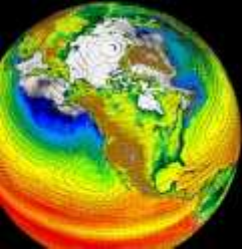
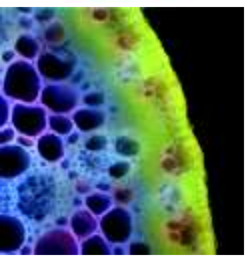



Workshop Report: Genome Engineering for Material Synthesis

Caroline Ajo-Franklin, Brian Fox, Mike Jewett, Huimin Zhao

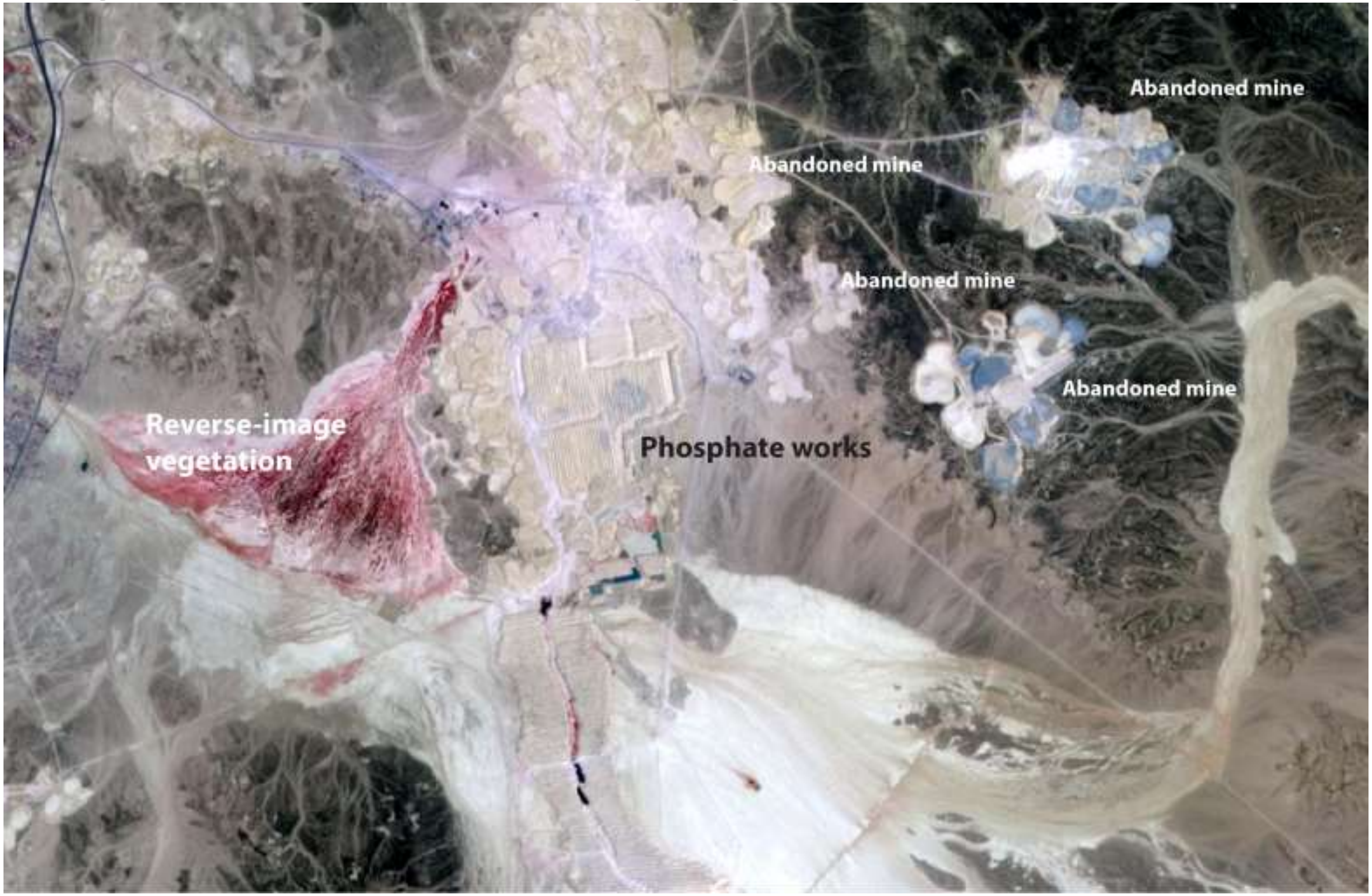
BERAC Spring Meeting

April 26, 2019

By 2050, the demand for materials will grow by 50-100%

The crisis of aging U.S. infrastructure will also drive need for materials

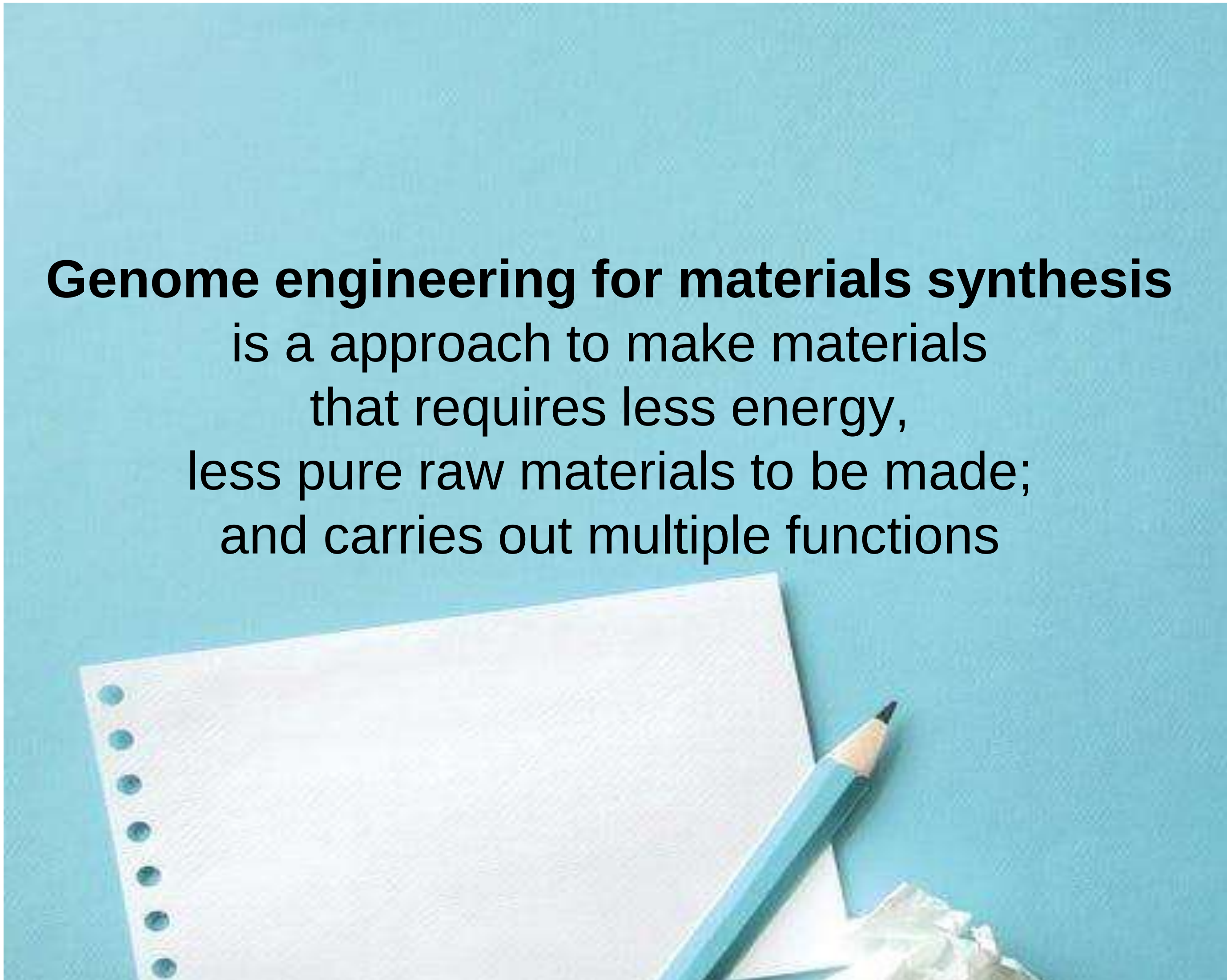
Extracting raw minerals in an environmentally benign way is challenging



https://visibleearth.nasa.gov/view.php?id=8824

Vaccari & Strigul / Chemosphere 84 (2011) 792

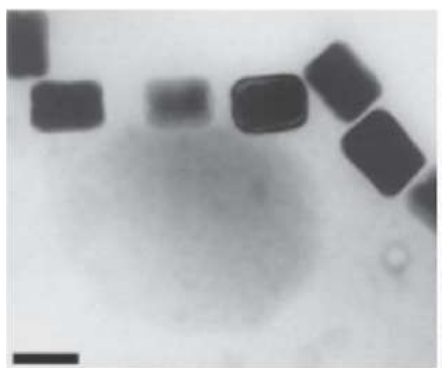
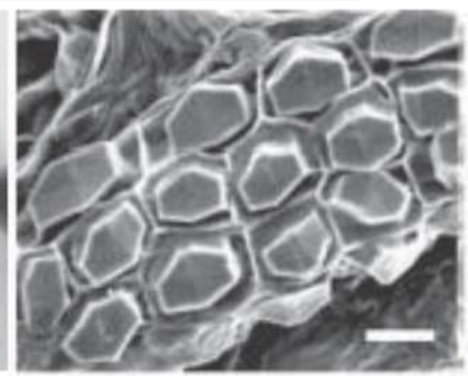
The scientific opportunity



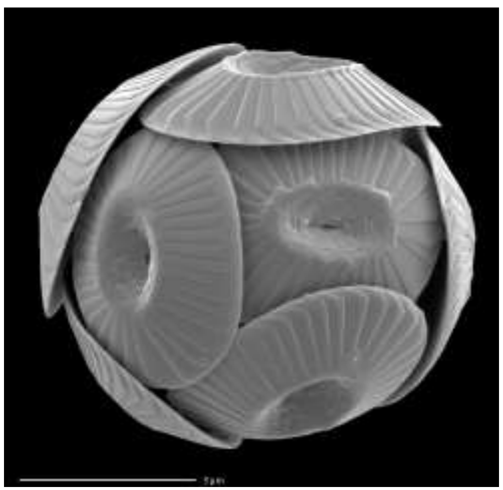
Genome engineering for materials synthesis
is a approach to make materials
that requires less energy,
less pure raw materials to be made;
and carries out multiple functions

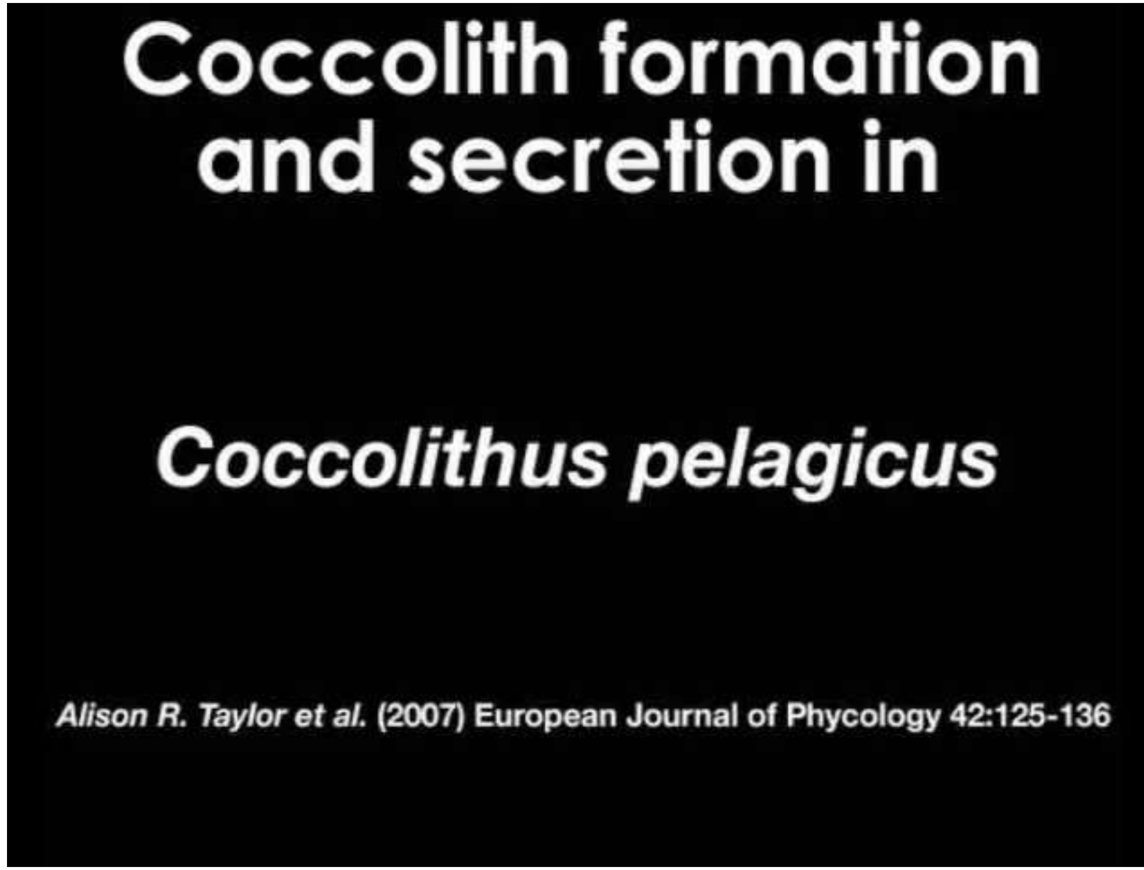
Naturally-occurring genome-encoded materials have the properties we seek



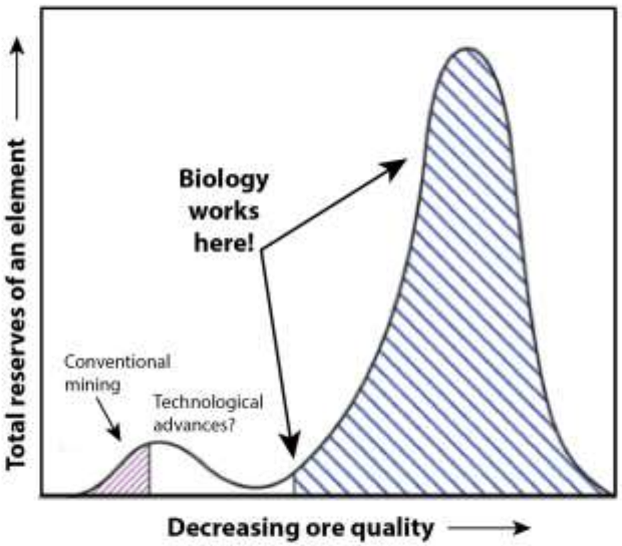
Biological systems synthesize materials with little energy input

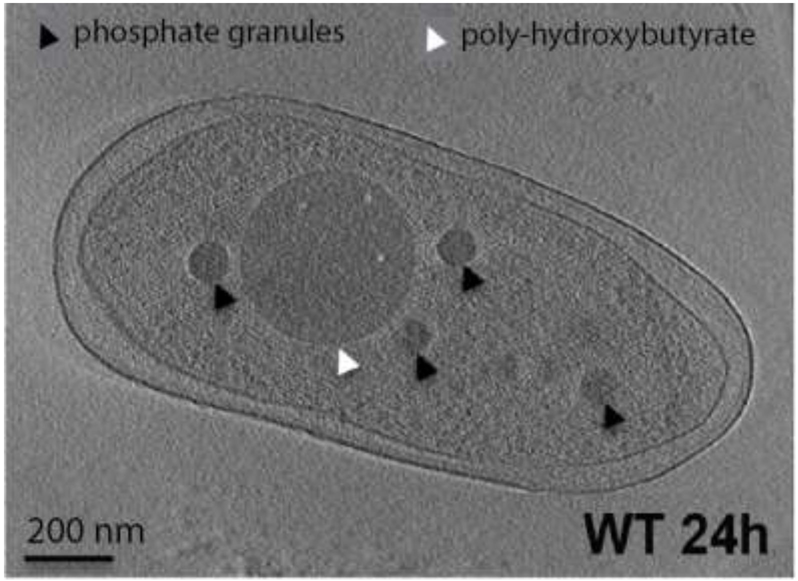




Taylor, et al. European Journal of Phycology. 42:125-136 (2007).

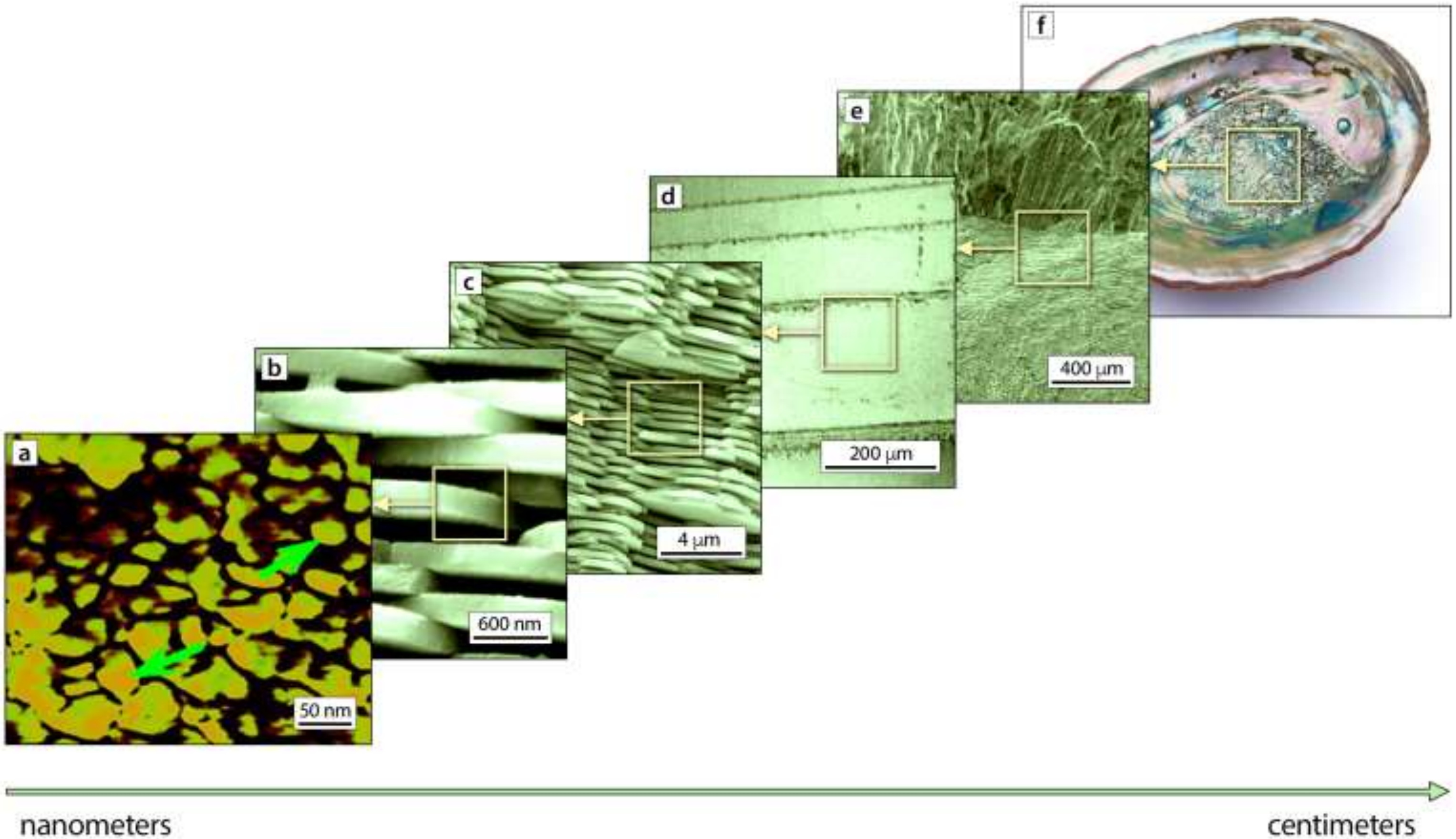
Biological systems scavenge raw materials from dilute sources





A.M. Diederen, TNO Defence, Security and Safety, http://astro1.panet.utoledo.edu/~khare/sustainability/dierden-paper-1.html and modified with permission; Racki, L. R., Tocheva, E. I., 272 Dieterle, M. G., Sullivan, M. C., Jensen, G. J., and Newman, D. K. (2017) Proc Natl Acad Sci 274 U S A 114, E2440-E2449

Biological systems make multifunctional materials using hierarchical structures



Adapted from: A. Meyers, et al. Journal of the Mechanical Behavior of Biomedical Materials 2011, 4:626-657.

Technological advancements that enable this opportunity now

- **New DNA technologies** have radically improved the speed, throughput, and accuracy of DNA sequencing leading to discovery of new organisms;

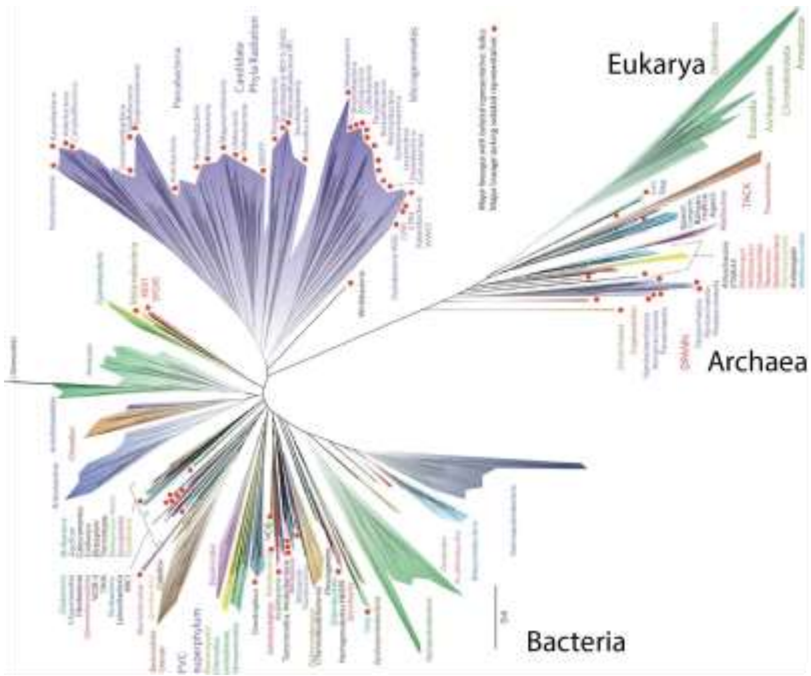
- **Gene synthesis** supports combinatorial assemblies of genes and regulatory circuits with optimized codon usage for specific host organisms;

- **CRISPR-based technologies** transform our ability to edit the genomes of organisms in simple, precise, fast, and scalable ways;

- New **quantitative and scalable measurement technologies** for bioprospecting, single cell -omics, multi-modal spectroscopy, microscopy and crystallography; and

- **Tools for *in-vivo* characterization** have enabled discoveries and mechanistic insights that were previously unattainable

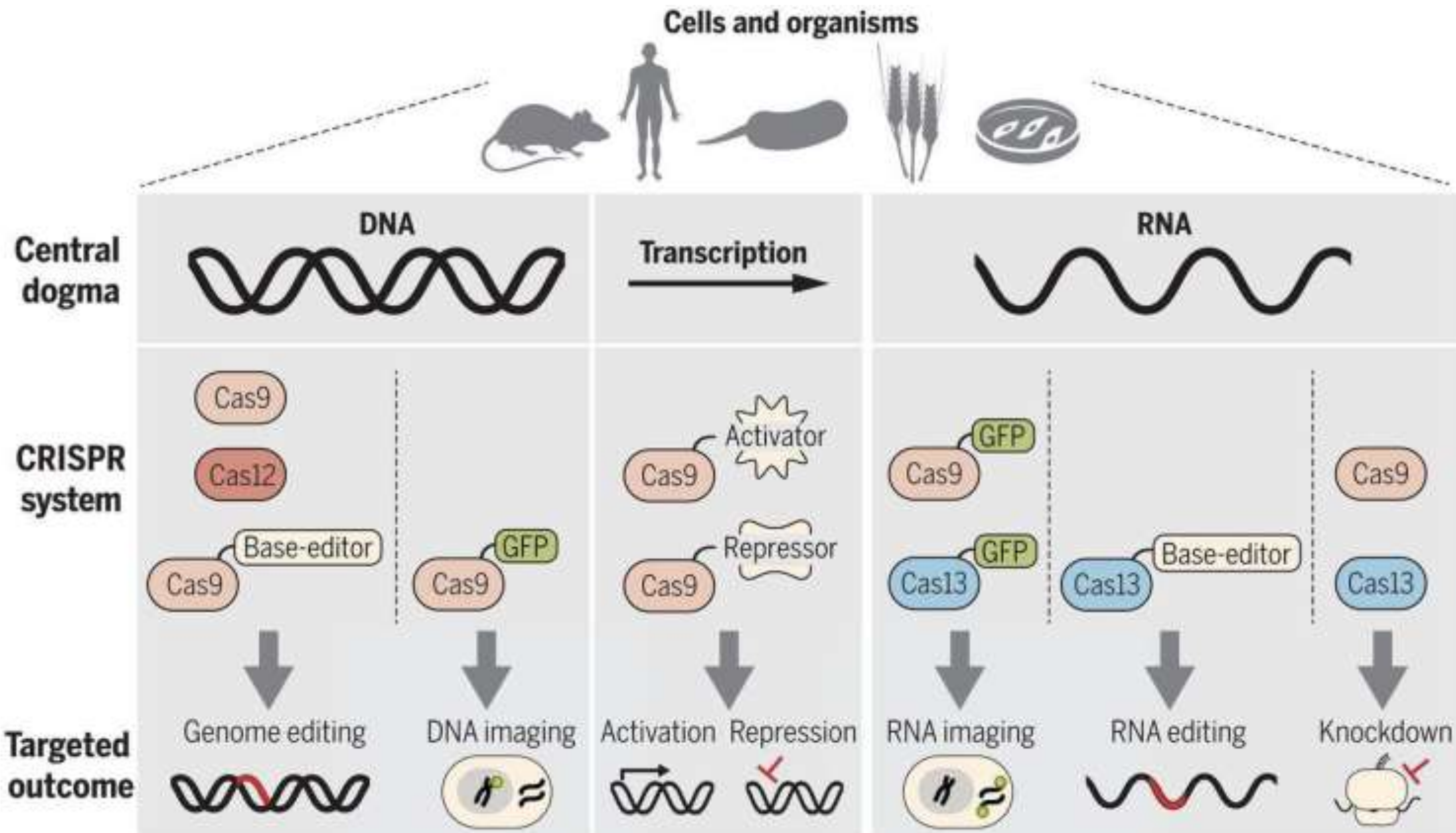
New technologies have radically improved DNA sequencing & synthesis



Hug, L. A., et al. 2016. “A New View of the Tree of Life,” *Nature Microbiology* **1**, 16048 231 (CC BY 4.0)

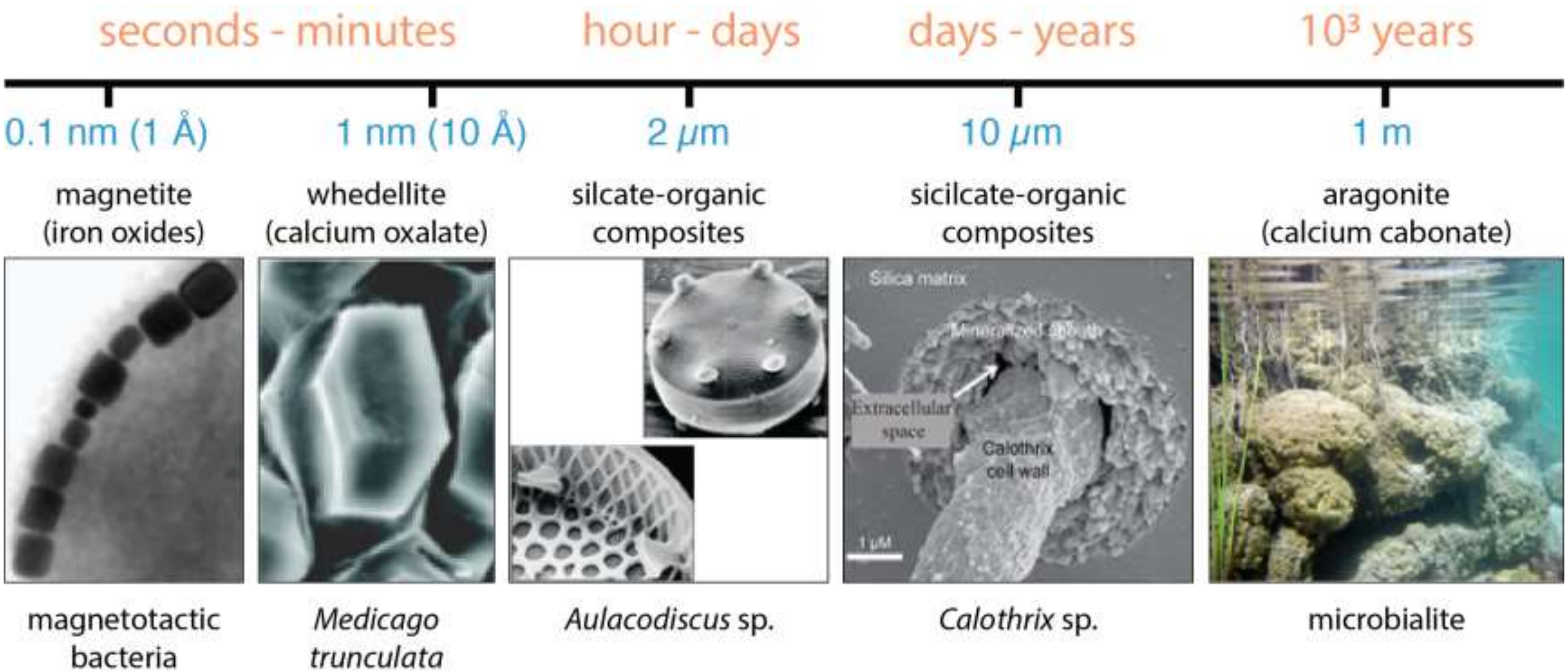
Bioeconomy Capital, www.bioeconomycapital.com/bioeconomy-dashboard/ (CC BY-ND 4.0).

Simple, precise, fast and scalable genome editing is now possible using CRISPR

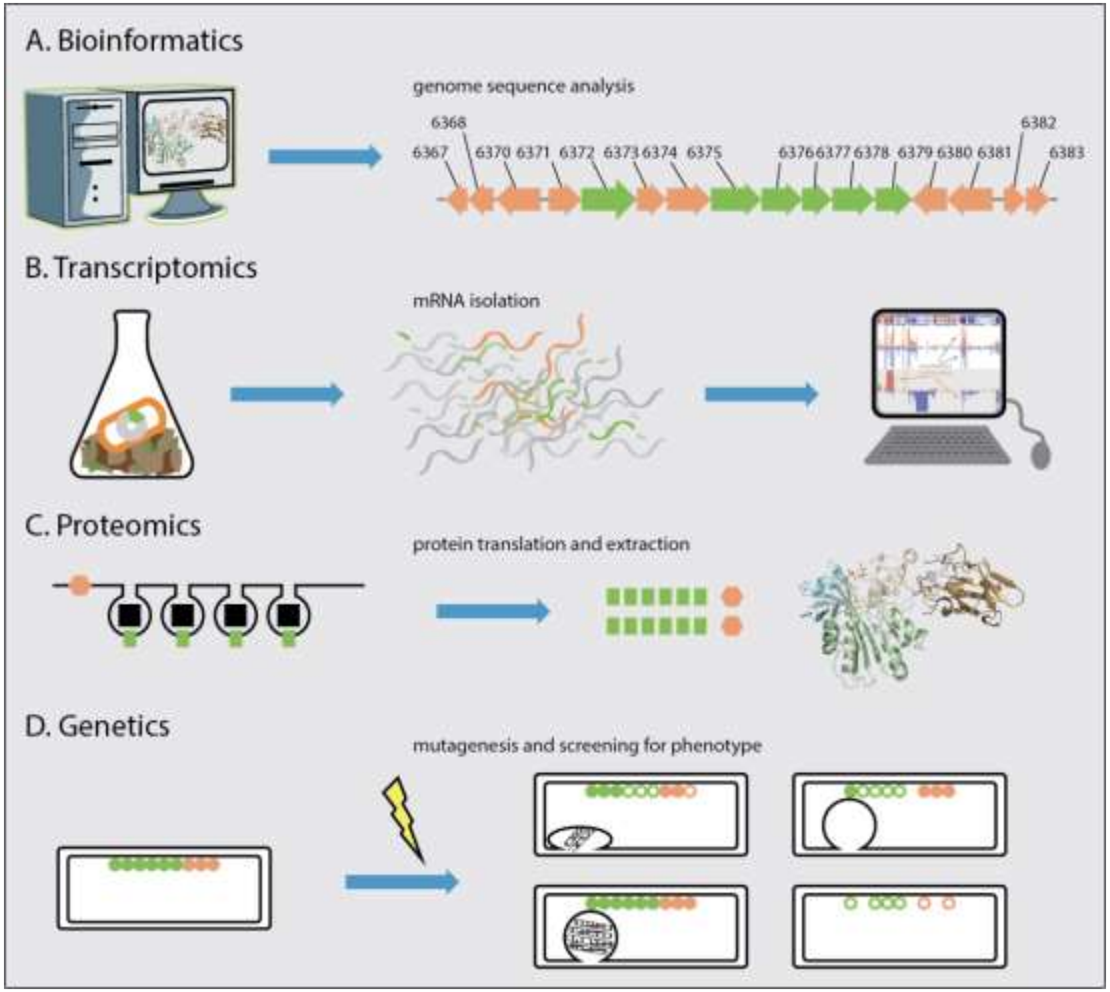


Knott, G. J., and J. A. Doudna. 2018. “CRISPR-Cas Guides the Future of Genetic Engineering, Science 189 361(6405), 866–69.

New advances allow us to study biology across scale and time



New approaches allow us to identify organisms, genes and proteins



Summary: Biological knowledge gaps

1. **Full taxonomy of species** capable of producing biominerals;

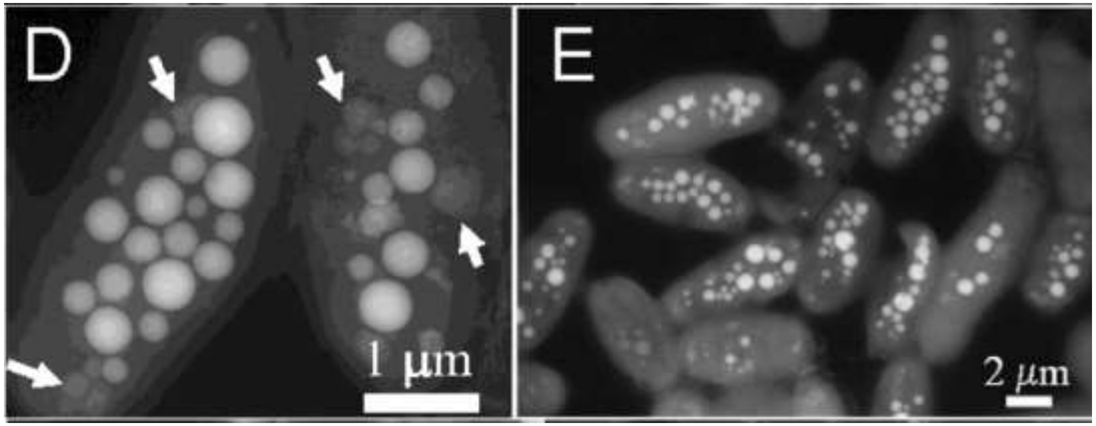
2. **Catalog of genes and regulatory networks** controlling transport, modification and synthesis of inorganic biomaterials;

3. **Intracellular metabolic processes** governing the transport, modification, assembly, and/or storage of inorganic biomaterials;

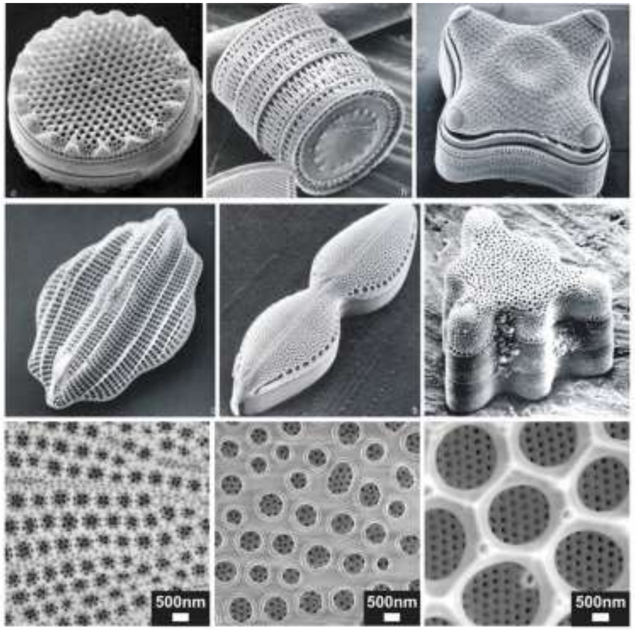
4. **Mechanisms** used by microbes and plants to acquire inorganic materials and specific inorganic biominerals;

5. **Engineered organisms and pathways** resulting in new inorganic materials.

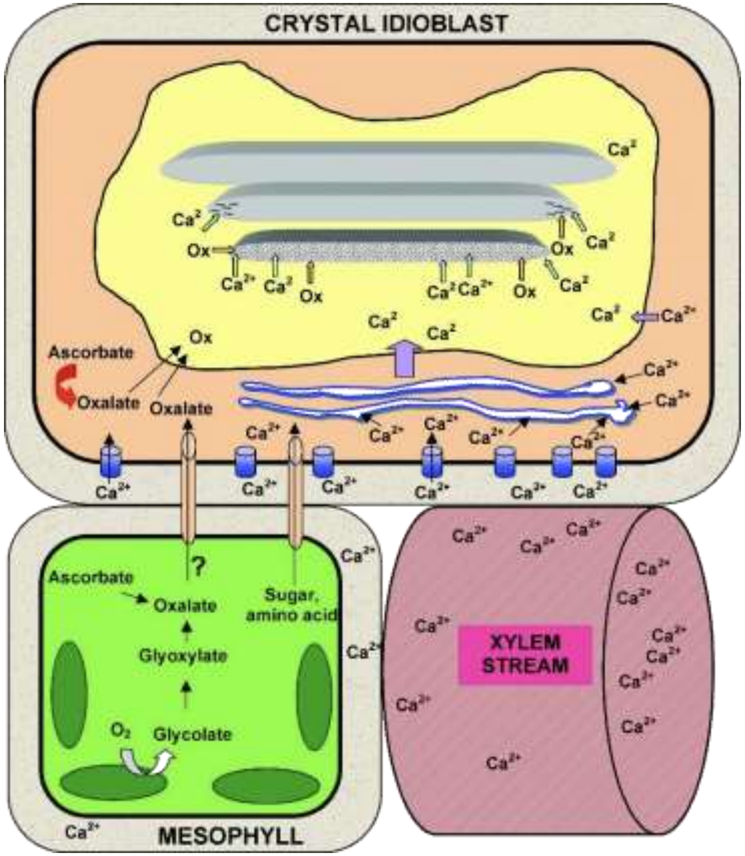
Biological knowledge gaps: What is made by who?

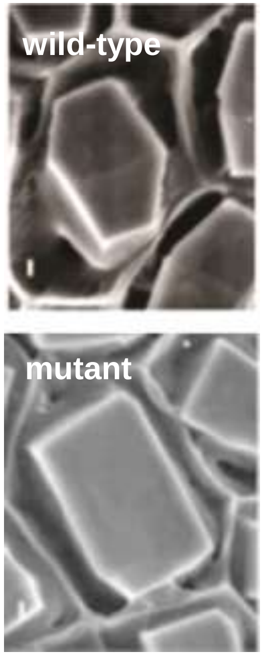


Benzerara, K. *et al.* Intracellular Ca-carbonate biomineralization is widespread in cyanobacteria. *Proc. Natl. Acad. Sci. U. S. A.* **111**, 10933–10938 (2014).



Biological knowledge gaps: How is this made? What are the minimal requirements?





McConn, M. M. & Nakata, P. A. *Planta* **215**, 380–386 (2002).
Franceschi, V. R. & Nakata, P. A. *Annu. Rev. Plant Biol.* **56**, 41–71 (2005).

Summary: Technology needs

1. New capabilities in **cultivation, single-cell and -omics methods for discovery** of inorganic biominerals and the genetic potential underlying their synthesis;

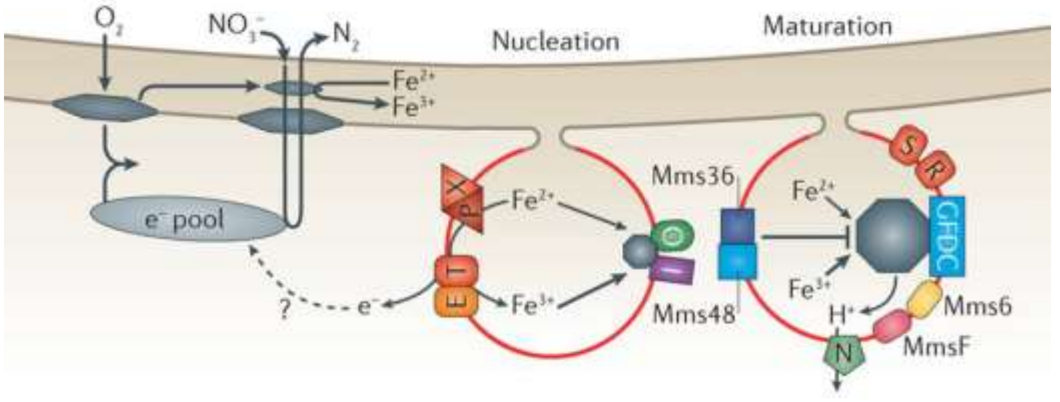
2. **Computational systems biology and biodesign tools** that provide a systems-level understanding and forward engineering of inorganic material synthesis;

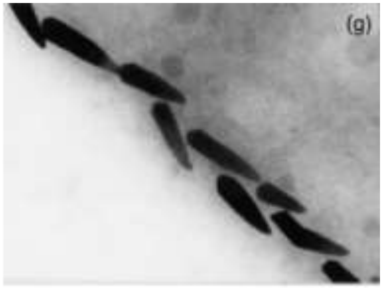
3. Capabilities to **manipulate organisms with a breadth of capabilities**, including control of transport, spatial patterning, and timing;

4. Technologies to support **high-throughput or massively parallel determinations of the function** of pathways used for inorganic synthesis; and

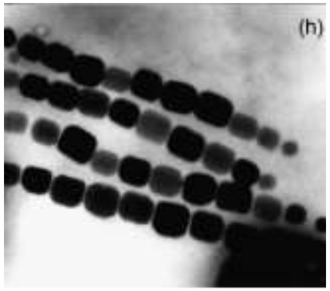
5. **Intentionally-aligned structural and functional tools** to characterize inorganic biomaterials.

We need computational tools for forward engineering



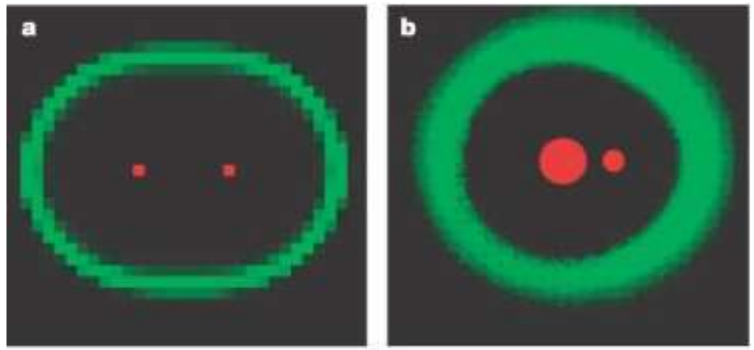


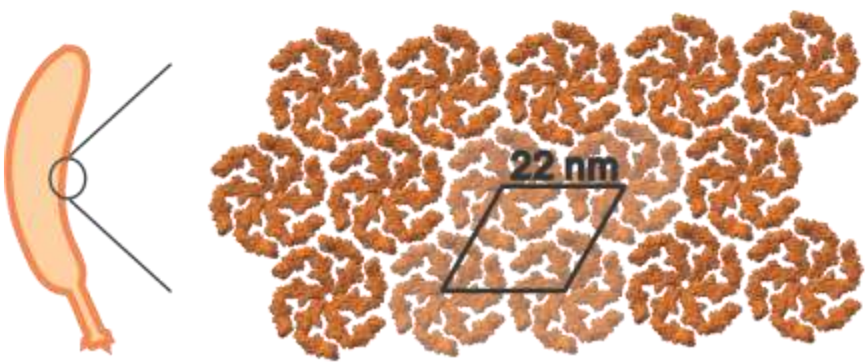
OR

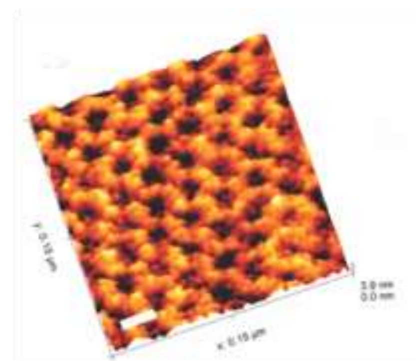


Uebe, R. & Schüler, D. *Nat. Rev. Microbiol.* **14**, 621–637 (2016).
Schüler, D. 2008. *FEMS Microbiology Reviews* **32**(4), 654–72.

We need new biosystems design capabilities in spatial patterning & transport

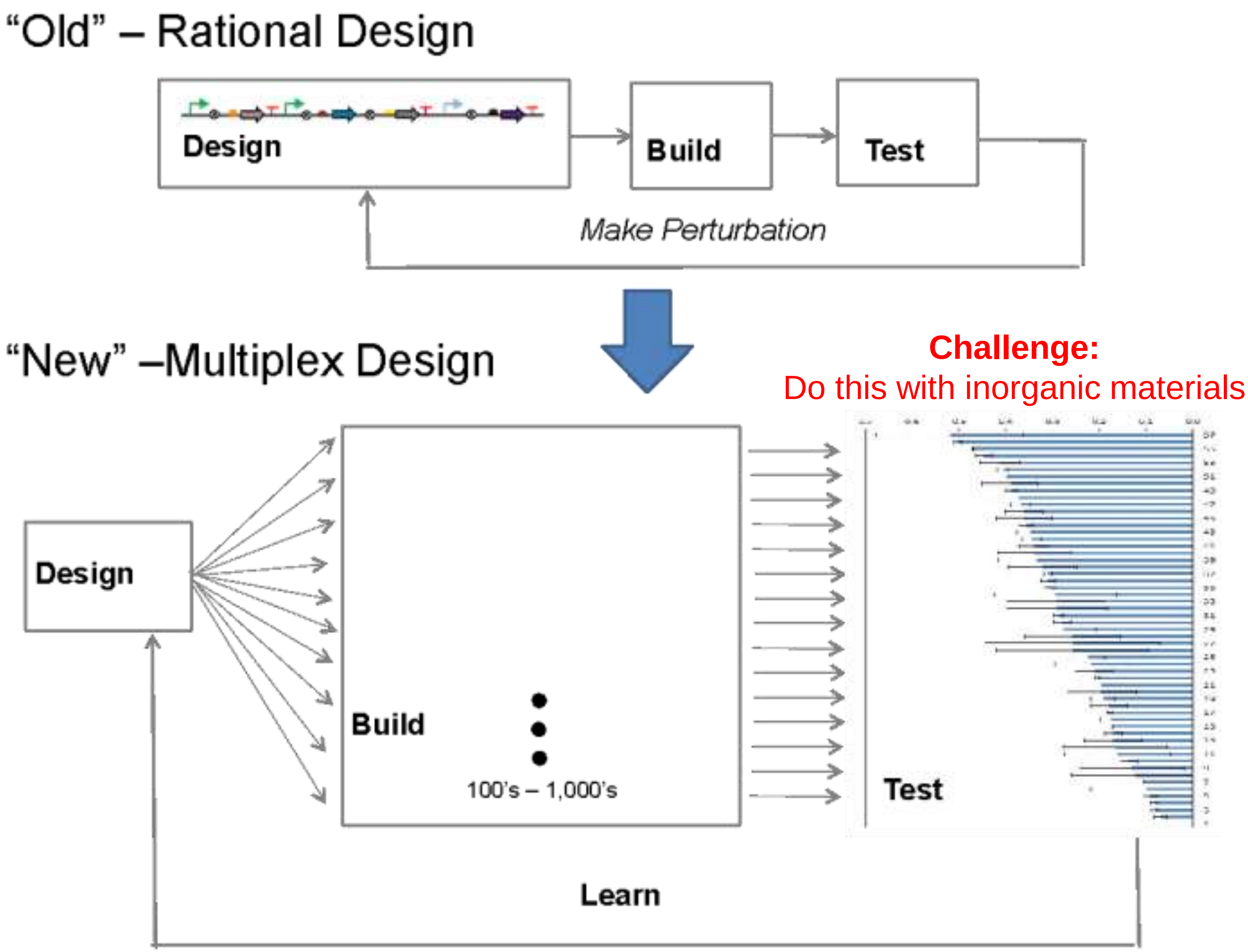




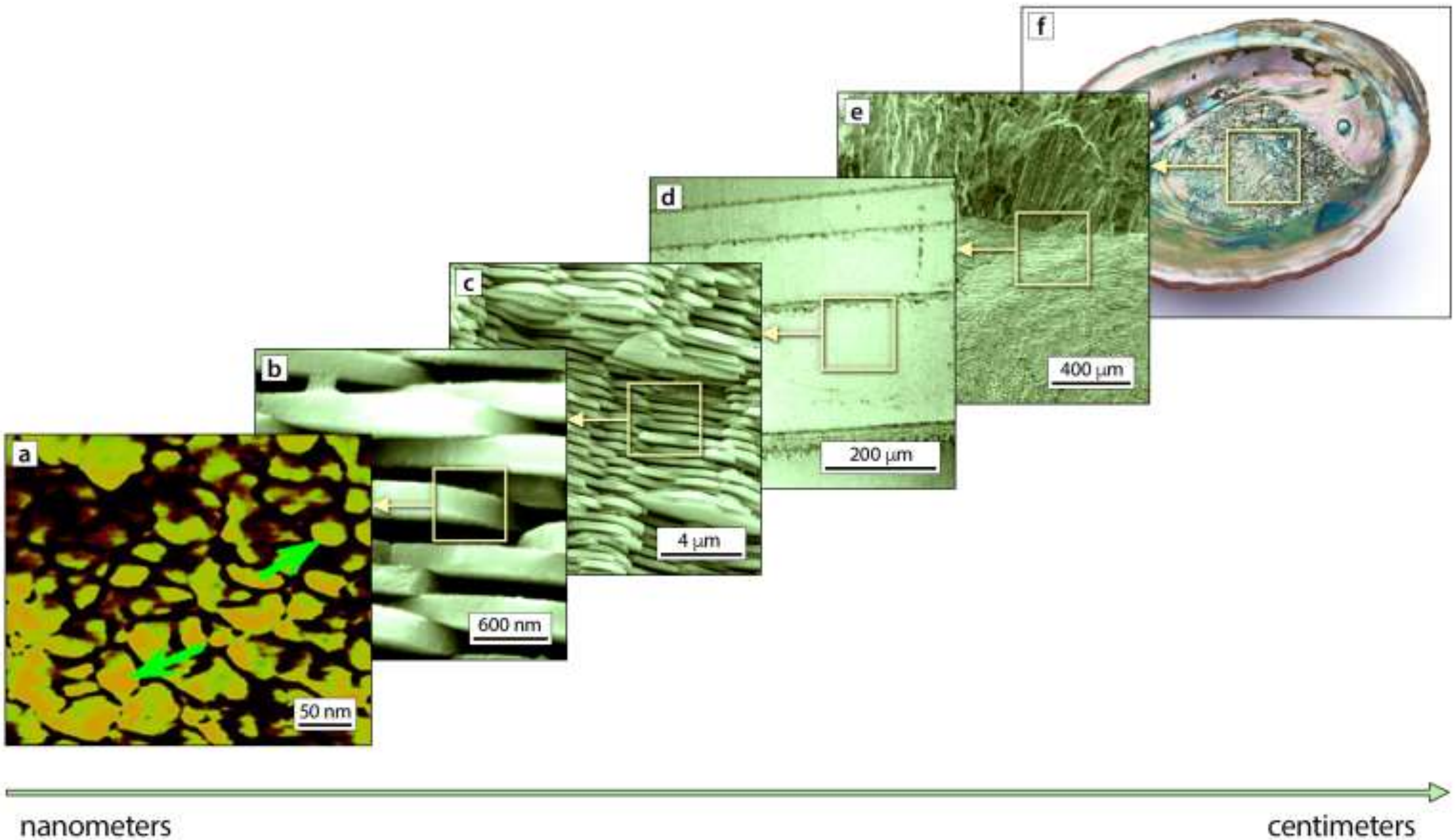


Basu, S., Gerchman, Y., Collins, C. H., Arnold, F. H. & Weiss, R. *Nature* **434**, 1130–1134 (2005).
Charrier, M., et al. 2019. *ACS Synthetic Biology* **8**(1), 181–190.

Technologies are needed to support high-throughput ‘test’ for inorganic synthesis



Intentionally-aligned imaging across scales is needed



Adapted from: A. Meyers, et al. Journal of the Mechanical Behavior of Biomedical Materials 2011, 4:626-657.

Materials that could be made

- **Sustainable versions of existing materials:**

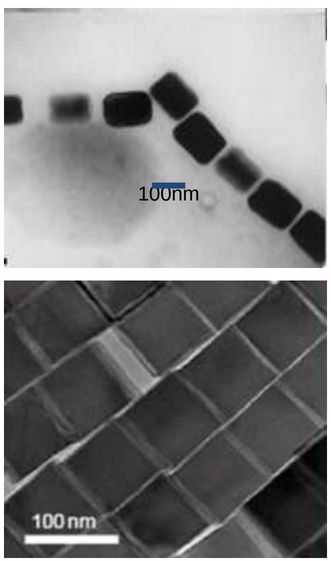
- functionalized nanoparticles
- photonic crystals and metamaterials
- lightweight-strong composite materials

- **Completely novel materials**

- Self-healing cell-inorganic composites
- Ion-specific chelators, transporters, and carrier proteins
- Novel classes of sequence-defined polymers for hybrid materials

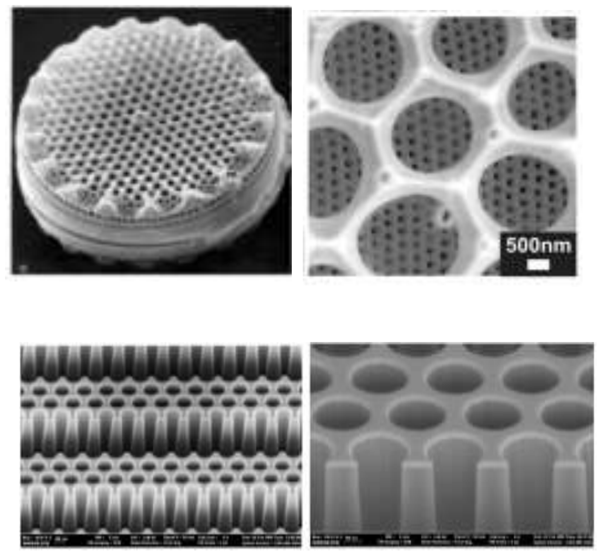
Specific examples of genome engineered materials (GEMs)

Sustainable Fe_3O_4 nanoparticles



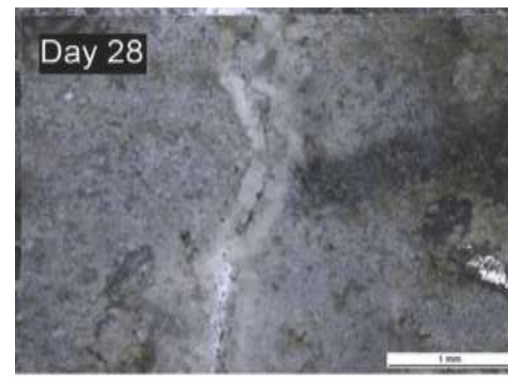
Yan, et al. *Microbiol. Res.* (2012).
Hyeon, et al. *Acc. Chem. Res.* (2015).

Diatoms for photonic crystals



Kröger & Scrutton,. *Curr Opin Chem Biol*. (2007).
Cabrini. *et al. Phys. Rev. Lett.* (2009).

Self-healing
concrete that regains strength



Jonkers,et al. *Advanced Materials Interfaces* (2018).

Summary

Genome engineering offers materials synthesis that requires less energy, less pure raw materials to be made, and carries out multiple functions.

Recent advances in **gene synthesis, editing, and multiscale characterization** technologies enable genome engineering for materials synthesis.

We identified **knowledge gaps and technology gaps** needed to enable GEMS.

Both **sustainable versions of existing materials and completely novel materials** could be GEMS targets.

Acknowledgements



- **Workshop participants**

- *Co-Chairs*
- Caroline Ajo-Franklin, Brian G. Fox, Michael Jewett, Huimin Zhao

- *Writing Team*
- Co-Chairs plus Pupa Gilbert, Arash Komeili, Filipe Natalio, Olga Ovchinnikova, Claudia Schmidt-Dannert, John Shanklin

- *Conference Participants*
- Writing Team plus Arpita Bose, Oleg Gang, Laurie Gower, Farren Isaacs, Derk Joester, Jay Keasling, Nils Kröger, Sanat Kumar, Kevin Morey, Philippe Noirot, Wil Srubar, Lance Stewart, Yasuo Yoshikuni

- *Department of Energy, Office Biological and Environmental Research, Biological Systems Science Division*
- Todd Anderson, Pablo Rabinowitz, Seema Singh

- *Oak Ridge National Laboratory*
- Holly Haun, Betty Mansfield, Stacey McCray