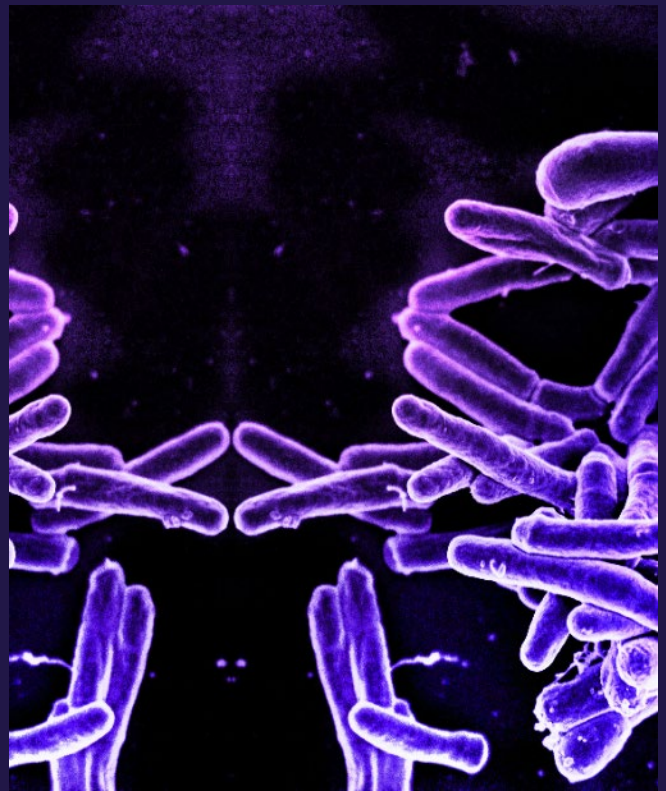
SEPTEMBER 2025

Day 2
Opening Remarks

Dr. Nicholas Adams, co-chair
Dr. Harshini Mukundan, co-chair



Patent Search

Platform:	U.S. Patent and Trademark Office (USPTO)
Country:	United States
Search String:	(mirror ADJ biology OR mirror ADJ image* OR mirror ADJ cell*).ab. AND (chiral OR achiral OR DNA OR protein OR enzyme OR lipid OR ligand OR "nucleic acid" or ribosome or "cell booting" or "protein synthesis using recombinant express").ab.

17

patent results

Platform:	WIPO - Search International and National Patent Collections
Country:	China
Search String:	(("mirror image" or "mirror biology" or "mirror cell*") AND (chiral OR achiral OR DNA OR protein OR enzyme OR lipid OR ligand OR "nucleic acid" or ribosome or "cell booting" or "protein synthesis using recombinant express")

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patent results

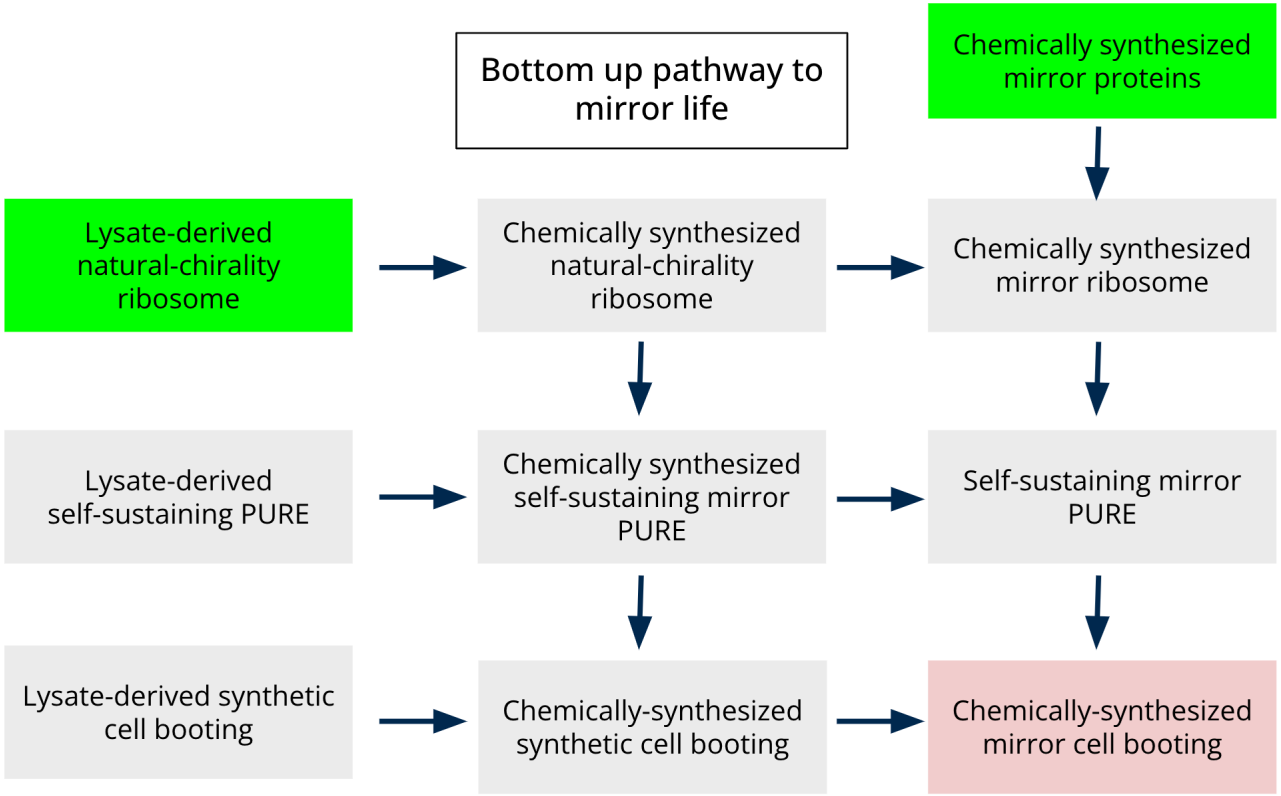


Figure credit: Kevin Esvelt

Lexicon

Workshop Terms and Concepts

- **Molecular chirality**
  - A property of a molecule that cannot be superimposed on its mirror image (also called “handedness”); molecules of “left” and “right” chirality are called L- and D-isomers or L- and D-enantiomers
- **Mirror biology**
  - Synthetic biological molecules and cellular components of the opposite chirality from those found in nature
    - **L-DNA**: Synthetic DNA of the opposite chirality from natural D-DNA
    - **D-proteins** and **D-peptides**: Synthetic proteins/peptides of the opposite chirality from natural L-proteins
- **Mirror life**
  - A synthetic self-replicating organism made entirely from molecules of the opposite chirality from natural life
- **Risk measures**
  - **Biosafety:** Prevention of infections in biomedical settings or release of organisms into the environment
  - **Biosecurity**: Prevention of deliberate misuse of biological material and biotechnology to cause harm

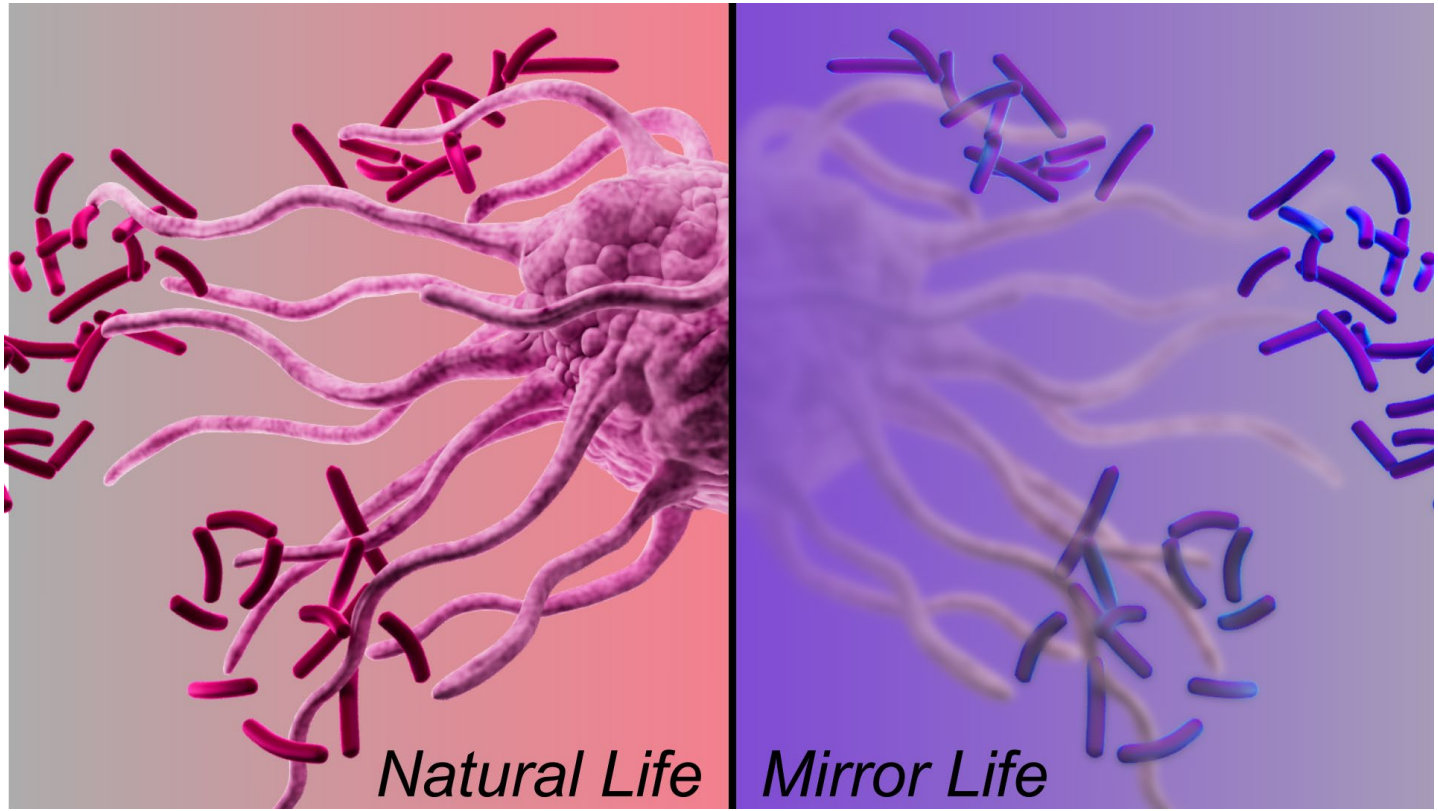


Figure 1 – 3D Illustration Mirror Bacteria: A schematic of interactions between bacteria and macrophage, which is a component of the innate immune system. The left side of the schematic illustrates interactions with natural chirality cells where macrophages recognize the bacteria as foreign bodies to engulf, digest, and present antigens to trigger an adaptive immune response. The right side of the schematic illustrates interactions with self-replicating mirror bacteria and natural chirality macrophages. The exact interactions between mirror bacteria and a natural macrophage are not known. While a macrophage may identify mirror cells as foreign bodies, it is not clear to what degree it will be able to engulf the mirror bacteria, digest the mirror components, and present the mirror antigens.

Our Purpose

Workshop Tasks and Team

- **Task**
  - Our charge is to provide an objective assessment of the current state, trajectories, and potential impacts of mirror biology

- **Team**
  - We have assembled a diverse group of experts to guide discussions on the basic science of mirror biology, as well as the promises and risks of enabling technologies along the pathway to mirror life

SEPTEMBER 2025

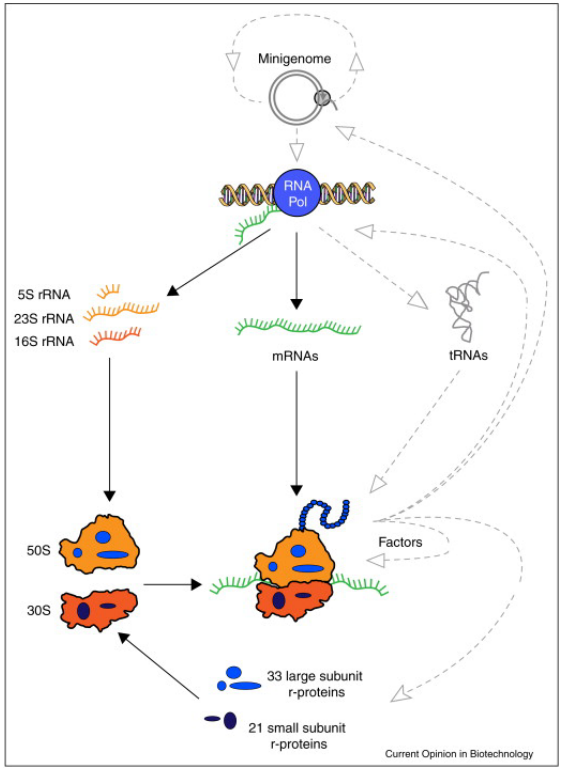
Mirror Biology: Technology Overview and Framing

Dr. Michael C. Jewett

A chemical structure model of a naturally occurring amino acid, L-tryptophan (left), is shown with its mirror image (right). ILLUSTRATION: N. BURGESS/*SCIENCE*

Building with biology

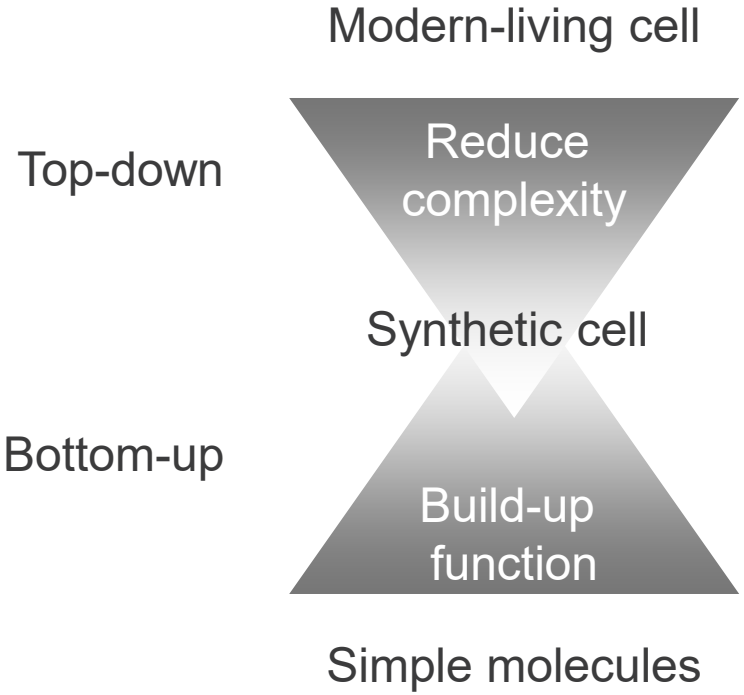
- Building biology tests understanding and opens new application spaces
- Building cells has captivated scientists for decades



Jewett and Forster, Current Opinion in Biotechnology, 2010

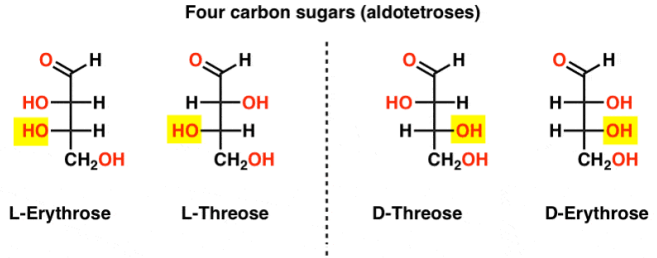
“Top-down” versus “bottom-up”

- “Top-down” = reduction of bacterial genomes *in vivo*
- “Bottom-up” = integration of DNA/RNA/protein/membrane syntheses *in vitro*.

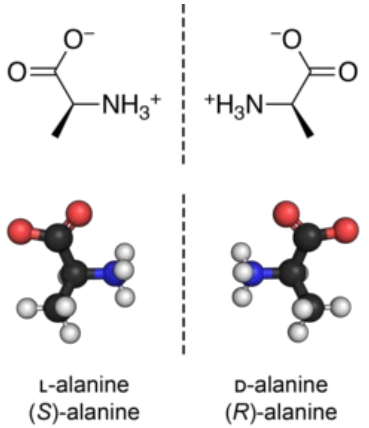


What is mirror biology? The concept of homochirality

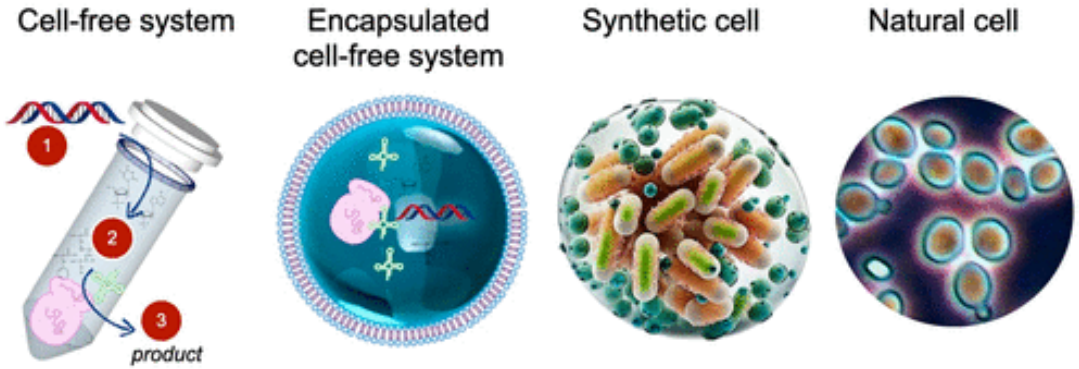
- The essential building blocks of life exist almost exclusively in one mirror-image form



→ Sugars: Sugars in biology are predominantly D-chiral (right-handed)
→ Nucleotides: The components of DNA and RNA are almost all right-handed (D-form), based either D-deoxyribose for DNA or D-ribose for RNA
→ Amino acids: The building blocks of proteins are almost all left-handed (L-form).



Making mirror components versus making mirror cells



- **Molecules and polymers** (e.g., DNA, RNA, peptides, proteins, sugars, membranes, etc.)
- **Processes to make molecules and polymers** (e.g., replication, transcription, translation, etc.)
- **Integration of processes to enable self-replication**

Rothschild *et al., ACS Synthetic Biology,* 2024.

What are the risks with mirror life?

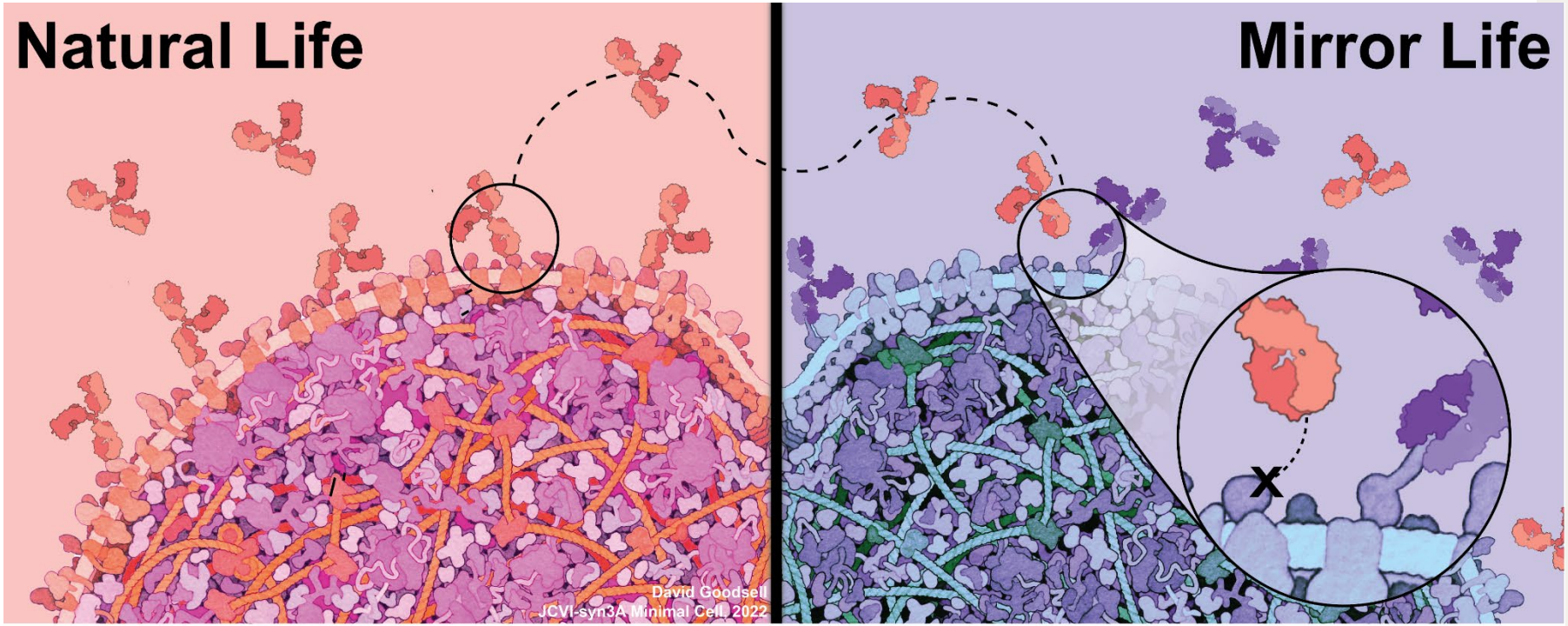


Figure 2 – 2D Cell Surface Proteins: A schematic of interactions between antibodies, which is part of the adaptive immune system, and proteins on the surface of a bacterial cell. The left side of the figure illustrates interactions of an antibody (orange) with a natural chirality bacterial cell surface protein, but lack of interaction of antibodies that bind to mirror image cell surface proteins (blue). The right side illustrates a self-replicating mirror bacterium cell surface protein binding to antibodies specific to that protein (blue), but not to antibodies that bind to the natural chirality protein (orange). Naturally, antibodies are highly diverse by design, specifically enabling them to be created against a wide variety of antigens and at least one study suggests that some antibodies preferentially bind left-handed amino acids whereas others bind right-handed amino acids. These findings raise the possibility of the body creating antibodies that recognize mirror proteins on the surface of self-replicating mirror cells . The experiments to test this possibility have not been conducted.

What can be done to minimize risk and maximize the benefits of mirror biology?

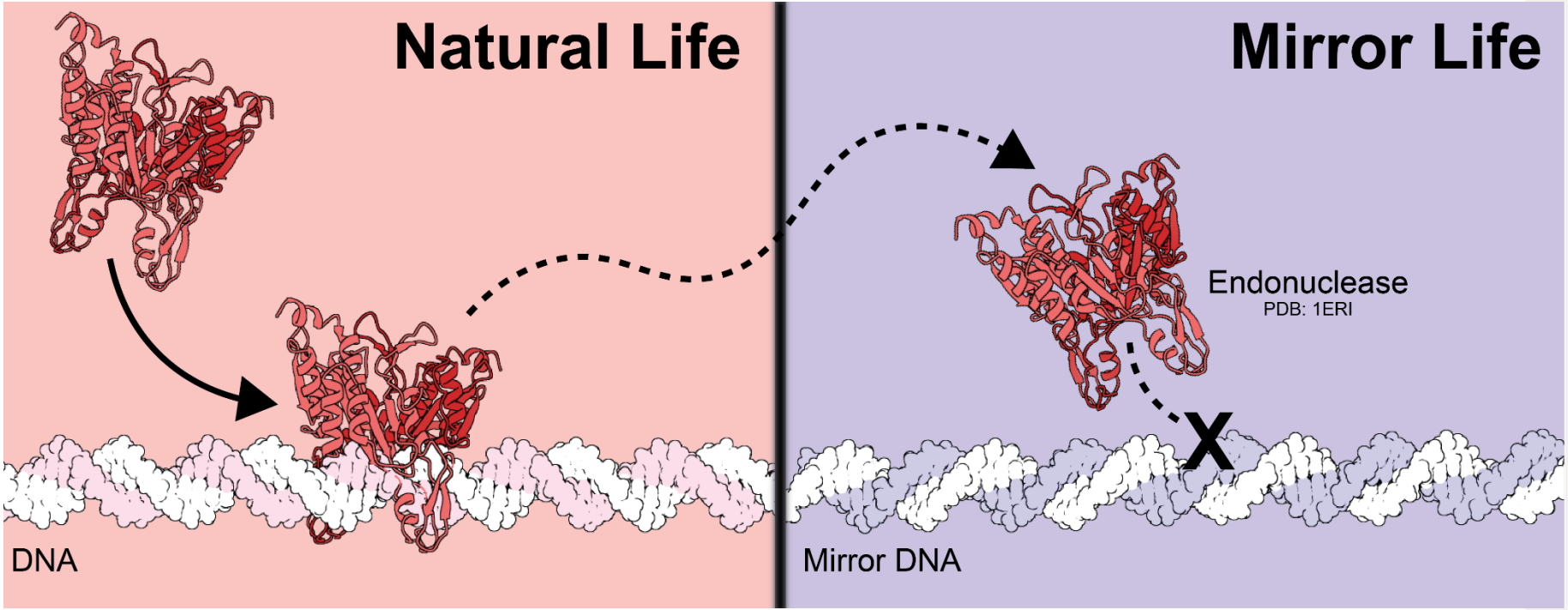


Figure 3 - 2D Mirror Life DNA: A schematic of molecular interactions of an endonuclease, which is an enzyme that cuts DNA, and DNA. The endonuclease pictured in this schematic is of EcoR1 and its structure was retrieved from the Protein Data Bank database. The left side of the figure illustrates binding of natural chiral molecules (DNA and an endonuclease). The right side of the figure illustrates the inability of the natural form of the endonuclease to bind to the mirror DNA molecule (left-handed DNA).

Artwork Attributions

Figures 1-3: Planning Committee Provided Figures. Design by Iwasa J. and Torrez, R. University of Utah Animation Lab. 2025.

Figure 1 – 3D Illustration Mirror Bacteria:

Creation of the Macrophage and bacteria in Autodesk Maya (2025.3.1) Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License

Figure 2 – 2D Cell Surface Proteins:

Acknowledgement: Illustration by David S. Goodsell, RCSB Protein Data Bank. doi: 10.2210/rcsb_pdb/goodsell-gallery-042

Updated resources for exploring experimentally-determined PDB structures and Computed Structure Models at the RCSB Protein Data Bank (2025) Nucleic Acids Research, 53: D564–D574 doi: 10.1093/nar/gkae1091

Molecular graphics modified with UCSF ChimeraX v1.7, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from National Institutes of Health R01-GM129325 and the Office of Cyber Infrastructure and Computational Biology, National Institute of Allergy and Infectious Diseases.

UCSF ChimeraX: Tools for structure building and analysis. Meng EC, Goddard TD, Pettersen EF, Couch GS, Pearson ZJ, Morris JH, Ferrin TE. Protein Sci. 2023 Nov;32(11):e4792.

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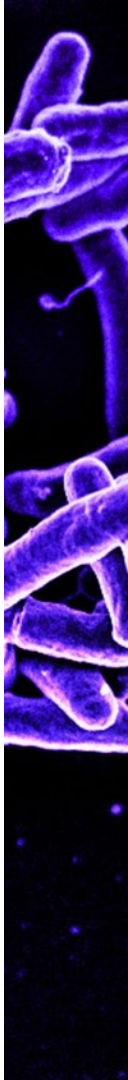
Molecular graphics built with Avogadro: an open-source molecular builder and visualization tool. Version 1.2. http://avogadro.cc/

Marcus D Hanwell, Donald E Curtis, David C Lonie, Tim Vandermeersch, Eva Zurek and Geoffrey R Hutchison; “Avogadro: An advanced semantic chemical editor, visualization, and analysis platform” Journal of Cheminformatics 2012, 4:17.



Backup Slides

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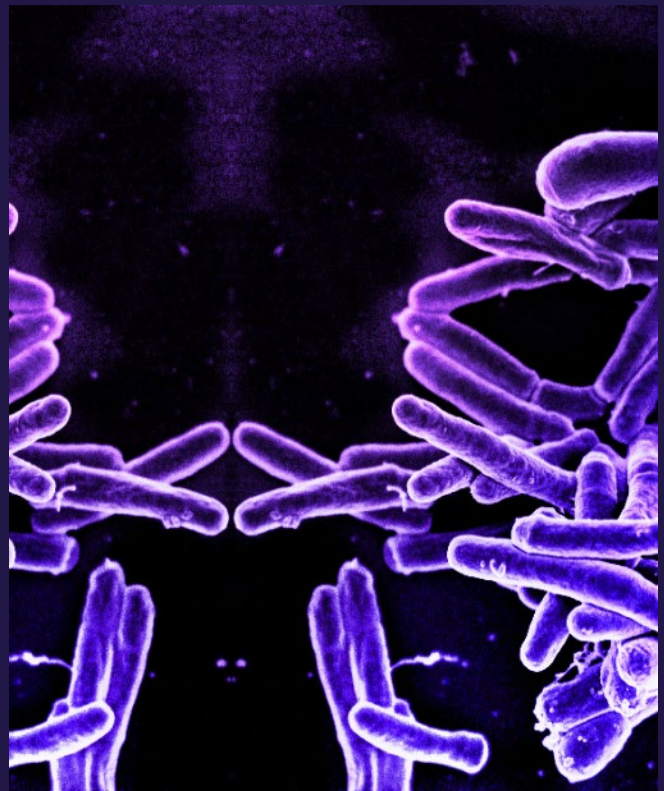

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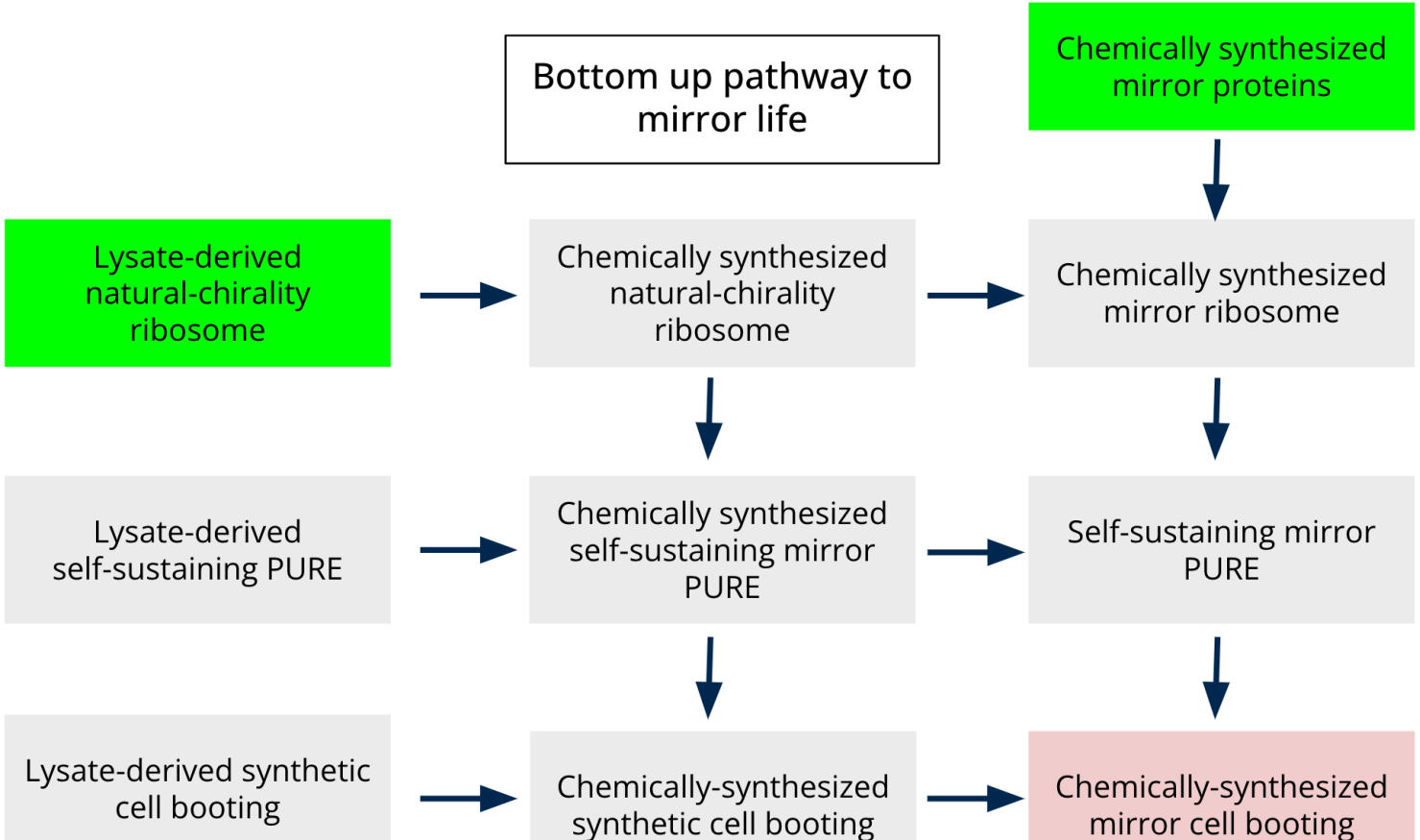
Bottom up pathway to mirror life
Chemically synthesized mirror proteins
Lysate-derived natural-chirality ribosome
Chemically synthesized natural-chirality ribosome
Chemically synthesized mirror ribosome
Lysate-derived self-sustaining PURE
Chemically synthesized self-sustaining mirror PURE
Self-sustaining mirror PURE
Lysate-derived synthetic cell booting
Chemically-synthesized synthetic cell booting
Chemically-synthesized mirror cell booting

NATIO
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