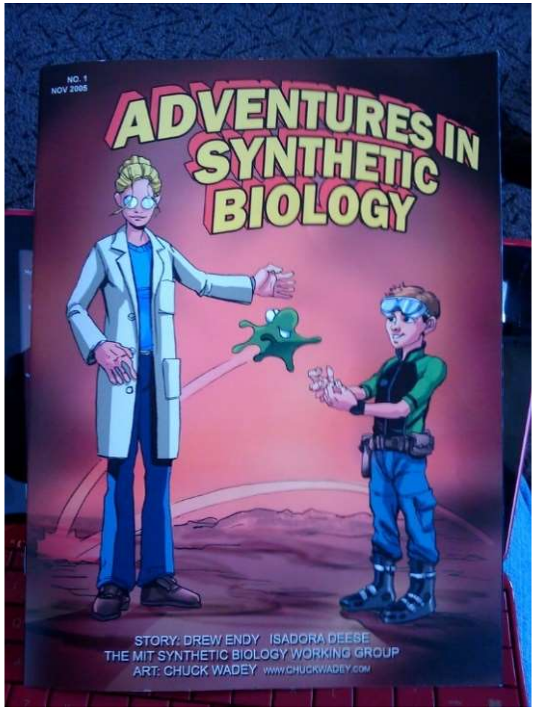
What is Synthetic Biology?

UE2.1 Biological Parts and Devices

http://web.mit.edu/endy/www/scraps/comic/AiSB.vol1.pdf



Yeh, B.J., and Lim, W.A. (2007). Nat. Chem. Biol.

Manish Kushwaha

25 September, 2024

What is Synthetic Biology?

- The first reported use of the term "Synthetic Biology" dates as long back as 1910-1912, by French Biologist Stéphane Leduc.
- Waclaw Szybalski is credited for popularizing it in 1974.
- However, it has re-appeared as a new biological discipline at the turn of the millennium (2000).

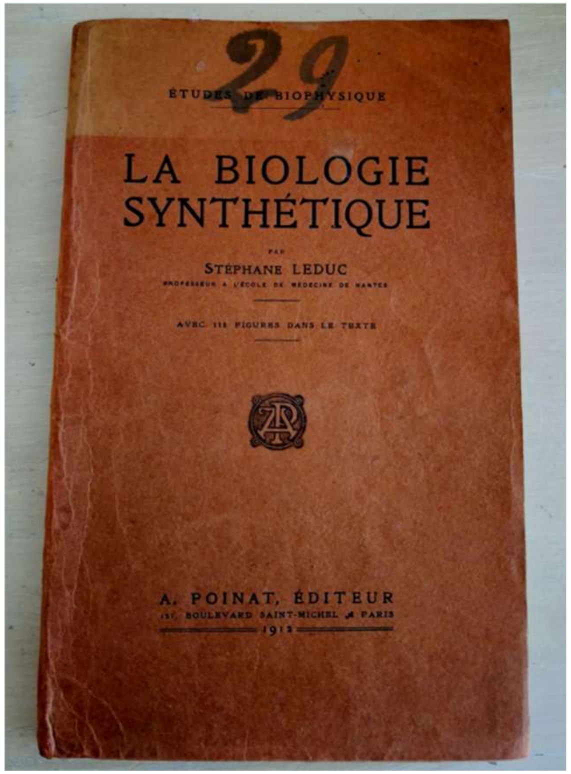


Image credit
@ad_am_ara

What is Synthetic Biology?

- Like any other new discipline, **its definition is still evolving**. It has variously been described as a discipline:

1) "Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures—from individual molecules to whole cells, tissues and organisms. In essence, synthetic biology will enable the design of 'biological systems' in a rational and systematic way." (NEST High-Level Expert Group, 2005)

2) "where ICT, biotechnology and nanotechnology meet and strengthen each other" (De Vriend, 2006)

3) "that uses engineering principles to design and assemble biological components" (Wellhausen & Oye, 2007)

4) "towards Biotechnology 2.0" (Zakrzewski et al., 2013)

5) "Synthetic biology is an emerging area of research that can broadly be described as the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems." (The Royal Society, 2014)

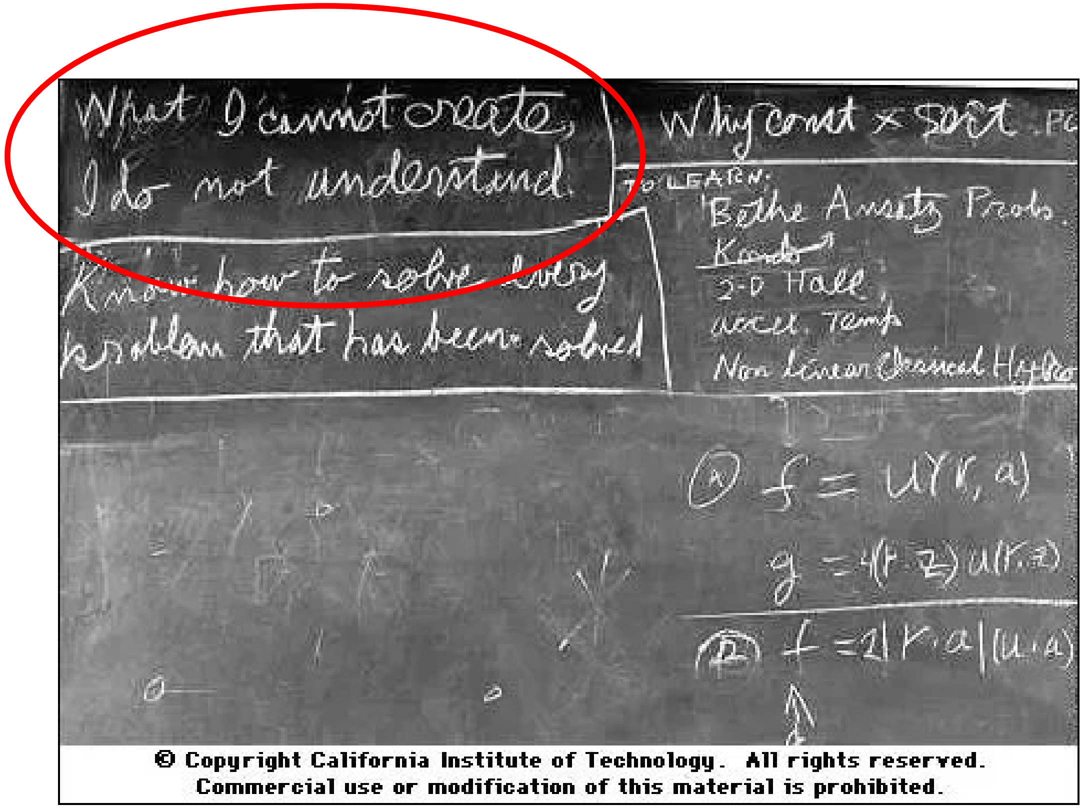
What place could Synthetic Biology have in the Sciences?

"… at the moment of its birth, a science not only gets rid of a certain number of obstacles but also eliminates and masks a certain amount of existing knowledge and wisdoms. It's as if applying a new grid, which allows for the appearance of phenomena that had been previously masked while at the same time masking already existing knowledge …"

-Michel Foucault

A televised debate (1971)
Debate Noam Chomsky & Michel Foucault - On human nature [Subtitled]
https://www.youtube.com/watch?v=3wfNI2L0Gf8

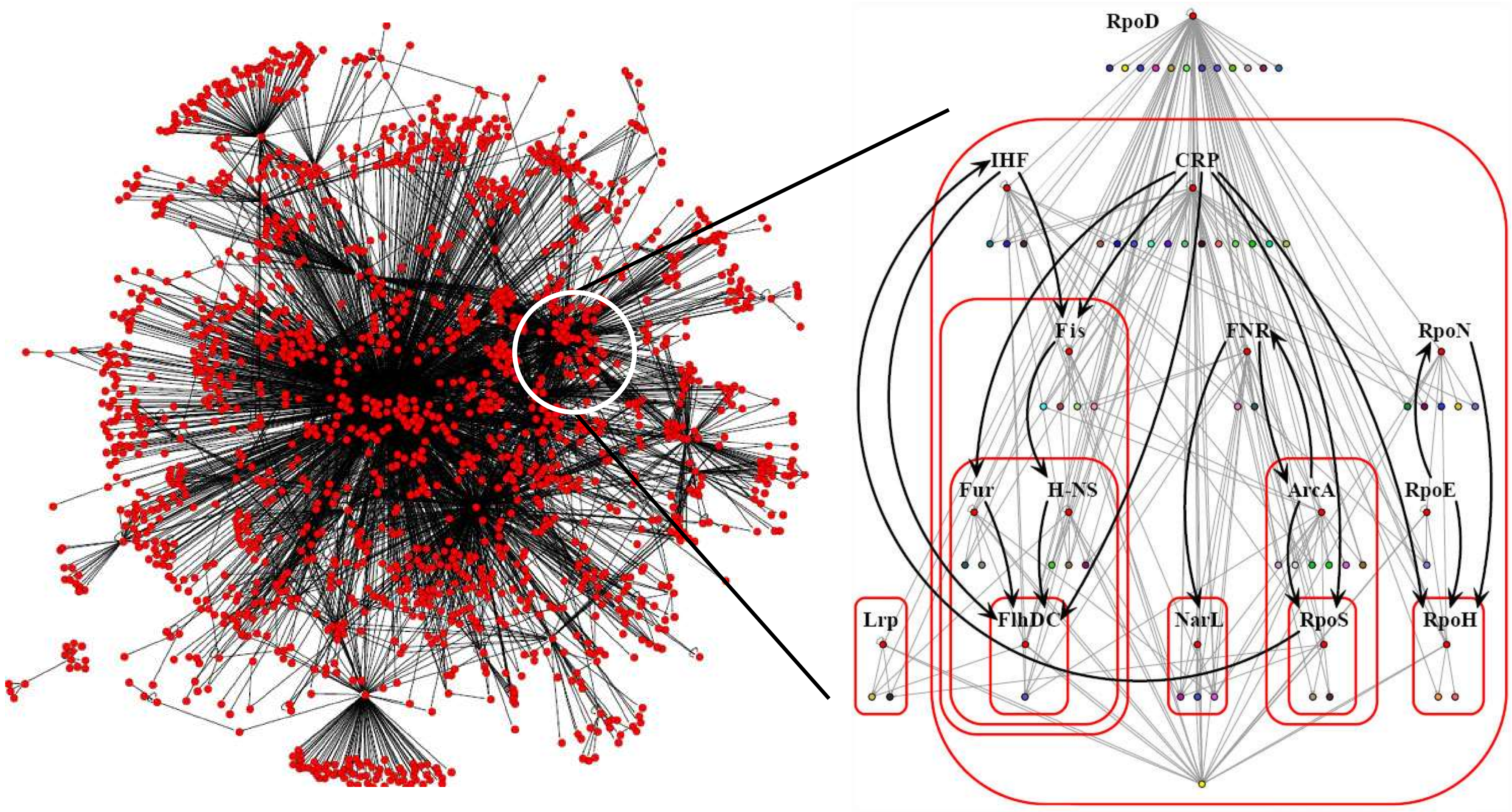
A rallying cry for Synthetic Biology



“What I cannot create, I do not understand.”

-Richard Feynman

Gene Regulatory Networks are Complex



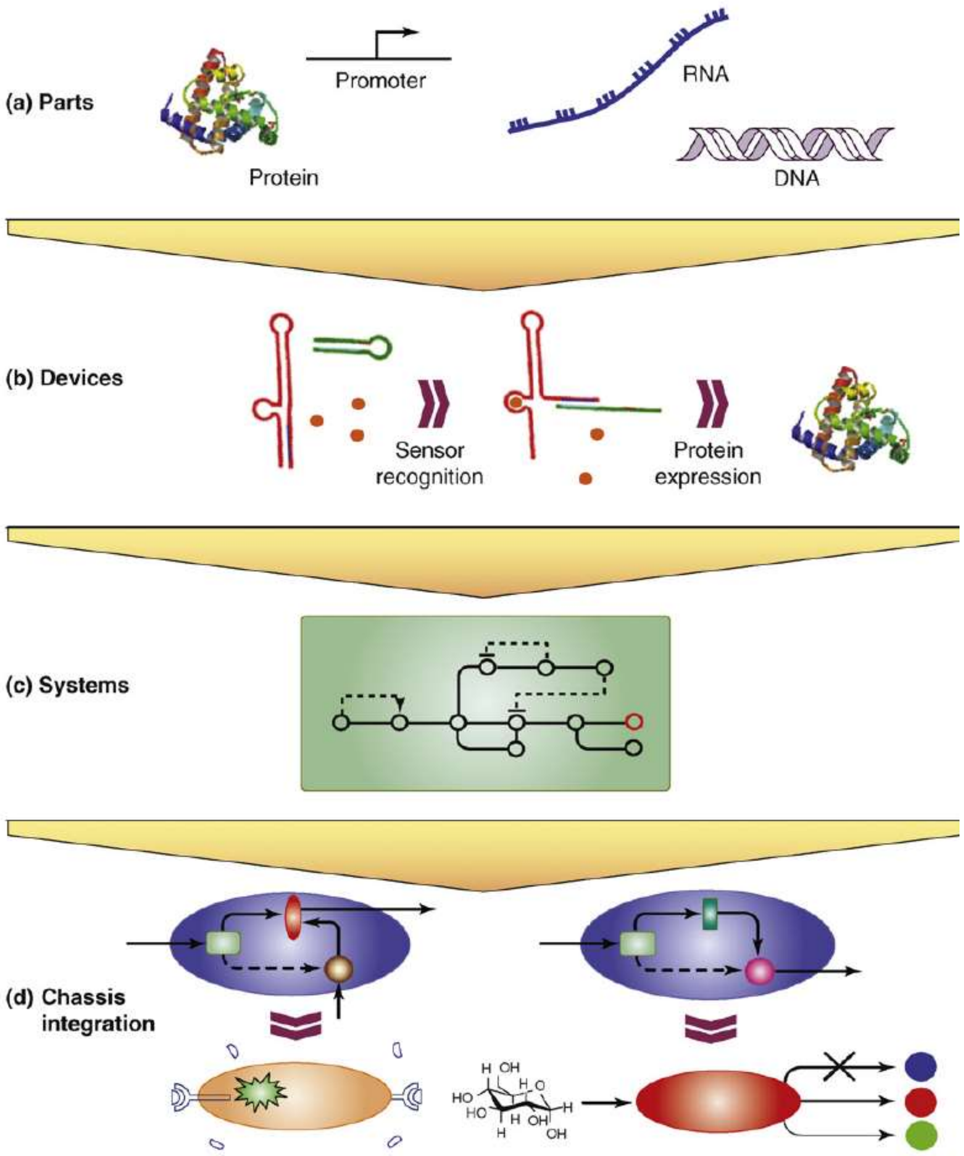
TOP

DOWN

- Decomposing interactions can help understand complex behaviour
- But, this is NOT easy!

RegulonDB (Salgado *et al*., 2006. NAR.)

A different approach: Building up Complexity



BOTTOM

UP

- Starting with simpler parts, complex behaviour can be engineered

(Leonard *et al*, 2008. Trends in Biotech.)

What could Synthetic Biology be masking?

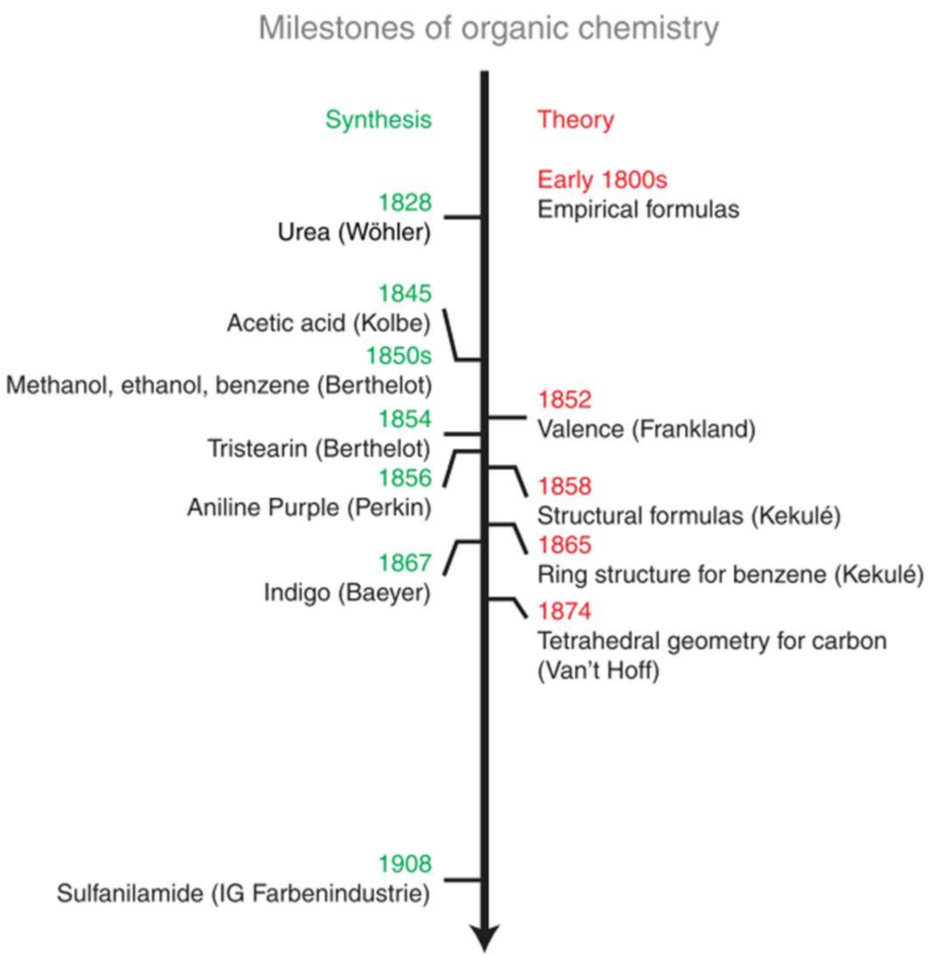
- “Synthetic biologists frequently cite genius physicist Richard Feynman “What I cannot create I do not understand”. This leitmotiv, however, does not necessarily imply that “What I can create, I do understand”, since the ability to create is essential but not sufficient to full understanding.”

(Do I Understand What I Can Create? Schmidt, 2009.)

- Starting with a fixed idea of what is to be achieved, which is at the core of synthetic biology, may inhibit discovery research while being essential to the creation of new objects, whether physical or biological.

(Where Synthetic Biology Came From and Where It Needs to Go. Way, Collins, Keasling, Silver. 2014.)

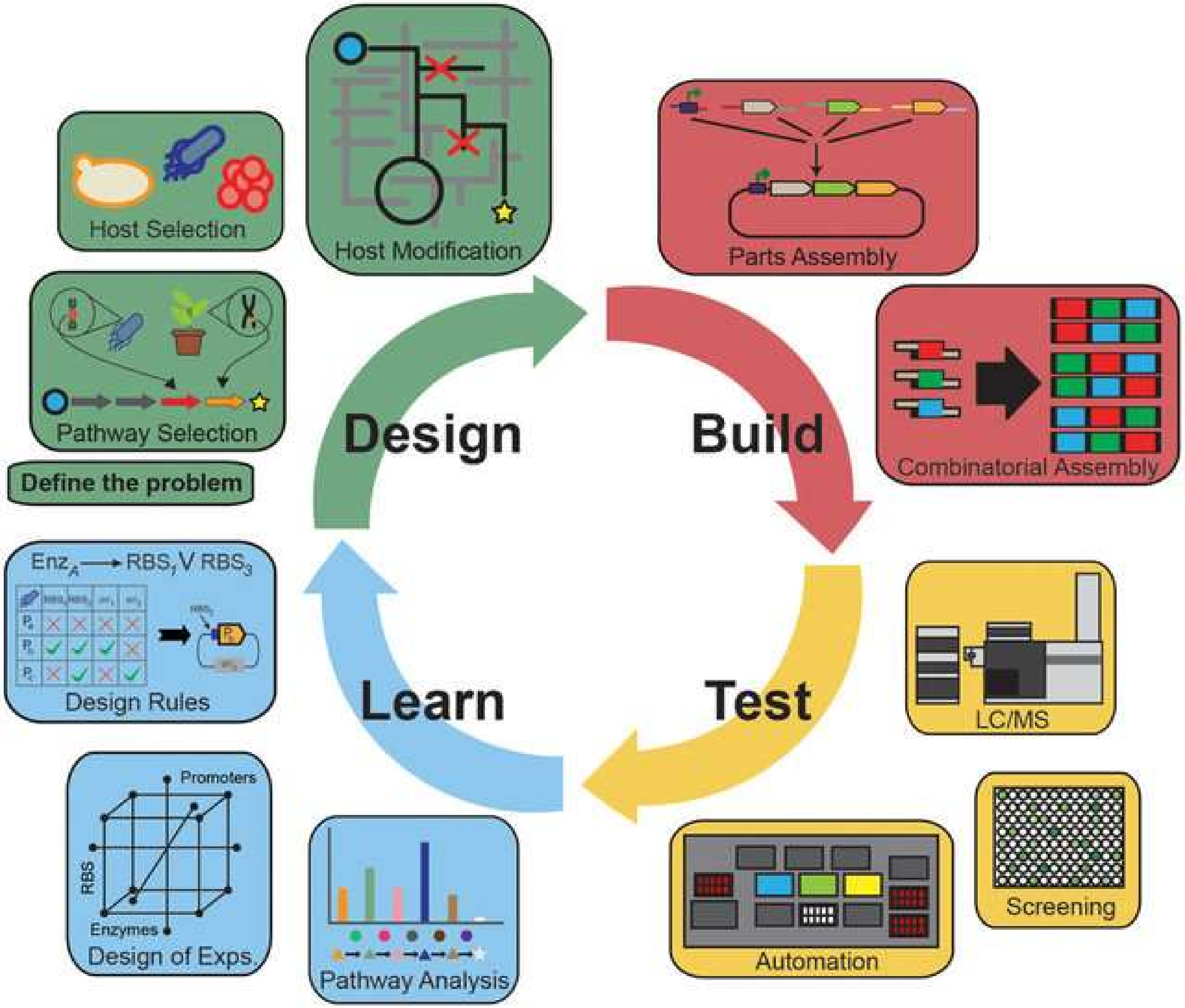
Yet, creating and learning can go hand in hand



- Synthetic DNA led directly to the discovery of the genetic code (Khorana, 1965)
- Chemical synthesis of active RNase A showed that primary sequence is sufficient to confer tertiary structure (Merrifield, 1971)
- Complete chemical synthesis of poliovirus DNA (Wimmer, 2002)
- Complete chemical synthesis of bacterial genome (Venter, 2010)

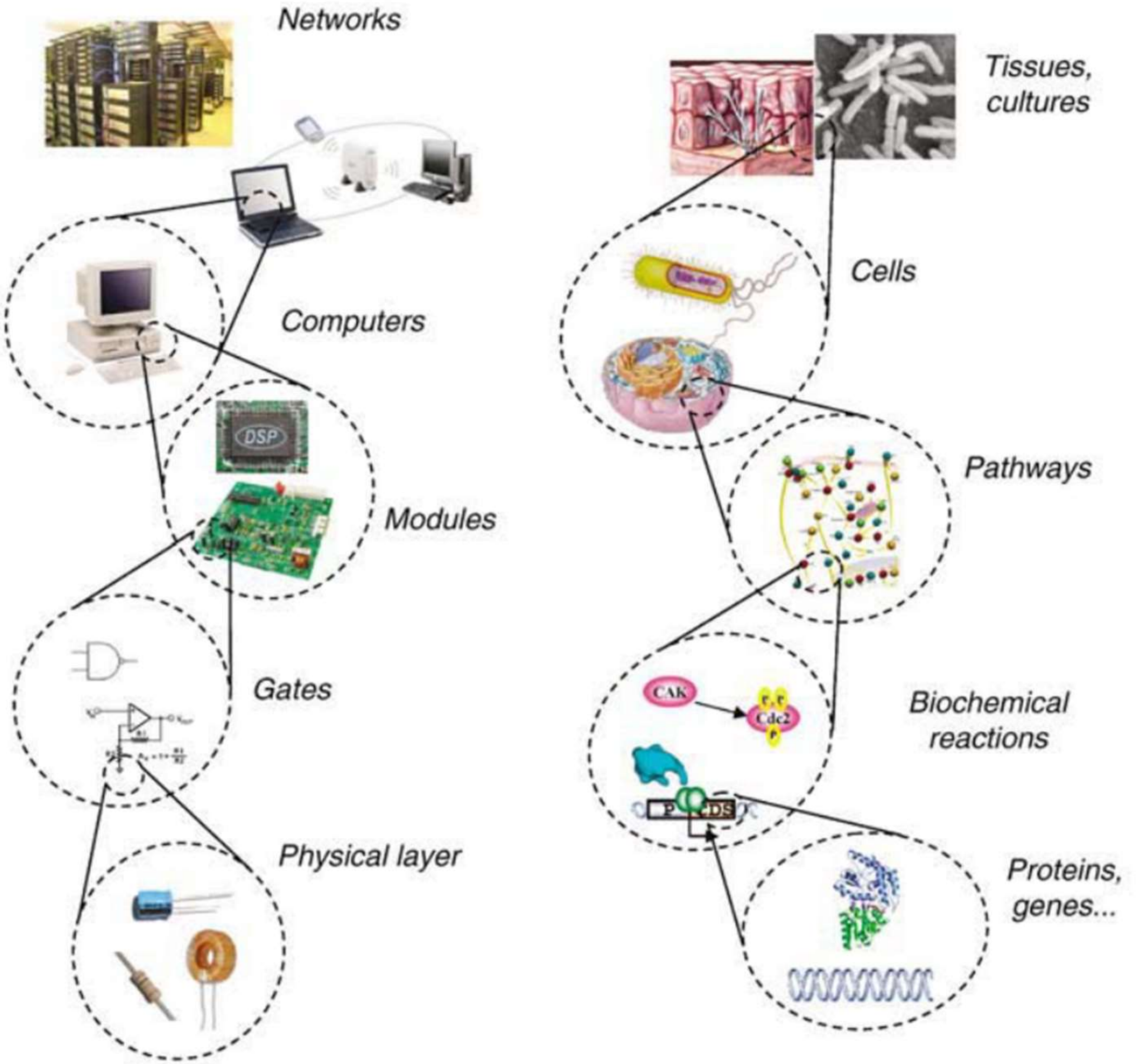
Yeh, B.J., and Lim, W.A. (2007). Nat. Chem. Biol.

DBTL cycles improve creation and knowledge



Petzold et al. (2015). Frontiers in Bioengineering and Biotechnology.

Synthetic biology
"Parts" Hierarchy for Biological Functions



Andrianantoandro et al. (2006). Molecular systems biology.

A Specification sheet

BS.1768 UNIFIED HEXAGON HEAD BOLTS / SCREWS

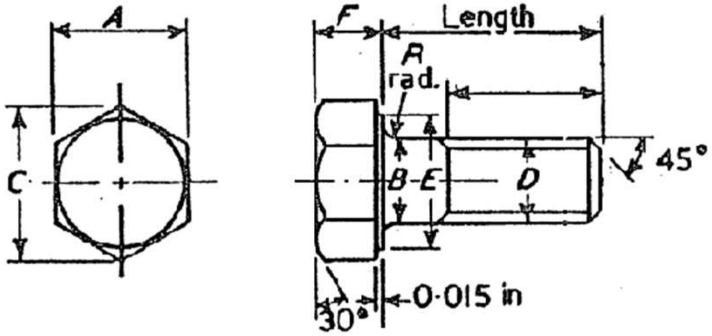


Fig. 1. Hexagon Head Bolt, Washer Faced

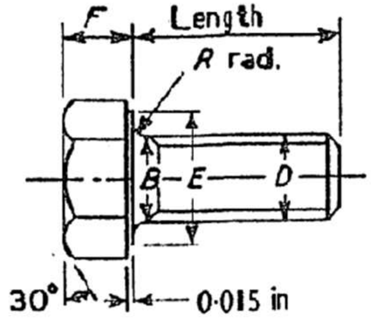


Fig. 2. Hexagon Head Screw, Washer Faced

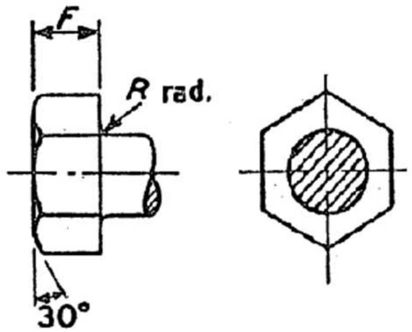
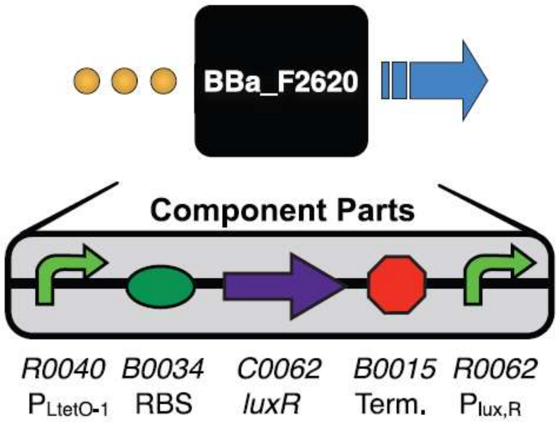


Fig. 3. Full Bearing Alternative Type of Head Permissible on Bolts and Screw

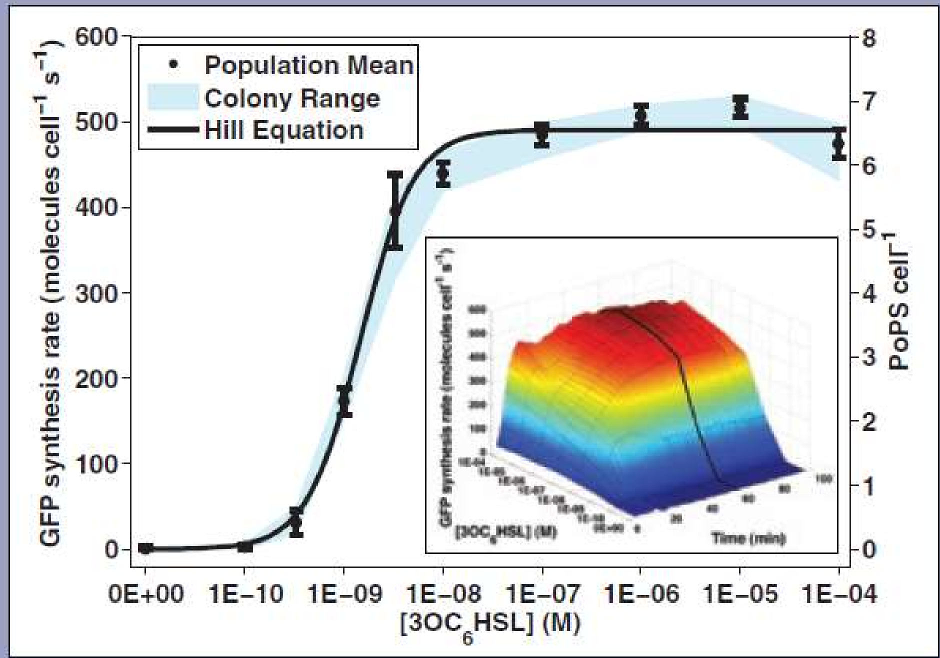
Nominal Size, D	Number of Threads per Inch		Diameter of Unthreaded Portion of Shank B		Width Across Flats A		Width Across Corners C	Diameter of Washer Face E		Thickness of Head F		Radius Under Head R	
Inch	UNC	UNF	MAX	MIN	MAX	MIN ‡	MAX	MAX	MIN	MAX	MIN	MAX	MIN
1/4	20	28	0.2500	0.2465	0.4375	0.4305	0.505	0.421	0.411	0.163	0.153	0.025	0.015
5/16	18	24	0.3125	0.3090	0.5000	0.4930	0.577	0.483	0.473	0.211	0.201	0.025	0.015
3/8	16	24	0.3750	0.3715	0.5625	0.5545	0.650	0.545	0.535	0.243	0.233	0.025	0.015
7/16	14	20	0.4375	0.4335	0.6250	0.6170	0.722	0.605	0.595	0.291	0.281	0.025	0.015
1/2	13	20	0.5000	0.4960	0.7500	0.7420	0.866	0.730	0.720	0.383	0.313	0.025	0.015
9/16*	12	18	0.5625	0.5585	0.8125	0.8045	0.938	0.792	0.782	0.371	0.361	0.045	0.020

https://www.beaconcorporation.co.uk/products/bolts-setscrews/bs1768-dimensions/

A Specification sheet for genetic parts



The 'datasheet' for genetic parts



$$P_{out} = \frac{P_{max}[3OC_6HSL]^n}{K^n + [3OC_6HSL]^n}$$

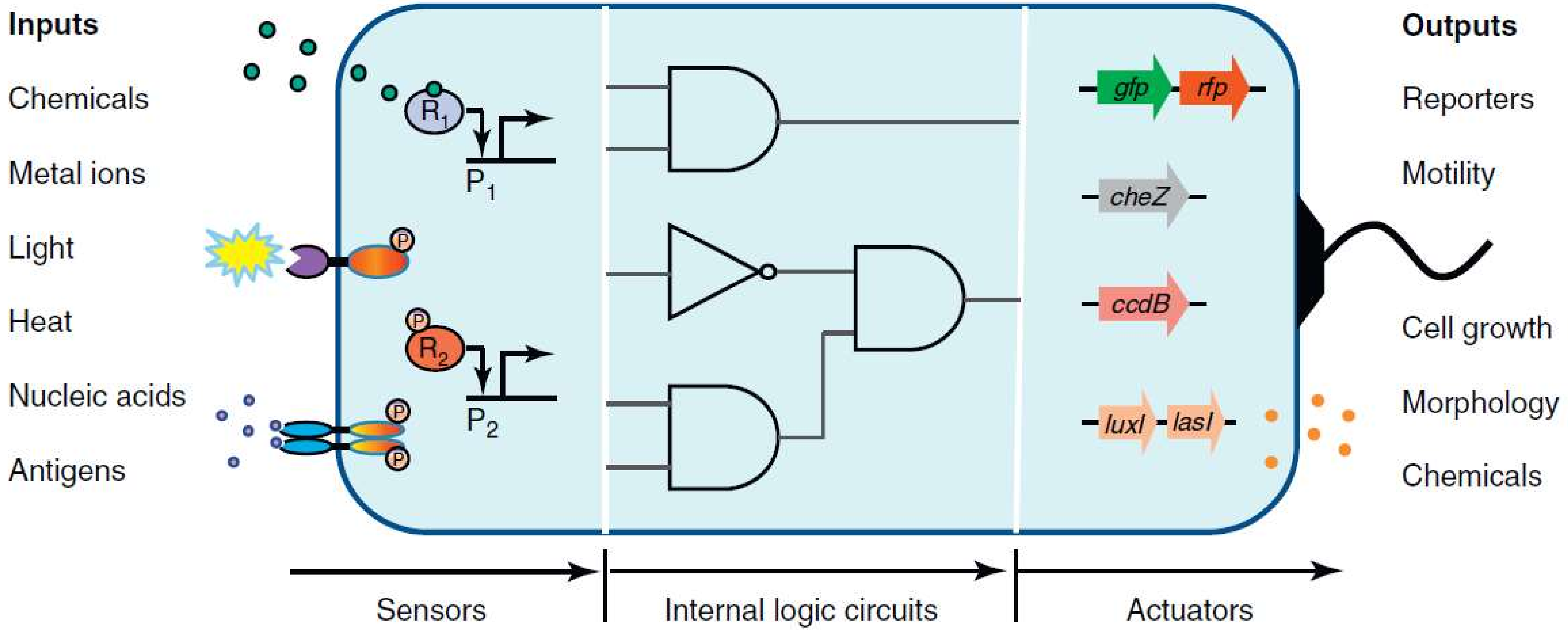
P_{max}: **6.6** PoPS cell^{-1}

K: **1.5E-09** M $3OC_6HSL$

n: **1.6**

(Canton *et al.*, 2008. Nat. Biotech.)

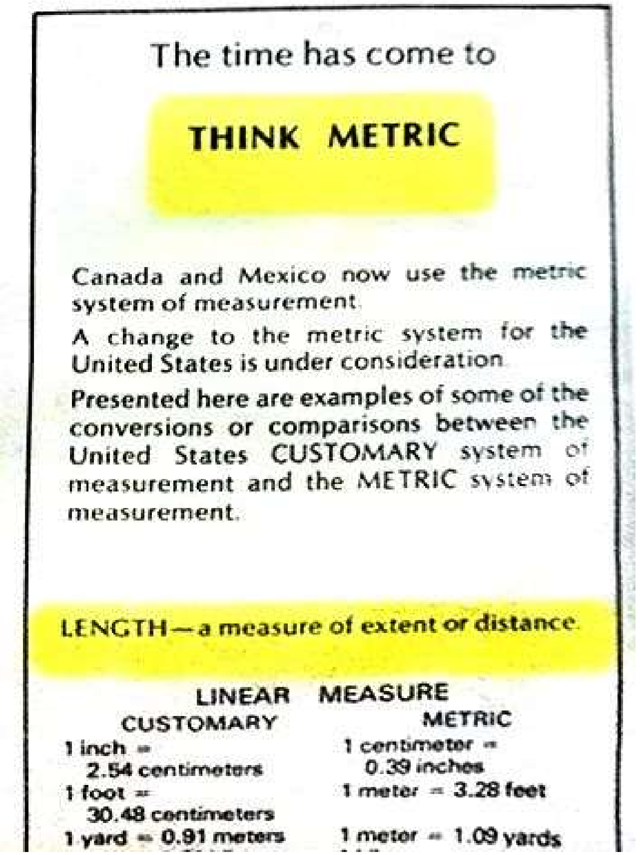
Engineering a Synthetic Genetic Network: Connecting the Parts



(Wang & Buck, 2012. Trends in Microbiology)

Standardisation in Synthetic Biology

- Well-characterised biological parts, like parts of a machine, can be re-used in novel contexts with similar functionality.
- Use of standardised symbols, metrics, terminology allow unambiguous understanding of the properties or behaviour of the engineered systems



The time has come to

THINK METRIC

Canada and Mexico now use the metric system of measurement.

A change to the metric system for the United States is under consideration.

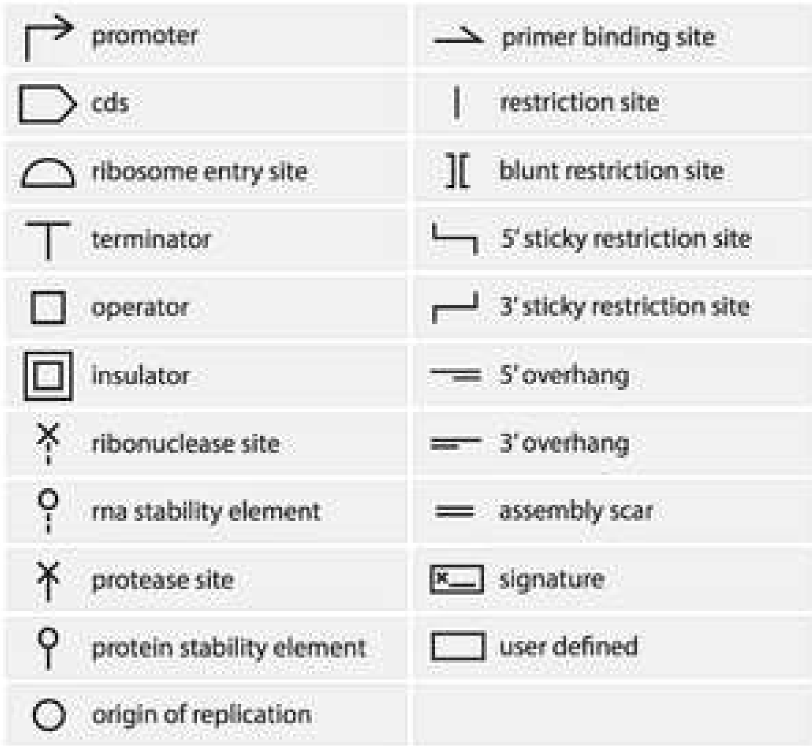
Presented here are examples of some of the conversions or comparisons between the United States CUSTOMARY system of measurement and the METRIC system of measurement.

LENGTH—a measure of extent or distance.

LINEAR MEASURE

CUSTOMARY	METRIC
1 inch = 2.54 centimeters	1 centimeter = 0.39 inches
1 foot = 30.48 centimeters	1 meter = 3.28 feet
1 yard = 0.91 meters	1 meter = 1.09 yards

1980s AA Road Map in the USA



Synthetic Biology Open Language (SBOL) standard visual symbols

BioBricks FOUNDATION

iGEM

Parts Registry

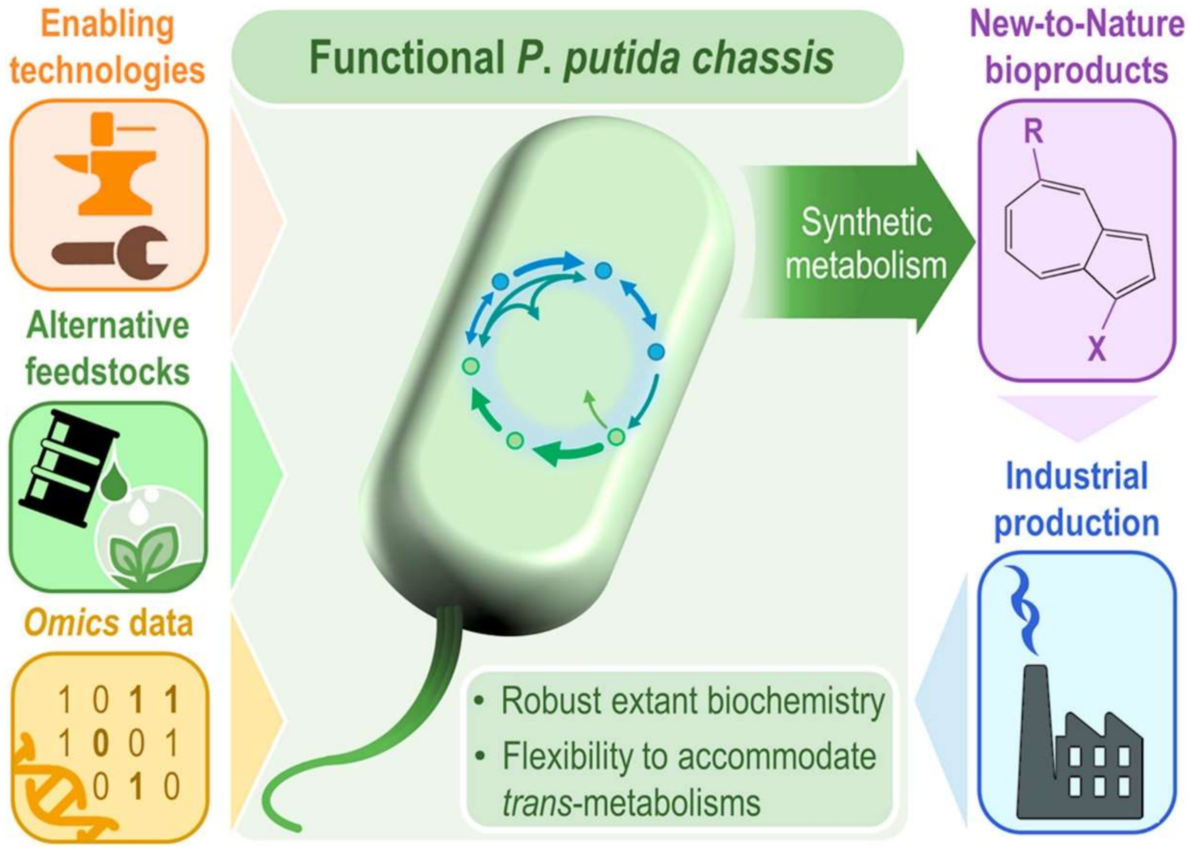
OpenPlant

RoBOOST

“Chasses” in Synthetic Biology

- “the basic functionalities of a bacterial genome provide a chassis on top of which forward engineered biological systems can be implanted”

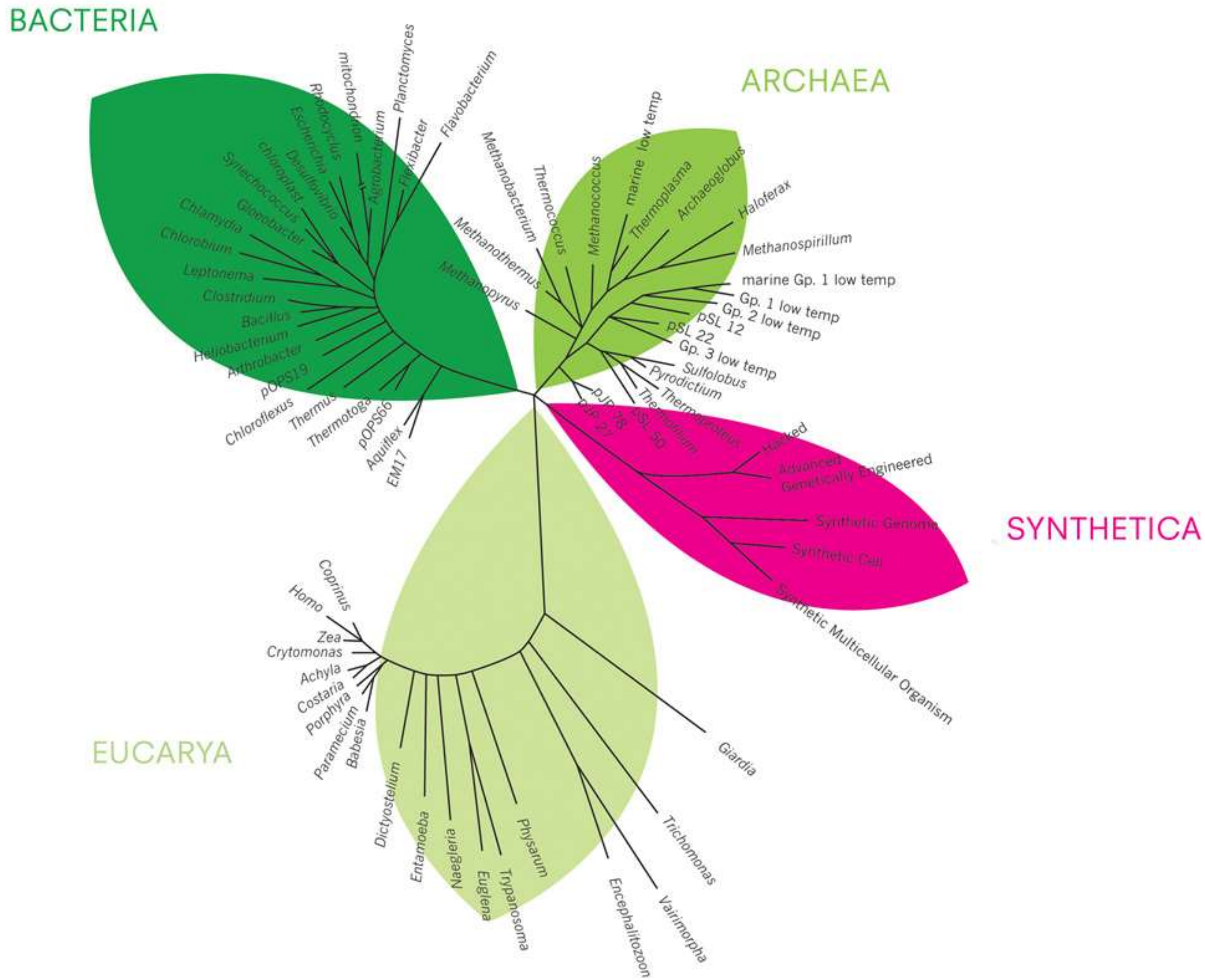
(Víctor de Lorenzo, 2011. Bioengineered bugs.)



Nikel & de Lorenzo, 2018. Metabolic Engineering.

“Chasses” in Synthetic Biology

- Towards a new Kingdom?



“The Synthetic Kingdom”, 2009. Alexandra Daisy Ginsberg.
https://daisyginsberg.com/work/synthetic-kingdom

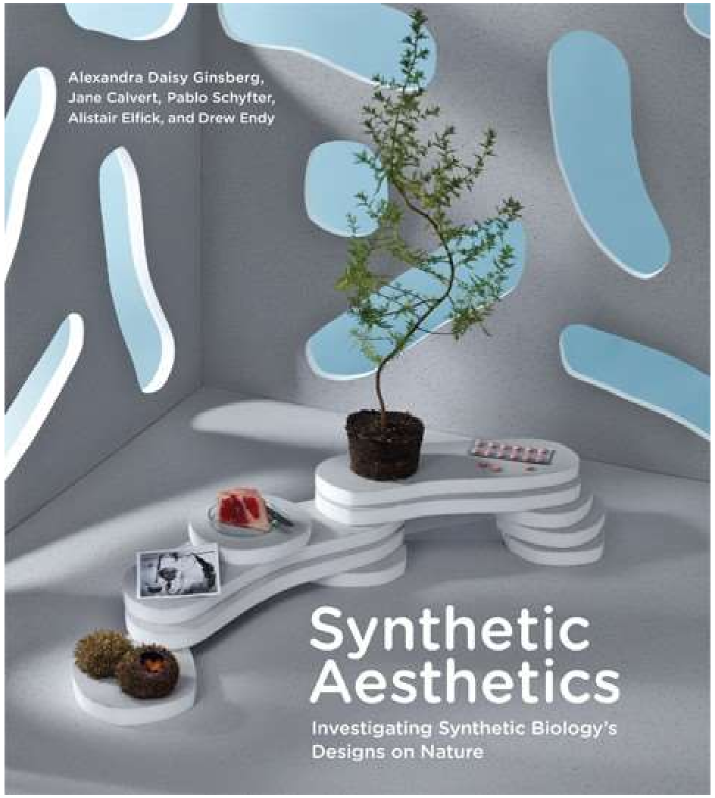
iGEM

- The International Genetically Engineered Machine (iGEM) is an international competition
- Student teams develop synthetic biology projects over each summer
- They present their work at the Giant Jamboree in October/ November.

iGEM

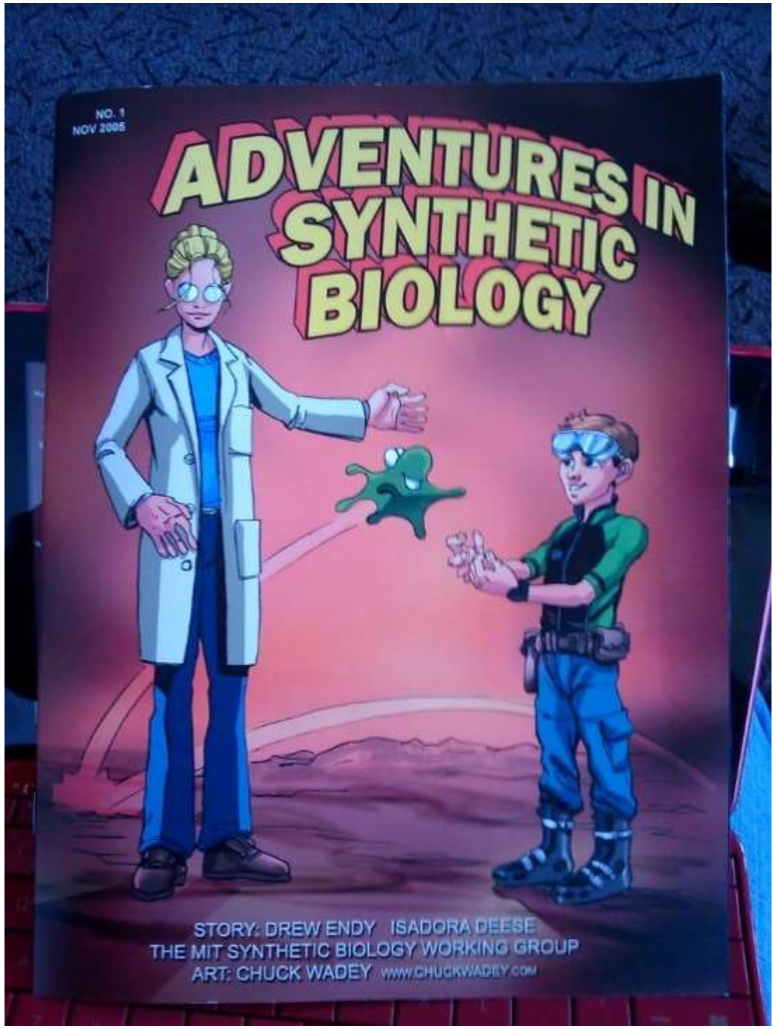
Synthetic Biology: The Society

https://www.labiotech.eu/best-biotech/bioart-exhibitions/



http://web.mit.edu/endy/www/scraps/comic/AiSB.vol1.pdf

Bio-art in Synthetic Biology



The story telling

Synthetic Biology: The Society

Public Engagement

Antonina Khodzhaeva, SYNENERGENE Forum
www.ecsite.eu

The VR experience, WISB
Cheltenham Science Festival, 2018

Governance and Regulation: *Biosafety, Biological Diversity*

- Redford *et al.*, 2019. Genetic frontiers for conservation: An assessment of synthetic biology and biodiversity conservation. Technical assessment. Gland, Switzerland: IUCN.
- Keiper & Atanassova, 2020. Regulation of Synthetic Biology: Developments Under the Convention on Biological Diversity and Its Protocols. Front. Bioeng. Biotechnol.
- Li *et al.*, 2021. Advances in Synthetic Biology and Biosafety Governance. Front. Bioeng. Biotechnol.

Synthetic Biology: the First Decade

2000: Two papers in *Nature* report synthetic biological circuits, a genetic toggle switch and a biological clock, by combining genes within *E. coli* cells.[12][13]

2003: The most widely used standardized DNA parts, BioBrick plasmids, are invented by Tom Knight.[14] These parts will become central to the International Genetically Engineered Machine (iGEM) competition founded at MIT in the following year.

2003: Researchers engineer an artemisinin precursor pathway in *E. coli*.[15]

2004: First international conference for synthetic biology, Synthetic Biology 1.0 (SB1.0) is held at MIT.

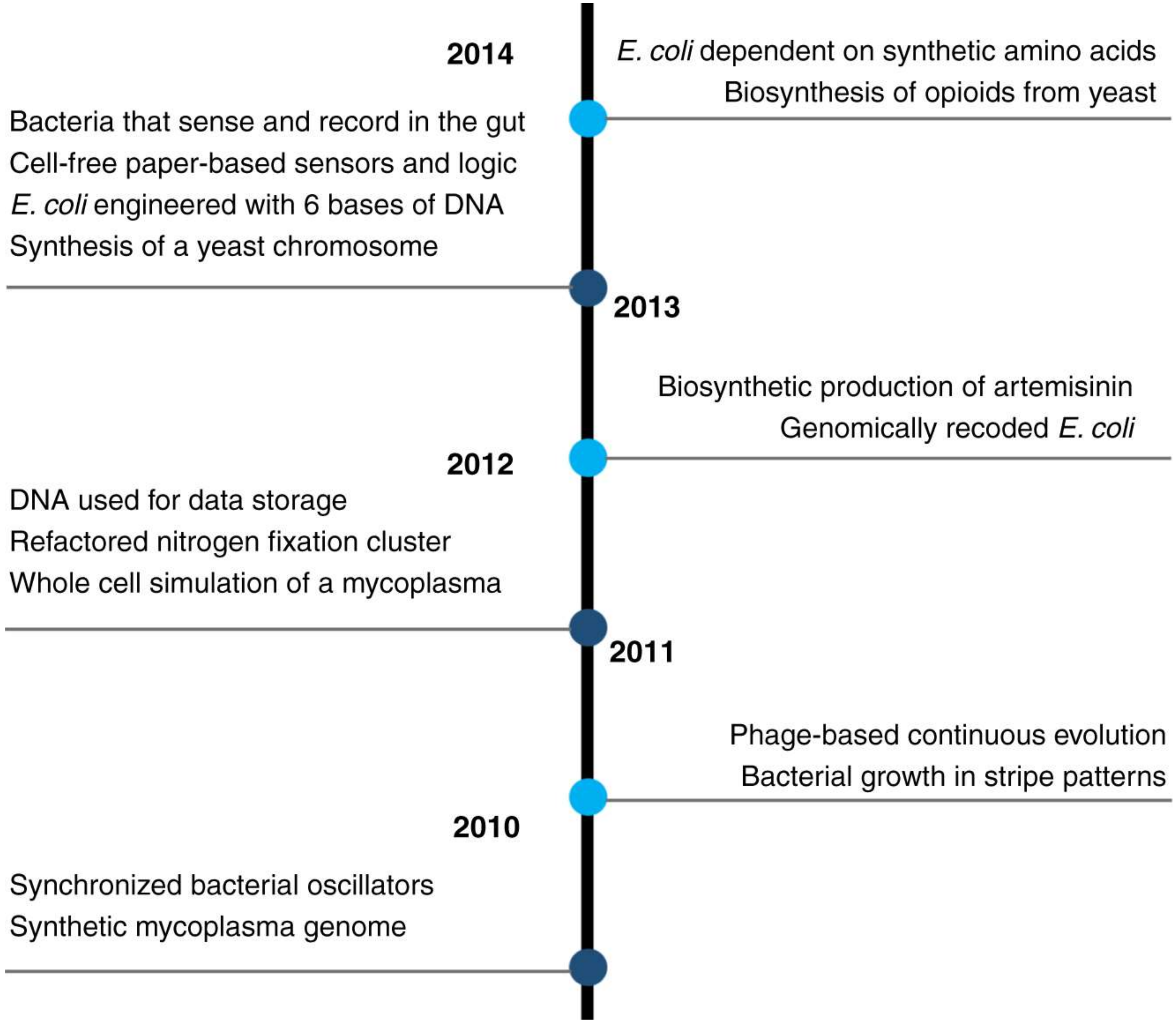
2005: Researchers develop a light-sensing circuit in *E. coli*.[16] Another group designs circuits capable of multicellular pattern formation.[17]

2006: Researchers engineer a synthetic circuit that promotes bacterial invasion of tumour cells.[18]

Non-exhaustive list of Key landmarks

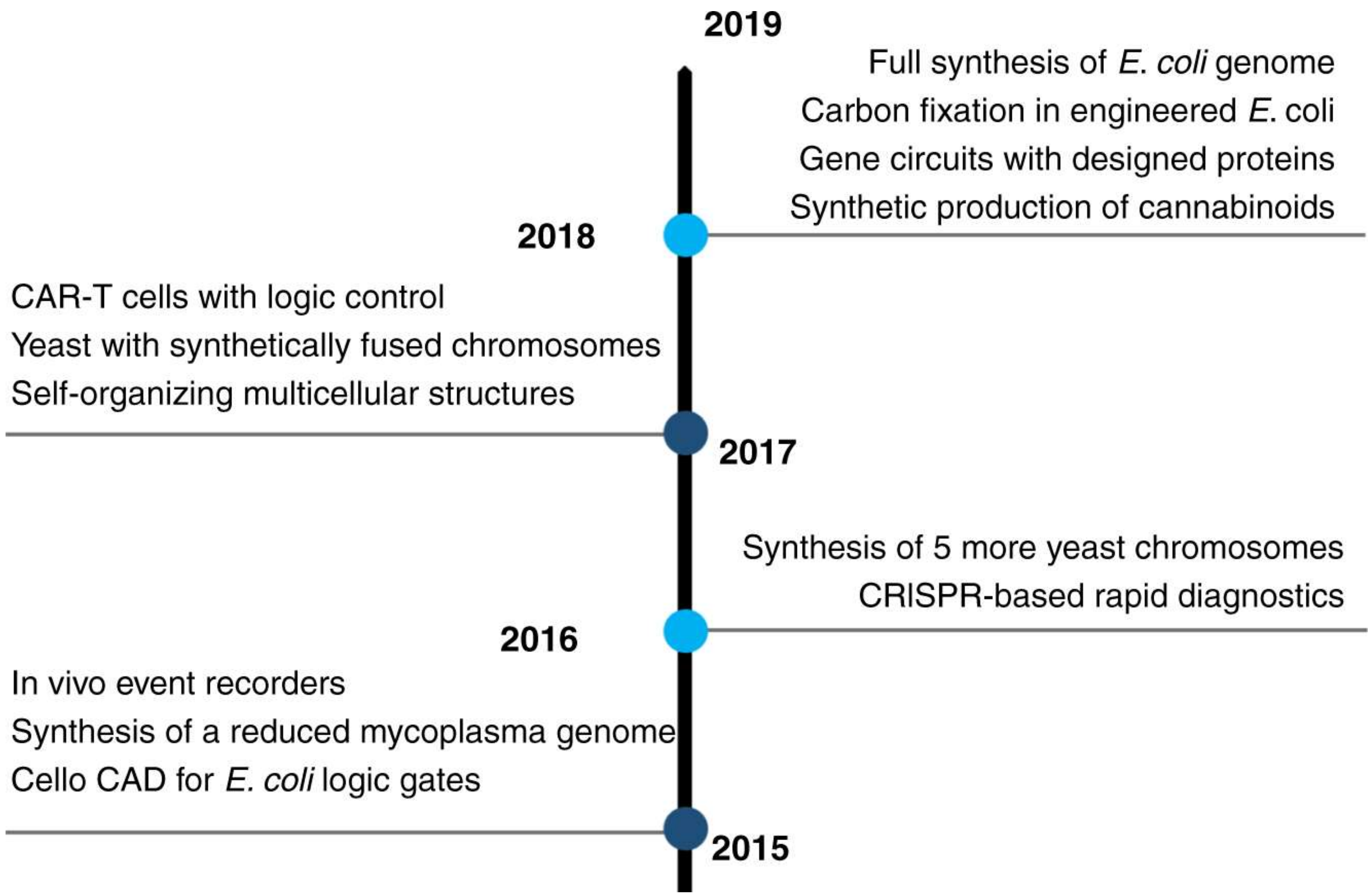
https://en.wikipedia.org/wiki/Synthetic_biology (25/09/2024)

Synthetic Biology: the Second Decade



Key landmarks (Meng & Ellis, 2020. Nat. Comms.)

Synthetic Biology: the Second Decade



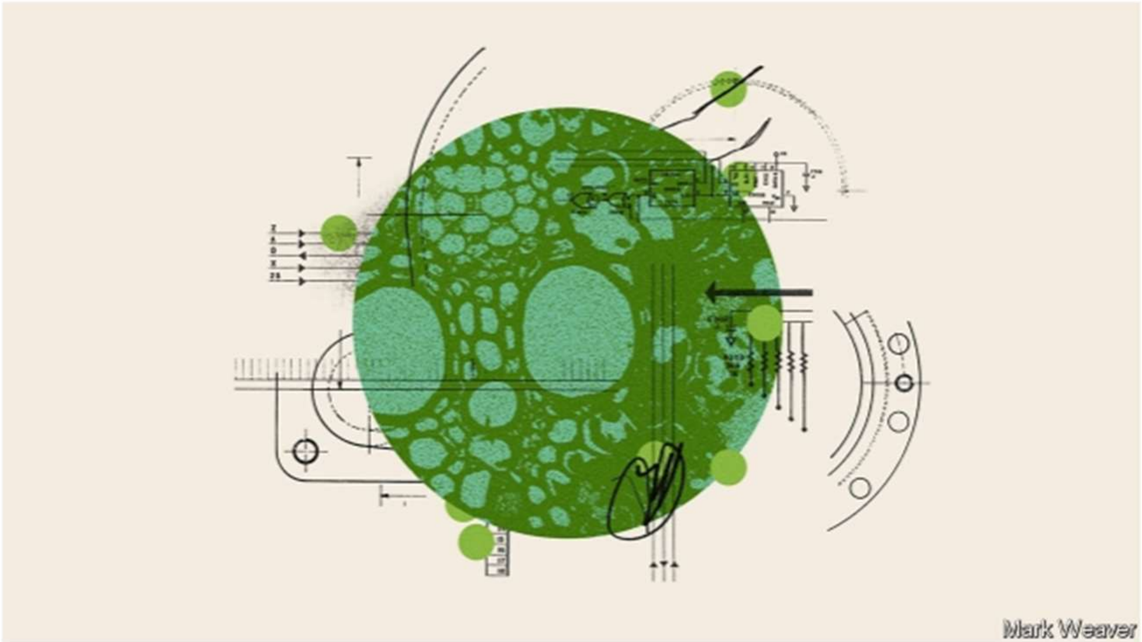
Key landmarks (Meng & Ellis, 2020. Nat. Comms.)

Synthetic Biology: Promise for the Future

Synthetic biology

The engineering of living organisms could soon start changing everything

Synthetic biology has only just begun, says Oliver Morton

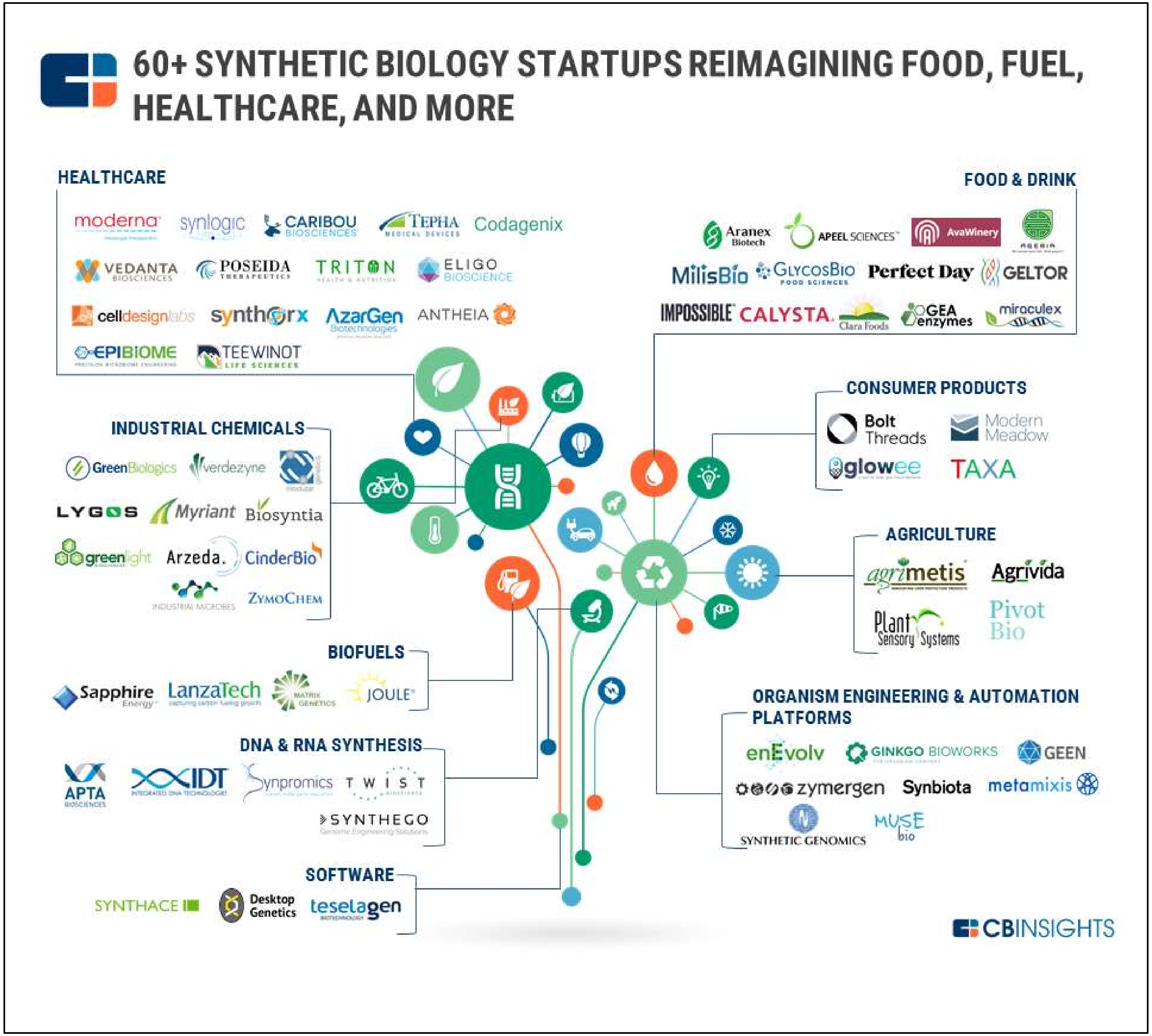


Print edition | Technology Quarterly ›

Apr 4th 2019

The Economist
https://www.economist.com/technology-quarterly/2019/04/04/the-engineering-of-living-organisms-could-soon-start-changing-everything

Synthetic Biology: Industry



CB insights, 2017

https://www.cbinsights.com/research/synthetic-biology-startup-market-map/

Questions welcome.

manish.kushwaha@inrae.fr