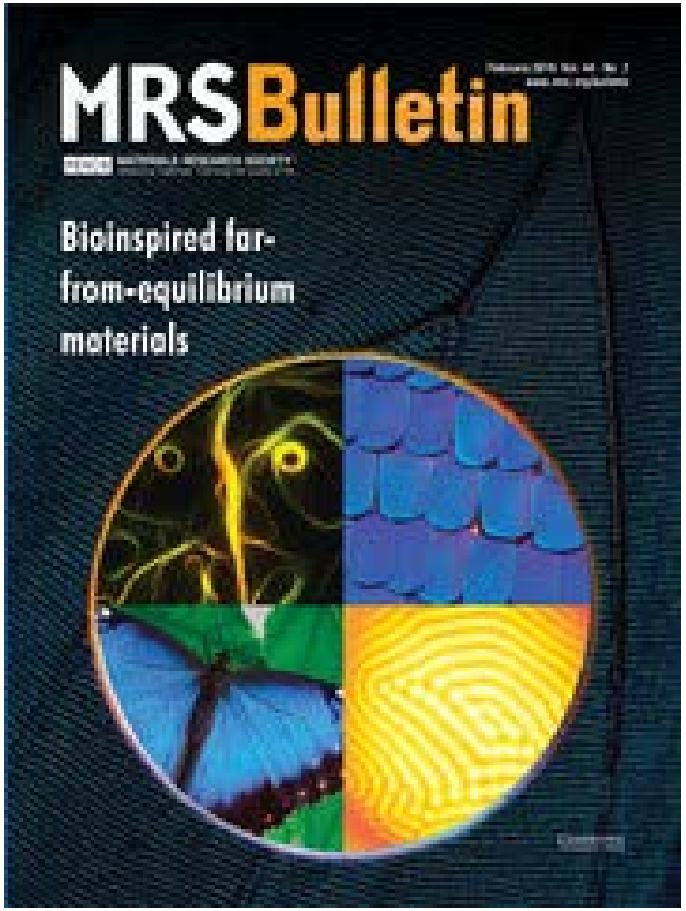
Biomaterials: Frontiers

Profound fundamental questions:

- Biomimicry (concrete mimicking seashells; on-demand biocomposites)
- Far-from-equilibrium Thermodynamics
- Information and Complexity
- Active Matter and Emergence
- *Biomachines that never were*

Traditional materials science explores uniform, equilibrated static condensed-matter structures.

Highly structured dynamical states that are out of equilibrium are ubiquitous in biology.



Bioinspired Far-From-Equilibrium Materials
Volume 44 - Issue 2 - February 2019

NSF's 10 Big Ideas: URoL

GOALS:

- To enable discoveries that will allow us to better understand biological interactions and identify *causal, predictive relationships across all scales* – so-called "rules" for how life functions
- To develop new *research tools and infrastructure*
- To train the next generation of researchers to approach scientific inquiry in a way that *crosses scales and scientific disciplines*
- To foster *collaboration and convergent research* across the Foundation

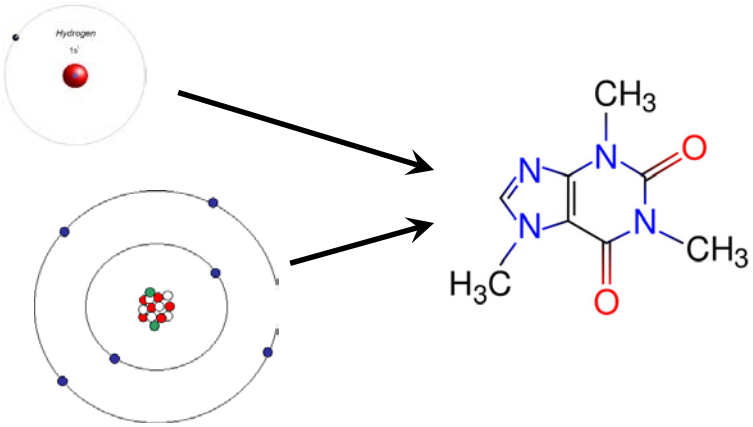
NSF's 10 Big Ideas: URoL

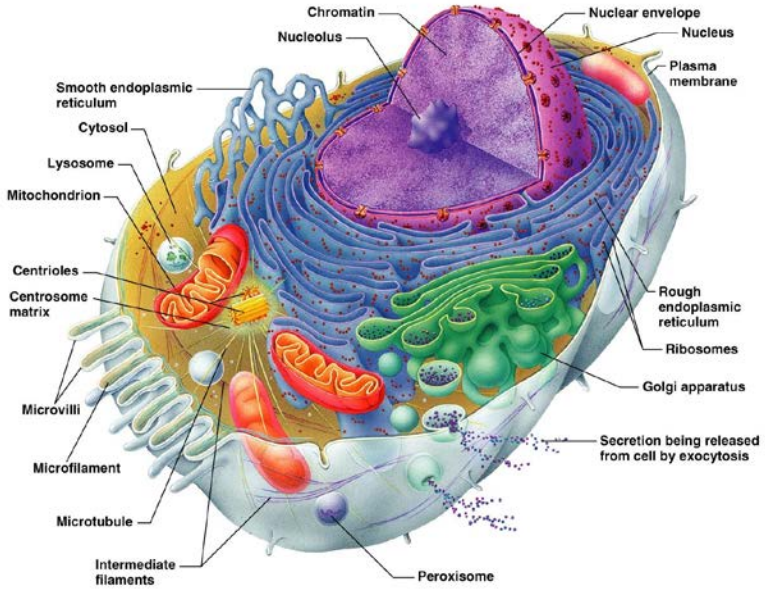
SOME CHARACTERISTICS:

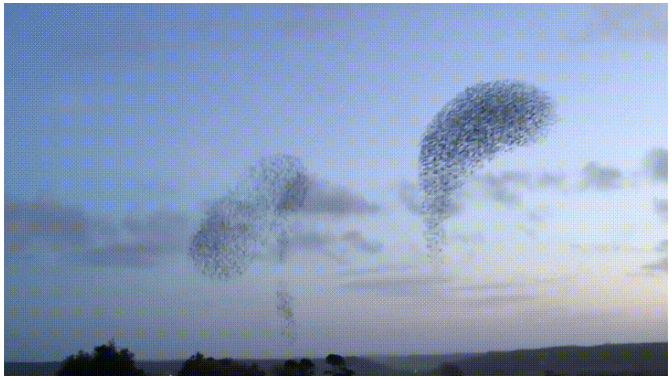
- Addresses a *fundamental question* in the life sciences
- *Crosses vastly different scales* (spatial, temporal, levels of biological organization, and complexity)
- Generates results that will be *broadly generalizable* beyond the system under investigation, so that a rule can be formulated
- Enables the *forecasting/prediction of change* in a biological system

NSF's 10 Big Ideas: URoL

WHY?







National Science Foundation-CMP/DMR

NSF's 10 Big Ideas: URoL

CURRENT:

URoL: Epigenetics (NSF 18-600) $15M

- To enable innovative research and to promote *multidisciplinary* education and workforce training in the broad area of epigenetics.
- BIO, ENG, MPS
- Proposals under review

URoL: Building a Synthetic Cell (NSF 18-599) $15M

- *Ideas Lab* to facilitate the generation and execution of innovative *multidisciplinary* research projects aimed at designing, fabricating, and validating synthetic cells that express specified phenotypes
- BIO, ENG, MPS
- Proposals under review

Planning for FY20 to FY23 are underway

MPS Activities

PHYSICS: PHYSICS OF LIVING SYSTEMS (PoLS)
Focus on fundamental physical processes that living systems utilize to perform their functions in dynamic and diverse environments.

CHEMISTRY: CHEMISTRY OF LIFE PROCESSES (CLP)
Focus on research at the interface of chemistry and biology, understanding of the molecular underpinnings of life processes.

MATHEMATICS: Joint Initiatives – Harnessing the Data Rev. (HDR)

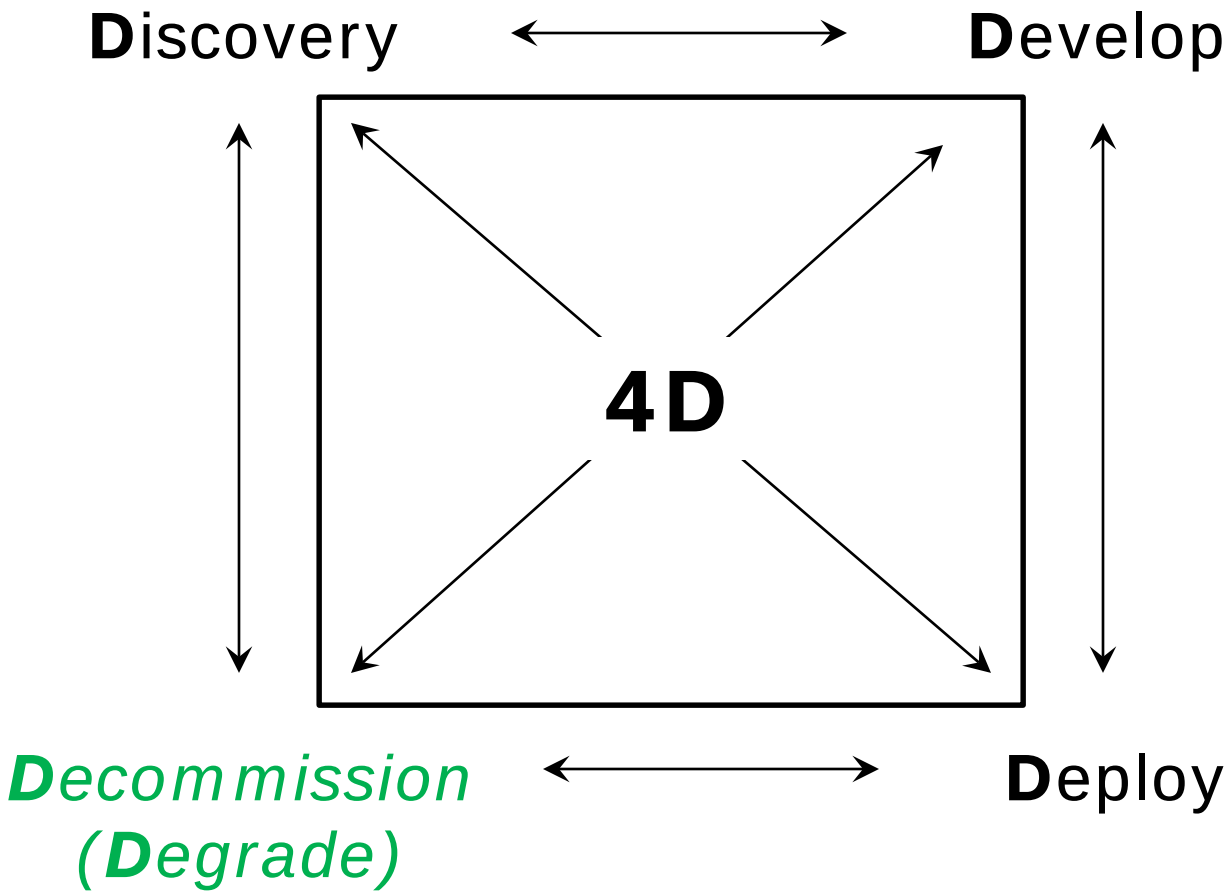
- Initiative to Support Research at the Interface of the Biological and Mathematical Sciences (DMS/NIGMS)
- Initiative on Generalizable Data Science Methods for Biomedical Research (DMS/NLM)

MATERIALS RESEARCH:

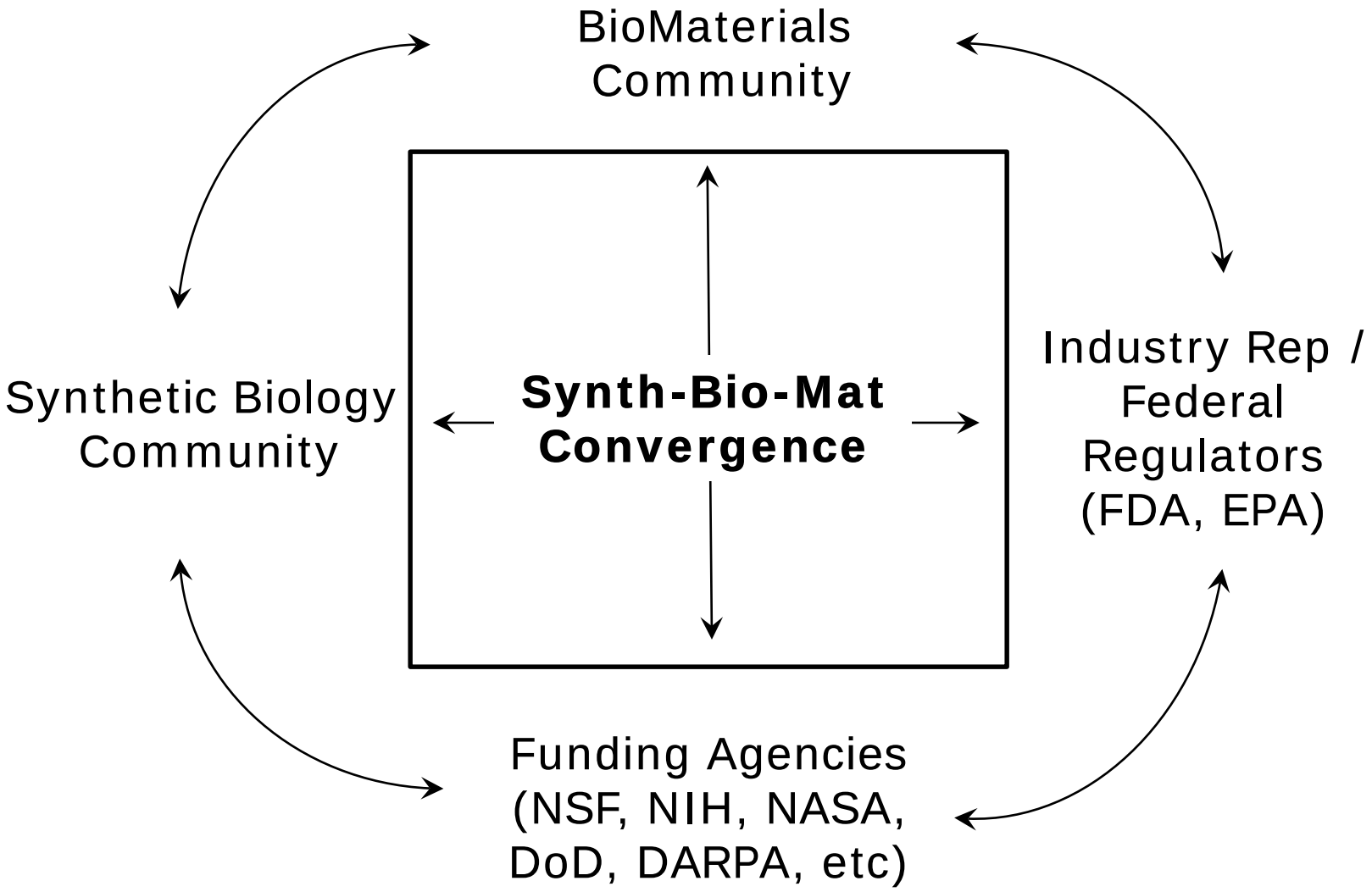
BIOMATERIALS (BMAT) + SOFT (CMP & CMMT)

SQUARE-TABLE (**ST**) Concept

Research Paradigm



Square-Table Concept



Square-Table Concept

MATERIALS RESEARCH: The palette that makes our knowledge real.

NSF (BMAT, CMP, CBET, MCB, PHY, CHE); NIH-NIBIB; NIST; FDA; NASA; DARPA; AFOSR

SQUARE-TABLE (**ST**): bridging *Synthetic Biology* and *Biomaterials*

- ST1-2018: Experimental format; *Living Interfaces*
  - Discussion breakout around guiding questions (*real square tables*)
  - Report back to entire group
  - Repeat
  - Mix/Remix of Researchers, Program Directors, Regulators, etc.
  - Final half-day produce draft of outcomes
  - Encourage self-assembly!
- Follow up **ST** meetings thru MULTIPLIER support:
  - ST2-2019: *Programmable Interfaces*
  - ST3-2019: Convergence of existing major efforts (Centers and Institutes) to develop *Research Collaborative Networks*

National Science Foundation-CMP/DMR

ST1-2018: LIVING INTERFACES

ST1-2018: GENERAL OUTCOMES

- Emulating nature for new materials with unique functionalities
- Controlling the organization of matter at all scales
- Designing the interface between biomaterials and biological systems to modulate responses
- Relying on inherent biological mechanisms
- Connecting to non-biological mechanisms
- Improved “gold” standard
- New experimental and theoretical techniques

ST1-2018: SPECIFIC OUTCOMES

- **New Classes of Functions**
  - Materials that Communicate
  - Non-Equilibrium Materials
  - Materials that Evolve

- **New / Augmented Compositions**
  - Reinvented Composites to include cells
  - Reinvented Feedstock to include renewables

- **Potential "Moon-Shots"**
  - Self-healing/Restructuring Materials
  - Materials that Incorporate Living Matter
  - Materials in the Body
  - Bio-Reference Materials

- **Blue-Print / Road-Map Recommendations**

- **Review Articles / <u>Whitepapers</u> (under review)**

MPS-AC SynthBioMat Subcommittee

NEED: The wide diversity of Perspectives, Disciplines, Efforts is extremely valuable BUT what is the Big-Picture?

Internally: Broad MPS efforts – Who sees it all?

Externally: Cross-NSF activities – How best to coordinate?

SOLUTION:
A subcommittee of MPS-AC focused on Synthetic Biology & Biomaterials could address both the internal and external need. It would provide a focal point … *these ideas live in people's heads not on hard-drives.*

STRATEGY:
The SynthBioMat Subcommittee, composed of a broad representation of the MPS-AC, would be tasked to review the current activities in this area and help advise on opportunities for MPS.