Synthetic Biology: Principles and Applications

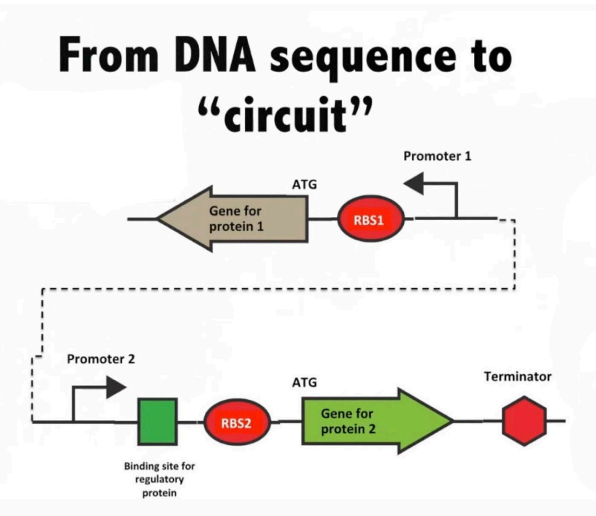
Have you ever wondered what synthetic biology is and why it's so important? When explaining synthetic biology, people often compare it to building a puzzle or LEGO set, but I prefer to think of it as writing a novel.

With just 26 letters in the alphabet, we can create over a billion words, yet crafting a novel is more than just stringing words together. You need to thoughtfully select your characters, plot, and setting to tell a unique story and create something meaningful. Similarly, in synthetic biology, we work with the basic building blocks — like DNA sequences — but it's how we arrange them that matters. By designing new functions and abilities in organisms, each genetic modification plays a role, just like each chapter in a novel. Together, they build toward the final goal: an organism engineered to solve real-world problems.

Synthetic biology is a field of science that involves redesigning organisms for useful purposes by engineering them to have new abilities, harnessing the power of nature to solve problems in medicine, manufacturing, agriculture and so much more.

DNA to Circuits

One of the fundamental concepts of synthetic biology is manipulating biological parts, whether by breaking down DNA sequences or working with proteins. This approach allows scientists to reassemble these components in specific ways to create new functions and capabilities.



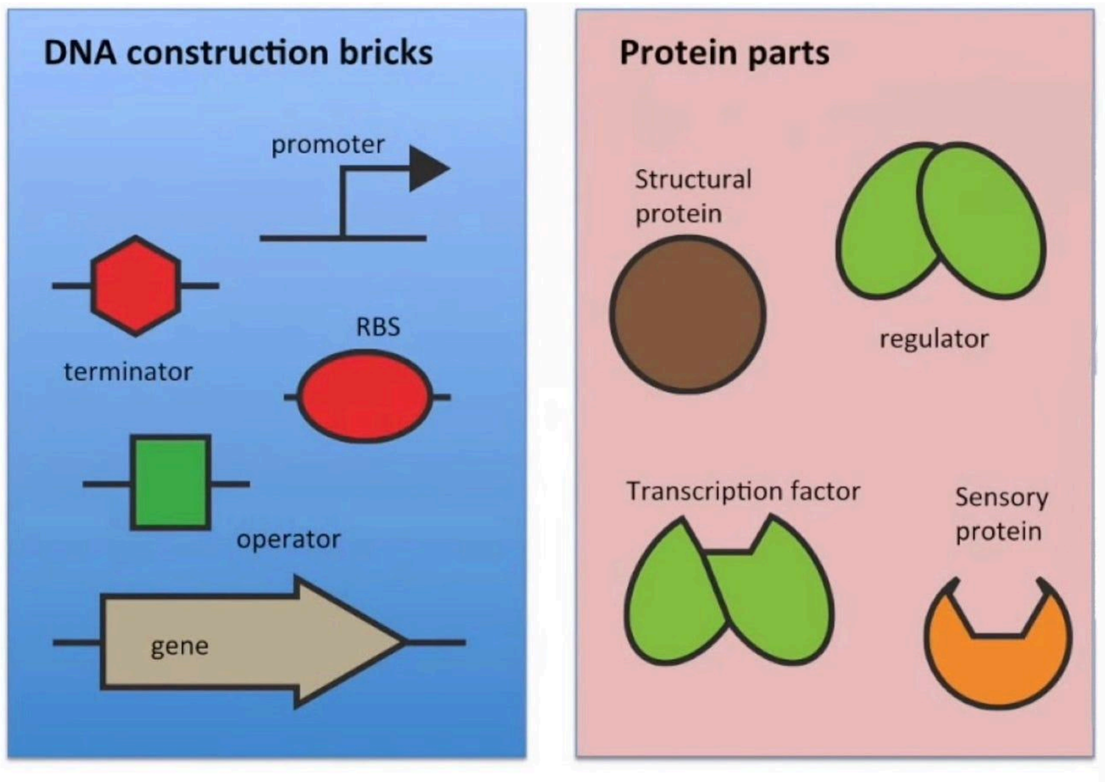
In the sequences above, DNA has been broken down schematically, illustrating the following: **genes**, which are coding regions essential for producing proteins, are typically represented as small arrows in diagrams, often colour-coded for clarity — in this example is the green for one gene and brown for another. The synthesis of these genes is regulated by **promoters**, which serve as signals for starting protein synthesis and are also depicted as different arrows.

Additionally, **ribosome binding sites** (RBS1 and RBS2) are crucial signals indicated in these schematics, guiding the ribosomes to initiate the translation of the corresponding proteins.

Translation *is the process by which cells create proteins using messenger RNA (mRNA). After DNA is copied into mRNA, the cell uses various components, including ribosomes, to read the mRNA sequence. These components work together to assemble the corresponding amino acids into proteins, resulting in newly formed proteins that perform important functions within the cell.*

Furthermore, synthetic biologists may require additional elements, such as a binding site for a regulatory protein and a terminator, which serves as a signal for RNA polymerase to stop transcription.

Circuit Parts



In synbio, scientists can break down a sequence into its components, allowing them to study these parts in their natural context within a living organism. They can also rearrange these components into different configurations for further research.

By breaking down the previous sequence, we can identify the essential DNA building blocks needed for assembly. This process allows us to study these components and assemble them in different ways.

However, we also need to incorporate protein parts, such as structural proteins, regulator proteins that signal the cell when to initiate transcription, transcription factors, and sensory proteins, depending on the specific objectives.

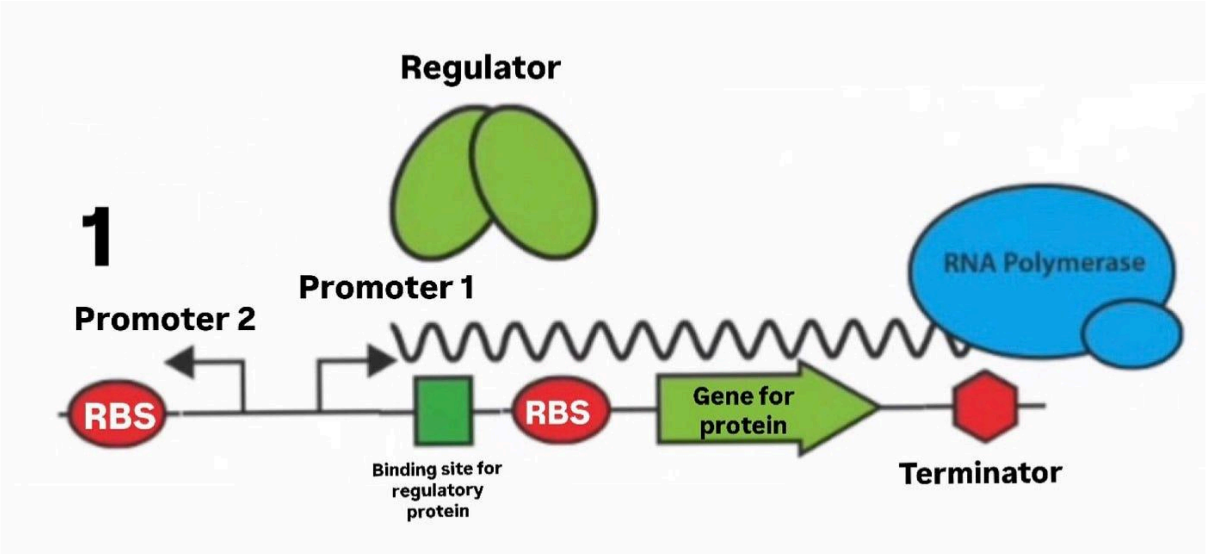
Rules and Models

The second concept in synbio is the use of rules and models. It's not enough to simply dissect a DNA sequence and know the exact arrangement of the A's, C's, G's, and T's in an organism's genome or in a section of DNA we aim to construct. We also need to understand how these sequences interact with each other and how they function together. This is done by identifying the rules that the cell follows to make the sequence operational.

To achieve this, synthetic biology employs specific rules, such as logical conditions that determine whether a gene is turned on or off. Additionally, it utilises models that aim to predict how a specific stretch of DNA — including promoters, terminators, and binding sites — operates within the cell.

Let's revisit the same DNA circuit we discussed earlier, along with the various components necessary for its operation within the genome. This will help us understand what these elements mean for the cell in the following steps.

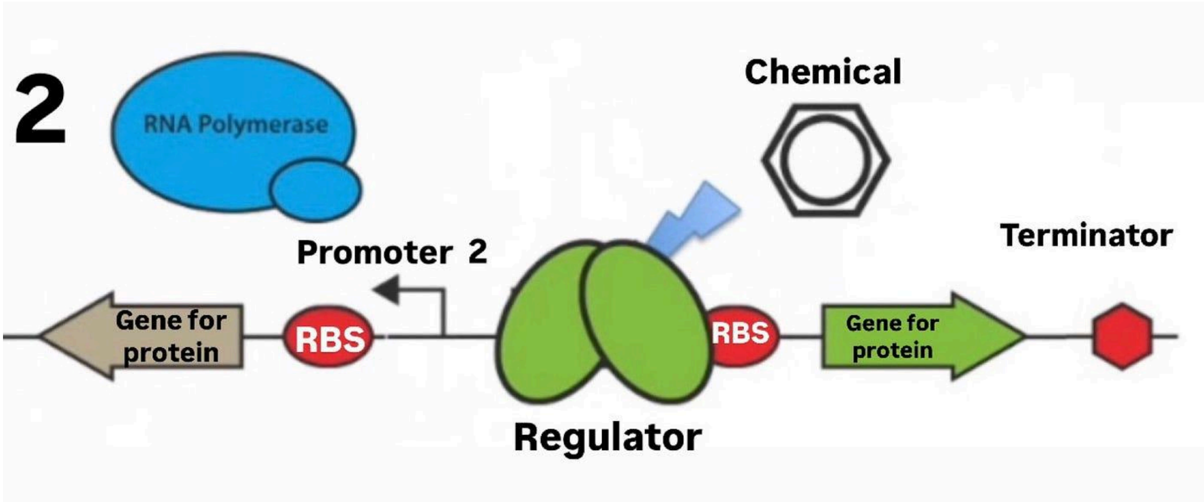
Step 1



The initial signal for the cell to begin interpreting a DNA sequence is the transcription of a specific gene, which, in this example, is the green gene. This process starts when the enzyme RNA polymerase binds to a region of the DNA known as the **promoter**. Once attached, RNA polymerase moves along the DNA strand, synthesizing a complementary strand of messenger RNA (mRNA) until it encounters a **terminator sequence**, which signals the end of transcription.

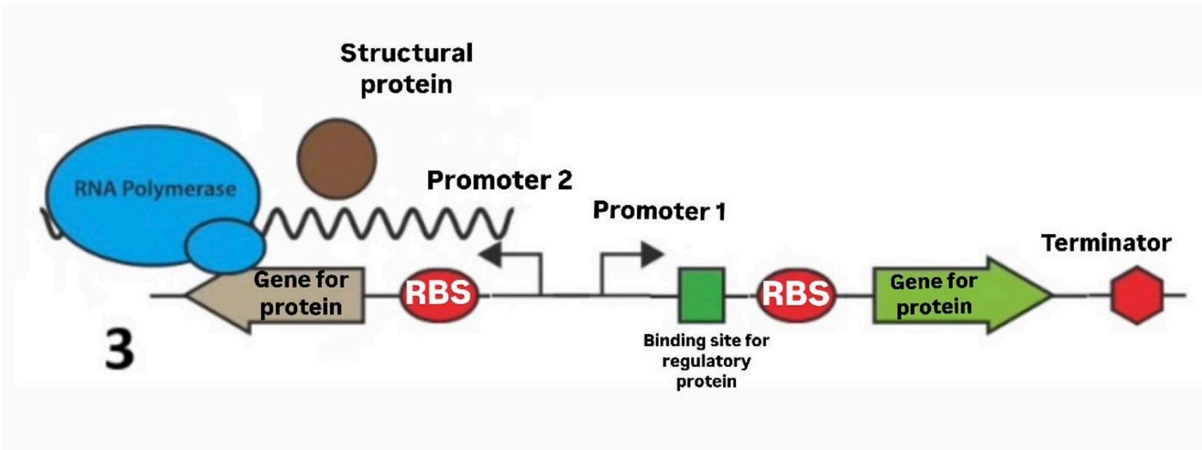
After the mRNA is produced, it is then translated into a protein, in this case, a **regulator**. The role of this regulator protein is to bind to the DNA at a particular site, the binding site.

Step 2



By binding to the binding site, the regulator protein can influence the transcription of other genes, either enhancing or suppressing their expression. This sensory protein is specifically designed to detect particular chemicals that interact with it, allowing it to guide RNA polymerase to a different promoter, **promoter 2**, to initiate further transcription.

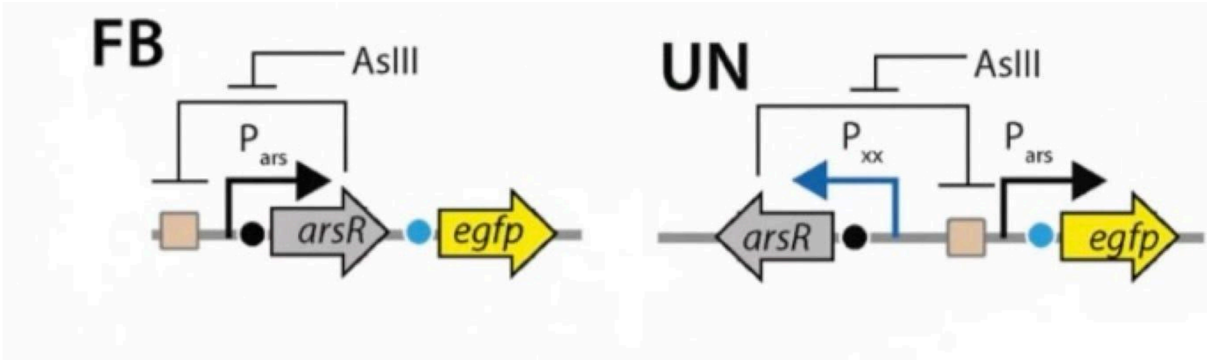
Step 3



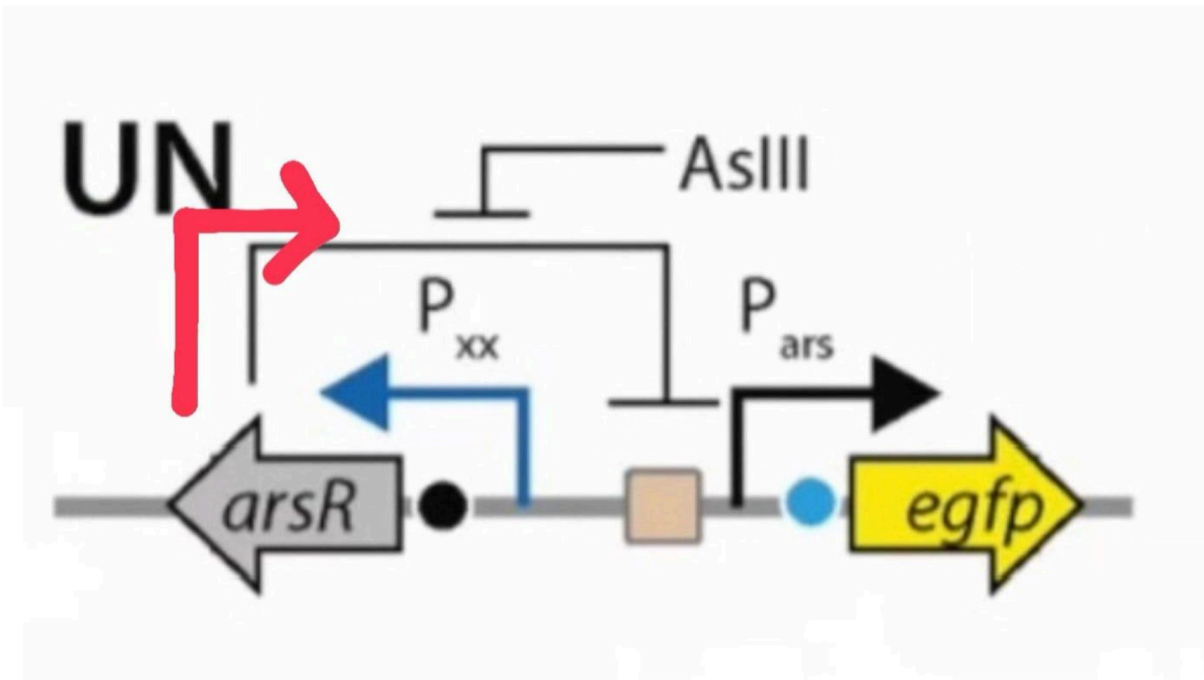
Once the regulator protein has successfully drawn RNA polymerase to promoter 2 and RNA polymerase is bound to this promoter, it initiates the transcription of the gene, leading to the production of the specific protein.

So as seen, this simple schematic structure provides instructions to the cell: it indicates where to begin, initiates protein production, and facilitates the binding of that protein to intercept signals, leading to the transcription of another protein. It's a straightforward process that follows a specific set of rules.

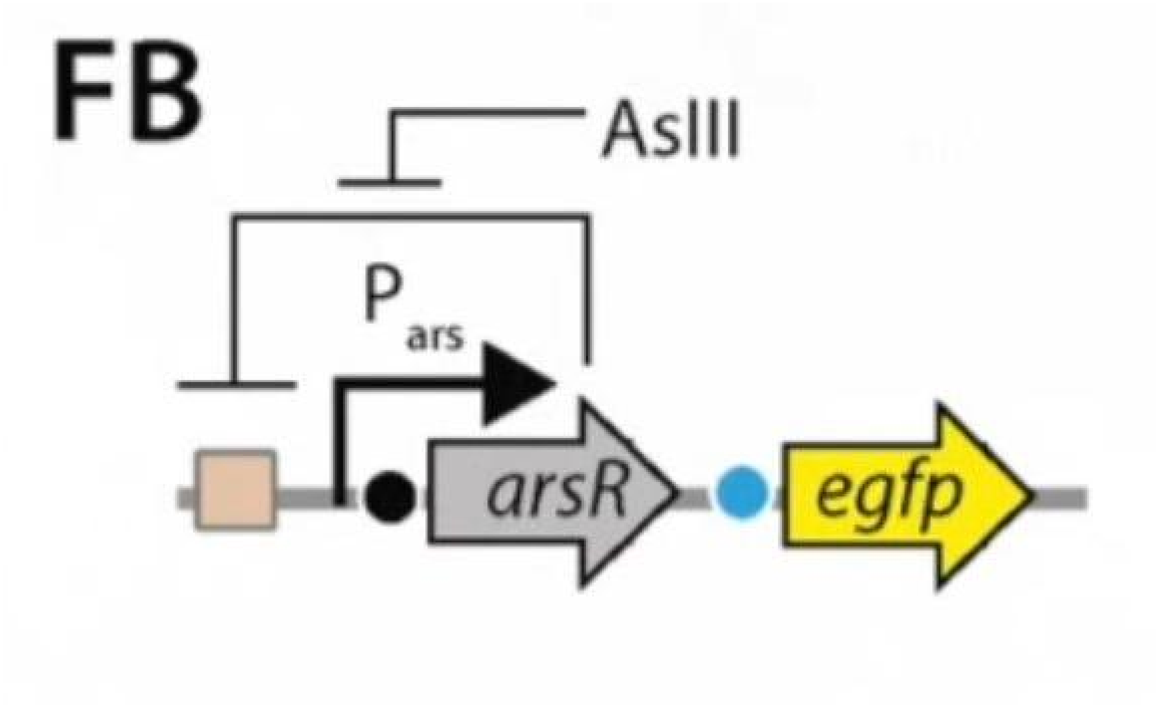
Predictions of the DNA Circuits



The rules can also be represented in a mathematical model, allowing us to predict the behaviour of certain circuits. For instance, look at two basic circuits, **FB** (Feedback) and **UN** (Uncoupled): one has two genes arranged in opposite directions, as shown on the right, while the other has the same genes positioned opposite to one another, as illustrated on the left.

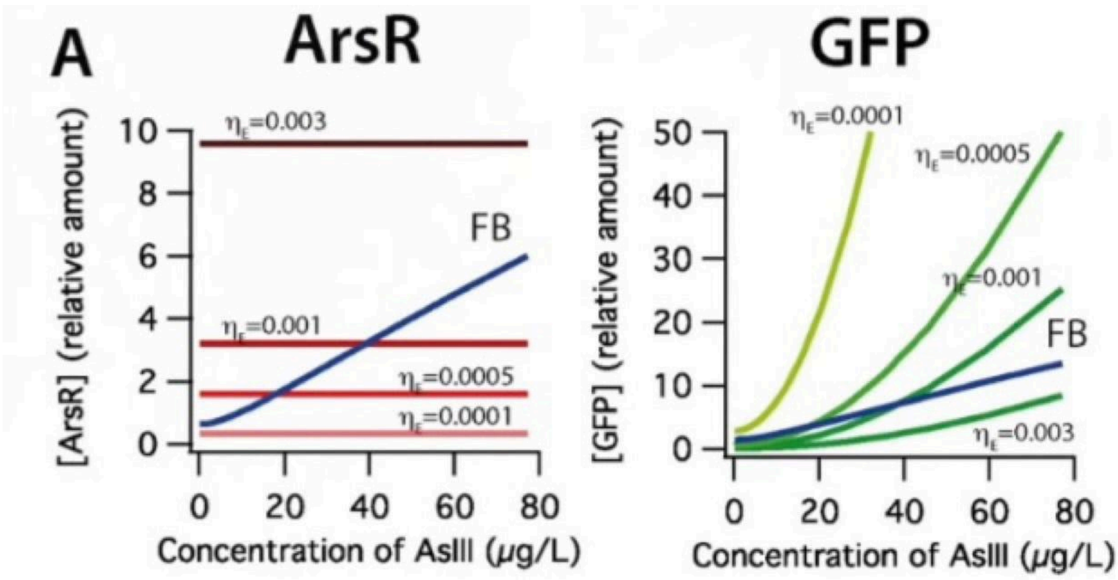


Now, the rules set by the UN circuit indicate that this “arsR” gene codes for a protein that will then prohibit the transcription of the yellow gene.



In this other case, this protein will inhibit its own synthesis and the gene that is in yellow behind it.

However, in the other case, it cannot stop its own synthesis because it doesn’t bind to the promoter that controls its transcription.



Subsequently, the model predicts that in the case of the FB circuit, the system's response will depend on a signalling molecule — in this case, arsenic (AsIII). The graph on the left shows that as the concentration of As increases, the amount of the ArsR protein increases, and there will also be an increase in GFP protein production, as seen in the graph on the right.

*A **signalling** molecule is a chemical that cells use to communicate with each other or to trigger specific processes within the cell.*

In the UN circuit, the ArsR gene is controlled by a different factor, not by itself. As shown in the left graph, ArsR is produced consistently, regardless of arsenic concentration. However, GFP production is still influenced by arsenic levels, with higher arsenic concentrations leading to more GFP protein, as illustrated in the graph.

With those examples, we have observed that these basic genetic circuits provide specific instructions to the cell, which will execute them if the circuit has the required components and we have seen in the graphs how these genetic circuits operate according to the instructions they provide, particularly in relation to **genetic regulation** and **environmental signals**.

Standards

The third concept of synthetic biology is the establishment of standards. This is needed for collaboration across different laboratories and industries. It is similar to how units of measurement in physics ensure clarity in scientific communication to help with innovation within the field.

In synthetic biology, the establishment of standards allows researchers to collaborate effectively on shared components, functioning like a universal language. Regardless of their background or location, scientists can work with these standards, which facilitate communication and understanding between them. A key aspect of these standards is the standardization of genetic parts like interchangeable DNA sequences with defined functions used to construct biological circuits. Just as units like metres and kilograms provide a common framework in physics, enzyme standards ensure consistency in enzymatic reactions across various applications.

Research Areas in Synbio

Currently, synthetic biologists are focused on integrating biological parts using established rules and models. They aim to understand the functionality and significance of these constructions, but the process is complex and often fragmented across different research areas such as the following:

- Standard parts and methods
- DNA synthesis and design of genomes or genome parts
- Minimal cells and host production platforms ("chassis")
- Protocells and artificial life
- Xeno-DNA/-biology
- Do-it-yourself biology

Standard Parts and Methods

This is the creation of new models and complex engineering strategies relies on having well-characterized standard parts. The more parts we have and the better we understand them, the more effectively we can produce innovative structures in synthetic biology.

DNA Synthesis and Genome Design

Current advancements in DNA synthesis enable biologists to create genetic sequences and send them electronically to synthesis companies for production. This process accelerates the assembly of genetic components. Researchers are now exploring the design of entire genomes, which continues to be a complex challenge due to our incomplete understanding of the rules that regulate genome assembly.

Minimal Cells and Host Production Platforms ("Chassis")

In synthetic biology, the term "chassis" refers to minimal cells or host production platforms. Just like a car can run with different types of seats, these chassis can support various components, such as bacteria or yeast, with its researchers aiming to create minimal cells stripped of unnecessary complexity, allowing them to focus on essential functions and components.

Protocells and Artificial Life

The study of protocells and artificial life focuses on understanding the origins of life. Although the exact origins remain a mystery, synthetic biologists aim to recreate certain life forms, which could significantly enhance our understanding of life's emergence and the various pathways leading to it.

Xeno-DNA/Biology

Xeno-biology explores the modification of DNA and proteins by incorporating non-standard amino acids. By doing so, researchers aim to create proteins with new functionalities that are not currently possible, opening up exciting possibilities for innovation.

Do-It-Yourself Biology

Synthetic biology has fostered a do-it-yourself culture, encouraging both amateurs and enthusiasts to engage with biology. This movement enables people to build simple instruments, join organized groups, and explore biological phenomena, expanding the reach and understanding of the field.

Having explored what synthetic biology is and studied some examples and research areas, let's look into the reasons behind these efforts. What are the applications of synthetic biology?

Potential Applications

There is significant optimism that synthetic biology can lead to the development of innovative solutions beneficial for both human and animal health. Substantial investments are being directed toward various applications, including pharmaceuticals, vaccines, gene therapy, tissue engineering, probiotics, and diagnostics.

However, many other important fields are also being explored, such as agriculture. Researchers are focusing on developing plants that are resistant to diseases and drought, as well as those that provide better feedstocks for animals. Additionally, with synthetic biology, we can enhance CO2 sequestration, as seen with algae, and improve chemical production and diagnostics. But not just that; synthetic biology is also being used to make bioenergy and biofuels more scalable and affordable, and there is significant interest in creating unique chemicals and new substances by combining DNA and proteins to develop materials with previously unseen properties.

Furthermore, synthetic biology has enabled various environmental management applications, from biosensors and bioremediation to waste treatment, by engineering specific organisms to perform tasks beyond their natural capabilities. One promising application could involve using engineered bacteria to reduce air pollution. Inspired by the fascinating characteristics of Bacillus cereus, I envision a synthetic biology approach to enhance this bacterium's ability to capture particulate matter (PM2.5) from coal power plant emissions, frequently used in Poland. B. cereus naturally produces a sticky extracellular matrix within its biofilm, which could potentially trap PM2.5 particles — pollutants responsible for 50,000 deaths annually in Poland and a nine-month reduction in life expectancy. The bacterium's biofilms, which form at the air-liquid interface, can interact with airborne particles. Additionally, its strong adhesion to surfaces such as stainless steel and glass may allow it to effectively capture particles within filtration systems. Incorporating these engineered biofilms into filtration systems could present a new method to reduce the release of harmful particles into the atmosphere. Although this idea remains in the early conceptual phase, I am excited to begin its development and turn it into a reality.

Conclusion

Synthetic biology enables us to assemble biological components into complex systems, enhancing our understanding of life and expanding the functional capacities of organisms. This field goes far beyond engineering individual proteins, allowing us to design entire pathways that can perform functions once thought impossible. The potential applications of synthetic biology are extended and hold the promise of revolutionary scientific advancements. Projects like engineering *Bacillus cereus* to capture PM2.5 particles from coal plant emissions exemplify this potential. While not every initiative may achieve the desired results, unexpected breakthroughs are often around the corner, bringing tangible progress. The best part? Some promising outcomes are already within reach, meaning we don't have to wait decades to see significant benefits from synthetic biology.