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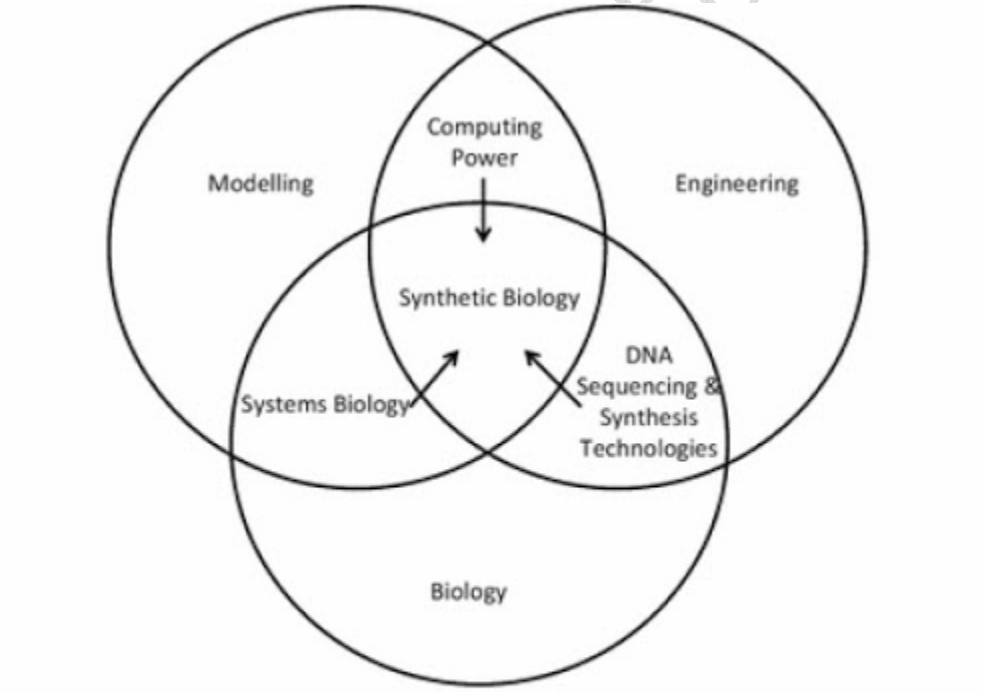
SYNTHETIC BIOLOGY :

Synthetic biology is the design and construction of new biological entities such as enzymes, genetic circuits, and cells or the redesign of existing biological systems. Synthetic biology builds on the advances in molecular, cell, and systems biology and seeks to transform biology in the same way that synthesis transformed chemistry and integrated circuit design transformed computing. The element that distinguishes synthetic biology from traditional molecular and cellular biology is the focus on the design and construction of core components (parts of enzymes, genetic circuits, metabolic pathways, etc.) that can be modeled, understood, and tuned to meet specific performance criteria, and the assembly of these smaller parts and devices into larger integrated systems to solve specific problems.



Synthetic biology is a set of research activities at the intersection of engineering, computational modelling, and biological sciences. It builds on a variety of technologies and tools including improvements in DNA sequencing, cheaper gene synthesis technologies, increased computational power, and a better understanding of biological systems gained through systems biology

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Applications OF SYNTHETIC BIOLOGY :

- Early synthetic biology designs, namely the genetic toggle switch and repressilator, showed that regulatory components can be characterized and assembled to bring about complex, electronics-inspired behaviours in living systems (for example, memory storage and timekeeping).

- Through the characterization and assembly of genetic parts and biological building blocks, many more devices have been constructed, including switches, memory elements, oscillators, pulse generators, digital logic gates, filters and communication modules.

- Advances in the field are now allowing expansion beyond small gene networks to the realm of larger biological programs, which hold promise for a wide range of applications, including biosensing, therapeutics and the production of biofuels, pharmaceuticals and biomaterials.

- Synthetic biosensing circuits consist of sensitive elements that bind analytes and transducer modules that mobilize cellular responses. Balancing these two modules involves engineering modularity and specificity into the various circuits.

- Biosensor sensitive elements include environment-responsive promoters (transcriptional), RNA aptamers (translational) and protein receptors (post-translational).

- Biosensor transducer modules include engineered gene networks (transcriptional), non-coding regulatory RNAs (translational) and protein signal-transduction circuits (post-translational).

- The contributions of synthetic biology to therapeutics include: engineered networks and organisms for disease-mechanism elucidation, drug-target identification, drug-discovery platforms, therapeutic treatment, therapeutic delivery, and drug production and access.

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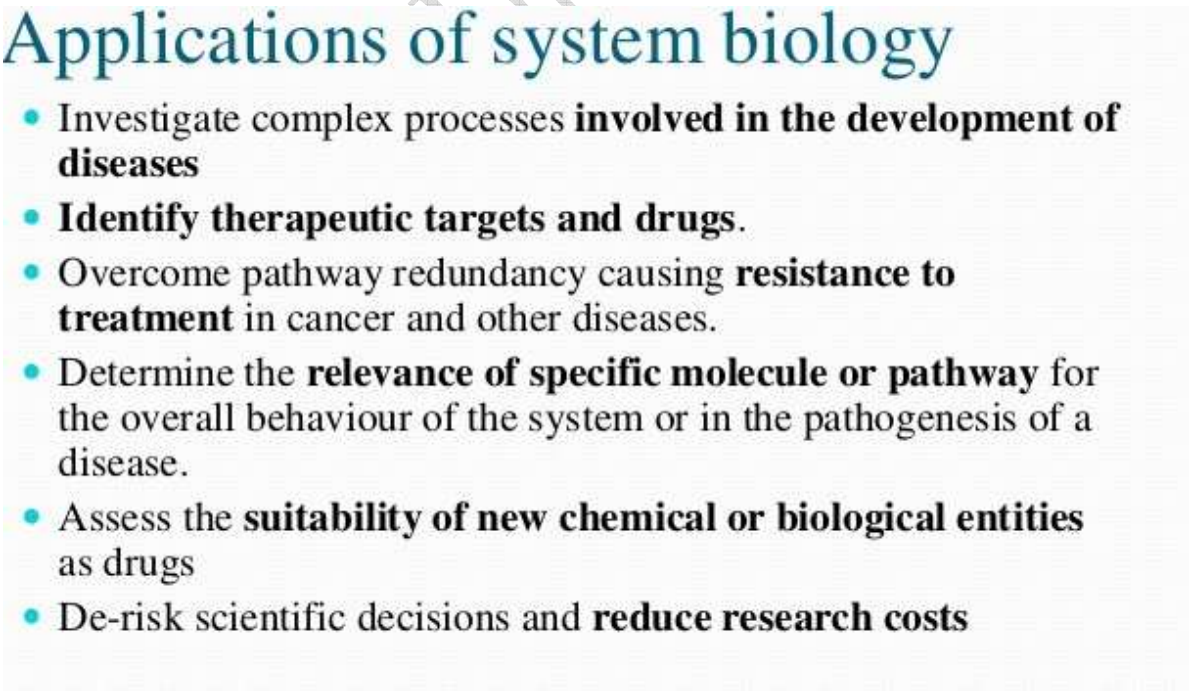
- In the microbial production of biofuels and pharmaceuticals, synthetic biology has supplemented traditional genetic and metabolic engineering efforts by aiding the construction of optimized biosynthetic pathways.

- Optimizing metabolic flux through biosynthetic pathways is traditionally accomplished by driving the expression of pathway enzymes with strong, inducible promoters. New synthetic approaches include the rapid diversification of various pathway components, the rational and model-guided assembly of pathway components, and hybrid solutions.

SYSTEMS BIOLOGY:

Systems biology is a biology-based interdisciplinary study field that concentrates on the systematic studying of the complex interactions in biological systems, using a new perspective (holism instead of reduction).



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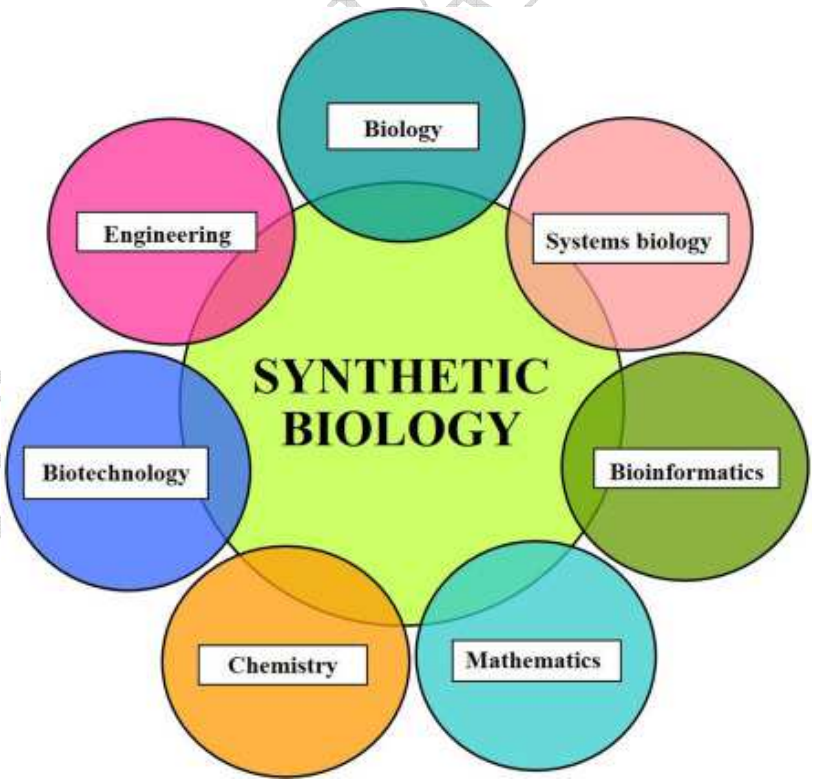
Synthetic Biology vs. Systems Biology

- **Systems biology** studies complex biological systems as integrated wholes, using tools of modeling, simulation, and comparison to experiment. The focus tends to be on natural systems, often with some (at least long term) medical significance.

- **Synthetic biology** studies how to build artificial biological systems for engineering applications, using many of the same tools and experimental techniques. ***But the work is fundamentally an engineering application of biological science, rather than an attempt to do more science***. The focus is often on ways of taking parts of natural biological systems, characterizing and simplifying them, and using them as a component of a highly unnatural, engineered, biological system.



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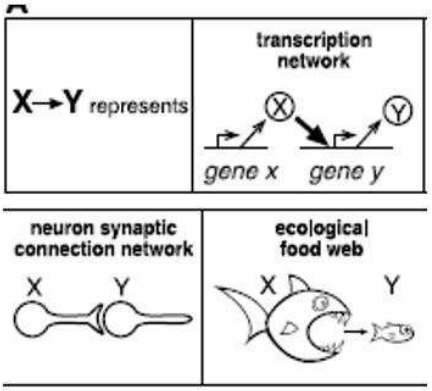
NET WORKNG IN BIOLOGY:

Biological systems are often represented as networks which are complex sets of binary interactions or relations between different entities. Essentially, every biological entity has interactions with other biological entities, from the molecular to the ecosystem level, providing us with the opportunity to model biology using many different types of networks such as ecological, neurological, metabolic or molecular interaction networks

Many Types of Biological Networks

- **protein – protein**
  - **nodes are proteins**
  - **links are interactions**
- **metabolic networks**
  - **nodes are small molecules metabolites**
  - **links are reactions**
- **neuronal networks**
  - **node are neurons**
  - **links are synaptic connections**
- **transcription networks**
  - **nodes are genes**
  - **links are activation or repression of gene expression**



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QUORUM SENSING :

Quorum sensing is a gene regulation mechanism used by bacteria. They utilize this mechanism to communicate with bacterial cells and sense their own population density. They produce and secrete small molecules known as autoinducers to sense the population density. Using this method, they regulate the expression of virulence genes. Moreover, autoinducers are small diffusible signalling molecules, mainly N-acyl-homoserine lactones (AHL). They trigger the expression of virulence genes.

Quorum sensing is important for many physiological activities of bacteria. Quorum sensing molecules induce processes such as symbiosis, virulence, competence, conjugation, antibiotic production, motility, sporulation, nitrogen fixation and biofilm formation, etc.

Furthermore, quorum sensing is common in both gram-negative and gram-positive bacteria. However, they secrete different molecules as autoinducers. Gram-negative bacteria mediate quorum sensing through acylated homoserine lactones while gram-positive bacteria mediate it through processed oligo-peptides

cooperative behaviour	group-derived benefits	microbe examples	higher organism comparisons
chemical communication (quorum sensing)	coordinated population behaviour	*Vibrio fischeri, Pseudomonas aeruginosa, Staphylococcus aureus*, etc.	pheromone production in many social animals

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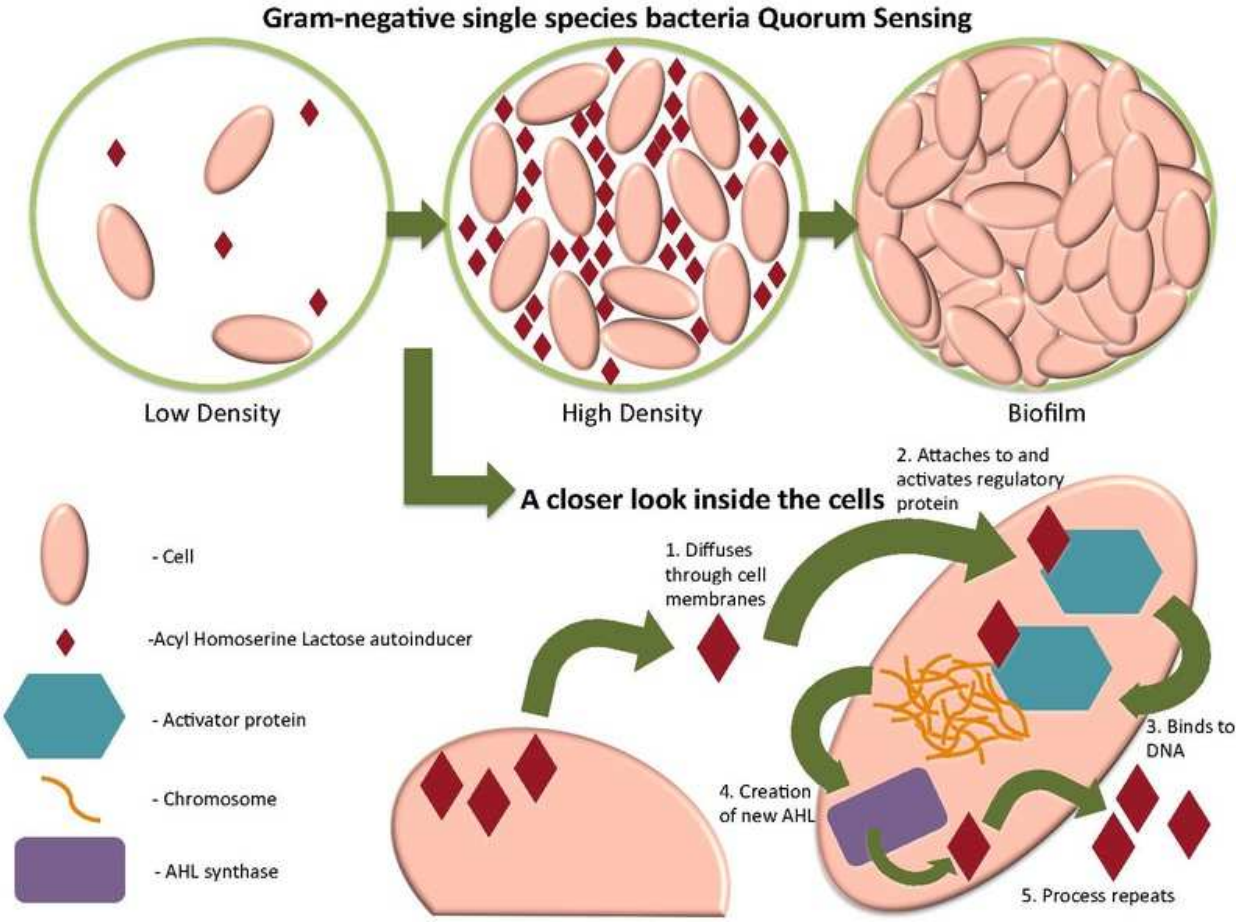

Quorum sensing can be divided into at least 4 steps:

(1) production of small biochemical signal molecules by the bacterial cell;

(2) release of the signal molecules, either actively or passively, into the surrounding environment; (3) recognition of the signal molecules by specific receptors once they exceed a threshold concentration, leading to

(4) changes in gene regulation.

One common consequence of quorum sensing induction of gene expression is increased synthesis of the proteins involved in signal molecule production. Increased synthesis of the signal molecule creates a positive feedback loop, which is why quorum signals are commonly called autoinducers.

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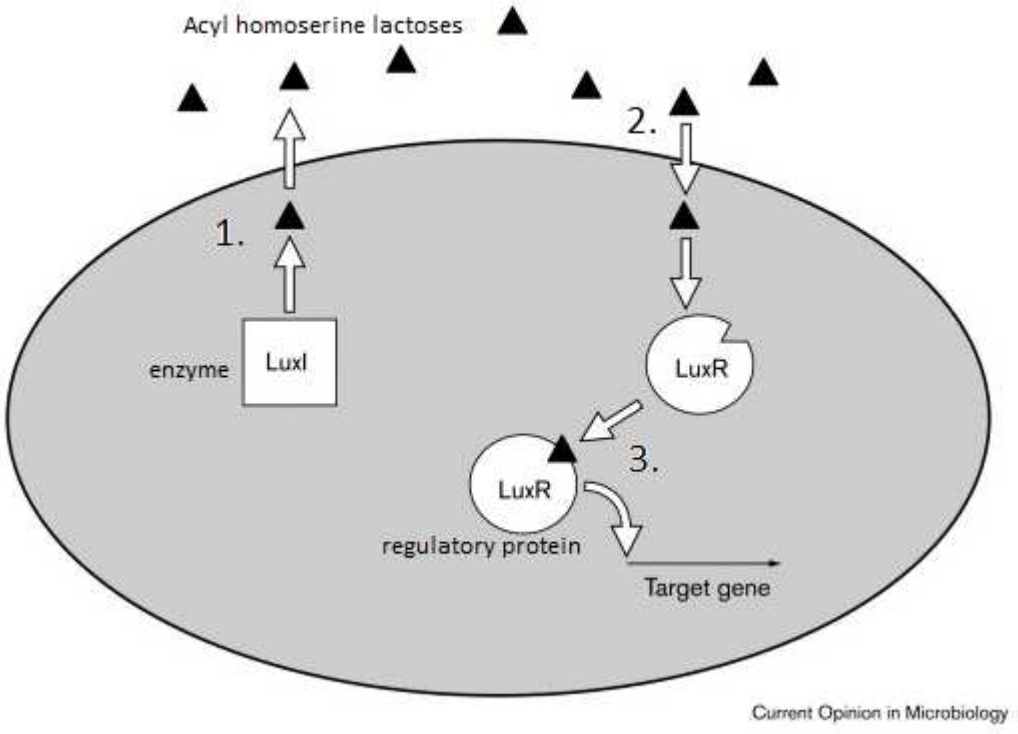
Qurum sensing in Gram negative bacteria :

1. Acyl homoserine lactoses are synthesized by enzymes and move through the bacterium membrane via passive diffusion.
2. When a significant concentration of lactoses is reached, it binds and activates a regulatory protein on the cell membrane.
3. The regulatory protein then binds to a specific DNA site and influences the target gene. It also induces more production of the lactose signaling molecules.



Qurum sensing in Gram positive bacteria :

1. Oligopeptides are cleaved into small functional units and secreted out of the bacterium through a transporter protein.
2. Signal oligopeptides are detected by a sensor protein on the bacterium's surface when they reach a significant concentration.
3. The protein becomes phosphorylated and the phosphate is transferred to a response regulator protein.
4. The phosphorylated regulator protein binds to a specific DNA site and alters transcription in the target gene.

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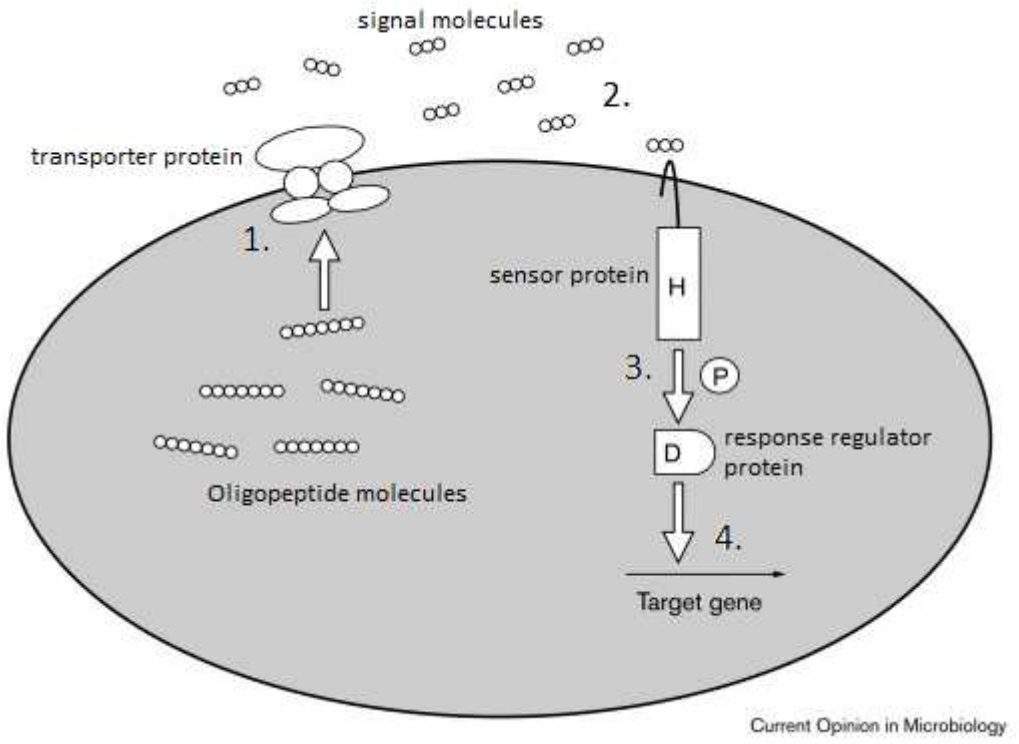

Quorum Sensing Molecules

The concentration of the low weight extracellular molecules which facilitate quorum sensing is proportional to the size of the bacterial population. A small population produces a low concentration of sensing molecules, while a large population produces a high concentration of sensing molecules. These molecules are responsible for information exchange and inducing gene expression among bacterial populations.

1. Acyl homoserine lactones are present mainly in Gram negative bacteria and are in control of their own synthesis. There is a lot of diversity in this group, with different bacteria species being able to produce unique lactones; however, some bacteria species produce the same lactones. The head group consists of the homoserine lactone and is conserved among all types of lactones; the tail goup is the acyl function group and is a variable region that determines the specificity of the receptor.

2. Oligopeptide molecules are present mainly in Gram positive bacteria. Their synthesis is dependent on ribosomes and their peptides can be modified.
3. Pseudomonas quinolone signal is a quorum sensing molecule specific to the *Psuedomonas* species. High concentrations of these molecules are produced. They are transported via membrane vesicles.
4. Auto inducer two is a quorum sensing molecule used by many Gram negative bacteria to facilitate communication between different species

Artificial cell :

Artificial cells refer to a class of artificial structures where biologically active components, for example, proteins, genes, enzymes, or other cellular structures, are encapsulated in artificial membranes. Polymer, protein, lipid, and their conjugates have been used to create artificial membranes. Small molecules can diffuse rapidly across the membrane, while active components inside the membrane are protected against antibodies or tryptic enzymes outside.

Up till now, two main fundamental approaches have been considered for the construction of an artificial cell: A top-down approach and a bottom-up approach .

The top-down approach starts from a living organism, stripping down the genome to the lowest number of genes that are required to maintain the essential properties of the cellular life, or totally replacing the genome with a synthetic one .

In contrast, the bottom-up approach starts from scratch . It constructs a ‘living’ artificial cell by assembling biological and/or non-biological molecules. These two approaches are very different but complementary to each other, fabricating a broad range of artificial cells from a simple protocell to an engineered living life.

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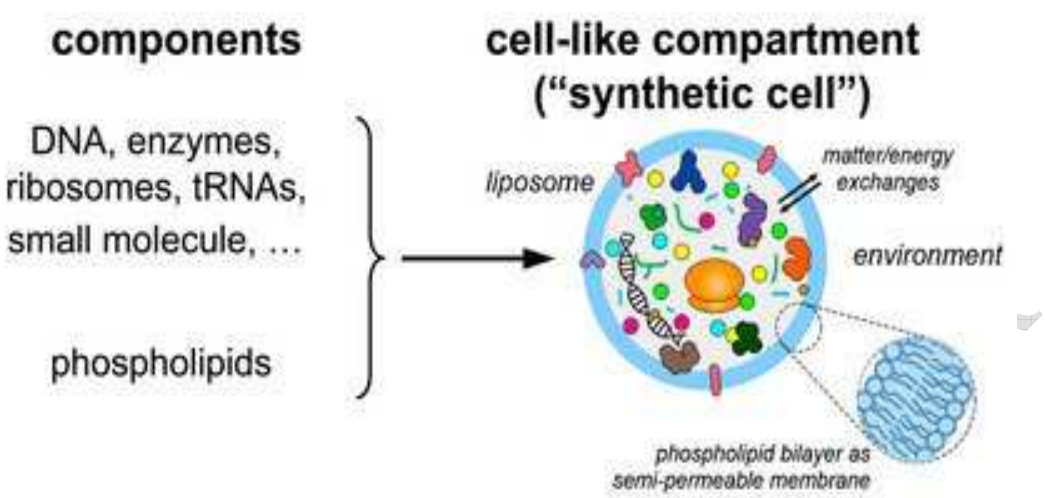
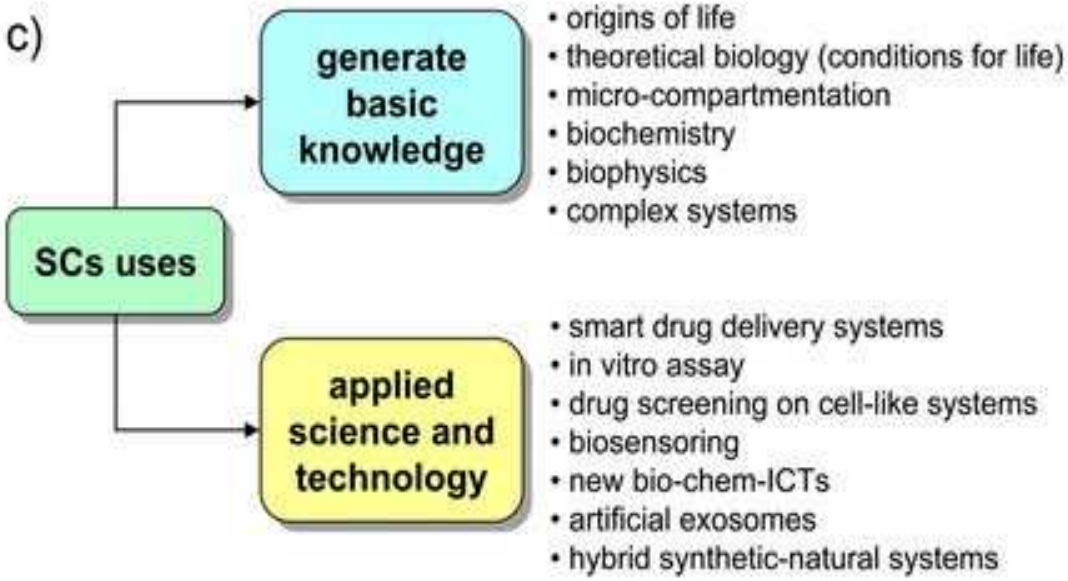


b)

Components	Examples
Primitive-like	Fatty acids, isoprenoids, ribozymes, short peptides, …
Biological	DNA, ribosomes, enzymes, tRNAs, phospholipids, …
Artificial	Polymers, surfactants, PNAs, inorganic catalysts, …

c)



The potential benefits that artificial cells may bring include:

(i) providing plausible theory for the origin of life,
(ii) providing a less-interfering way to investigate and understand the cellular life,
(iii) connecting the non-living to the living world,

(iv) Replacing engineered organisms to produce pharmaceuticals and fuels,

(iv) biomedical applications such as replacement or supplement of deficient cells, drug delivery or medical imaging, and

(vi) adding new functions that are absent in biological cells. Undoubtedly, further development of artificial cells will bring attractive opportunities to many fields such as biotechnology, medicine, and industry.