Introduction to Bioengineering
BIOE/ENGR.80
Stanford University

Spring 2020 Class Slides

Day 2
8 April 2020

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What makes living matter unique?

1. **Physics of living matter**
2. Opportunities & challenges
3. The here & now

Planetary-Scale Natural Nanotechnology

Biology is already many places

~90 terawatts via photosynthesis*

Reproducing, growing, & healing materials

Massively functional

Living ramifications

*electrobiosynthesis will remove this cap

Enable humanity to provide for itself

Stabilize & recover natural biodiversity

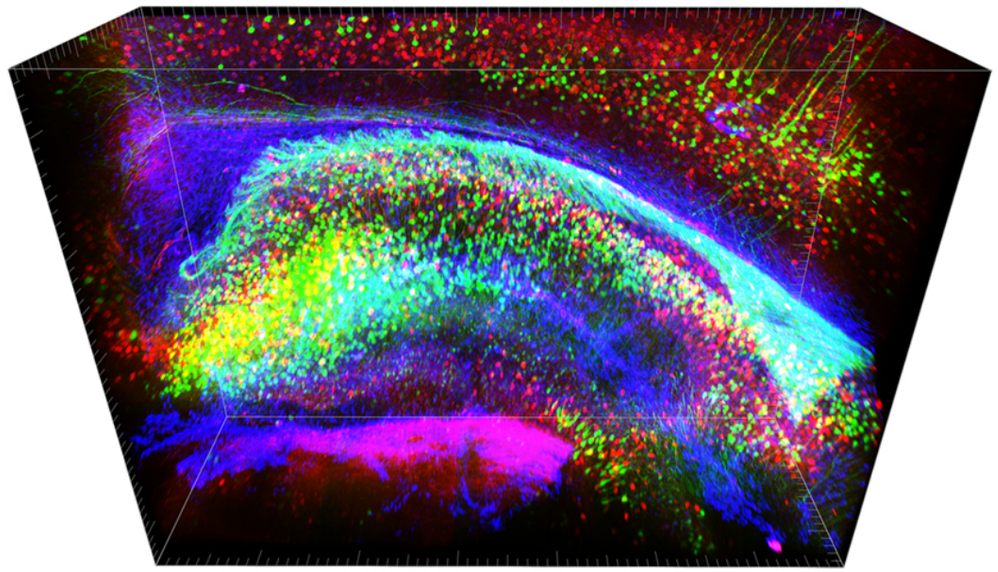
Take infectious & other diseases off the table

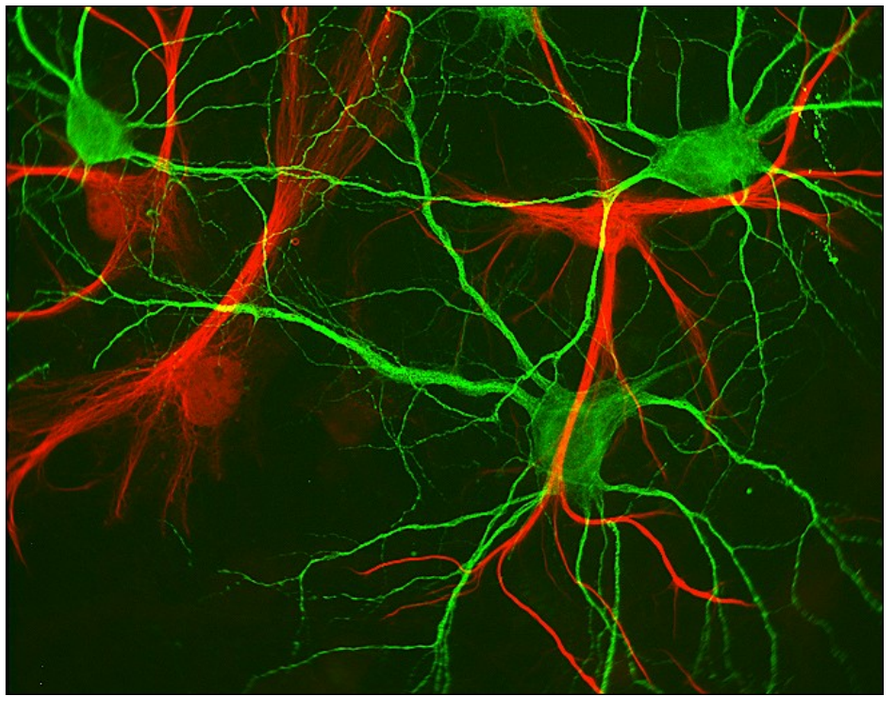
Enable a culture of citizenship

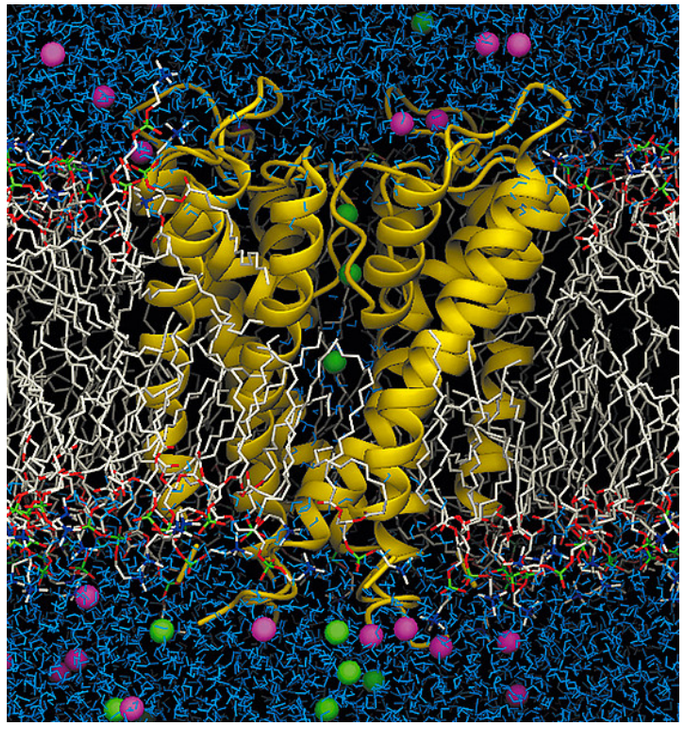
Understand life via building

The living bridges of Cherrapunji, India are made from the roots of the Ficus elastica tree. (http://rootbridges.blogspot.com/)

Take a microscope and keep zooming in

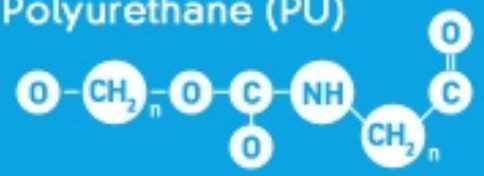
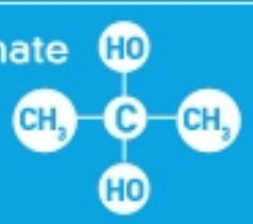






Organized over 10 orders of magnitude - 0.1 nanometers to meters

MATERIALS USED TO MAKE A CAR

Leather							Polyester (PET)
Cotton	Stainless steel	Fe Iron	Al Aluminium	Pd Palladium	O Oxygen	C Carbon	Polyurethane (PU) 
Timber	Steel	Pb Lead	Cu Copper	Si Silicon	H Hydrogen	Xe Xenon	Poly-carbonate (PC) 
Natural Rubber	Quartz	Cr Chromium	Zn Zinc	Mn Manganese	N Nitrogen	Ne Neon	Poly-propylene (PP)
Natural							Polymers

Cars are global products

MATERIALS USED TO MAKE A CAR

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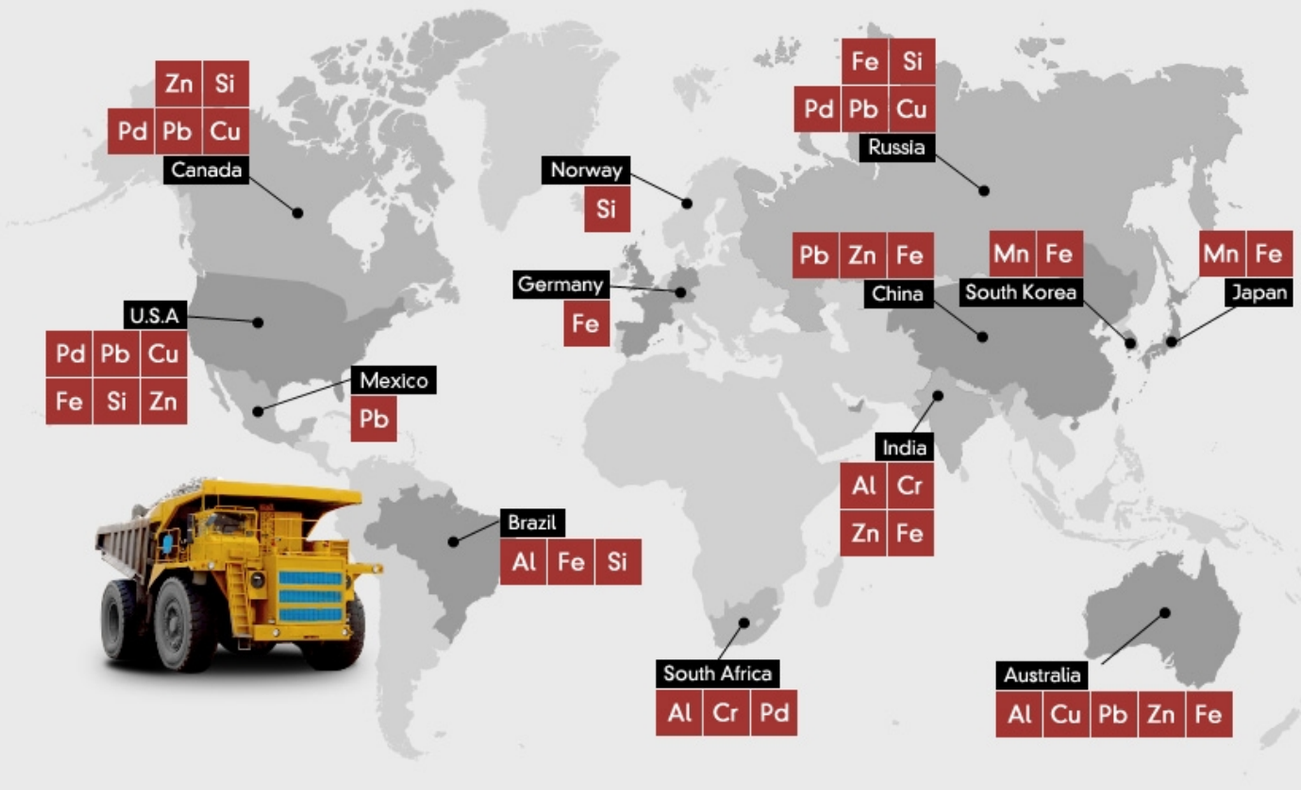
Natural Rubber	Quartz	Cr Chromium	Zn Zinc	Mn Manganese	N Nitrogen	Ne Neon	Poly-propylene (PP)
Natural							Polymers

WHERE IN THE WORLD DO THE RAW MATERIALS COME FROM?



MATERIALS IN A CAR

Al	Radiator, intake manifold, cylinder heads, engine block, bumpers, wheels, body panels	Cotton	Car covers, car seat covers, seats	Natural Rubber	Tyres, wiper blades, engine mounts, seals, hoses and belts	Leather	Car seats, interiors	Steel	Car body
Stainless Steel	Car mufflers, decorative trims, exhaust silencers, catalytic converters	Xe	Light bulbs: headlights	Poly-ester	Seat covers, carpets	Poly-carbonate	Electrical insulator, decorative bezels, optical reflectors, laminated for bullet resistant windows	Poly-propylene	Bumpers, car batteries

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MATERIALS USED TO MAKE A TREE
(light/air/carbon/nitrogen/water)

MATERIALS & INPUTS ARE LOCAL

What's physically special re: "living matter"?

Lots and lots of parts;
Computation is ultra energy efficient and massively parallel

Light/air/carbon/nitrogen/water precursors

Intricately organized on multiple time and spatial scales

Self-mixing

Self-organizing

Self-replicating

Self-healing

Each component can reproduce the whole

Breakout #1

- how many unique physical aspects?
- most interesting / important microscopic?
- most interesting / important macroscopic?

What makes living matter unique?

1. Physics of living matter
2. **Opportunities & challenges**
3. The here & now

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You are what you eat!

We eat what we are...

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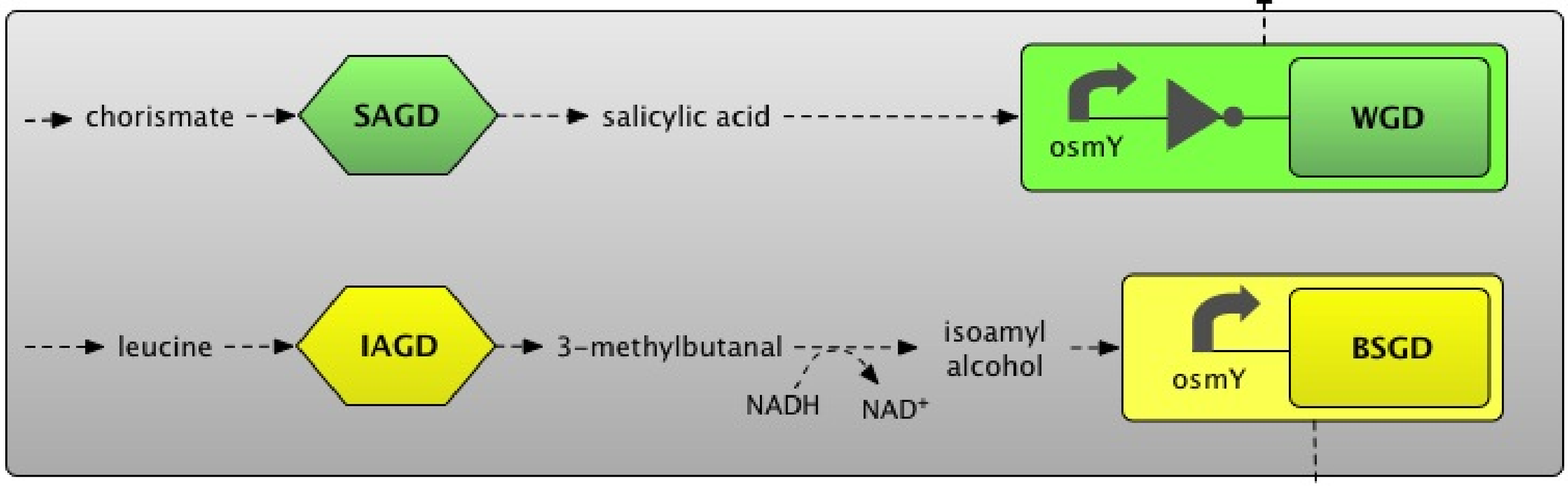
indole deficient tnaA5^{-} chassis



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Living cells make cells (& other things)

We don’t fully understand any cell.

SYNTHETIC BIOLOGY

Design and synthesis of a minimal bacterial genome

Clyde A. Hutchison III,[1*†] Ray-Yuan Chuang,[1†‡] Vladimir N. Noskov,[1] Nacyra Assad-Garcia,[1] Thomas J. Deerinck,[2] Mark H. Ellisman,[2] John Gill,[3] Krishna Kannan,[3] Bogumil J. Karas,[1] Li Ma,[1] James F. Pelletier,[4§] Zhi-Qing Qi,[3] R. Alexander Richter,[1] Elizabeth A. Strychalski,[4] Lijie Sun,[1||] Yo Suzuki,[1] Billyana Tsvetanova,[3] Kim S. Wise,[1] Hamilton O. Smith,[1,3] John I. Glass,[1] Chuck Merryman,[1] Daniel G. Gibson,[1,3] J. Craig Venter[1,3*]

We used whole-genome design and complete chemical synthesis to minimize the 1079–kilobase pair synthetic genome of *Mycoplasma mycoides* JCVI-syn1.0. An initial design, based on collective knowledge of molecular biology combined with limited transposon mutagenesis data, failed to produce a viable cell. Improved transposon mutagenesis methods revealed a class of quasi-essential genes that are needed for robust growth, explaining the failure of our initial design. Three cycles of design, synthesis, and testing, with retention of quasi-essential genes, produced JCVI-syn3.0 (531 kilobase pairs, 473 genes), which has a genome smaller than that of any autonomously replicating cell found in nature. JCVI-syn3.0 retains almost all genes involved in the synthesis and processing of macromolecules. Unexpectedly, it also contains 149 genes with unknown biological functions. JCVI-syn3.0 is a versatile platform for investigating the core functions of life and for exploring whole-genome design.

EMBARGOED UNTIL 2PM U.S. EASTERN TIME ON THE THURSDAY BEFORE THIS DATE:

Minimal Cells—Real and Imagined

John I. Glass, Chuck Merryman, Kim S. Wise, Clyde A. Hutchison III, and Hamilton O. Smith

Synthetic Biology and Bioenergy Group, J. Craig Venter Institute, La Jolla, California 92037

Correspondence: jglass@jcvi.org

EPILOGUE

Recently, Bruce Alberts, former president of the United States National Academy of Sciences, wrote about the astonishing finding that 149 genes in the JCVI-Syn3.0 minimal cell were of unknown function. "Hundreds of talented young scientists should be leaping to fill this huge gap in understanding of fundamental biological mechanisms, perhaps earning several Nobel Prizes along the way. Over the long term, such results are certain to lead to powerful new approaches for improving human health and welfare" (Alberts 2016). Having a minimal bacterial cell has been a long-standing goal of cell biologists. No longer are we limited to working with imaginary minimal cells or naturally occurring or naturally occurring organisms with small genomes as surrogates. A minimal cell has now been constructed. Clearly, there is much about its biology that biologists do not understand. First principles of cellular life are waiting to be discovered.

What don't biologists understand about biology?

Breakout #2

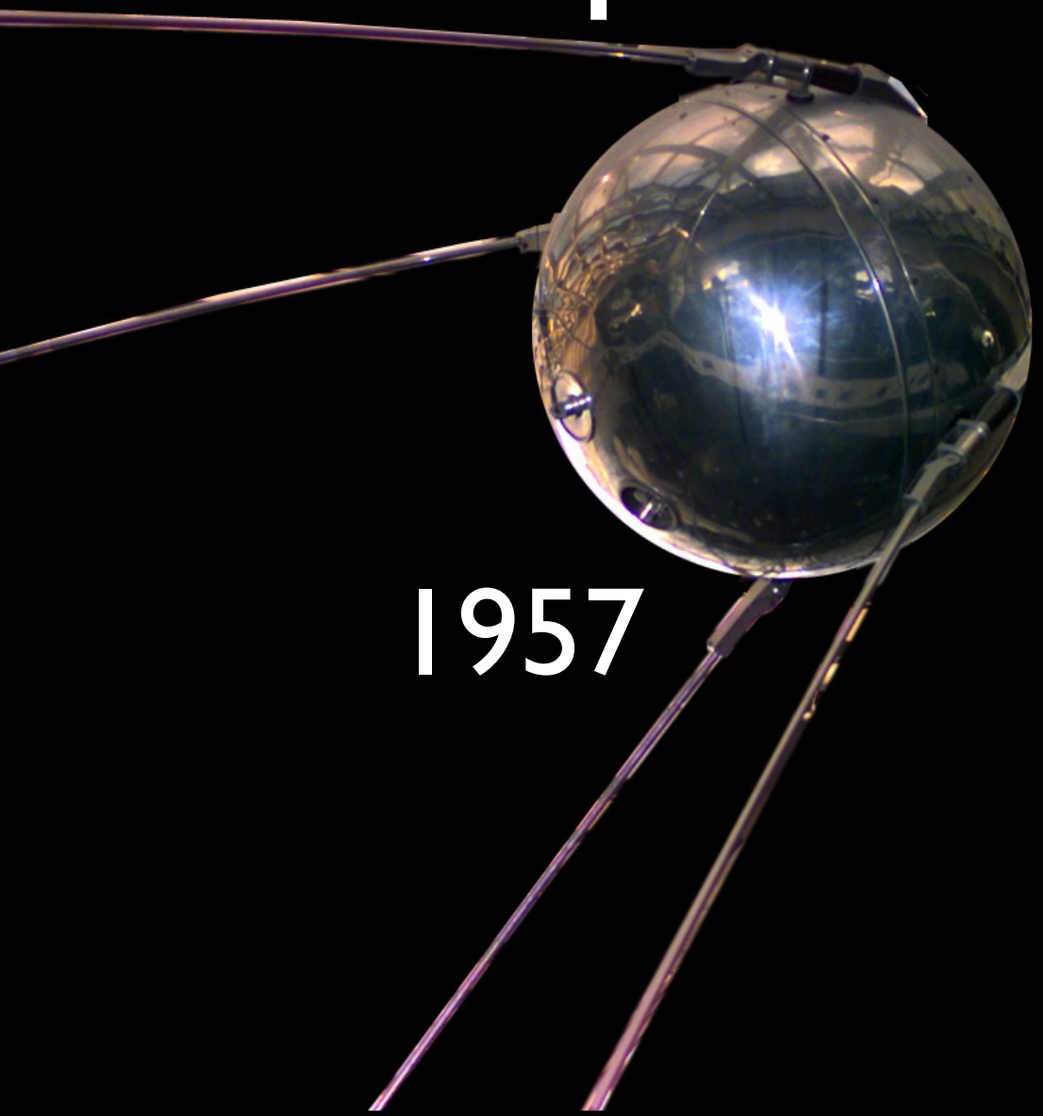
- most important opportunity?
- most important challenge?
- most frightening opportunity/challenge?
- most exciting opportunity/challenge?

What makes living matter unique?

1. Physics of living matter
2. Opportunities & challenges
3. **The here & now**

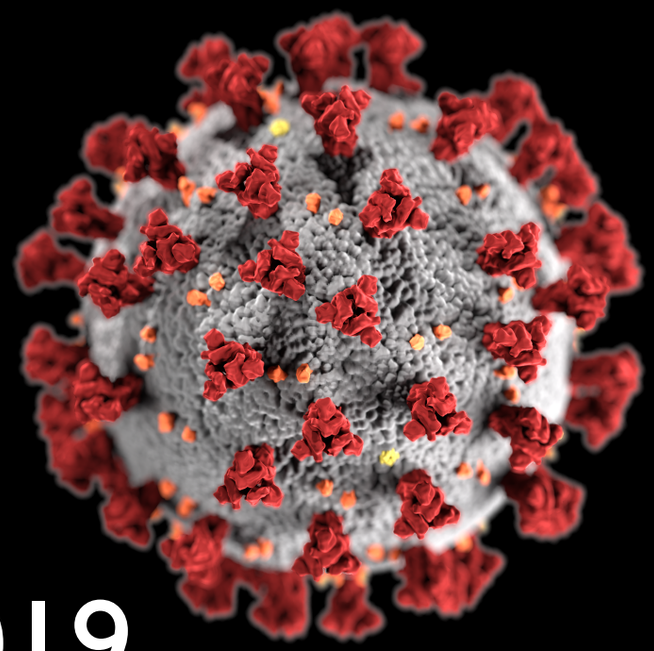
“Surprise!”

Sputnik

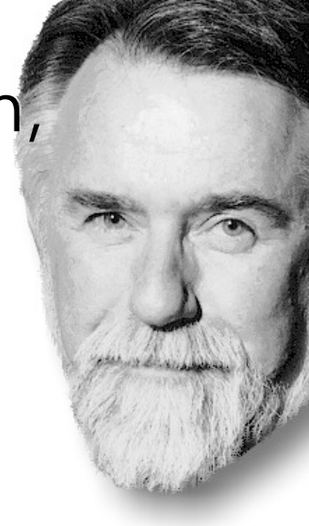


1957

COVID-19



2019



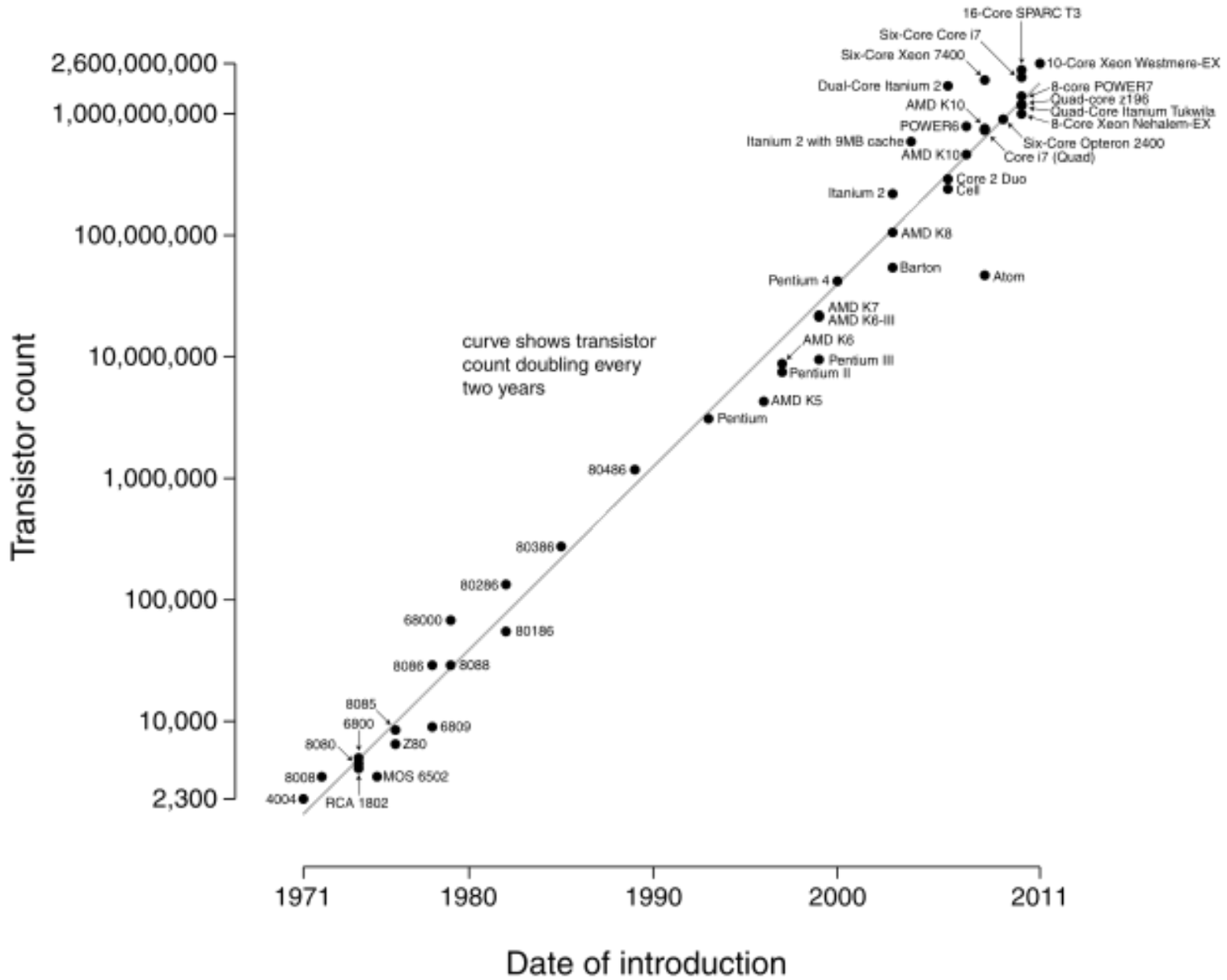
“When the group moved to California to become part of Lucasfilm, **we got close to making a computer-animated movie again in the mid-1980s** – this time about a monkey with godlike powers but a missing prefrontal cortex. We had a sponsor, a story treatment, and a marketing survey. We were prepared to 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/

Pace of change…



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

Breakout #3

- what about the “here & now” do you think will matter most for bioengineering or bioengineers for the next ten years?

Before Friday's class

Preclass for Friday

A specific skill we wish you to learn or improve is how to quickly and effectively benefit from research reports that appear routinely on the "front lines" of bioengineering. To gain or improve your research manuscript analysis skills please study the two papers listed below. NOTE — we are not asking you to read these papers. Rather, simply apply the first five points as noted below. Your two objectives are to see if you can identify the main claim in the paper (only by skimming and thinking about the title and the abstract) and then to see if you can determine *where* in the paper the evidence is presented that supports the main claim (only by skimming and thinking about what is presented in the figures or illustrations). Please practice the method outlined below before class on Friday on the two papers given here.

How to read a research paper:

(0) DO NOT SIT DOWN AND READ THE ENTIRE PAPER. STOP. DO WHAT FOLLOWS INSTEAD.

(1) Read the title. Does it make any sense? Note words you don't understand.

(2) Read the abstract. Find the single most apparent or remarkable claim.

(3) If you fail to find any main claim from the abstract don't bother reading the paper.

(4) Skim the figures, looking for evidence in support of the main claim.

(5) If you can't find clear and apparent evidence in support of the main claim stop spending time on the paper.

STOP HERE REGARDLESS AND DECIDE IF YOU HAVE MORE TIME TO SPEND ON THE PAPER