Introduction to Bioengineering
BIOE/ENGR.80
Stanford University

Spring 2020 Class Slides

Day 14
6 May 2020

Week 5 look ahead

CONCEPT
SKILL

DNA sequencing (reading)

DNA synthesis (writing)

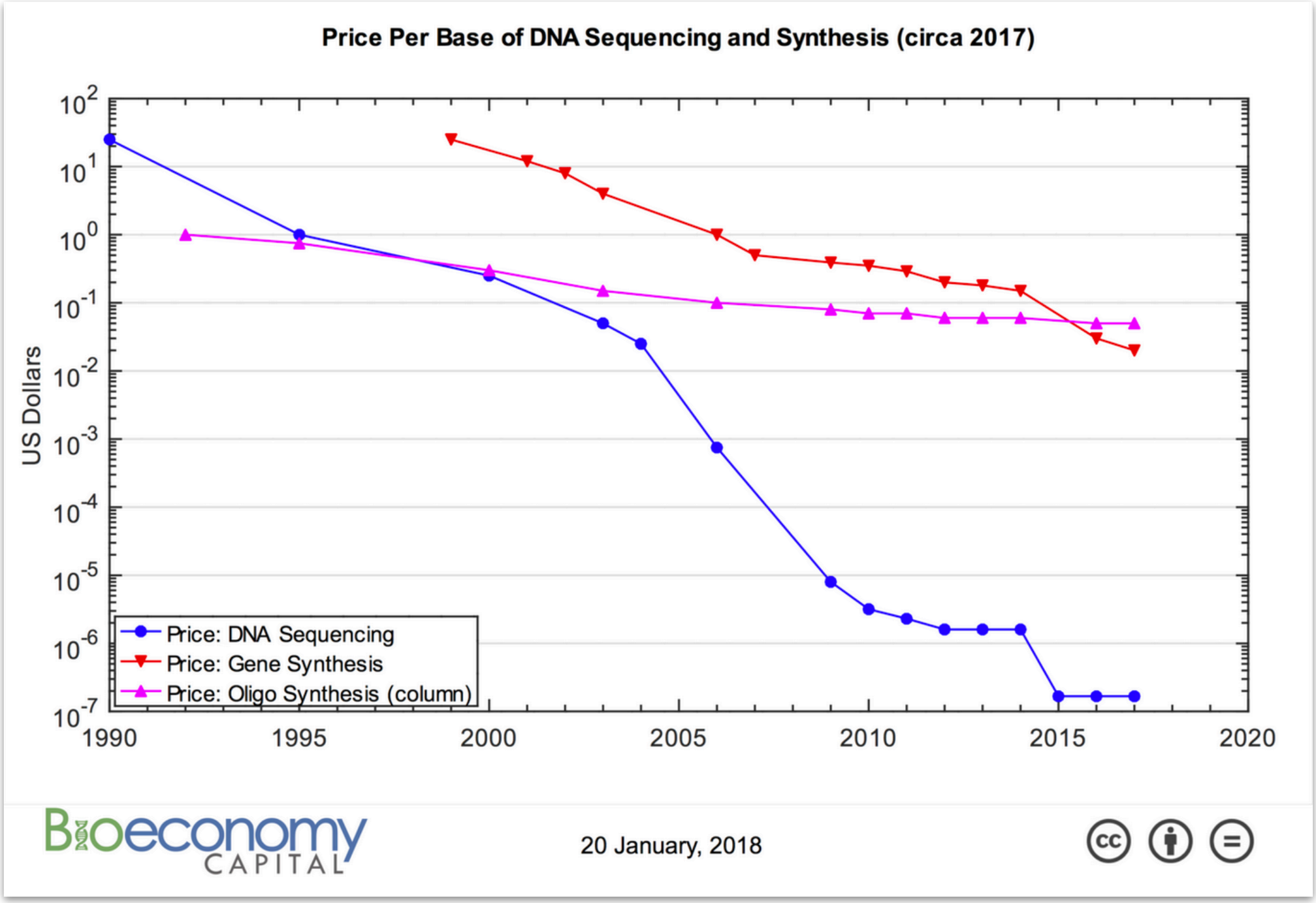
WE ARE HERE

Surfing exponentials

Interconvertibility of matter and information

Team rules & priority setting tools

DNA read/write increasingly affordable



Q. what becomes possible as DNA read/ write becomes more affordable?

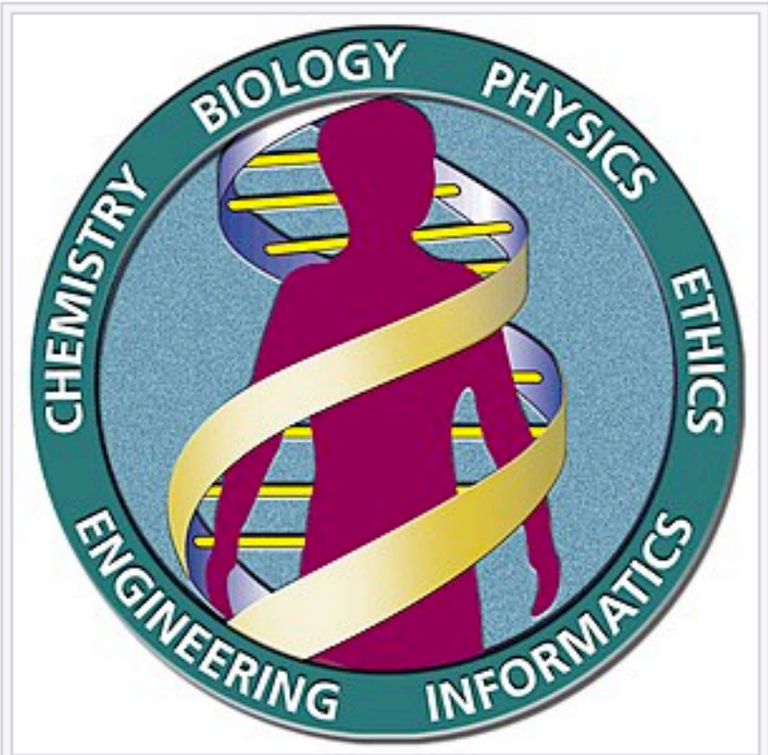
1990, DNAr @ $2/base, $6 billion!

Human Genome Project

From Wikipedia, the free encyclopedia

The **Human Genome Project** (**HGP**) was an international scientific research project with the goal of determining the base pairs that make up human DNA, and of identifying and mapping all of the genes of the human genome from both a physical and a functional standpoint.[1] It remains the world's largest collaborative biological project.[2] After the idea was picked up in 1984 by the US government when the planning started, the project formally launched in 1990 and was declared complete on April 14, 2003.[3] Funding came from the US government through the National Institutes of Health (NIH) as well as numerous other groups from around the world. A parallel project was conducted outside the government by the Celera Corporation, or Celera Genomics, which was formally launched in 1998. Most of the government-sponsored sequencing was performed in twenty universities and research centers in the United States, the United Kingdom, Japan, France, Germany and China.[4]

The Human Genome Project originally aimed to map the nucleotides contained in a human haploid reference genome (more than three billion). The "genome" of any given individual is unique; mapping the "human genome" involved sequencing a small number of individuals and then assembling these together to get a complete sequence for each chromosome. Therefore, the finished human genome is a mosaic, not representing any one individual.

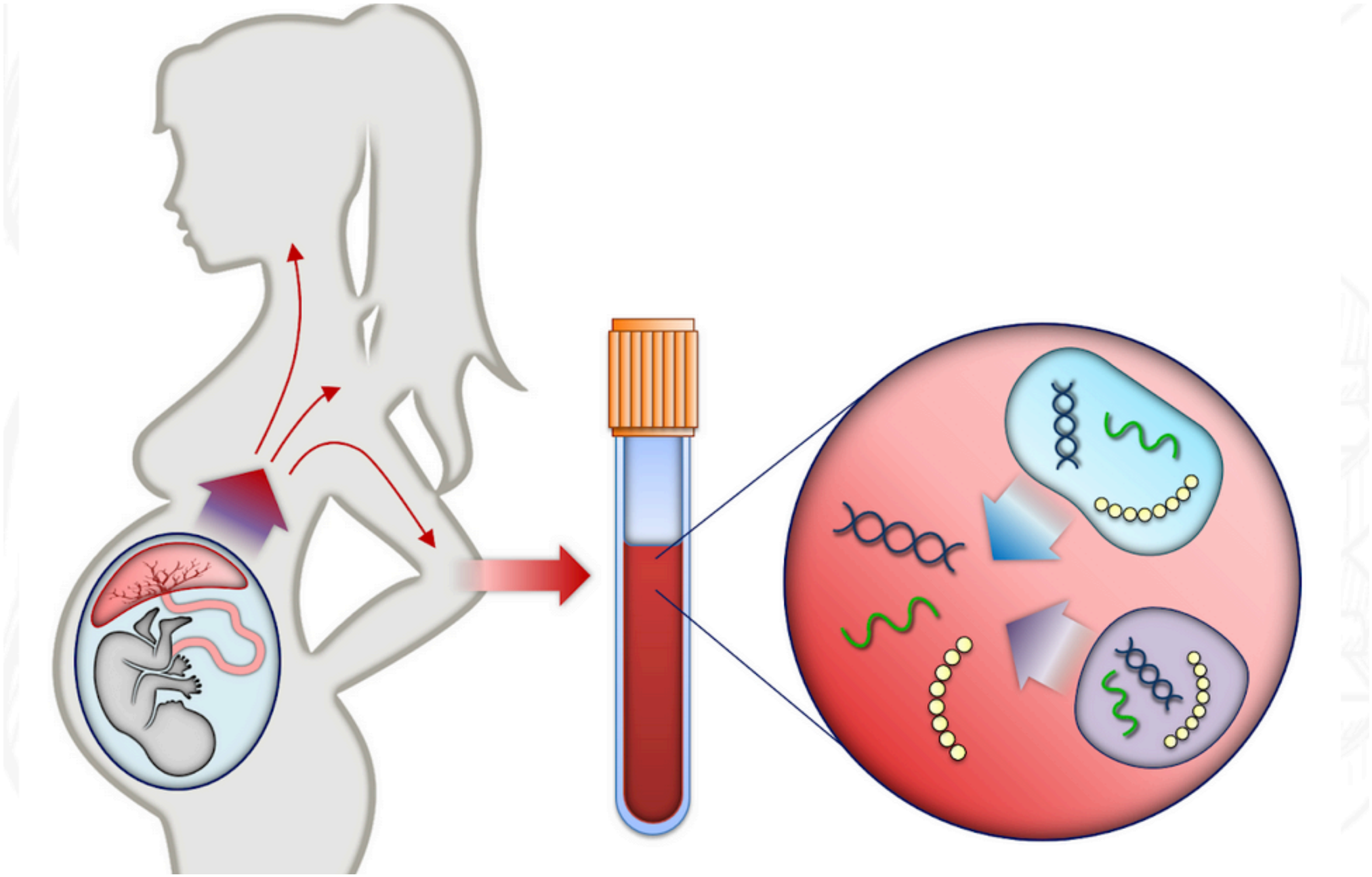


Logo of the Human Genome Project

A. can set out to sequence human genome for first time…

https://en.wikipedia.org/wiki/Human_Genome_Project

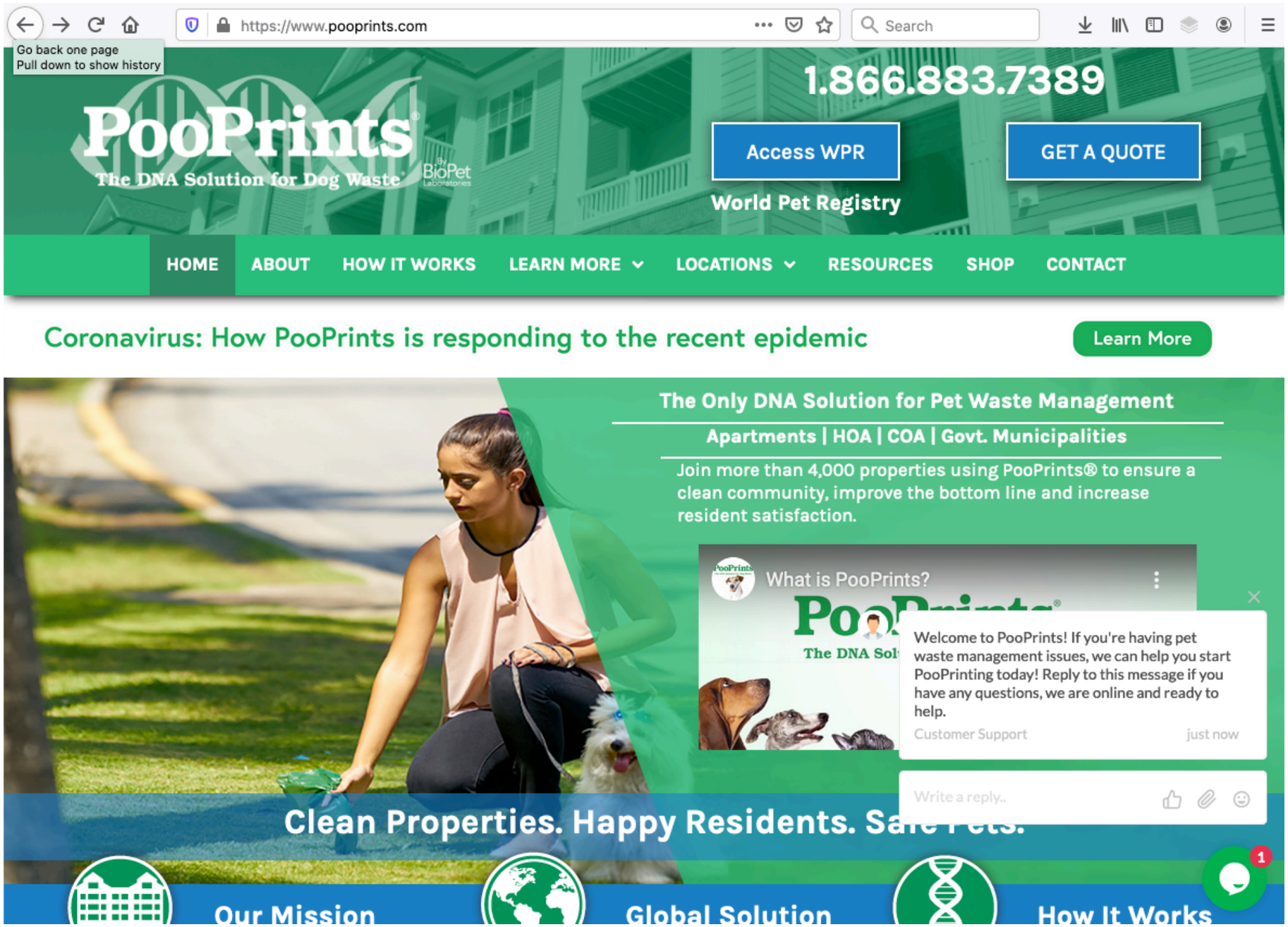
2011-15, DNAr @ $1E-6/base, $1000!



A. can determine properties of fetus from fetal DNA circulating in woman's blood.

https://geneton.sk/en/trisomytest-non-invasive-prenatal-screening/

2020, DNAr @ $1E-7/base…



A. can register your dog's DNA and assign blame to neighbors who don't clean up after their pets.

https://www.pooprints.com/

20??, DNAr @ $???/base…

ESSAY

An Estimate of the Total DNA in the Biosphere

Hanna K. E. Landenmark*, Duncan H. Forgan¤, Charles S. Cockell

United Kingdom Centre for Astrobiology, School of Physics and Astronomy, University of Edinburgh, Edinburgh, United Kingdom

¤ Current address: School of Physics & Astronomy, Physical Science Building, North Haugh, St Andrews, United Kingdom
* s1046113@sms.ed.ac.uk

Abstract

Modern whole-organism genome analysis, in combination with biomass estimates, allows us to estimate a lower bound on the total information content in the biosphere: 5.3×10^{31} ($\pm 3.6 \times 10^{31}$) megabases (Mb) of DNA. Given conservative estimates regarding DNA transcription rates, this information content suggests biosphere processing speeds exceeding yottaNOPS values (10^{24} Nucleotide Operations Per Second). Although prokaryotes evolved at least 3 billion years before plants and animals, we find that the information content of prokaryotes is similar to plants and animals at the present day. This information-based approach offers a new way to quantify anthropogenic and natural processes in the biosphere and its information diversity over time.

5.3×10^{31} Megabases of DNA

A. when should we expect to have sequenced all DNA on earth?

https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002168

2003, DNAw @ $4/base, $4000/gene!

MIT News

ON CAMPUS AND AROUND THE WORLD

Browse or Search

Maia Mahoney, left, a sophomore in electrical engineering and computer science, confers with graduate student Reshma Shetty of the Biological Engineering Division during the January IAP course, "Synthetic Biology Lab: Engineered Genetic Blinkers."

Class aims to engineer blinking life in the lab

February 13, 2003

When four MIT biology and engineering faculty members designed a daring new IAP course for this year, they jokingly nicknamed it "phage wars."

A. can afford to synthesize genes for undergraduates for the first time…

https://en.wikipedia.org/wiki/Human_Genome_Project

2010, DNAw @ $0.50/base

($500,000/small bacterial genome!)

RESEARCH ARTICLE

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2]*

We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including "watermark" sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.

crude *M. mycoides* or *M. capricolum* extracts, or by simply disrupting the recipient cell's restriction system (*8*).

We now have combined all of our previously established procedures and report the synthesis, assembly, cloning, and successful transplantation of the 1.08-Mbp *M. mycoides* JCVI-syn1.0 genome, to create a new cell controlled by this synthetic genome.

Synthetic genome design. Design of the *M. mycoides* JCVI-syn1.0 genome was based on the highly accurate finished genome sequences of two laboratory strains of *M. mycoides* subspecies *capri* GM12 (*8*, *9*, *11*). One was the genome donor used by Lartigue *et al.* [GenBank accession CP001621] (*10*). The other was a strain created by transplantation of a genome that had been cloned and engineered in yeast, YCpMmyc1.1-Δ*typeIIIres* [GenBank accession CP001668] (*8*). This project was critically dependent on the accuracy of these sequences. Although we believe that both finished *M. mycoides* genome sequences are reliable, there are 95 sites at which they differ. We

A. can afford to synthesize a small bacterial genome from scratch…

https://science.sciencemag.org/content/329/5987/52

2017/18, DNAw @ $0.10/base

($1,000,000/eukaryotic genome)

Building a synthetic cell with 164 undergraduates.

Anton Jackson-Smith, Katie Bodner, Patrick Brennock, Timothy Abbott, Nathan Kipniss, Wen Torng, Alex Trevino, Linfeng Yang, Xue Yuan, Amara Aarif, Anthony Agbay, Khalid Ahmad, Kyu Ahn, Alexander Akesson, Stephen Aman, Cameron Andrews, Sruti Arulmani, Niranjan Balachandar, Peter Ballmer, Jon Bartlett, Elena Bauer, Tanner Beason, Michael Becich, Jeff Bennett, Melat Birbo, Alessandra Blanco, Kaylee Blevins, Catherine Borsting, Ari Brown, Camila Camacho, Matthew Carter, Moratwa Chamme, Ri Chen, Xingkai Chew, Selin Chiragzada, In Cho, Francis Choi, Ying Chow, Abbey Cutchin, Karen Dai, Nathan Dale, Jeffrey Dalli, Robel Daniel, Trevor Danielson, Sabar Dasgupta, Gordon Dean, Shelly Deng, Jonah Eisenberg, Clayton Ellington, Marina Elmore, Suzy Emerson, Harrison Enright, Tommy Fan, Dylan Faulkner, Erica Fearon, Gabbi Fisher, Steph Flamen, Boomer Fleming, Thomas Fleming, Monique Foung, Eva Frankel, Natalie Gable, Luisa Galhardo, Kelsey Garcia, Valerie Garcia, Geronimo Garcia, Eleanor Glockner, Samuel Gold, Dhruti Gopaluni, Autumn Greco, Maria Gutierrez Peñaloza, Maverick Handley, Cody Hankins, Cynthia Hao, Taylor Harris, Avina Harry, Cayla Hatton, Maddie Hayes-Lattin, Tyler Hochman, Hikaru Hotta, Michelle Howard, Grace Hsieh, Andrew Huang, Jessica Hui, Kenzi Inman, Starr Jiang, Dorothy Kang, Anjini Karthik, Asad Khaliq, Somya Khare, Yong-hun Kim, Diana Kim, Robert Kimmelman, Max Kucera, Josh Lange, Minku Lee, Catherine Lee, Alice Li, Angela Li, Sungmoon Lim, Jessica Lindsay, Cindy Liu, Frank Lou, Lanting Lu, Marissa MacAvoy, Brandon Maddick, Morgan Mahlock, Cody Maly, Josh Marchok, Bryce Marion, Paola Martinez, Eric Matsumoto, Demetri Maxim, Lauren Maymar, Lucy Maynard, Brittany McGee, Joey McKenna, Wills McMahon, Anna Mitchell, Healey Montague-Alamin, Scott Morris, Michael Morrissey, Dana Murphy, Sanura N'Jaka, Anika Naidu, Meredith Nelson, Regina Nguyen, Ariadne Nichol, Wesley Olmsted, Nicolai Ostberg, Danny Pantuso, Veeral Patel, Neil Patel, Nick Pena, Reinaldo Perez, Sasha Perigo, Patricia Perozo, Addie Petersen, Emanuel Pinilla, Austin Poore, Sruthi Raguveer, Anish Rao, Helena Roberts-Mataric, Feddi Roth, Blake Salvador, Trina Sarkar, Julia Schaepe, Aisha Sharif, Pretom Shome, Noor Siddiqui, Isaiah Smith, Tyler Smith, Travis Sosa, Meera Srinivasan, Millie Stefanowicz, Sharman Tan, Lena Tarhuni, Amelia Traylor, Trey Turner, Victoria Valverde Rambaud, Luisfer Varela Eleta, Andrea Villarreal, Quinton Wessells, Ashley Westerfield, Megan Wilson, Amy Wu, Kelsie Wysong, Michael Xie, Dennis Xu, Ale Young, Molly Zhang, Crystal Zheng, Lillian Zhu, **Jan Liphardt**, **Drew Endy**

Introduction

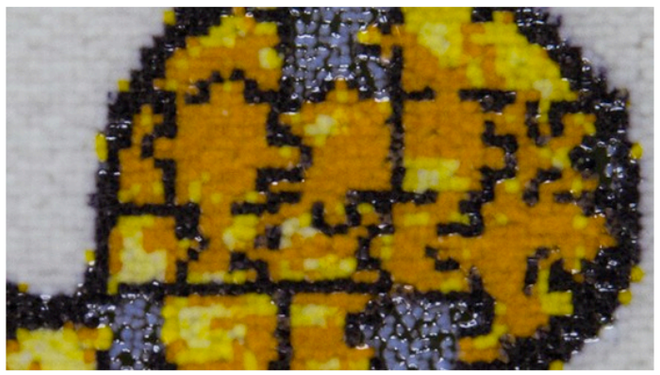
BIOE 80 is an introductory bioengineering class at Stanford. This spring, we added a 'Build-A-Cell' final project component to the class: each student would be responsible for designing and documenting several genes considered essential to a growing and dividing cell. We will synthesize the students' DNA constructs, and test them independently and in concert in a cell-free reaction system. We intend to iterate the design and build every time the class runs, increasing the speed and complexity of development as our capacity and understanding grows.

nature communications

Search | E-alert | Submit | Login

COLLECTION | 22 MAY 2018

Yeast 2.0



Synthetic biology aims to redesign and reconstruct biological systems for new, useful end goals. One of the ambitious projects currently underway is Sc2.0: the design and synthesis of a complete eukaryotic genome - *Saccharomyces cerevisiae*.

This collection highlights... show more

Commentary and Perspectives

EDITORIAL
OPEN ACCESS
22 MAY 2018
Nature Communications

Building better yeast

The Sc2.0 project has set out to synthesise the *Saccharomyces cerevisiae* genome, with each chromosome redesigned along agreed principles. In this collection of papers, the researchers involved show how SCRaMbLE—Synthetic Chromosome Rearrangement and Modification by... show more

A. can afford to enable undergrads to attempt building cells, can rebuild single-cell eukaryotes…

https://science.sciencemag.org/content/329/5987/52

20??, DNAw @ $???/base

8 June 2015 **BioE 80 – Final Exam** **Total Points: 100**

0. Your Name (2 points):

1. Nature+Nurture or Fab-a-Family? (20 points):

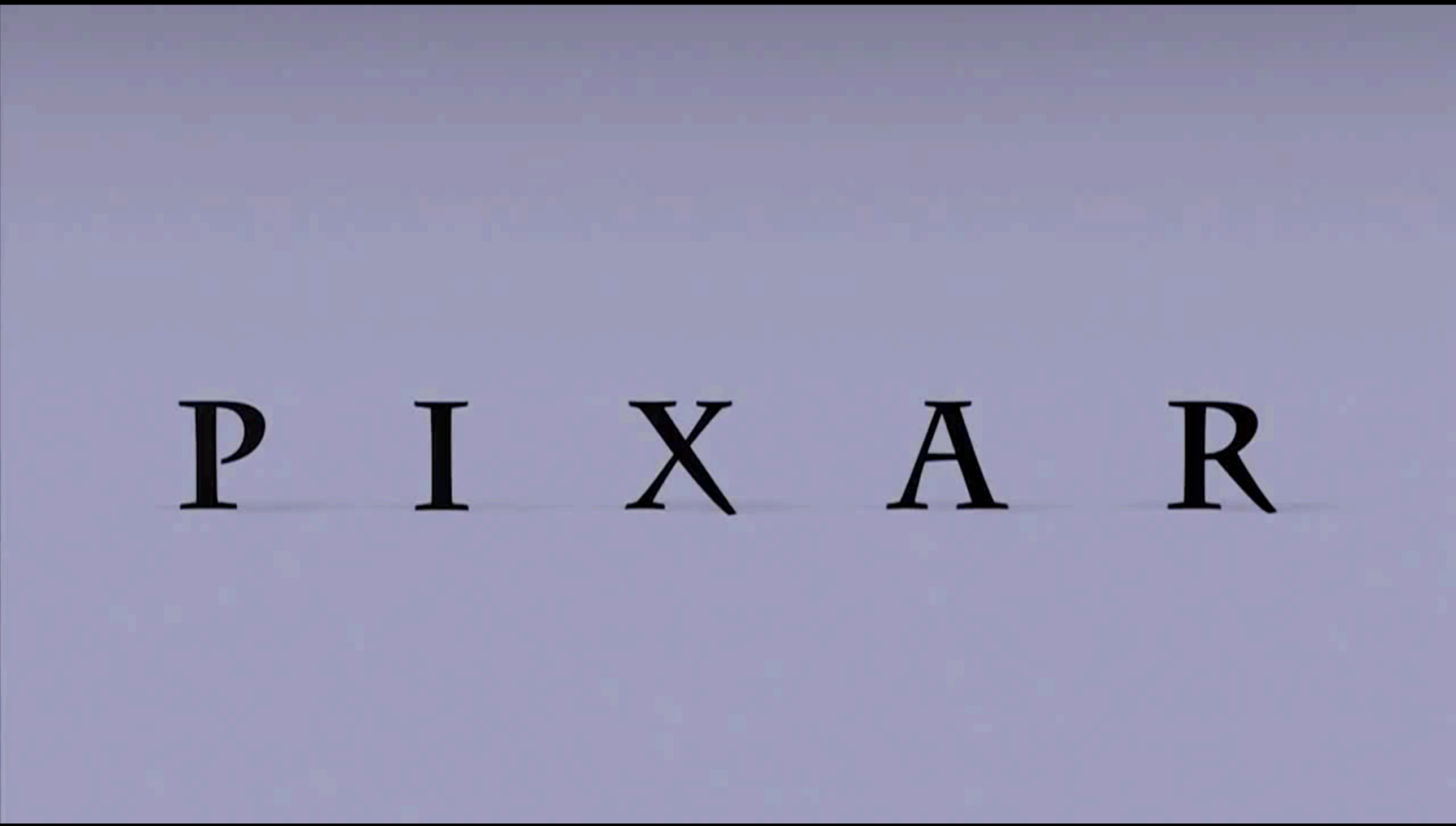
Over the past 12 years the price of synthesizing genes has dropped from $4 to $0.04 per base pair; presume the future price for DNA synthesis will continue to drop two fold every two years.

Meanwhile, Stanford's undergraduate tuition is approximately $50,000 per year up from $25,000 in 2000. Presume Stanford's tuition will continue to double every 15 years.

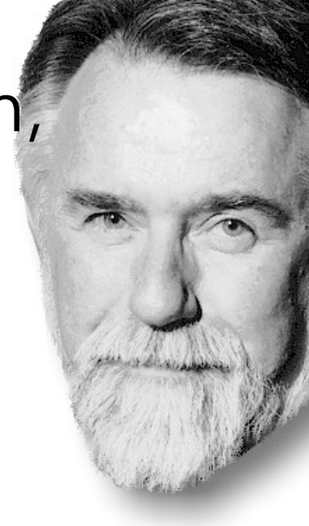
1a. If a human genome is 4 billion base pairs long then when will the cost of synthesizing the DNA encoding an entire human genome be roughly the same as the tuition cost associated with attending Stanford for one year? Hint: use the facts given, keep your math simple, and write it out. An approximate answer is fine.

A. when should we expect to be capable of synthesizing a human genome from scratch…

How to surf accelerating waves?



Luxo Jr., Pixar Animation Studios



“When the group moved to California to become part of Lucasfilm, **we got close to making a computer-animated movie again in the mid-1980s** – this time about a monkey with godlike powers but a missing prefrontal cortex. We had a sponsor, a story treatment, and a marketing survey. We were prepared to make a screen test: Our hot young animator John Lasseter had sketched numerous studies of the hero monkey and had the sponsor salivating over a glass-dragon protagonist.

But when it came time to harden the deal and run the numbers for the contracts, **I discovered to my dismay that computers were still too slow:** The projected production cost was too high and the computation time way too long. **We had to back out of the deal.** This time, we [knew enough] to correctly apply Moore’s Law – [] **we had to wait another five years to start making the first movie**. And sure enough, **five years later Disney approached us to make Toy Story**.”

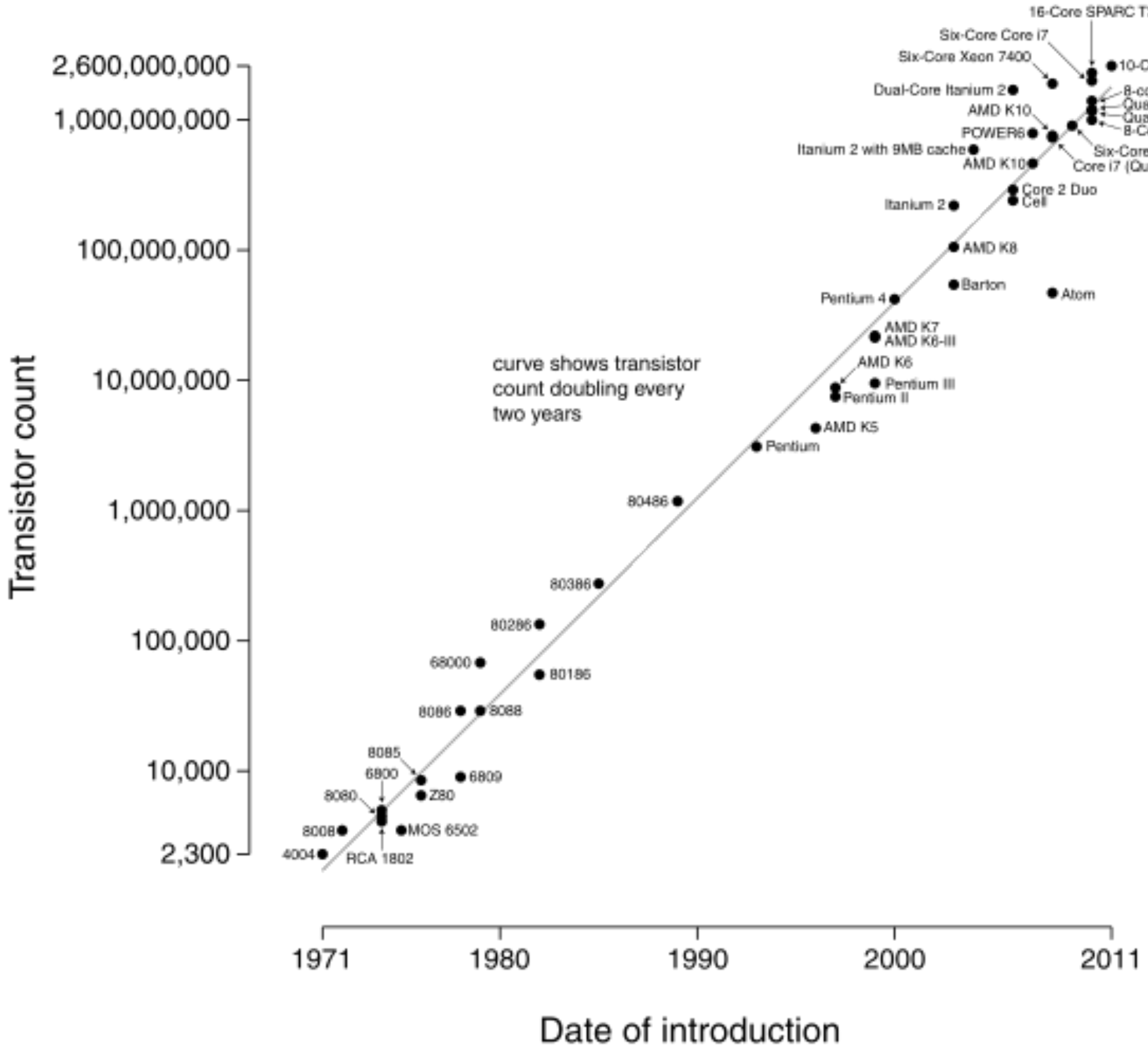
– Alvy Ray Smith

http://www.wired.com/2013/04/how-pixar-used-moores-law-to-predict-the-future/

How much cheaper did computer rendering of animated movies get between ~1985 and ~1990?

What information do you need to answer this question?

Microprocessor Transistor Counts 1971-2011 & Moore's Law



http://en.wikipedia.org/wiki/Moore%27s_law

How to surf accelerating waves?

Take away lesson… for Toy Story to arrive in theaters in 1995,
people had to be making smart decisions in 1985… how?
By understanding underlying trends in key tools.
What smart decisions should bioengineers be making today?

But wait…

Not just quantitative change…

Qualitatively new opportunities emerge…

To begin to ponder…
Life goes via four regimes

1. Natural lineages

3. Edit w/ intention

2. Screen & breed

ATCG ···· 0101 ···· ATCG

SEQUENCE

SYNTHESIZE

4. Networked & lineage agnostic

Download & print COVID from the web

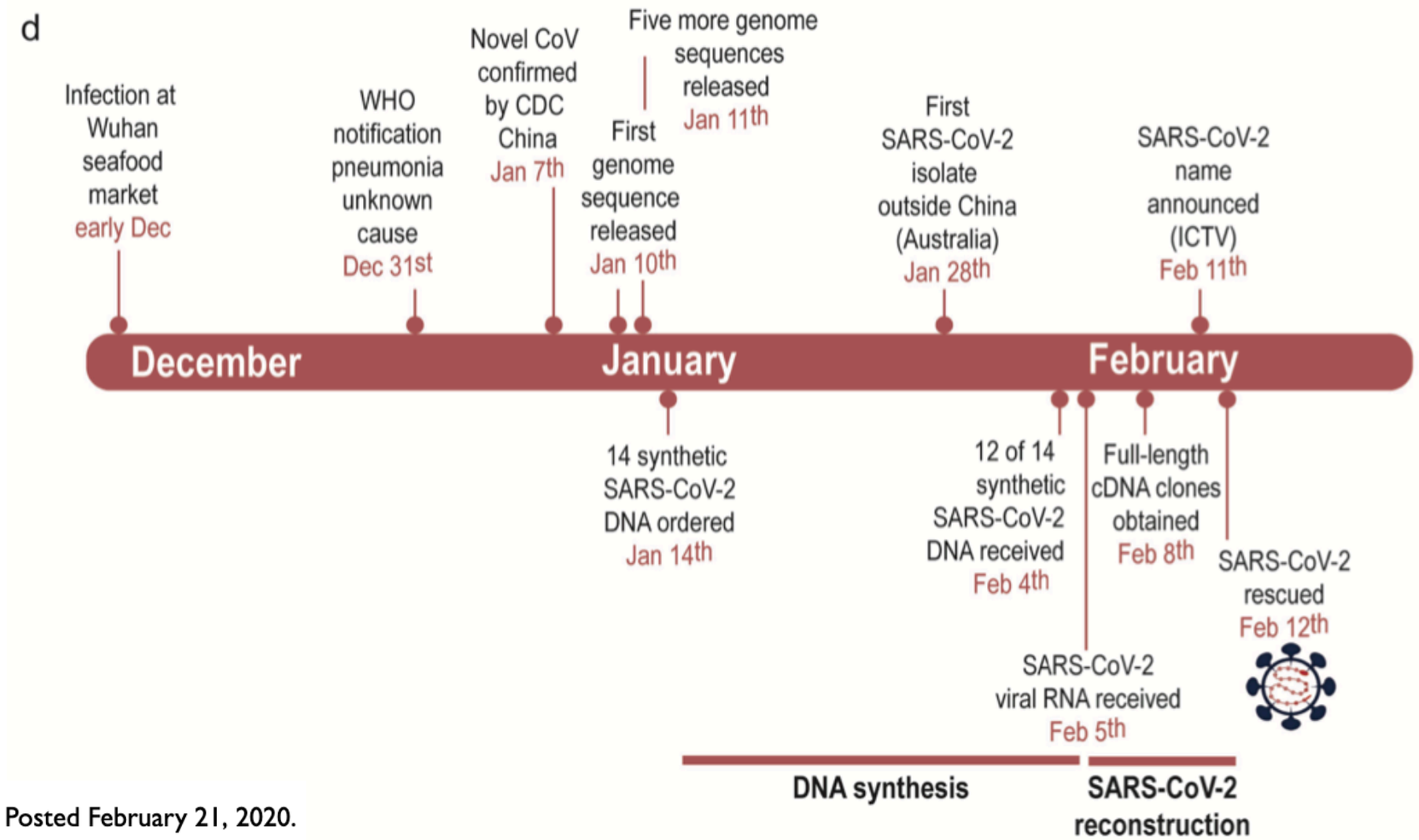
New Results

Comment on this paper

Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform

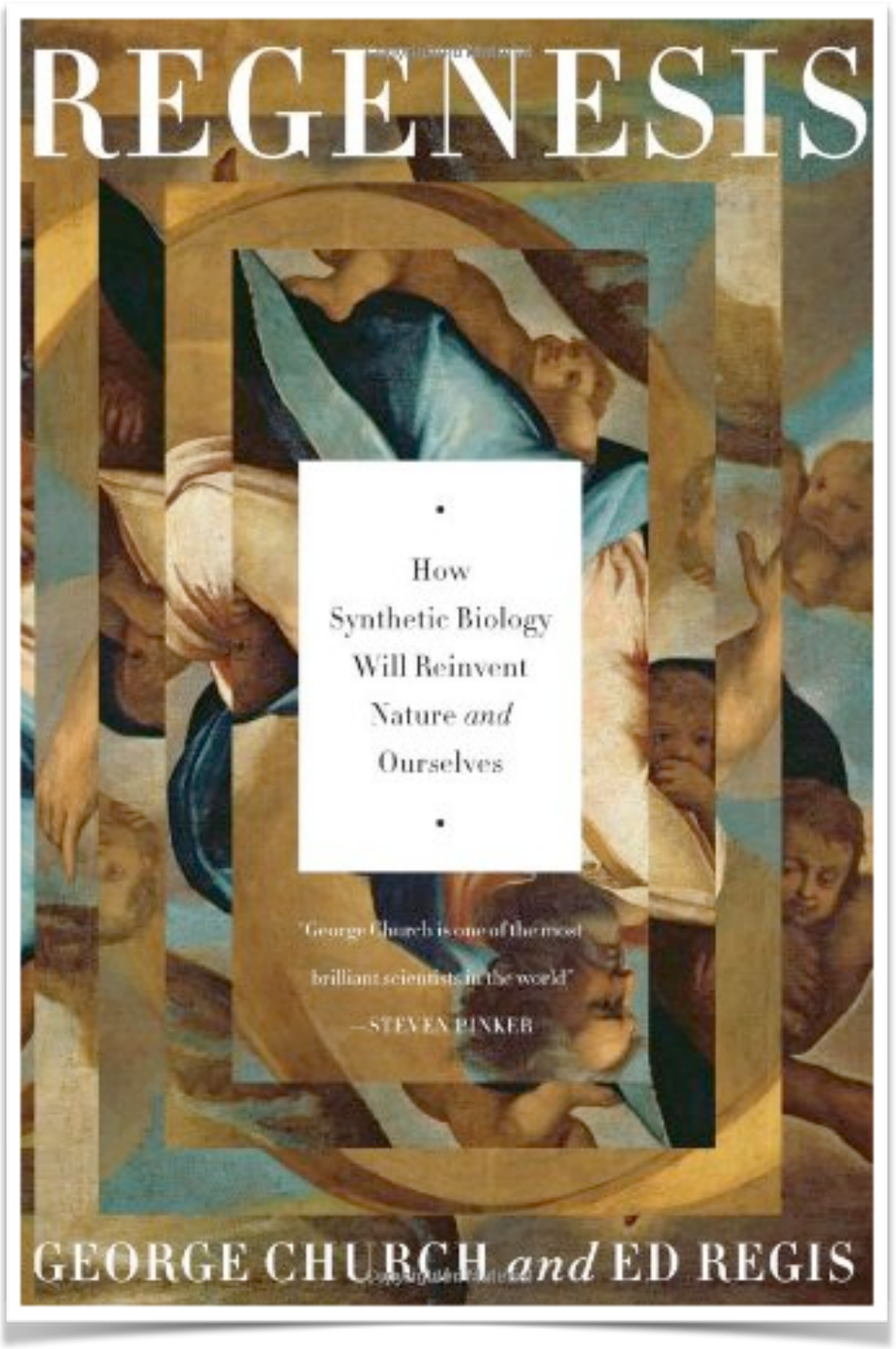
Tran Thi Nhu Thao, Fabien Labroussaa, Nadine Ebert, Philip V'kovski, Hanspeter Stalder, Jasmine Portmann, Jenna Kelly, Silvio Steiner, Melle Holwerda, Annika Kratzel, Mitra Gultom, Laura Laloli, Linda Hüsser, Manon Wider, Stephanie Pfaender, Dagny Hirt, Valentina Cippà, Silvia Crespo-Pomar, Simon Schröder, Doreen Muth, Daniela Niemeyer, Marcel A. Müller, Christian Drosten, Ronald Dijkman, Joerg Jores, Volker Thiel

doi: https://doi.org/10.1101/2020.02.21.959817



Posted February 21, 2020.

DNA as an abiotic tape for storing arbitrary digital data. Storage market > biotech.



SCIENCE

The First Book To Be Encoded in DNA

Two Harvard scientists have produced 70 billion copies of a book in DNA code --and it's smaller than the size of your thumbnail.

By Kharunya Paramaguru | Aug. 20, 2012 | 5 Comments

Despite the fact there are 70 billion copies of it in existence, very few people have actually read the book *Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves in DNA*, by George Church and Ed Regis. The reason? It is written in the basic building blocks of life: Deoxyribonucleic acid, or DNA.

Church, along with his colleague Sriram Kosuri, both molecular geneticists from the Wyss Institute for Biologically Inspired Engineering at Harvard, used the book to demonstrate a breakthrough in DNA data storage. By copying the 53,000 word book (alongside 11 jpeg images and a computer program) they've managed to squeeze a thousand times more data than ever previously encoded into strands of DNA, as reported in the August 17 issue of the journal *Science*. (To give you some idea of how much information we're talking about, 70 billion copies is more than three times the total number of copies for the next 200 most popular books in the world combined.)

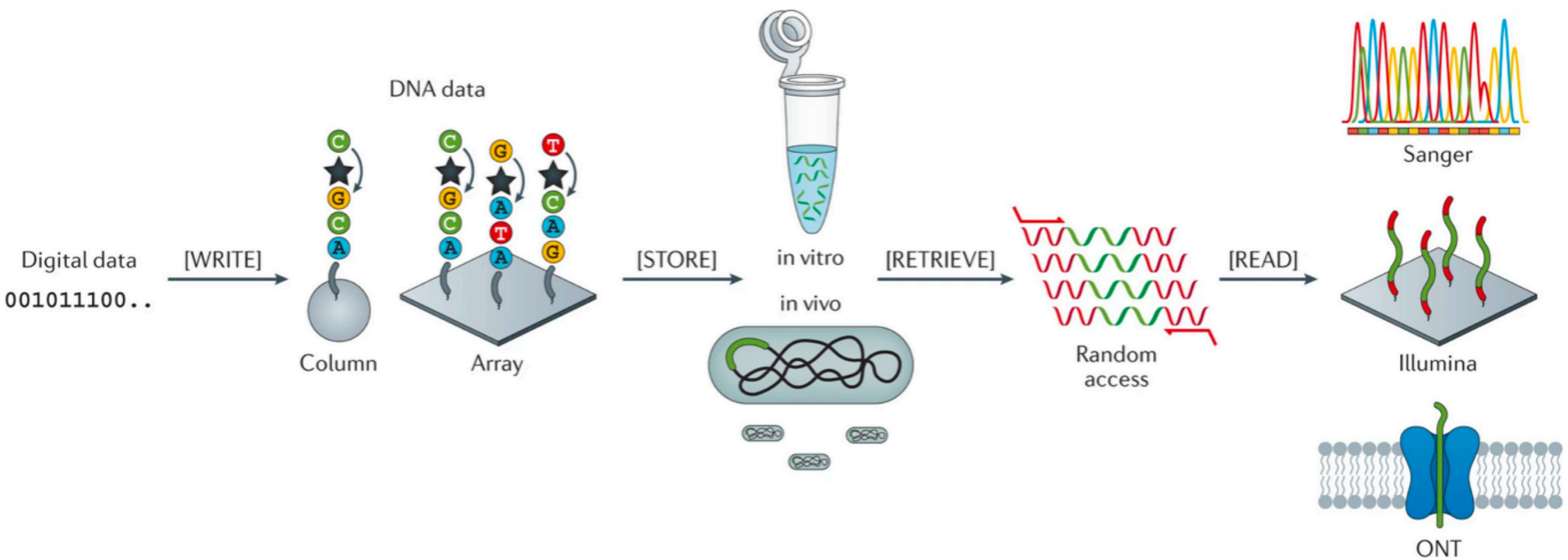
Lisa Poole / AP FILE

In his lab at the Harvard Medical School in Boston, George Church, Harvard Medical School Genetics professor, shows DNA sequence data for Dr. John Halamka, chief information officer, following a news conference on Monday, Oct. 20, 2008 where a group of mostly scientists and researchers said they will post their medical records and DNA sequence of some of their own genes online for the sake of research. Both George Church and Dr. Halamka are part of the group that plan to post their medical and DNA sequence of some of their own genes online.

Encode a library in a test tube

Fig. 2: Overview of the major steps of digital data storage in DNA.

From: Molecular digital data storage using DNA



Review Article | Published: 08 May 2019

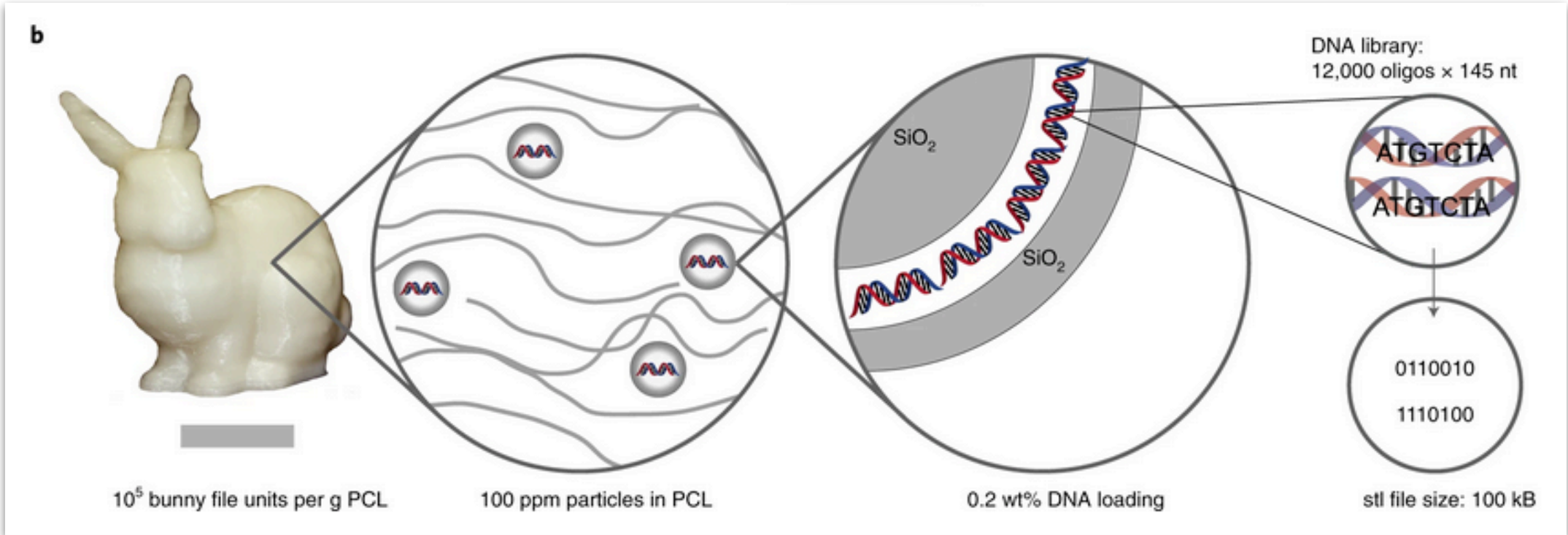
Molecular digital data storage using DNA

Luis Ceze ✉, Jeff Nivala & Karin Strauss

Nature Reviews Genetics **20**, 456–466(2019) | Cite this article

The world will generate 160 zettabytes of data in 2025. That's more bytes than there are stars in the observable universe. Conventional storage media like flash-drives and hard-drives do not have the longevity, data density, or cost efficiency to meet the global demand. CATALOG is building the world's first DNA-based platform for massive digital data storage and computation.

Embed arbitrary info. in arbitrary objects

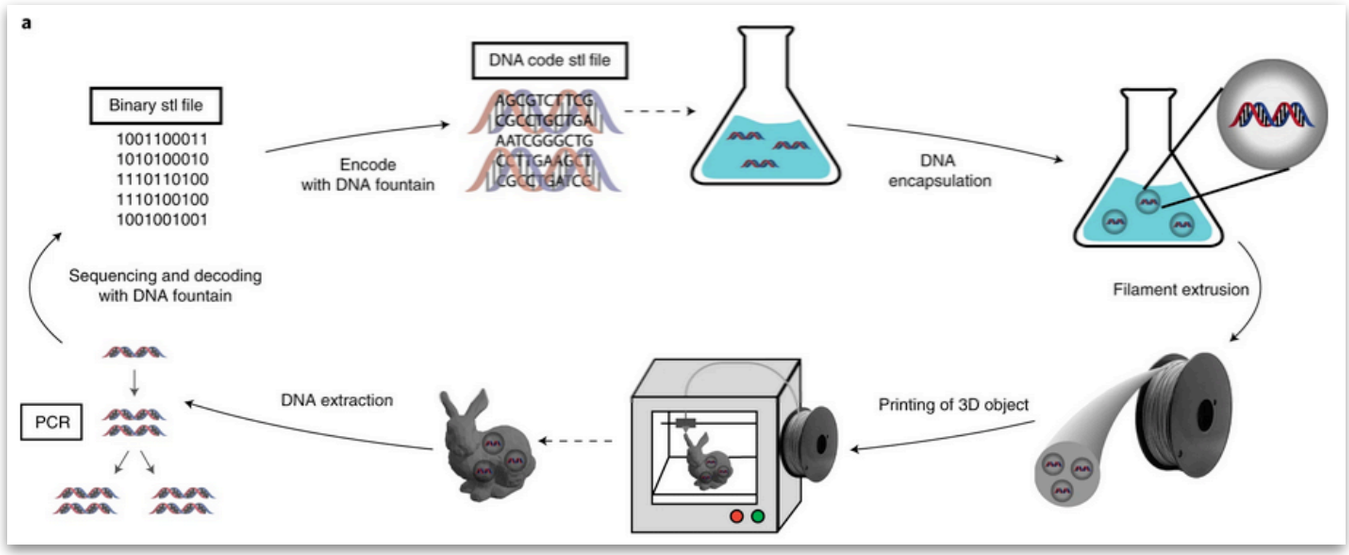


Letter | Published: 09 December 2019

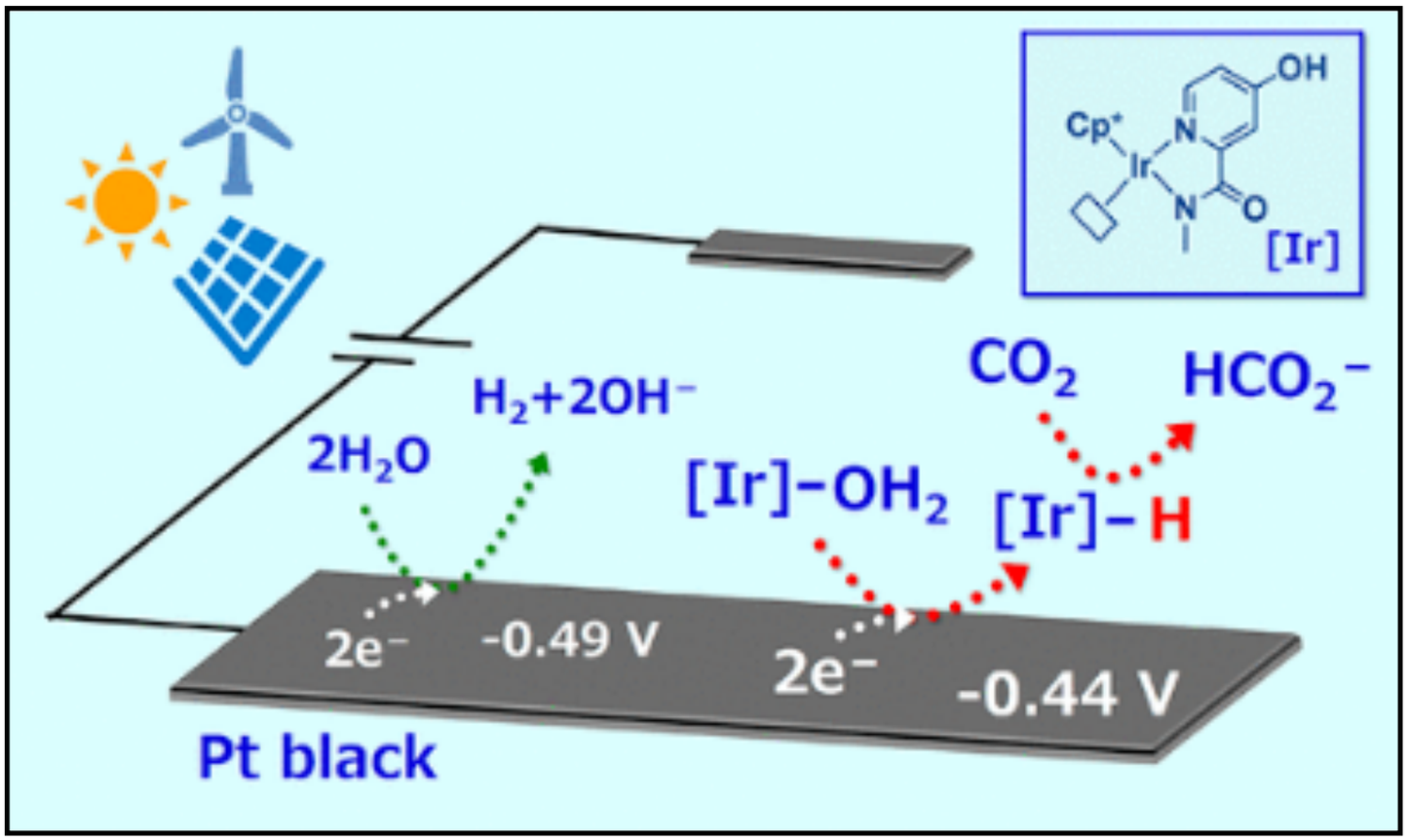
A DNA-of-things storage architecture to create materials with embedded memory

Julian Koch, Silvan Gantenbein, Kunal Masania, Wendelin J. Stark, Yaniv Erlich ✉ & Robert N. Grass ✉

Nature Biotechnology **38**, 39–43(2020) | Cite this article

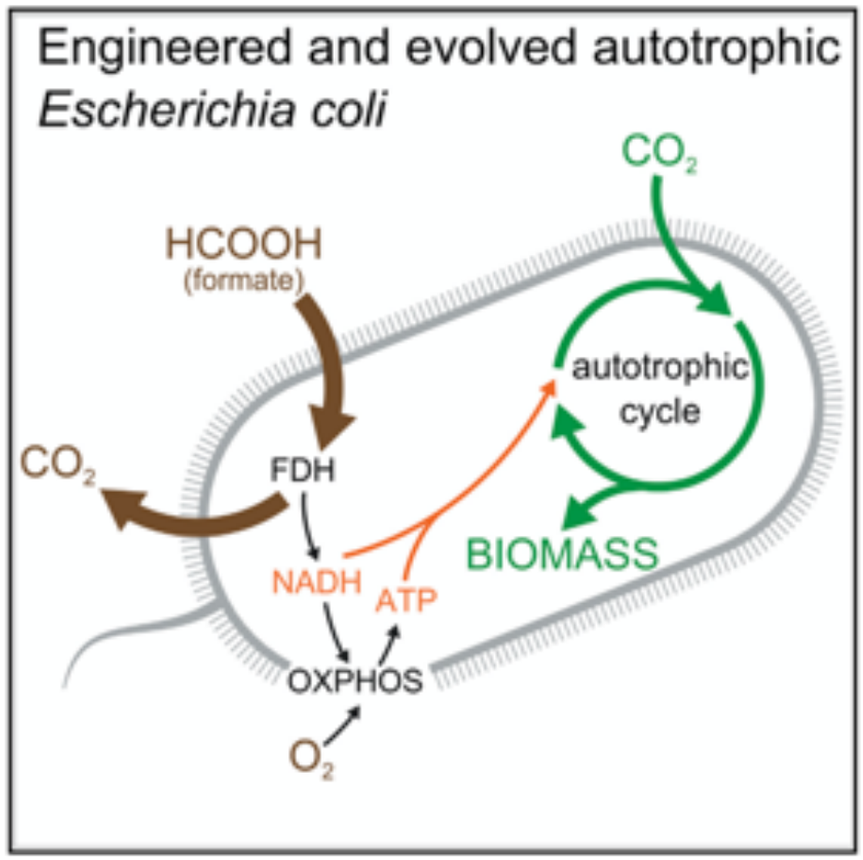


From electricity to formate,
from formate to bio-stuff



Electroreduction of Carbon Dioxide to Formate by Homogeneous Ir Catalysts in Water

Ryoichi Kanega*, Naoya Onishi, Lin Wang and Yuichiro Himeda*



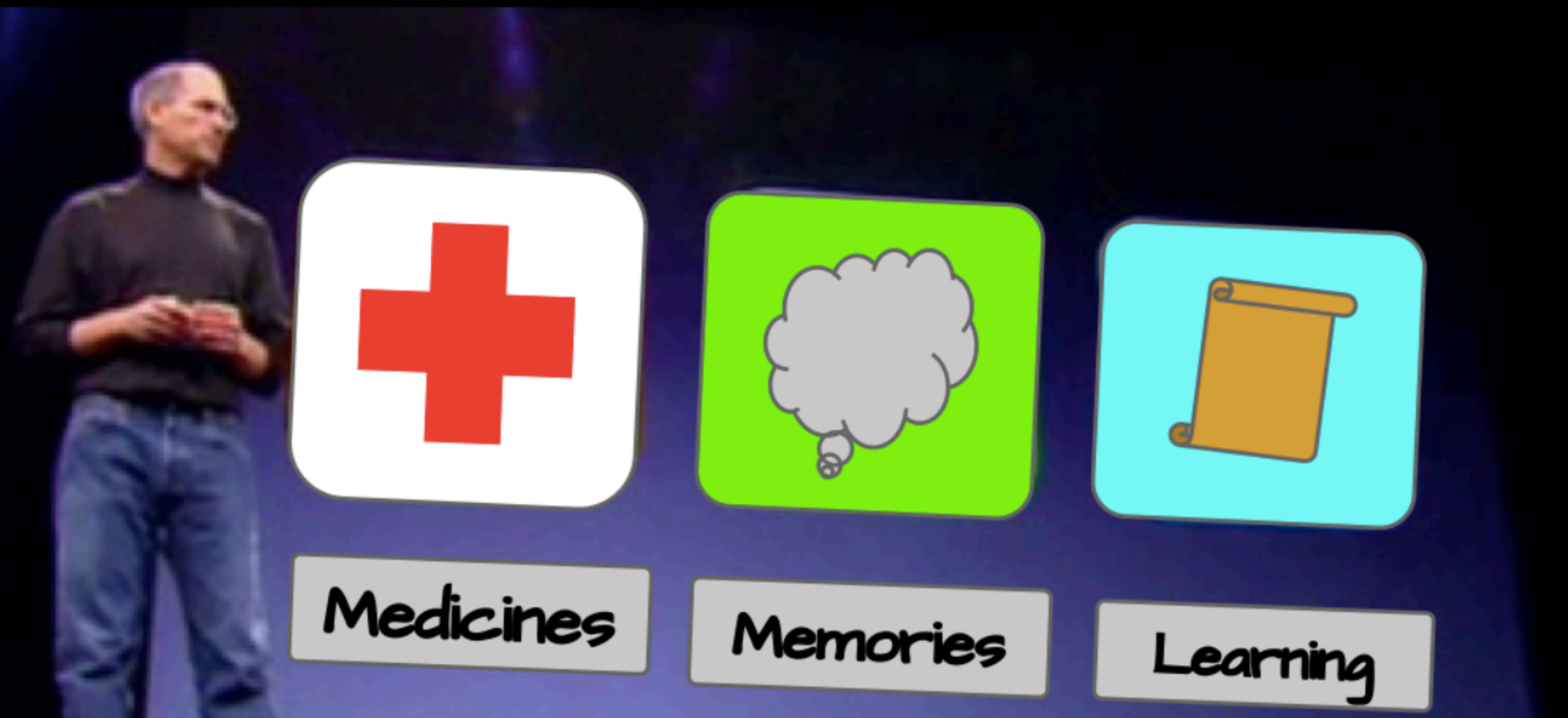
Gleizer et al., 2019, Cell *179*, 1255–1263
November 27, 2019 © 2019
https://doi.org/10.1016/j.cell.2019.11.009

~1 kWh electricity = ~ 1 (to 30) grams biomass

~$0.11 = ~ 1 (to 30) courses of antibiotics

Who will make the world's first
personal biology synthesizer (aka, the PB)?

"Today we are introducing three
revolutionary products…"



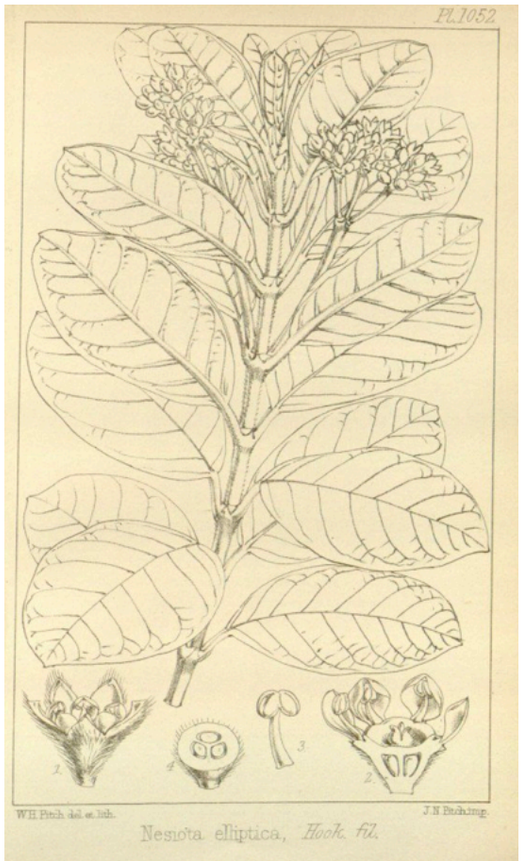

N°5
INÉVITABLE
N°5
CHANEL
PARIS
PARFUM

Rewriting Life

Would You Feel Sexy Wearing *Eau de Extinction*?

Synthetic biologists seek to make perfumes from extinct trees and flowers.

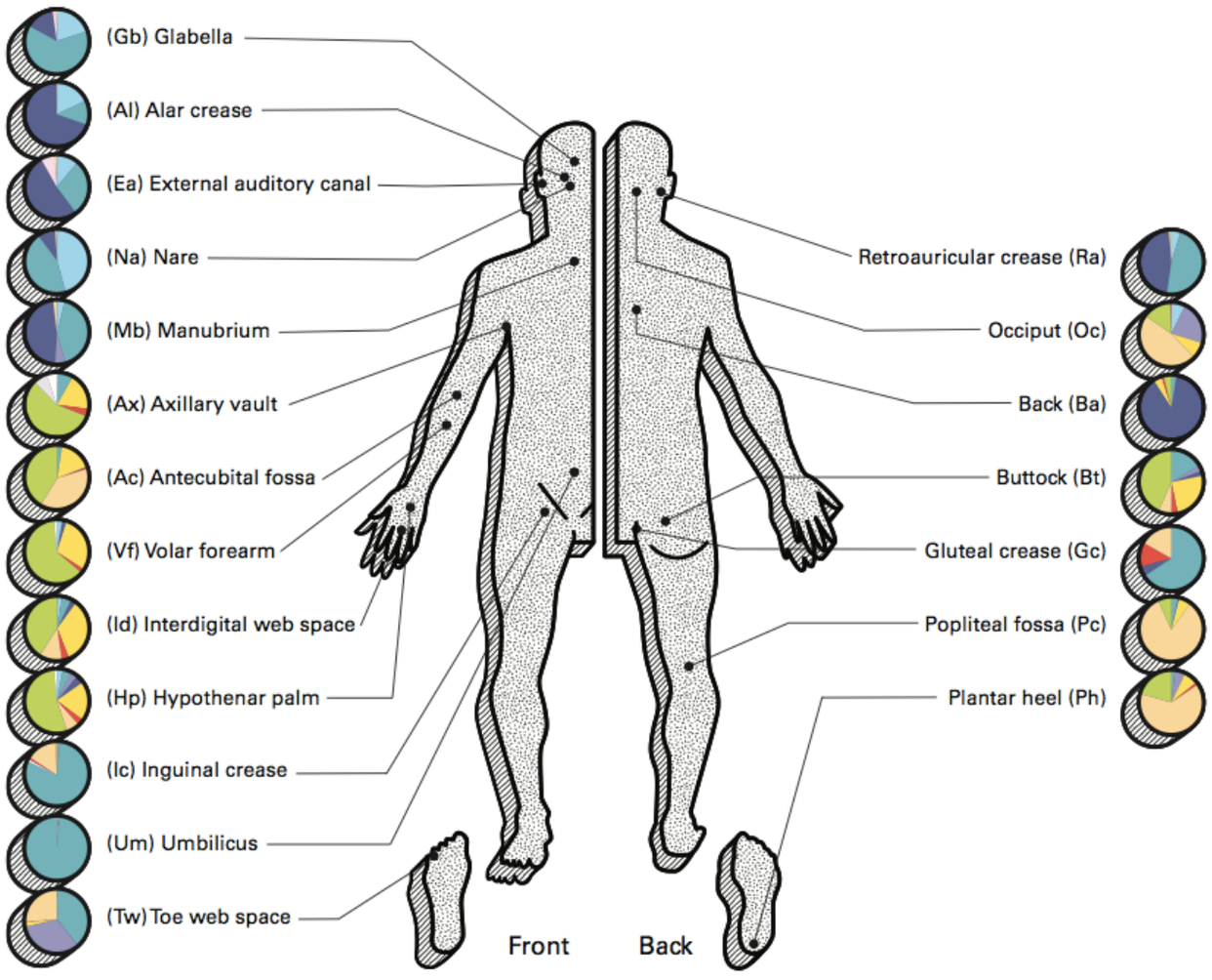
by Monique Brouillette December 5, 2016



To locate new terpene-making genes, in May of this year Agapakis and colleagues scoured the archives of the Harvard University Herbarium, which houses more than five million preserved plant specimens. They selected samples of a dozen species that have gone extinct in the last two centuries, including a Hawaiian hibiscus and *Nesiota elliptica*, a flowering olive bush native to the island of St. Helena's in the South Atlantic, which disappeared from the wild in 1994 and went extinct in 2003.

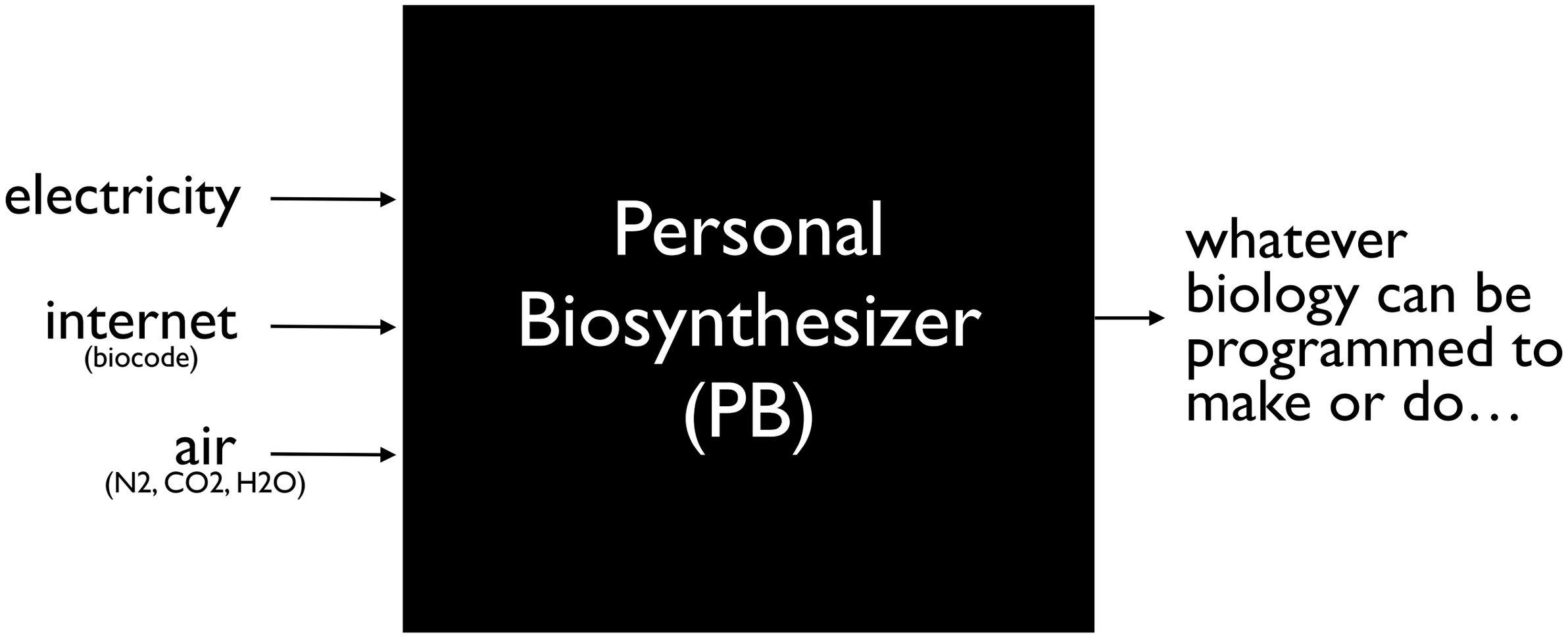
What if skin microbes could be programmed to make living perfumes?

(that monitor blood sugar level, infection, other)



https://www.smithsonianmag.com/smart-news/what-happens-when-you-culture-bacteria-eight-year-olds-hand-180955528/

Q. How will this box change the world?



Q. What will the "PB" + the "bionet" lead to?

A. "design anywhere, grow everywhere"

Friday — Team Project — Priority Setting

First 15’ of class will be discussion with pioneering leader of organization whose mission is to help individuals understand their DNA.

Be here to learn what this person has learned about making decisions and setting priorities!