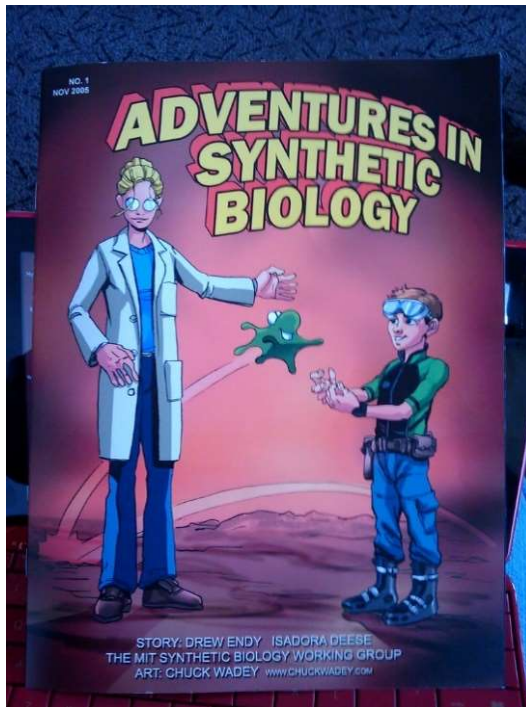


What is Synthetic Biology?

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.

J. Iwasa

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).

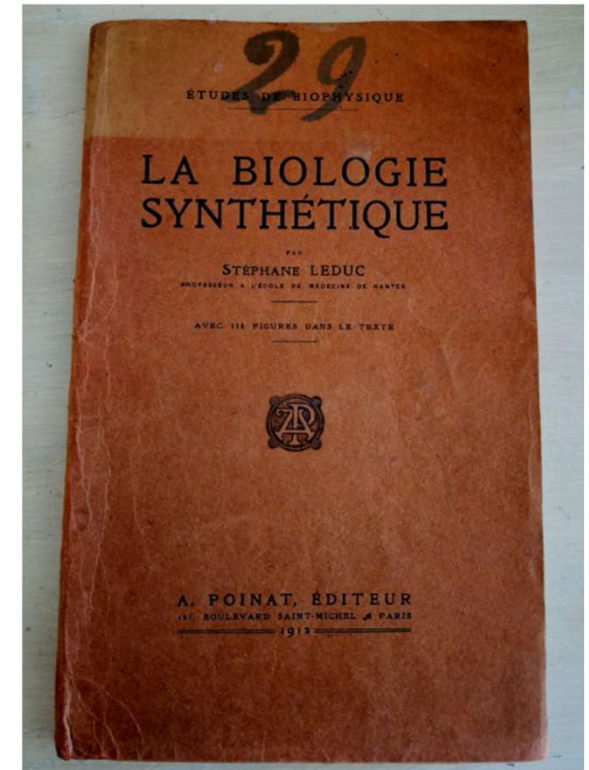



Image credit
@ad_am_ara 

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

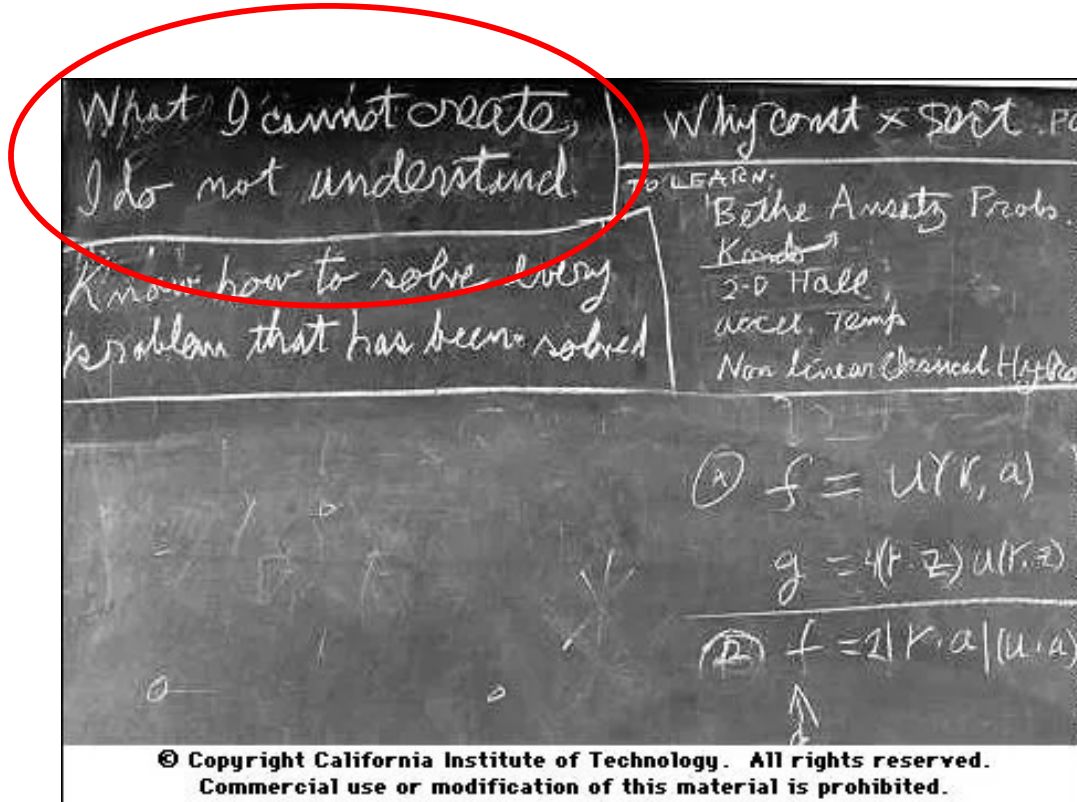


A televised debate (1971)

Debate Noam Chomsky & Michel Foucault - On human nature [Subtitled]

<https://www.youtube.com/watch?v=3wfNI2L0Gf8>

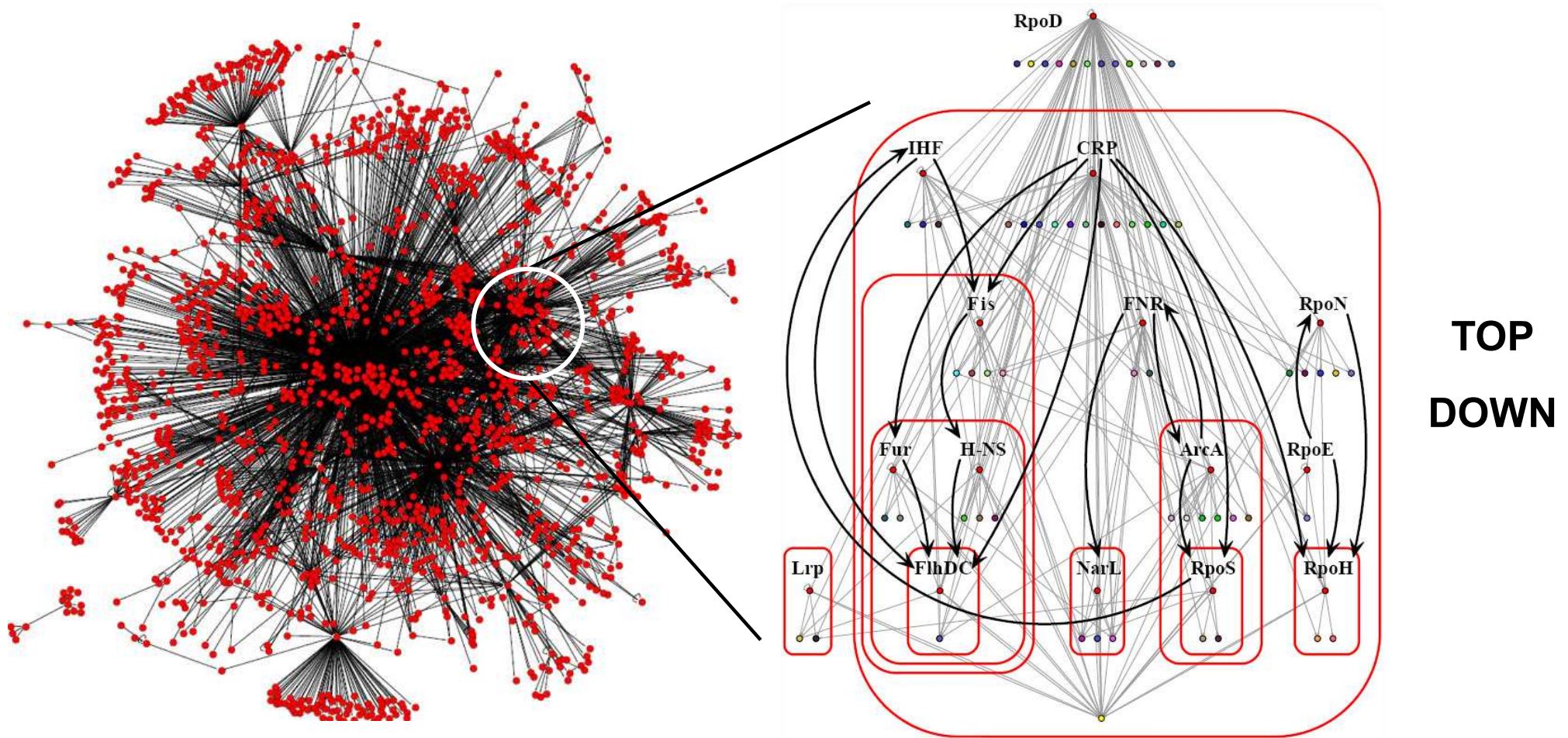
A rallying cry for Synthetic Biology



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

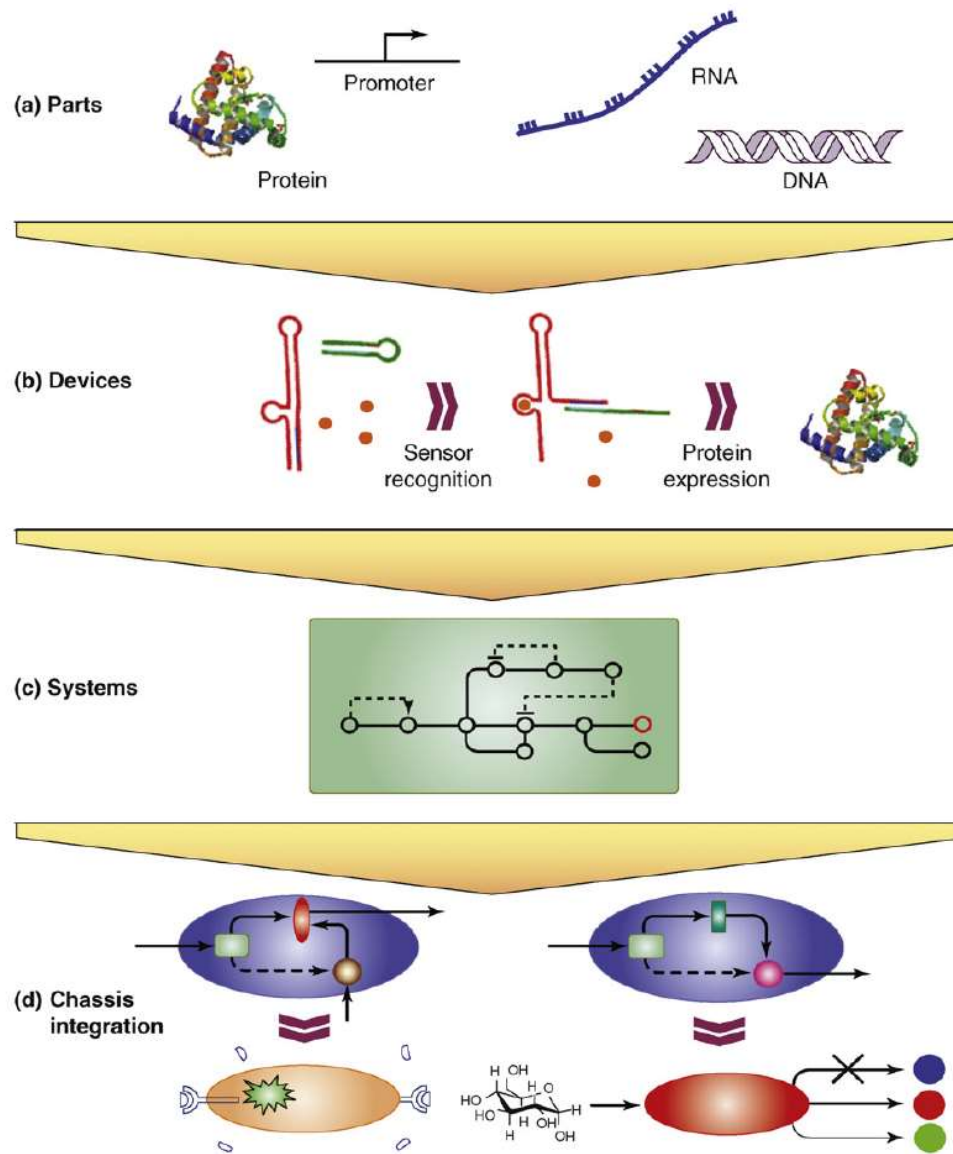
-Richard Feynman

Gene Regulatory Networks are Complex



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

A different approach: Building up Complexity



**BOTTOM
UP**

- Starting with simpler parts, complex behaviour can be engineered

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.”

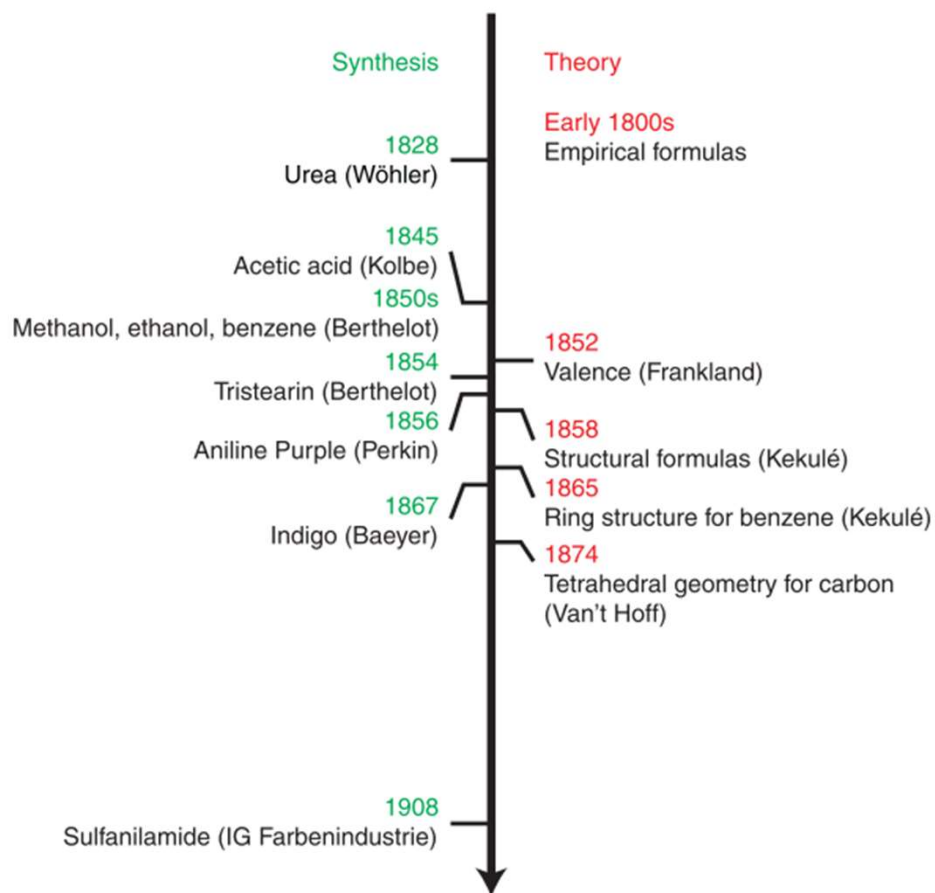
(Do I Understand What I Can Create? Schmidt, 2009.)

- 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.)

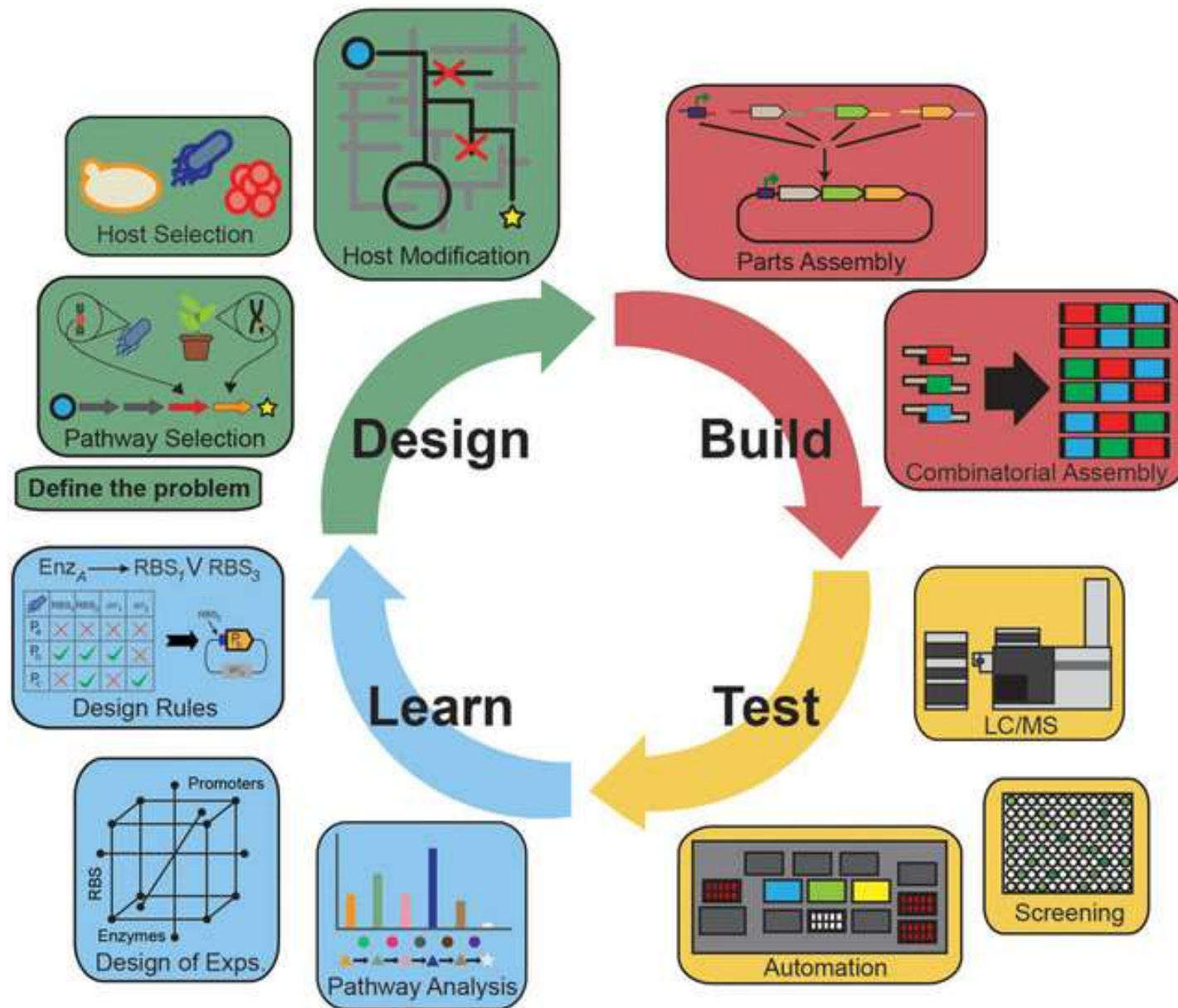
Yet, creating and learning can go hand in hand

Milestones of organic chemistry



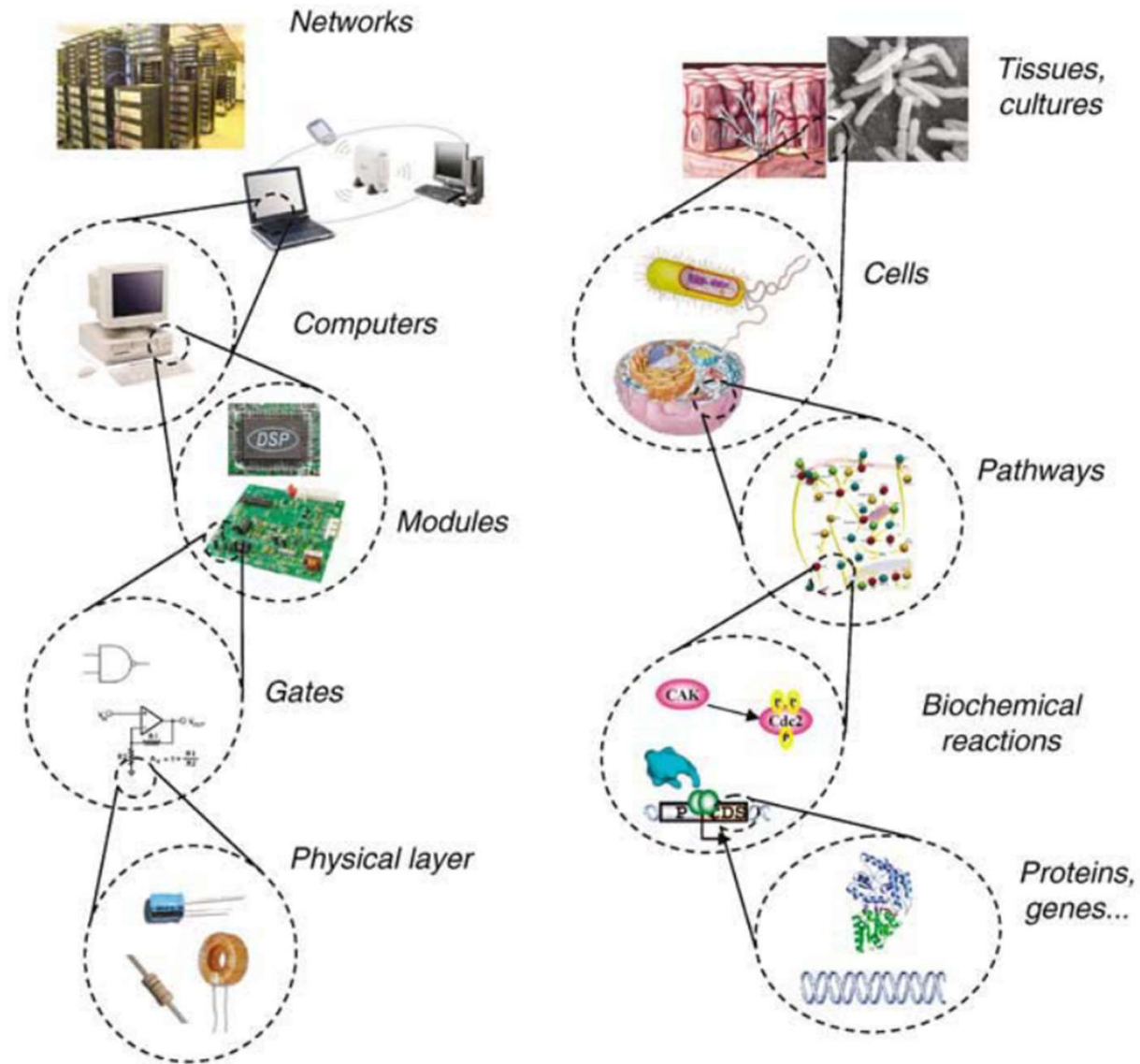
- Synthetic DNA led directly to the discovery of the genetic code (Khorana, 1965)
- Chemical synthesis of active RNase A showed that primary sequence is sufficient to confer tertiary structure (Merrifield, 1971)
- Complete chemical synthesis of poliovirus DNA (Wimmer, 2002)
- Complete chemical synthesis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

DBTL cycles improve creation and knowledge



Synthetic biology

“Parts” Hierarchy for Biological Functions



A Specification sheet

BS.1768 UNIFIED HEXAGON HEAD BOLTS / SCREWS

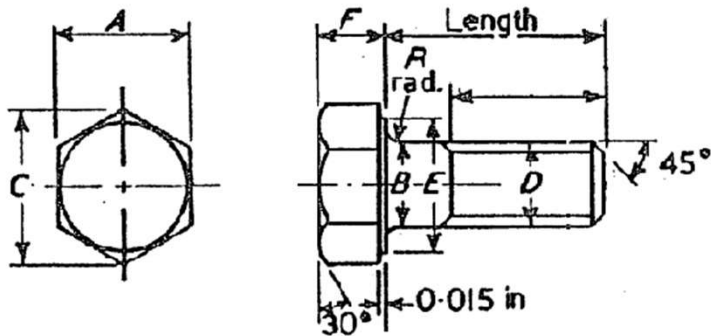


Fig. 1. Hexagon Head Bolt, Washer Faced

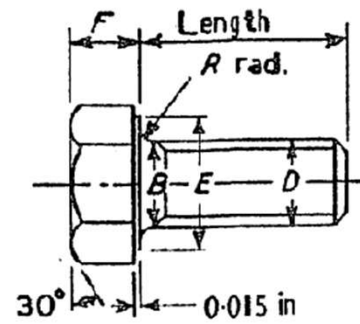


Fig. 2. Hexagon Head Screw, Washer Faced

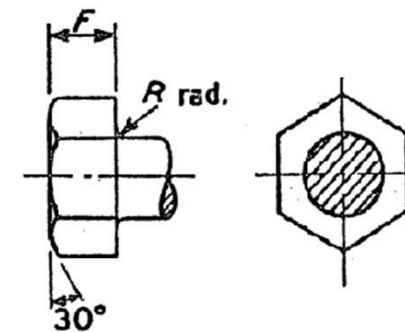


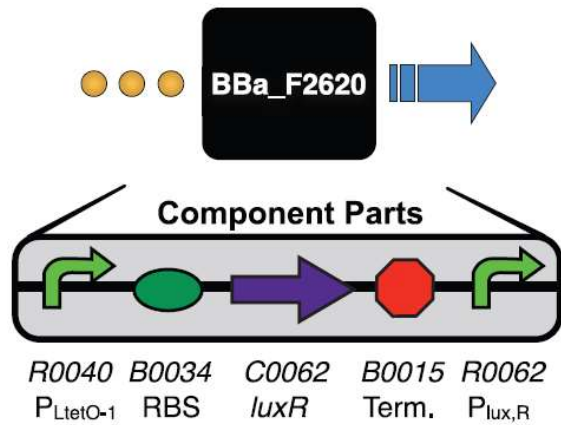
Fig. 3. Full Bearing Alternative Type of Head Permissible on Bolts and Screw

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	
	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

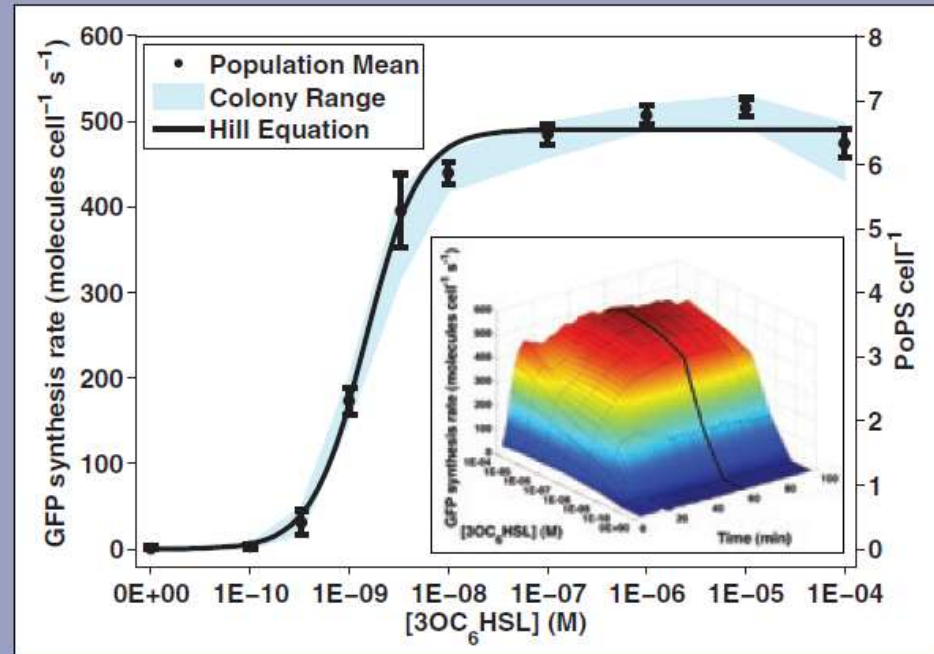
<https://www.beaconcorporation.co.uk/products/bolts-setscrews/bs1768-dimensions/>

A Specification sheet for genetic parts

The 'datasheet' for genetic parts



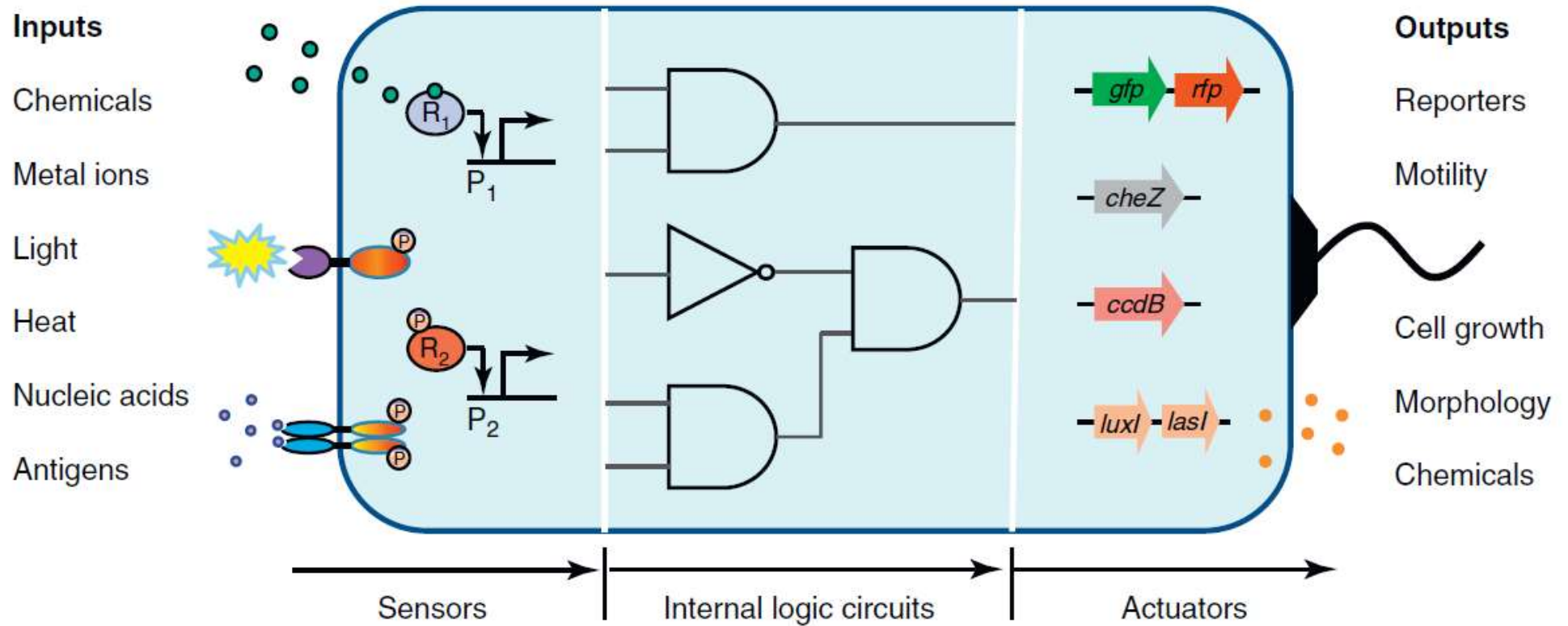
Static Performance*



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

P_{max} : 6.6 PoPS cell⁻¹
 K : 1.5E-09 M 3OC₆HSL
 n : 1.6

Engineering a Synthetic Genetic Network: Connecting the Parts



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

 promoter	 primer binding site
 cgs	 restriction site
 ribosome entry site	 blunt restriction site
 terminator	 5' sticky restriction site
 operator	 3' sticky restriction site
 insulator	 5' overhang
 ribonuclease site	 3' overhang
 rna stability element	 assembly scar
 protease site	 signature
 protein stability element	 user defined
 origin of replication	

Synthetic Biology Open Language (SBOL)
standard visual symbols



Parts Registry



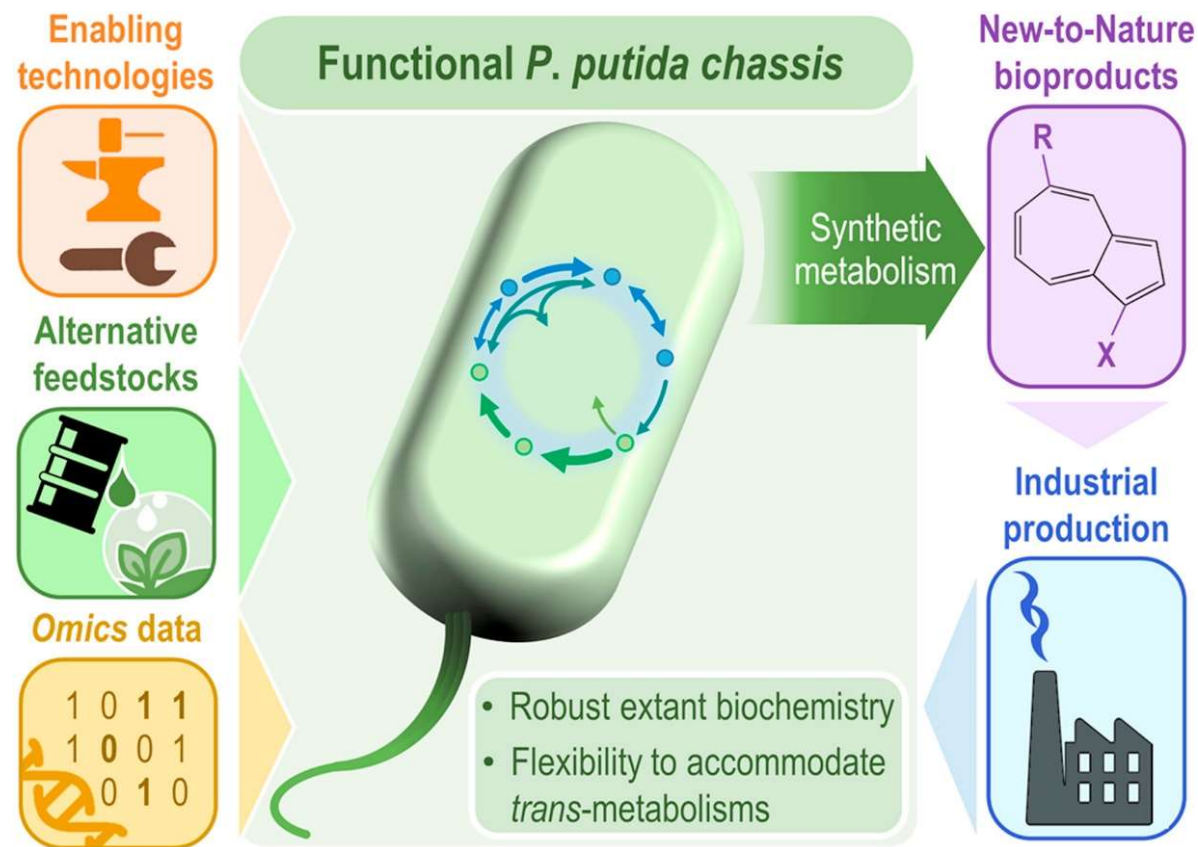
OpenPlant



“Chasses” in Synthetic Biology

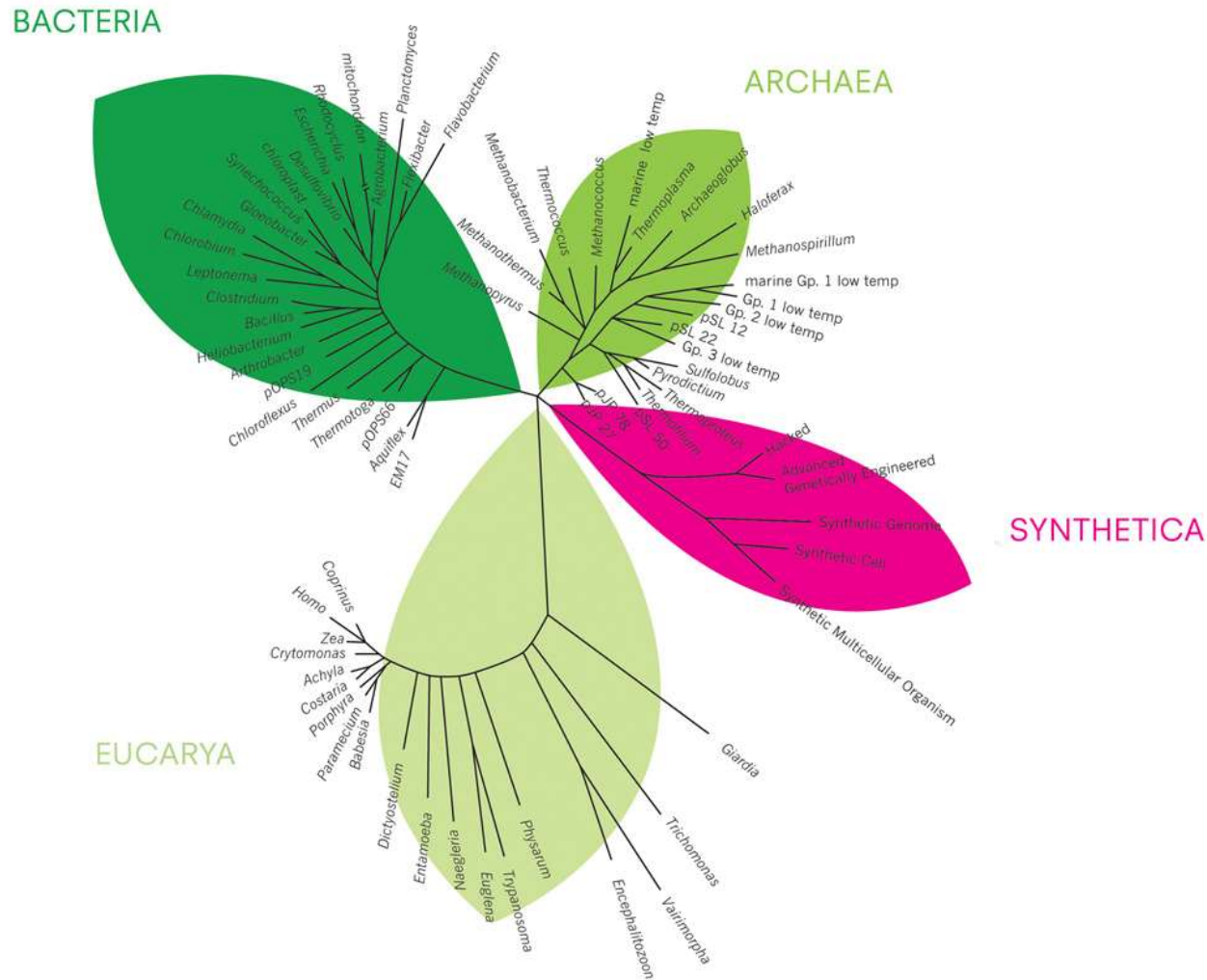
- “the basic functionalities of a bacterial genome provide a chassis on top of which forward engineered biological systems can be implanted”

(V́ctor de Lorenzo, 2011. Bioengineered bugs.)



“Chasses” in Synthetic Biology

- Towards a new Kingdom?



“The Synthetic Kingdom”, 2009. Alexandra Daisy Ginsberg.

<https://daisyginsberg.com/work/synthetic-kingdom>

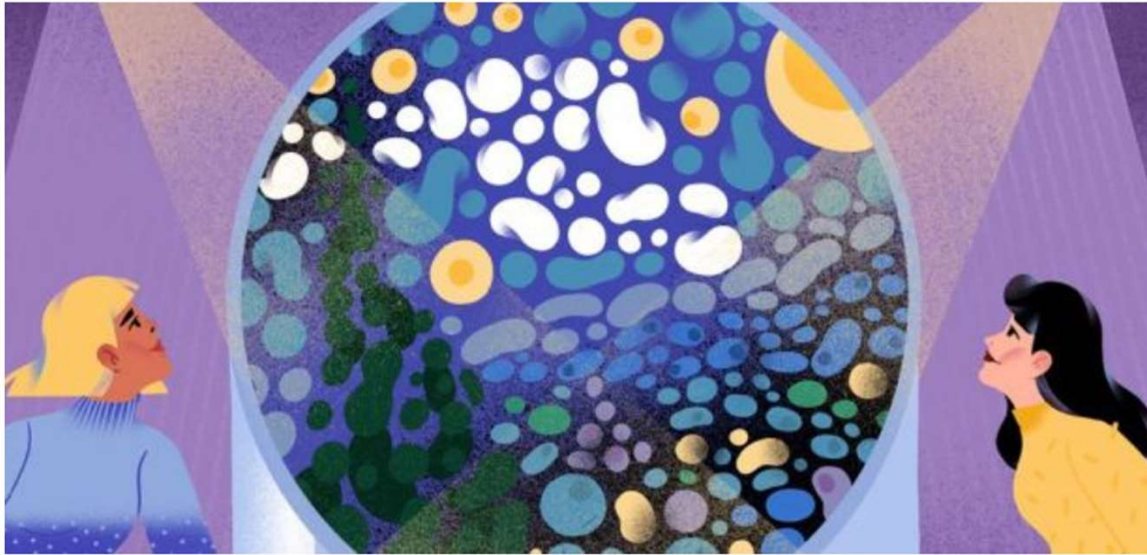
iGEM

- 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.



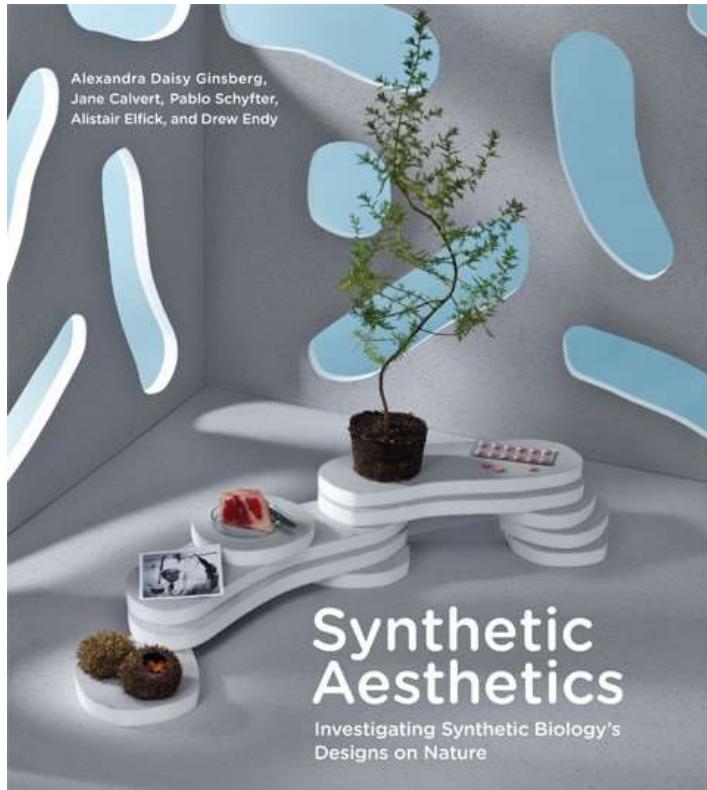
Synthetic Biology: The Society

Bio-art in Synthetic Biology



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

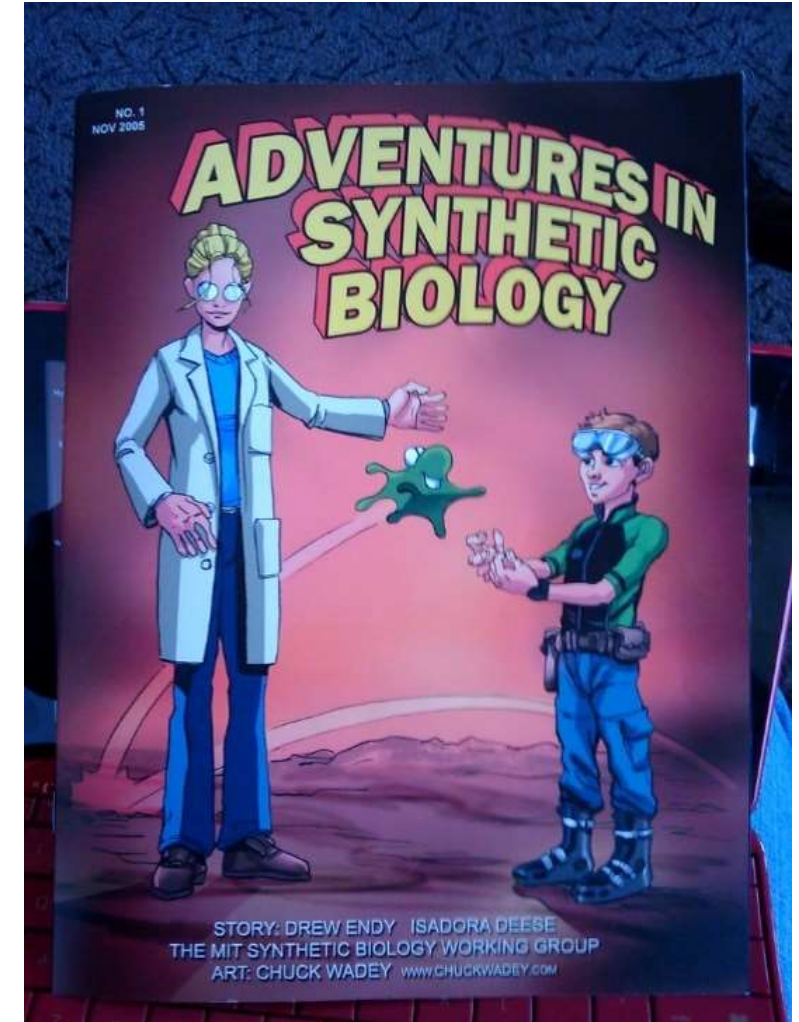
<http://web.mit.edu/indy/www/scrap/comic/AISB.vol1.pdf>



Alexandra Daisy Ginsberg,
Jane Calvert, Pablo Schyfter,
Alistair Ellick, and Drew Endy

Synthetic Aesthetics

Investigating Synthetic Biology's
Designs on Nature



The story telling

NO. 1
NOV 2005

ADVENTURES IN SYNTHETIC BIOLOGY

STORY: DREW ENDY ISADORA DEESE
THE MIT SYNTHETIC BIOLOGY WORKING GROUP
ART: CHUCK WADEY WWW.CHUCKWADEY.COM

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.

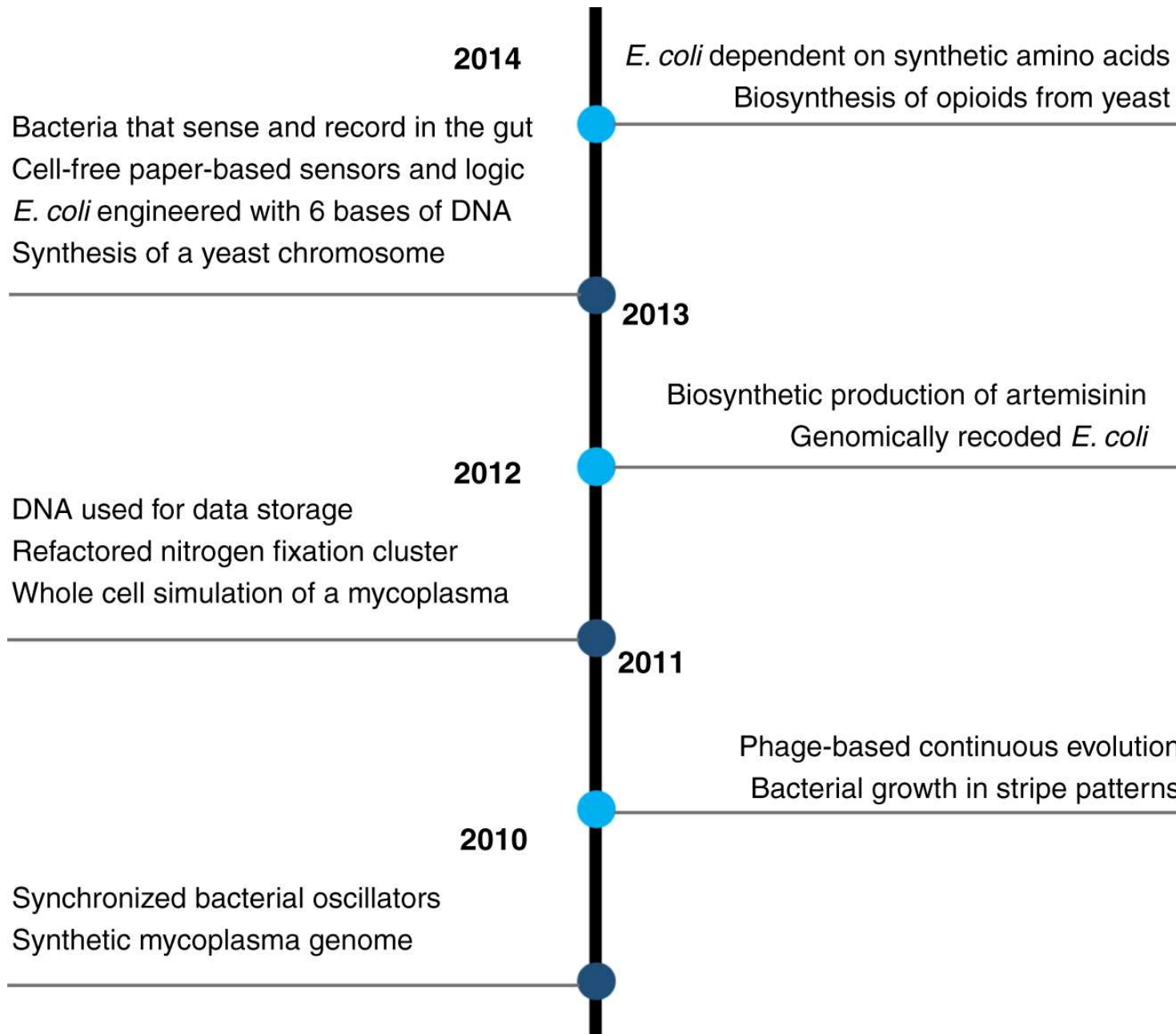
2005: Researchers develop a light-sensing circuit in *E. coli*.^[16] Another group designs circuits capable of multicellular pattern formation.^[17]

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

Non-exhaustive list of Key landmarks

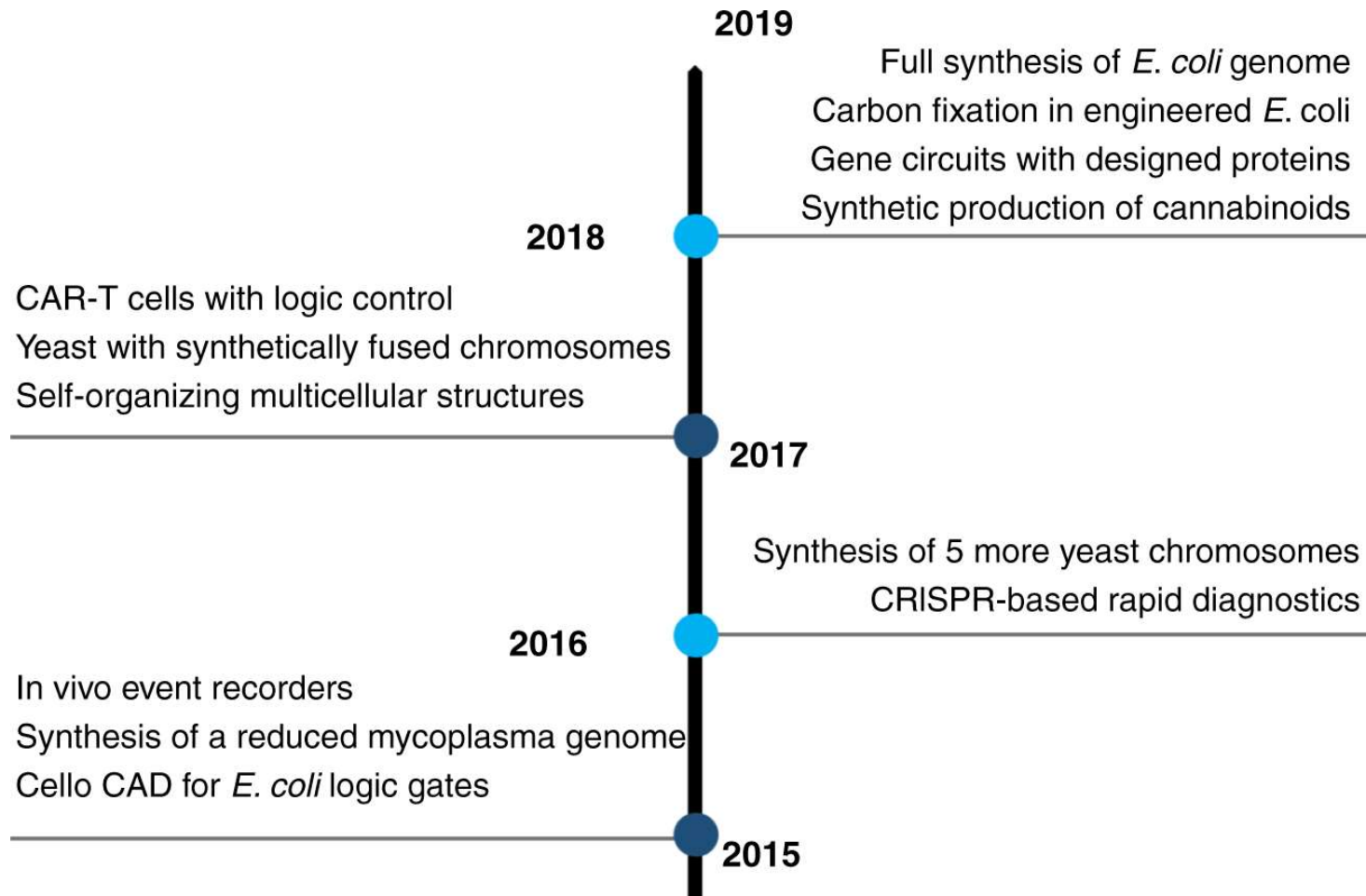
https://en.wikipedia.org/wiki/Synthetic_biology (25/09/2024)

Synthetic Biology: the Second Decade



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

Synthetic Biology: the Second Decade



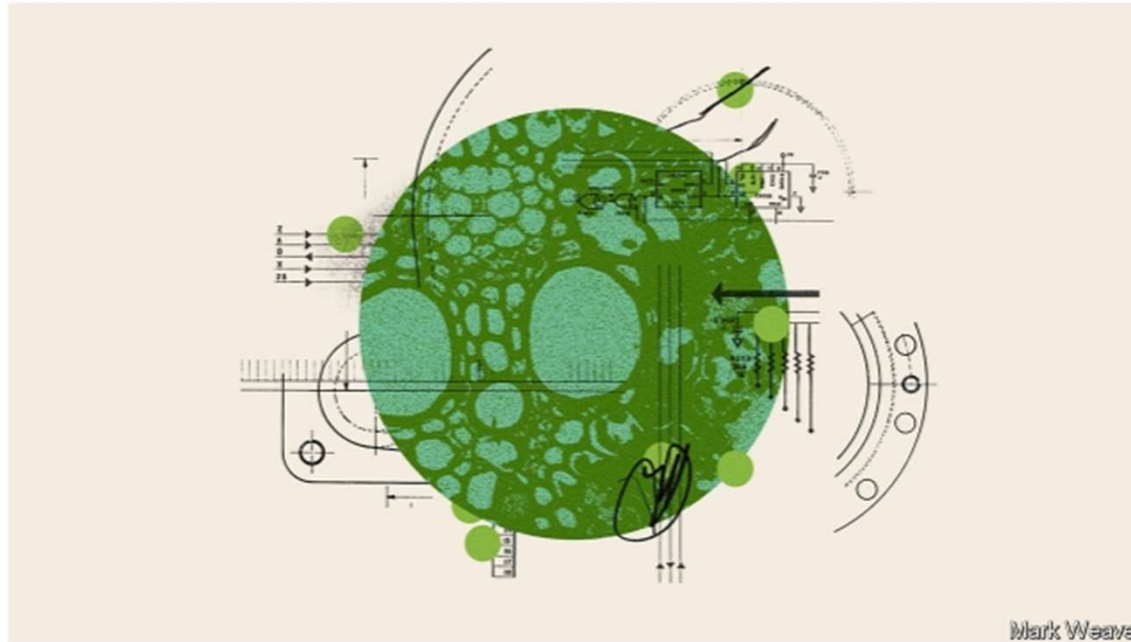
Key landmarks (Meng & Ellis, 2020. Nat. Comms.)

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



Mark Weaver

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

60+ SYNTHETIC BIOLOGY STARTUPS REIMAGINING FOOD, FUEL, HEALTHCARE, AND MORE

HEALTHCARE



FOOD & DRINK



INDUSTRIAL CHEMICALS



CONSUMER PRODUCTS



AGRICULTURE



BIOFUELS



DNA & RNA SYNTHESIS



ORGANISM ENGINEERING & AUTOMATION PLATFORMS



SOFTWARE



Questions welcome.

manish.kushwaha@inrae.fr