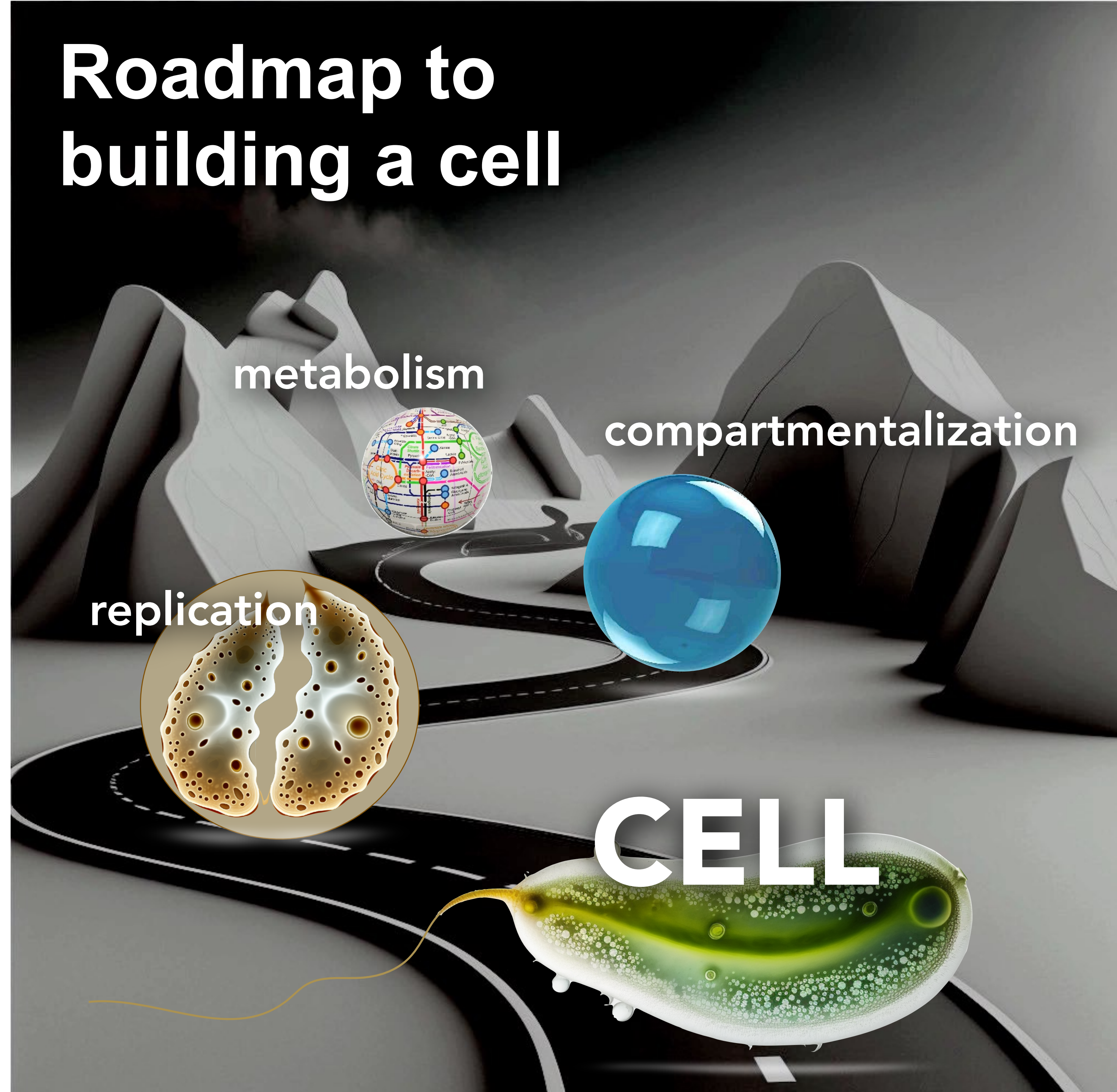


Rothschild, L.J., Averagesch, N.J.H.,
Strychalski, E., Moser, F., Glass, J.I.,
Cruz Perez, R., Yekinni, I.O., Rothschild-
Mancinelli, B., Roberts Kingman, G.A.,
Wu, F., Waeterschoot, J., Ioannou, I.A.,
Jewett, M.C., Liu, A.P., Noireaux, V.,
Sorenson, C., and Adamala, K.P. 2024.

Building Synthetic Cells – from the Technology Infrastructure to Cellular Entities.

ACS Synthetic Biology. 13, 4, 974–997.
[https://pubs.acs.org/doi/epdf/
10.1021/acssynbio.3c00724](https://pubs.acs.org/doi/epdf/10.1021/acssynbio.3c00724)

Roadmap to building a cell



What Is Life?



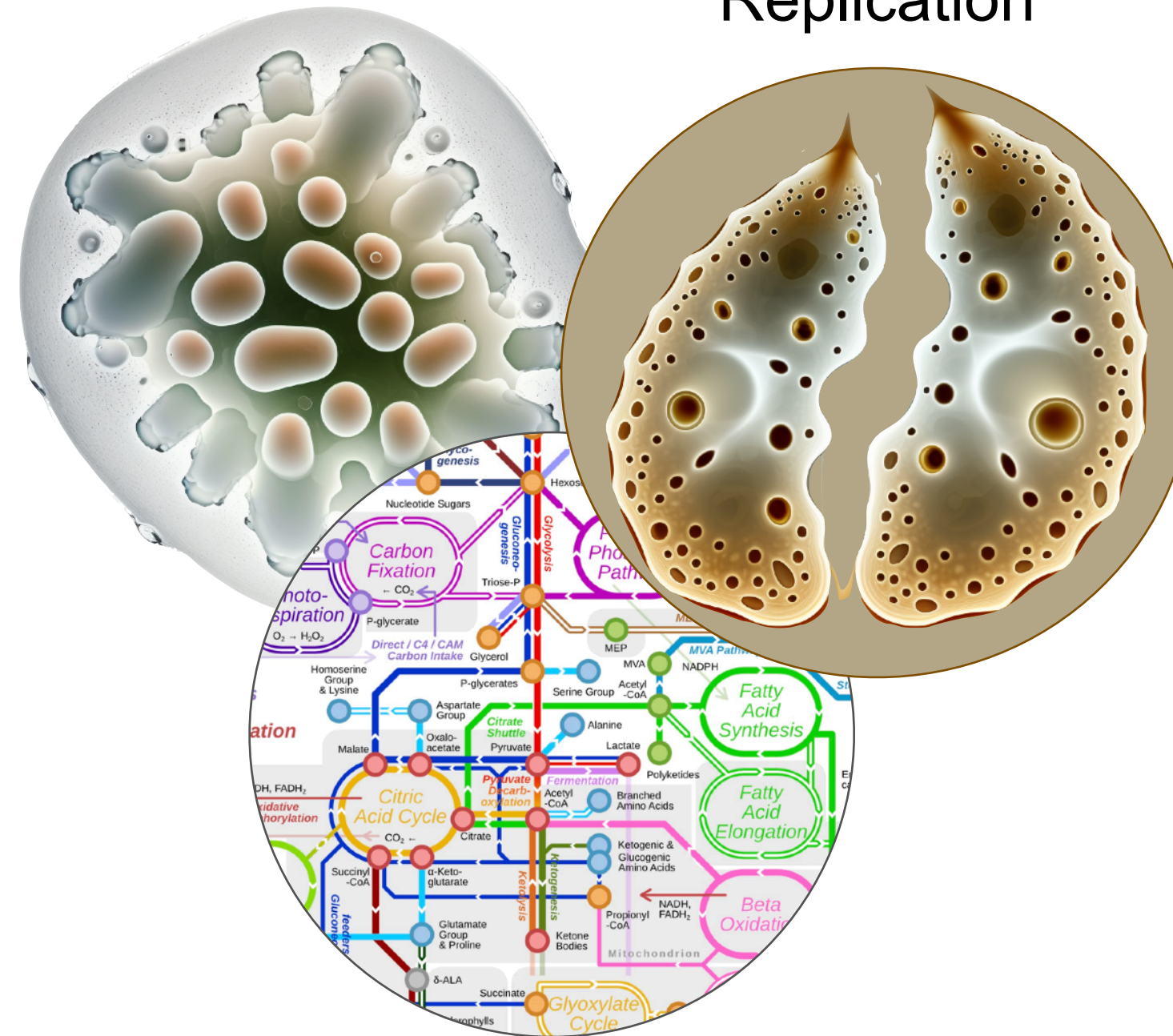
What is life?

Primary properties

Emergent properties

Compartmentalization

Replication

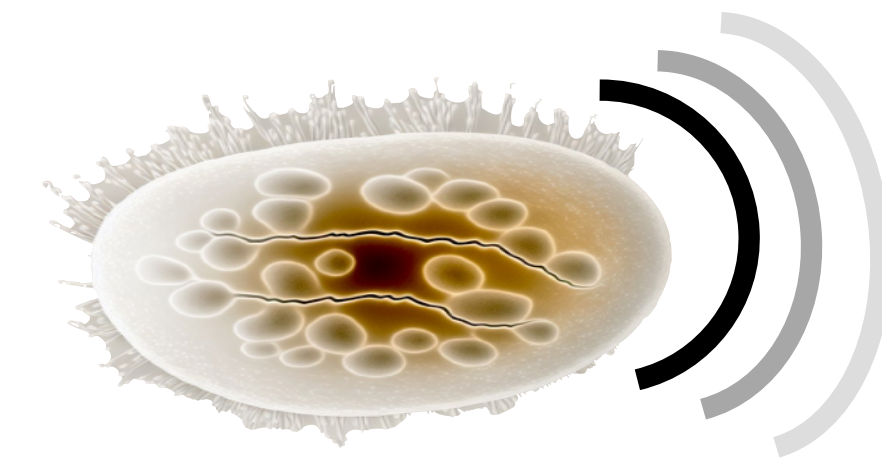


Metabolism

Evolution



Responsiveness



Movement



★ Tibor Ganti's model

What Is Life?



Operational Definition

What Is Life?

- Life is an emergent process based on physical components, not just an object

*Operational
Definition*

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- Life is a population level phenomenon

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- The process includes fighting entropy a la Schrödinger (1944) and creating disequilibria (atmospheric, isotopic, chirality...)

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- It also needs energy and time

*Operational
Definition*



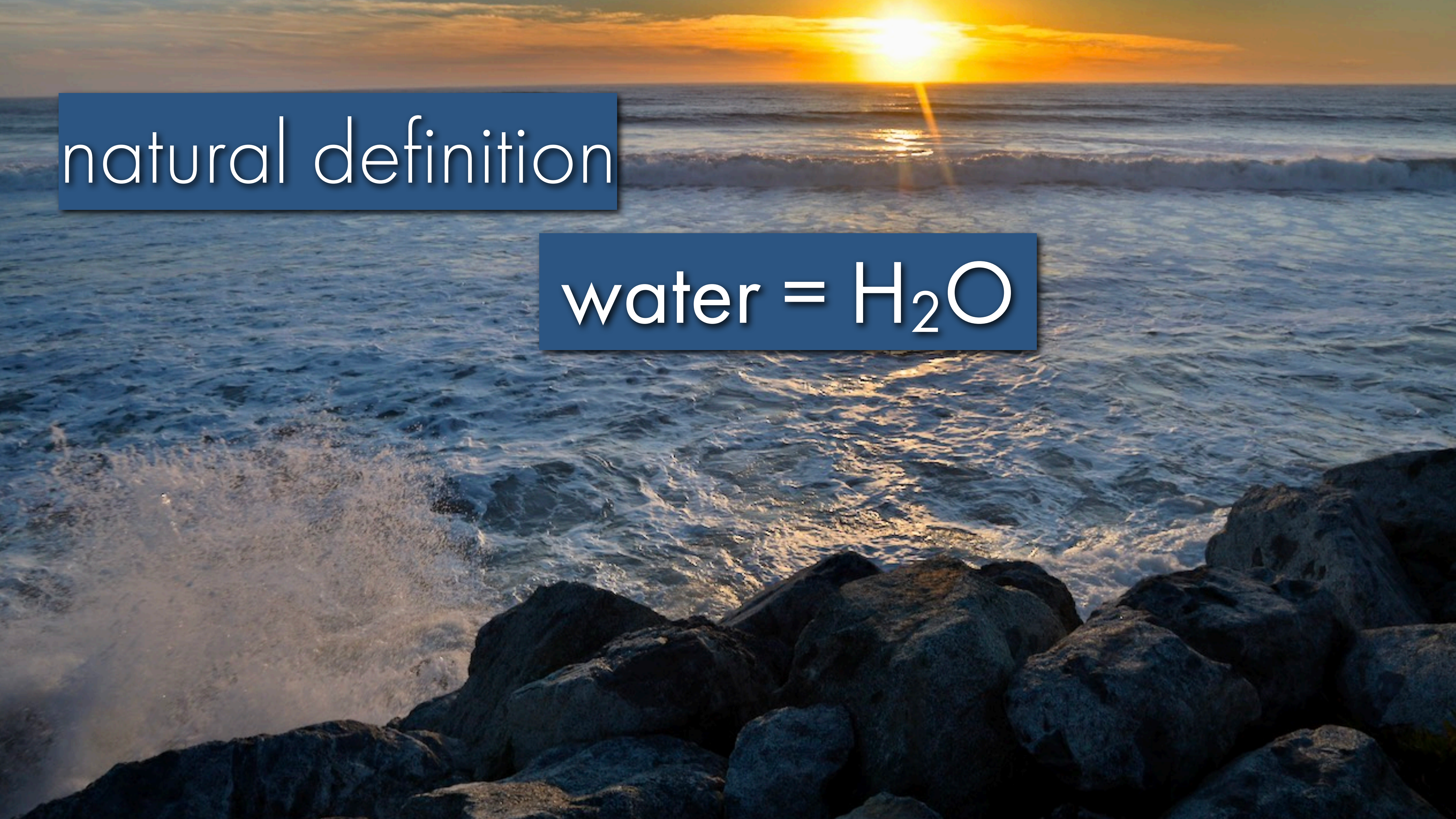
Non
natural definition

Non

natural definition

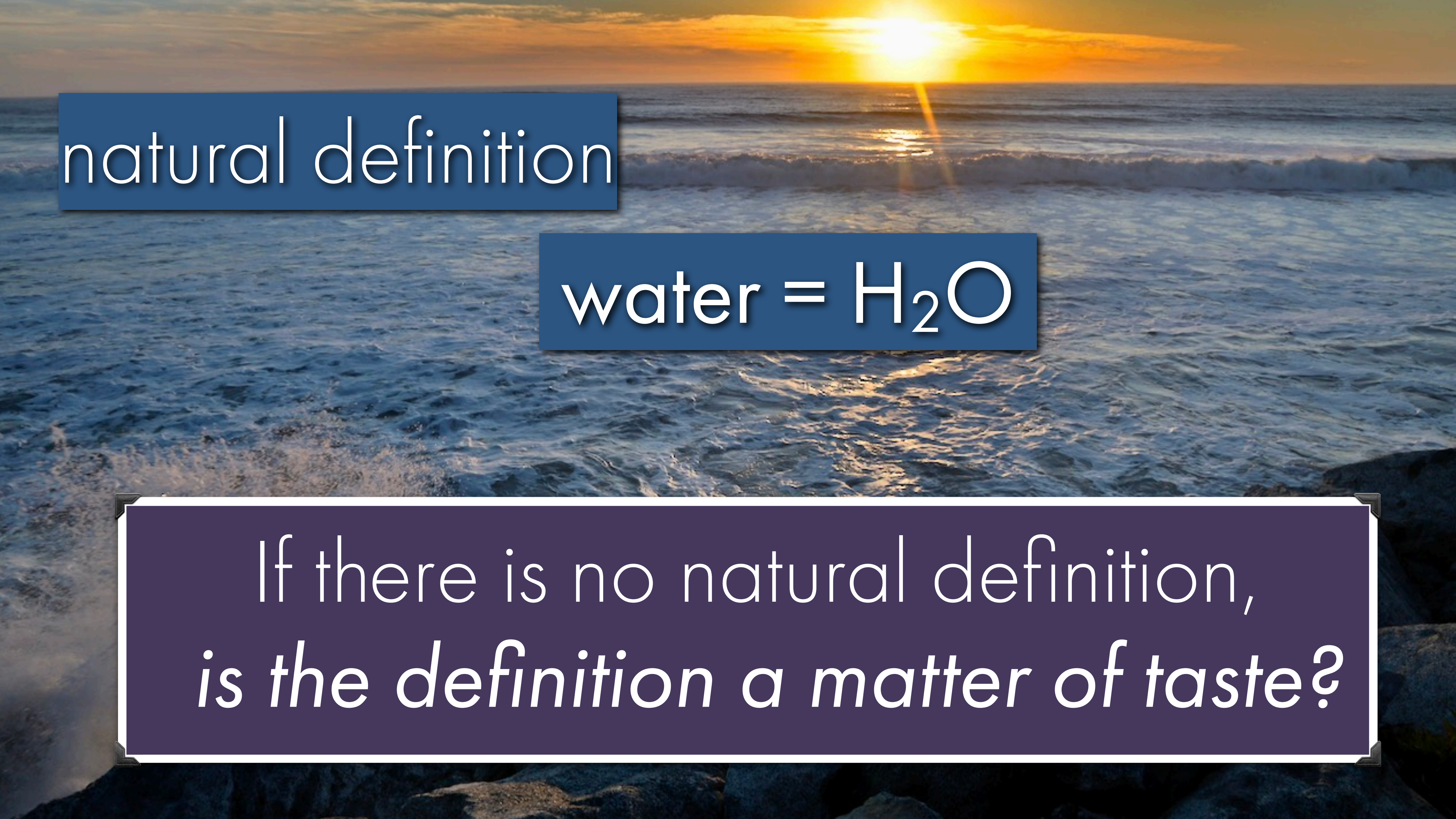
“Water is sometimes sharp and sometimes strong, sometimes acid and sometimes bitter, sometimes sweet and sometimes thick or thin, sometimes it is seen bringing hurt or pestilence, sometimes health-giving, sometimes poisonous. It suffers change into as many natures as are the different places through which it passes. And as the mirror changes with the colour of its subject, so it alters with the nature of the place, becoming noisome, laxative, astringent, sulfurous, salty, incarnadined, mournful, raging, angry, red, yellow, green, black, blue, greasy, fat or slim....”

da Vinci, 1513



natural definition

water = H_2O

A background image of a sunset over the ocean. The sun is a bright yellow-orange orb on the horizon, casting a long, shimmering reflection across the dark blue water. Gentle waves are visible in the foreground. The sky is a mix of orange, yellow, and light blue.

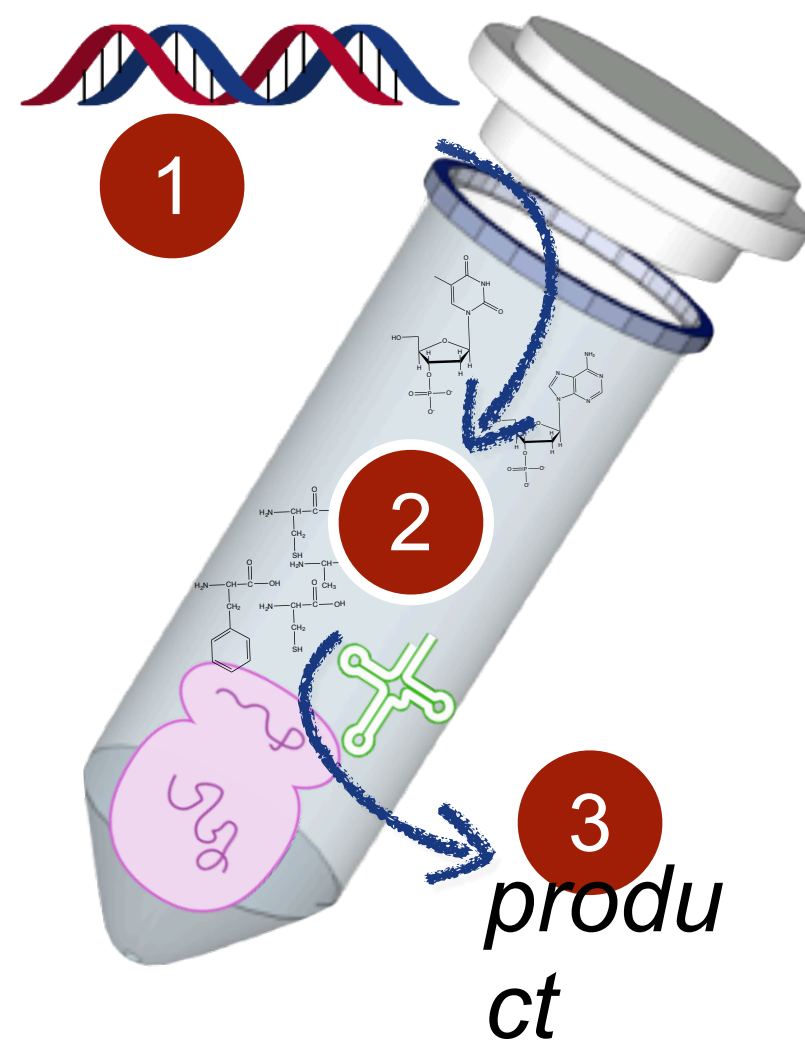
natural definition

water = H₂O

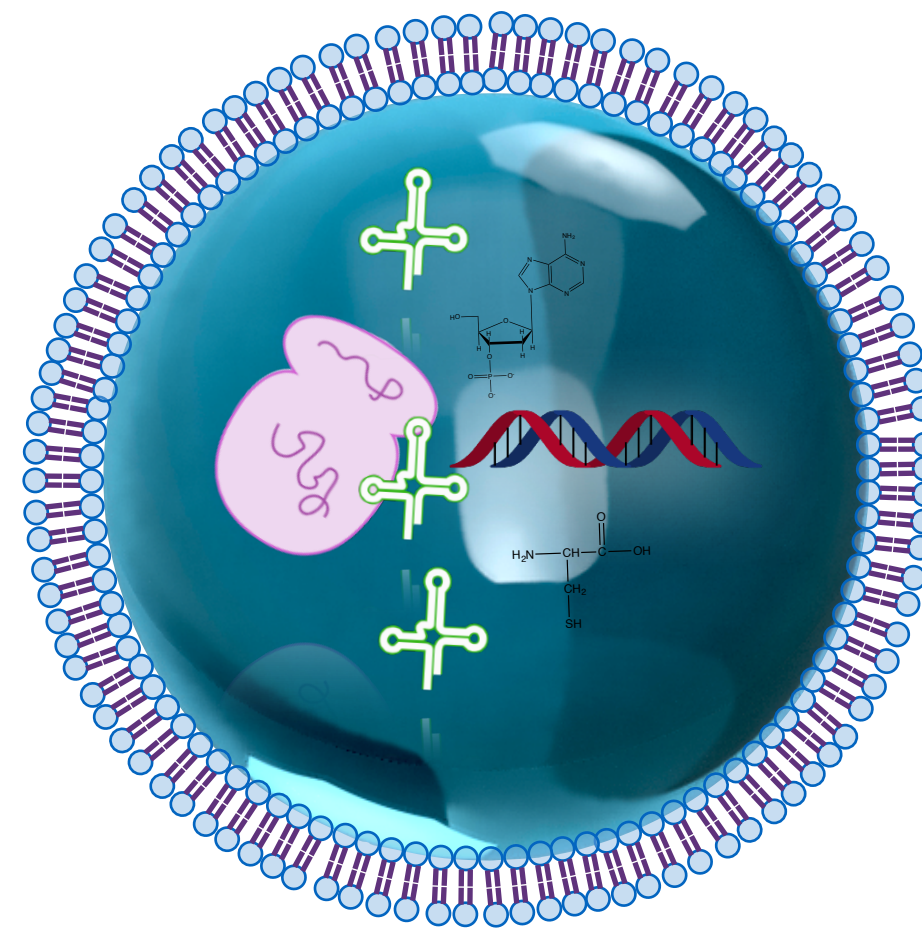
If there is no natural definition,
is the definition a matter of taste?

Four different platforms for studying cellular processes

Cell-free system



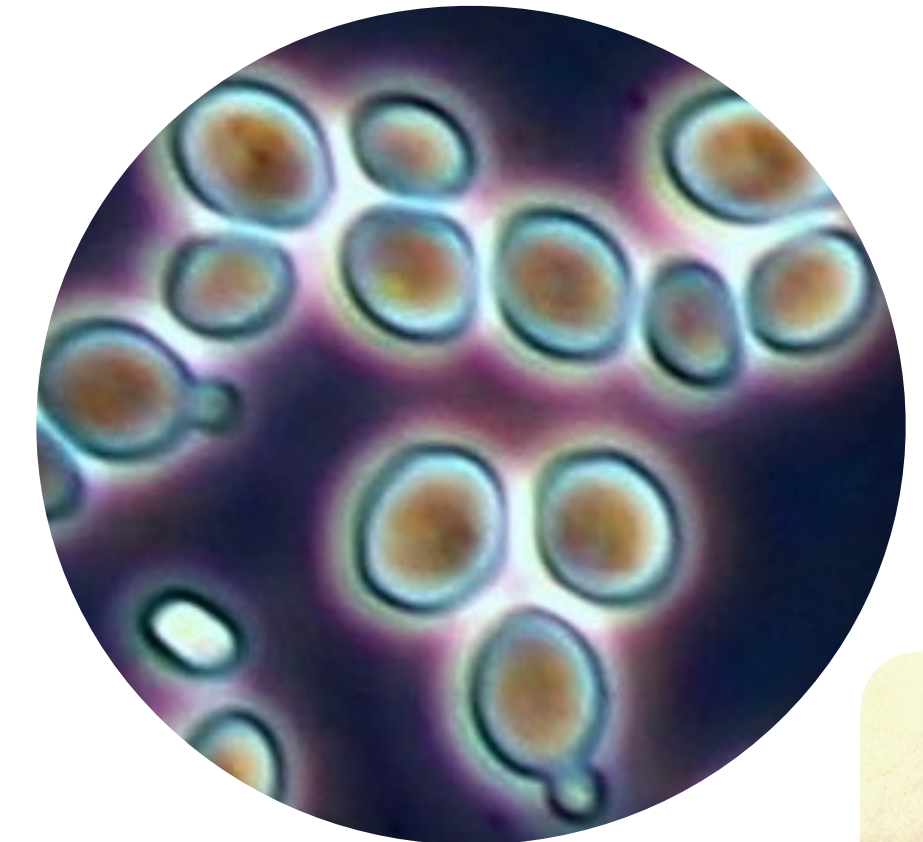
Encapsulated cell-free system



Synthetic cell

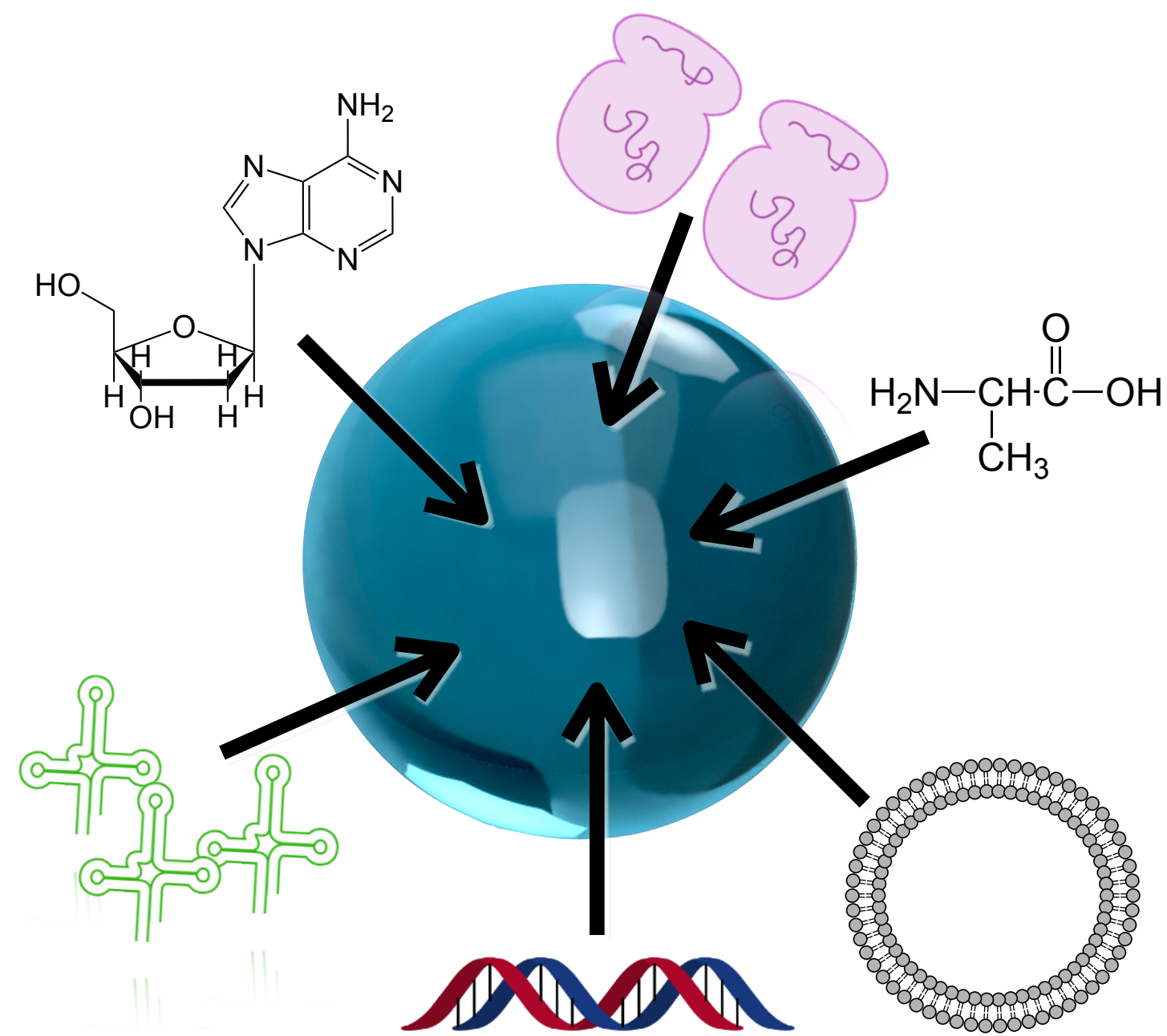


Natural cell

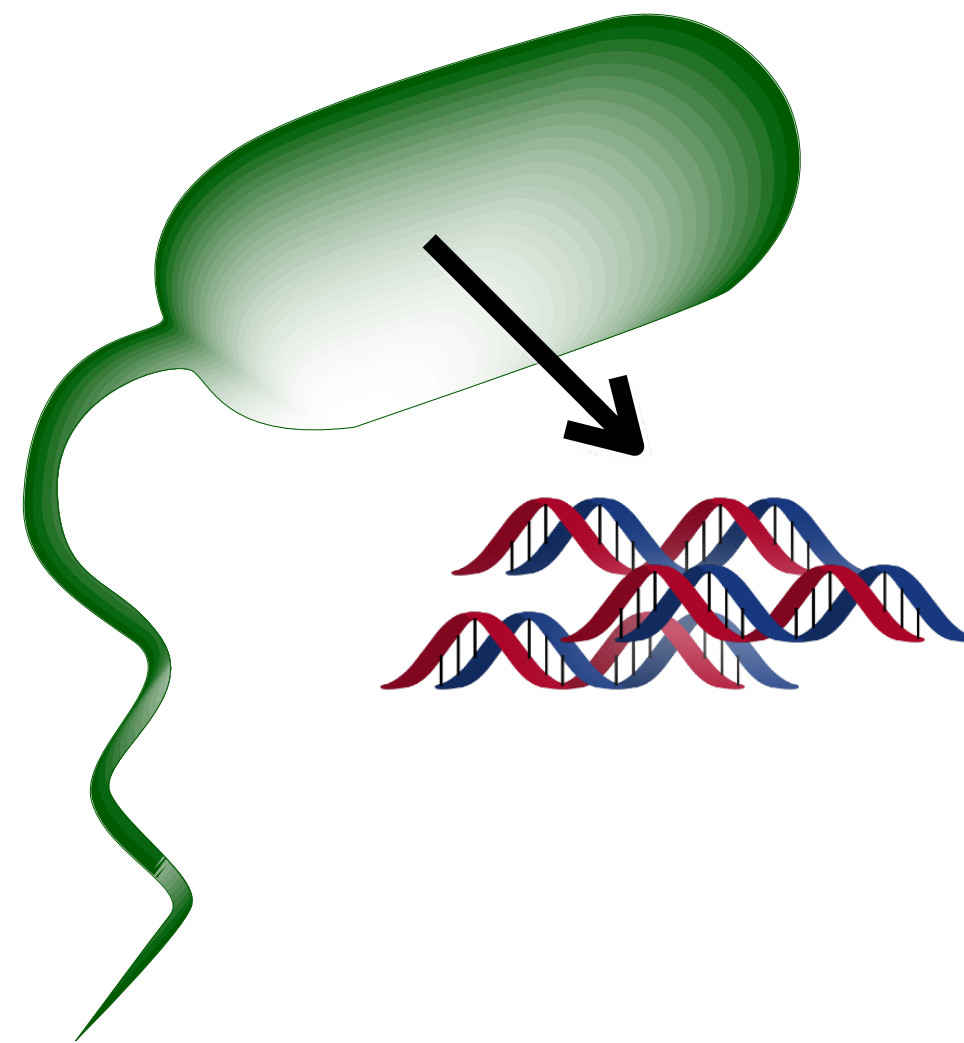


Three different approaches

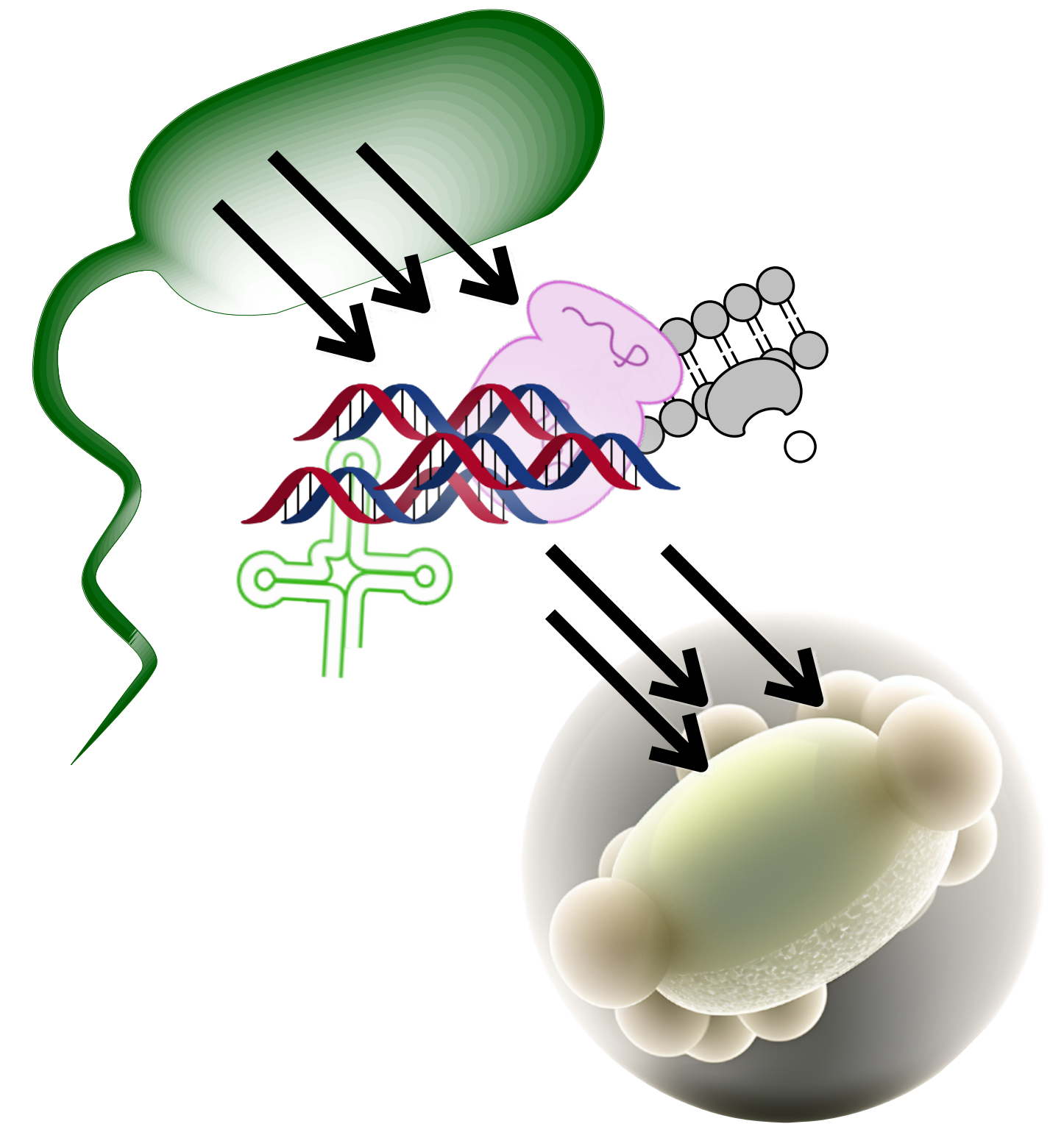
Bottom up



Top down



Middle out



Current

Today's capabilities

Compartmentalization:

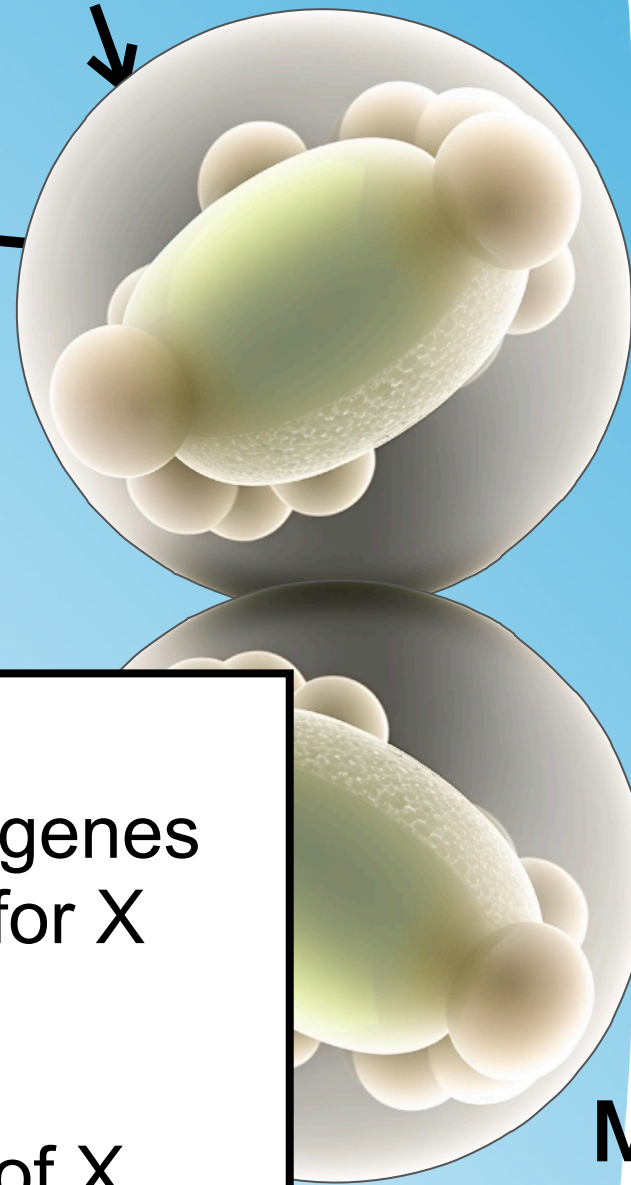
Creation of inter-communicating vesicle within-vesicle structures

Metabolism

Partial metabolic pathways expressed in cell free systems and in artificial organelle

Replication

- Translation of X genes within a system for X hours
- Transcription
- DNA replication of X size in X systems for X generations
- Limited capability of cytoskeleton driven segregation of DNA



Scaling up functionalities of each component

- Develop a modular roadmap with the minimum requirement for each component
- Increase robustness and complexity of each component to achieve minimum requirement
- Requires top-down, bottom-up, and middle-out strategies

synthetic cells



integration
definition of
success
safety/regulatory

Integration of components

- Develop common integration framework and effort coordination
- Implement multiple design-test-build cycles of component development and integration
- Leverage computational modeling and

Infrastructure and technological development

Microfluidics

Microscopy

Automation and
robotics systems

Biochemistry and
biophysics tools

Genetic tools

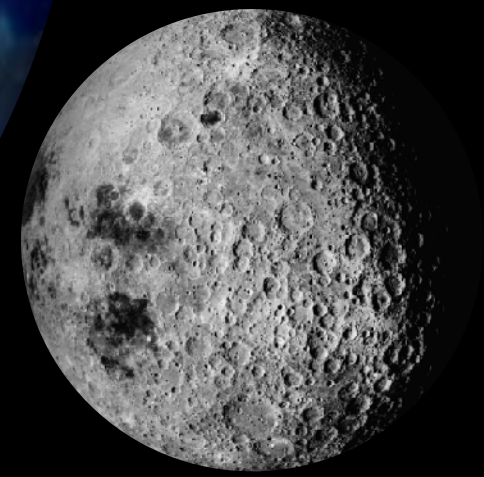
Computational
modeling and
AI

Gap

Goal

Morphogenesis to
orthogonal life

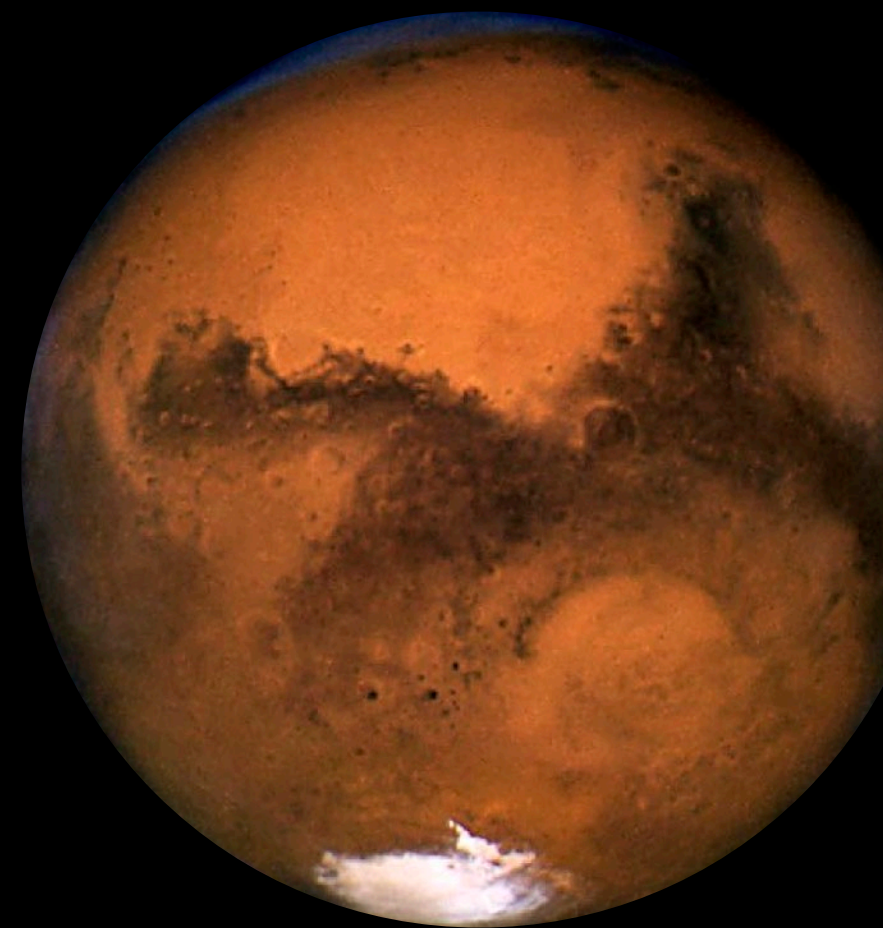


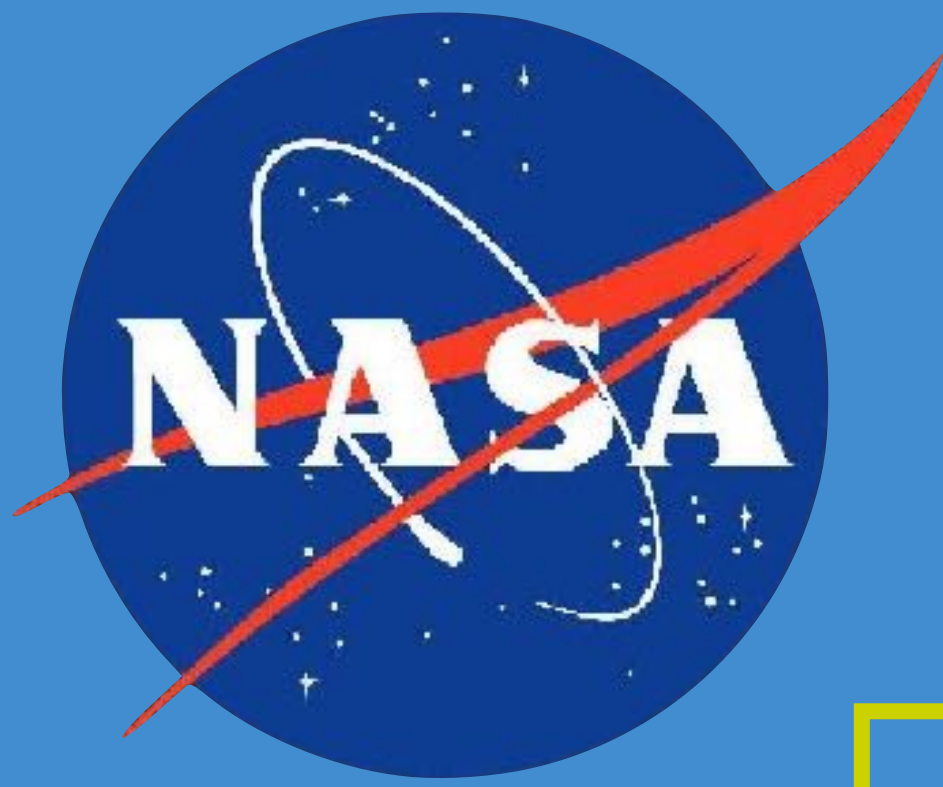


Synthetic cells: key for space applications

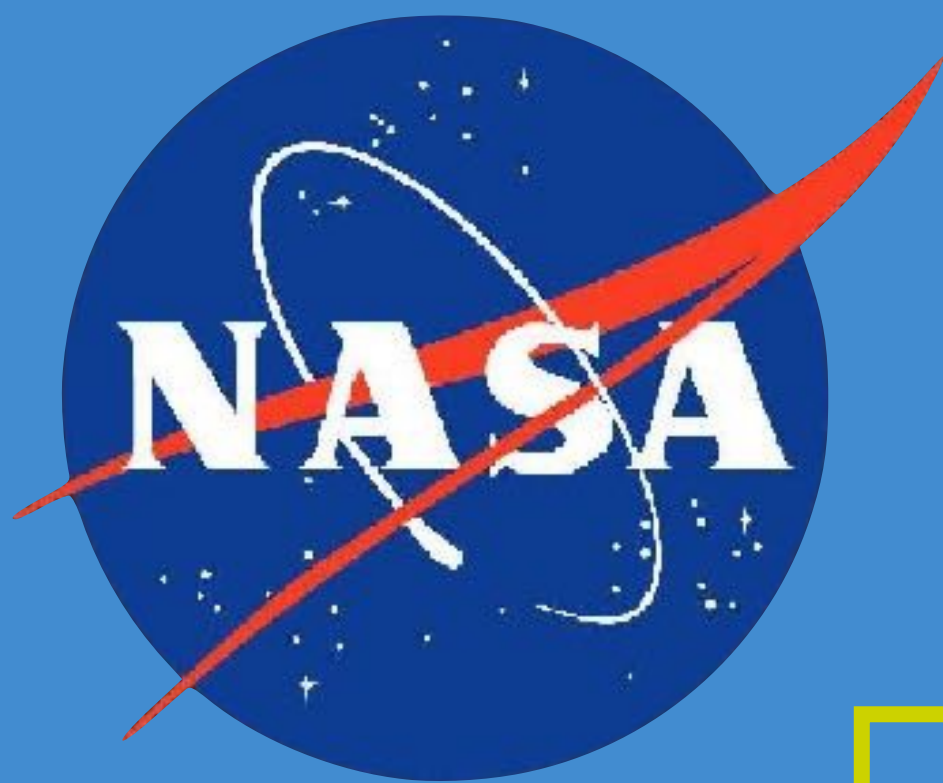


Lynn J. Rothschild
NASA Ames Research Center
Moffett Field, CA USA
22 July 2025
@lynnjrothschild



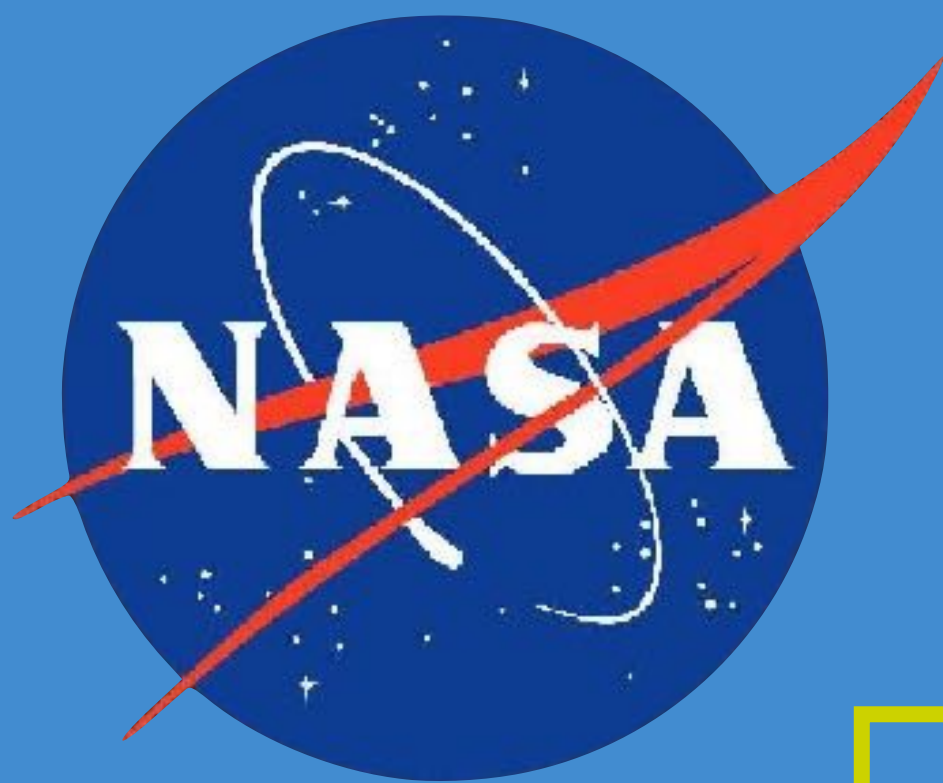


National Aeronautics and Space Administration



aeronautics: green aviation
- biofuels, novel materials

National Aeronautics and Space Administration

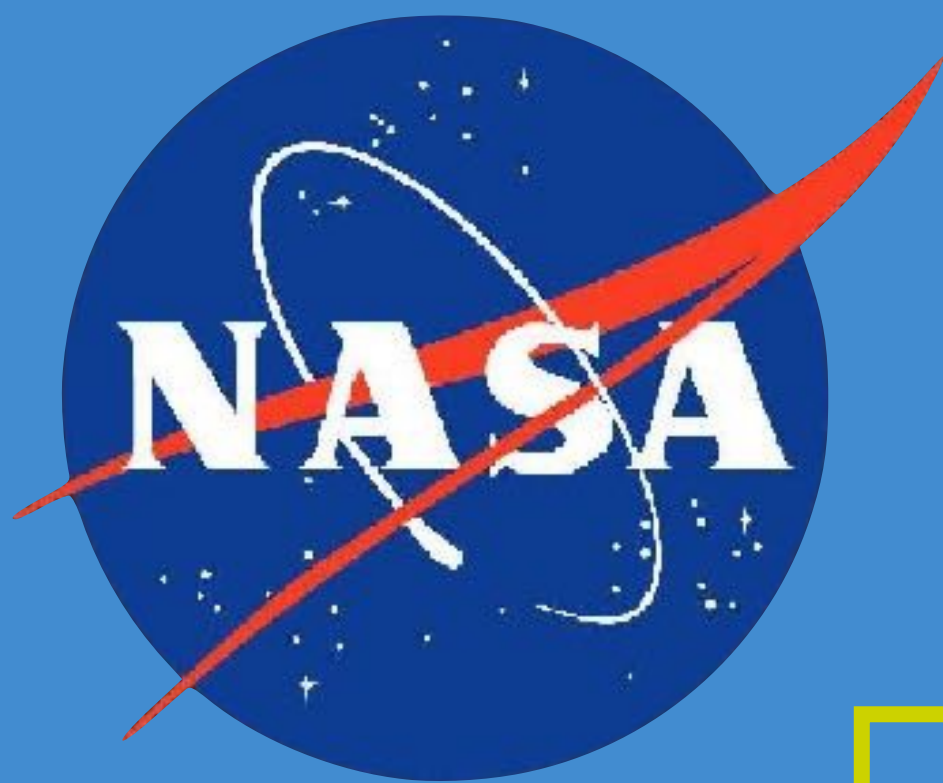


aeronautics: green aviation
- biofuels, novel materials

National Aeronautics and Space Administration



Exploration issues:
Upmass, reliability in
extreme environments



aeronautics: green aviation
- biofuels, novel materials

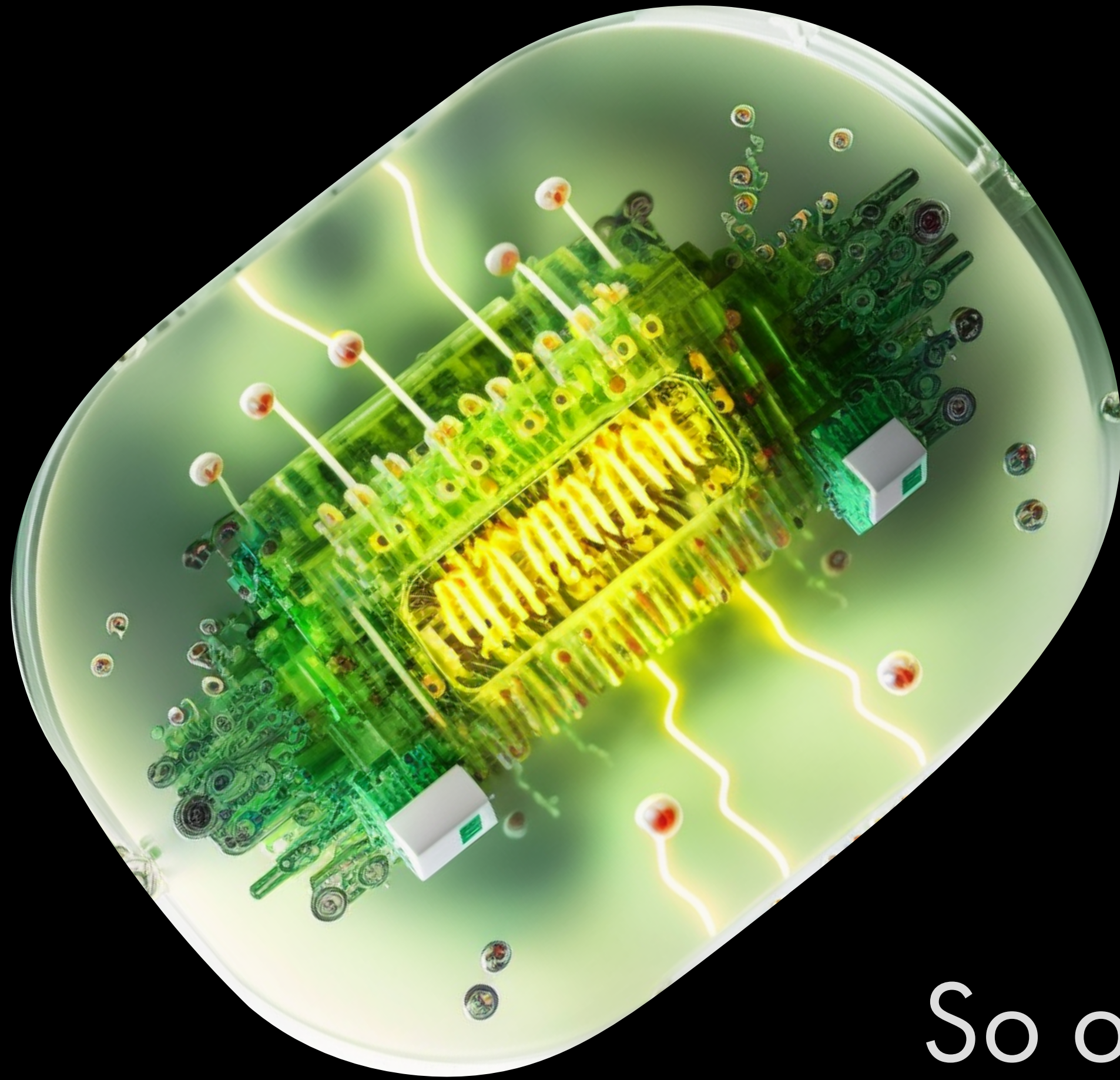
National Aeronautics and Space Administration



Exploration issues:
Upmass, reliability in
extreme environments



Science issues: can't
rerun origin and
evolution of life; what
might be out there?



Life is a self-replicating micro machine that does carbon chemistry and nanotech

Naturally evolved life will not suffice

So our lab uses Life 1.5, aka synthetic bio

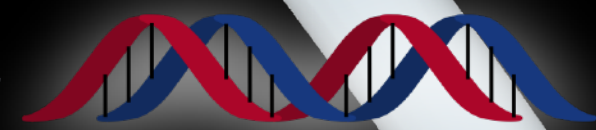
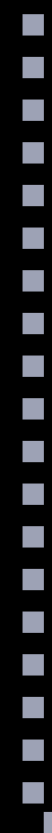
The solution? **Life 2.0, aka synthetic cells**



- Chemistry: plastics to toxic chemicals
- Drugs: production and delivery (ex. Astropharmacy)
- Nanotechnology (ex. Biowires)
- Generating electricity
- Material production (ex. Fungal biocomposites)
- Biomining
- Detoxifying lunar and martian water
- Food/flavor/scent production

Vision: Life 1.5 / 2.0
Key for Human Exploration

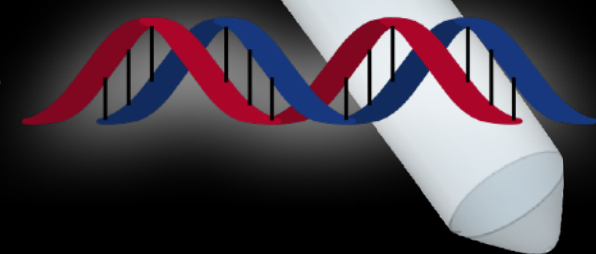
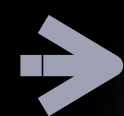
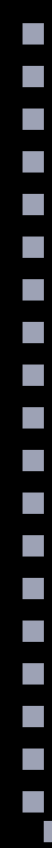
..00101101110100..



We **SEND**
DIGITAL
INFORMATION to
make **DNA**

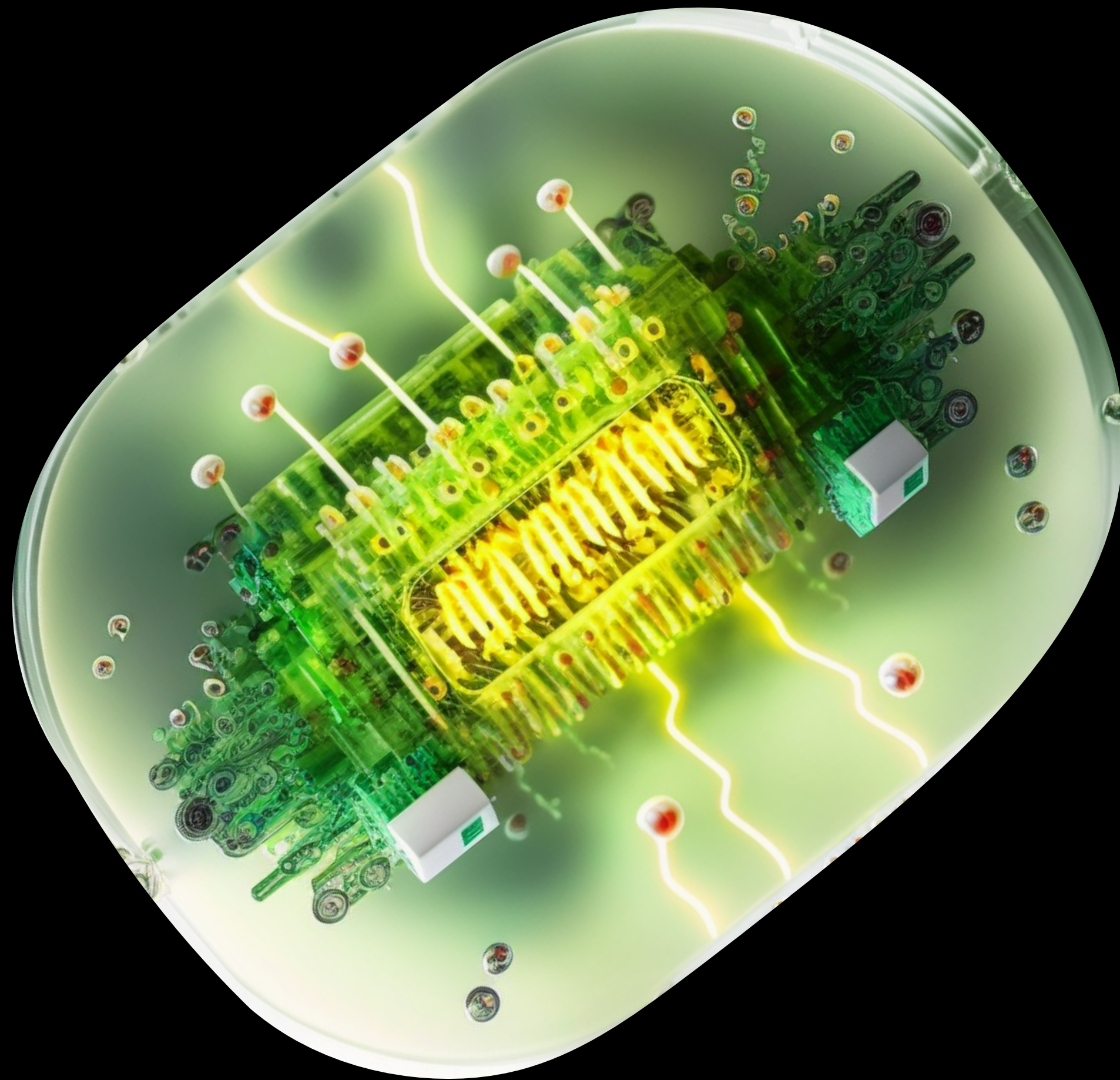


..00101101110100..



The Ultimate Massless Exploration:

*Send Digital Information To
Make Cells*



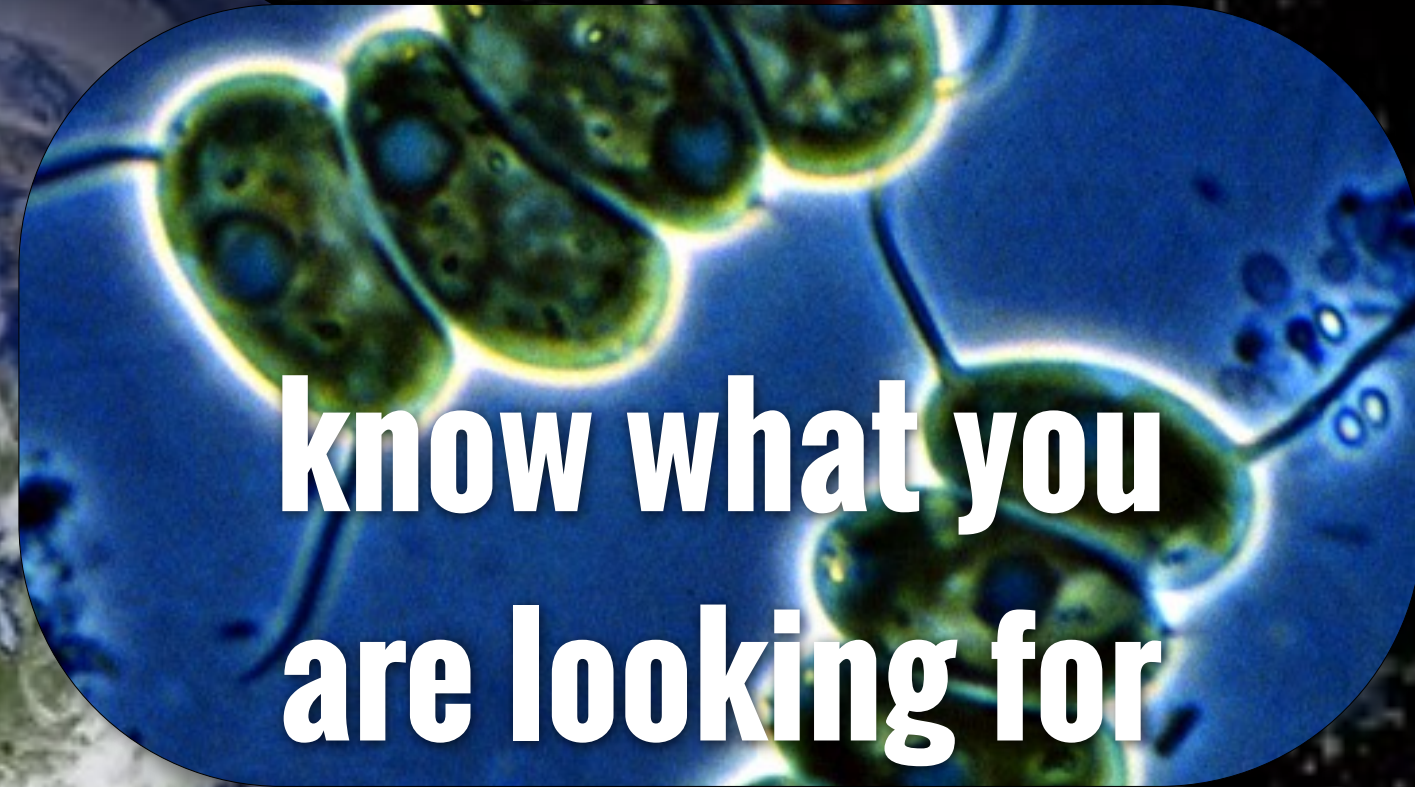
synthetic cells
allows us to answer
the 'What if?'
Questions

Vision: Science



*how to search
for life beyond
Earth*





**know what you
are looking for**

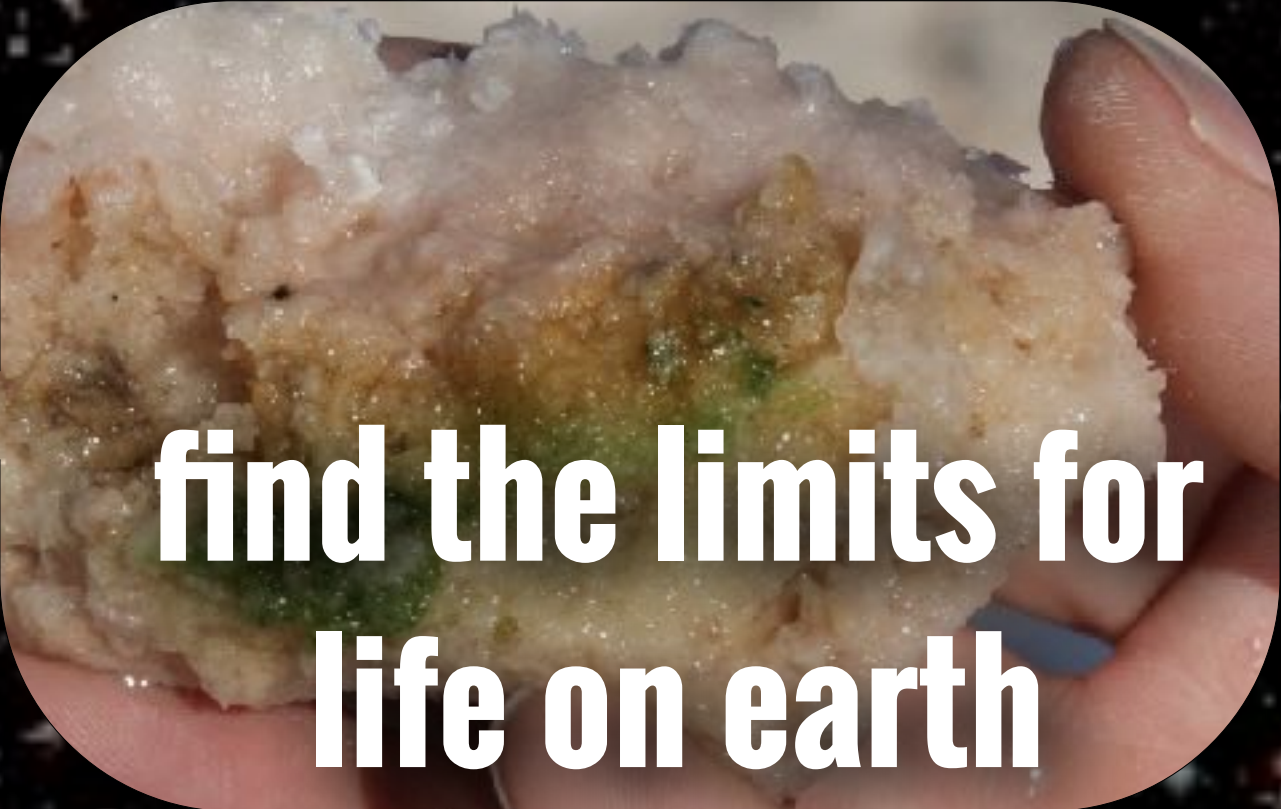
*how to search
for life beyond
Earth*



how to search for life beyond Earth



**know what you
are looking for**

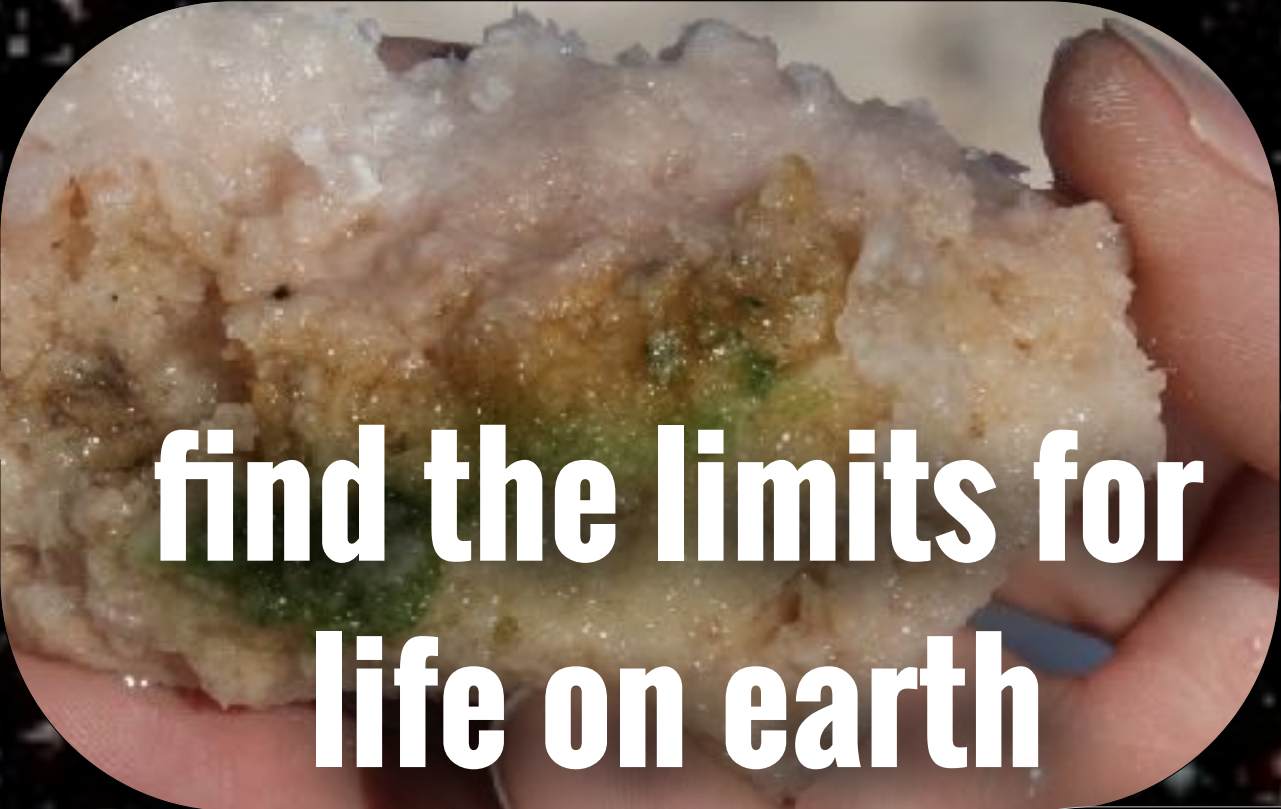


**find the limits for
life on earth**

how to search for life beyond Earth



**know what you
are looking for**



**find the limits for
life on earth**



**map extremophiles
to other habitable
bodies**



**know what you
are looking for**

*how to search
for life beyond
Earth*

If there are tempting locations
beyond the capability of
extant, naturally evolved
extremophiles, why not make
synthetic cells?



how to search for life beyond Earth



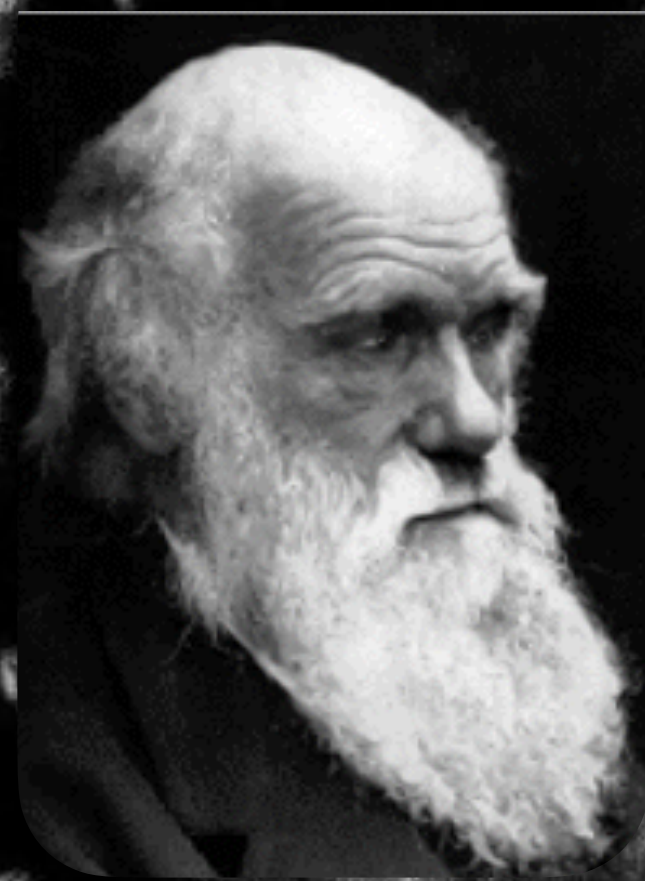
**know what you
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**make synthetic
extremophiles**

The only successful
origin of cells so far
was the handiwork
of evolution



- How?
- Why?
- Are there alternative components, functions? Hint: look at the raw materials that were available.
- This should help us find life elsewhere

With Special Thanks to

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Garrett Roberts Kingman (Hell Cell, perchlorate detox)

Rolando Perez (fungal work)

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Jess Snyder (bio printing, Astropharmacy)

Alina Kunitskaya (Astropharmacy)

Devan Nisson (Astrobiology)

Ivan Paulino-Lima (Hell Cell, biomining)

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Kosuke Fujishima (origin of life, iGEM)

Nils Aversch (polymers)

Daiki Horikawa (tardigrades)

Stephan Leuko (extremophiles)

Charles Cockell (DNA synthesis)

Jamie Foster (UV effects)

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Kiran Mahurkar (biomaterials)

Paloma Lenz (Biomining)

Ginger Buck (Biomining)

Hanna Krivic (mycotecture, astropharm)

Becca Blum (astropharmacy)

Dorra Omrani (astropharmacy)

Cagn Walker (baselining earth)

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Kat Korengay (mycotecture)

Karoli Clever (fungal)

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Monika Lipinská (mycotecture)

Julia van Etten (algal extremophiles)

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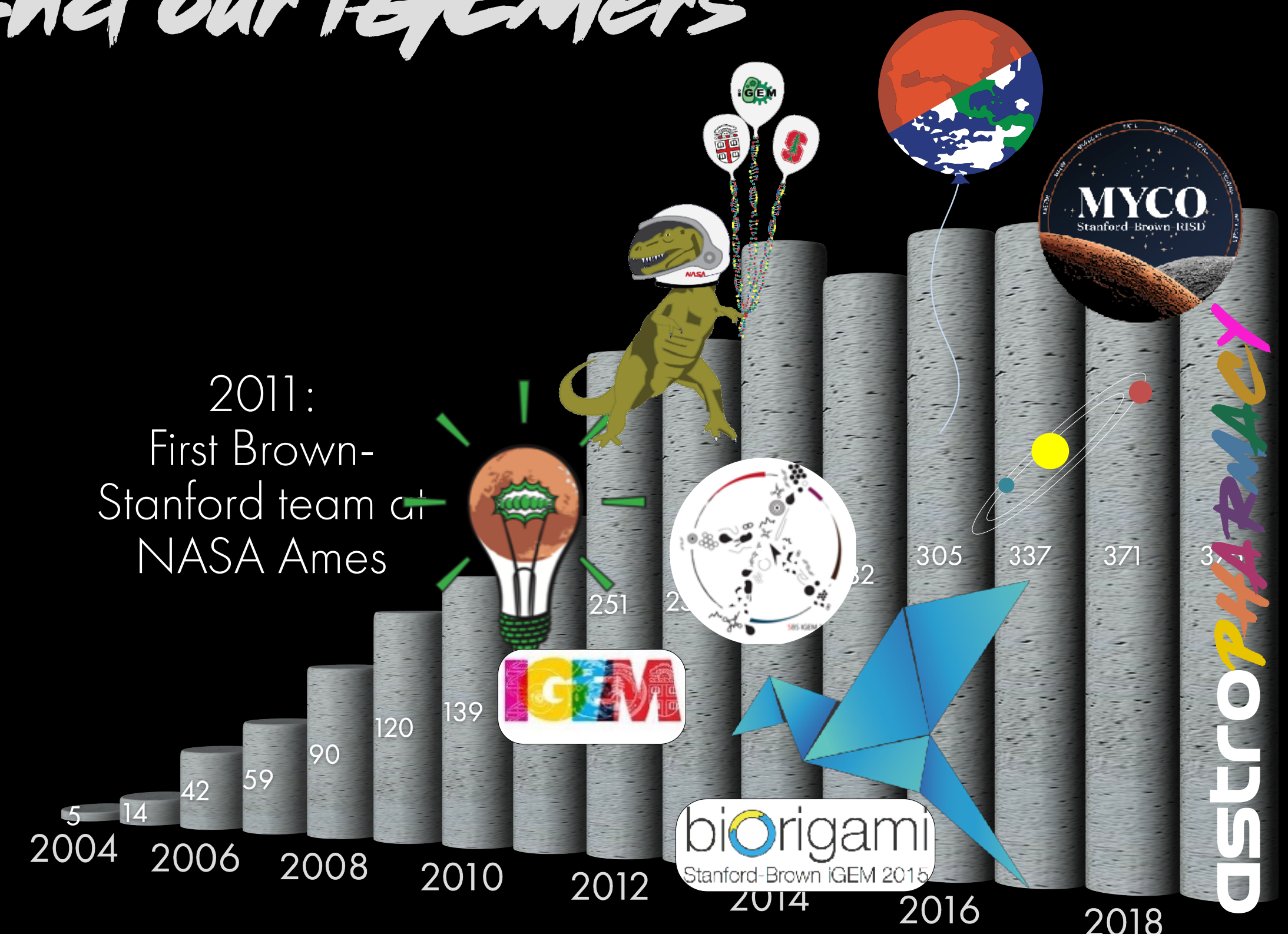
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Rocco Mancinelli (BAERI)

And many other wonderful undergrads, including

And our iGEMers

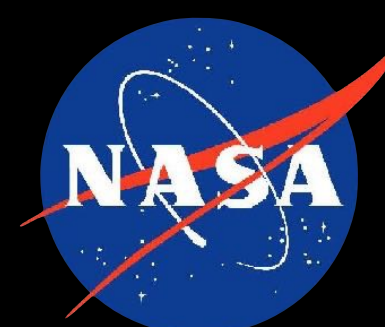


2011:
First Brown-
Stanford team at
NASA Ames

- ★ Our past projects
- ★ 2011: Synbio Enabled Mars Colony
- ★ 2012: The transit of synthetic astrobiology
- ★ 2013: BioCommunication
- ★ 2014: Towards a biodegradable UAS (drone)
- ★ 2015: BiOrigami

- ★ 2016: BioBalloon
- ★ 2017: Mars: Getting there & staying there
- ★ 2018: Mycotecture off planet
- ★ *most of have won major awards, press attention, Maker Faire awards, etc.

Funders:



TRANSLATIONAL
RESEARCH INSTITUTE FOR
SPACE HEALTH

