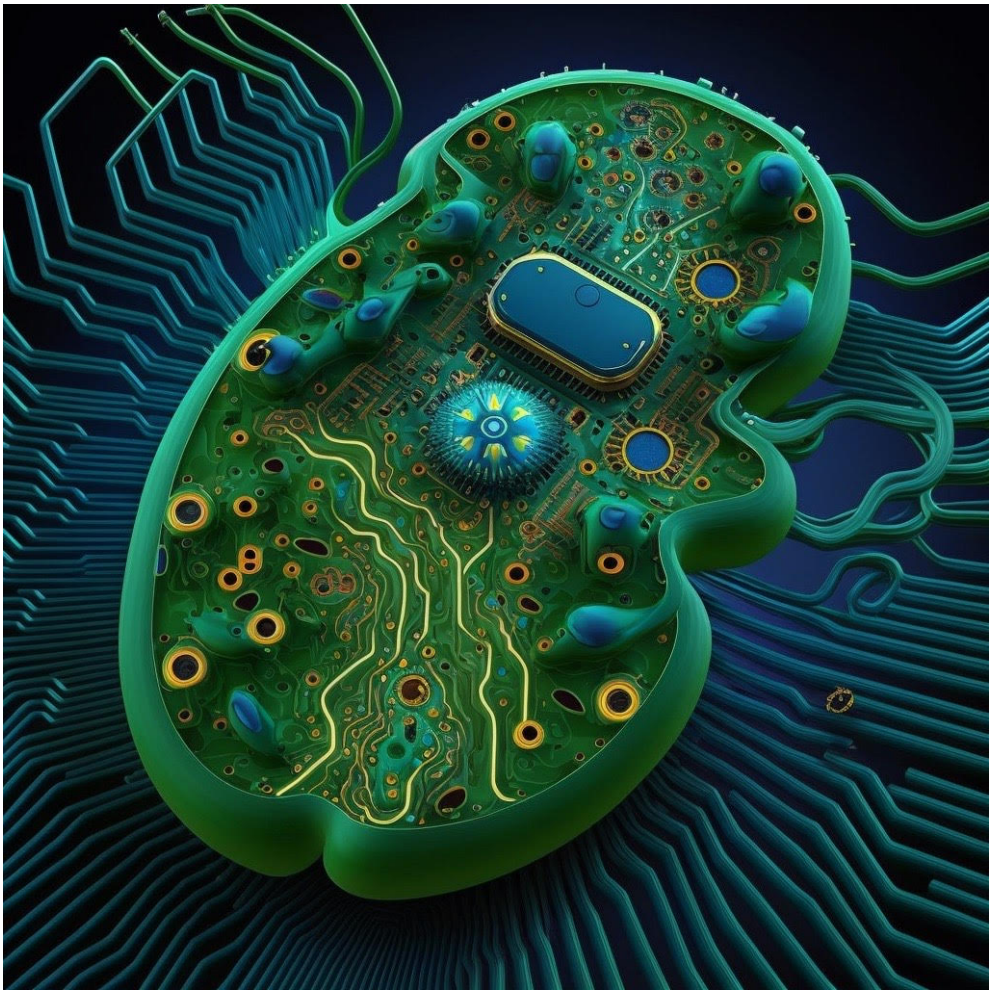
Synthetic Cells

How can we use cells, the building blocks of life, to create something brand new?



Kate Adamala and Carlise Sorenson

Department of Genetics, Cell Biology and Development, University of Minnesota Minneapolis, USA

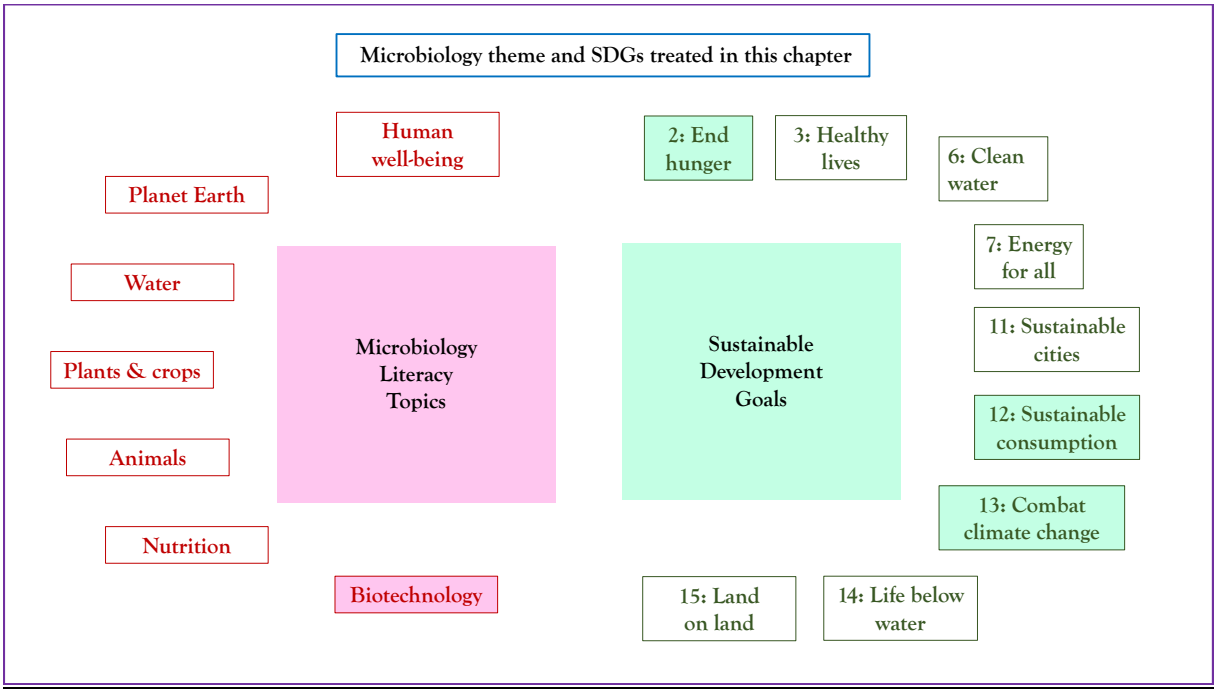
Synthetic Cells

Storyline

Making living cells from scratch is one of the most exciting frontiers of science. The ability to make a living cell from non-living building blocks will teach us about what is life, how life started, how we can study and modify living cells.

The Microbiology and Societal Context

The microbiology: intracellular biology; biochemistry. *Sustainability issues:* health equity; accessibility to healthcare and diagnostics; waste treatment; bioeconomy.

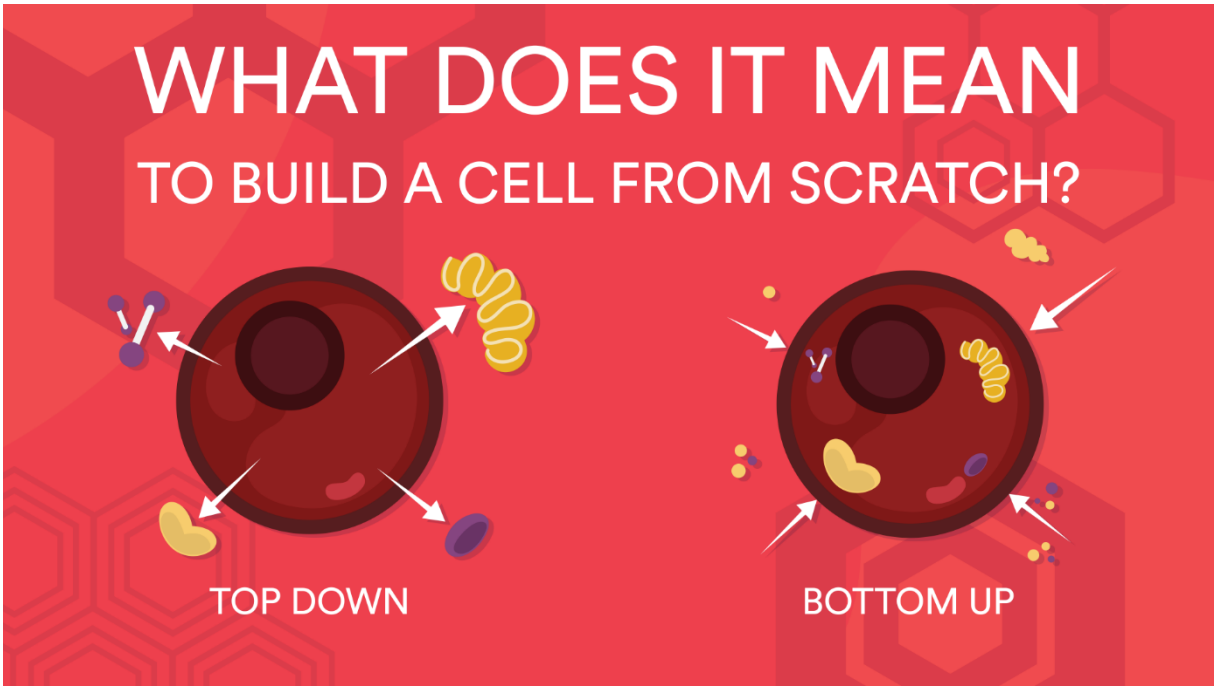


Synthetic Cells: the Microbiology

1. ***Cells: the building blocks of life, and what makes them tick.*** Cells represent the simplest building blocks of larger complex creatures on earth. Still, they are not fully understood by scientists. There are many complex biochemical interactions taking place within a cell that allows it to grow, divide, and reproduce its genome, as well as sometimes sense and respond to its environment. While some of these biochemical processes have been characterized by scientists, we have still barely begun to scratch the surface of the mystery of complex cellular mechanisms and pathways. Understanding these mechanisms is a crucial step towards utilizing cellular functions for a wide range of biotechnology tools and technologies.

2. ***What are synthetic cells and how are they created?*** To approach this task, researchers have been developing what have become known as synthetic cells. There are several approaches to creating a synthetic cell. There is the top-down approach, wherein researchers begin with a complete living cell and slowly remove parts to create a minimal cell. There is also the bottom-up approach where researchers start from scratch and use synthetic, or man-made, components to build up a cell from the bottom until it achieves the requirement of a living cell. Additionally, there is the middle-out approach that combines practices and methods from both top-down and bottom-up.

Creating a synthetic cell is a large and daunting task. Researchers have broken this challenge down into compartmentalized goals: achieving smaller cellular features and traits that can then be combined to create a specifically designed cell.



3. ***Why are they being developed?*** Synthetic cells offer great benefit to both basic science – research for the sake of knowledge and greater understanding of natural systems – as well as to bioengineering and development of applied synthetic cell-based technologies.

Experimenting on living systems and cells has been a critical cornerstone of biological research. These experiments ask scientists difficult questions about how we view and understand living things as we gain control and ability to "program" specific features in a cell to determine the mechanisms behind how it works. These experiments are not about creating something new, but to replicate features found in natural cells and learn more about life's origins and complex components involved in life's building blocks.

Bioengineering is the deliberate manipulation of biological systems for real world applications and uses. Natural cells provide a lot of interesting features (such as being able to move and react to their environments by changing shape or releasing chemicals) that have long been utilized for our own ends for creating new materials, medicines, and diagnostic tools that can detect the presence of diseases, to name just a few examples.

Synthetic cells offer a unique opportunity to take advantage of these features (making/processing/metabolizing chemicals, movement and shape changes, detecting environmental changes, etc.) without the interference of unknown parts and reactions present in living cells.

Synthetic cells provide a method for testing individual biological parts outside the complexity of a natural cell. We can isolate biochemical reactions or specific pieces of organelles to better analyze their unique properties.

A complete understanding of cellular processes is important and useful to humans for several reasons:

a. Humans are a home to many living systems that must be *kept in balance* for survival and health. Learning more about these systems and how to control/manipulate them offers unique health and medicine advantages.

b. Living cells can *replicate* quickly and exponentially. This means they can be cultivated rapidly for the creation of sustainable materials made from these cells.

c. Living cells perform *complicated chemistry* and organize the cascading sequences of coordinated reactions far beyond the capacity of current technologies. Unlocking the secrets to this organization will allow for improved system processes.

d. Living cells have the capacity to *evolve* and demonstrate a capacity for optimization that can be utilized as an algorithm to enhance our own technologies.

e. Living systems are able to *react and respond/adapt* to changes in the environment around them. This provides an opportunity for testing and adapting smaller components of natural systems under different controlled conditions.

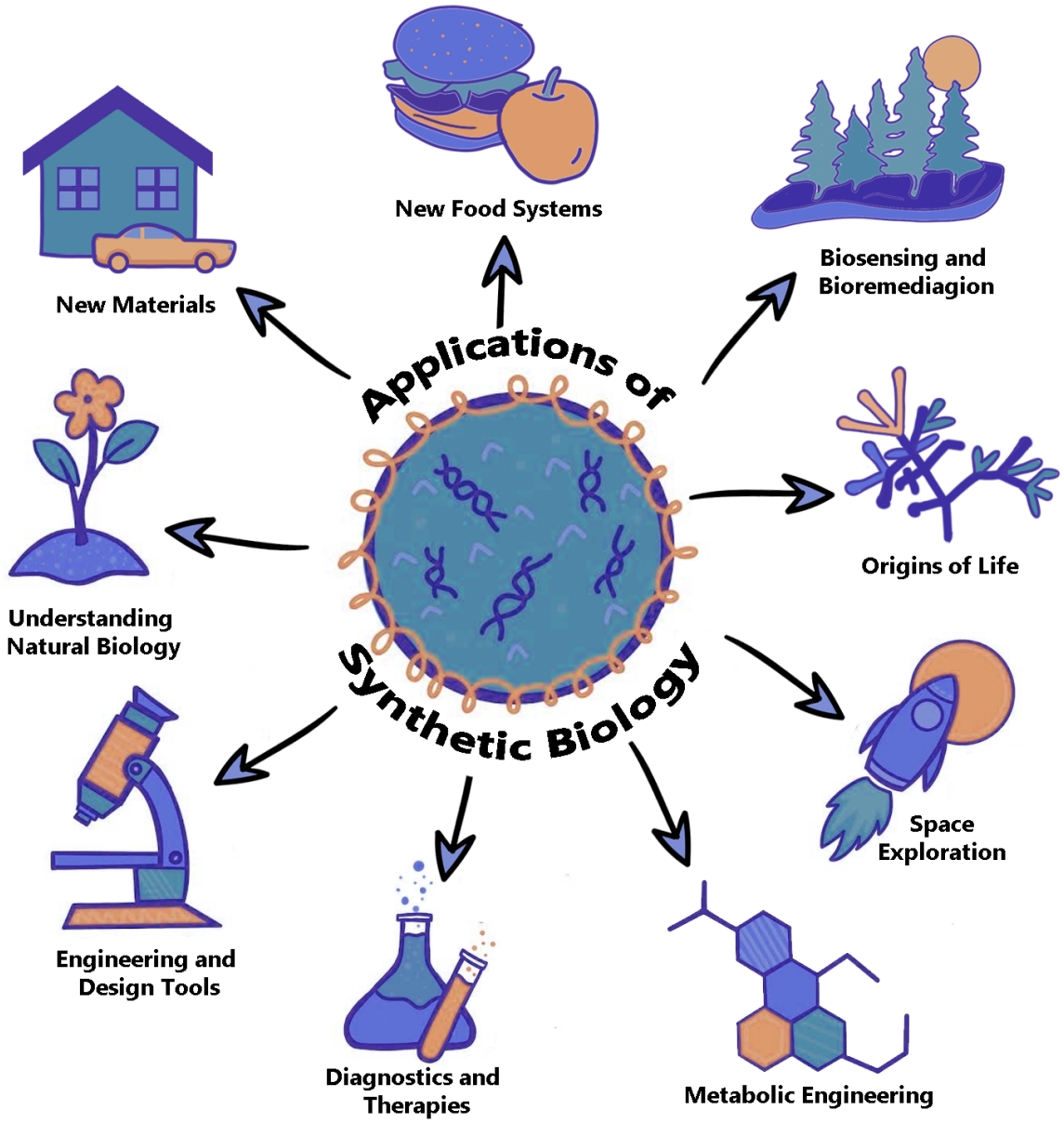
4. What are the broader applications?

a. Food Systems: Synthetic cell technologies can be used to enhance current food systems to offer more control over crop production and reduce the environmental impact of farming by minimizing dependence on fertilizers and pesticides.

b. **Biosystems** and **Bioremediation**: Synthetic cell tools are being developed that will aid in waste management and help us to clean up areas impacted by pollution by industrial chemicals, fertilizers, heavy metals, and microplastics. Synthetic cells may offer a unique method of remediating and cleaning the environment of chemicals that natural cells cannot tolerate or process.

c. Space Exploration. The unknown environments and atmospheres of space are great obstacles to expansive space travel. Synthetic cells may unlock unique opportunities to create specialized biological methods for food and energy production, and resource recycling, beyond our planet and expand the ecosystems we deem “livable.”

d. Metabolic Engineering and Biomanufacturing. Natural cells are nature's incredible biomanufacturers, creating countless chemicals and compounds of great value. With an improved understanding of the biochemical pathways that produce these compounds we can enhance their production using synthetic cell systems. The controllability of synthetic cell systems offers great benefits in the purity and efficiency of synthesis. This means eliminating any extra, unnecessary, chemical production to make one specific compound with greater purity and less energy input.



e. Diagnostics and Therapeutics. Synthetic cells have demonstrated great potential as "smart release" drug delivery systems. Because they are "programmable", a synthetic cell can hold onto a medicine and be used to only release the medicine where needed most in the body – at the exact point of care – instead of dosing the entire body and potentially creating negative side effects.

Synthetic cells also offer a unique opportunity to "3D print" new tissue or organs and help the medical industry to overcome the shortage of organ availability for organ transplants in a safely controlled and ethical way.

f. New Materials. The programmable biological features of synthetic cells can be utilized to create novel materials. Textiles can be made with cellular traits, such as

antibacterial/antifungal capabilities, or even with embedded biosensors to detect exposure to chemicals or viruses.

Using synthetic cells instead of natural cells in creating new materials offers greater control and therefore improved biosecurity compared to natural cells, especially if the synthetic cell systems used are coded to include a "kill switch."

g. Engineering and Design Tools. A wide variety of traits and features found in natural cells can be recreated in synthetic cells and combined as needed to develop many new tools, such as biosensors utilizing a cell's ability to detect environmental changes and respond in a programmable manner (e.g.: exhibiting luminescence when exposed to a specific chemical or virus). There are an almost limitless number of ways these cellular traits can be utilized to create novel bio-tools.

h. Understanding Natural Biology**.** Natural cells, even the simplest of organisms, are such complex bio-machines that researchers are still struggling to fully understand the intricacies of how a living cell works in detail. A synthetic cell offers an opportunity to single out smaller pieces of the puzzle at a time to test and learn from outside of the confusing background noise within a living cell. A deeper understanding of cellular biochemical pathways will allow researchers to better understand our own cells and to better utilize new cell features.

5. Cellular features of interest

a. **Replication**. Cells need to replicate their DNA, wherein a double stranded DNA molecule is copied into two identical DNA molecules. This creates a "sister genome" and is the first crucial step in the process through which cells pass on their genetic makeup.

b. Self-replicating **translation system.** A well replicated genome is all well and good, but does the cell no good without a translation system to go along with it and read the code. A cell's translation system utilizes mRNA to send the information from the cell's genome to ribosomes which will process the information to make proteins.

c. Evolution. Evolution is a key feature of interest in living systems. It is an intriguing process through which a cell's DNA experiences slight changes over time and pass along new genetic features to offspring or sister cells.

d. Compartmentalization. A cell holds within it various organelles, separated by distinct compartments, wherein different cell functions can occur independently without interference from other intracellular processes. This is an important feature when a cell is doing many things at once.

e. Sensing and responding to environment - Shape changes and motility. A cell's ability to modify and mold its shape is a powerful mechanism for movement and reacting to the environment. These properties can be utilized across a variety of fields to create synthetic systems that move and change shape in response to specific stimuli (such as chemical or light exposure, temperature changes, etc.)

Relevance for Sustainable Development Goals and Grand Challenges

- **Goal 3. Ensure healthy lives.** Deeper understanding of the intricate intracellular biochemical processes that dictate our cells, the building blocks that create all living things, will allow us to better understand and treat illnesses and diseases. Synthetic cells have also proven to

be an effective means to quickly develop easy diagnostic tools. Furthermore, the ability of synthetic cells to be freeze-dried allows for medicines, vaccines, and diagnostic tools to be transported across difficult geographical boundaries to secluded and underserved communities.

- **Goal 12. Sustainable Consumption.** Cells are highly efficient mini-bioreactors that have been producing useful compounds and chemicals since they evolved. If we understand how these compounds are created, we can engineer a synthetic cell that develops it for us with less energy and fewer resources needed. Cells can also be designed to "eat" harmful or toxic materials such as plastics, oils, and hazardous chemicals. These features can be utilized to process dangerous waste or clean up environments impacted by hazardous human waste.
- **Goal 13. Combat Climate Change.** Natural cells have evolved many unique ways of surviving and thriving across earth's varied and sometimes extreme ecosystems. Adaptations such as energy efficient metabolism of greenhouse gases and sustainable energy production and capture from waste materials can be harnessed and improved for energy production and more efficient manufacturing and supply chains that will counter climate change.

Pupil Participation

1. ***Class Discussion.*** What is currently understood about how different cells function and interact with their environment?

2. ***Pupil stakeholder awareness***

a. Understanding and modification of complex biochemical cellular functions can help address the SDGs. What cellular features are of interest to you personally?

b. Can you think of any ways you interact with cellular biotechnologies? What foods do you eat that utilize cellular processes? What medicines were uniquely designed for targeted cellular impacts?

3. ***Exercises***

a. Looking at the SDGs, how can we take advantage of the cellular functions towards environmental, social, and economic sustainability? What are the challenges and opportunities?

b. Consider some of the bizarre living cells found in natural life (extremophiles, octopus skin cells, koala digestive systems that break down toxic leaves, etc.). Consider an issue relevant to the SDGs and design a cell that will help address it using features present in living systems.

The Evidence Base, Further Reading and Teaching Aids

https://www.youtube.com/watch?v=7er7saHVFW0&t=63s

Glossary

Bioremediation: the use of either naturally occurring or deliberately introduced microorganisms or other forms of life to consume and break down environmental pollutants, in order to clean up a polluted site.

Bioengineering: a discipline that applies engineering principles of design and analysis to biological systems and biomedical technologies

Biosystem: **a living organism or any complete system of living things that can, directly or indirectly, interact with others.**

Replication: the process by which the genome's DNA is copied in cells

Translation system: the process that takes the information passed from DNA as messenger RNA and turns it into specific molecules that allow/create different functions/features in a cell

Synthetic Cells: An artificial cell or minimal cell is an engineered particle that mimics one or many functions of a biological cell