Synthesizing Abiotic Life in the Chemistry Laboratory

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and

Origins of Life Initiative

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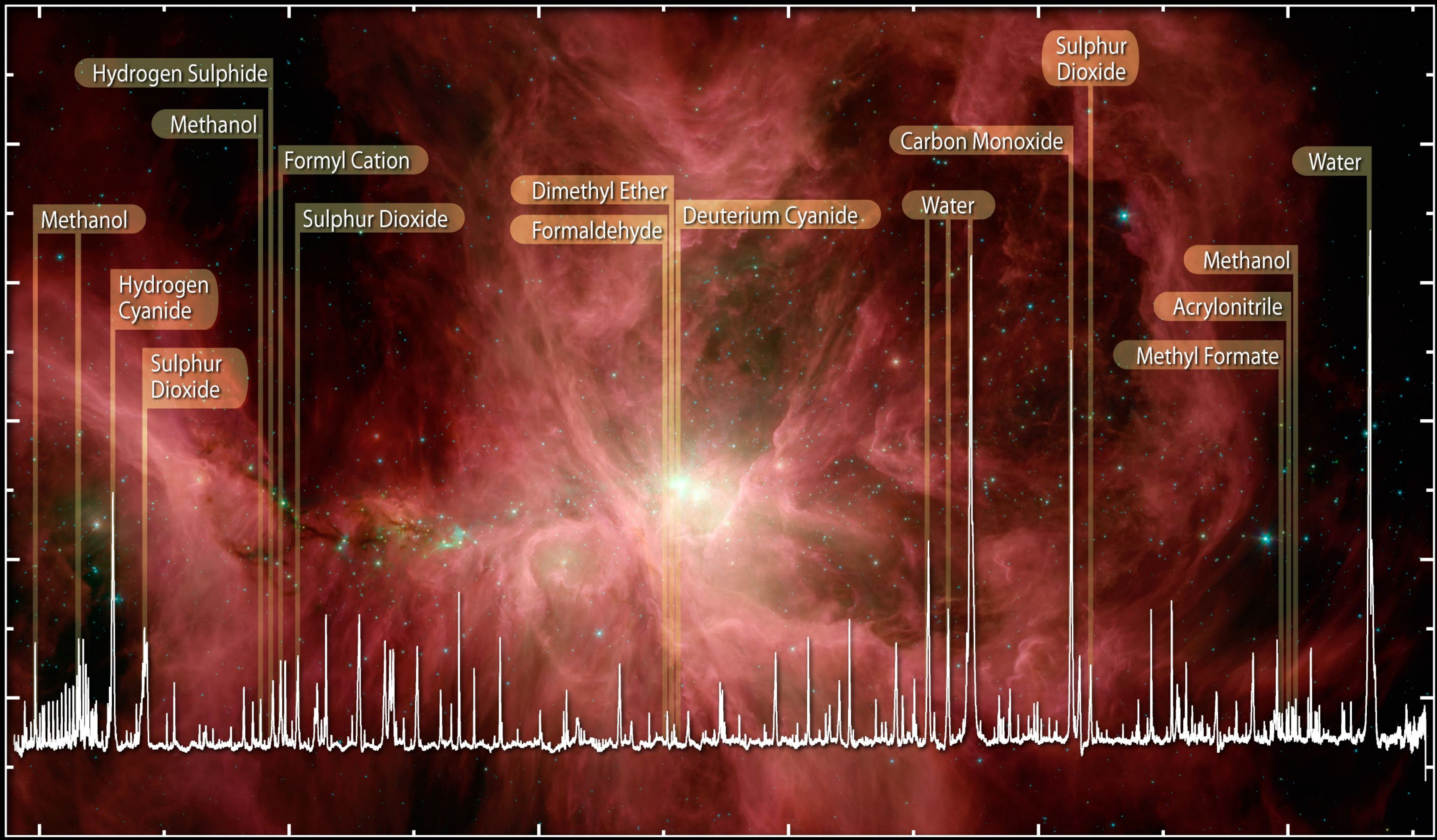
Cambridge, Massachusetts

Synthetic Cells at the Frontier: Navigating Innovation and Risk

National Academies of Science, Engineering and Medicine

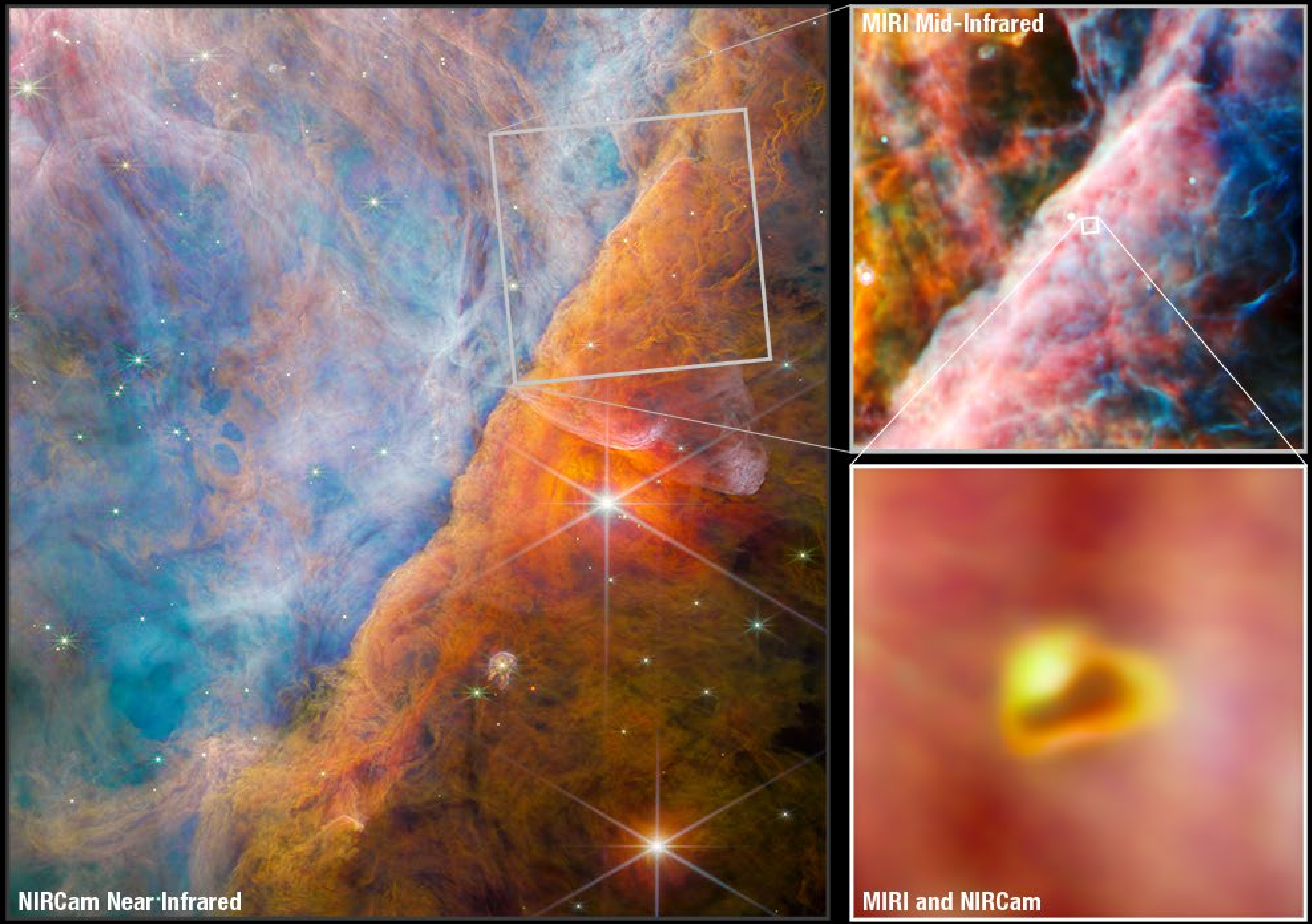
July 22, 2025, Washington, DC



We now know many details about the chemical complexity in the Interstellar Medium (ISM)

HIFI Spectrum of Water and Organics in the Orion Nebula

© ESA, HEXOS and the HIFI consortium E. Bergin

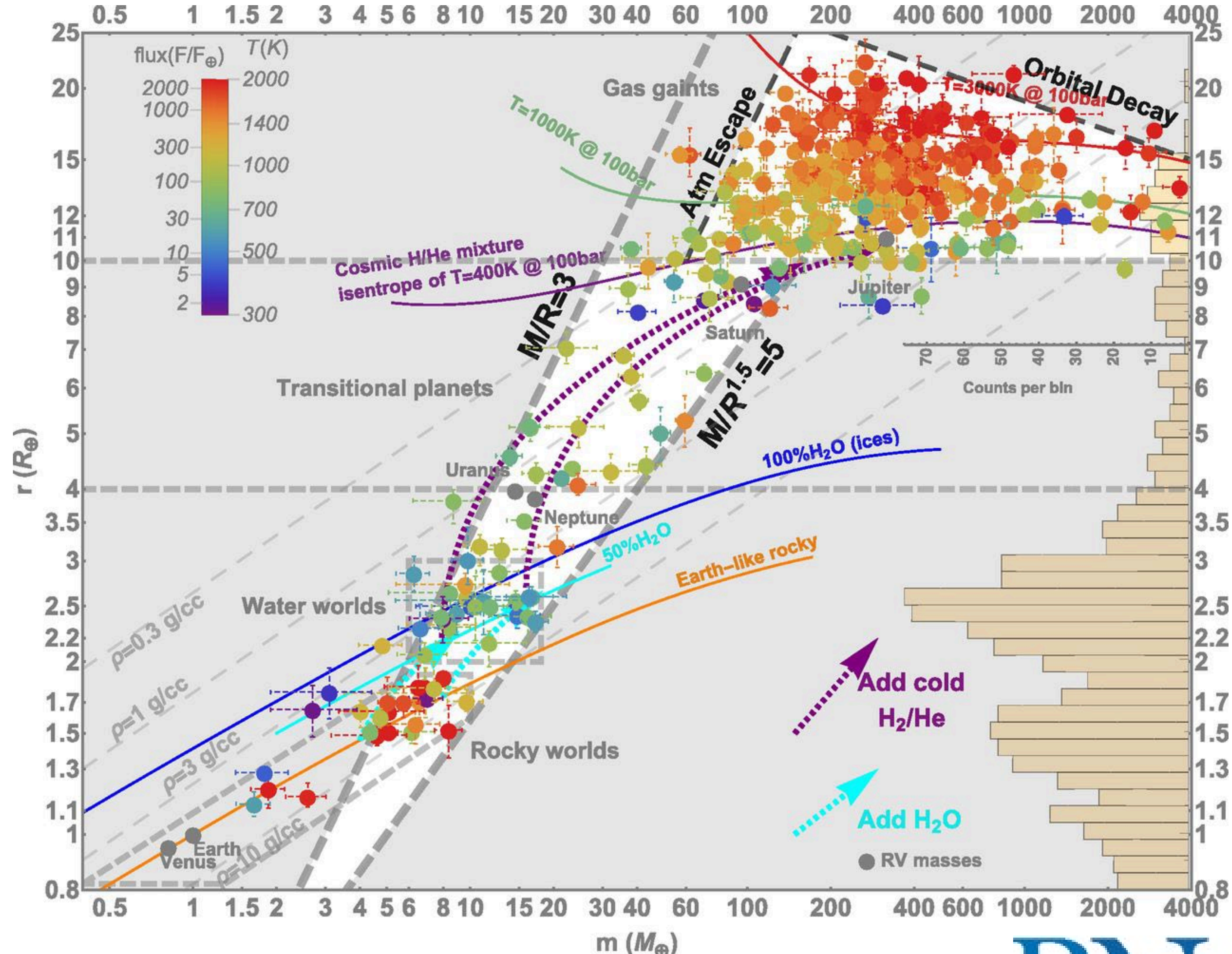


Discovery of Methyl CH_3^+ in the Orion Nebula's star d203-506 protoplanetary disk, a small red dwarf bombarded by strong UV light

Orion Bar Collage (NIRCam and MIRI Images)

NASA/ESA James Webb Space Telescope, July 2023

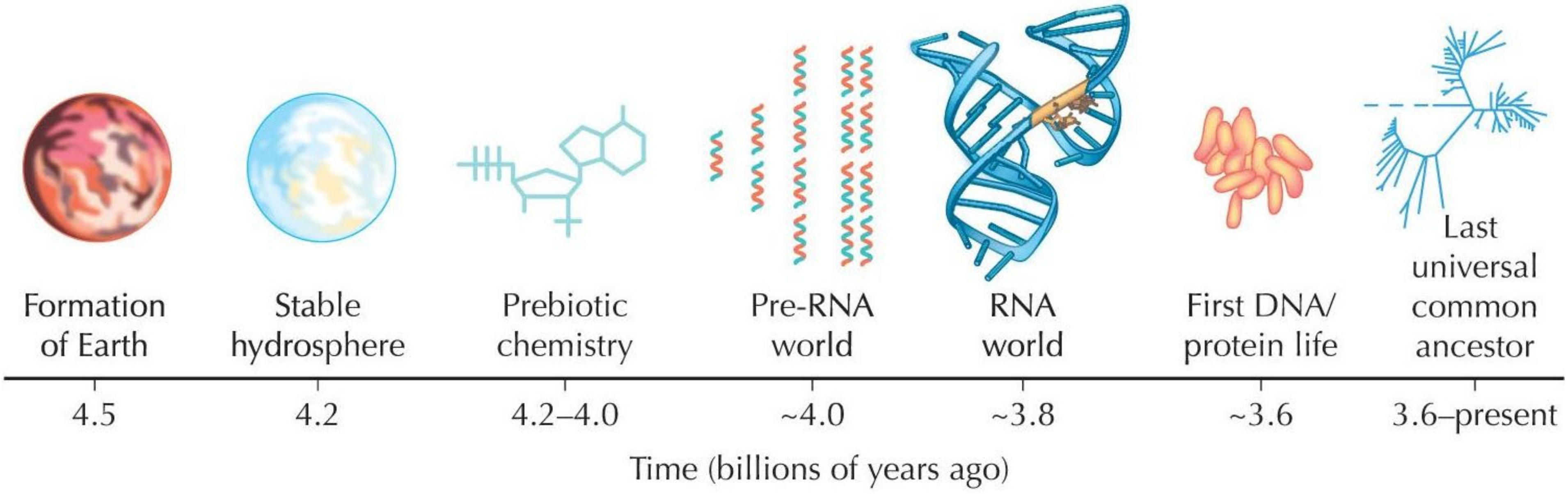
The mass–radius variations among selected exoplanets with masses determined by the radial-velocity (RV) method and densities constrained to better than ±50% (1-σ).



Li Zeng et al. PNAS doi:10.1073/pnas.1812905116

PNAS

The co-evolution of Earth, environment and life: from its birth 4,567 million year ago to LUCA



Protocell (LBB, Generalized Biology) era: lots of speculation

(Modified from G. Joyce, ~ 2002)

What characterizes All Life?

- Information (generation, transmission, storage, use for control and not re-inventing “the wheel”)
- Metabolism (making parts and energy …)
- Programmed/Controlled Self-reproduction
- Evolution (adaptive and non-adaptive)

Refs.: Eigen, Küppers, JP-M, Mariscal-Doolittle, Nurse

At least since LUCA implemented and unified in the Cell Division Cycle via biochemistry using standard physico-chemical processes.

1. All the above is based on and uses standard physico-chemical processes

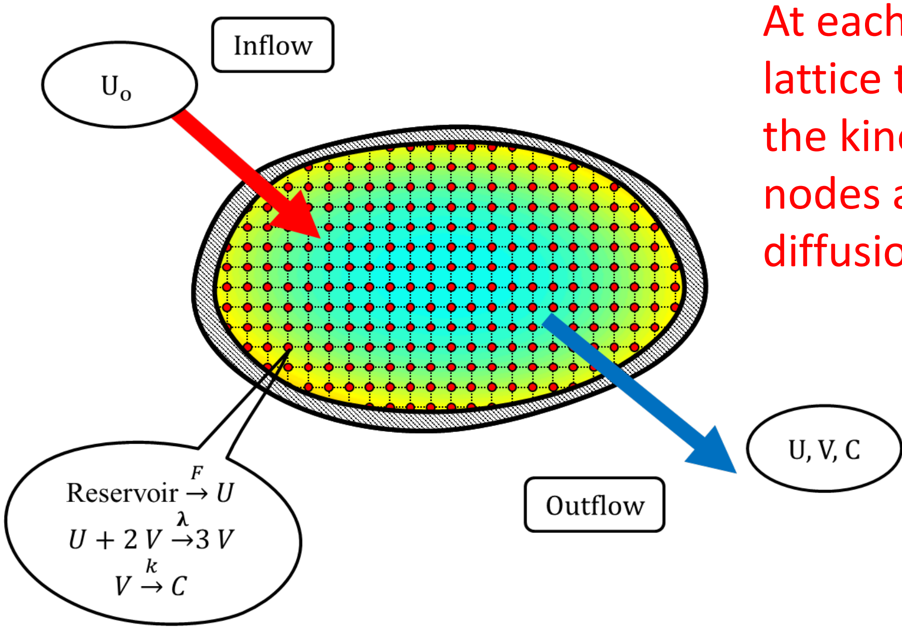
2. But … there is a huge leap in “complexity” from chemistry to biochemistry, and on to extant life

3. Does the extensively validated fundamental physics tenet that “the complexity at the surface is a reflection of a very deep simplicity” also hold here?

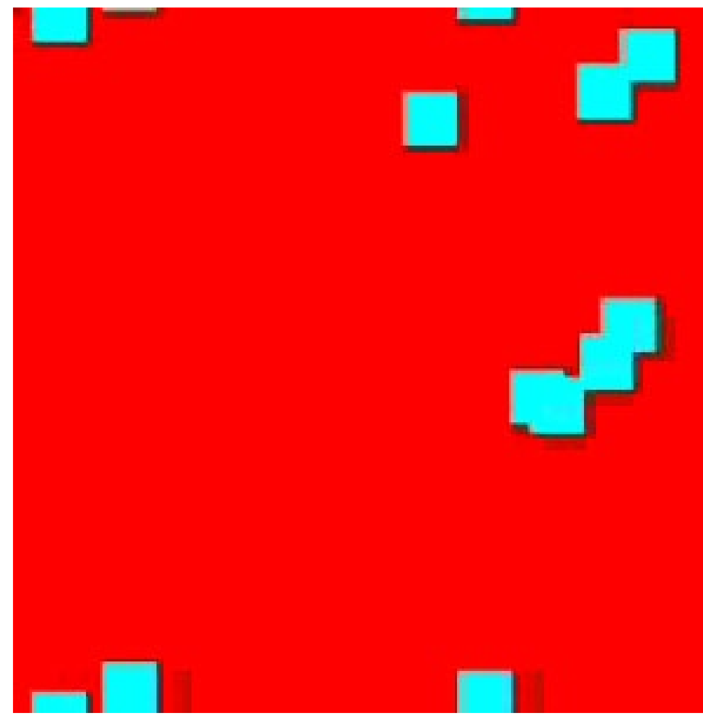
- We may ask: what is the simplest chemistry-based life-mimic system we can synthesize in a 1-pot reaction using small molecules?
- Can we “engineer”/”integrate”/”unify” these functional properties into an aqueous artificial chemical system without biochemistry?

- Where do we start? Bring in the methods and power of physics

A mass-action kinetics minimal model incorporating waste and unifying the four properties



At each node in the spatial lattice there is one instance of the kinetic equations. The nodes are interconnected by diffusion



$$\frac{\partial u}{\partial t} = -\lambda\, uv^2 + F(u_0 - u) + \eta_u + D_u \nabla^2 u$$

$$\frac{\partial v}{\partial t} = +\lambda\, uv^2 - (F + k)v + \eta_v + D_v \nabla^2 v$$

$$\frac{\partial c}{\partial t} = k\, v - F\, c + \eta_c + D_c \nabla^2 c$$

Munuzuri and JP-M, Physics of Life Reviews 2022
Lesmes, Hochberg, Morán and Pérez-Mercader, PRL-2003, PRE 2004

How to “translate equations” into chemistry and boot-up a non-biochemistry operated artificial living system?

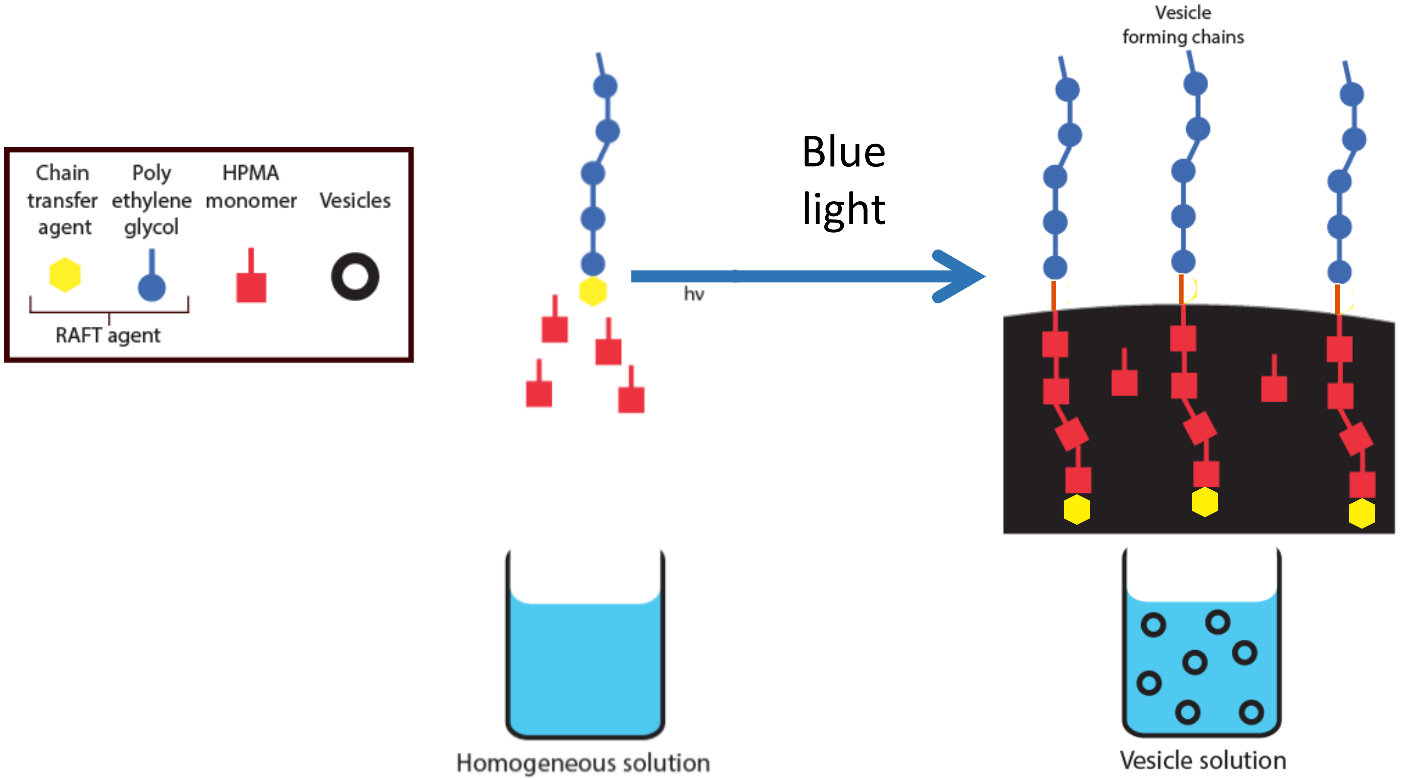
- Autonomously from a heterotrophic state of high entropy
  - Concentration problem/Arithmetic demon
  - How can this be overcome?
- What is the set of initial or boundary conditions?
- Dynamical Self-assembly driven encapsulation

Oparin/Miller/Urey, Ireland, Serratosa

NO BIOLOGICAL MATERIALS ALLOWED

(Except for researchers)

PISA: Polymerization Induced Self-Assembly



(1) Wan, W. M.,Sun, X. L. and Pan, C. Y., Formation of Vesicular Morphologies via Polymerization Induced Self-Assembly and Re-Organization, *Macromol. Rapid Commun.*, **31**, 399 (2009)

(2) Blanazs, A., Madsen, J., Battaglia, G., Ryan, A. J. and Armes, S. P. Mechanistic insights for block copolymer morphologies: how do worms form vesicles *J. Am. Chem. Soc*. **133**, 16581-16587 (2011)

(4) Charleux, B., Delaitre, G,, Rieger, J., D'Agosto, F., Macromolecules 45, 6753-6765 (2012)

(5) Yeow, J., Xu, J. and Boyer, C., Polymerization-Induced Self-Assembly Using Visible Light Mediated Photoinduced Electron Transfer–Reversible Addition–Fragmentation Chain Transfer Polymerization, *ACS Macro Lett.* **4**, 984–990 (2015)

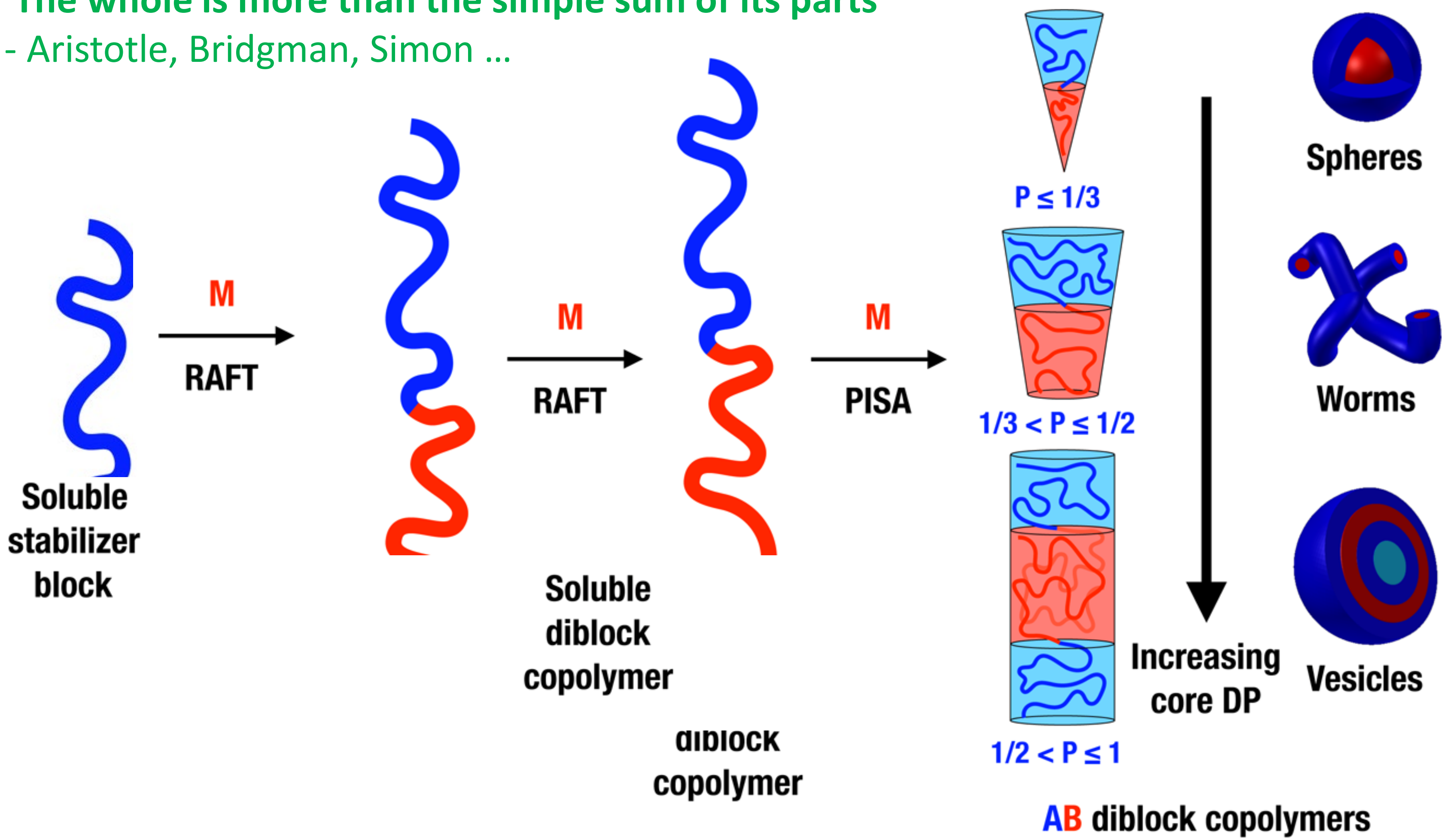
(6) Szymanski, J. and Pérez-Mercader, J. Direct Optical Observations of Vesicular Self-Assembly in Large-Scale Polymeric Structures During Photocontrolled Biphasic Polymerization. *Polymer Chemistry* **7**, 7211-7215 (2016)

(7) Szymanski, J. and Pérez-Mercader, J. Straightforward Synthesis Route to Polymersomes with Simple Molecules as Precursors. *Langmuir.* **30**, 11267-11271 (2014)

Polymerization Induced Self-Assembly (PISA): an out of equilibrium dynamical phase transition under the control of chemistry

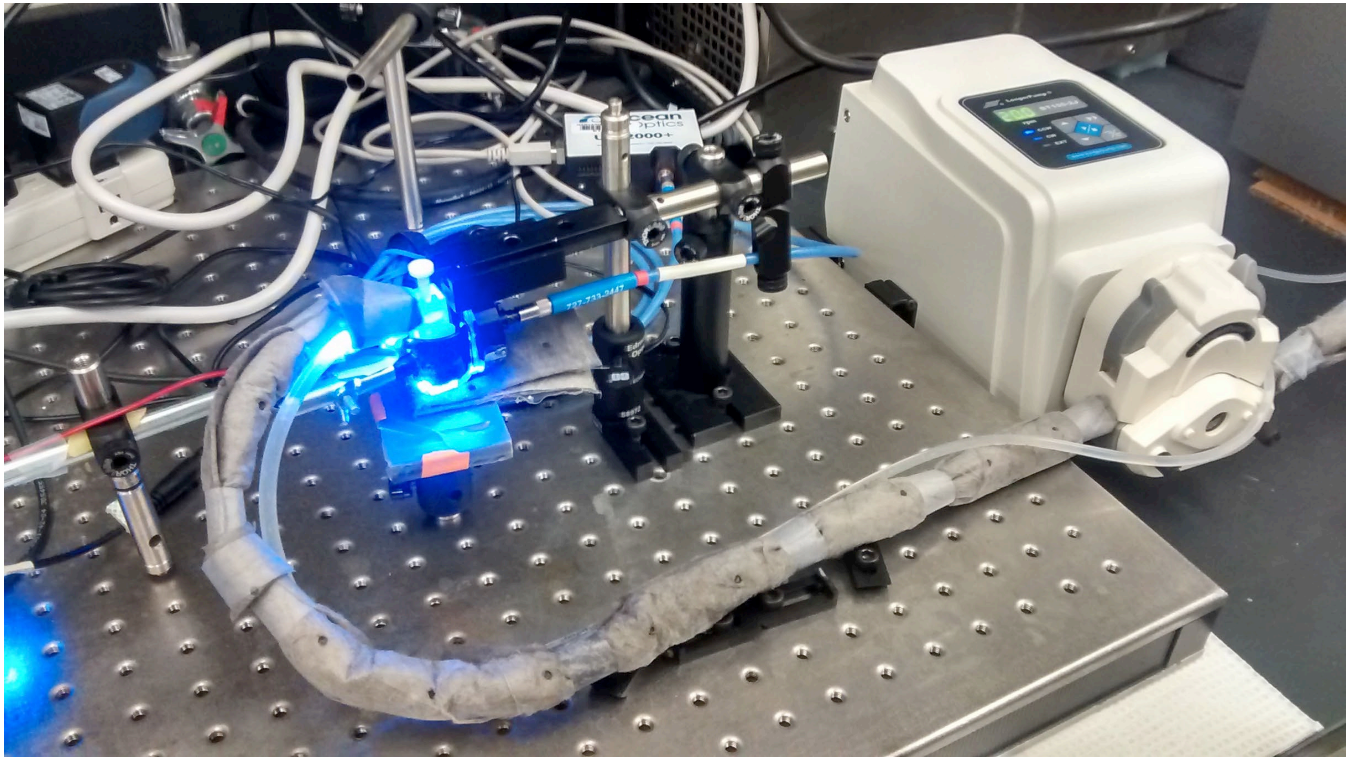
"The whole is more than the simple sum of its parts"

- Aristotle, Bridgman, Simon …



S. L. Canning, G. N. Smith and Steven P. Armes, *Macromolecules* 2016, 49, 1985.

Experimental workflow



CCD image acquisiton

blue light

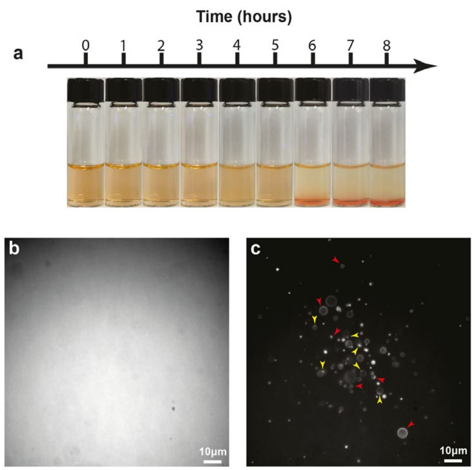
16 hours of polymerization in a thermostated and illuminated vial

Mixed: water, HPMA/AN monomer, PEG, RAFT agent (cont. sulphur), ruthenium(II) tris(2,2'-bipyridyl) chloride

Sample withdrawn, stained with fluorescent dye and observed with a microscope under continued illumination in an "oxygen starved" medium

Albertsen, Szymanski and JP-M, Scientific Reports, 2017

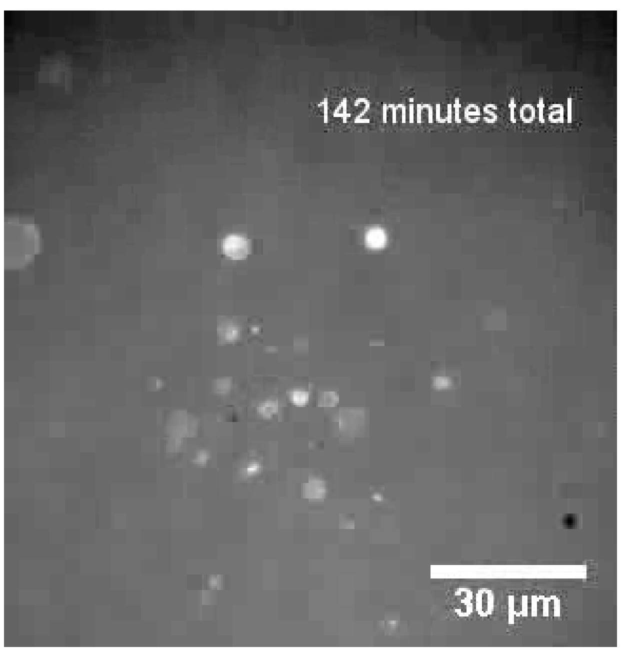
An autopoietic "warm little pond"

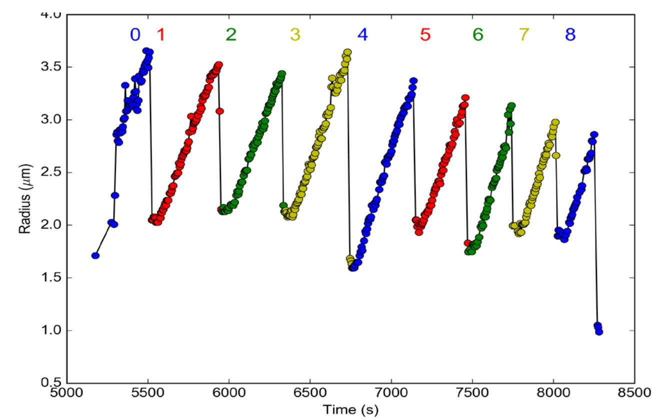


From a homogeneous, and heterotrophic mixture of non-biochemical molecules, including fuels

"Booted-up" out of equilibrium by light

To a phase-separated autopoietic ecosystem of life-mimics





Periodic vesiculation-growth-implosion cycles promoted by chemiosmosis and illumination (which control underlying chemistry, system and population behavior)

Albertsen, Szymanski and JP-M, Scientific Reports, 2017

A form of what we call BIChOSS (“bugs” in Spanish):
Biologically Inspired Chemically Operated Synthetic System

Supporting Video No. 1

for

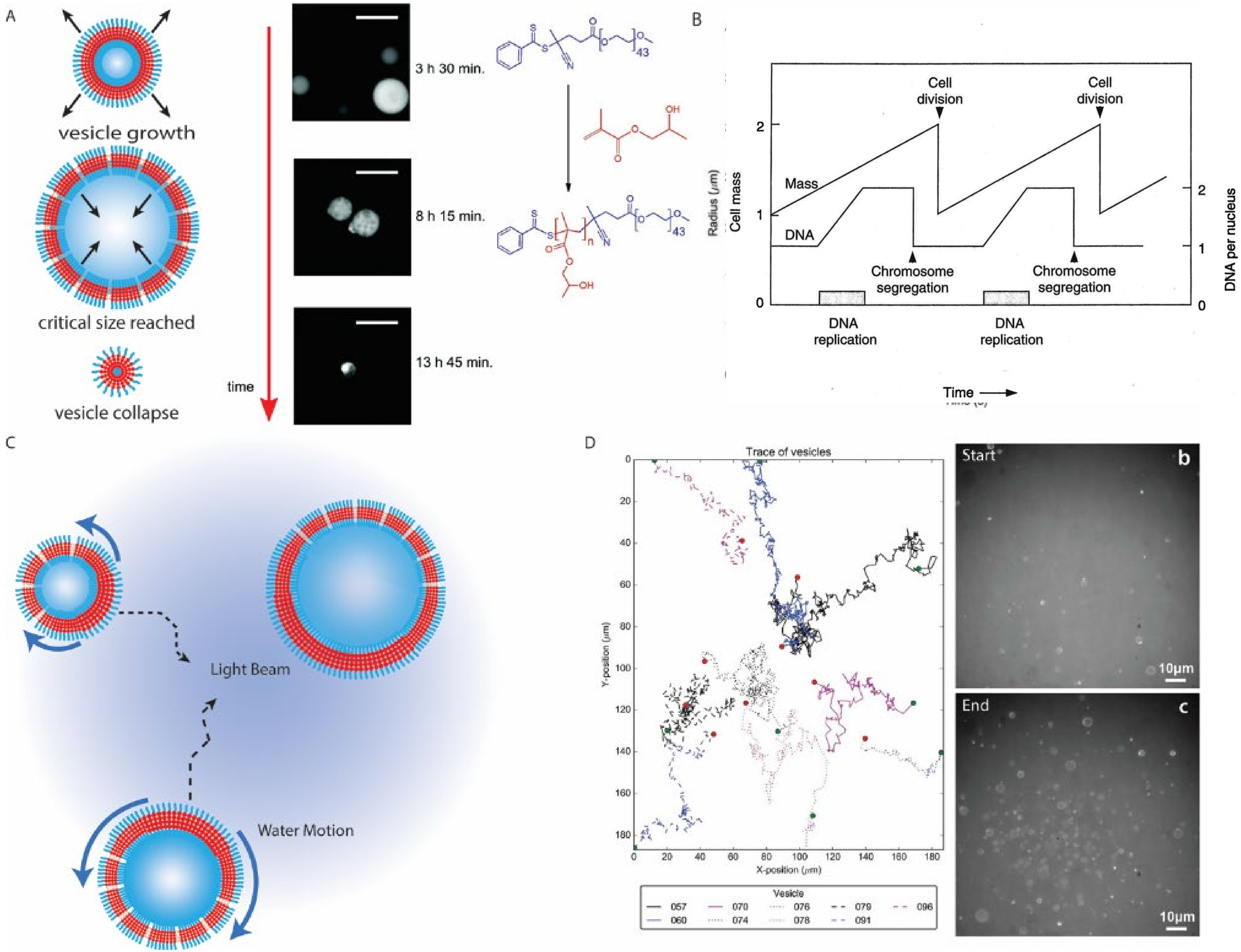
EMERGENT PROPERTIES OF GIANT VESICLES FORMED BY A POLYMERIZATION-INDUCED SELF-ASSEMBLY (PISA) REACTION

by

Anders N. Albertsen, Jan K. Szymański,
and
Juan Pérez-Mercader

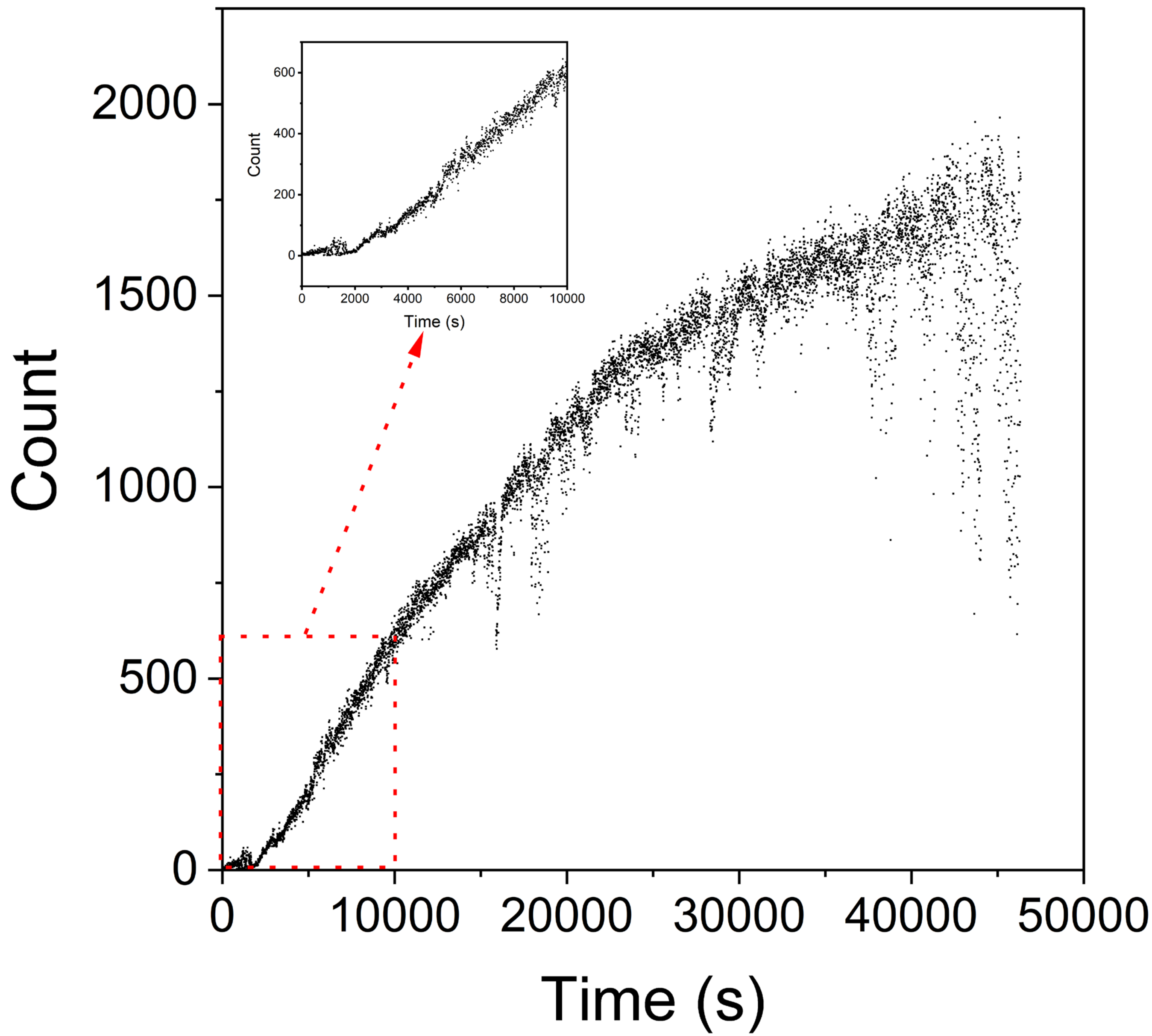
From a Homogeneous Non-biochemical Soup to the Emergence of the Fundamental Features of Life, including Adaptation.
Physics and Chemistry Working together at micron scales

Albertsen, Szymanski and JP-M, Scientific Reports, 2017



A
vesicle growth
critical size reached
vesicle collapse
time
3 h 30 min.
8 h 15 min.
13 h 45 min.
B
Cell division
Cell division
Mass
DNA
Cell mass
DNA per nucleus
Chromosome segregation
Chromosome segregation
DNA replication
DNA replication
Time
C
Light Beam
Water Motion
D
Trace of vesicles
Y-position (μm)
X-position (μm)
Vesicle
057
060
070
074
076
078
079
091
096
Start
b
10μm
End
c
10μm

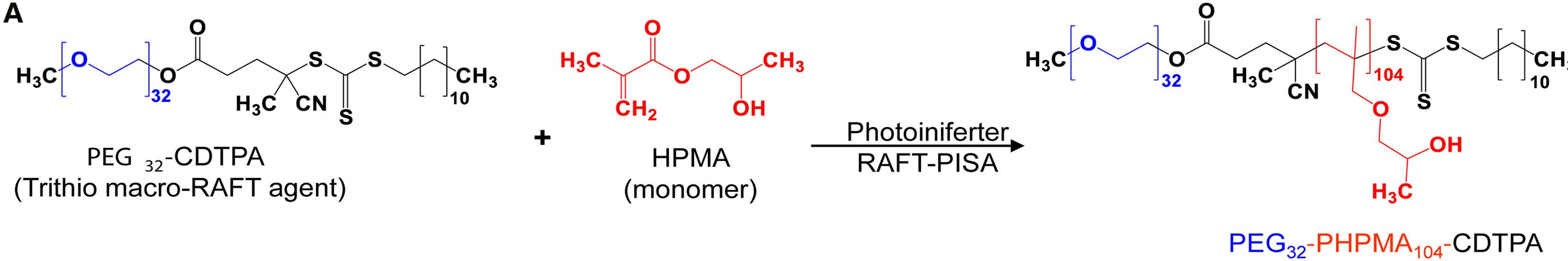
Time change of the population size (number of individuals)



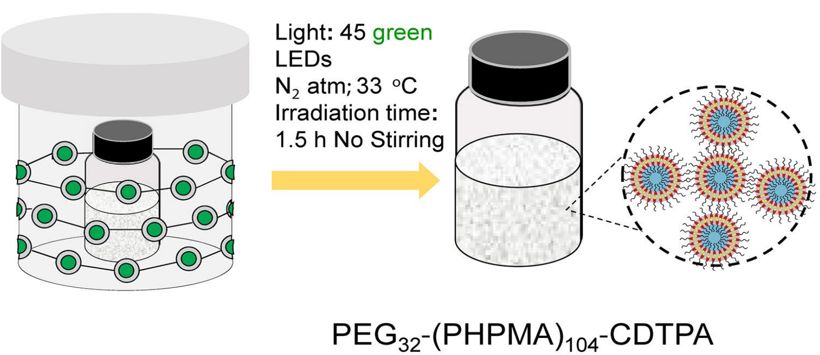
Lin, Katla and JP-M, Comms. Chem. 2021

Another example: Self-booted (autopoietic) Population of Abiotic, and Self-reproducing Synthetic Artificial Cells

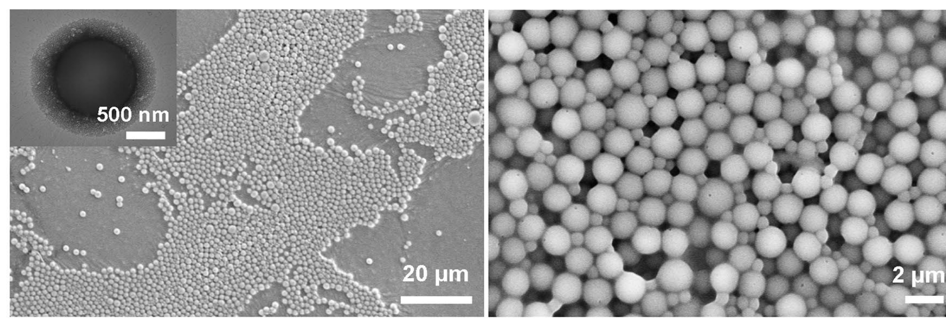
A



B



C

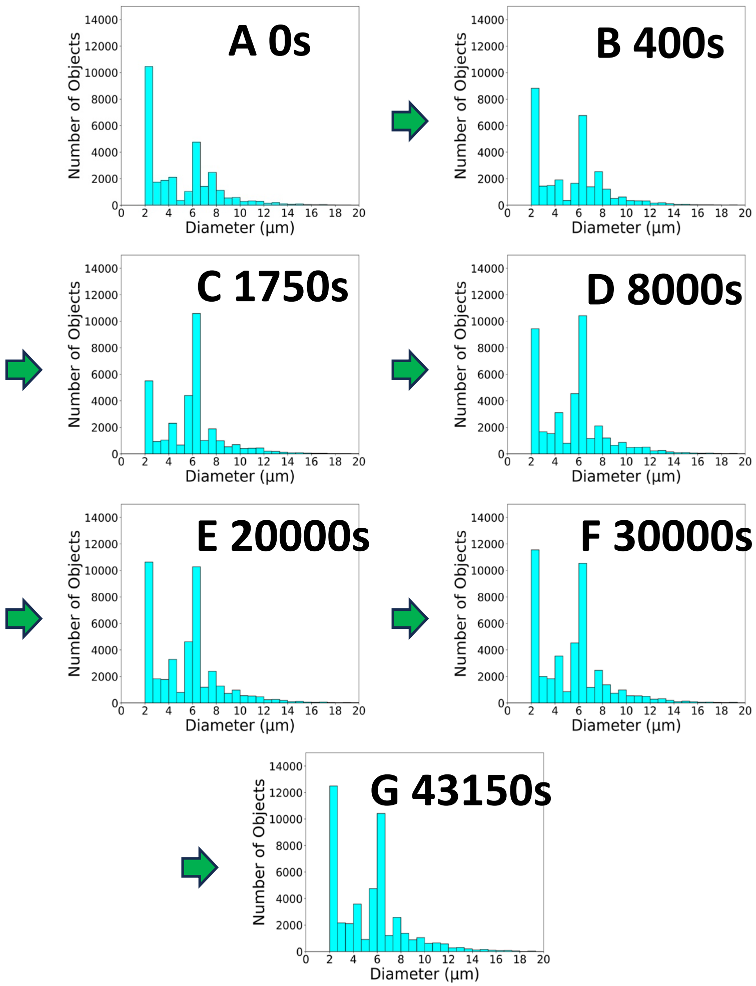


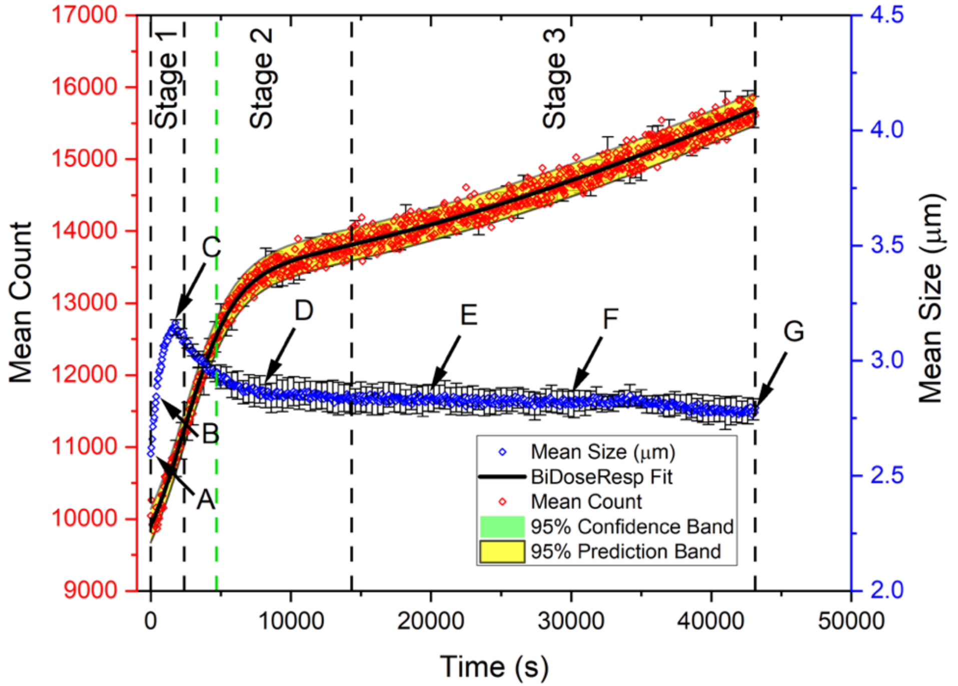
SEM images showing the low magnification and TEM (inset) image showing the hollow core of the vesicular cells.

Cell PRESS

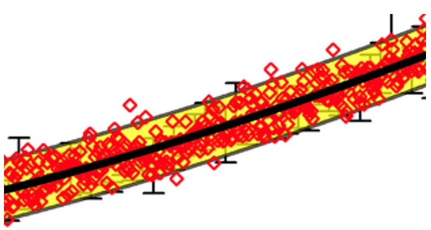
Katla, Lin and JP-M, Cell Reports Physical Science 2023 and PNAS 2025

Time development of Synthetic Abiotic Cell Population and Their Diameters During Three Experiments

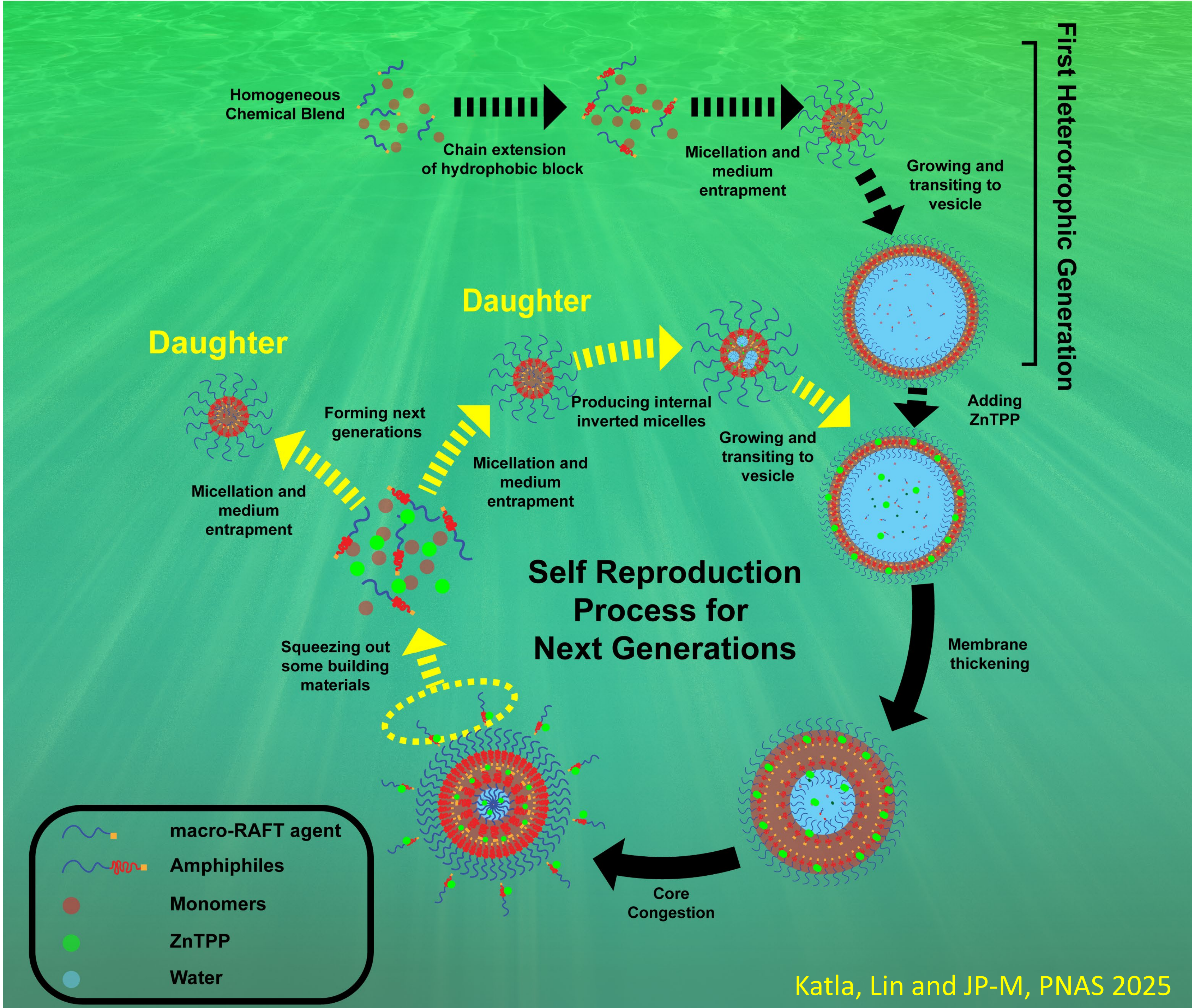




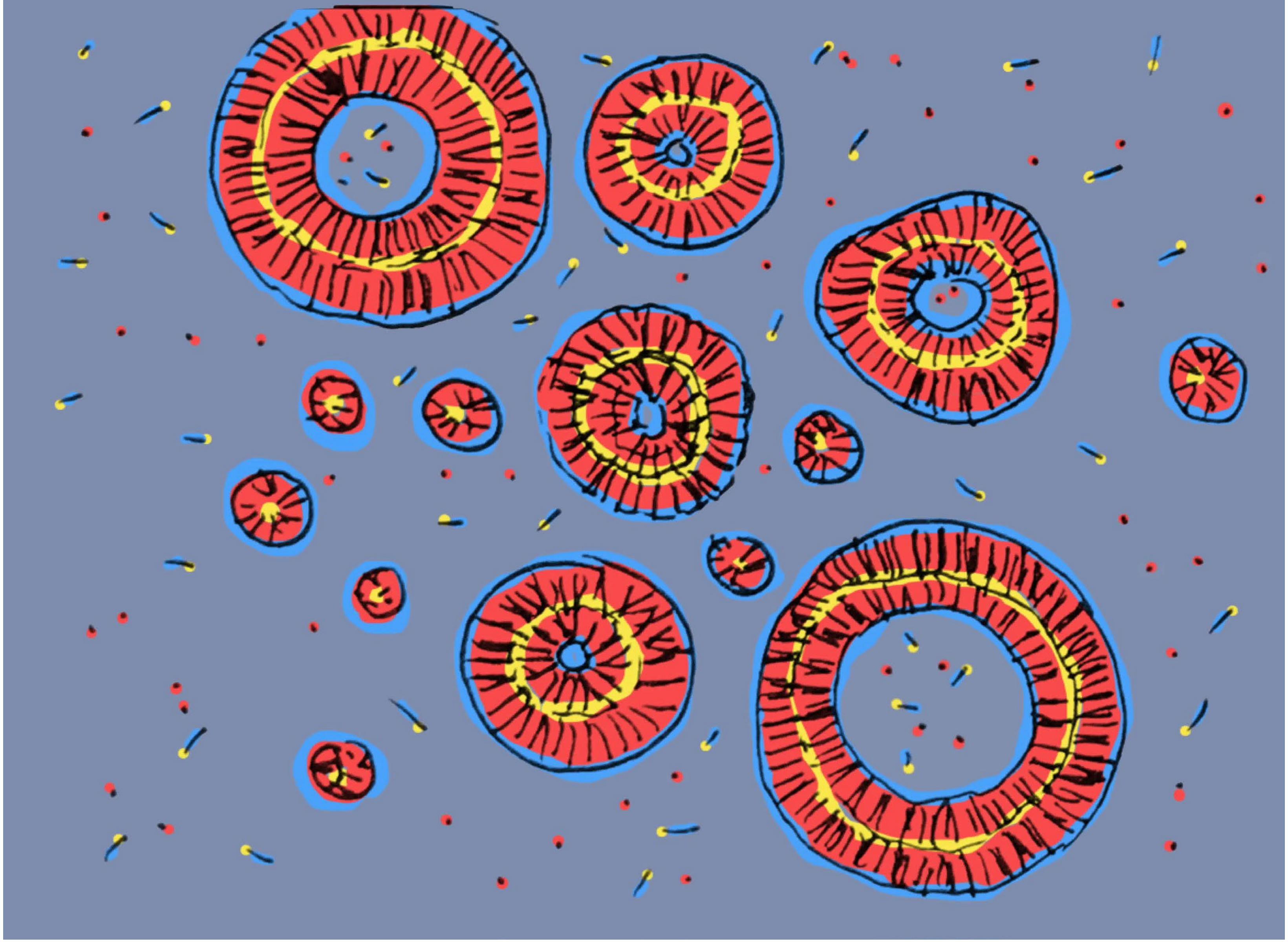
Detail of SDOM errors for 3 repetitions of experiments



Katla, Lin and JP-M, PNAS 2025

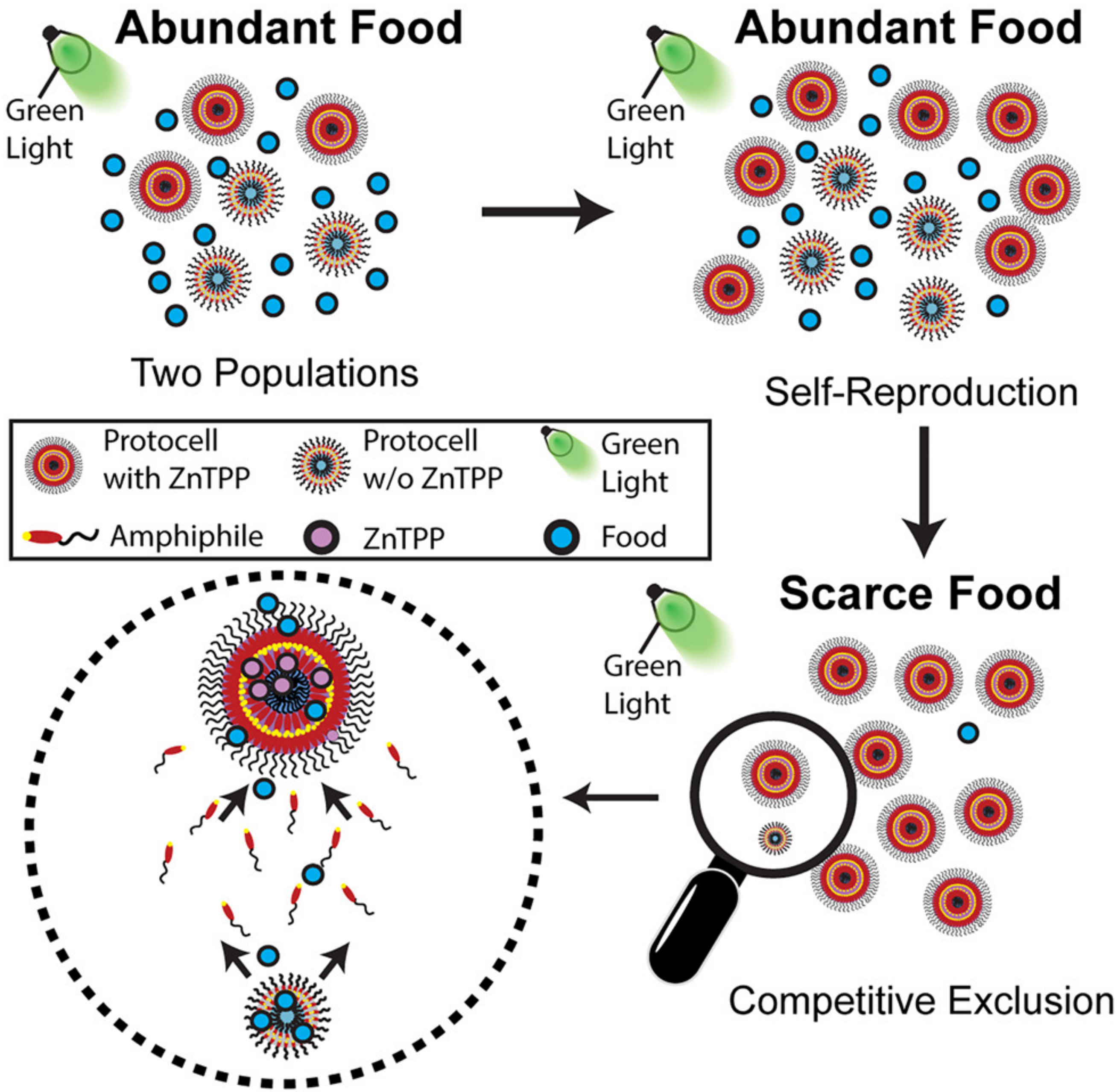


Katla, Lin and JP-M, PNAS 2025



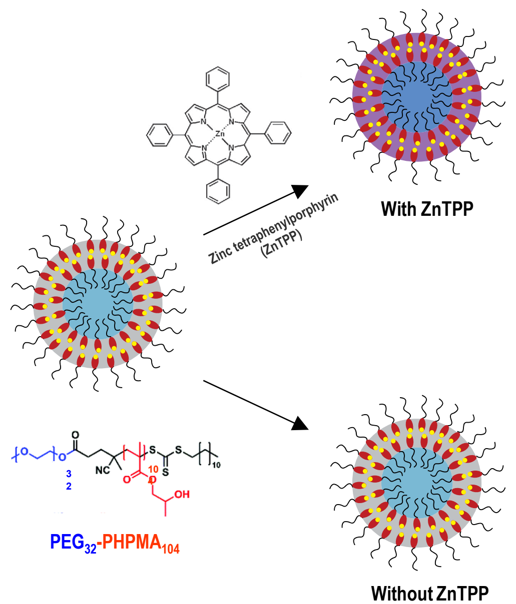
A cartoon view of living RAFT polymerization of an amphiphile from three molecules and the induced self-organization, self assembly, evolution and reproduction of vesicles in PISA

Images by Janet Iwasa. Video-montage by Alec Pawling. Work in progress, 2025

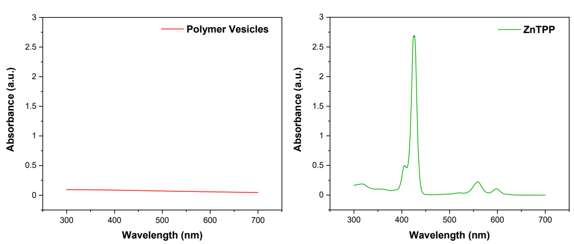


Katla, Lin and JP-M, Cell Reports Physical Science 2023

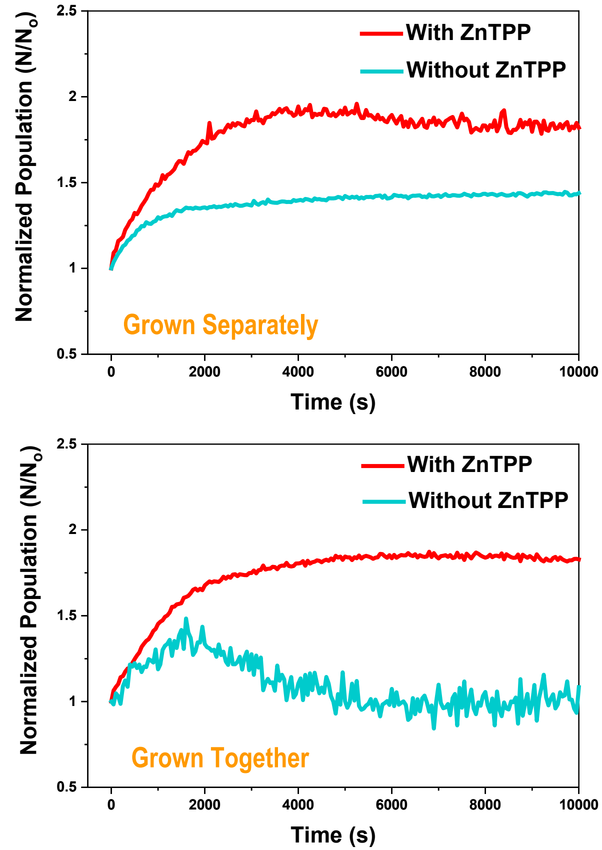
Gause's Competitive Exclusion Principle and Darwin's "struggle for life"



UV-Vis Absorption Spectra

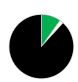


Competition in Polymer Vesicles

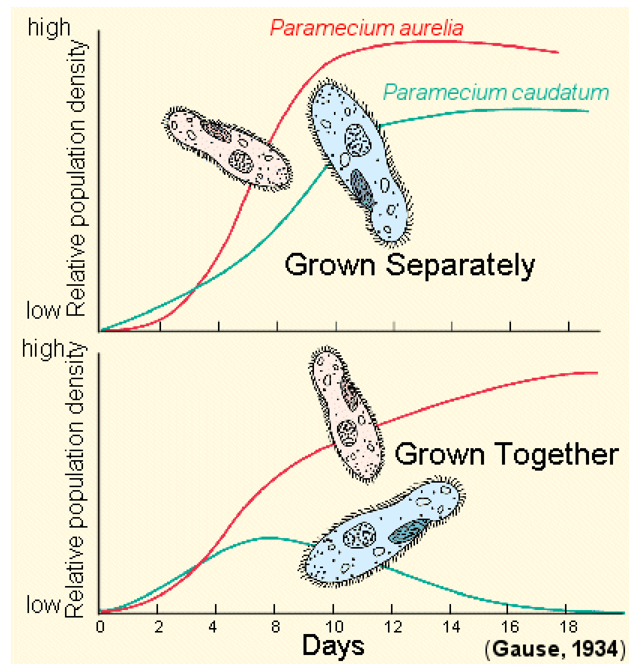


Light Irradiation Conditions:

Green = 1 s
White = 0.5 ms
Dark = 10 s



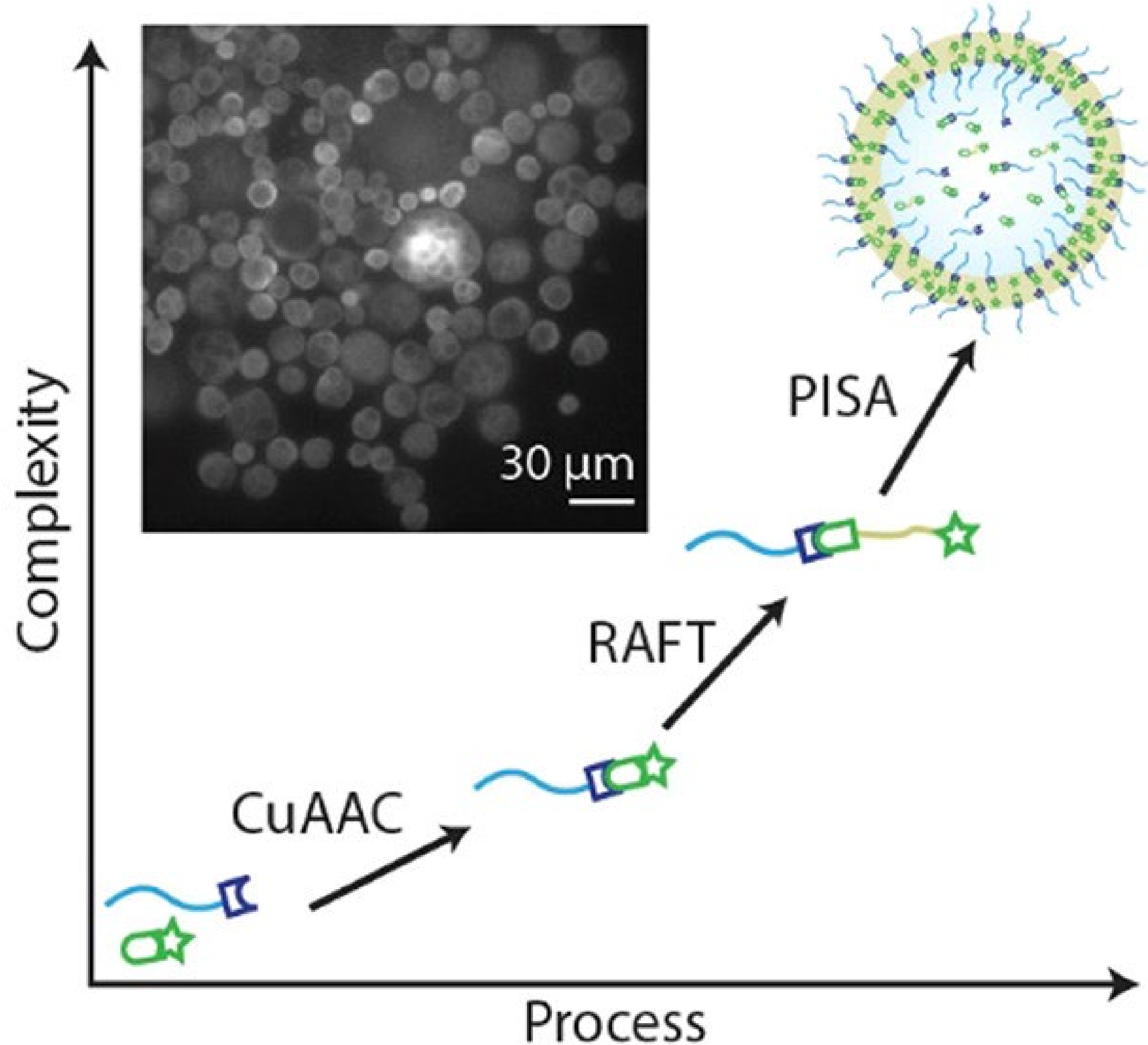
Competition in Paramecium Species



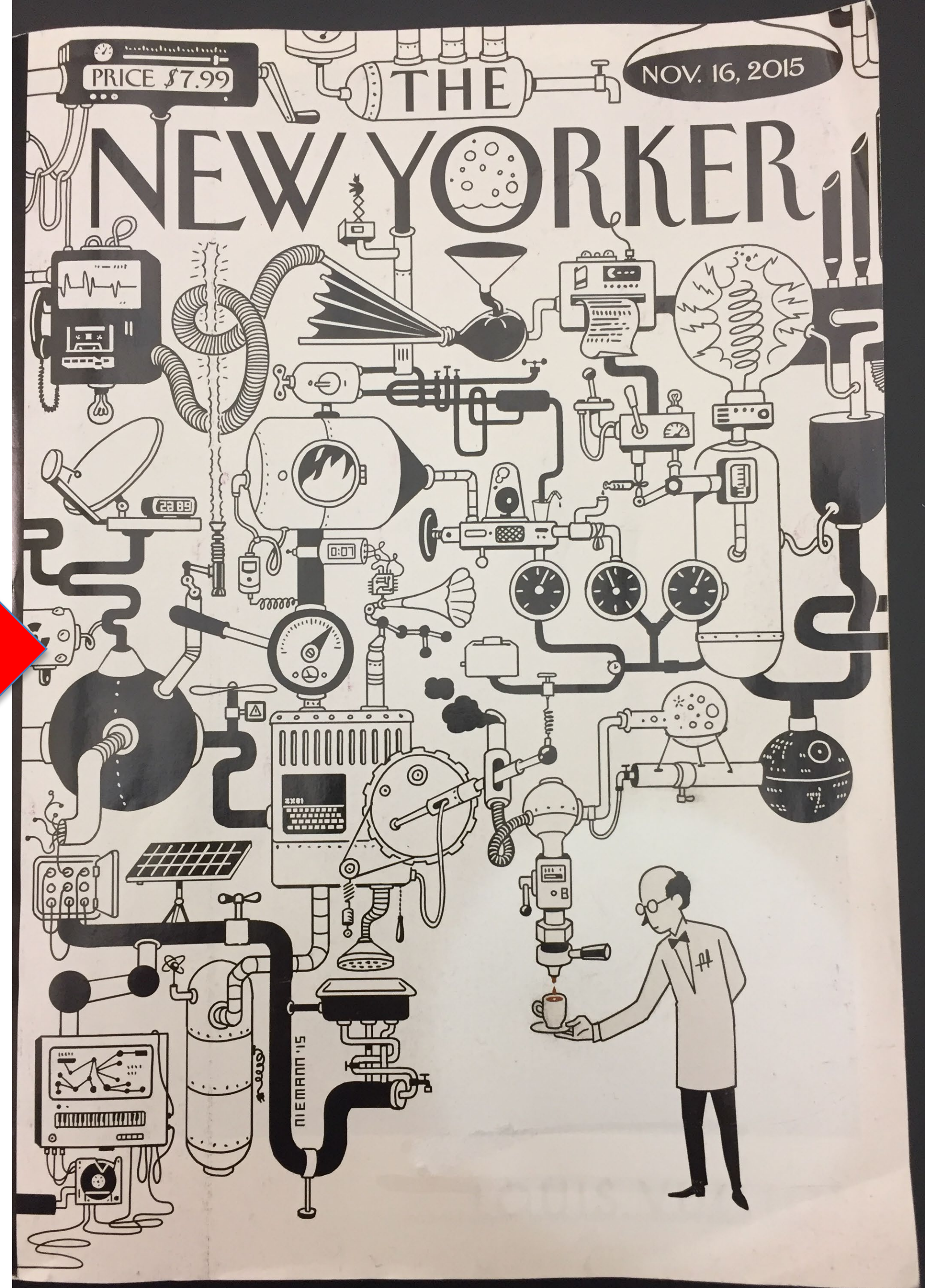
Gause, G. F. (1934). *The Struggle For Existence* (1st ed.). Baltimore: Williams & Wilkins.

Katla, Lin and JP-M, Cell Reports Physical Science 2023

Adding a second feedback loop using click chemistry enables Adaptation and a path forward for chemical evolution



S. Pearce and J. P-M, ACS Central Science 2021
S. Pearce, C. Lin and JP-M, ACS Nano Letters 2024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THE
NEW YORKER
NOV. 16, 2015
NIEMANN '15

“The origin of life maybe a virtually automatic consequence of carbon chemistry and the physics of self-organizing systems – given favorable environments and requisite inorganic constituents.” (S. J. Gould, NYT editorial, August 11, 1996)

There are literally thousands of chemicals that can implement these abiotic PISA-based systems “living” in their “heterotrophic” “little warm ponds”

They can exist in a large class of organic solvents

They mostly take advantage of chemiosmosis, the hydrophobic effect and presence of defects

They can be adaptive and “evolve” by degradation, competition and or co-option of materials in their medium to generate catalysts

Growing community: China, Australia, Europe (incl. UK)

Some applications:

Drug delivery, mining, microplastic management, origin of life studies, exoplanets, life in the Universe/astrobiology, why life?

Thanks to these Postdoctoral Fellows and Associates in the Perez-Mercader Group between 2013 and 2025:

- Jan Szymanski
- Anders Albertsen
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- Alberto Munuzuri
- Gourab Goshal
- Frederick Cooper
- Yuandu Hu
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- Kaixuan Ren
- Sudhina Guragain
- Bishnu Bastakoiti
- Gong Cheng
- Eszter Poros-Tarcali
- Chenyu Lin
- Sai Krishna Katla
- Samuel Pearce
- Kumar Siddharth

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