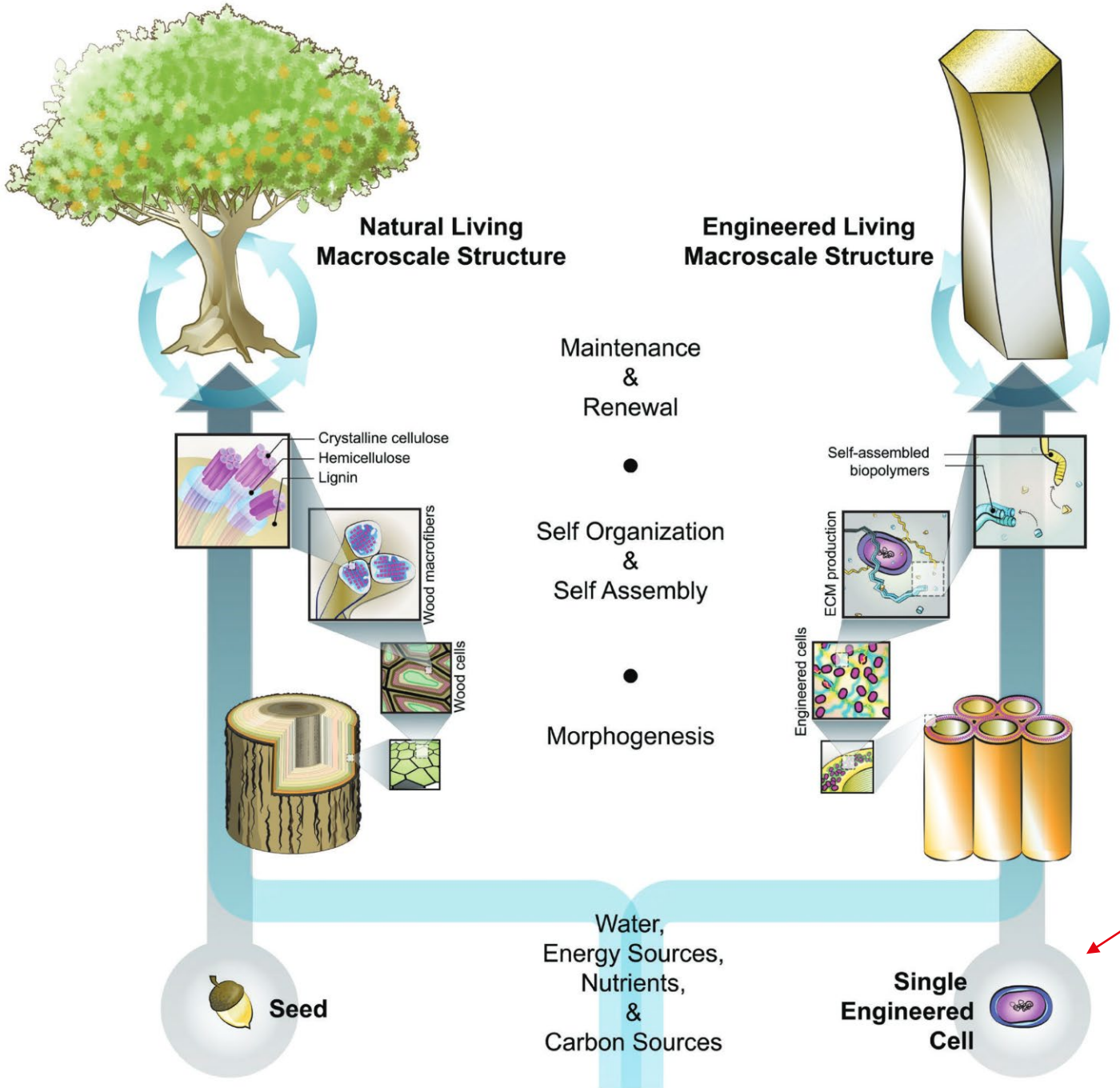
ELM Basics MSE 493

Prof. Tiffany Abitbol

2024



ELMs as bioinspired materials engineering

Uses tools of synthetic biology

DOI: 10.1002/adma.201704847

OK, so what is an ELM? - *recap*

- Living cells **form or assemble the material**
- These living cells are materials factories, drawing energy from their environment: to create biopolymer building blocks and to guide material formation and maintenance
- Allows for stimuli-responsiveness over the course of the lifetime of the cells (adaptive gene expression)
- Composed of cells OR of extracellular secretions (like biofilm)
- If desired, can be processed or programmed to kill the living cells at a given time, keeping the material intact (no concern for maintenance or potential biohazard threats)

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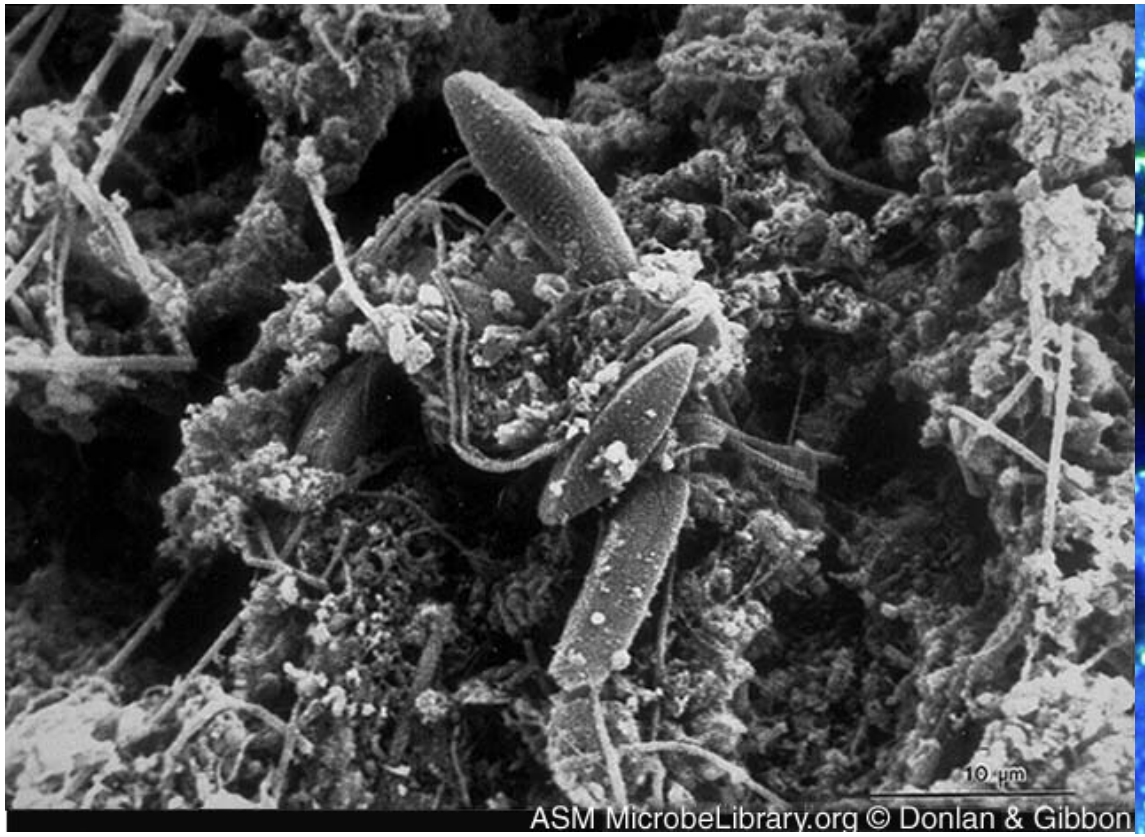
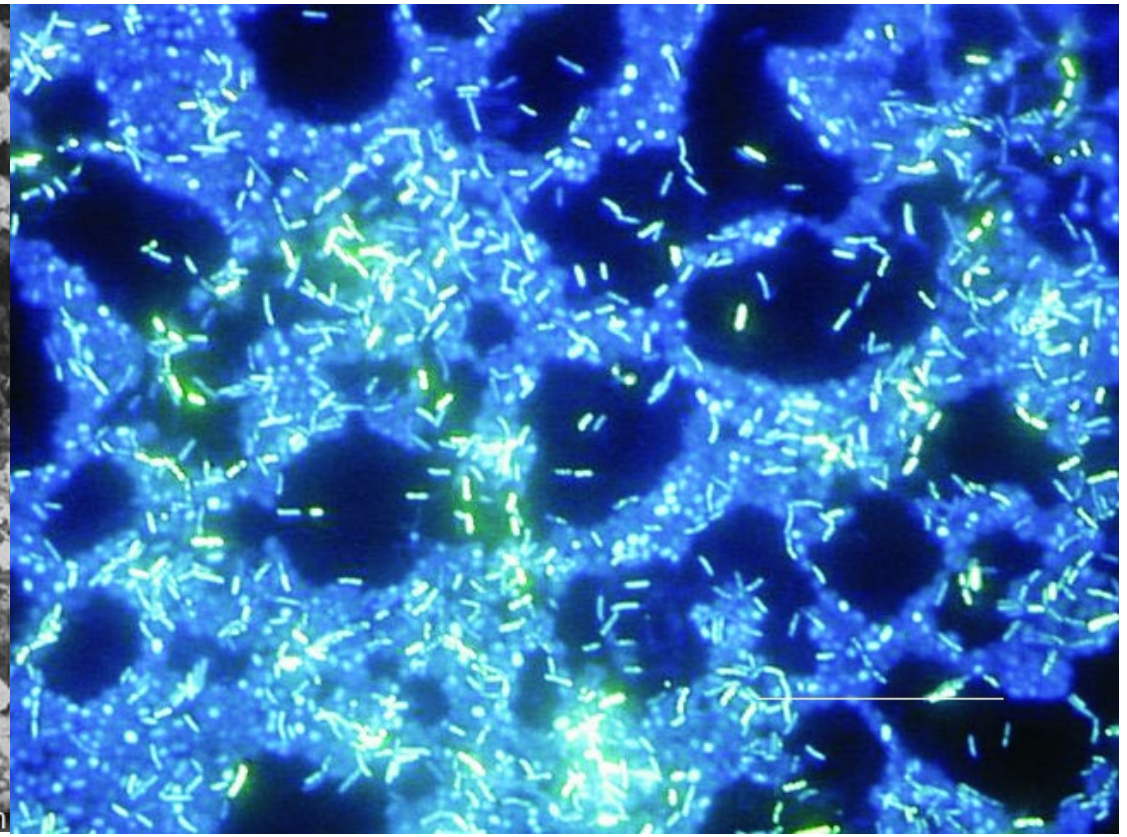
Biofilms



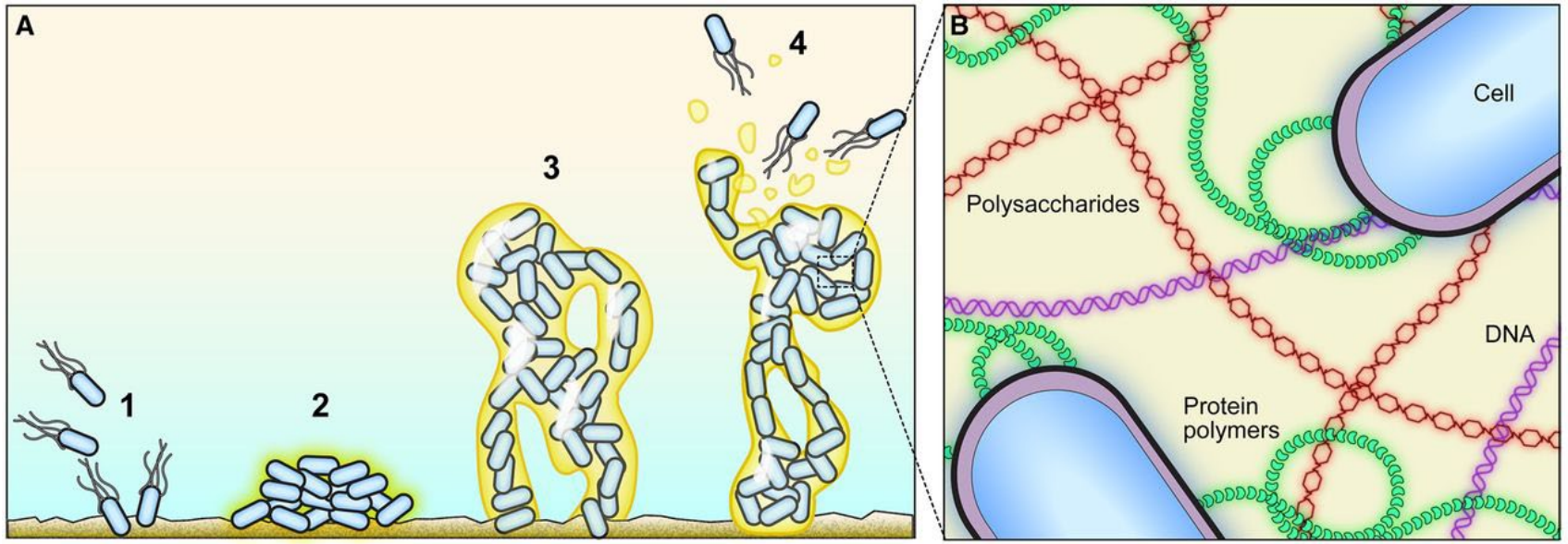


Biofilms on steel surfaces

doi: 10.3201/eid0809.020063

Biofilms

https://doi.org/10.1042/BST20160348



- A community of surface-associated microbial cells
- Protect microorganisms by encapsulation in extracellular matrix (ECM)
- Attach (1), ECM generation (2), mature biofilm (3), and biofilm dispersal for colonization (4)
- Three main components: collectively called extracellular polymeric substances (EPS) = polysaccharides, DNA, self-assembled protein polymers

A stimuli-responsive material made from cells encapsulated into a polymeric matrix is an ELM.
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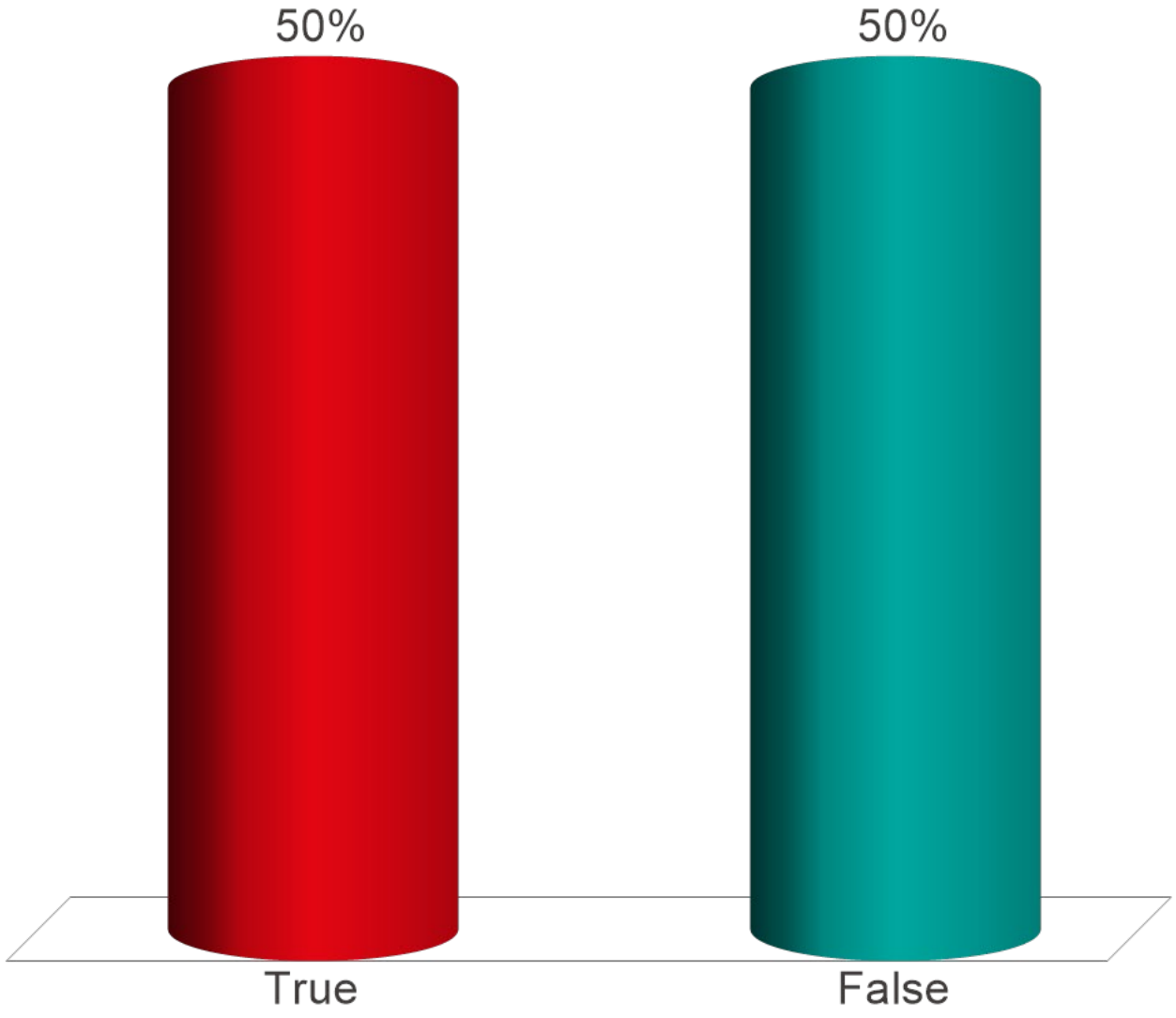
Session ID: MSE493 (no space)

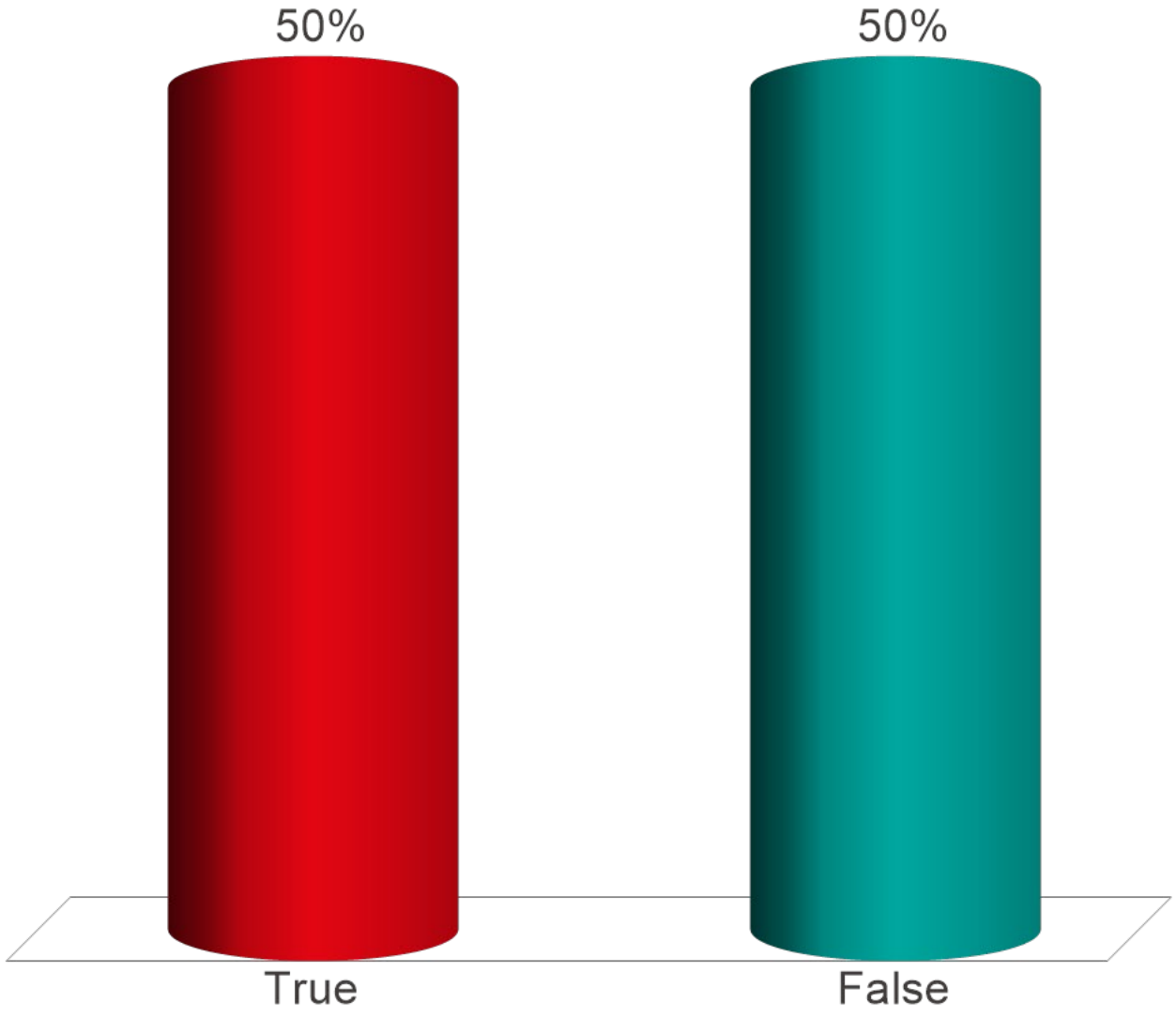
A. True
B. False



A stimuli-responsive material made from genetically engineered cells encapsulated into a polymeric matrix is an ELM.

go to: ttpoll.eu
Session ID: MSE493 (no space)

A. True
B. False



OK, so what is not an ELM?

- There are many examples of “biohybrids” in the literature where the biological component is “just one element” of the final material **and does not actively create or modulate the bulk material structure**

REVIEW
Engineered Living Materials

ADVANCED MATERIALS
www.advmat.de

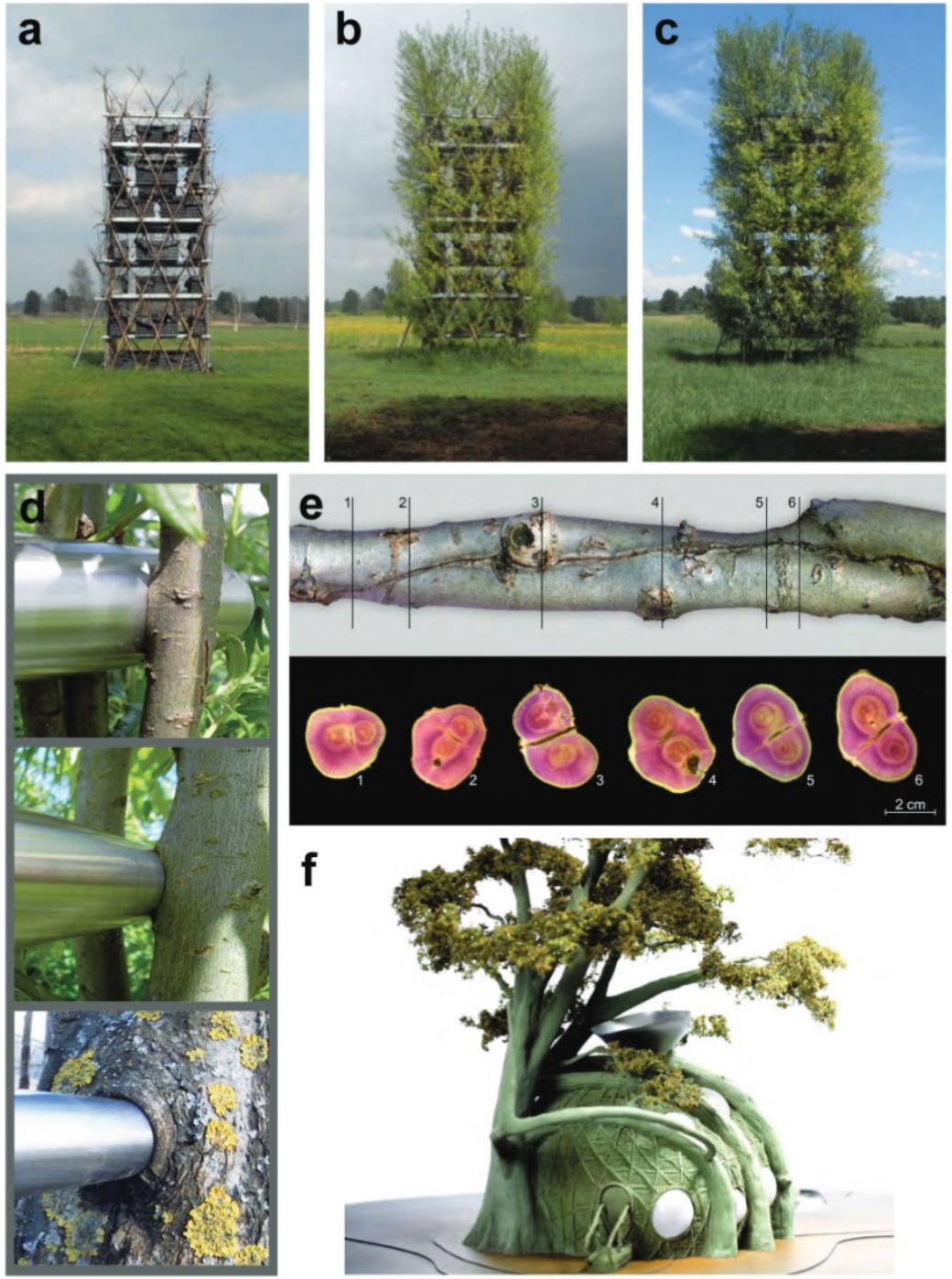
Engineered Living Materials: Prospects and Challenges for Using Biological Systems to Direct the Assembly of Smart Materials

*Peter Q. Nguyen, Noémie-Manuelle Dorval Courchesne, Anna Duraj-Thatte, Pichet Praveschotinunt, and Neel S. Joshi**

DOI: 10.1002/adma.201704847

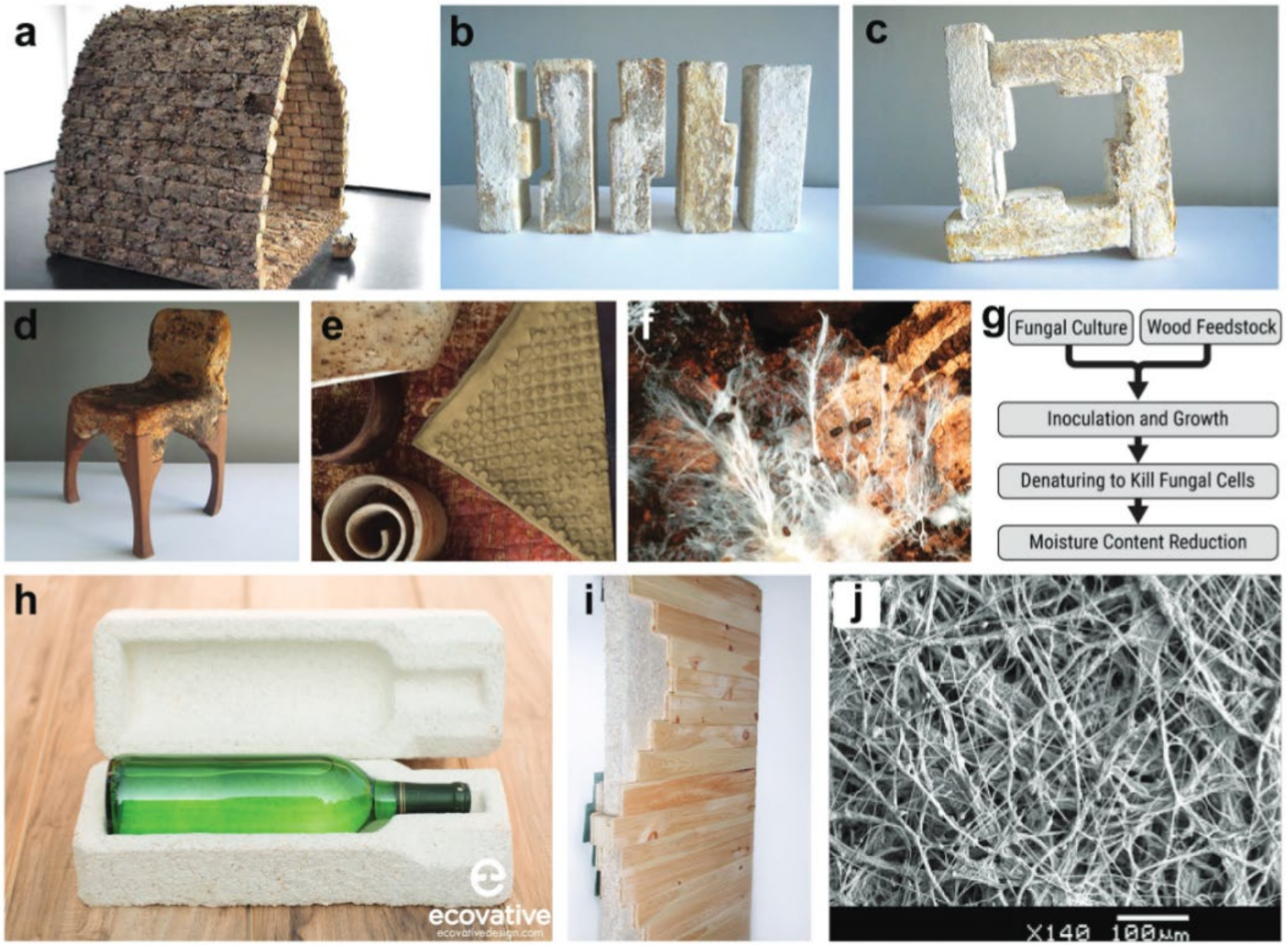
Be aware!

- In this course, we sometimes cover topics that are not ELM’s under the strict definition as put forth in this review
- Indeed, not all papers agree



Lignocellulosic living organisms as ELMs

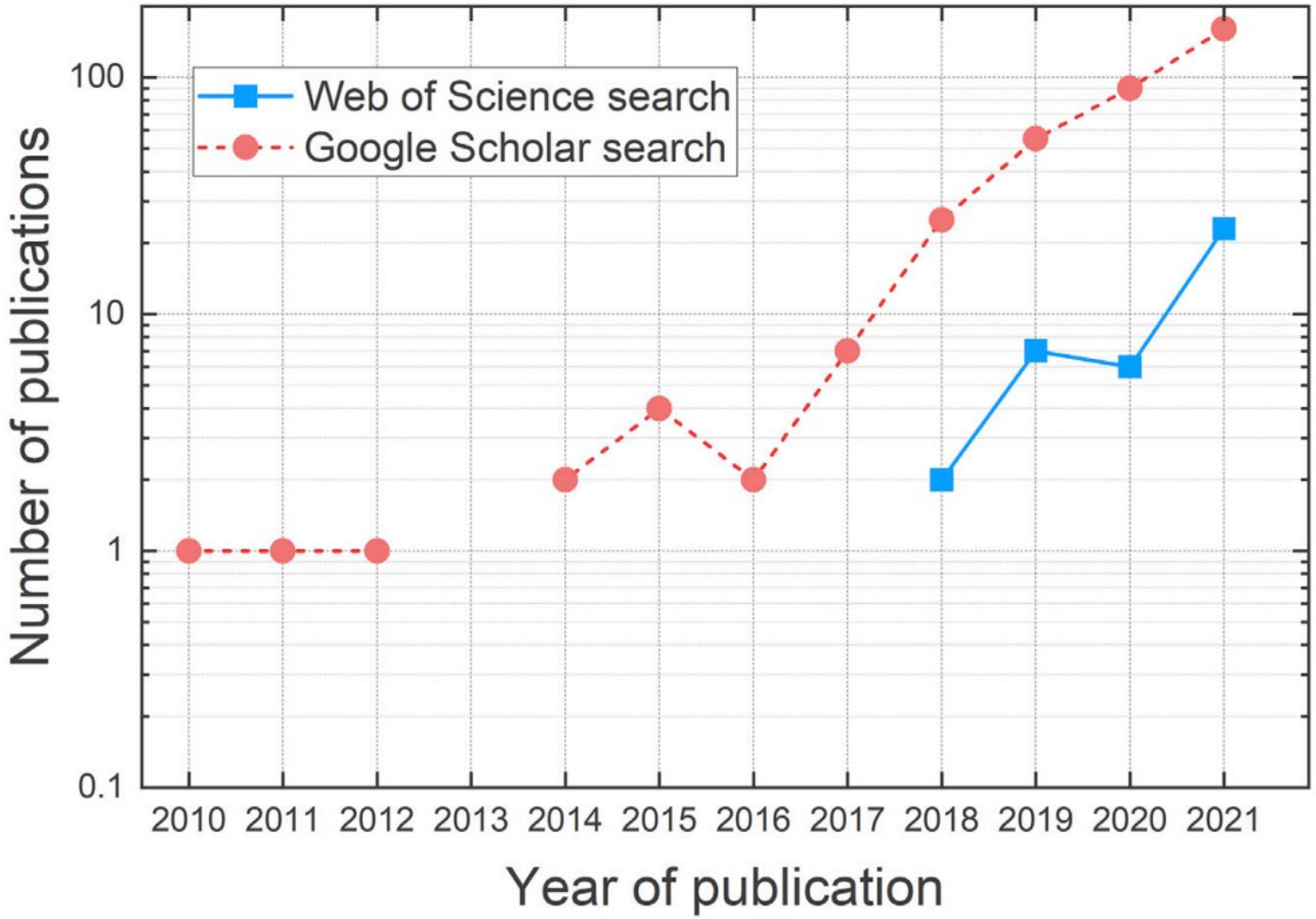
DOI: 10.1002/adma.201704847



Mycelium-based ELM materials

DOI: 10.1002/adma.201704847

ELMs - an emergent field of materials science



Annual number of publications obtained from a Web of Science and Google Scholar search using "engineered living materials" as keywords.

https://doi.org/10.1016/j.xcrp.2022.100807

1st use of term in 2017

Biochemical Society Transactions (2017) **45** 585–597
DOI: 10.1042/BST20160348

PORTLAND PRESS

Review Article

Synthetic biology engineering of biofilms as nanomaterials factories

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[1]Wyss Institute for Biologically Inspired Engineering, Harvard University, Boston, MA 02115, U.S.A. and [2]School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138, U.S.A.

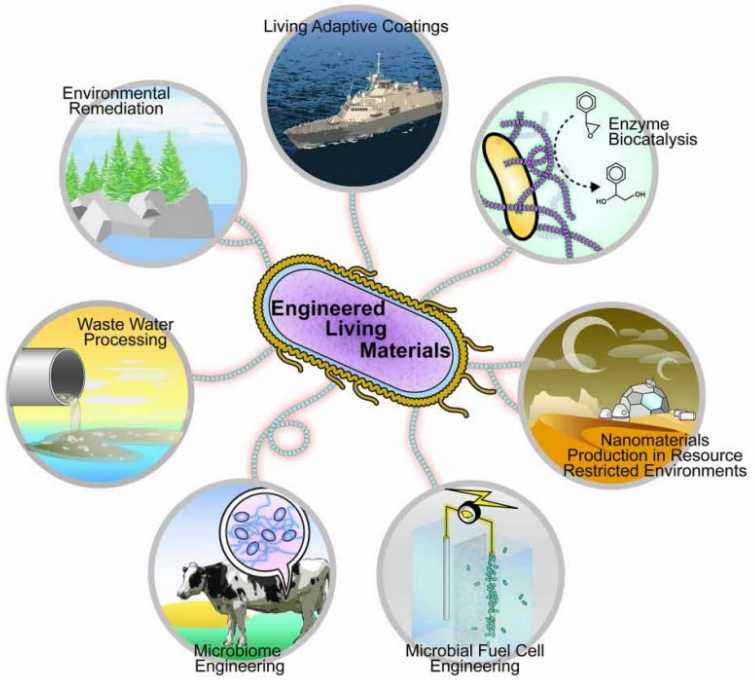
Correspondence: Peter Q. Nguyen (peter.nguyen@wyss.harvard.edu)

https://doi.org/10.1042/BST20160348

https://wyss.harvard.edu/

1st use of term in 2017

"An integration of *nanomaterials science* and *synthetic biology approaches* could allow the development of *nanomaterial-producing systems* that are able to *adapt dynamically to stimuli, modulate their properties over time, and heal themselves*, much like tissues are capable of doing. Such engineered systems can be thought of as '**engineered living materials**', materials that have *integrated living and non-living components*, respectively, the cells and the materials they generate."
– *Peter Q. Nguyen*



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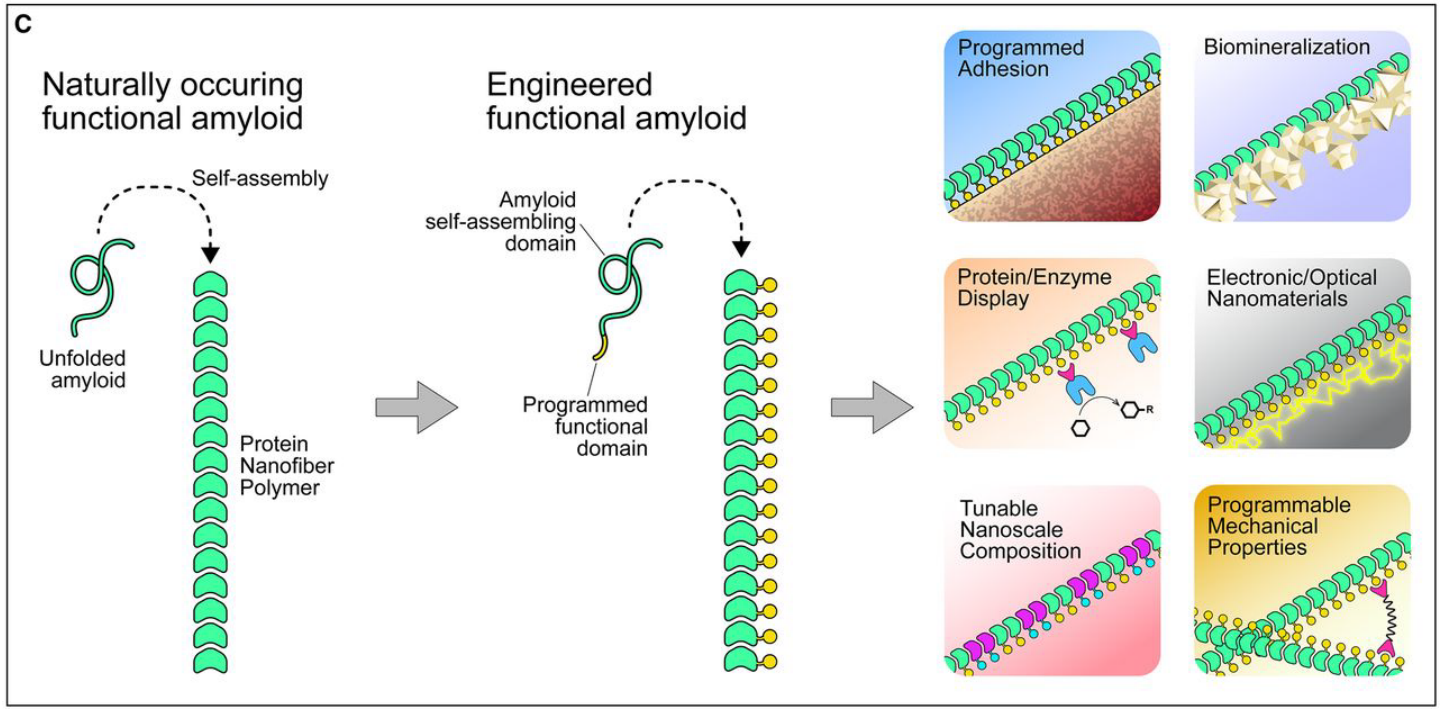
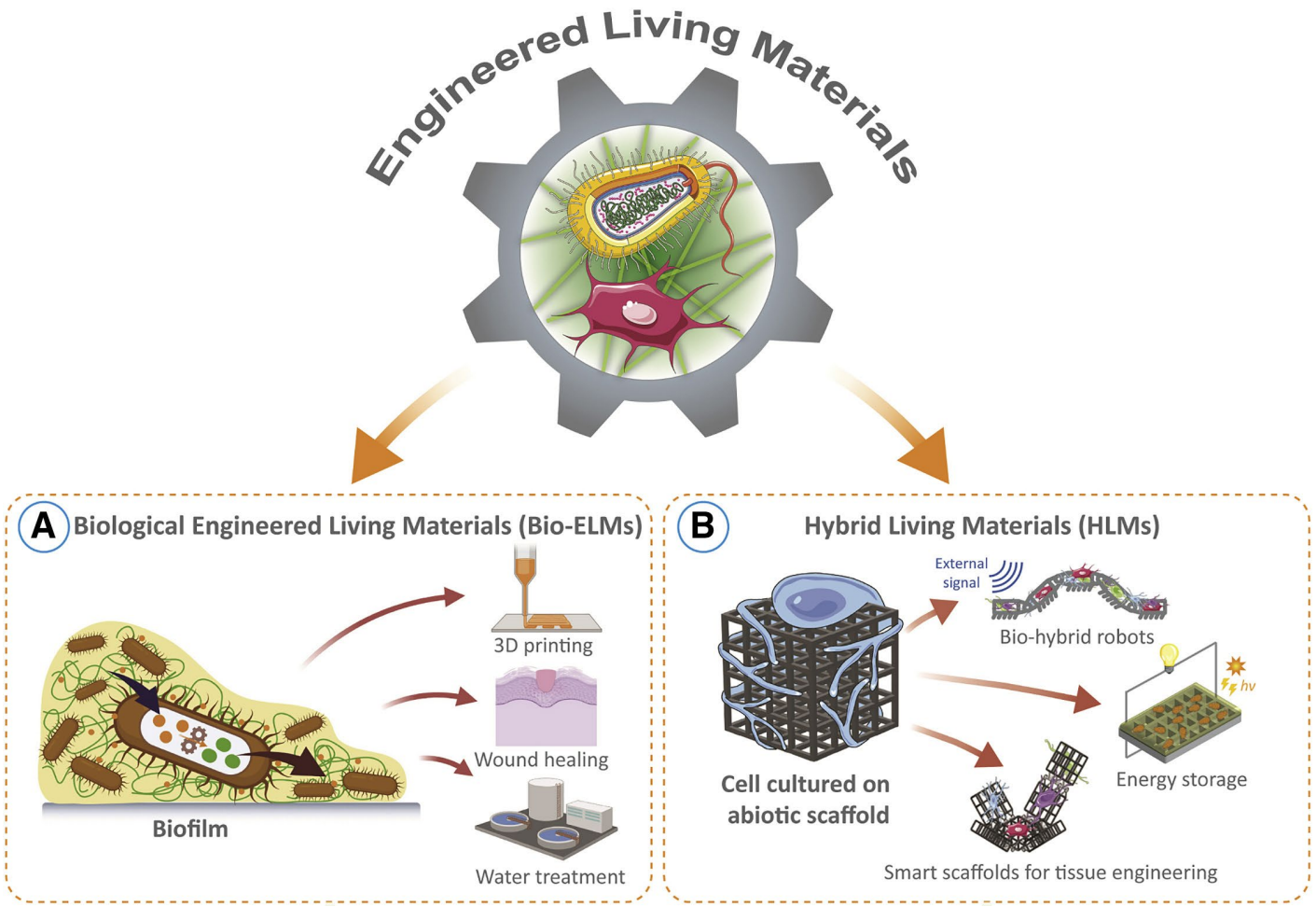


Programmable nanomaterials – expanding the **synthetic biology toolkit** for biofilm materials

https://doi.org/10.1042/BST20160348

Other common definitions



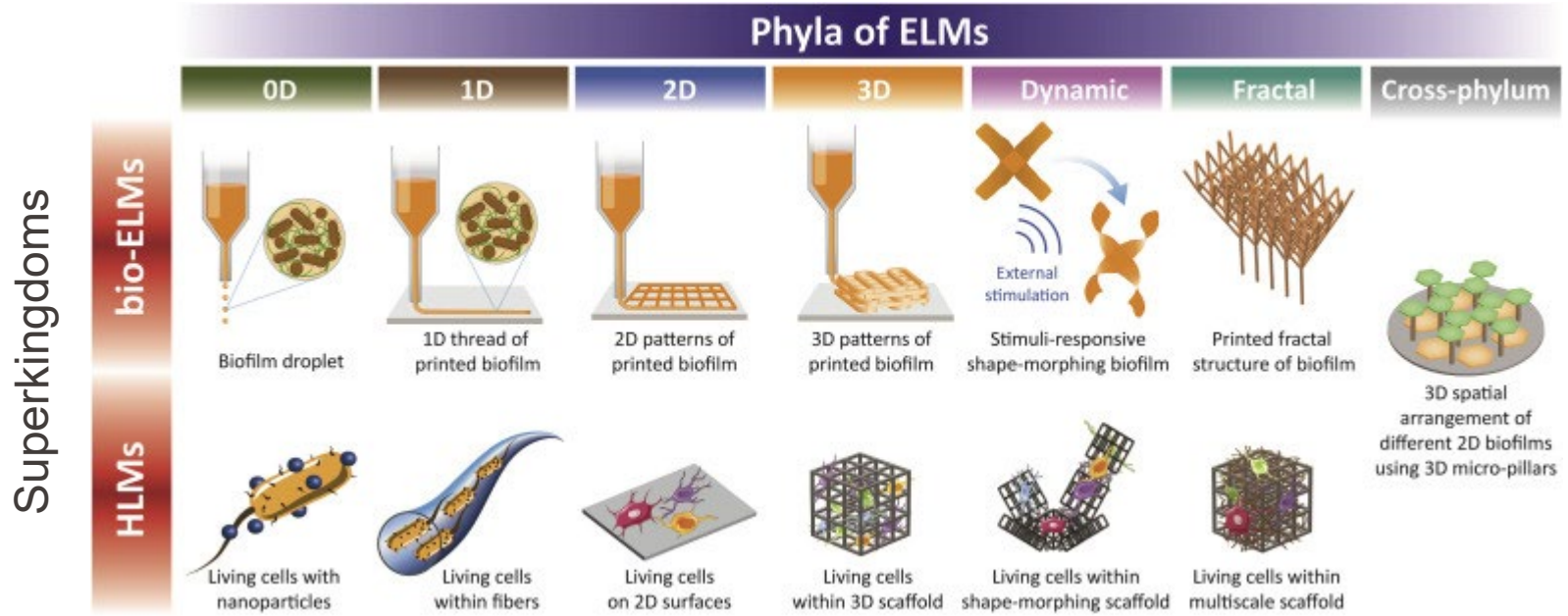
https://doi.org/10.1016/j.xcrp.2022.100807

Defines ELMs as:

- Bio-ELMs – self-assembly of living cells
- Hybrid ELMs – incorporating living cells in a scaffolding structure (not a true ELM according to previous definition on slides 3 & 8 – but who's keeping track?)

Proposed taxonomy of ELMs

Domain – *superkingdom* – kingdom – *phylum* – class – family



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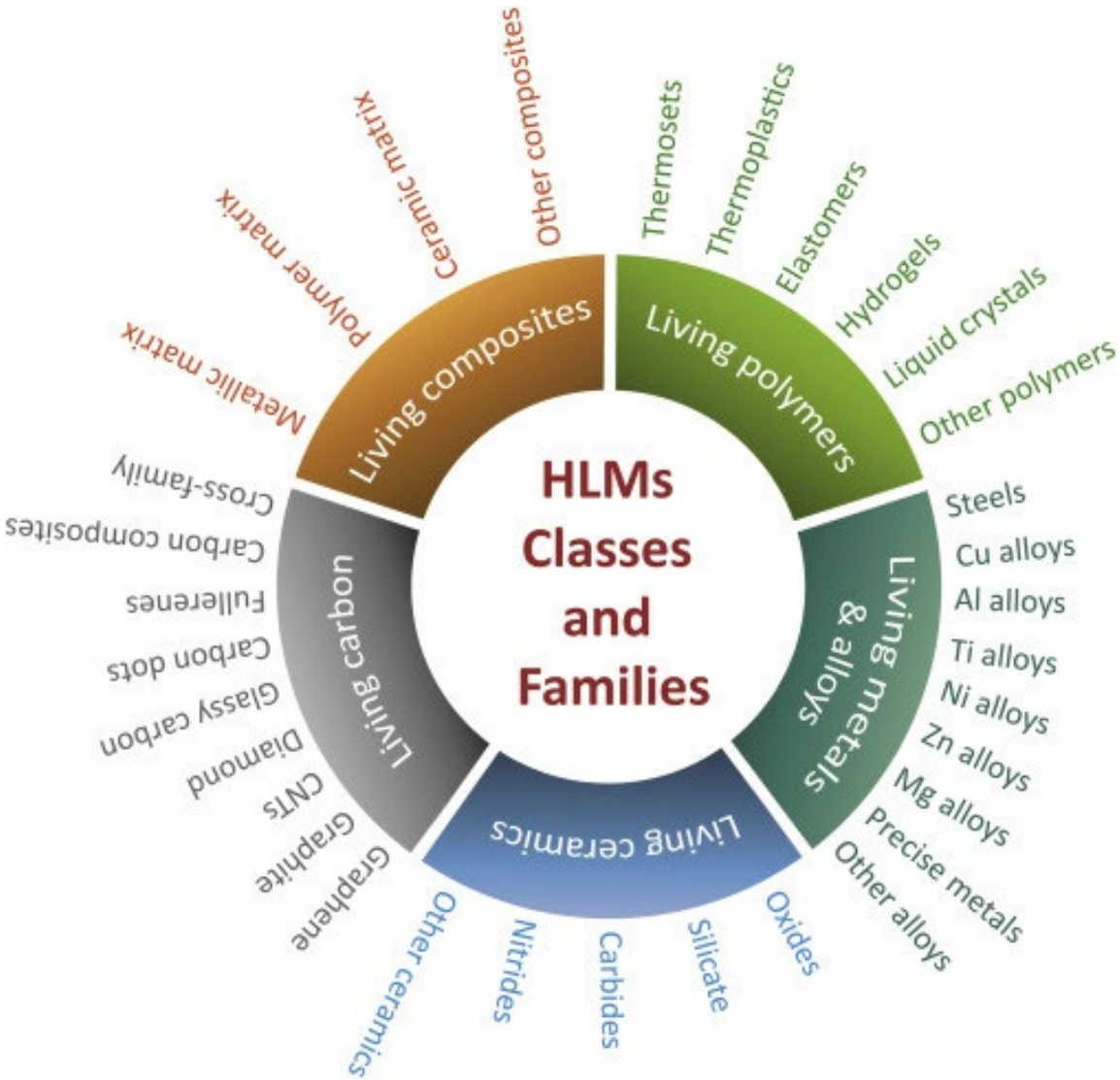
Proposed taxonomy of ELMs

Domain – superkingdom – kingdom – phylum – *class* – *family*



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Proposed taxonomy of ELMs

Table 1. *Continued*

Pioneering examples of engineered living materials (ELMs)		Classification according to proposed taxonomy					
Described ELMs	Purpose/application field	Domain	Superkingdom	Kingdom	Phylum	Class	Family
Sand-hydrogel scaffolds with photosynthetic cyanobacteria[42]	smart buildings	bacterial	hybrid living materials	eubacterial ELMs	3D ELMs	living composites	living polymer matrix composite
Bacteria cultured on polymeric scaffolds growing ceramics[43]	materials production	bacterial	hybrid living materials	eubacterial ELMs	3D ELMs	living composites	living ceramic matrix composite
Self-healing, bacterial-loaded concrete[44]	smart buildings	bacterial	hybrid living materials	eubacterial ELMs	3D ELMs	living ceramics	living concrete

Table 1. *Continued*

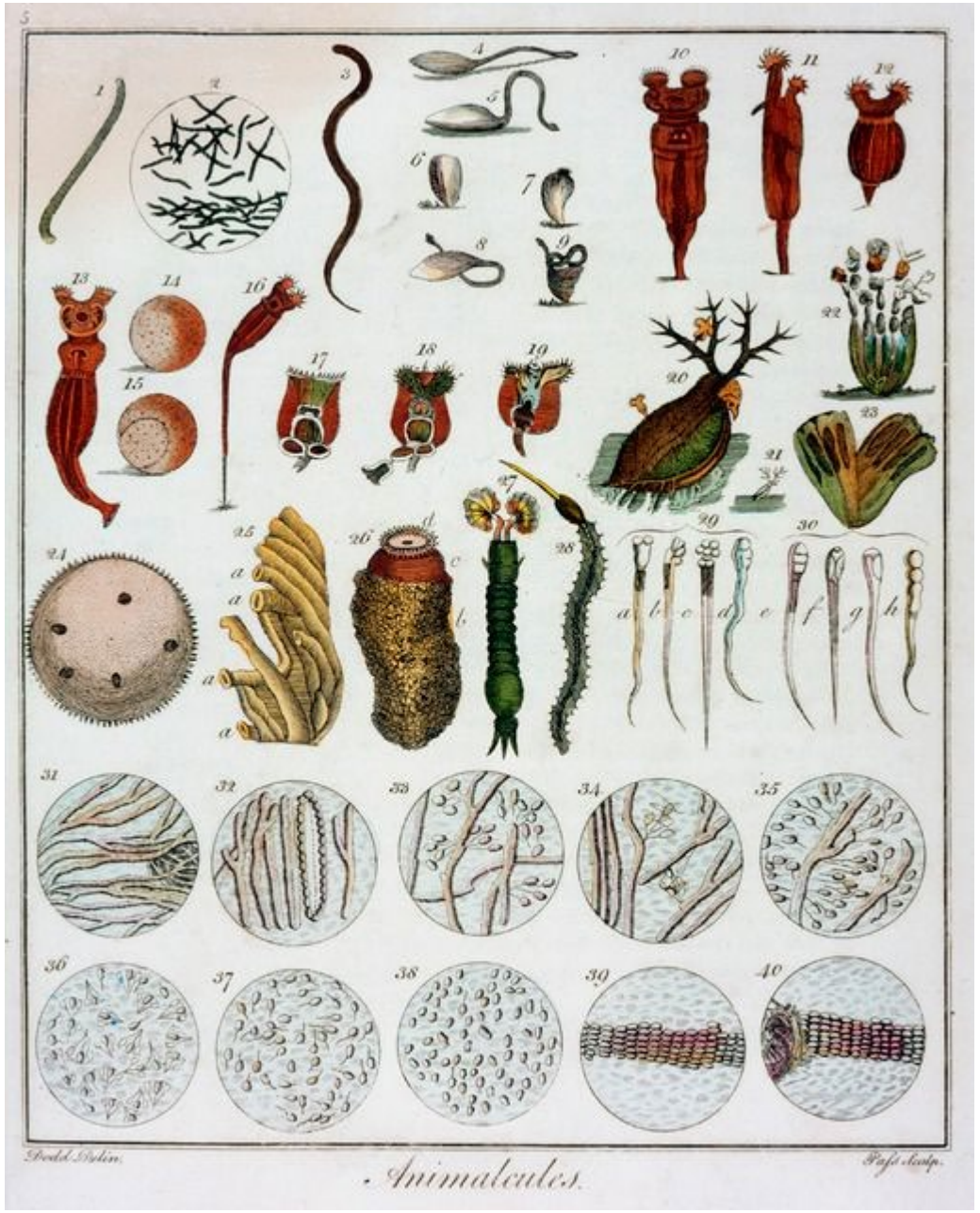
Pioneering examples of engineered living materials (ELMs)		Classification according to proposed taxonomy					
Described ELMs	Purpose/application field	Domain	Superkingdom	Kingdom	Phylum	Class	Family
Musculoskeletal cells attached to hair[83]	robotics	eukaryotic	hybrid living materials	animal ELMs	1D ELMs	living polymers	living elastomers
3D printed bio-ink containing cardiac tissue[84]	smart surfaces and structures	eukaryotic	hybrid living materials	animal ELMs	dynamic ELMs	living polymers	living hydrogels
Cardiomyocytes with CNTs[18]	robotics	eukaryotic	hybrid living materials	animal ELMs	dynamic ELMs	living carbon	living CNTs
Mycelium-based composites (fungi into organic substrate)[85]	materials production	eukaryotic	hybrid living materials	fungal ELMs	3D ELMs	living polymers	other living polymers (fibers)
Bioprinted bioinks with baker's yeast[86]	biotechnology and bioprocessing	eukaryotic	hybrid living materials	fungal ELMs	3D ELMs	living polymers	living thermoplastics

https://doi.org/10.1016/j.xcrp.2022.100807

At the heart of ELMs are living cells

‘wee animalcules’

1st described by Leuwenhoek in 1676



Animalcule

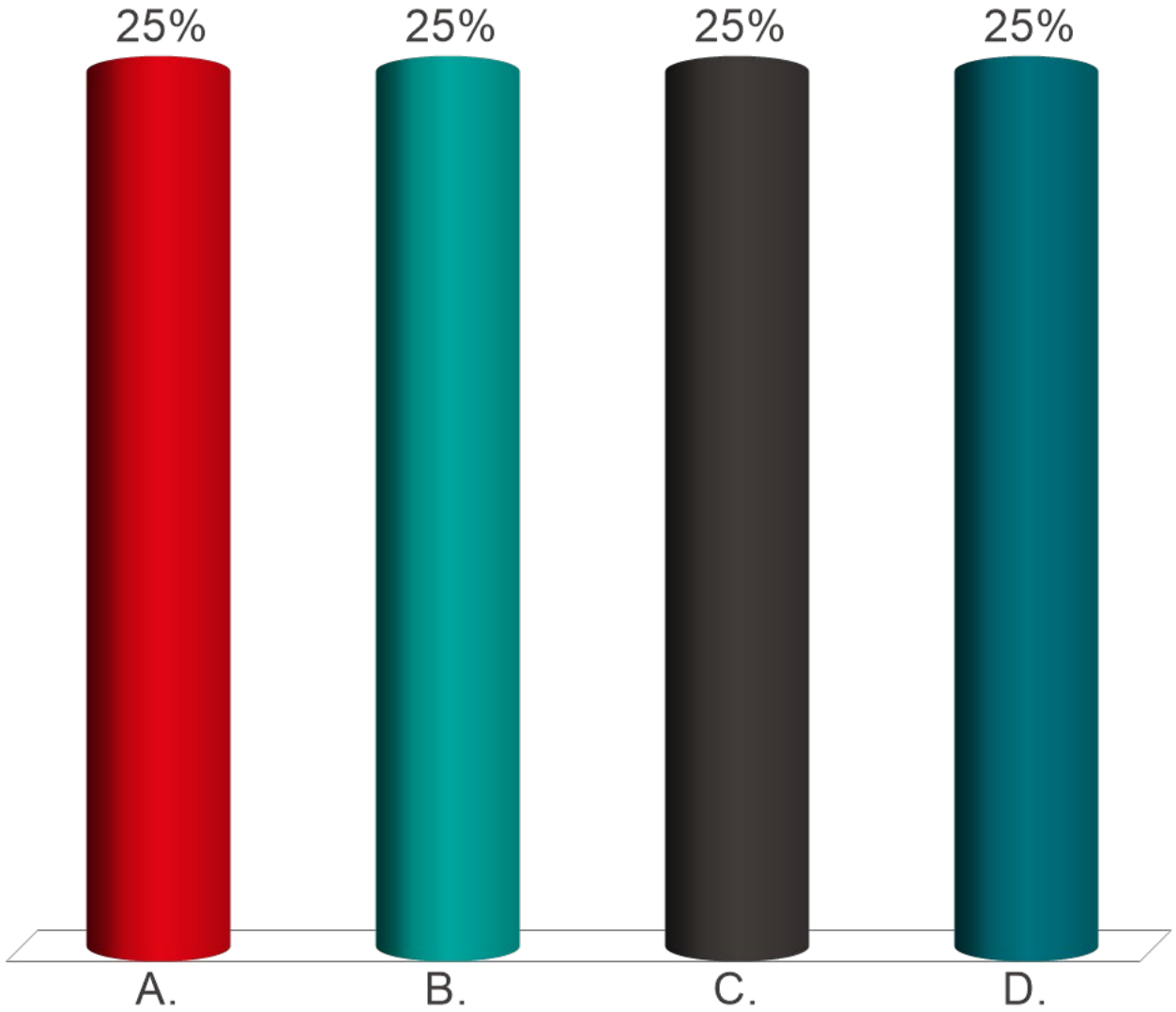
Where do cells come from? go to: ttpoll.eu Session ID: MSE493 (no space)

A. Spontaneous generation when food is left out

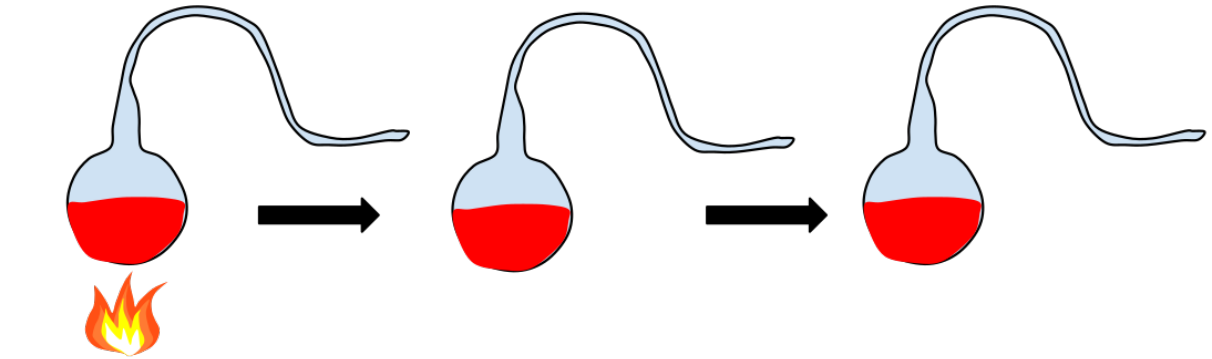
B. From space via meteor showers

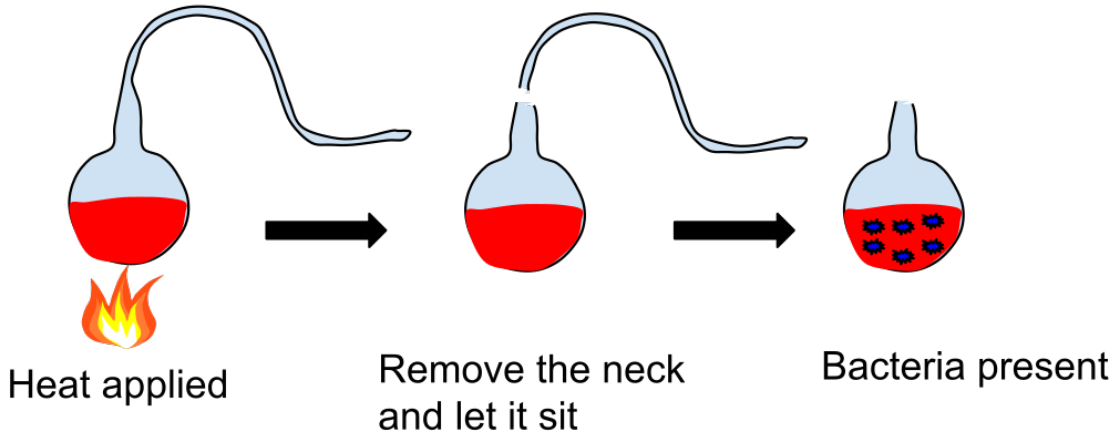
C. From invisible seeds that plant themselves in living organisms

D. From pre-existing cells, through a process of division



Spontaneous generation?

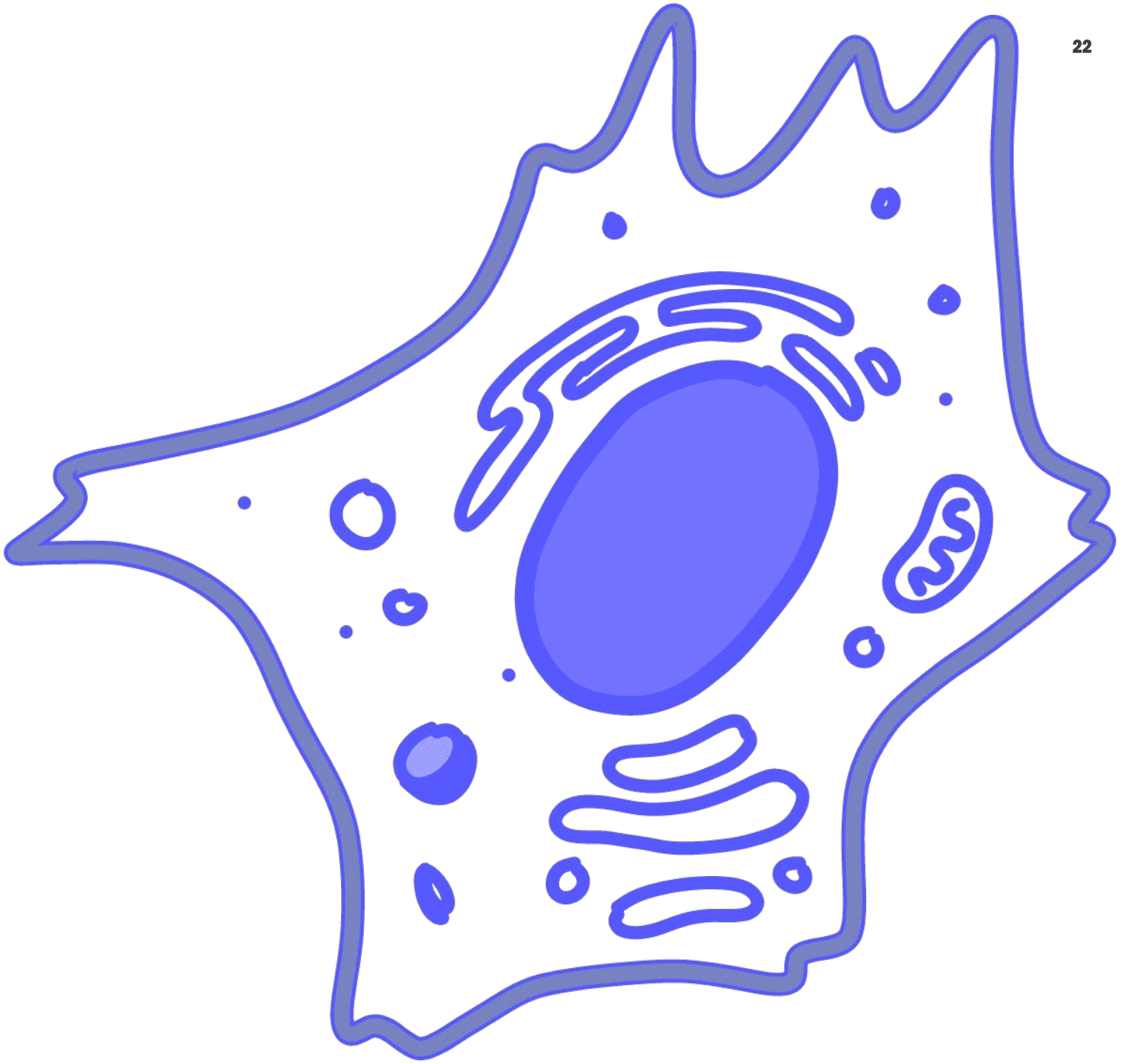




Louis Pasteur_1859

Cell theory

- All living organisms are made up of one or more cells
- The cell is the basic biological structure of life
- Cells arise from pre-existing cells (Biogenic law)

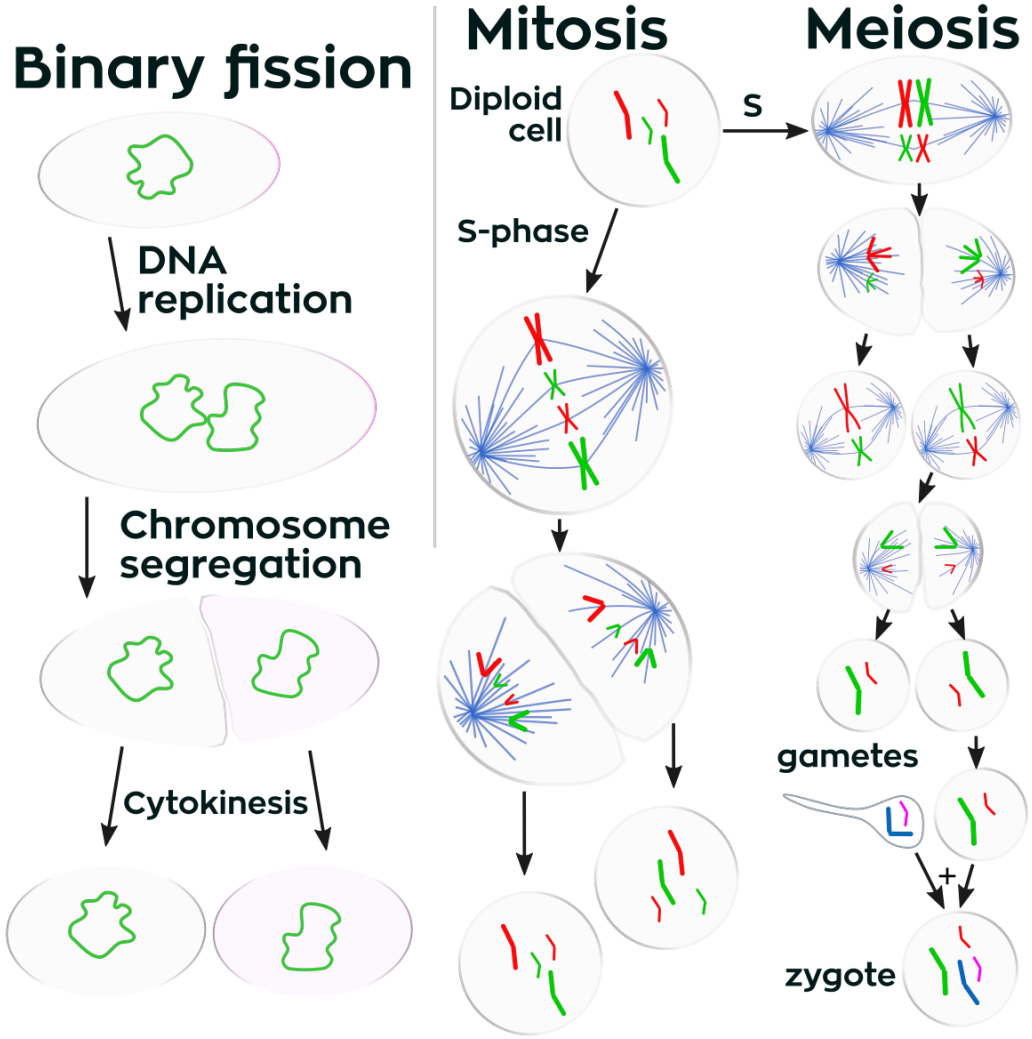


doi: 10.1042/EBC20200059

Cell division

Prokaryotes -

Binary Fission: DNA replication, cell elongation, septum formation, cell splitting



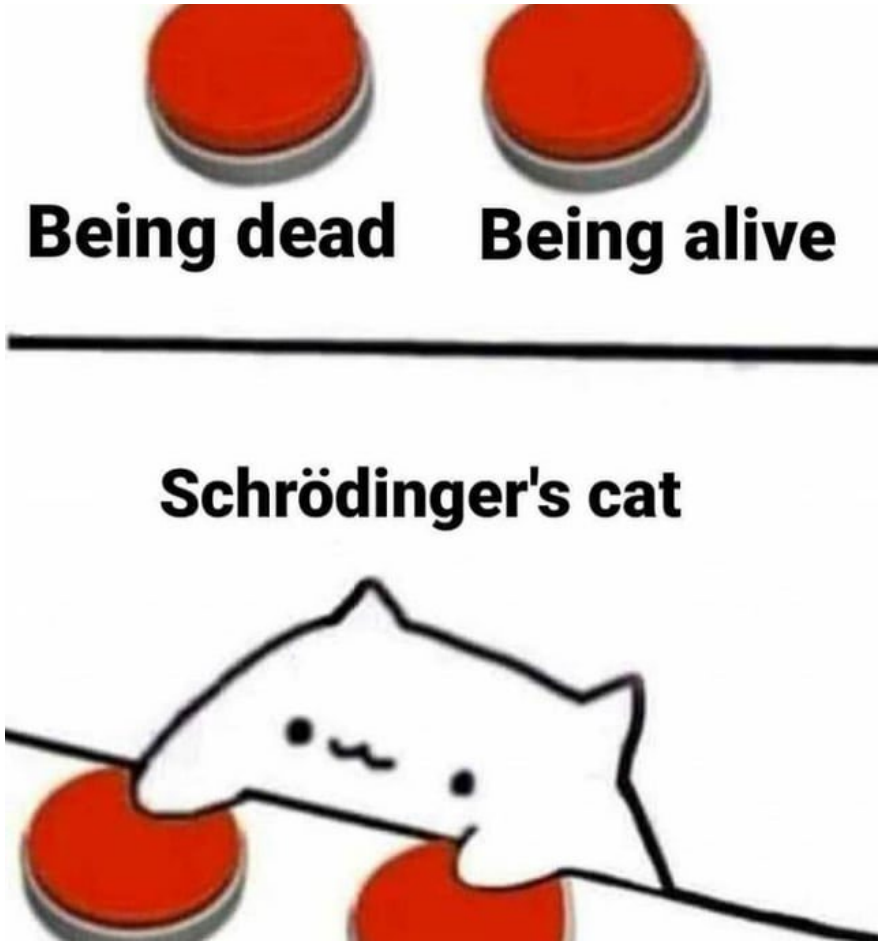
Eukaryotes -

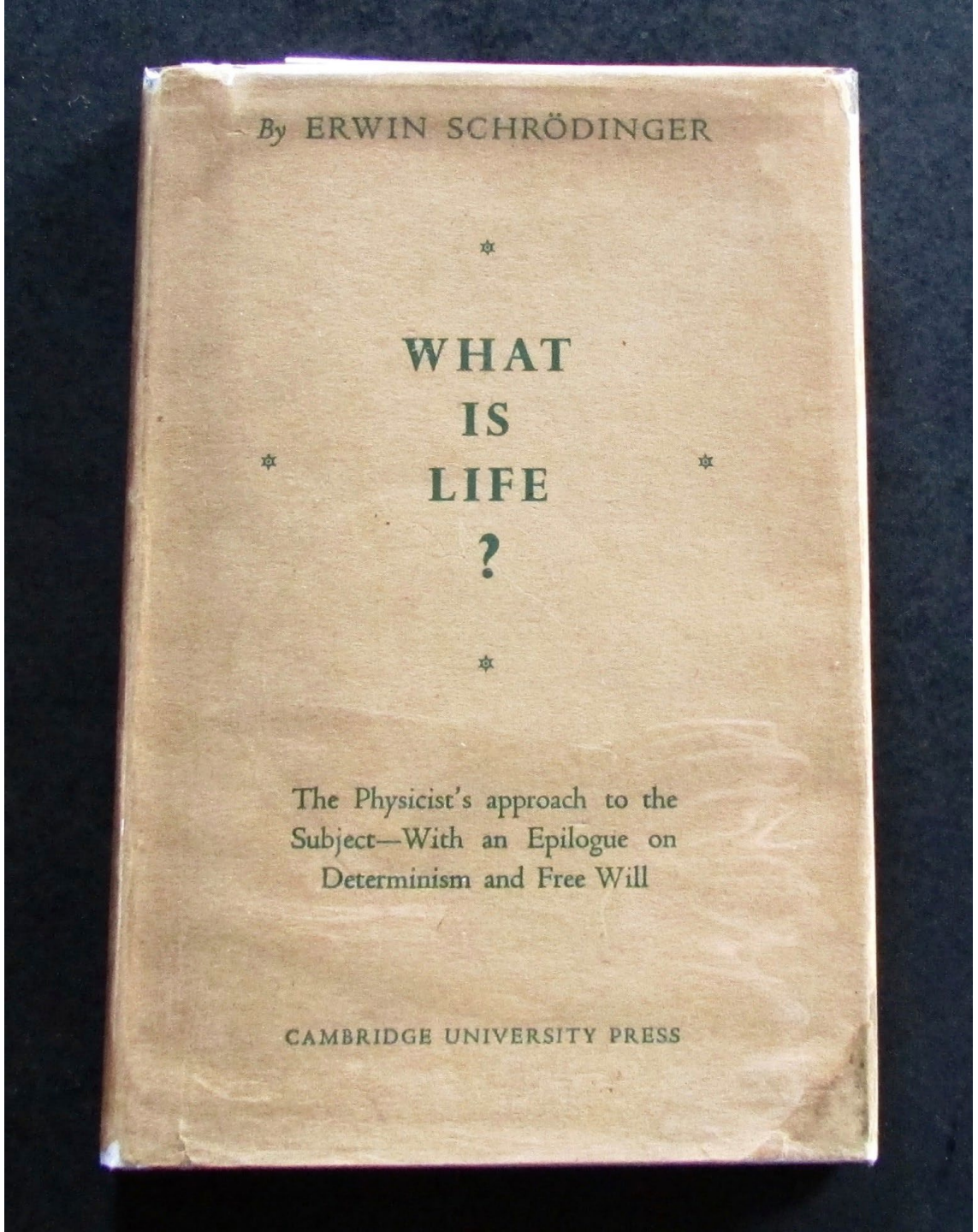
Mitosis: single cell divides to give two identical daughter cells, essential for growth, tissue repair, and asexual reproduction

Meiosis: single cell divides into 4 daughter cells with half the number of chromosomes as the parent cell (haploid), essential for sexual reproduction

Cell division

What is life?


Being dead
Being alive
Schrödinger's cat


By ERWIN SCHRÖDINGER
WHAT
IS
LIFE
?
The Physicist's approach to the Subject—With an Epilogue on Determinism and Free Will
CAMBRIDGE UNIVERSITY PRESS

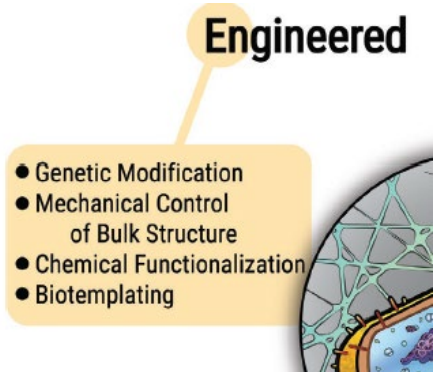
What is life?

- 2nd law of thermodynamics: entropy increases in any closed system over time
- Cells are open systems
- Metabolic pathways enable cells to get the energy they need to create and maintain their order, pushing disorder into their surroundings (heat and waste)
- In 1944, Schrödinger was the first to propose that cells contained a "**codescript**"
- Codescript consisted of well-ordered atoms, referred to as an 'aperiodic crystal', contained all information to determine development of individual
- Watson & Crick give credit to Schrodinger for inspiration leading to the discovery of DNA in 1953

doi: 10.1042/EBC20200059

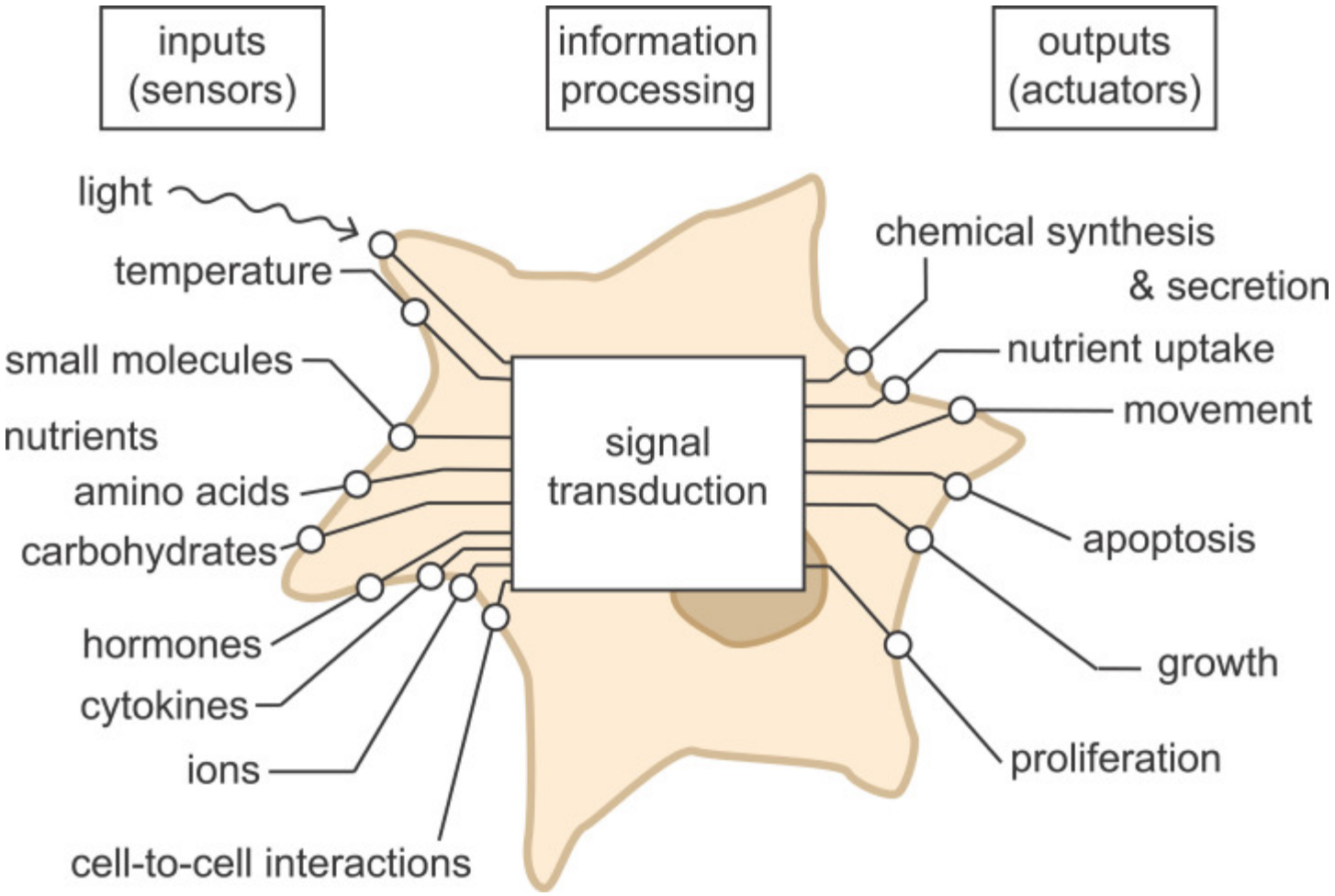
Synthetic biology (from 2010 article)

- Circuit-like connectivity of **biological parts**
- Describe biological parts with math and to apply electric circuit analogies to biological pathways
- Make biological parts with tools like recombinant DNA technology
- Synthetic biology's broad goal "engineering or wiring biological circuitry – for manifesting logical forms of cellular control"
- Some practical applications: biosensing, therapeutics, biofuels, pharmaceuticals, novel biomaterials



https://doi.org/10.1038/nrg2775

Living



Cells make sense of their environment

doi: 10.1042/EBC20200059

Synthetic Biology or "Engineering Life"

- Previous slide: cells as information processing systems, with sensors and actuators
- Synthetic biology applies engineering principles to biology
- Uses engineering concepts of standardization, modularity, and abstraction
- DNA is the code for the building part, a biological part or 'biopart'
- Parts are used to build devices
- Devices can be used and combined into biological systems

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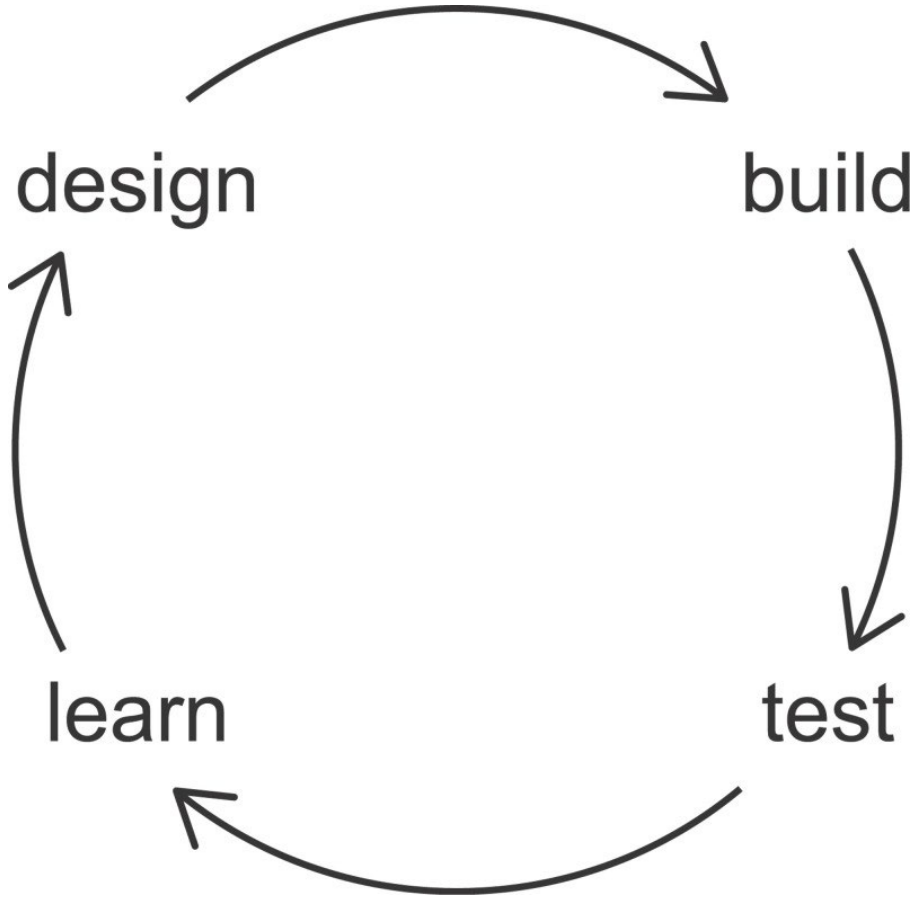
Iterative approach



"What better way is there to learn how something is constructed than to try to build it yourself?"

doi: 10.1042/EBC20200059

Synthetic Biology or "Engineering Life"

- Cell is needed to provide energy to the biopart and to mediate inputs from outside the cell
- In synthetic biology, the environment of the cell can be provided by an "off the shelf" standard part, called a ***chassis***
- Chassis is the cellular host that receives the engineered bioparts and devices; they propagate and express genetic information
- The chassis provides the energy to run the synthetic system and is thought of as the 'hardware', the bioparts and devices as the 'software'

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Chassis

A chassis is the load-bearing framework of a manufactured object, which structurally supports the object in its construction and function. Wikipedia

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- *Escherichia coli* (*E. coli*) model microbe in molecular biology and the go-to chassis in synthetic biology
- 'Laboratory workhorse' – easy to maintain and grow, fast doubling time of 20 min
- Sequenced genome of 4.6 Mb (1 Mb = 1 000 000 bp)
- Synthetic gene circuits can easily be introduced into bacterium's cytoplasm using DNA plasmids
- Other common chassis: *B. subtilis* (bacterium), *S. cerevisiae* (yeast)
- Needs to be well characterized and understood to avoid unwanted interactions

Synthetic biology/computer science analogy – programmable microbes

Synthetic Biology	Computer Science
DNA	Code
Genes, bioparts	Software
Cells, chassis	Hardware
Genetic engineering	Software development
Modular DNA	Modular code
Run a genetic program	Run the code

Turning cells into computers