

SOFT

Sense of Future Trends

Progress is not a point but an asynchronous continuum of punctuated equilibria, perhaps an unevenly braided canvas of communities embracing change, chance, choice, and character.

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To Whom It May Concern: **SOFT** was created for students aspiring to become professional catalysts to improve, globally, the quality of life and living. The content is biased in its focus on science and the issues related to lives of 80% of the world's population with actual problems (not the fictitious idiosyncrasies of the 20% affluent world). Examples are limited by the knowledge on the part of the author. Most ideas are borrowed and presented here only as suggestions. The author neither created these examples nor has made any scientific contribution. Exercise caution in reviewing the author's proposals and predictions because the author may be best described as a successful failure in almost all professional efforts as well as in research and in his career in science. Opinions are due to the author alone and doesn't represent the views of the institutions with which the author may be affiliated.

After reading through this document will you learn anything you didn't know?

There is nothing “new” here.
It is a re-telling of facts already
known to many, in some form.

Mathematics, science and
engineering is catalytic to the
progress of human civilization.

You knew that, already. Didn't you?

This is my version of the same old story.

If I have wasted your time, I'm sorry. I apologize.

Think “SOFT” as
a heap of data ...

CREATE YOUR
OWN STORY ...

DATA



SORTED



ARRANGED



PRESENTED
VISUALLY



EXPLAINED
WITH A STORY



Future → Forward

FEWSH

Food Energy Water Sanitation Healthcare



F	Food
E	Energy
W	Water
S	Sanitation
H	Healthcare

Your contribution to society matters.

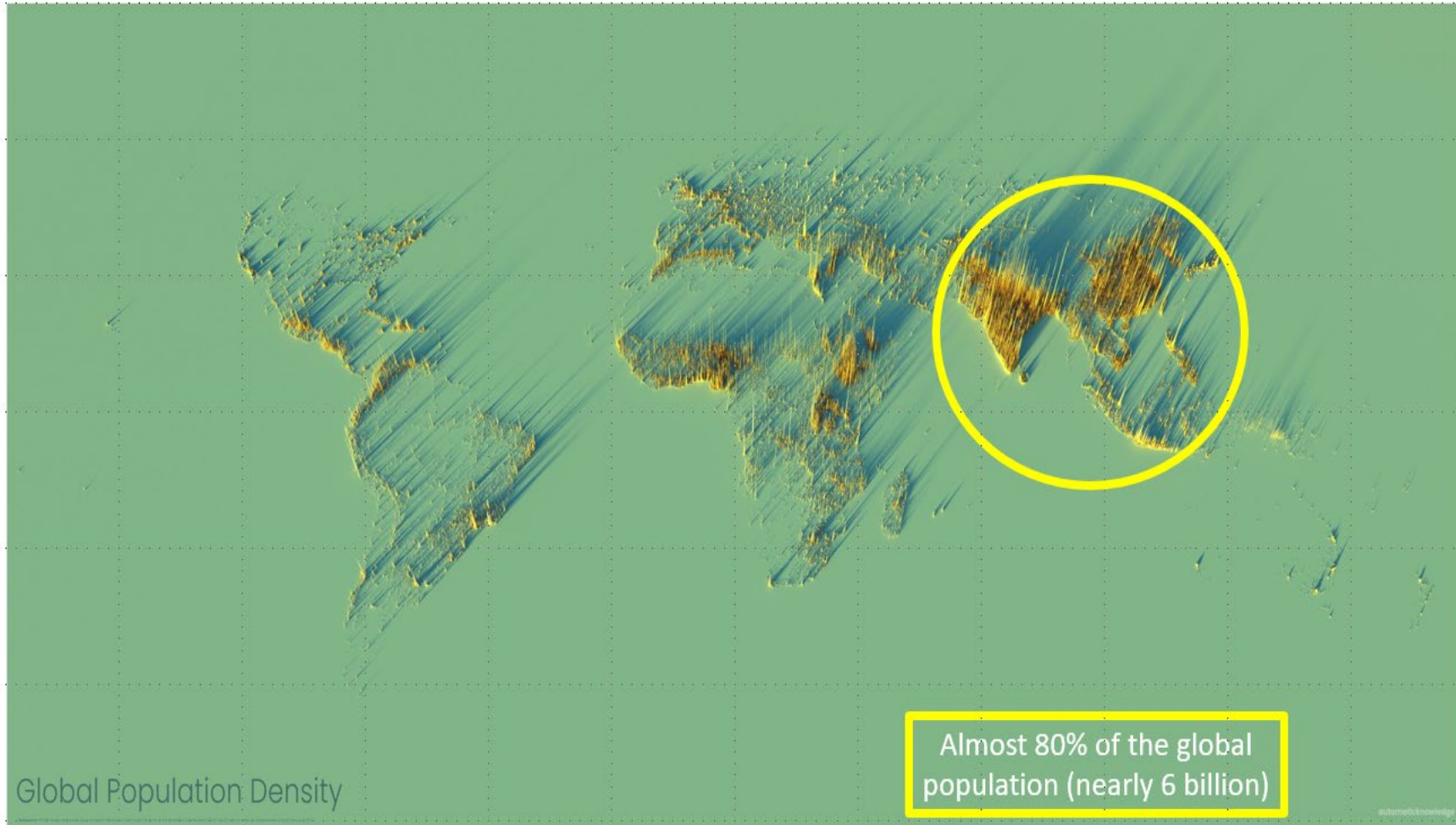
Science and Scientists for Society

Why the emphasis on FEWSH

We are neither discounting nor discarding space stations, deep sea explorations, asteroid mining, autonomous transportation or other engineering marvels from the affluent world.

Focus on FEWSH offers a life-line to 80% of the less-affluent global population. Asia and Africa will continue to contribute to the global population (may exceed 10 billion by 2100).

I am, however, advocating that we discard and disregard fake artificial intelligence (AI) which has viciously infected almost everything, the stupid hype associated with “smart cities” and technical tools that increase the carbon footprint (egg-minders sending SMS to mobile apps).



Key threads this discussion includes

INFORMATION and CONNECTIVITY

Attempt to review, learn, compare, criticize and evaluate science through the lens of

Information

The Information Age is all around us. It started with the Big Bang, created the Solar System and it may persist *ad infinitum* as long as the Solar System continues its physical existence. Information is the fundamental fabric of intellectual connectivity. Our understanding of the difference between hydrogen and oxygen is based on information. The difference between bauxite and the material of the Coke can is information. Information is the differentiator between Apple Newton PDA which died prematurely vs the almost identical Palm Pilot that climbed the summit of popularity. Information changes when the car you are driving is suddenly crushed in a collision. Think about the approximately 500 inhabitants of Mureybet, Syria in 8000BC and compare their information content to the approximately 1500 modern day inhabitants of Dingle village in County Kerry (Ireland) which boasts of at least 50 pubs in this miniscule hamlet near the Atlantic. Described by Claude Shannon in 1948 as informational entropy, it has been shown that the interpretation of entropy (formula) provided by Ludwig Boltzmann (the Boltzmann equation) becomes the Shannon equation, thus mathematically linking entropy and information.

Attempt to review, learn, compare, criticize and evaluate science/engineering in terms of

Connectivity

Connectivity is fundamentally pervasive between almost every entity – physical, metaphysical and cyberphysical. Connectivity transcends the sub-nano realm and the super-macro domain. Doesn't it define the astronomical universe, all biological systems and everything conceptual in between? The mobility of ancient civilizations to explore new worlds were physical connections between atoms. The bargain hunter's app to compare prices between various retailers is the new sense of value which connects bits with atoms. All things and processes are about connectivity. Invention and innovation was, is and will be about connecting the dots, real and/or virtual, perceived and/or imagined. Human thought, technological progress and the future of synaptic relationships are likely to be manifestations of connectivity, convergence and confluence of concepts. The sense of connectivity is germane to life. Its ubiquity makes us oblivious to its quintessential nature. To evoke the central theme of connectivity, therefore, is not an insight but rather recognizing the fabric of the future (SOFT) hiding in plain sight. Connect the dots!

What this discussion excludes

THE BS AND NONSENSE ABOUT FAKE AI (ARTIFICIAL INTELLIGENCE) CLAIMS

<https://bit.ly/BS-about-AI>

<https://bit.ly/BS-about-AI>

Articles in support of the fact that the propaganda about artificial intelligence (fake AI) may be a scientific absurdity.

Datta, Shoumen Palit Austin (2016) Intelligence in Artificial Intelligence • <https://arxiv.org/ftp/arxiv/papers/1610/1610.07862.pdf>

Datta, Shoumen Palit Austin, Tausifa Jan Saleem, Molood Barati, María Victoria López López, Marie-Laure Furgala, Diana C. Vanegas, Gérald Santucci, Pramod P. Khargonekar and Eric S. McLamore (2021) *Data, Analytics and Interoperability between Systems (IoT) is Incongruous with the Economics of Technology: Evolution of Porous Pareto Partition (P3)*. Chapter 2 in “*Big Data Analytics for Internet of Things*” 1st ed. Editors Tausifa Jan Saleem and Mohammad Ahsan Chishti. Publisher: Wiley Inc., 2021.

Book - Wiley Online Library <https://onlinelibrary.wiley.com/doi/book/10.1002/9781119740780>

Book Chapter 2 – Wiley Online Library <https://onlinelibrary.wiley.com/doi/abs/10.1002/9781119740780.ch2>

Book Chapter 2 – free from MIT Library – PDF copy of “P3” in the MIT Library <https://dspace.mit.edu/handle/1721.1/123984>

Published: 2 April 2021 ▪ Print ISBN: [9781119740759](https://doi.org/10.1002/9781119740759) ▪ Online ISBN: [9781119740780](https://doi.org/10.1002/9781119740780) ▪ DOI: [10.1002/9781119740780](https://doi.org/10.1002/9781119740780)

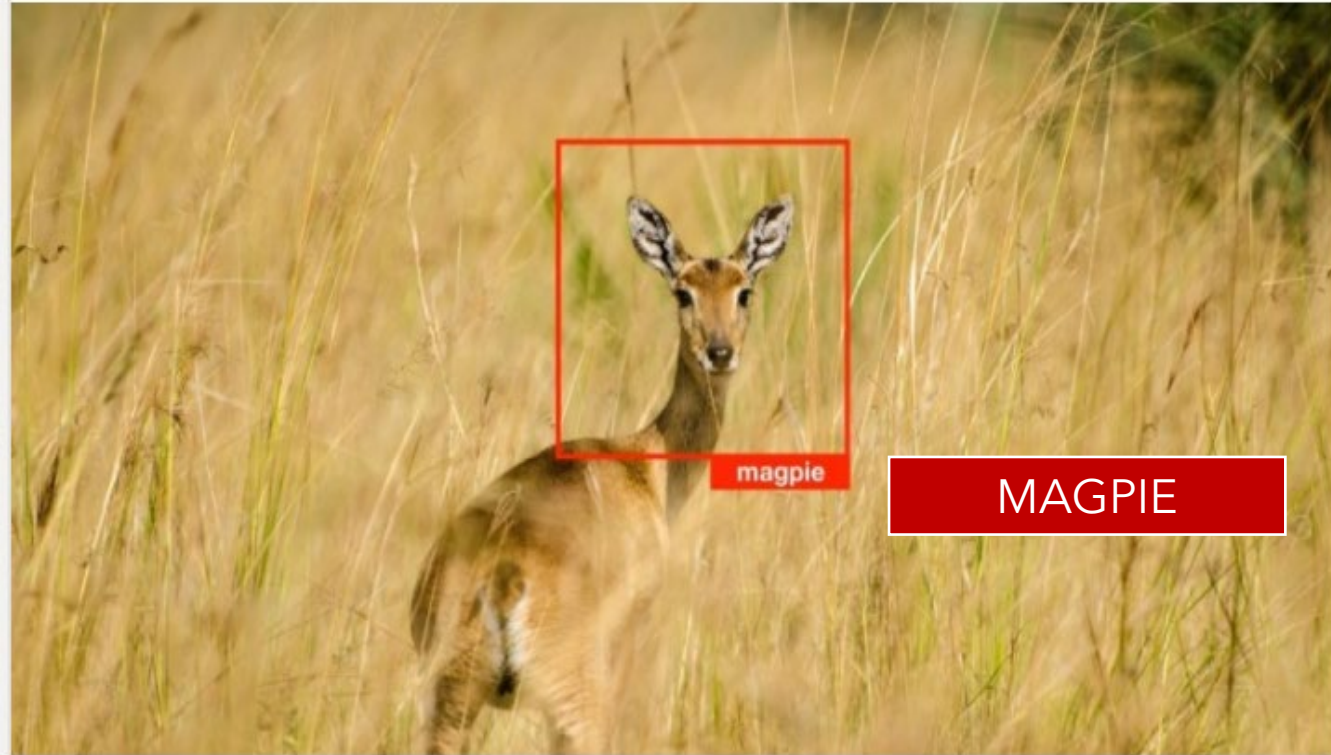


MIT Technology Review

933,582 followers

1w •

The 10 most cited AI data sets are riddled with errors.



AI datasets are filled with errors. It's warping what we know about AI

<https://bit.ly/BS-about-AI>



nytimes.com/2021/07/16/technology/what-happened-ibm-watson.html

The New York Times

What Ever Happened to IBM's Watson?

IBM's artificial intelligence was supposed to transform industries and generate riches for the company. Neither has panned out. Now, IBM has settled on a humbler vision for Watson.

SALESMAN SPOTTING



AI

CHARLATAN

<https://bit.ly/BS-about-AI>

SNAKE OIL SALES

technologyreview.com/2021/07/30/1030329/machine-learning-ai-failed-covid-hospital-diagnosis-pandemic/

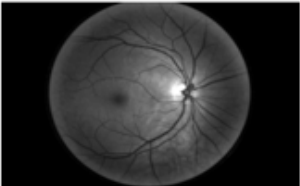
MIT Technology Review

Artificial intelligence / Machine learning

Hundreds of AI tools have been built to catch covid. None of them helped.

MIT Technology Review

Related Story



Google's medical AI was super accurate in a lab. Real life was a different story.

If AI is really going to make a difference to patients we need to know how it works when real humans get their hands on it, in real situations.

It never happened—but not for lack of effort. Research teams around the world stepped up to help. The AI community, in particular, rushed to develop software that many believed would allow hospitals to diagnose or triage patients faster, bringing much-needed support to the front lines—in theory.

In the end, many hundreds of predictive tools were developed. None of them made a real difference, and some were potentially harmful.

That's the damning conclusion of multiple studies published in the last few months. In June, the Turing Institute, the UK's national center for data science and

AI, put out a report summing up discussions at a series of workshops it held in late 2020. The clear consensus was that AI tools had made little, if any, impact in the fight against covid.

Not fit for clinical use <https://bit.ly/BS-about-AI>

A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models

Evangelia Christodoulou ^a, Jie Ma ^b, Gary S. Collins ^{b, c}, Ewout W. Steyerberg ^d, Jan Y. Verbakel ^{a, e, f}, Ben Van Calster ^{a, d}  

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[https://www.jclinepi.com/article/S0895-4356\(18\)31081-3/fulltext](https://www.jclinepi.com/article/S0895-4356(18)31081-3/fulltext)

Accepted 5 February 2019, Available online 11 February 2019.

Real emphasis is on

MATH

SCIENCE

ENGINEERING

FEWSH

is the outcome from

MATH

SCIENCE

ENGINEERING

Female teachers' math anxiety affects girls' math achievement

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Edited* by Edward E. Smith, Columbia University, New York, NY, and approved December 17, 2009 (received for review September 23, 2009)

People's fear and anxiety about doing math—over and above actual math ability—can be an impediment to their math achievement. We show that when the math-anxious individuals are female elementary school teachers, their math anxiety carries negative consequences for the math achievement of their female students. Early elementary school teachers in the United States are almost exclusively female (>90%), and we provide evidence that these female teachers' anxieties relate to girls' math achievement via girls' beliefs about who is good at math. First- and second-grade female teachers completed measures of math anxiety. The math achievement of the students in these teachers' classrooms was also assessed. There was no relation between a teacher's math anxiety and her students' math achievement at the beginning of the school year. By the school year's end, however, the more anxious teachers were about math, the more likely girls (but not boys) were to endorse the commonly held stereotype that "boys are good at math, and girls are good at reading" and the lower these girls' math achievement. Indeed, by the end of the school year, girls who endorsed this stereotype had significantly worse math achievement than girls who did not and than boys overall. In early elementary school, where the teachers are almost all female, teachers' math anxiety carries consequences for girls' math achievement by influencing girls' beliefs about who is good at math.

education | mathematics | gender | stereotype | modeling

*This US-centric view
may be applicable to
the "Western" world.
Is it applicable to
female math teachers
in Asia and Africa?*

If you
wish to
choose
only
one ...

Future of FEWSH

Science begins with

MATHEMATICS

If you excel in mathematics

you can do almost anything

However, no matter how good or promising something may seem, nothing by itself is a panacea. Solutions for life are not points but fabrics of convergence which may change or evolve.

But, ...

Mathematics improves your analytical thinking which is central to almost everything in the professional arena where skills are essential.

Mathematics is the salt of science and engineering.

But, knowledge without compassion is inhuman.

Compassion without knowledge is ineffective.

Taken together ...

Mathematics improves analytical thinking which is central to almost everything in the professional arena. Mathematics *is* the salt of the earth. But, knowledge without compassion is inhuman. Compassion without knowledge is ineffective. Intellectual balance for social good is a convergence of the analytical mind with magnanimity. Arts, humanities, and philosophy enriches our humanity. Languages, linguistics and music are the heart and soul of communication. Understanding economics helps.

It is a widely held belief that science and the fruits from science (engineering, technology) may catalyze new developments to lift the lives of billions of people and provide solutions for remediable injustices in an ethical, egalitarian, civil society.

Hence, one purpose of this talk/presentation is to discuss science.

I will present a few examples of potential scientific strides in each of these FIVE categories (FEWSH), which are not in silos but inextricably linked in our daily lives, agnostic of where we live.

These examples are selected from millions of potential clues from ongoing research and development, globally. What I/we know is insignificant. The unknown unknowns are so immense that I do not even know how to begin to describe the things which may be possible in the future. The latter excludes ideas that may appear impossible, at this time. If we know about an idea then it is no longer in the realm of unknown unknowns.

It is your mission to take your imagination to a plane where you can begin to think about development in terms of thoughts none has thought before, inventions that we have not imagined, yet.

F

Food

E

Energy

W

Water

S

Sanitation

H

Healthcare

Science and Scientists for Society

Before suggesting how to build your foundation to deal with the challenges of FEWSH

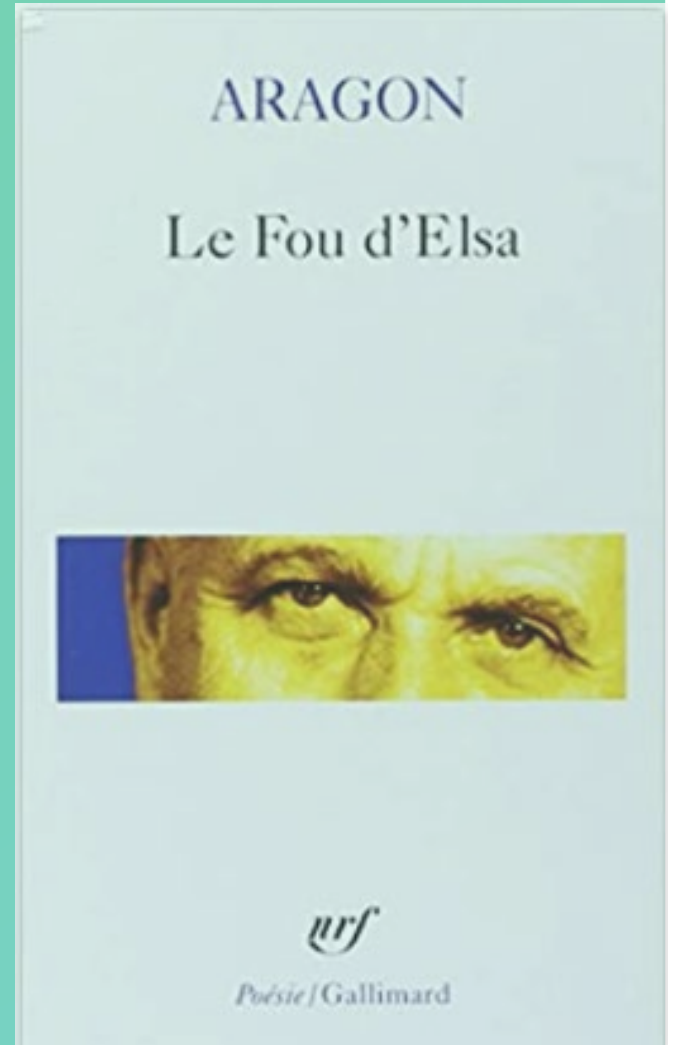
Let me remind you that women are the foundation of any civil society.

You ought to know about the
foundation of global society.

Underpinning for global economic growth and development:

La femme est l'avenir de l'homme

woman is the future of man



Discussion

Number 0

Mathematics begins with zero

The education of a boy may change the
fate of a man. The education of a girl
may change the destiny of a nation.

It matters.

WIDE

Women In Decision Economy

In the 1960's the Rockefeller Foundation funded a meal program for school children in southern India. Poor families began sending not only "boys" but also the girls to school. The girls became educated women and created educated families, educated boys and an educated society. But, poverty was not discouraged by this march of reason and educational resources still consisted of paper and pencil. Mathematics had no problem with just paper and pencil. The children were fed on a diet of mathematics. Half a century later the trinity of food, poverty and mathematics evolved as a force of consilience. Their synergistic convergence resulted in making parts of southern India (Tamilnadu, Kerala) the software capital of the 21st century world. The literacy rate in the state of Kerala (92%) is higher than in Massachusetts (90%).



MATHEMATICS for MOTHERS

MATH-HERS

Pronounced “MATTERS”

Why it matters? <https://bit.ly/MATH-HERS>

Discussion: Snippets of Examples

Number 1



F

Food

Your contribution to society matters.

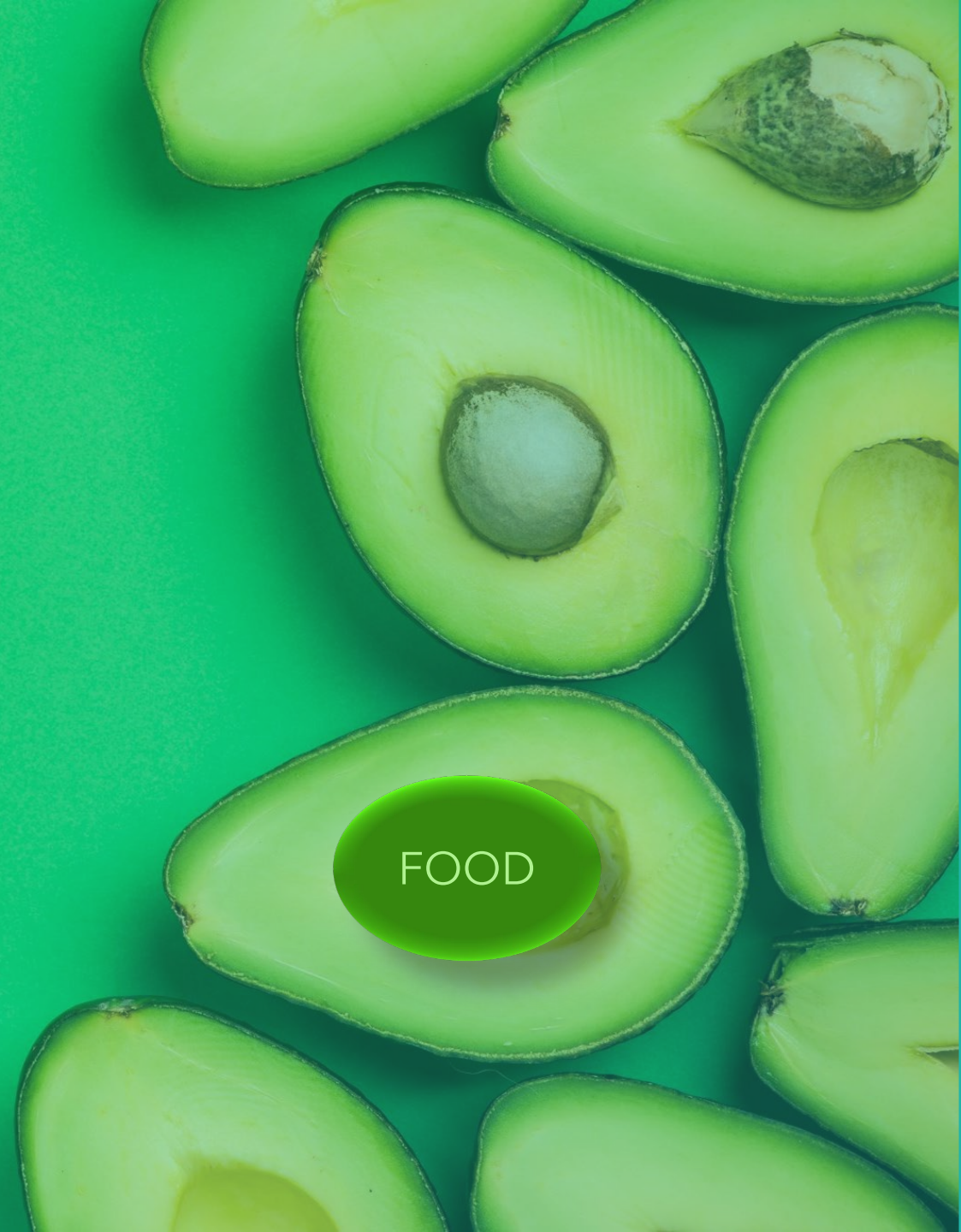
Science and Scientists for Society

WISE

Women in Science & Engineering

Each year \$285 billion worth of food is thrown away in the US. Food produced with scarce resources (water, slaughtered animals, soil). 54 million tons of food won't be on the plates of people who go hungry every day. 54 million tons of food trashed in the US, each year.

<http://eosfoundation.org/combating-hunger>



a vulture waiting for a starving boy to die to eat him. Taken by Kevin Carter who later committed suicide. Sudan, 1993.



<http://100photos.time.com/photos/kevin-carter-starving-child-vulture>

<http://content.time.com/time/magazine/article/0,9171,165071,00.html>

<https://www.nytimes.com/1994/07/29/world/kevin-carter-a-pulitzer-winner-for-sudan-photo-is-dead-at-33.html>

US centric discussion: cost of food ...

Report

<https://www.rockefellerfoundation.org/wp-content/uploads/2021/07/True-Cost-of-Food-Full-Report-Final.pdf>

Explore

www.rockefellerfoundation.org/report/true-cost-of-food-measuring-what-matters-to-transform-the-u-s-food-system/

A \$1 dollar plate of bean stew costs the equivalent of \$320 in South Sudan



The real price of a plate of bean stew is \$321.7 in South Sudan. The result is hunger. Image: REUTERS/Andreea Campeanu

<https://www.weforum.org/agenda/2017/10/a-plate-of-bean-stew-costs-320-in-this-country/>

10 PrEP is in the MIT Library <https://dspace.mit.edu/handle/1721.1/123984>. Opinions are solely due to the author and does not represent the views of any institution.

2017

Food ■

- Reduce Waste

- Increase Production?



Food ■ Depends on Population

- Reduce Waste
- Increase Production?

The Lancet, British medical journal established in 1823.

ARTICLES | [VOLUME 396, ISSUE 10258, P1285-1306, OCTOBER 17, 2020](#)

Fertility, mortality, migration, and population scenarios for 195 countries and territories from 2017 to 2100: a forecasting analysis for the Global Burden of Disease Study

[Prof Stein Emil Vollset, DrPH](#) • [Emily Goren, PhD](#) • [Chun-Wei Yuan, PhD](#) • [Jackie Cao, MS](#) • [Amanda E Smith, MPA](#) • [Thomas Hsiao, BS](#) • [Catherine Bisignano, MPH](#) • [Gulrez S Azhar, PhD](#) • [Emma Castro, MS](#) • [Julian Chalek, BS](#) • [Andrew J Dolgert, PhD](#) • [Tahvi Frank, MPH](#) • [Kai Fukutaki, BA](#) • [Prof Simon I Hay, FMedSci](#) • [Prof Rafael Lozano, MD](#) • [Prof Ali H Mokdad, PhD](#) • [Vishnu Nandakumar, MS](#) • [Maxwell Pierce, BS](#) • [Martin Pletcher, BS](#) • [Toshana Robalik, BSc](#) • [Krista M Steuben, MS](#) • [Han Yong Wunrow, BSc](#) • [Bianca S Zlavog, BS](#) • [Prof Christopher J L Murray, DPhil](#)  

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[Open Access](#) • Published: July 14, 2020 • DOI: [https://doi.org/10.1016/S0140-6736\(20\)30677-2](https://doi.org/10.1016/S0140-6736(20)30677-2)

JUNE 17, 2019

World's population is projected to nearly stop growing by the end of the century

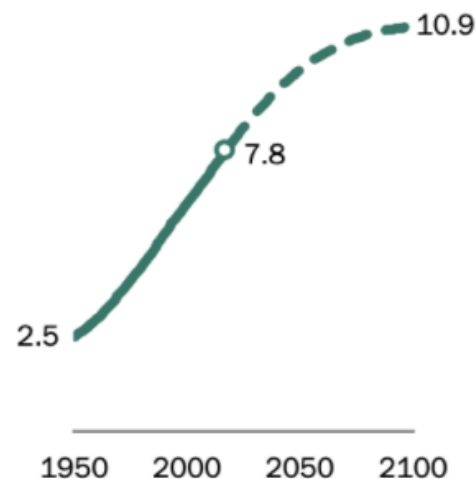
BY ANTHONY CILLUFFO AND NEIL G. RUIZ

For the first time in modern history, the world's population is expected to virtually stop growing by the end of this century, due in large part to falling global fertility rates, according to a Pew Research Center analysis of [new data from the United Nations](#).

By 2100, the world's population is projected to reach approximately 10.9 billion, with annual growth of less than 0.1% – a steep decline from the current rate. Between 1950 and today, the world's population grew between 1% and 2% each year, with the number of people rising from 2.5 billion to more than 7.7 billion.

World population growth is projected to flatten in coming decades

World population, in billions

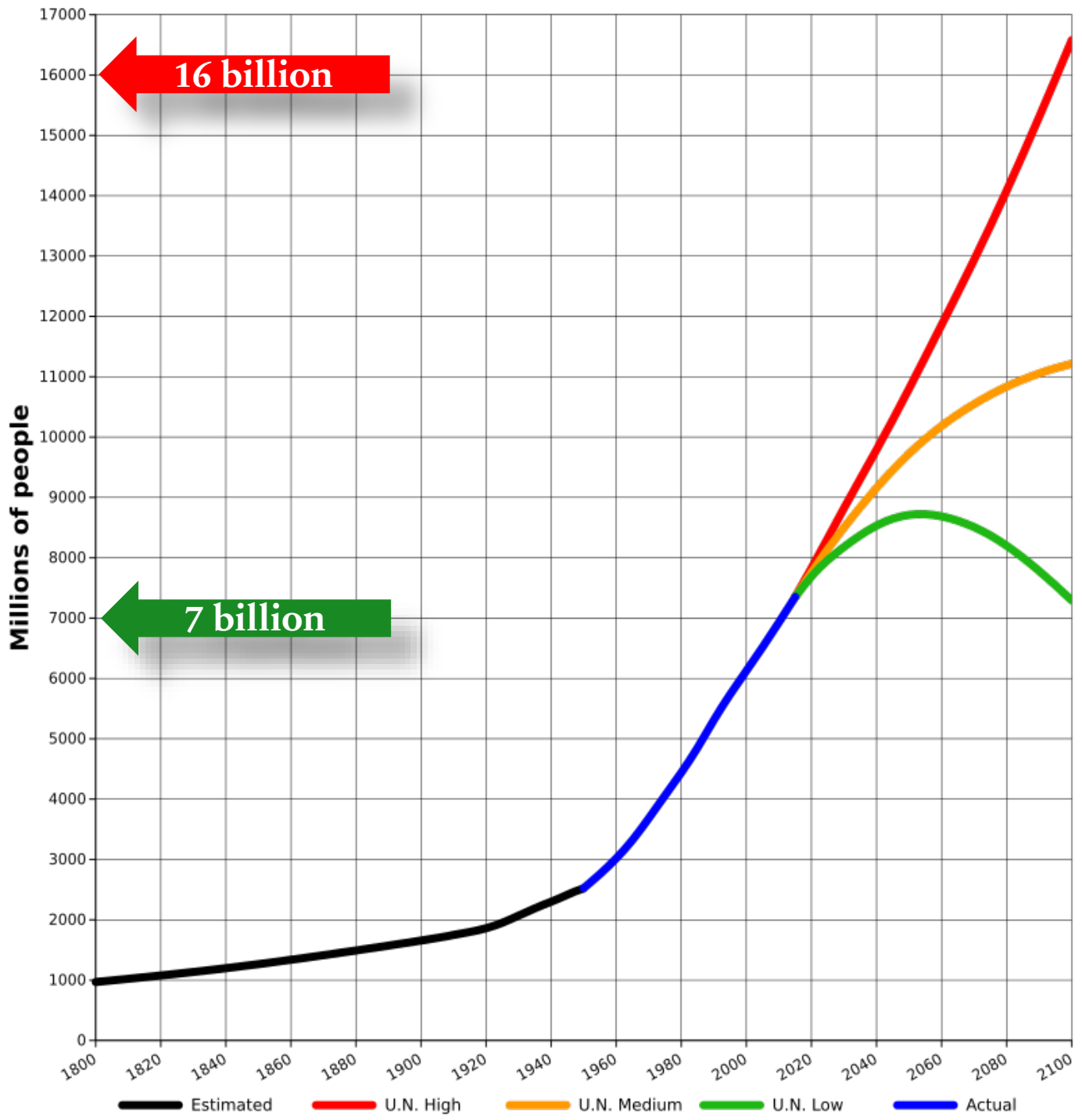


Population

🕒 This article is more than **11 months old**

World population in 2100 could be 2 billion below UN forecasts, study suggests

Changes in population structure due to improving equality and ageing societies will pose policy dilemmas



By 2100, the world population may rise to 16 billion or decline to 7 billion or as low as 6 billion.

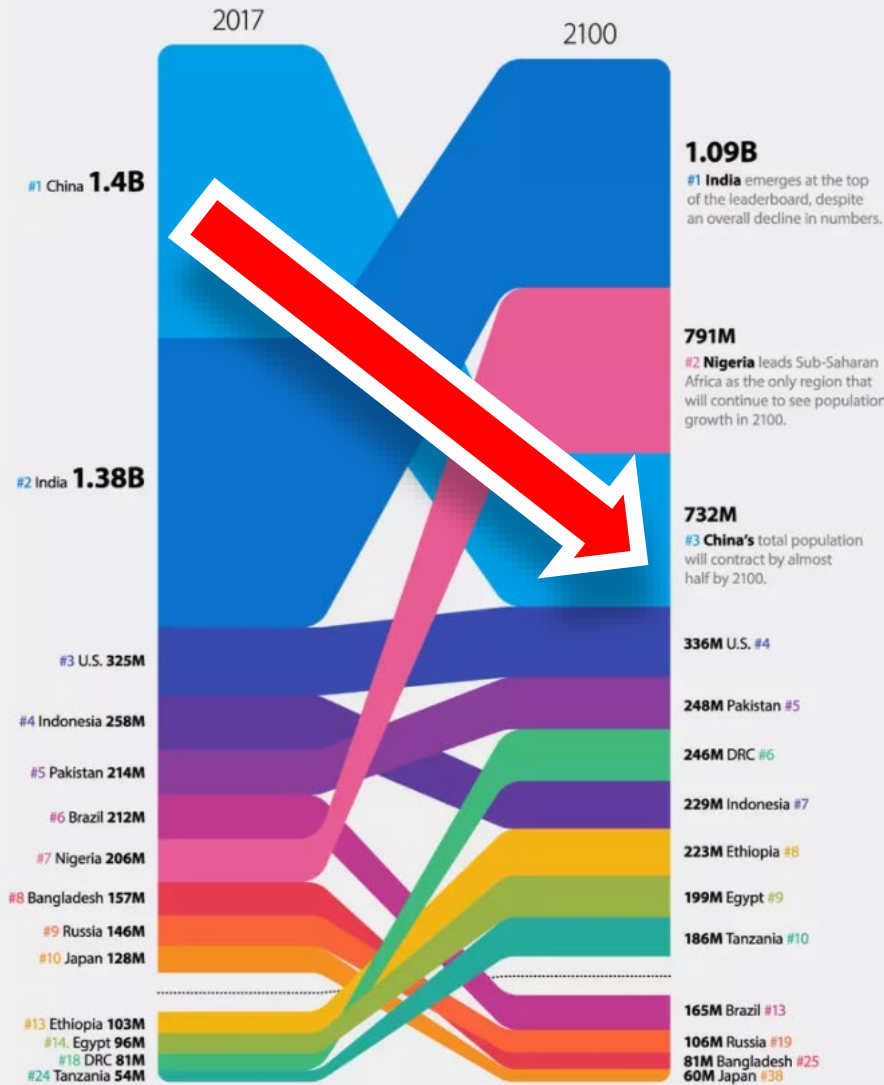
Food ■ feed 16 billion or 6 billion people ?

- Reduce Waste
- Increase Production?

FOOD



Top 10 Countries by Population



Number 1 in 2100
India ~1 billion

Various demographic factors, from lower fertility rates to higher life expectancies, are key reasons behind these differing estimates.

Food ■ SCIENCE

- Reduce Waste

- Packaging?

> [Toxicol Res \(Camb\)](#). 2020 Dec 3;9(6):808-822. doi: [10.1093/toxres/tfaa082](#). eCollection 2020 Dec.

FULL TEXT LINKS



Physical, chemical, and toxicological characterization of sulfated cellulose nanocrystals for food-related applications using *in vivo* and *in vitro* strategies

James D Ede ¹, Kimberly J Ong ¹, Marina R Mullen ², Sahar Pradhan ², Matthew Gibb ³,
Christie M Sayes ², Jo Anne Shatkin ¹

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- 3 Department of Environmental Science, Baylor University, One Bear Place #97266, Waco, TX 76798-7266, USA.

PMID: 33447365 PMCID: PMC7786165 (available on 2021-12-03) DOI: [10.1093/toxres/tfaa082](#)

Abstract

Cellulose nanocrystals (CNCs) are a next-generation cellulose product with many unique properties

Reduce food waste:
nano-material
science may
improve food
quality and
packaging

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Cellulose nanocrystals (CNCs) are a next-generation cellulose product with many unique properties

What do you need to know if you want to understand and evaluate this research paper?

What is cellulose?

What is a nano-crystal?

What is an *in vivo* assay?

What is an *in vitro* assay?

What is toxicology?

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To answer these questions you will need the foundation of knowledge provided by

MATHEMATICS
SCIENCE
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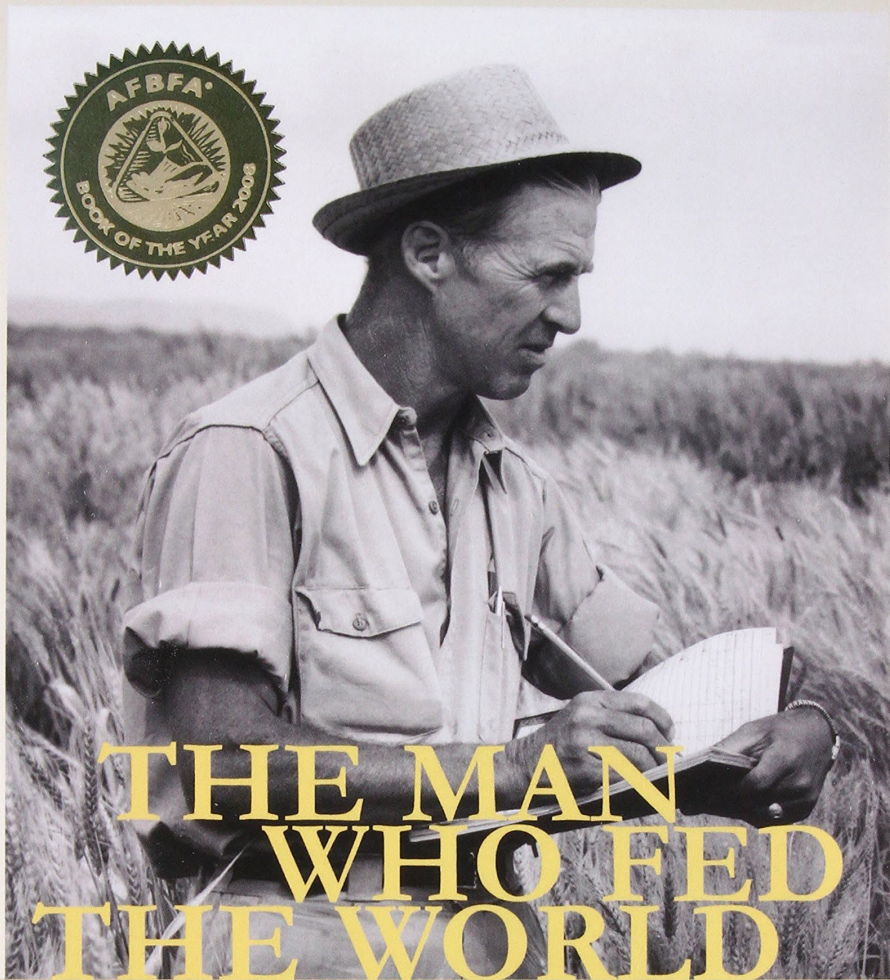
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**MATHEMATICS
SCIENCE
and
ENGINEERING**

Food ■ feed 16 billion or 6 billion people ?

- Increase Production?
 - Process
 - Soil, fertilizer, water, energy
 - Herbicides, pesticides
 - Seeds
 - Yield
 - Genetics



THE MAN WHO FED THE WORLD

Nobel Peace Prize Laureate Norman Borlaug
And His Battle to End World Hunger

An authorized biography by **Leon Hesser**

Foreword by **Jimmy Carter**

Dr. Norman Borlaug is credited with saving over a billion people from starvation. He was awarded the Nobel Peace Prize, the Presidential Medal of Freedom and the US Congressional Gold Medal.

Dr. Borlaug received the **Padma Vibhushan**, the highest civilian award the government of India can present to a non-citizen.

The immense complexity

Tomato

REVIEW

Noncoding RNAs: functional regulatory factors in tomato fruit ripening

Lili Ma^{1,2} · Jianlou Mu² · Donald Grierson³ · Yunxiang Wang⁴ · Lipu Gao¹ · Xiaoyan Zhao¹ · Benzhong Zhu⁵ · Yunbo Luo⁵ · Kai Shi⁶ · Qing Wang¹ · Jinhua Zuo¹

Received: 10 October 2019 / Accepted: 12 March 2020 / Published online: 24 March 2020

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Abstract

Tomato has emerged as the model system for investigations into the regulation of fleshy-fruit ripening and senescence, and the ripening process involving the coordinated regulation at the gene/chromatin/epigenetic, transcriptional, post-transcriptional and protein levels. Noncoding RNAs play important roles in fruit ripening as important transcriptional and post-transcriptional regulatory factors. In this review, we systematically summarize the recent advances in the regulation of tomato fruit ripening involved in ethylene biosynthesis and signal transduction, fruit pigment accumulation, fruit flavor and aroma, fruit texture by noncoding RNAs and their coordinate regulatory network model were set up and also suggest future directions for the functional regulations of noncoding RNAs on tomato fruit ripening.

Just
1
paper

Table 1 The ncRNAs related to ethylene pathway in tomato fruit

ncRNA	Target gene	Target description	Related pathway	References
miR159	Solyc08g081550.2.1	<i>1-Aminocyclopropane-1-carboxylate synthase (ACS)</i>	Ethylene pathway	Karlova et al. (2013)
miR171	Solyc12g011330.2.1	<i>Ethylene receptor (ETR)</i>	Ethylene pathway	Karlova et al. (2013)
miR172a	Solyc05g009450.1	<i>Ethylene-responsive transcription factor 118 (ERF118)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR1916	Solyc12g056430.1.1	<i>Ethylene-responsive transcription factor 10 (ERF10)</i>	Ethylene pathway	Karlova et al. (2013)
miR1917	Solyc03g096050.2.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 1(ACO1)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR1918	Solyc05g051180.1.1	<i>Ethylene-responsive transcription factor 2 (ERF2)</i>	Ethylene pathway	Karlova et al. (2013)
miR1919	Solyc05g052410.1.1	<i>Ethylene-responsive transcription factor 1 (ERF1)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR390	Solyc04g082510.2.1	<i>Serine/threonine protein kinase CONSTITUTIVE TRIPLE RESPONSE (CTR1)</i>	Ethylene pathway	Karlova et al. (2013)
miR394	Solyc08g081540.2.1	<i>1-Aminocyclopropane-1-carboxylate synthase (ACS)</i>	Ethylene pathway	Karlova et al. (2013)
miR395	Solyc12g038920.1.1	<i>Serine/threonine protein kinase (CTR1)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR396b	Solyc12g005940.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 2 (ACO2)</i>	Ethylene pathway	Karlova et al. (2013)
miR397	Solyc06g073580.2.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 1(ACO1)</i>	Ethylene pathway	Karlova et al. (2013)
mir398	Solyc04g050750.1.1	<i>Ethylene-responsive transcription factor 1 (ERF1)</i>	Ethylene pathway	Karlova et al. (2013)
miR403	Solyc02g031860.2.1	<i>Serine/threonine protein kinase (CTR1)</i>	Ethylene pathway	Karlova et al. (2013)
miR4376	Solyc03g117790.1.1	<i>Serine/threonine protein kinase (CTR1)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR472	Solyc12g009240.1.1	<i>Ethylene-responsive transcription factor 4 (ERF 4)</i>	Ethylene pathway	Karlova et al. (2013)
miR482e-3p	Solyc03g043890.2	<i>1-Aminocyclopropane-1-carboxylate synthase (ACS)</i>	Ethylene pathway	Karlova et al. (2013)

miR5301	Solyc08g066410.1.1	<i>Serine/threonine protein kinase (CTR1)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR5302	Solyc04g080910.1.1	<i>Ethylene-responsive transcription factor 13 (ERF13)</i>	Ethylene pathway	Karlova et al. (2013)
miR5303	Solyc09g066360.1.1	<i>Ethylene-responsive transcription factor 2 (ERF2)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR6022	Solyc06g068590.2.1	<i>Serine/threonine protein kinase (CTR1)</i>	Ethylene pathway	Karlova et al. (2013)
miR6023	Solyc03g118190.2	<i>Ethylene-responsive transcription factor 114 (ERF114)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR858	Solyc11g065590.1.1	<i>Ethylene receptor (ETR)</i>	Ethylene pathway	Wang et al. (2017a, b)
miR894	Solyc02g071470.2.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 1 (ACO1)</i>	Ethylene pathway	Karlova et al. (2013)
miR9470-3p	Solyc11g042580.1	<i>Ethylene-responsive transcription factor 021 (ERF021)</i>	Ethylene pathway	Karlova et al. (2013)
lncRNAZ018	Solyc01g095080.2	<i>1-Aminocyclopropane-1-carboxylate synthase 2 (ACS2)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ037	Solyc01g067540.1	<i>Ethylene-responsive transcription factor 086 (ERF086)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ113	Solyc12g005940.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 2 (ACO2)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ118	Solyc12g005940.1	<i>1-Aminocyclopropane-1-carboxylate oxidase 2 (ACO2)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ306	Solyc06g065820.2	<i>Ethylene response factor 1 (ERF1)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ307	Solyc06g065820.2	<i>Ethylene response factor 1 (ERF1)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ317	Solyc07g056580.2	<i>Ethylene receptor (ETR)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ327	Solyc07g056580.2	<i>Ethylene receptor (ETR)</i>	Ethylene pathway	Wang et al. (2017a, b)
lncRNAZ363	Solyc08g008100.2	<i>1-Aminocyclopropane-1-carboxylate synthase (ACS)</i>	Ethylene pathway	Wang et al. (2017a, b)
3:12165611 12167830	Solyc05g009450.1	<i>Ethylene-responsive transcription factor 118 (ERF118)</i>	Ethylene pathway	Wang et al. (2017a, b)
3:64444135 64445667	Solyc05g009450.1	<i>Ethylene-responsive transcription factor 118 (ERF118)</i>	Ethylene pathway	Wang et al. (2017a, b)
5:22621180 22630239	Solyc07g064890.1	<i>Ethylene-responsive factor (ERF)</i>	Ethylene pathway	Wang et al. (2017a, b)
6:39644680 39646142	Solyc05g009450.1	<i>Ethylene-responsive transcription factor 118 (ERF118)</i>	Ethylene pathway	Wang et al. (2017a, b)

Table 2 The miRNAs related to fruit color in tomato

ncRNA	Target gene	Target description	Related pathway	References
miR399	Solyc12g098710.1.1	<i>15-Cis-zeta-carotene isomerase (ZISO)</i>	Color pathway	Wang et al. (2017a, b)
miR414	Solyc12g098710.1.1	<i>15-Cis-zeta-carotene isomerase (ZISO)</i>	Color pathway	Wang et al. (2017a, b)
miR5300	Solyc12g098710.1.1	<i>15-Cis-zeta-carotene isomerase (ZISO)</i>	Color pathway	Karlova et al. (2013)
miR482	Solyc03g007960.2.1	<i>Beta-carotene hydroxylase 2 (CrtZ-2)</i>	Color pathway	Karlova et al. (2013)
miR1916	Solyc06g074240.1.1	<i>Chromoplast-specific lycopene beta-cyclase (CYC-B)</i>	Color pathway	Wang et al. (2017a, b)
miR390	Solyc06g074240.1.1	<i>Chromoplast-specific lycopene beta-cyclase (CYC-B)</i>	Color pathway	Karlova et al. (2013)
miR159	Solyc10g079480.1.1	<i>Lycopene beta-cyclase 2 (LCYB)</i>	Color pathway	Wang et al. (2017a, b)
miR156/157	Solyc02g077920.2.1	<i>Colorless non-ripening (CNR)</i>	Color pathway	Moxon et al. (2008)

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1757

Table 3 The ncRNAs related to fruit flavor in tomato

ncRNA	Target gene	Target description	Related pathway	References
miR396	Solyc01g068210.2.1	<i>Glutamate dehydrogenase (GLDH)</i>	Flavor pathway	Li et al. (2012)
miR397	Solyc01g068210.2.1	<i>Glutamate dehydrogenase (GLDH)</i>	Flavor pathway	Karlova et al. (2013)
miR158	Solyc03g094010.2.1	<i>Glutamate dehydrogenase (GLDH)</i>	Flavor pathway	Li et al. (2012)
miR6022	Solyc03g094010.2.1	<i>Glutamate dehydrogenase (GLDH)</i>	Flavor pathway	Li et al. (2012)
miR1917	Solyc06g059920.1.1	<i>Sesquiterpene synthase 2 SSTLE2</i>	Flavor pathway	Karlova et al. (2013)
miR5303	Solyc05g008910.2.1	<i>Glutamine amidotransferase (GATD)</i>	Flavor pathway	Karlova et al. (2013)
miR6024	Solyc05g008910.2.1	<i>Glutamine amidotransferase (GATD)</i>	Flavor pathway	Li et al. (2012)
miR414	Solyc07g042630.2.1	<i>Beta-Amyrin Synthase (β-AS)</i>	Flavor pathway	Karlova et al. (2013)
LncRNAZ063	Solyc10g078550.1	<i>Glutamate dehydrogenase (GATD)</i>	Flavor pathway	Wang et al. (2017a, b)
LncRNA192	Solyc03g096050.2	<i>Flavonol synthase (FLS)</i>	Flavor pathway	Wang et al. (2017a, b)
LncRNA291	Solyc06g069900.2	<i>Flavonol synthase (FLS)</i>	Flavor pathway	Wang et al. (2017a, b)
LncRNA135	Solyc02g083620.2	<i>L-ascorbate peroxidase 3 (APX3)</i>	Flavor pathway	Wang et al. (2017a, b)
LncRNA027	Solyc01g099150.2	<i>Lipoxygenase (LOX)</i>	Flavor pathway	Wang et al. (2017a, b)
LncRNA143	Solyc02g083270.2	<i>Vitamin K epoxide reductase (VKOR)</i>	Flavor pathway	Wang et al. (2017a, b)

ncRNA	Target gene	Target description	Related pathway	References
miR158	Solyc05g014000.2.1	<i>Pectate lyase (PL)</i>	Fruit texture	Wang et al. (2017a, b)
miR167	Solyc09g072820.2.1	<i>Cellulose synthase (CeSA)</i>	Fruit texture	Zuo et al. (2012)
miR1916	Solyc02g014300.1.1	<i>Pectinesterase (PE)</i>	Fruit texture	Karlova et al. (2013)
miR1917	Solyc02g061770.2.1	<i>Chitinase (CHI)</i>	Fruit texture	Karlova et al. (2013)
miR1918	Solyc10g049370.1.1	<i>Pectinesterase (PE)</i>	Fruit texture	Zuo et al. (2012)
miR394	Solyc12g015770.1.1	<i>Cellulose synthase (CeSA)</i>	Fruit texture	Zuo et al. (2012)
miR395	Solyc00g030000.1.1	<i>Cellulose synthase4 (CeSA4)</i>	Fruit texture	Wang et al. (2017a, b)
miR396	Solyc03g058910.2.1	<i>Pectate lyase (PL)</i>	Fruit texture	Wang et al. (2017a, b)
miR408	Solyc01g057220.2.1	<i>Pectinesterase (PE)</i>	Fruit texture	Wang et al. (2017a, b)
miR472	Solyc00g030000.1.1	<i>Cellulose synthase4 (CeSA4)</i>	Fruit texture	Wang et al. (2017a, b)
miR482	Solyc12g019220.1.1	<i>Polygalacturonase 7 PG7</i>	Fruit texture	Karlova et al. (2013)
miR5301	Solyc01g079180.2.1	<i>Pectinesterase (PE)</i>	Fruit texture	Karlova et al. (2013)
miR5303	Solyc02g080290.2.1	<i>Beta-glucosidase 47 β-Glu47</i>	Fruit texture	Wang et al. (2017a, b)
miR6022	Solyc01g091050.2.1	<i>Pectinesterase (PE)</i>	Fruit texture	Zuo et al. (2012)
miR6023	Solyc01g097270.2.1	<i>Chitinase (CHI)</i>	Fruit texture	Karlova et al. (2013)
miR6024	Solyc01g087280.1.1	<i>Polygalacturonase (PG)</i>	Fruit texture	Wang et al. (2017a, b)
miR6026	Solyc12g009420.1.1	<i>Polygalacturonase (PG)</i>	Fruit texture	Karlova et al. (2013)
miR858	Solyc09g098270.2.1	<i>Polygalacturonase (PG)</i>	Fruit texture	Zuo et al. (2012)
lncRNAZ033	Solyc01g087280.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ069	Solyc10g049450.1	<i>Pectinesterase-like (PE-like)</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ138	Solyc02g080210.2	<i>Pectinesterase-like (PE-like)</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ180	Solyc03g123620.2	<i>Pectinesterase 3 (PE3)</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ316	Solyc07g044870.2	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ346	Solyc08g042020.1	<i>Beta-glucosidase 31-like β-Glu31</i>	Fruit texture	Wang et al. (2018a, b, c)
lncRNAZ386	Solyc09g075060.2	<i>Beta-glucosidase 11-like β-Glu11</i>	Fruit texture	Wang et al. (2018a, b, c)
1:36612324 36616003	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)
10:60887167 60889411	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)
10:61293869 61299867	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)
2:32910844 32913066	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)
5:22621180 22630239	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)
6:3511784 3512526	Solyc02g068410.1	<i>Polygalacturonase QRT3 (PG)</i>	Fruit texture	Wang et al. (2017a, b)
8:144804 149694	Solyc12g096730.1	<i>Polygalacturonase-like (PG-like)</i>	Fruit texture	Wang et al. (2017a, b)

So many genes, *so little is known*

Tomato Fruit Ripening

Understanding just one process (ripening) in one fruit (tomato) requires knowledge of molecular biology, genetics, biochemistry, biophysics, plant physiology, soil chemistry and mathematics (always).

So many genes, *let us do something*



RNA breakthrough creates crops that can grow 50% more potatoes, rice



<https://news.uchicago.edu/story/rna-breakthrough-crops-grow-50-percent-more-potatoes-rice-climate-change>

A genetic tweak that targets RNA can grow crops that yield significantly more food and show increased drought tolerance, announced scientists from the University of Chicago, Peking University and Guizhou University.

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By [Louise Lerner](#)
Jul 22, 2021

RNA demethylation increases the yield and biomass of rice and potato plants in field trials

Qiong Yu^{1,10}, Shun Liu^{2,3,10}, Lu Yu⁴, Yu Xiao¹, Shasha Zhang¹, Xueping Wang¹, Yingying Xu¹, Hong Yu⁵, Yulong Li⁶, Junbo Yang¹, Jun Tang¹, Hong-Chao Duan¹, Lian-Huan Wei¹, Haiyan Zhang⁷, Jiangbo Wei^{2,3}, Qian Tang¹, Chunling Wang¹, Wutong Zhang¹, Ye Wang¹, Peizhe Song¹, Qiang Lu¹, Wei Zhang¹, Shunqing Dong¹, Baoan Song⁴✉, Chuan He^{2,3,8}✉ and Guifang Jia^{1,9}✉

RNA N⁶-methyladenosine (m⁶A) modifications are essential in plants. Here, we show that transgenic expression of the human RNA demethylase FTO in rice caused a more than threefold increase in grain yield under greenhouse conditions. In field trials, transgenic expression of FTO in rice and potato caused ~50% increases in yield and biomass. We demonstrate that the presence of FTO stimulates root meristem cell proliferation and tiller bud formation and promotes photosynthetic efficiency and drought tolerance but has no effect on mature cell size, shoot meristem cell proliferation, root diameter, plant height or ploidy. FTO mediates substantial m⁶A demethylation (around 7% of demethylation in poly(A) RNA and around 35% decrease of m⁶A in non-ribosomal nuclear RNA) in plant RNA, inducing chromatin openness and transcriptional activation. Therefore, modulation of plant RNA m⁶A methylation is a promising strategy to dramatically improve plant growth and crop yield.

Yu, Q., Liu, S., Yu, L. *et al.* RNA demethylation increases the yield and biomass of rice and potato plants in field trials. *Nature Biotech* (July 22, 2021) ♦ <https://doi.org/10.1038/s41587-021-00982-9>

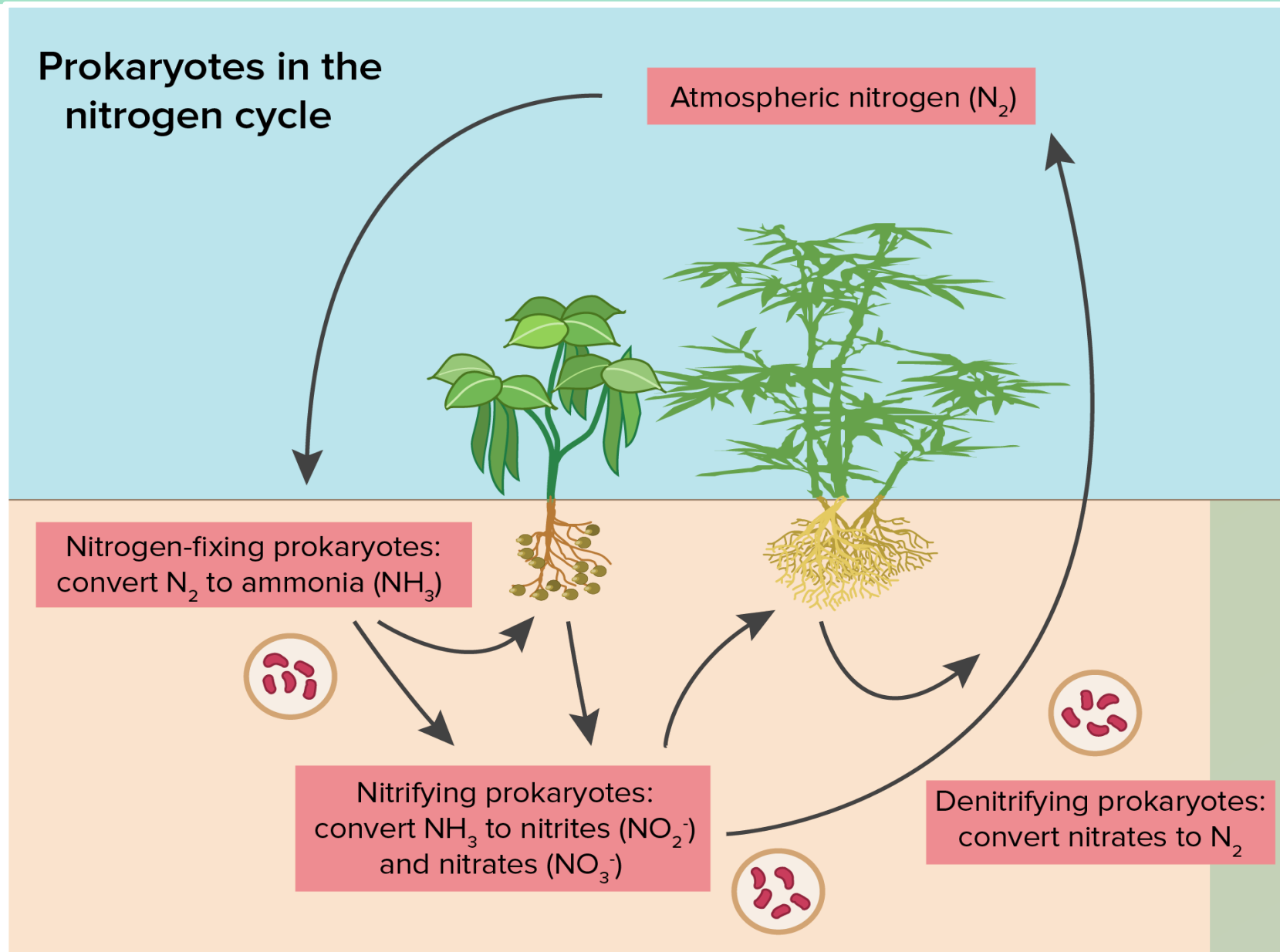
Soil Chemistry ??

Understanding the multifactorial dynamics of geo-bio-chemistry

SOIL GEOBIOCHEMICAL CYCLES

BIOTIC / ABIOTIC

WATER
CARBON
SULPHUR
NITROGEN
PHOSPHOROUS

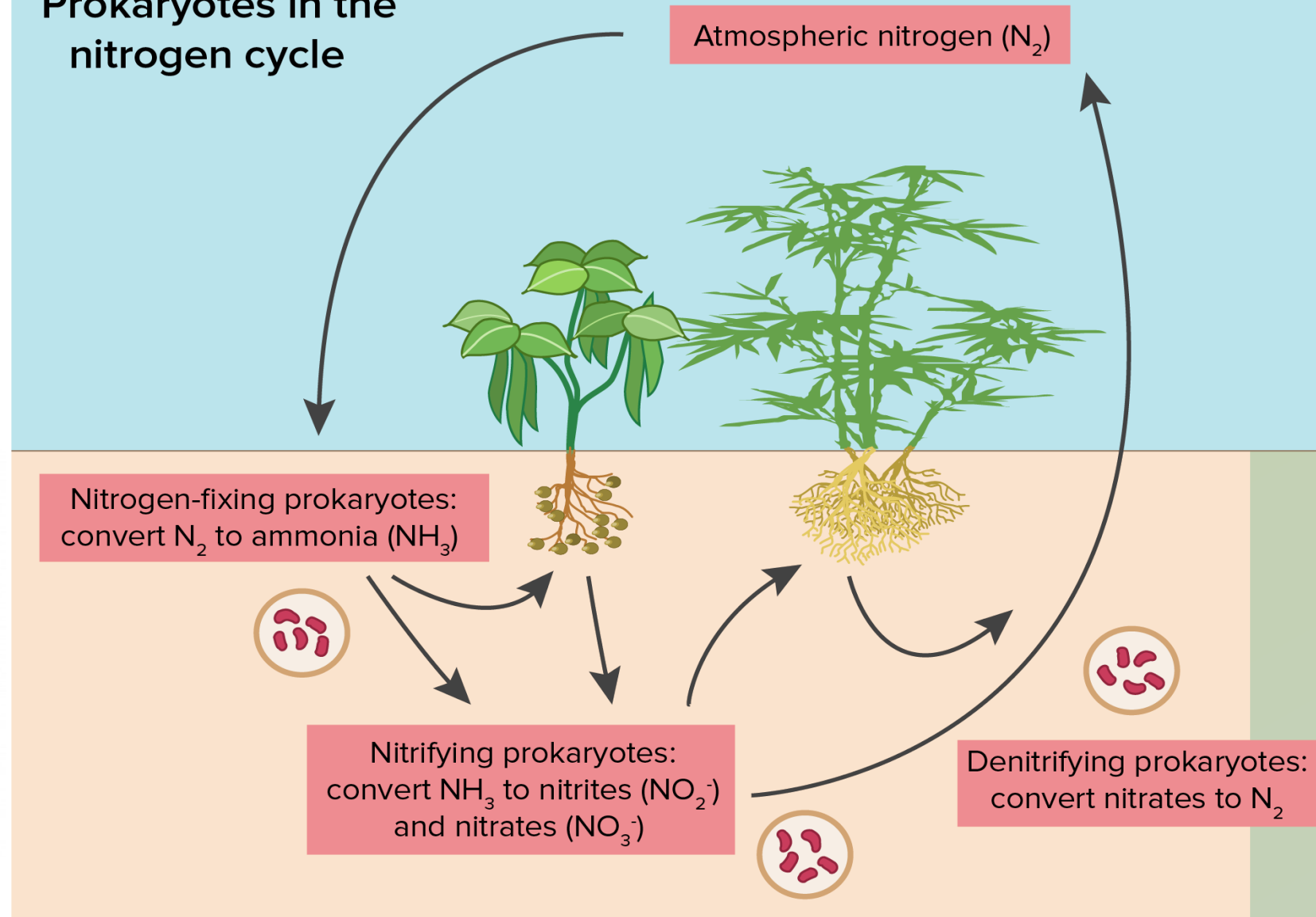


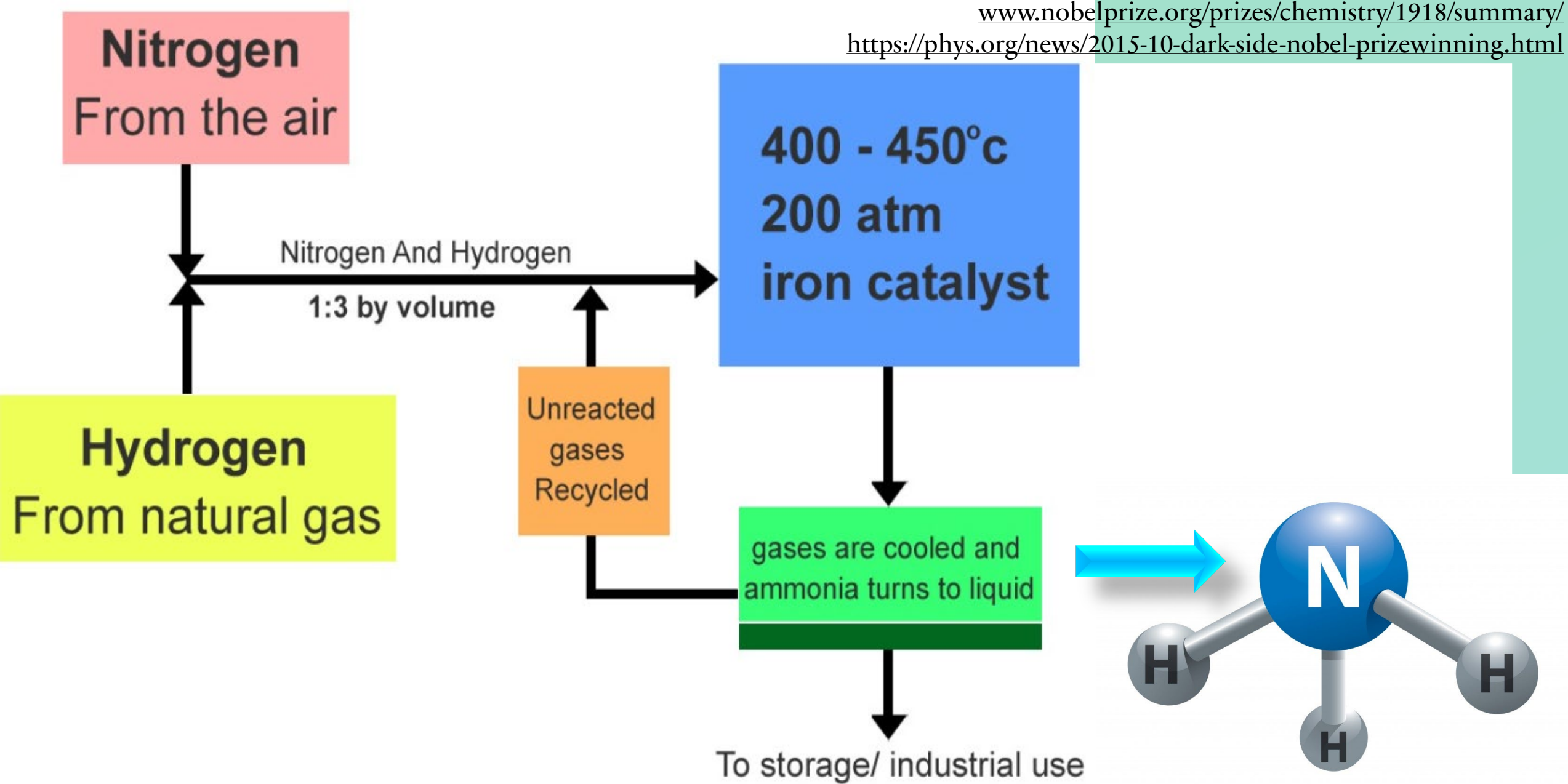
Second critical
contribution of
chemistry to
humanity?

What is the first?



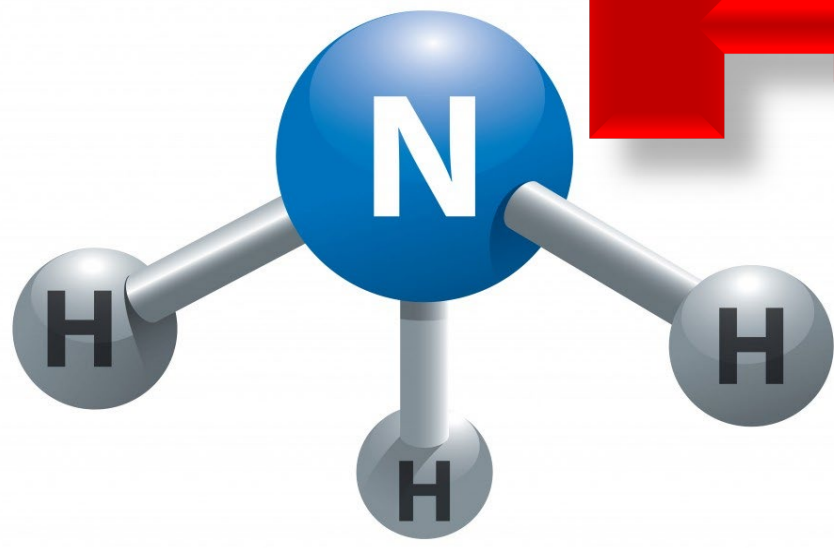
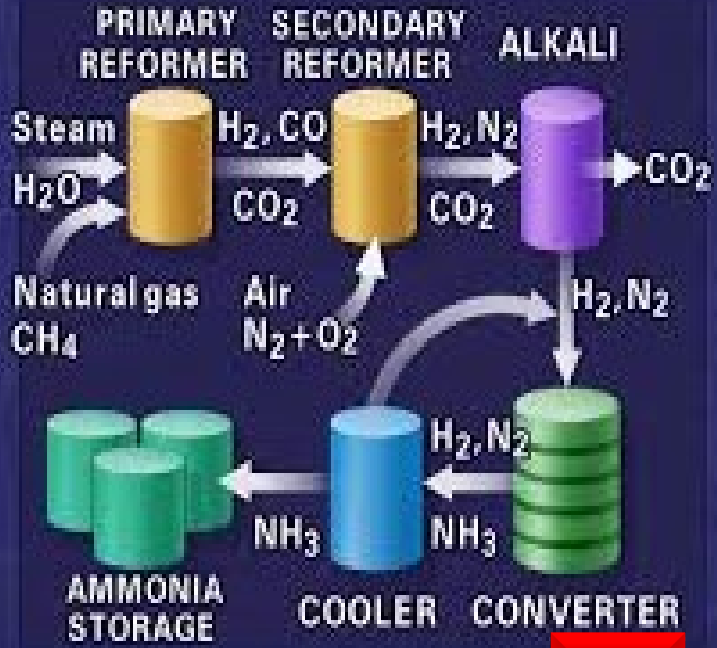
Prokaryotes in the nitrogen cycle



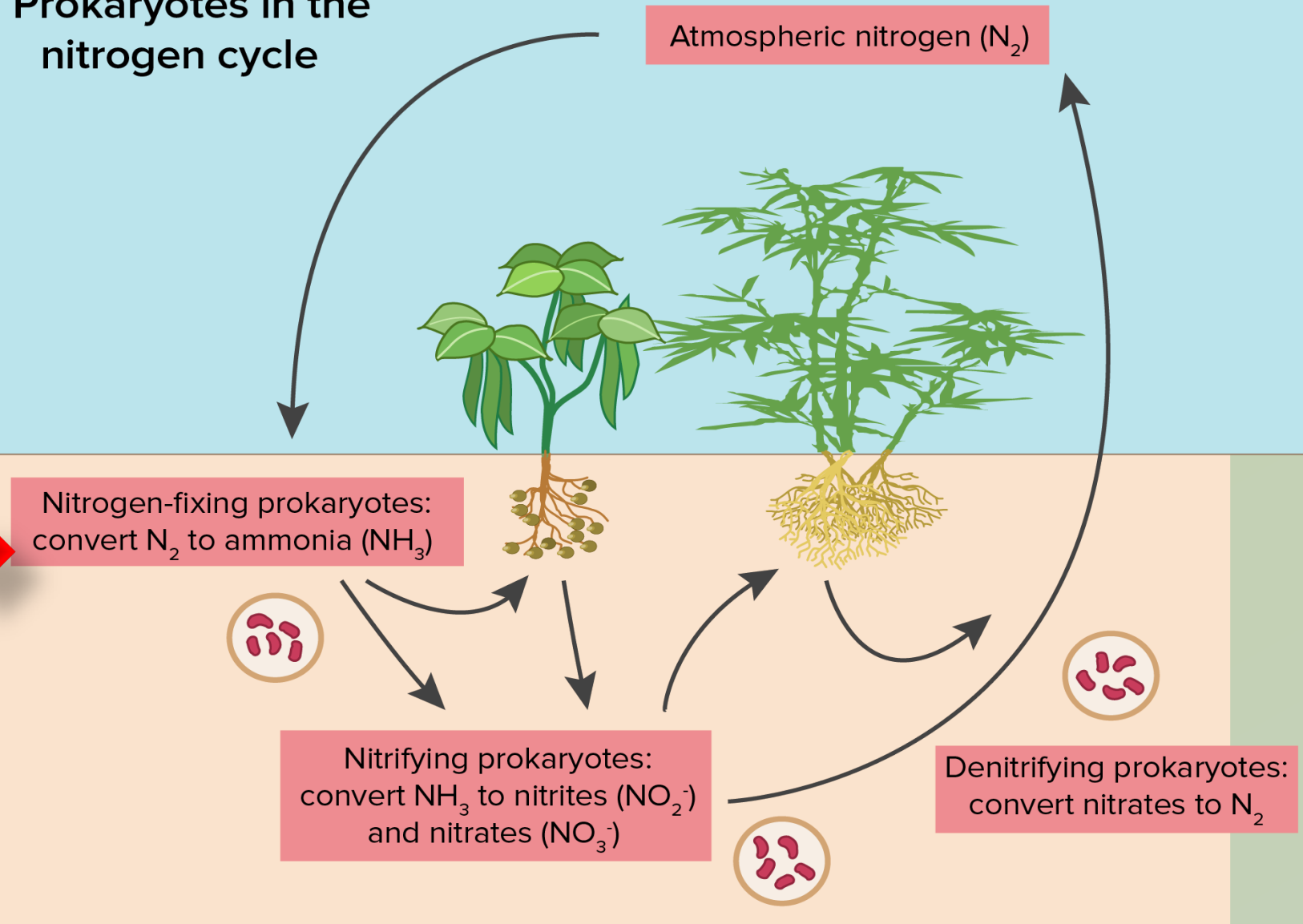


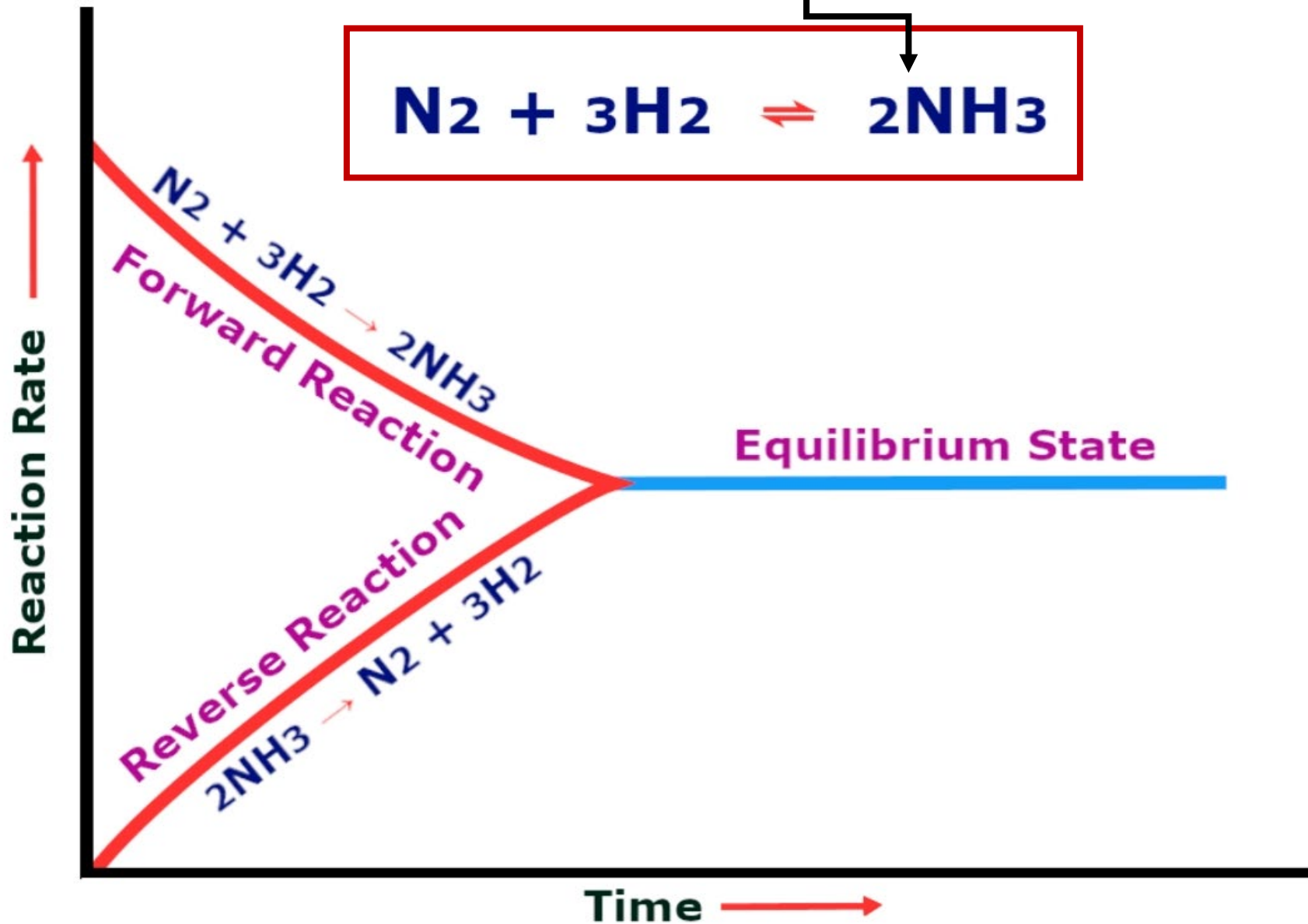
HABER-BOSCH PROCESS

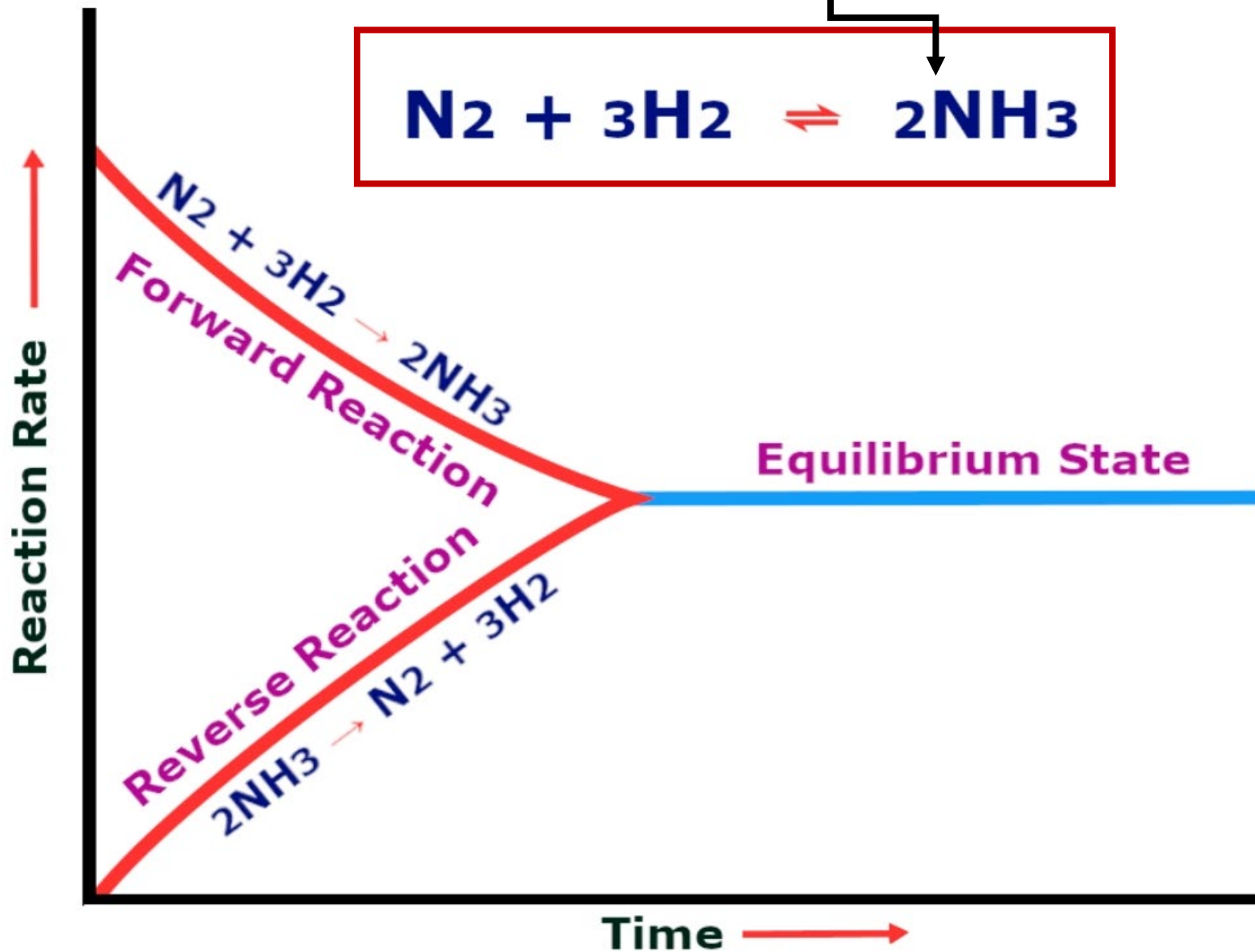
AMMONIA



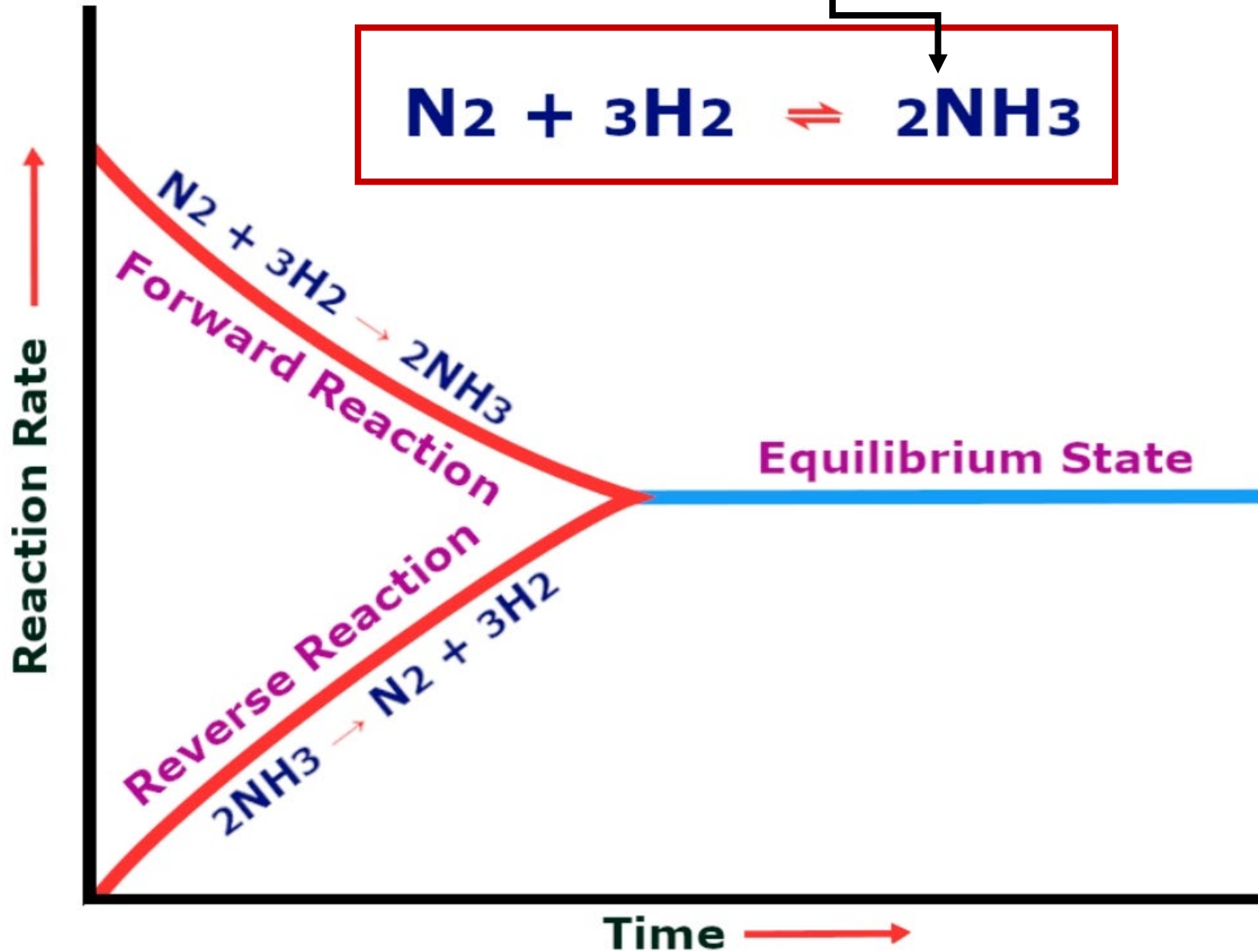
Prokaryotes in the nitrogen cycle



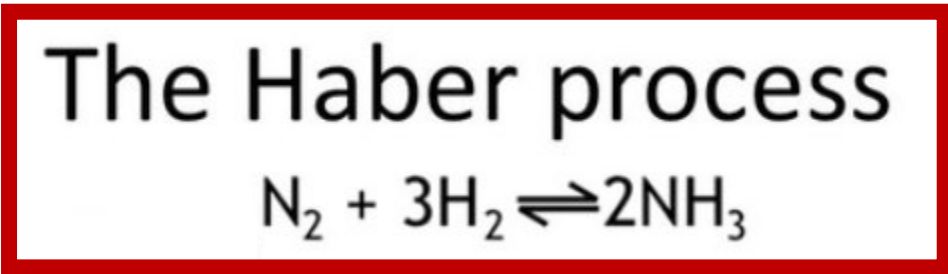
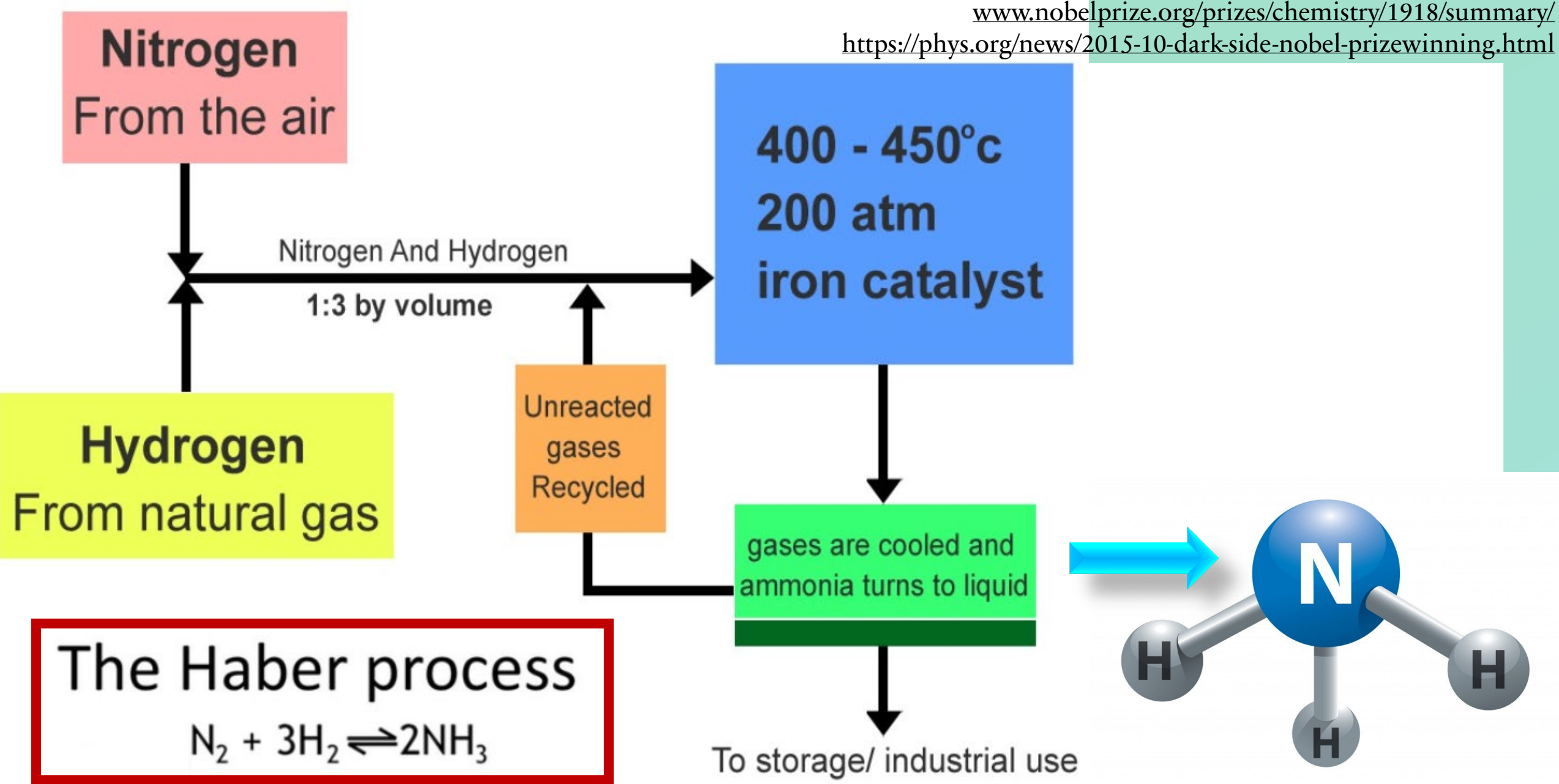




Are the two equations representing the same process of ammonia synthesis?



No.



HABER-BOSCH PROCESS

AMMONIA



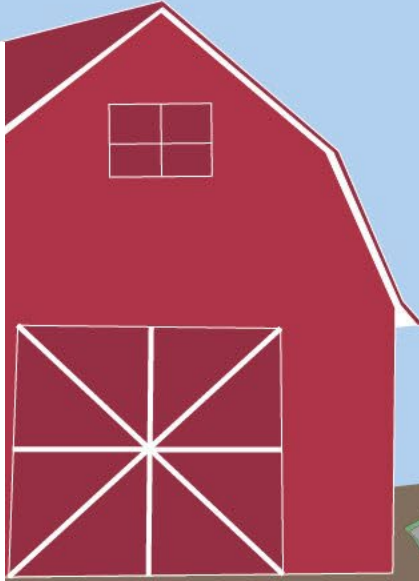
**BIOLOGICAL PROCESS
ENZYME CATALYZED**

Crop	Nodulating Bacteria
Alfalfa	<i>Sinorhizobium melilotii</i>
Beans	<i>Rhizobium leguminosarum biovar phaseoli</i> and <i>Rhizobium tropici</i>
Clover	<i>Rhizobium leguminosarum biovar trifolii</i>
Lotus	<i>Mesorhizobium loti</i>
Peas	<i>Rhizobium leguminosarum biovar viceae</i>
Soybean	<i>Bradyrhizobium japonicum</i> , <i>Bradyrhizobium elkanii</i> , <i>Rhizobium fredii</i>
Sesbania	<i>Azorhizobium caulinodans</i>

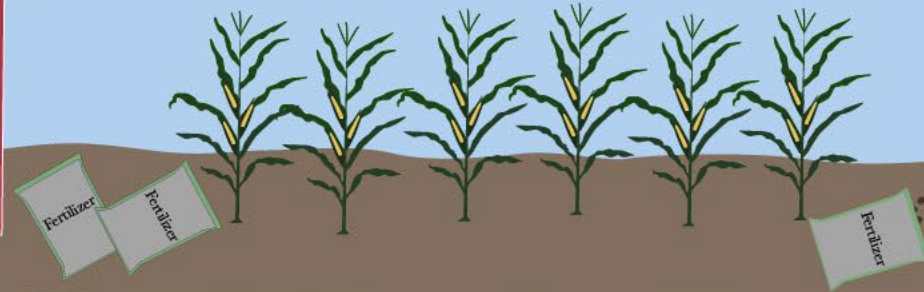
Social Costs of Nitrogen Pollution

How does nitrogen cause problems for people?

How can something so useful also be so detrimental?



A farmer applies fertilizer to her farm field. That fertilizer boosts the yields of her crops.



The nitrogen in that fertilizer isn't very good at staying put. That's when nitrogen starts to have "social costs." Some of that nitrogen is absorbed by crops, but some is lost to the environment.

Climate Change

- Some fertilizer ends up getting converted into N_2O , a potent greenhouse gas. This kind of nitrogen loss to the atmosphere causes climate change (and associated costs).

Air Pollution

- Fertilizer becomes ammonia and nitrogen oxides. These end up in the atmosphere as particulate matter and affect people breathing that air in downwind communities.

Surface Water Contamination

- Fertilizer seeps into lakes, streams and coastal water causing eutrophication, degraded recreational quality, and impacts on fish and shellfish.

Groundwater Contamination

- Increased levels of nitrogen in drinking water leads to increased treatment costs and health impacts.

WATER POLLUTION

Too much nitrogen and phosphorus in the water causes algae to grow faster than ecosystems can handle. Significant increases in algae harm water quality, food resources and habitats, and decrease the oxygen that fish and other aquatic life need to survive. Large growths of algae are called algal blooms and they can severely reduce or eliminate oxygen in the water, leading to illnesses in fish and the death of large numbers of fish. Some algal blooms are harmful to humans because they produce elevated toxins and bacterial growth that can make people sick if they come into contact with polluted water, consume tainted fish or shellfish, or drink contaminated water. www.epa.gov/nutrientpollution/issue

INEXTRICABLY LINKED

BALANCING
THE CYCLE ?

Science R&D may
provide solutions.

Who will imagine, invent,
innovate and implement?

YOU ?

Discussion: Snippets of Examples

Number 2



E

Energy

Your contribution to society matters.

Science and Scientists for Society

Even more shocking, almost 3 billion people – over a third of the world's population – don't have access to clean cooking facilities.

The UN estimate that almost 4 million people will die prematurely this year due to the use of unclean cooking fuels.

80% of the world's population today live in countries where energy consumption is so low, that increases in energy tend to go hand-in-hand with significant improvements in human development.

The world needs more energy to grow and prosper.

Access to safe, secure, affordable energy enriches lives.

ENERGY

In need of herculean transformation



This is just lame,
incremental and
inconsequential.
It's NOT radical.

Making electric cars more competitive with gas-powered ones will require a breakthrough battery that remedies those shortcomings. That, at least, is the argument of Jagdeep Singh, chief executive of QuantumScape, a Silicon Valley startup that claims to have developed just such a technology.

The company asserts it did so by solving a chemistry puzzle that has stumped researchers for nearly half a century: how to use lithium, the lightest metal on the periodic table, to boost the amount of energy that can be packed into a battery without posing a routine risk of fire or otherwise sacrificing performance. The company says it achieved this, in large part, by developing a solid version of the flammable liquid electrolyte.

VW was impressed enough to invest hundreds of millions of dollars in QuantumScape. The German auto giant also agreed to set up a joint venture with the company to mass-produce the batteries and says they'll be in its electric cars and trucks on the road by 2025.

A Radical Design Metaphor ?

“Swappable Atoms”

The Paradigm of Atoms to Bits

The form factor of energy, and its source, must/will undergo radical metamorphoses. One solution will not suit all.

New imagination. New ideas. New inventions. New innovations. New implementations.

New science? New engineering? New technologies?

Think radically different

Growth in India over the next decade will create new demand

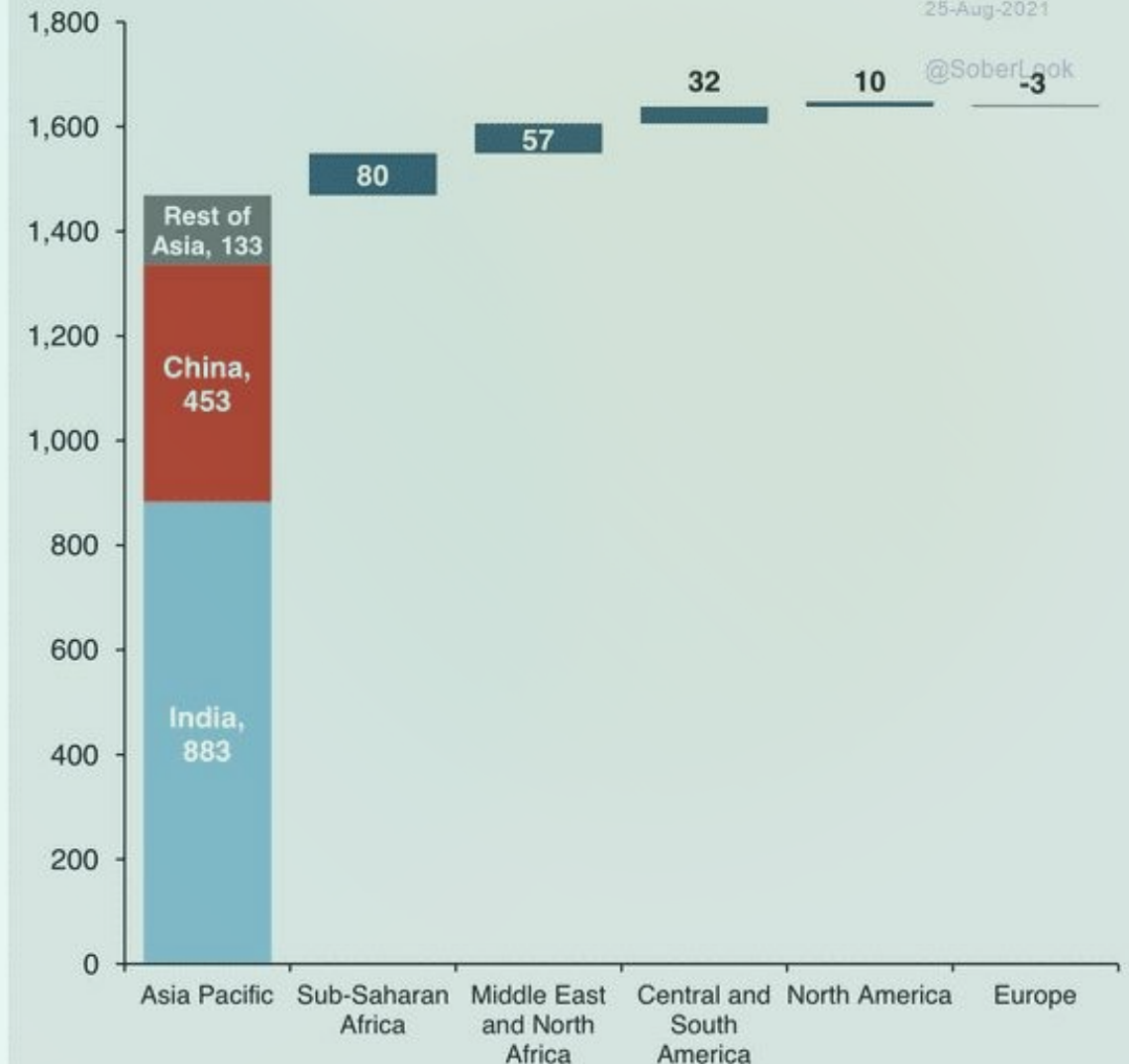
Regional contribution middle class growth: 2020 to 2030

Millions of people

The Daily Shot

25-Aug-2021

@SoberLook



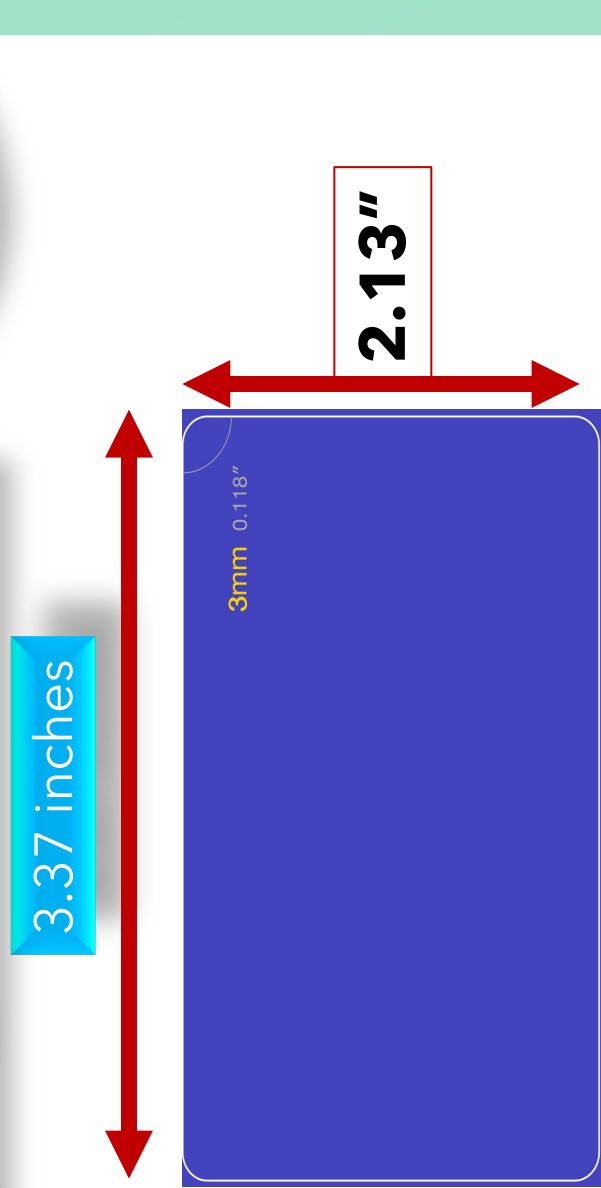
1956

5 MB hard
drive being
shipped out
of IBM



2020

16 million MB
16 TB hard drive slightly bigger than a credit card



Credit Card



1956



5 MB hard
drive air
lifted on to
PAN AM

A close-up photograph of a person's hand holding a red Seagate portable hard drive. The drive is rectangular and has the Seagate logo and name printed on the bottom left corner. The background shows a light blue button-down shirt and a dark grey textured surface.

2020

**16 million
MB**

16 TB hard
drive fits in
your palm
& pocket

Size of credit card

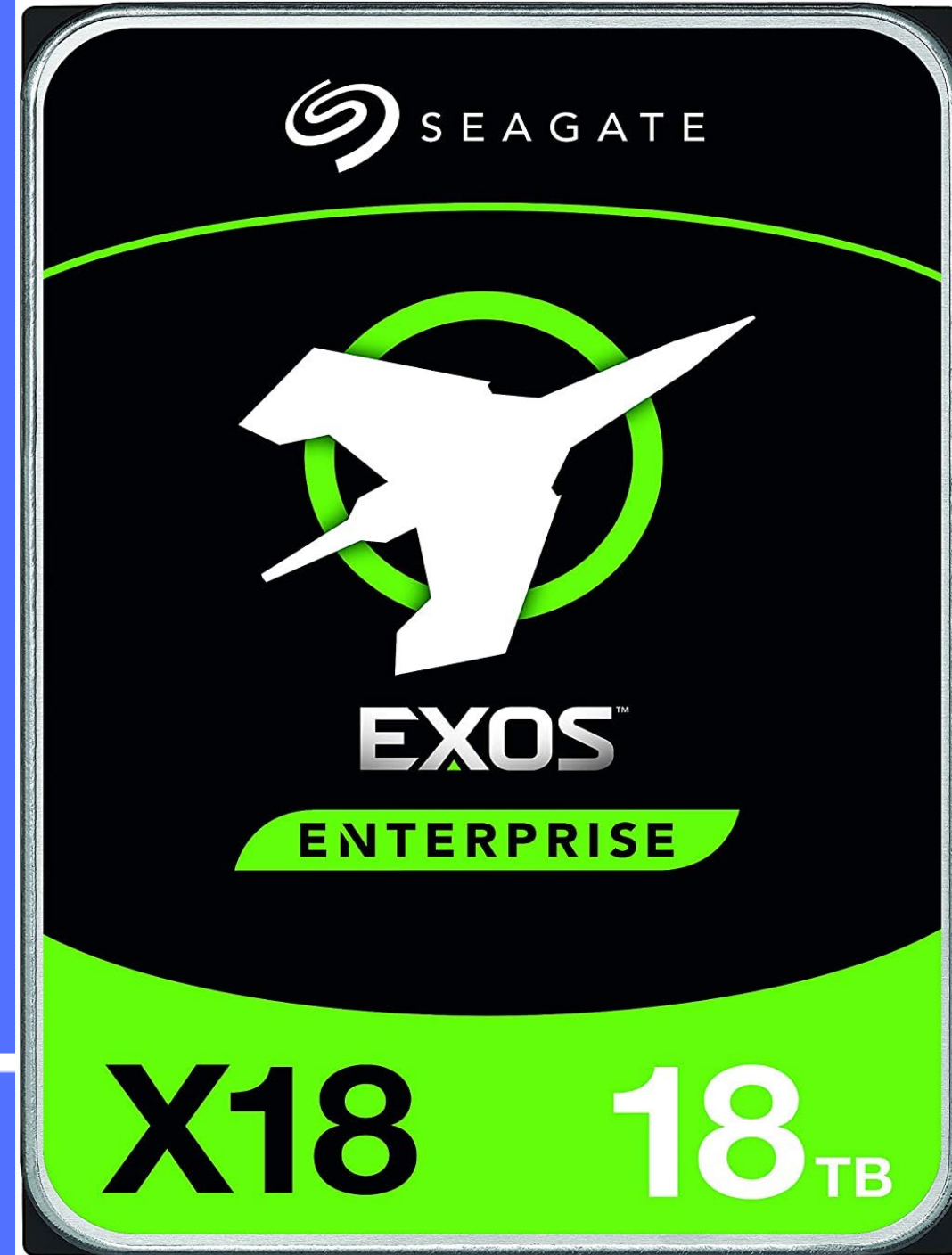


18TB HD 2X SIZE
of CREDIT CARD



TRANSFORMATION
IN ENERGY MUST
HAPPEN ON A
MASSIVE SCALE

18TB HD 2X SIZE
of CREDIT CARD



HYDROGEN GAS? SOLID?

ENERGY FROM HYDROGEN



HYDROGEN HYDROXIDE

Abundant. But, we don't know how to break down water (for energy-positive extraction of hydrogen).

Simplest things we don't know

We still do not know how to break down water to generate hydrogen and oxygen (in a manner which is energy positive and generates energy). Electrolysis of water consumes energy. It was first demonstrated in 1789 by Jan Rudolph Deiman and Adriaan Paets van Troostwijk (Dutch) using an electrostatic generator to produce a discharge between two gold electrodes immersed in water. Michael Faraday's laws of electrolysis are quantitative relationships which were published in 1833 (in UK).

Energy is an economic differentiator

*Leapfrogging the barriers
of conventional wisdom
and the dead weight of
old technology.*

Radical Energy Design Metaphor

“Swappable Atoms”

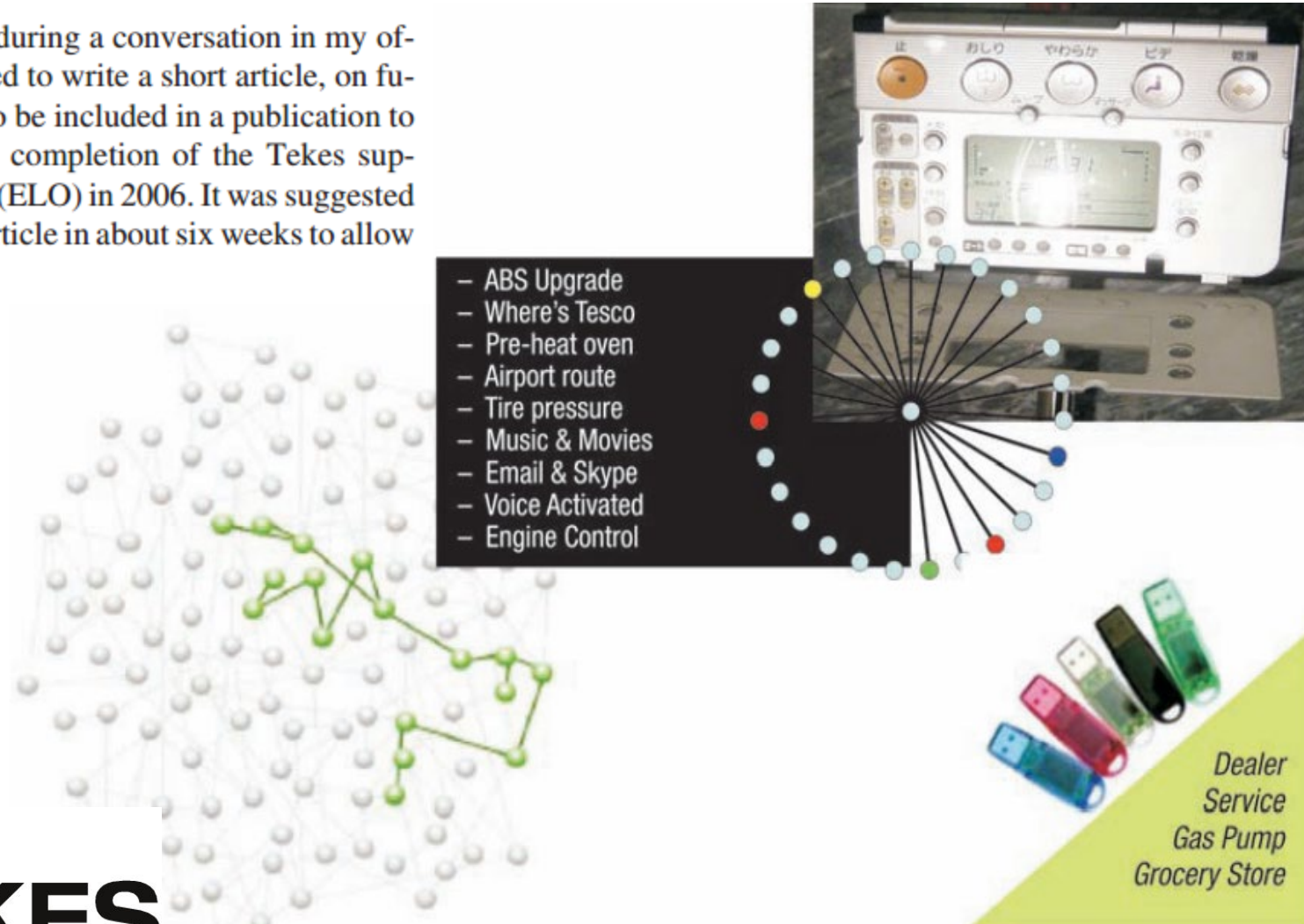
The Paradigm of Atoms to Bits? Not easy!

Replaces the “atoms” with low energy with high energy atoms.

2005 – Swap form factor for “atoms” (connect bits, cars, engines, toilets)

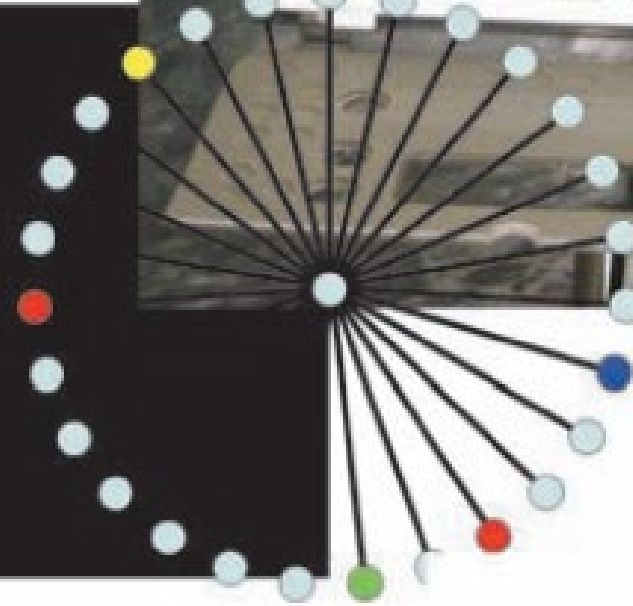
16 years later, swappable car batteries are in discussion, but form factor for energy is still large.

On 17th November 2005, during a conversation in my office at MIT, I was requested to write a short article, on future trends in e-business, to be included in a publication to accompany the successful completion of the Tekes supported e-logistics program (ELO) in 2006. It was suggested that I send the completed article in about six weeks to allow for translation in Finnish.



*Radical idea:
“portability”
of atoms, eg.
running
automobiles
on metallic
hydrogen as
fuel source.*

- ABS Upgrade
- Where's Tesco
- Pre-heat oven
- Airport route
- Tire pressure
- Music & Movies
- Email & Skype
- Voice Activated
- Engine Control



*Dealer
Service
Gas Pump
Grocery Store*

*Radical idea:
“portability”
of atoms, eg.
running
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on metallic
hydrogen as
fuel source.*

- ABS Upgrade
- Where's Tesco
- Pre-heat oven
- Airport route
- Tire pressure
- Music & Movies
- Email & Skype
- Voice Activated
- Engine Control

FUEL STICKS ??



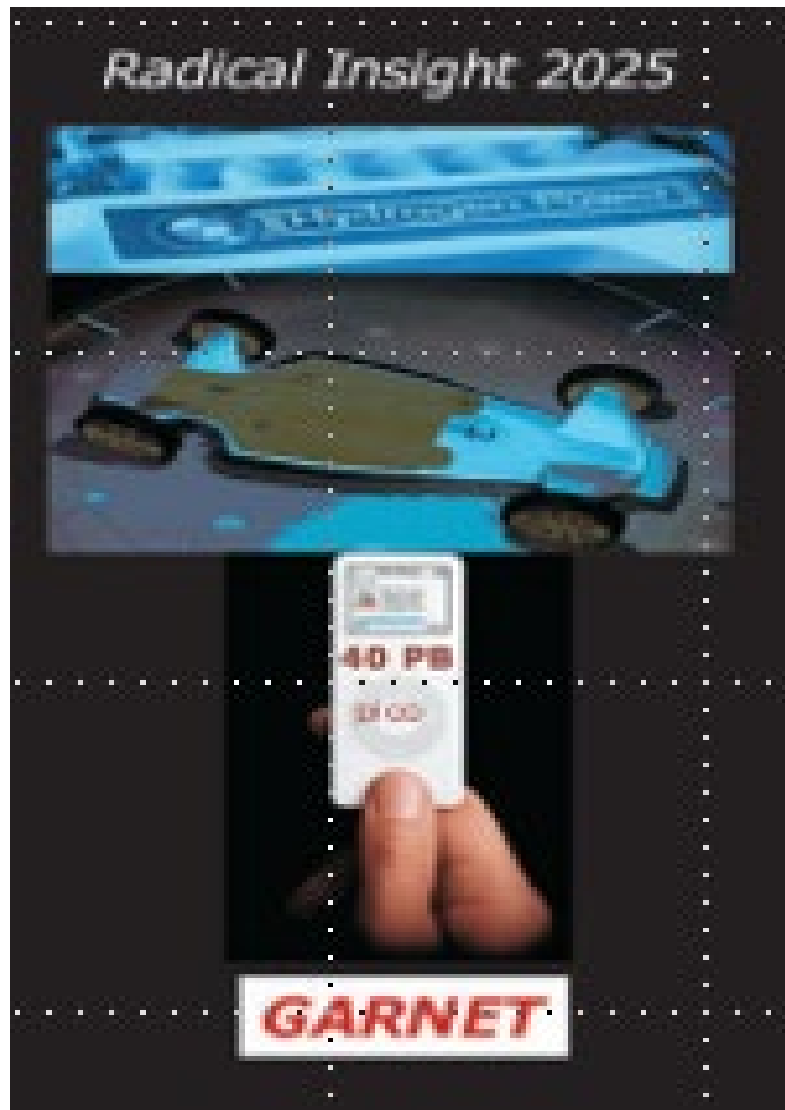
Dealer
Service
Gas Pump
Grocery Store



*Radical idea – “portability” of atoms
e.g. metallic hydrogen as fuel source.*

Wigner E. and Huntington H.B. On the possibility of a metallic modification of hydrogen. *J. Chem. Phys.*, 1935, v.3, 764–770.

Born	Wigner Jenő Pál November 17, 1902 Budapest, Austria-Hungary
Died	January 1, 1995 (aged 92) Princeton, New Jersey, US



S. Datta, published
by TEKES in 2006

<https://dspace.mit.edu/handle/1721.1/56251>

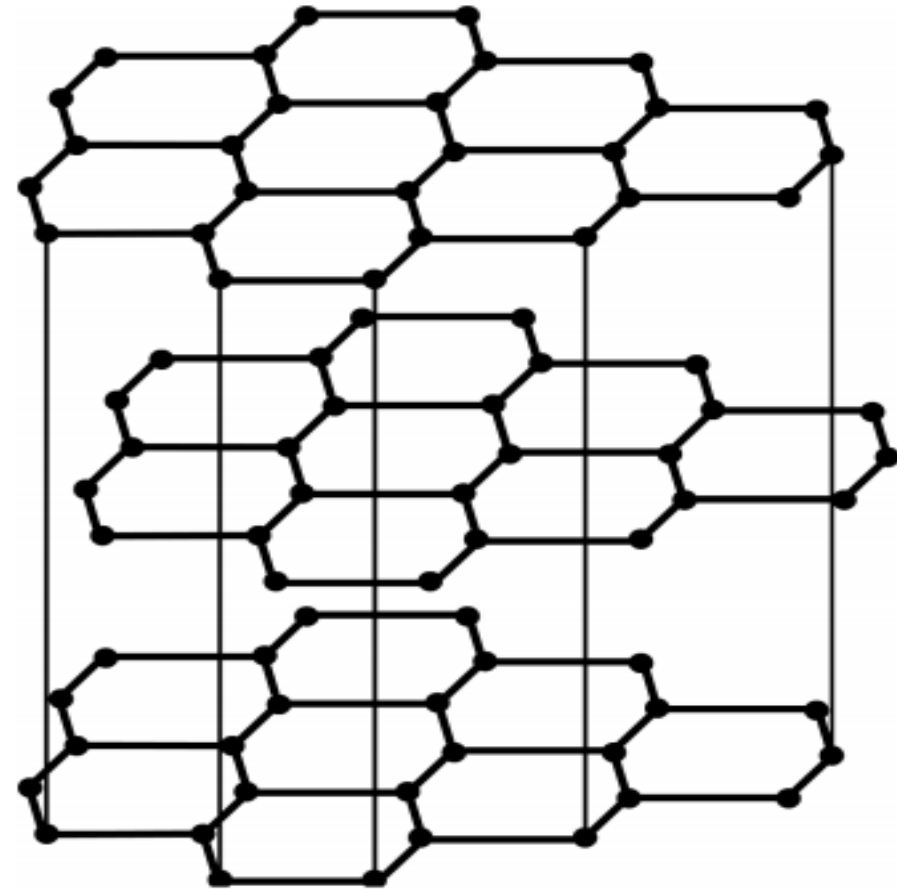


Fig. 1: Schematic representation of the layered lattice of graphite. Wigner and Huntington [19] would propose that most energetically favorable form of metallic hydrogen would assume this crystal structure.

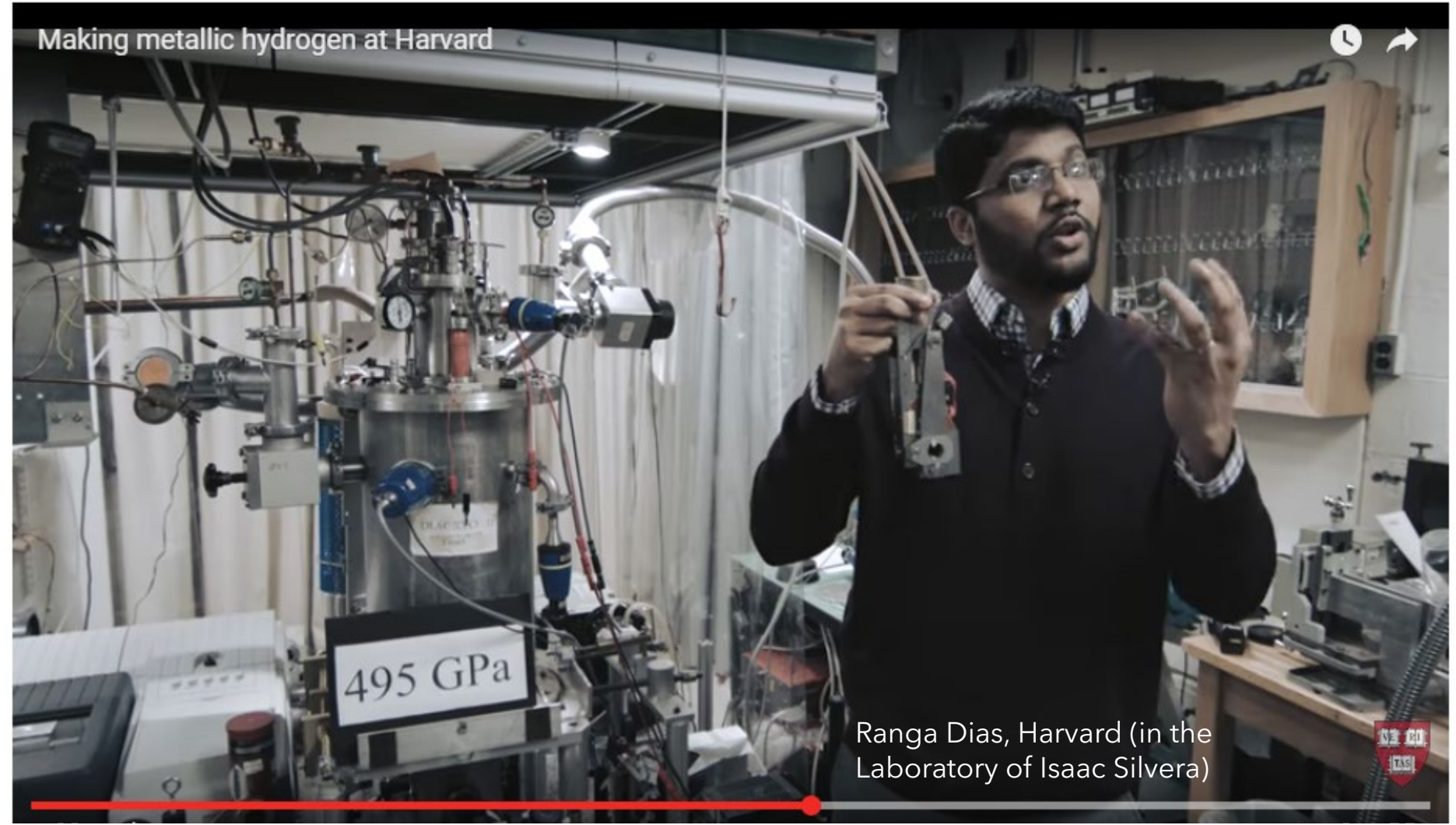
J. D. Bernal who first put forward the view that all substances go over under very high pressure into metallic or valence lattices” [19]. www.ptep-online.com/index_files/2011/PP-26-07.PDF

Rationale of “portability” of atoms was based on the theory of metastable metallic hydrogen

19. Wigner E. and Huntington H.B. On the possibility of a metallic modification of hydrogen. *J. Chem. Phys.*, 1935, v.3, 764–770.

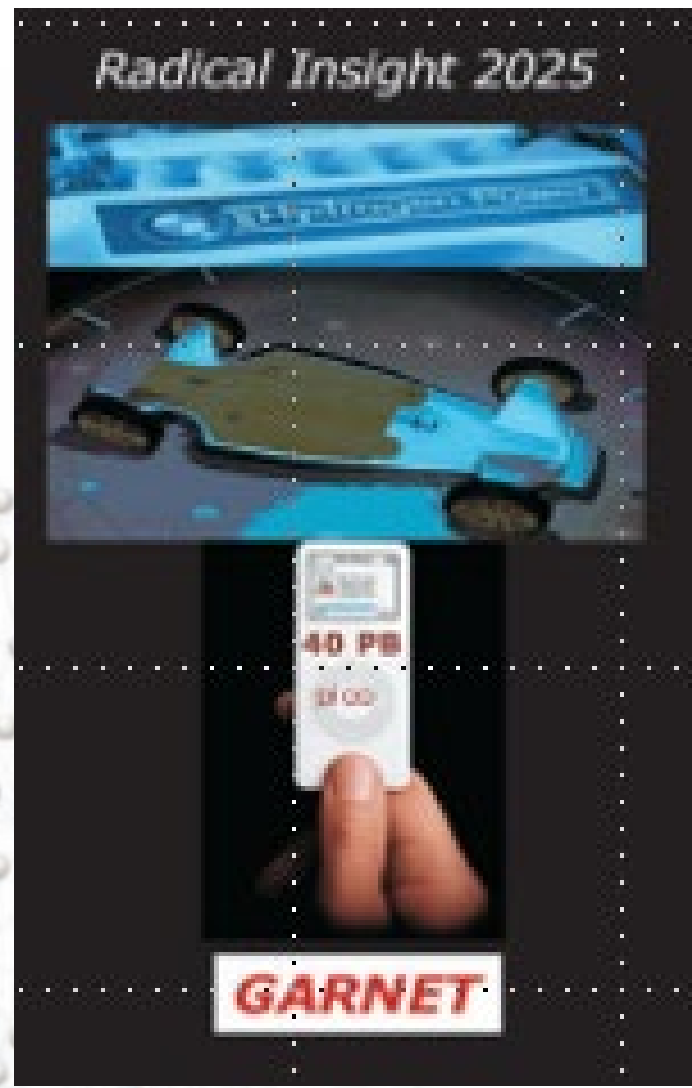
Harvard scientists announce they've created metallic hydrogen, which has been just a theory

January 26, 2017 |   

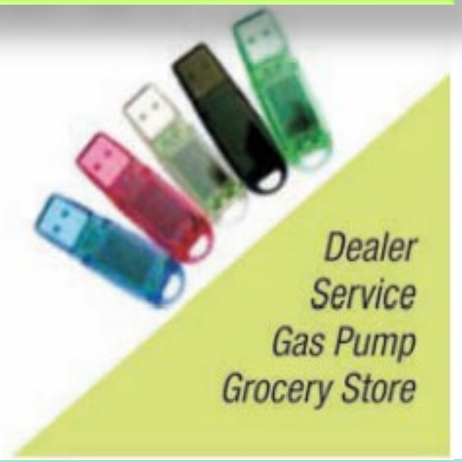


<http://news.harvard.edu/gazette/story/2017/01/a-breakthrough-in-high-pressure-physics/>

Drive cars, ship, plane, rocket, with metallic hydrogen in a fuel stick (USB flash drive format).



Swap anywhere to replenish fuel



What is the energy form factor now ?

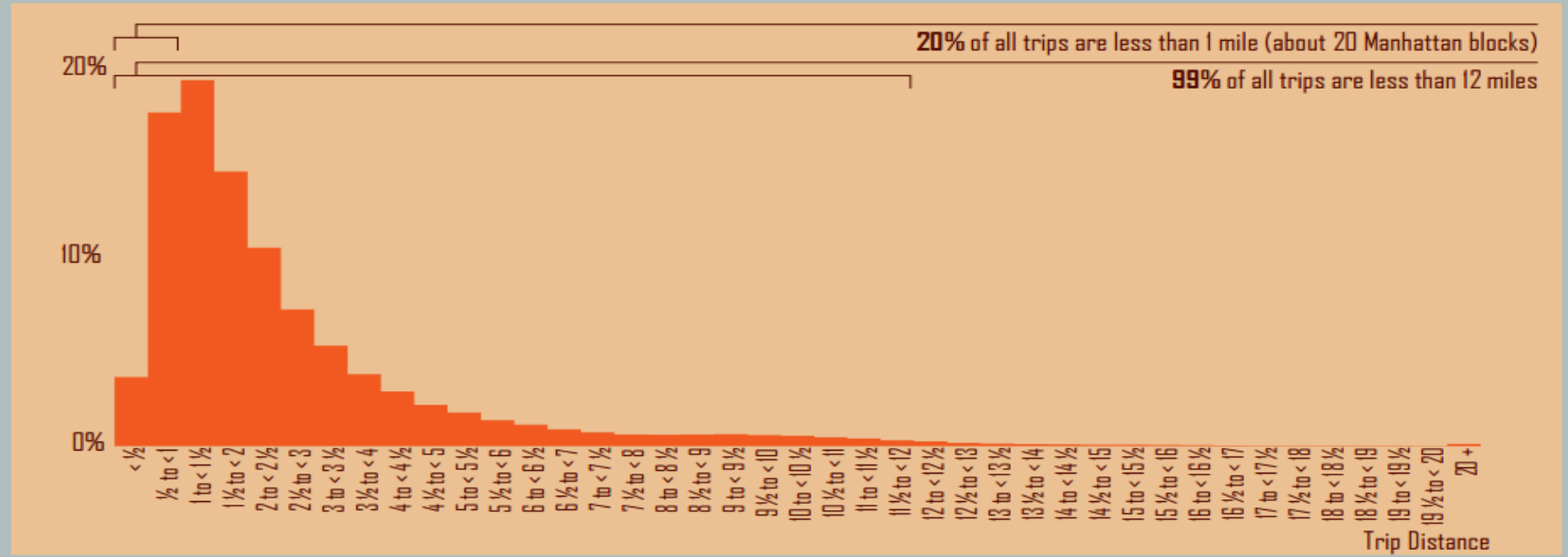
The case for taxicabs in cities.

Yellow taxis provide an average of

485,000
trips/day

Average taxi ride
approx. 2.6 miles

The average trip distance is **2.6** miles

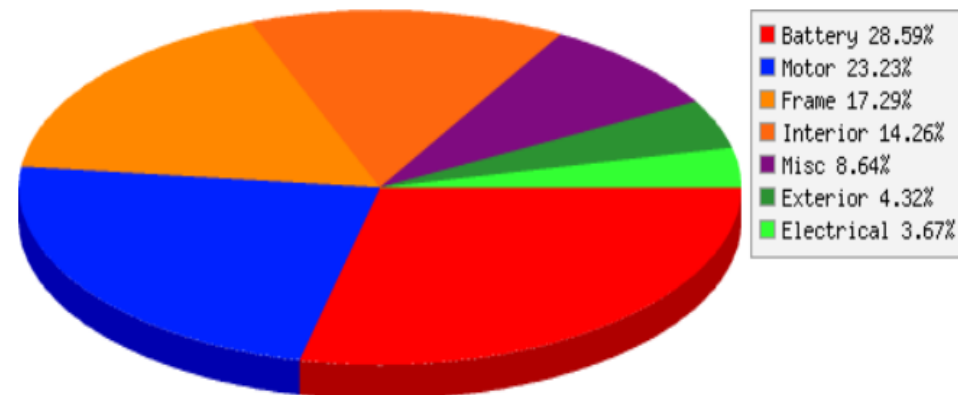


12 gallons **72 lb @ 6 lb/gal**

Smaller cars generally have gas tanks that hold **12 gallons** worth of gas, while larger cars can hold 15 or **16 gallons**. For the purpose of this story, let's say gas costs \$3.85 a gallon. A car with a **12-gallon** tank costs \$46.20 to fill up while a larger car with a 15-gallon tank costs \$57.75. Jul 5, 2013

How much energy (inventory) and weight of energy (gas or battery) is a vehicle carrying for an average 2.6 mile trip?

TESLA MODEL S WEIGHT – 4,600+ LB



Battery Pack

1323 lb

Aluminum Space Frame

- ~ 800 lb

Motor / Drivetrain

- ~ 350 lb - electric motor + inverter
- ~ 175 lb - differential
- ~ 250 lb - wheels + tires
- ~ 120 lb - brakes calipers, discs, lines
- ~ 80 lb - air suspension

Interior

- ~ 200 lb - front powered seats + rears
- ~ 190 lb - windshield, windows, hatch
- ~ 150 lb - pano glass and assembly
- ~ 80 lb - carpet, padding, mats
- ~ 40 lb - dash, trim, panels

Exterior

- ~200 lb - doors, frunk, hatch, body

Misc

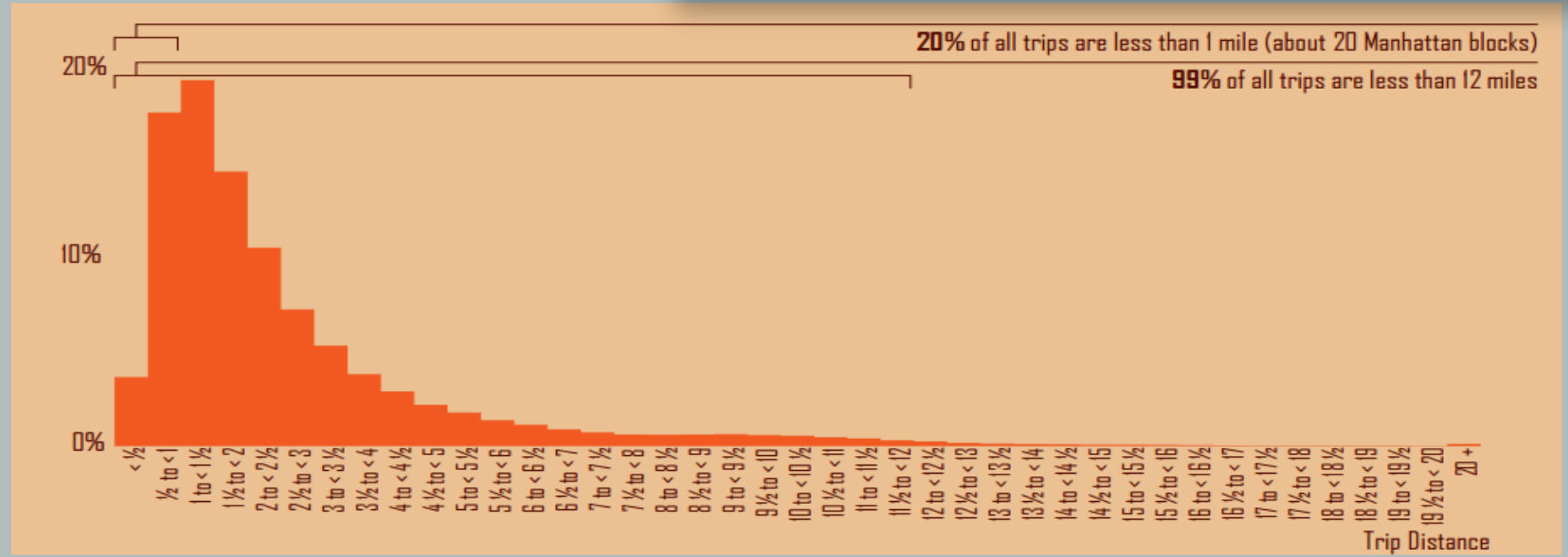


Yellow taxis provide an average of

485,000
trips/day

1300lb battery (weight)
even for 2.6 mile trip?

The average trip distance is **2.6** miles



Change is slow. But
change the equation.
Can we take baby steps?

EV, OR NOT TO BE?

India's electric vehicle revolution will begin with auto-rickshaws running on swappable batteries

<https://qz.com/1001518>



Changed the
equation!

SWAPPABLE ATOMS

swappable

batteries

Not quite metallic hydrogen but we are changing the equation in India. Aren't we?



<https://qz.com/1001518>

SWAPPABLE ATOMS – A DESIGN METAPHOR

→   Secure | <https://www.technologyreview.com/s/531911/isaac-asimov-asks-how-do-people-get-new-ideas/>

A person willing to fly in the face of reason, authority, and common sense must be a person of considerable self-assurance. Since he occurs only rarely, he must seem eccentric (in at least that respect) to the rest of us. A person eccentric in one respect is often eccentric in others.

Consequently, the person who is most likely to get new ideas is a person of good background in the field of interest and one who is unconventional in his habits. (To be a crackpot is not, however, enough

What about conventional hydrogen fuel cells and hydrogen storage?

← → ↻ 🔒 nature.com/articles/35104634 🔍

Published: 15 November 2001

Hydrogen-storage materials for mobile applications

Louis Schlapbach & Andreas Züttel 

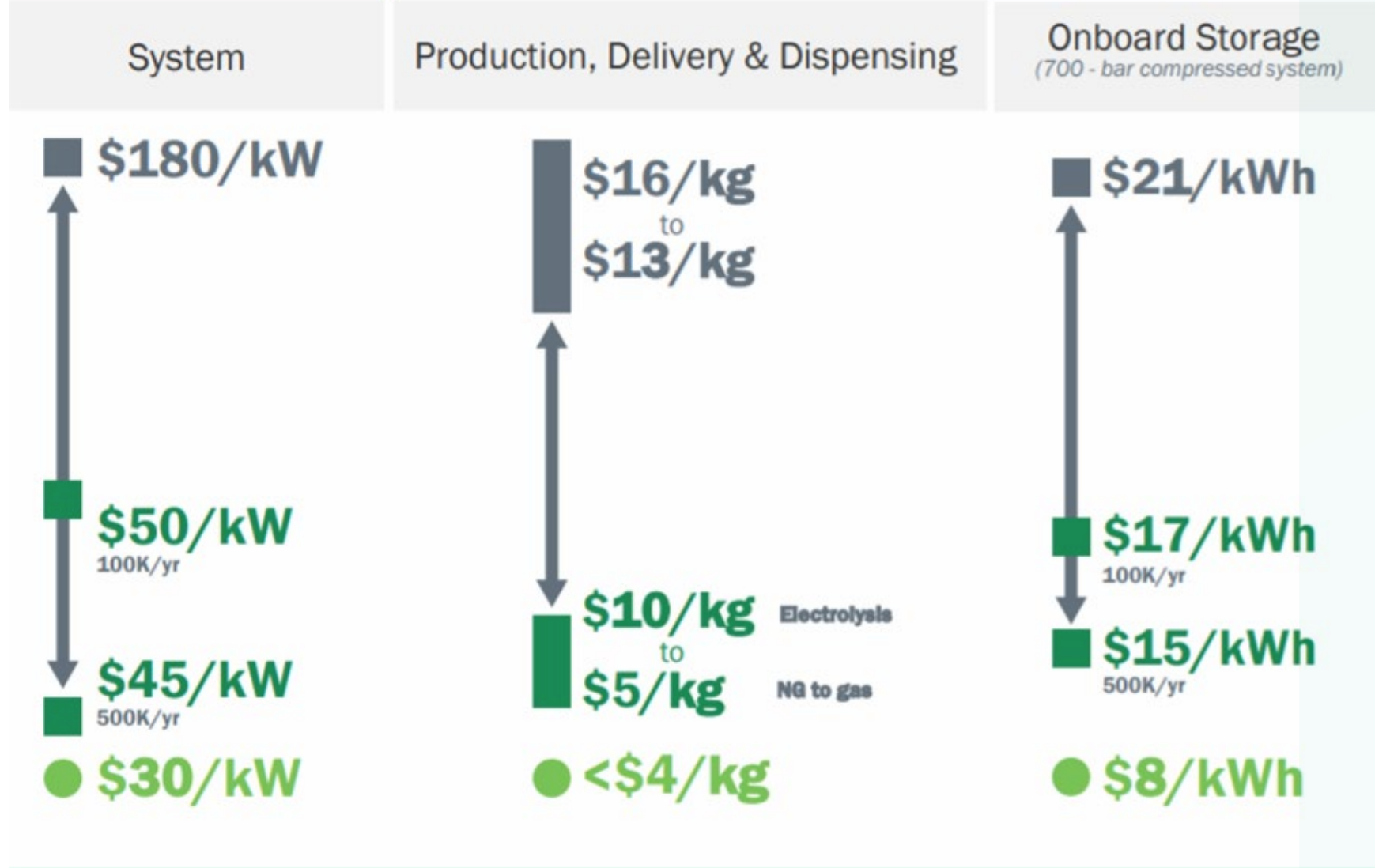
Nature **414**, 353–358 (2001) | <https://doi.org/10.1038/35104634>

>8,600 hydrogen fuel cell cars on US roads (6/2020).

FUEL CELL R&D

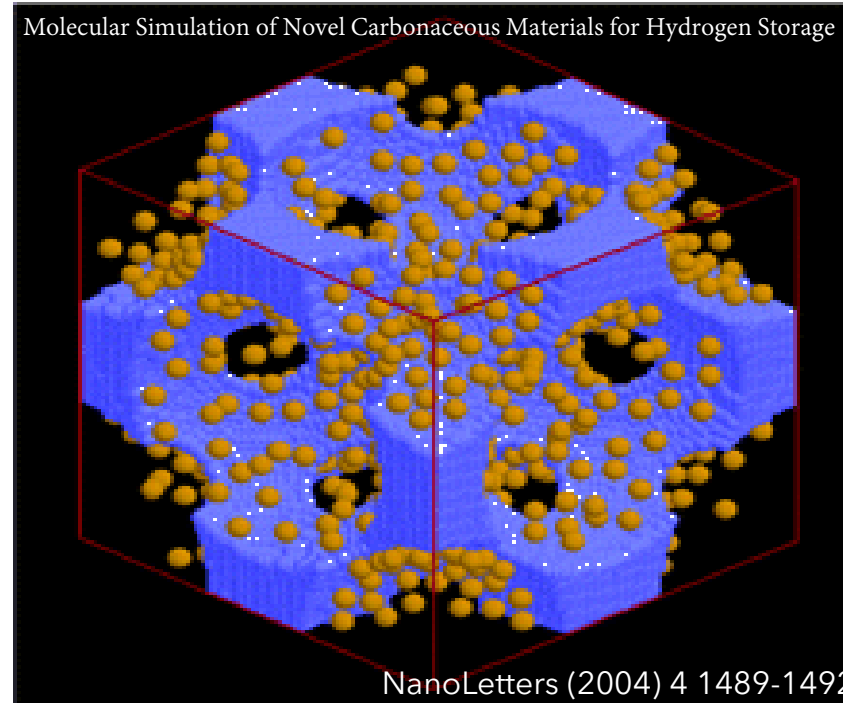
HYDROGEN R&D

www.energy.gov/sites/prod/files/2020/07/f77/hfto-progress-fact-sheet-june-2020-1.pdf



● Ultimate Targets ■ High-Volume Projection ■ Low-Volume Estimate

Adsorbed Hydrogen in the frame of the vehicle may even eliminate the need for fuel cell or tank



Hydrogen molecules (yellow) adsorbed in graphitic carbon inverse opal (GCIO, blue).

Liquid Fuel

Think Different

Glucose was first isolated in 1747 from raisins by Andreas Marggraf. The name *glucose* was coined in 1838 by Jean Dumas, from the greek *glycos*. Structure was first discovered by Emil Fischer in 1891.

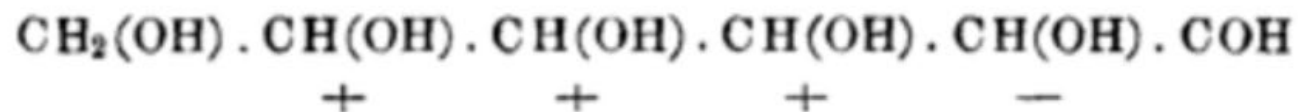


Glucose

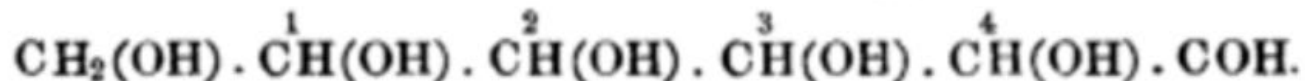
432. Emil Fischer: Ueber die Configuration des Traubenzuckers und seiner Isomeren. II.

[Mittheilung aus dem chemischen Laboratorium der Universität Würzburg.]
(Eingangen am 8. August.)

In der ersten Abhandlung¹⁾ habe ich für den Traubenzucker die Formel



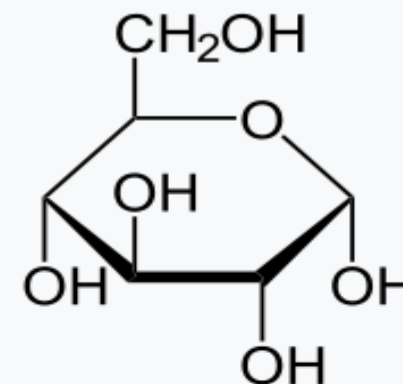
entwickelt. Die Bezeichnung der räumlichen Anordnung durch + und —, welche von van't Hoff eingeführt und von mir in unveränderter Form beibehalten wurde, kann aber bei solchen complicirten Molekülen leicht eine irrthümliche Auffassung zur Folge haben. Um dies zu verhüten, halte ich eine ausführlichere Interpretation der Formeln für nöthig und bezeichne für den Zweck die vier asymmetrischen Kohlenstoffatome mit den Zahlen 1 bis 4



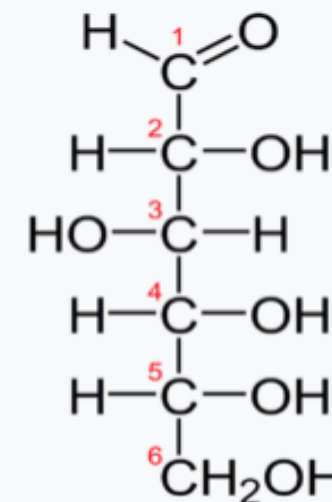
¹⁾ Diese Berichte XXIV, 1836.

Glucose Structure

D-Glucose



Haworth projection of α -D-glucopyranose



Fischer projection of D-glucose

Published: 03 November 1887

Synthesis of Glucose

A. E. TUTTON

Nature **37**, 7–8 (1887) | [Cite this article](#)

3220 [Accesses](#) | [Metrics](#)

Abstract

ANOTHER important acquisition to our store of knowledge has recently been made. Glucose, commonly called grape-sugar, has been artificially prepared by Drs. Emil Fischer and Julius Tafel in the chemical laboratory of the University of Würzburg. This happy achievement, which is announced in the number of the *Berichte* just received, is one which has long been looked forward to, and which cannot fail to give deep satisfaction in chemical circles all over the world. As is generally the case in syntheses of this description, not only has the sugar itself been actually prepared, but, what is at least quite as important, considerable light has been thrown upon that much-discussed question—the constitution of sugars. A most remarkable, and yet only to be expected, attribute of this artificial sugar is that it is found to be entirely incapable of rotating a beam of polarized light. As is well

Nov. 3, 1887]

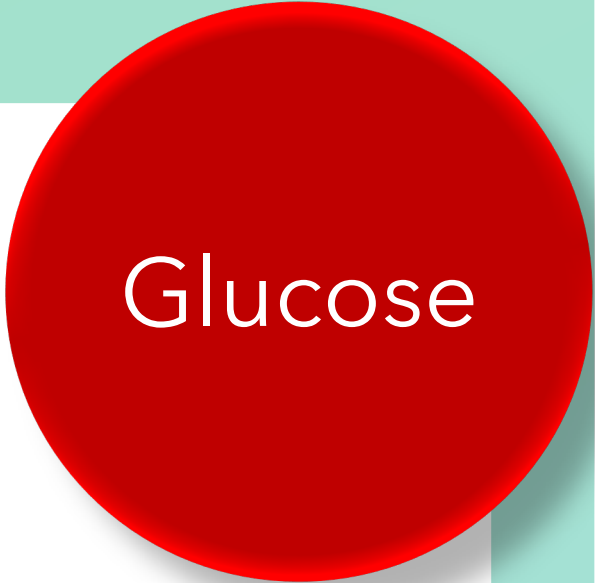
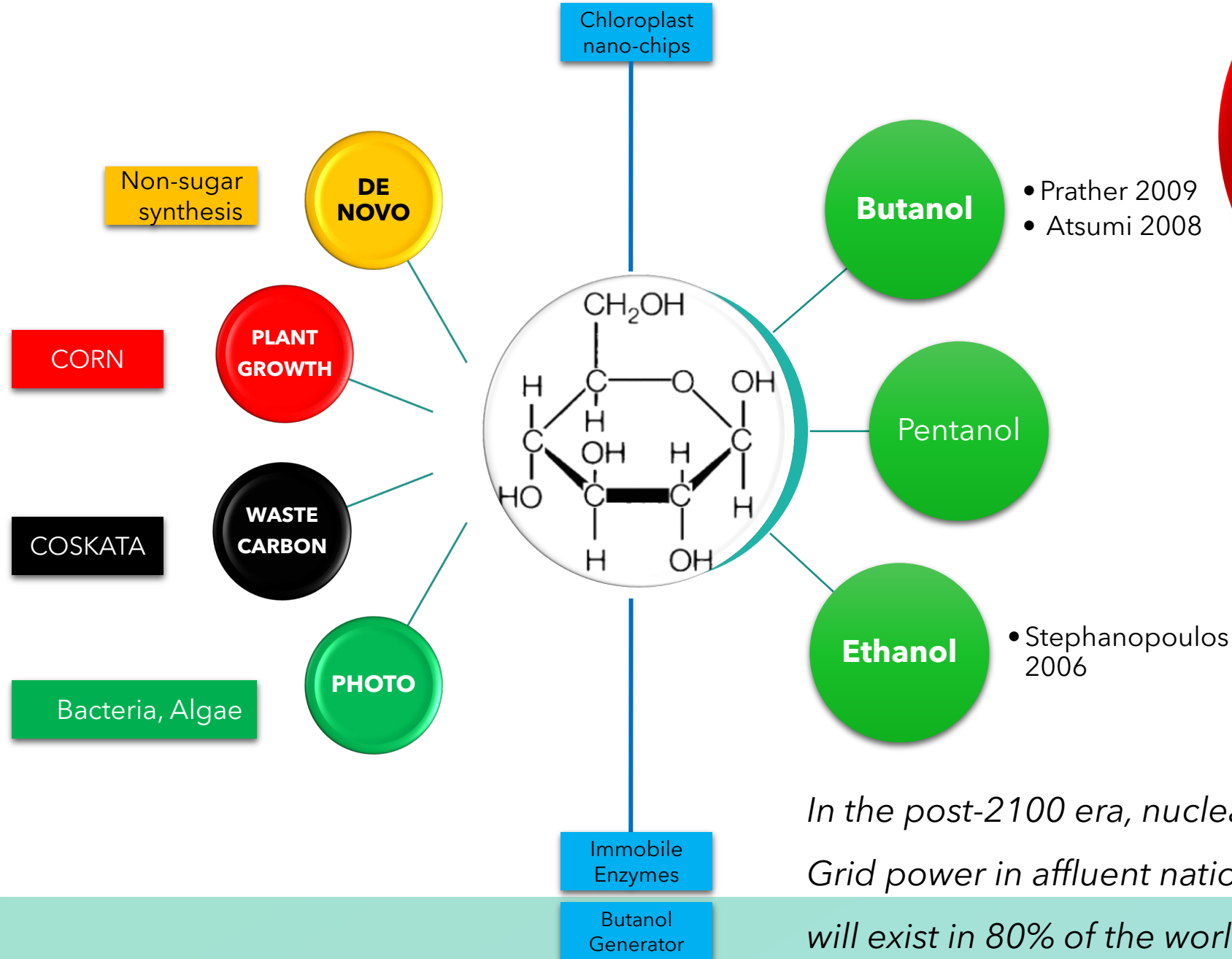
NATURE

SYNTHESIS OF GLUCOSE.

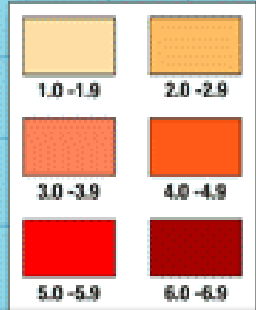
ANOTHER important acquisition to our store of knowledge has recently been made. Glucose, commonly called grape-sugar, has been artificially prepared by Drs. Emil Fischer and Julius Tafel in the chemical laboratory of the University of Würzburg.

We have known GLUCOSE since 1747, it was synthesized in 1887 and structure confirmed in 1891.

Yet we are still incapable of efficient *de novo* synthesis of glucose.



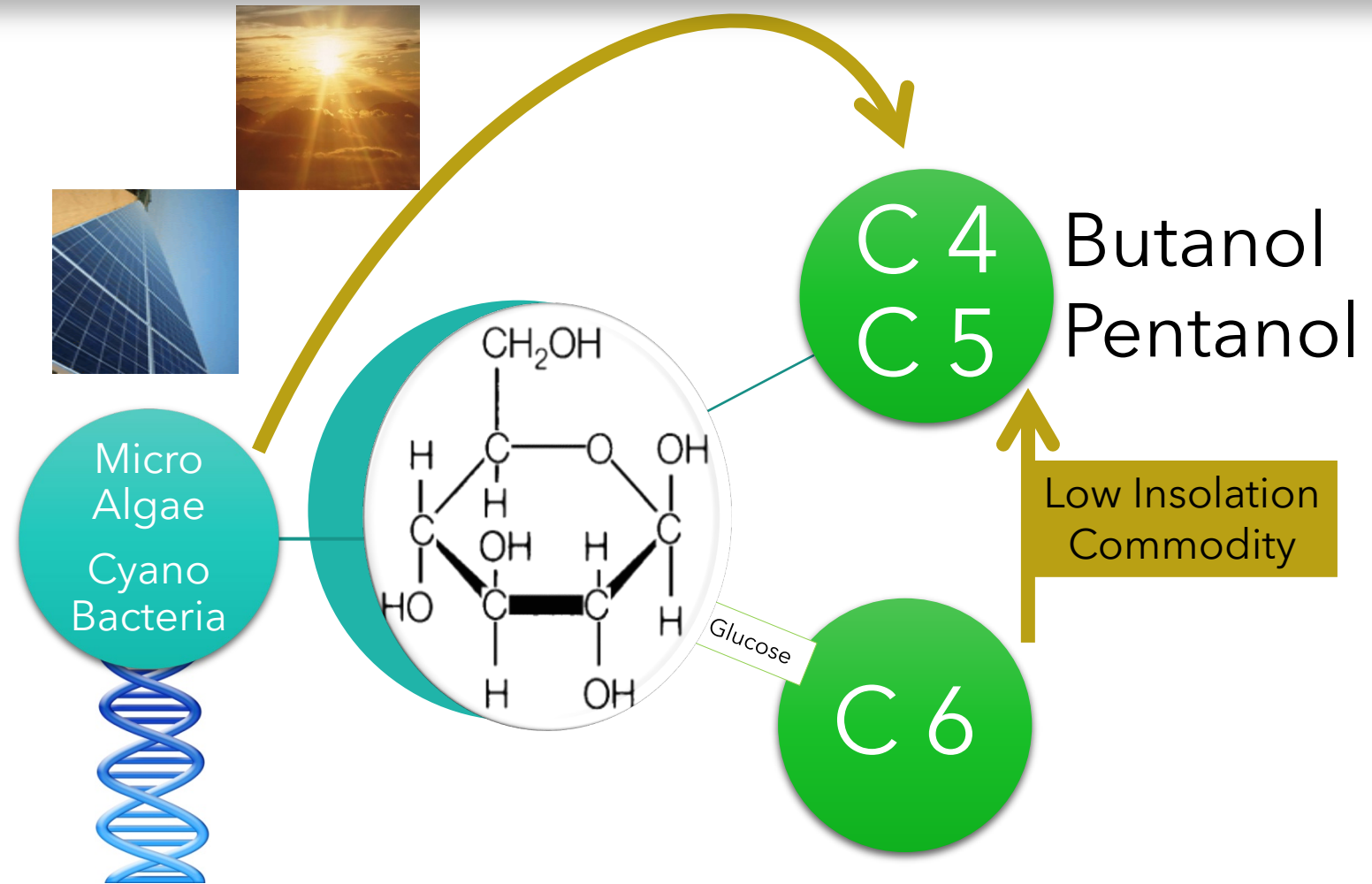
In the post-2100 era, nuclear fusion may dominate Grid power in affluent nations. Liquid fuel demand will exist in 80% of the world. Will it catapult glucose?



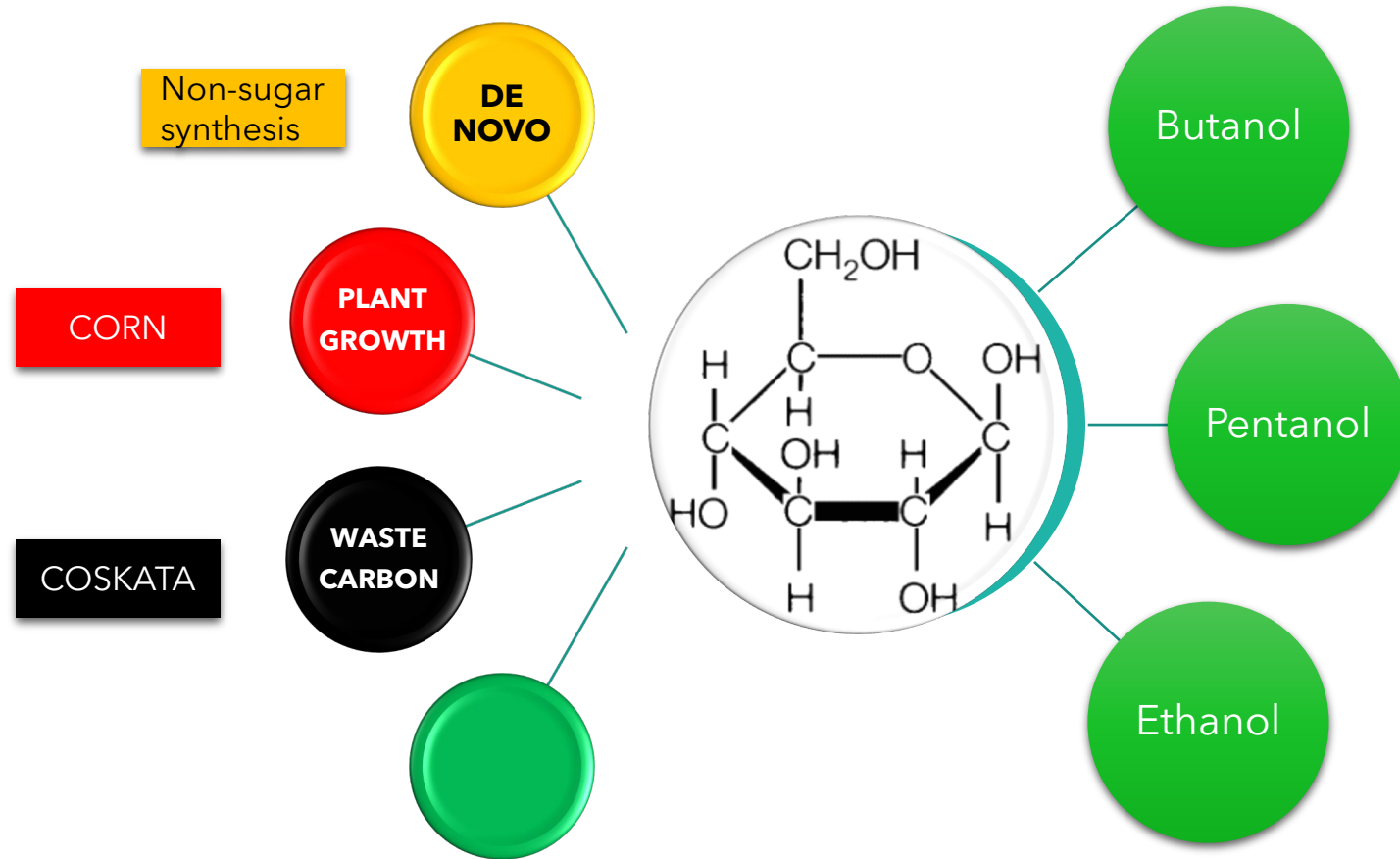
High Insolation Zones

SAHARA SOLAR CORPORATION

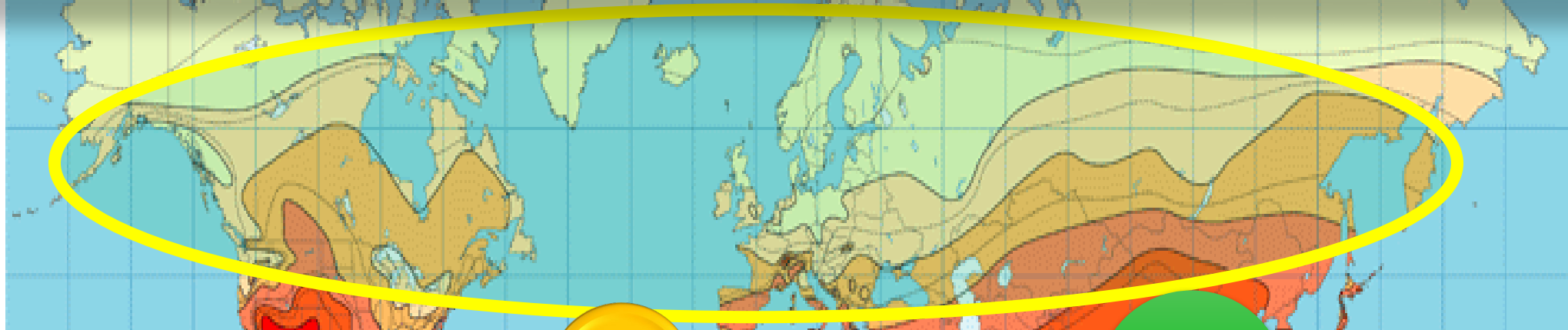
Photosynthetic Butanol Production in High Insolation Zones



Glucose as a Commodity for Liquid Fuel Supply Chain? Can Glucose serve as an intermediary in low insolation?



Glucose as an intermediary in Low Insolation Zones ?

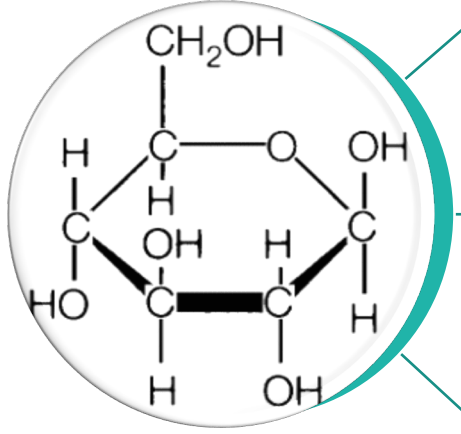


Non-sugar
synthesis

**DE
NOVO**

**PLANT
GROWTH**

**WASTE
CARBON**

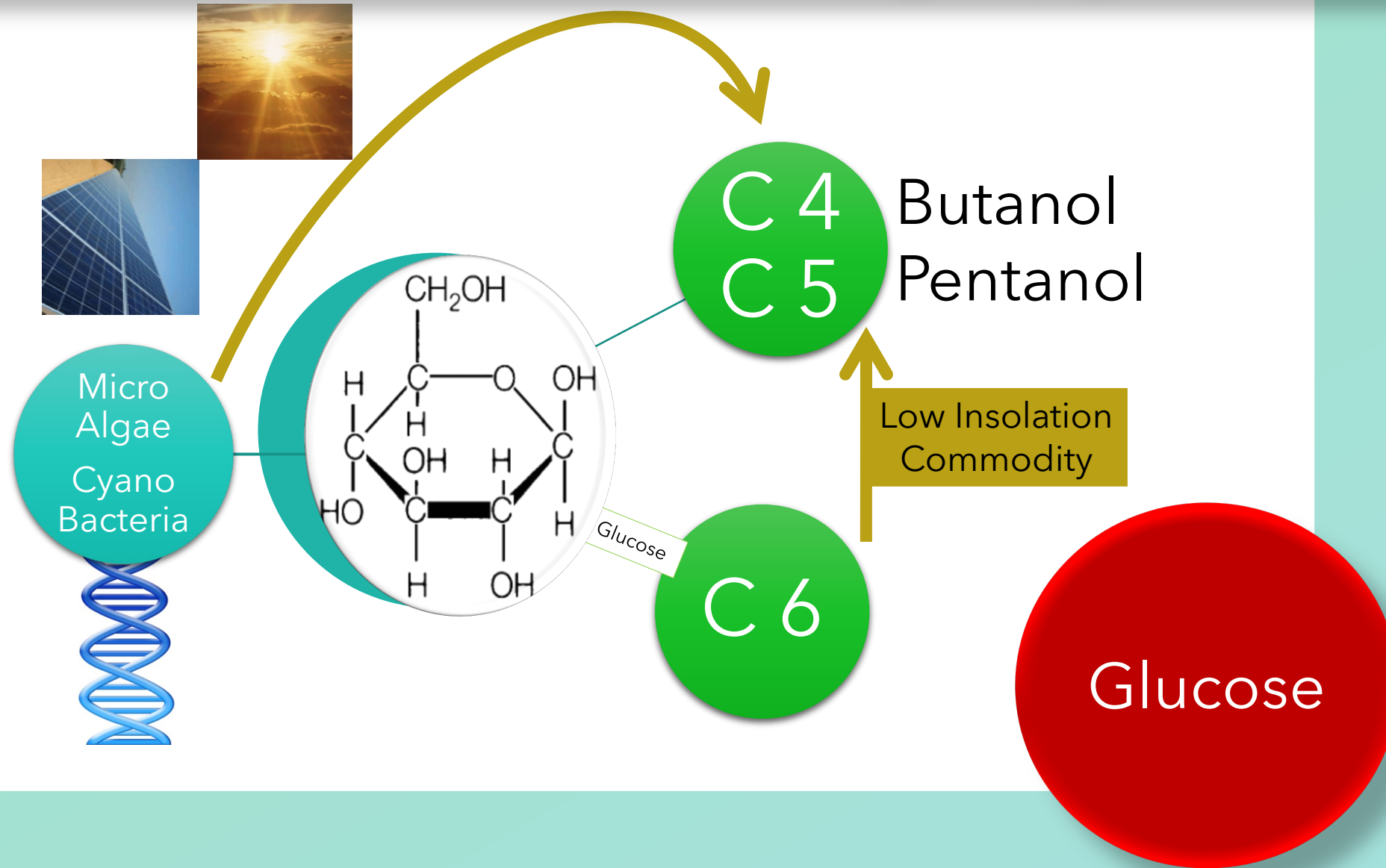


Butanol

Pentanol

Ethanol

Glucose from low insolation zones can be used to produce Butanol & Pentanol which can be used directly as liquid fuel

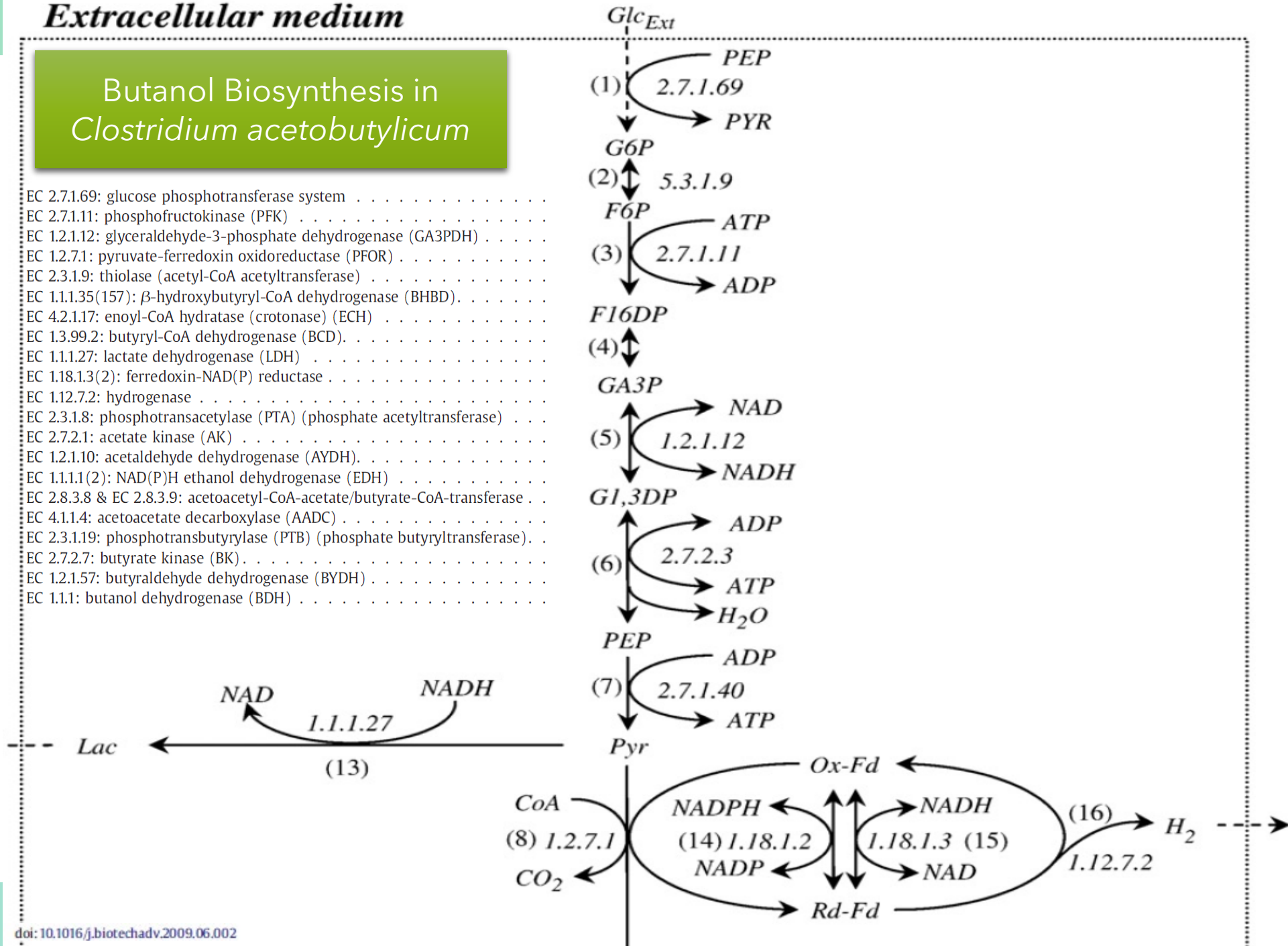


How difficult is it to produce
butanol and pentanol ?

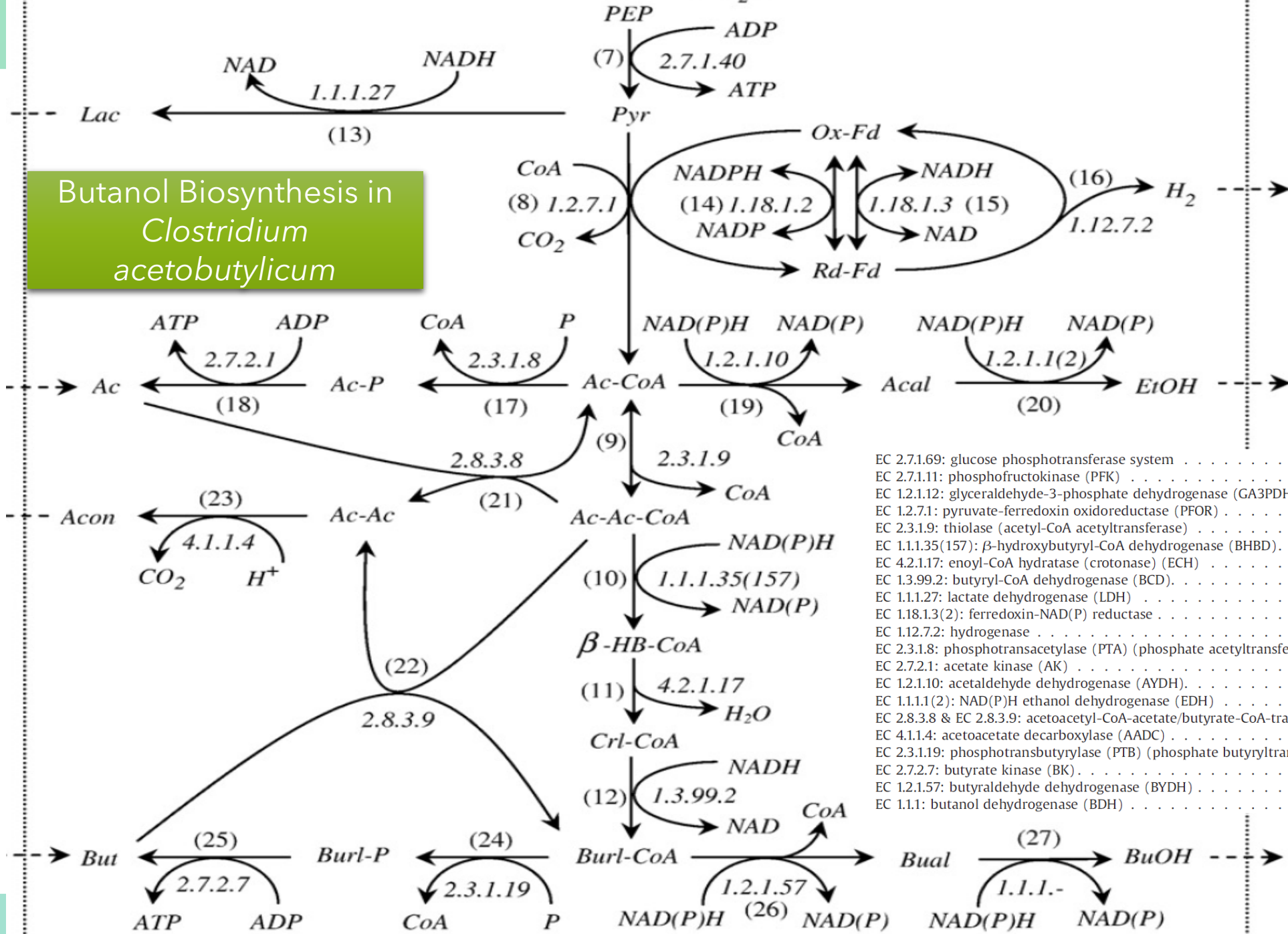
Extracellular medium

Butanol Biosynthesis in *Clostridium acetobutylicum*

- EC 2.7.1.69: glucose phosphotransferase system
- EC 2.7.1.11: phosphofructokinase (PFK)
- EC 1.2.1.12: glyceraldehyde-3-phosphate dehydrogenase (GA3PDH)
- EC 1.2.7.1: pyruvate-ferredoxin oxidoreductase (PFOR)
- EC 2.3.1.9: thiolase (acetyl-CoA acetyltransferase)
- EC 1.1.1.35(157): β -hydroxybutyryl-CoA dehydrogenase (BHBD).
- EC 4.2.1.17: enoyl-CoA hydratase (crotonase) (ECH)
- EC 1.3.99.2: butyryl-CoA dehydrogenase (BCD).
- EC 1.1.1.27: lactate dehydrogenase (LDH)
- EC 1.18.1.3(2): ferredoxin-NAD(P) reductase
- EC 1.12.7.2: hydrogenase
- EC 2.3.1.8: phosphotransacetylase (PTA) (phosphate acetyltransferase)
- EC 2.7.2.1: acetate kinase (AK)
- EC 1.2.1.10: acetaldehyde dehydrogenase (AYDH).
- EC 1.1.1.1(2): NAD(P)H ethanol dehydrogenase (EDH)
- EC 2.8.3.8 & EC 2.8.3.9: acetoacetyl-CoA-acetate/butyrate-CoA-transferase
- EC 4.1.1.4: acetoacetate decarboxylase (AADC)
- EC 2.3.1.19: phosphotransbutyrylase (PTB) (phosphate butyryltransferase).
- EC 2.7.2.7: butyrate kinase (BK).
- EC 1.2.1.57: butyraldehyde dehydrogenase (BYDH)
- EC 1.1.1: butanol dehydrogenase (BDH)



Butanol Biosynthesis in *Clostridium acetobutylicum*

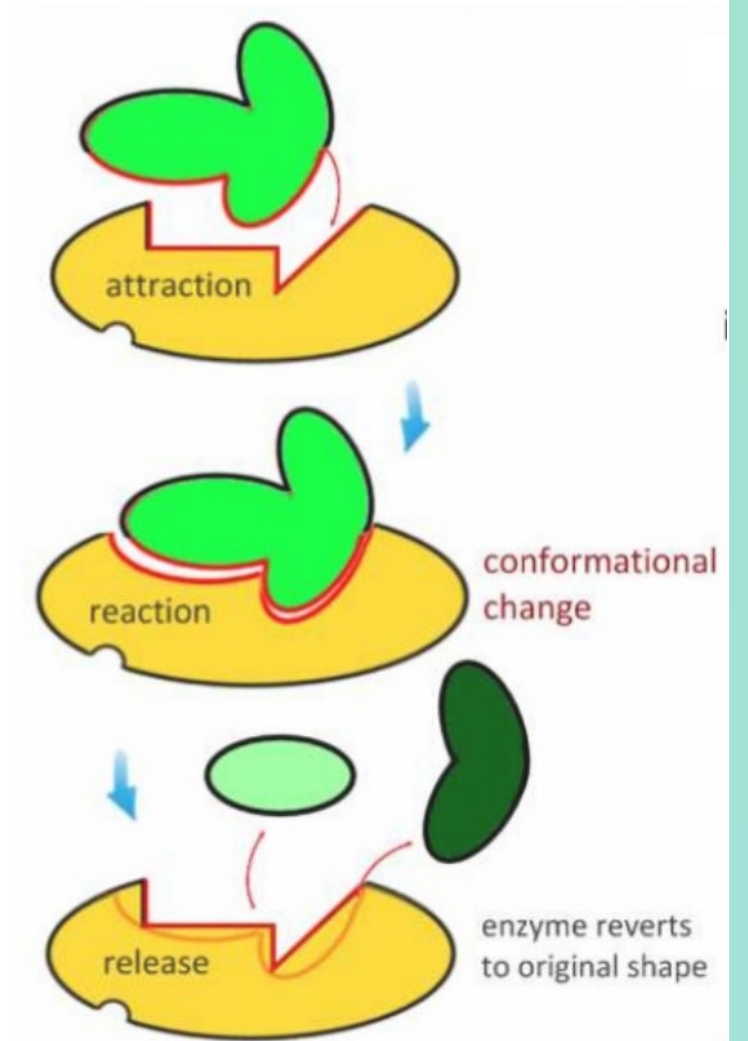


- EC 2.7.1.69: glucose phosphotransferase system
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- EC 1.2.1.12: glyceraldehyde-3-phosphate dehydrogenase (GA3PDH)
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- EC 2.3.1.8: phosphotransacetylase (PTA) (phosphate acetyltransferase)
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- EC 1.2.1.10: acetaldehyde dehydrogenase (AYDH)
- EC 1.1.1.1(2): NAD(P)H ethanol dehydrogenase (EDH)
- EC 2.8.3.8 & EC 2.8.3.9: acetoacetyl-CoA-acetate/butyrate-CoA-transferase
- EC 4.1.1.4: acetoacetate decarboxylase (AADC)
- EC 2.3.1.19: phosphotransbutyrylase (PTB) (phosphate butyryltransferase)
- EC 2.7.2.7: butyrate kinase (BK)
- EC 1.2.1.57: butyraldehyde dehydrogenase (BYDH)
- EC 1.1.1: butanol dehydrogenase (BDH)

Bio-mimicry?

Can we mimic these sequential enzyme-catalyzed steps in a cascade of immobilized enzymes (on material surfaces)?

ENZYMES



ENZYMES

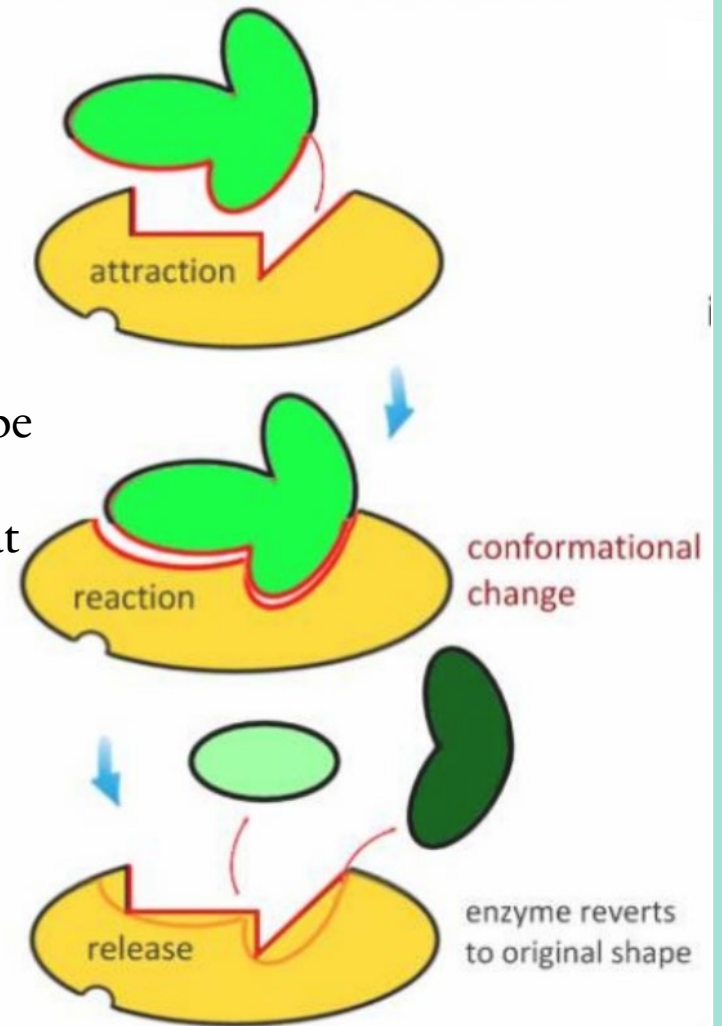
Biological Catalysts

French chemist Anselme Payen was the 1st to discover an enzyme, diastase, in 1833. In 1877, German physiologist Wilhelm Kühne (1837–1900) first used the term *enzyme*, which comes from Greek ἐνζυμον, "leavened" or "in yeast" to describe this process. To explain the specificity of enzymes, in 1894 Emil Fischer proposed that enzymes and substrates possess specific complementary geometric shapes that fit exactly into one another. But the "lock and key" model was modified in 1958 by Daniel Koshland who proposed the induced-fit mechanism of enzyme action.

Payen A, Persoz JF (1833). "Mémoire sur la diastase, les principaux produits de ses réactions et leurs applications aux arts industriels" [Memoir on diastase, the principal products of its reactions, and their applications to the industrial arts]. *Annales de chimie et de physique*. 2nd (in French). 53: 73–92.

Fischer E (1894). "Einfluss der Configuration auf die Wirkung der Enzyme" [Influence of configuration on the action of enzymes]. *Berichte der Deutschen Chemischen Gesellschaft zu Berlin* (in German). 27 (3): 2985–2993.

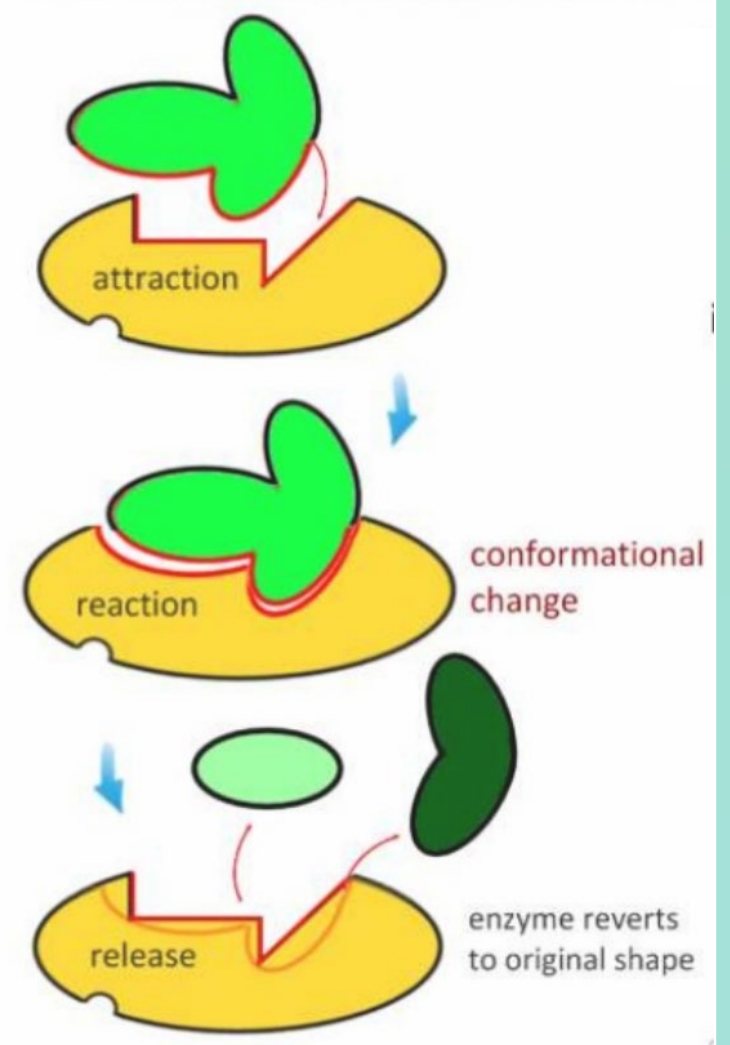
doi:10.1002/cber.18940270364



<https://www.jstor.org/stable/229596>

In 1958, Daniel Koshland suggested a modification to Emil Fischer's (1894) *lock and key* mechanism of enzyme action. Enzymes are flexible structures. In the **induced-fit model** active sites are continuously reshaped by interactions with the substrate as the substrate interacts with the enzyme.

The Induced-Fit Model



Proc Natl Acad Sci U S A. 1958 Feb; 44(2): 98–104.

PMCID: PMC335371

doi: [10.1073/pnas.44.2.98](https://doi.org/10.1073/pnas.44.2.98)

PMID: [16590179](https://pubmed.ncbi.nlm.nih.gov/16590179/)

Application of a Theory of Enzyme Specificity to Protein Synthesis*

D. E. Koshland, Jr.[†]

[Author information](#) ▶ [Copyright and License information](#) [Disclaimer](#)

BIOLOGY DEPARTMENT, BROOKHAVEN NATIONAL LABORATORY, UPTON, NEW YORK

[†] Visiting professor of chemistry, Cornell University, 1957-58.

* Research carried out at Brookhaven National Laboratory under the auspices of the U.S.

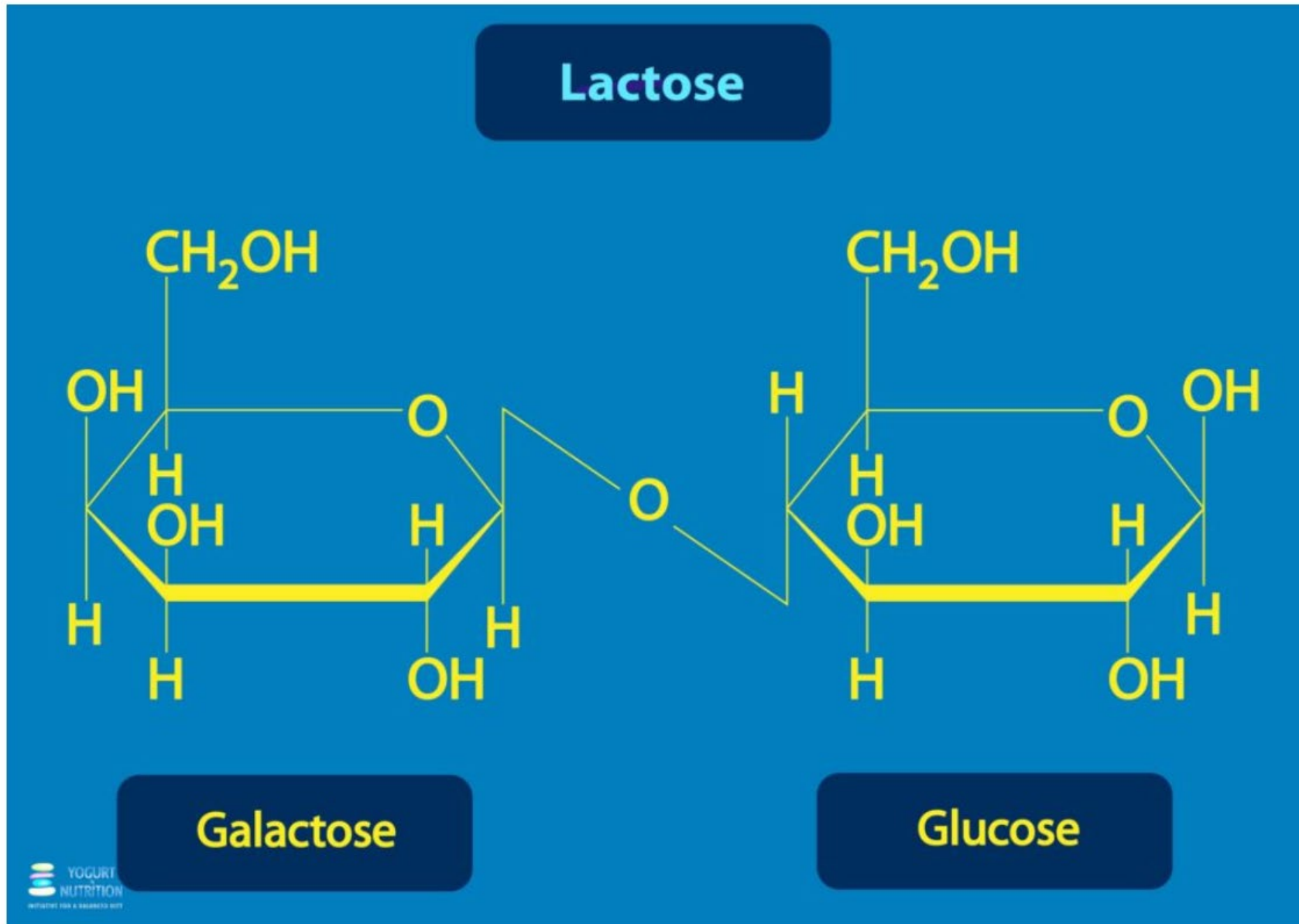
Atomic Energy Commission.

Immobilized enzymes

Application of enzymes tethered to surfaces.

Science for society.

The lactose is a carbohydrate (“sugar”) exclusively found in milk and dairy products. It is a disaccharide, composed of galactose and glucose. www.yogurtinnutrition.com/tag/lactose



Lactose malabsorption exists in **two-thirds of the world's population.** Data reveals regional pattern of **lactose intolerance.**

Lactose intolerance

Symptoms & causes

Diagnosis & treatment

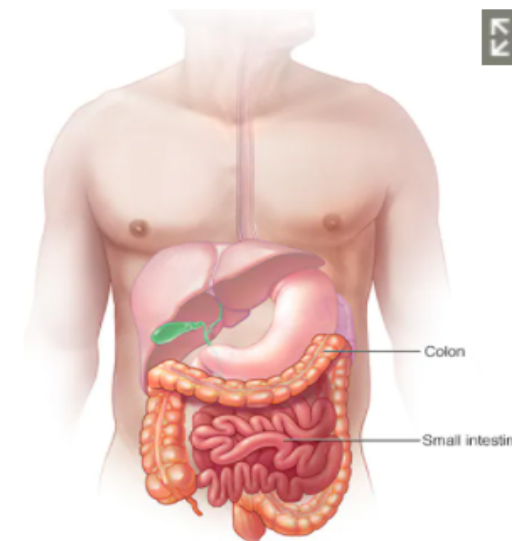
Doctors & departments

Overview

People with lactose intolerance are unable to fully digest the sugar (lactose) in milk. As a result, they have diarrhea, gas and bloating after eating or drinking dairy products. The condition, which is also called lactose malabsorption, is usually harmless, but its symptoms can be uncomfortable.

Too little of an enzyme produced in your small intestine (lactase) is usually responsible for lactose intolerance. You can have low levels of lactase and still be able to digest milk products. But if your levels are too low you become lactose intolerant, leading to symptoms after you eat or drink dairy. <https://www.niddk.nih.gov/health-information/digestive-diseases/lactose-intolerance>

Print



Small intestine

Lactose malabsorption exists in **two-thirds of the world's population.** Data reveals regional pattern of **lactose intolerance.**

LACTOSE IS THE SUGAR NATURALLY FOUND IN DAIRY



Milk
regular

12 g of lactose
(1 cup - 8 oz - 250 mL)



Yogurt
regular

5 g of lactose
(4.4 oz - 125 g)



Low-fat hard cheeses
like cheddar


traces of lactose
(1.6 oz - 45 g)

THE LANCET Gastroenterology & Hepatology

ARTICLES | [VOLUME 2, ISSUE 10, P738-746, OCTOBER 01, 2017](#)

Country, regional, and global estimates for lactose malabsorption in adults: a systematic review and meta-analysis

[Christian Løvold Storhaug, MS](#) [†] • [Svein Kjetil Fosse, MS](#) [†] • [Dr Lars T Fadnes, PhD](#)   • [Show footnotes](#)

Published: July 06, 2017 • DOI: [https://doi.org/10.1016/S2468-1253\(17\)30154-1](https://doi.org/10.1016/S2468-1253(17)30154-1) •  Check for updates

www.thelancet.com/action/showPdf?pii=S2468-1253%2817%2930154-1

Widespread Lactose malabsorption exists in **two-thirds of the world's population.** Data reveals regional patterns of **lactose intolerance.**

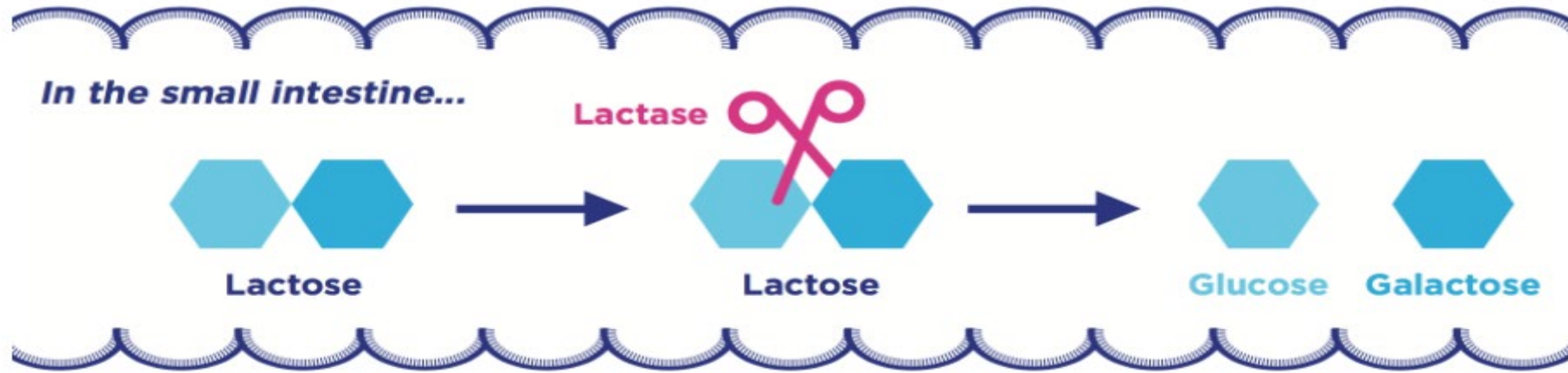
T G T A G T C C C T G

MOLECULAR GENETICS OF LACTOSE INTOLERANCE - IN OUR GENES
Please watch <https://www.youtube.com/watch?v=umiLaW5AmKg&t=4s>

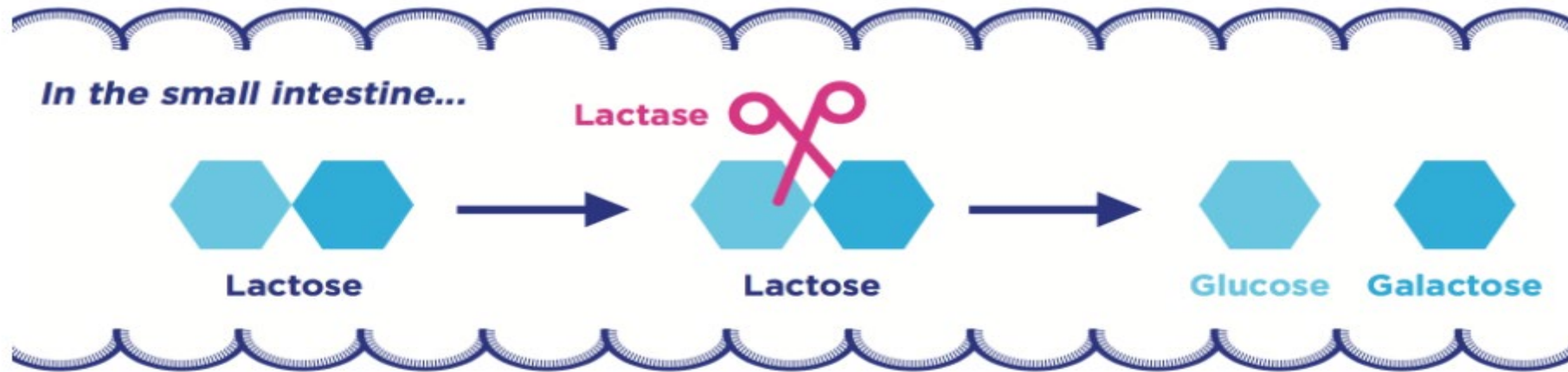
G T A G C C C C T G

Science for society offers a solution

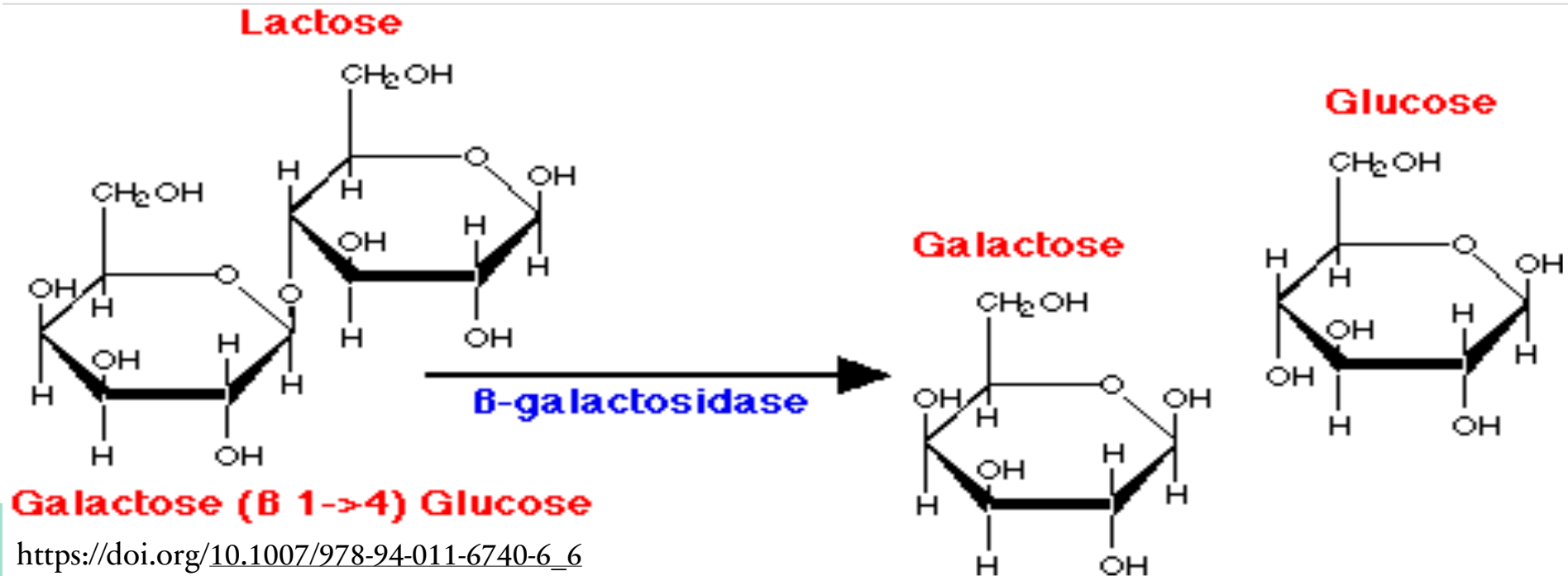
Lactase, an enzyme present in the small intestine, is necessary to split lactose into **glucose** and **galactose**, two simple sugars. <https://www.yogurtinnutrition.com/lactose-as-a-nutrient>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC322277/pdf/jcinvest00210-0168.pdf>



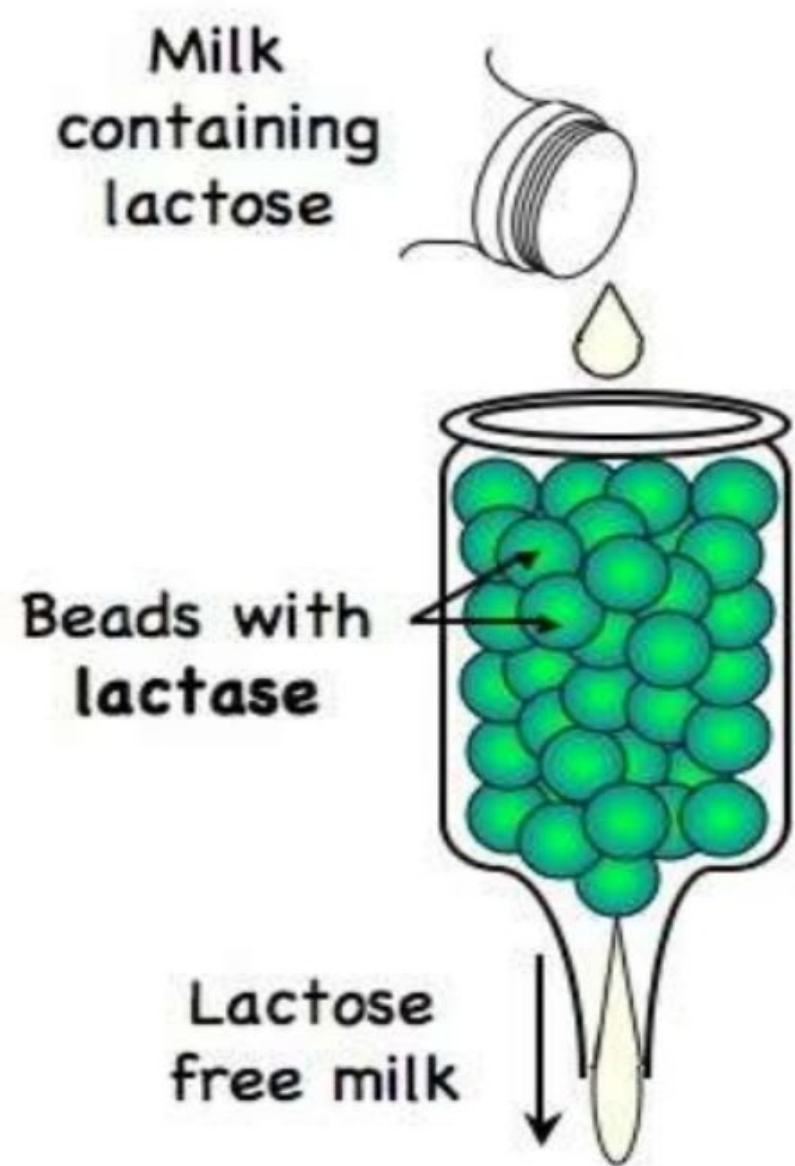
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<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC322277/pdf/jcinvest00210-0168.pdf>



Nijpels H.H. (1981) Lactases and their Applications. In: Birch G.G., Blakebrough N., Parker K.J. (eds) Enzymes and Food Processing. Springer, Dordrecht.

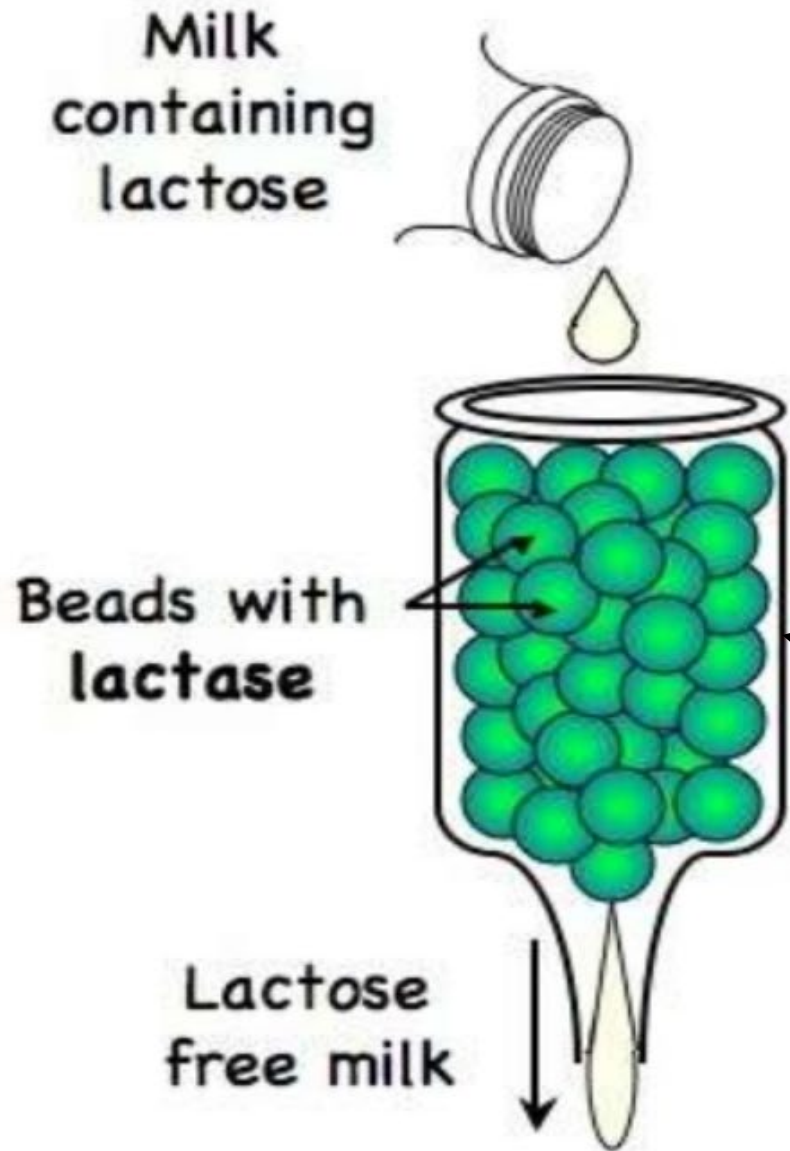


https://doi.org/10.1007/978-94-011-6740-6_6



Production of Lactose-free milk

- Lactase obtained from commonly from yeast (bacteria is an alternative)
- Lactase is bound to the surface of alginate beads
- Milk is passed (repeatedly) over the beads
- The lactose is broken down into glucose and galactose
- The immobilized enzyme remains to be used again and does not affect the quality of the lactose free milk



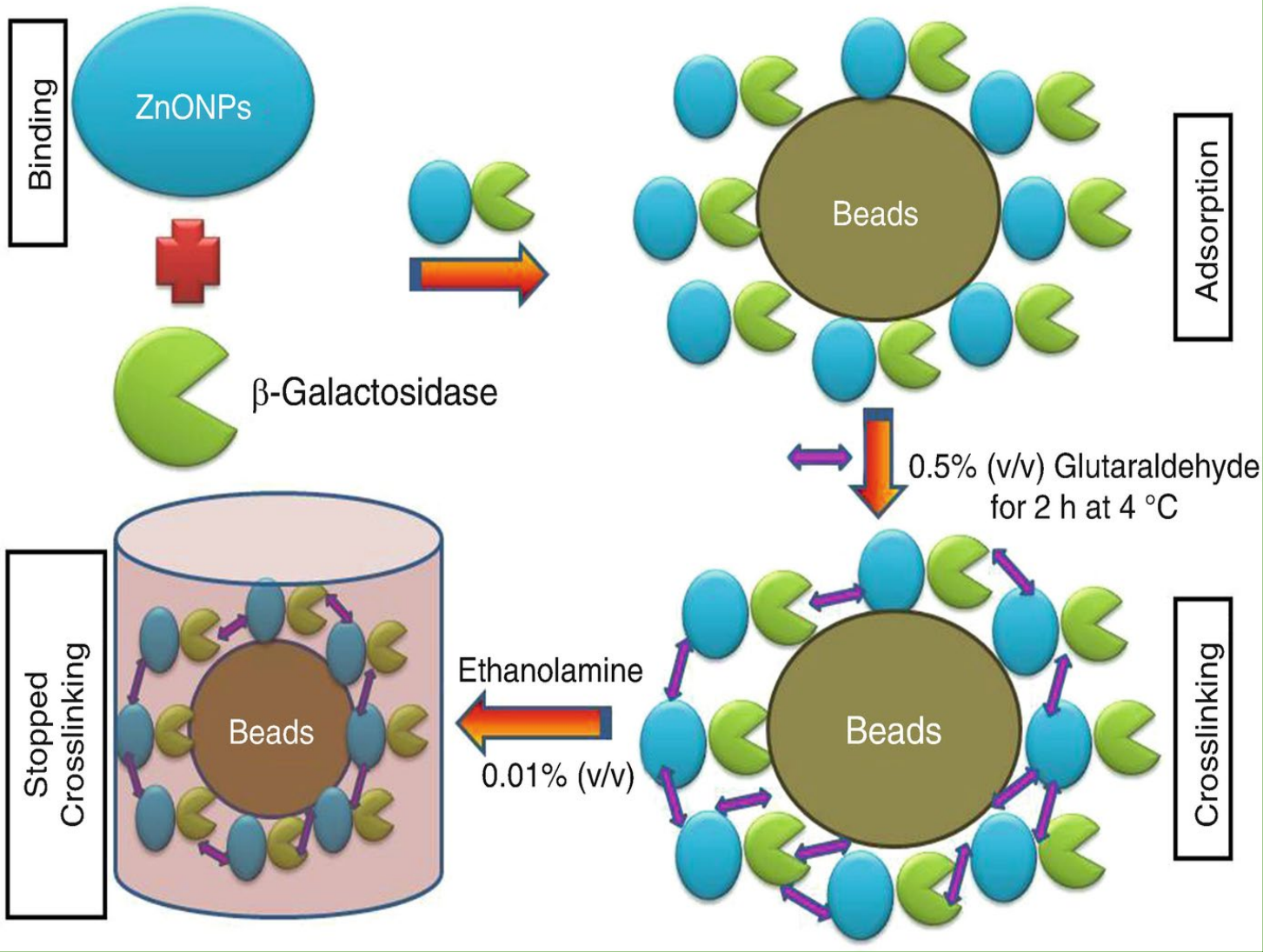
Production of Lactose-free milk

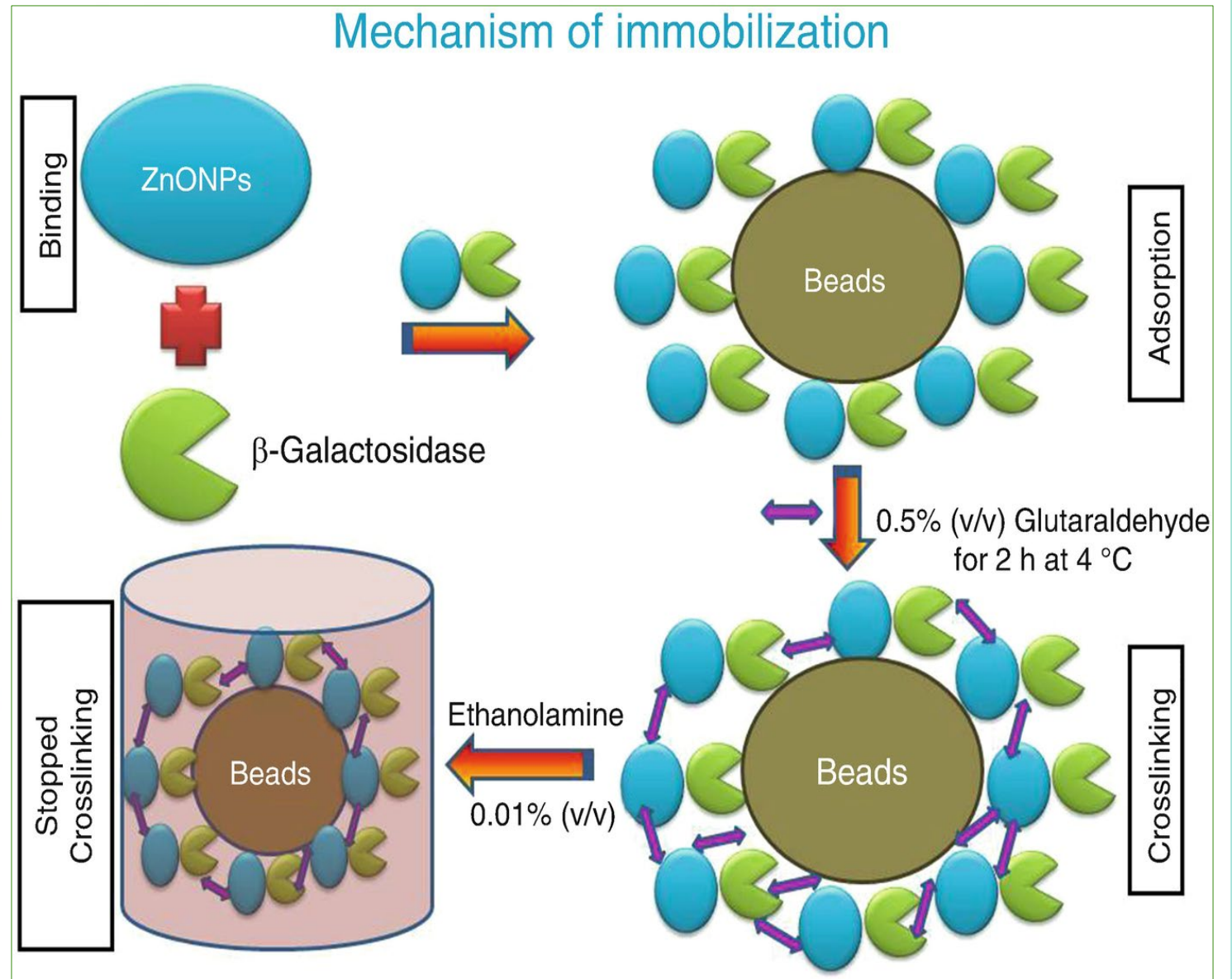
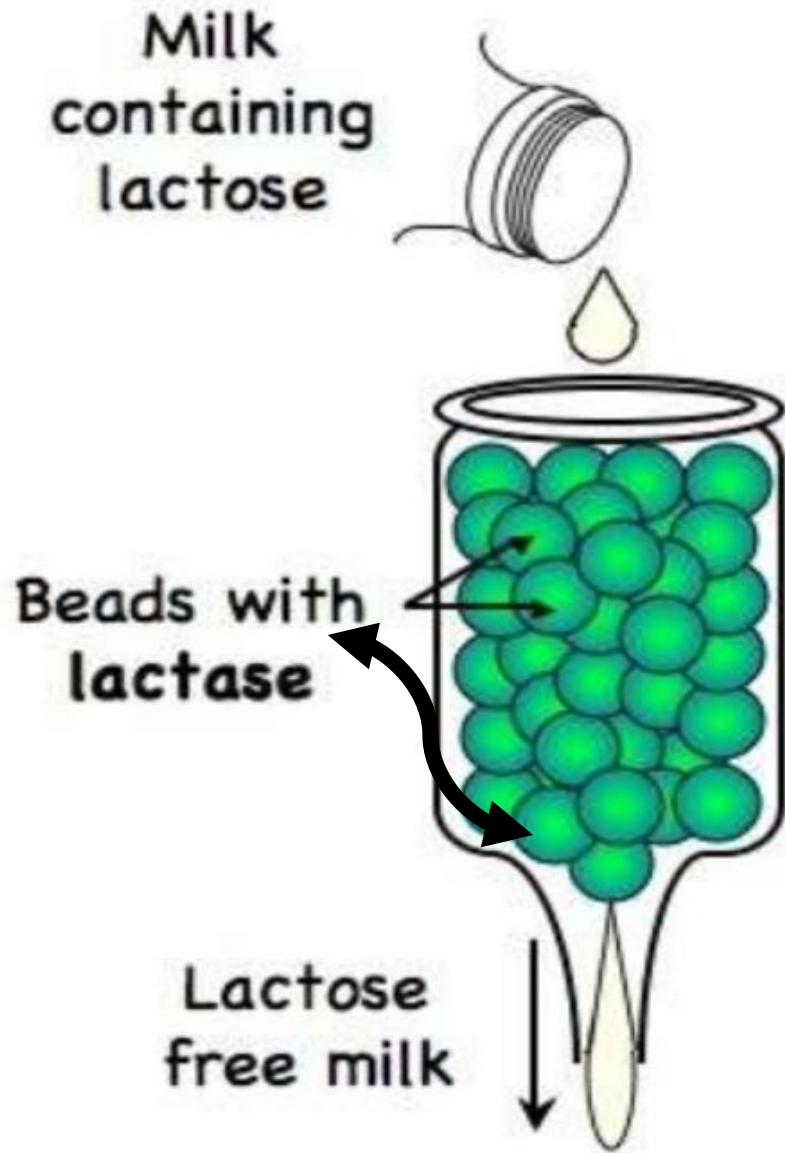
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<https://pubs.acs.org/doi/pdf/10.1021/acs.jafc.9b04385>

Immobilized Enzymes
Science for Society

Mechanism of immobilization

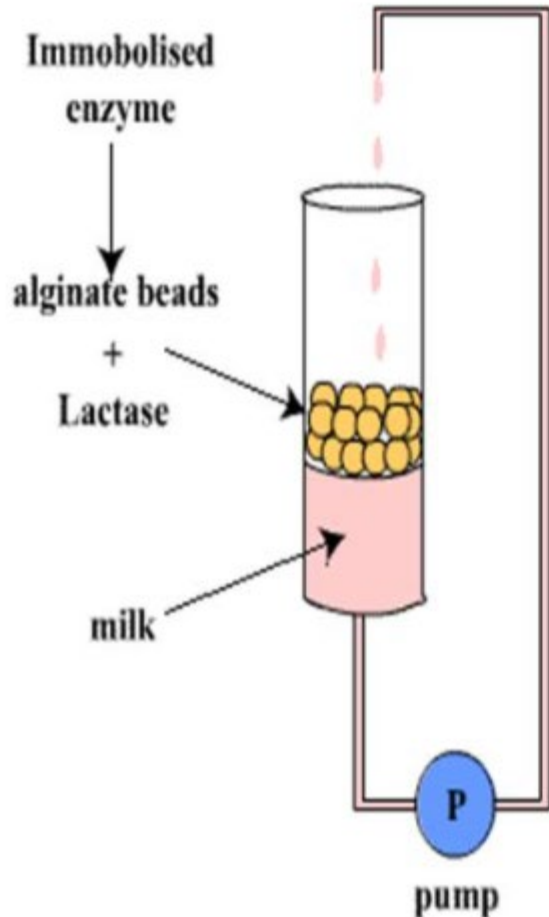






[Nanoscience and Biotechnology for Environmental Applications](#) pp 199-223 | [Cite as](#)

Nanoimmobilization of β -Galactosidase for Lactose-Free Product Development



- **Enzyme Immobilisation:**
- It is possible to make the process more efficient by immobilising the lactase on a recoverable surface such as alginate.
-
- First the Lactase is immobilised in alginate beads.
- Next the beads are placed in a container over which milk can be passed.
- The milk is collected and re-circulated (pump) to convert any remaining lactose to glucose and galactose.
- The circulation is maintained until all lactose has been converted.
- This model of an industrial process allow the lactase to be recovered and re-used (cheaper).
- Efficient conversion of lactose to glucose and galactose.
- reduced purification of milk since enzyme is retained and a high % lactose conversion is achieved.
- All these factors reduce cost particularly on the downstream processing and purification.
-

Vaithilingam Mohanasrinivasan

Request for the
Book Chapter

v.mohan@vit.ac.in

Science for
Society

Daniel Burnham
Architect, Chicago



**MAKE
NO LITTLE
PLANS**

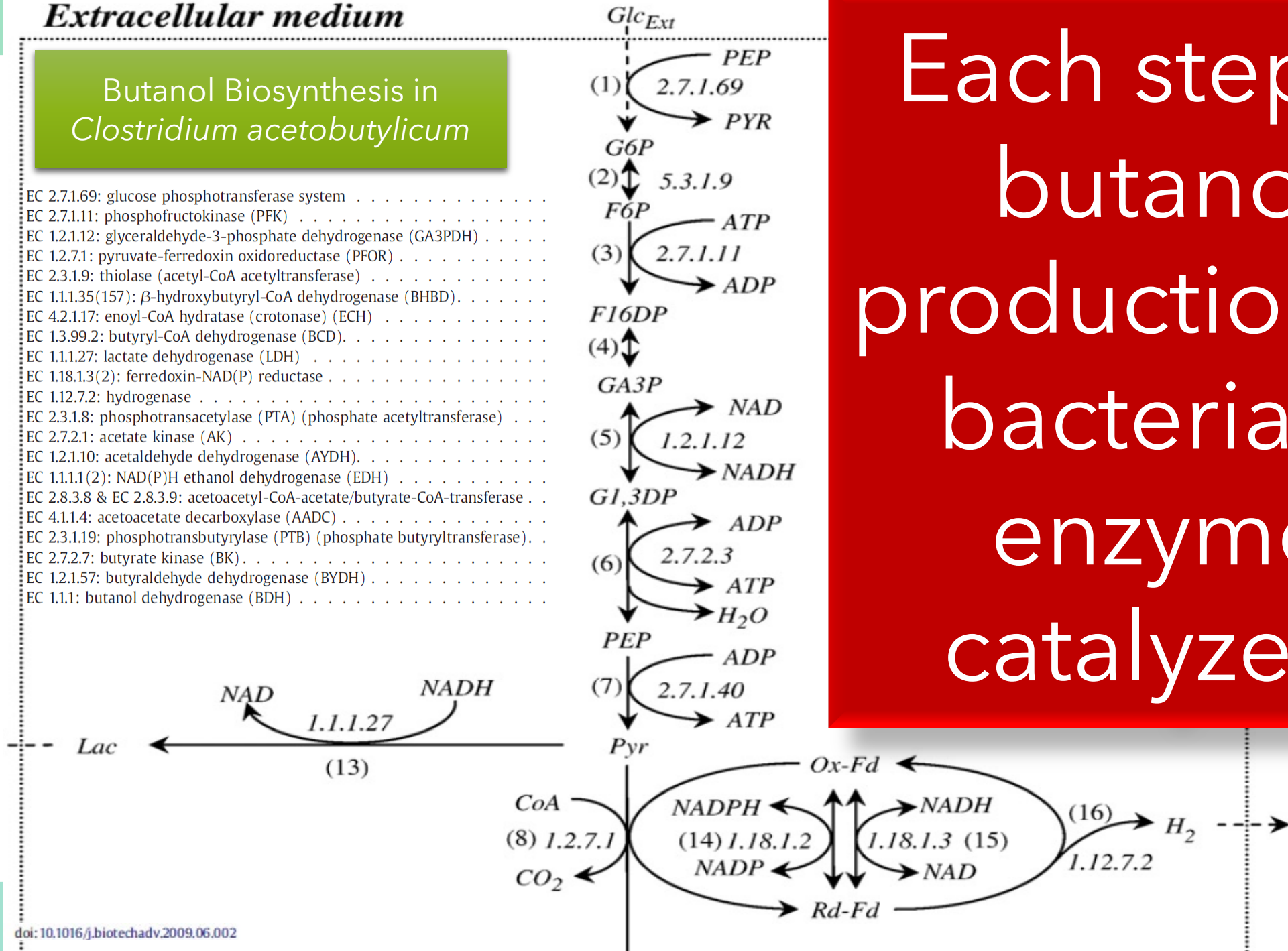
Think big.

Immobilized Enzymes
Science for Society

Extracellular medium

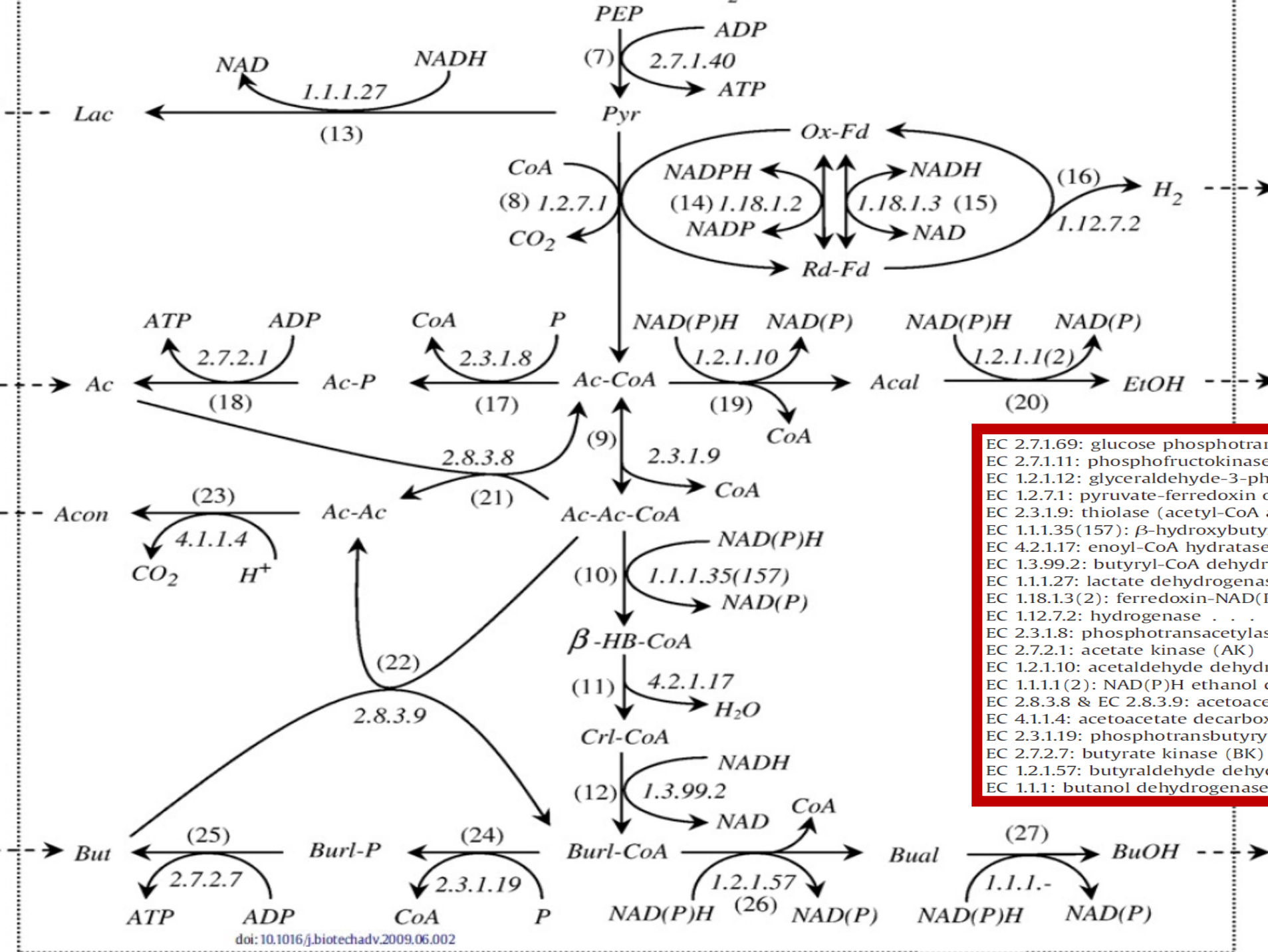
Butanol Biosynthesis in *Clostridium acetobutylicum*

- EC 2.7.1.69: glucose phosphotransferase system
- EC 2.7.1.11: phosphofructokinase (PFK)
- EC 1.2.1.12: glyceraldehyde-3-phosphate dehydrogenase (GA3PDH)
- EC 1.2.7.1: pyruvate-ferredoxin oxidoreductase (PFOR)
- EC 2.3.1.9: thiolase (acetyl-CoA acetyltransferase)
- EC 1.1.1.35(157): β -hydroxybutyryl-CoA dehydrogenase (BHBD).
- EC 4.2.1.17: enoyl-CoA hydratase (crotonase) (ECH)
- EC 1.3.99.2: butyryl-CoA dehydrogenase (BCD).
- EC 1.1.1.27: lactate dehydrogenase (LDH)
- EC 1.18.1.3(2): ferredoxin-NAD(P) reductase
- EC 1.12.7.2: hydrogenase
- EC 2.3.1.8: phosphotransacetylase (PTA) (phosphate acetyltransferase)
- EC 2.7.2.1: acetate kinase (AK)
- EC 1.2.1.10: acetaldehyde dehydrogenase (AYDH).
- EC 1.1.1.1(2): NAD(P)H ethanol dehydrogenase (EDH)
- EC 2.8.3.8 & EC 2.8.3.9: acetoacetyl-CoA-acetate/butyrate-CoA-transferase
- EC 4.1.1.4: acetoacetate decarboxylase (AACDC)
- EC 2.3.1.19: phosphotransbutyrylase (PTB) (phosphate butyryltransferase).
- EC 2.7.2.7: butyrate kinase (BK).
- EC 1.2.1.57: butyraldehyde dehydrogenase (BYDH)
- EC 1.1.1: butanol dehydrogenase (BDH)



Each step in butanol production by bacteria is enzyme catalyzed.

Each "EC" is an enzyme. Immobilize?



- EC 2.7.1.69: glucose phosphotransferase system
- EC 2.7.1.11: phosphofructokinase (PFK)
- EC 1.2.1.12: glyceraldehyde-3-phosphate dehydrogenase (GA3PDH)
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- EC 4.1.1.4: acetoacetate decarboxylase (AADC)
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- EC 2.7.2.7: butyrate kinase (BK)
- EC 1.2.1.57: butyraldehyde dehydrogenase (BYDH)
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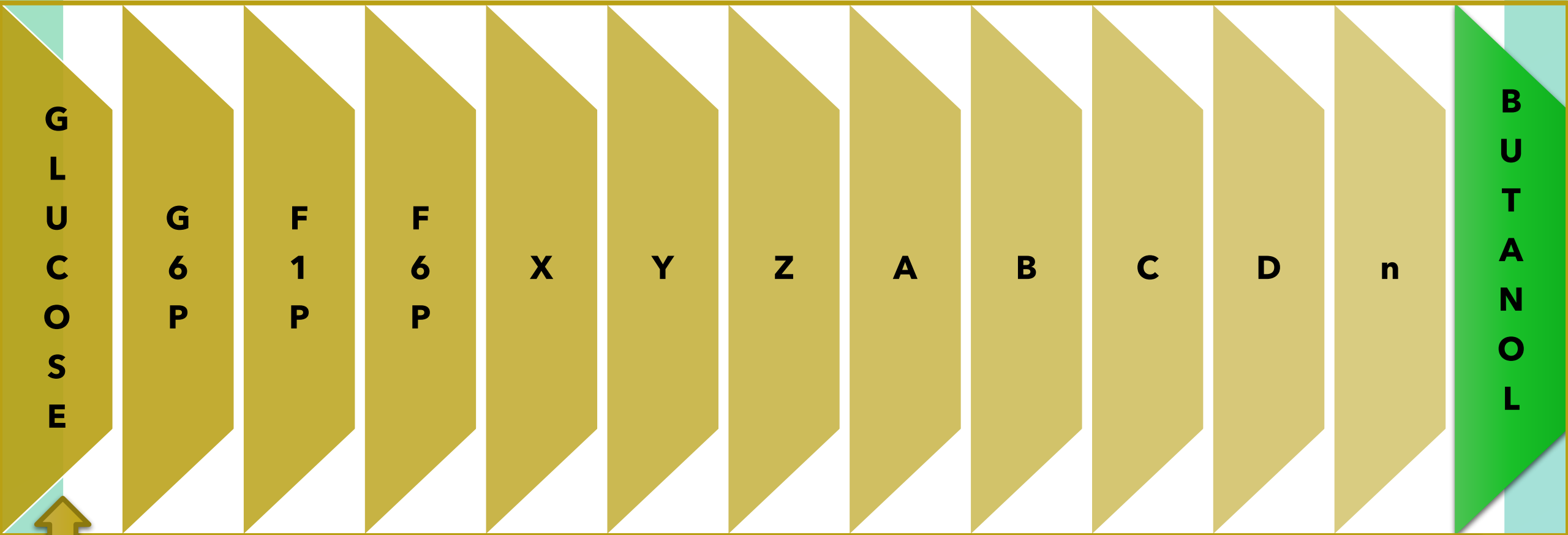
Butanol Biosynthesis in *Clostridium acetobutylicum*

Think big. Dream bigger.

Immobilized Enzymes
Science for Society

Hypothetical Immobilized Enzymatic Catalysis of Glucose to Butanol

Butanol Battery (*I thought ca. 2000 it was going to be real by 2020*)



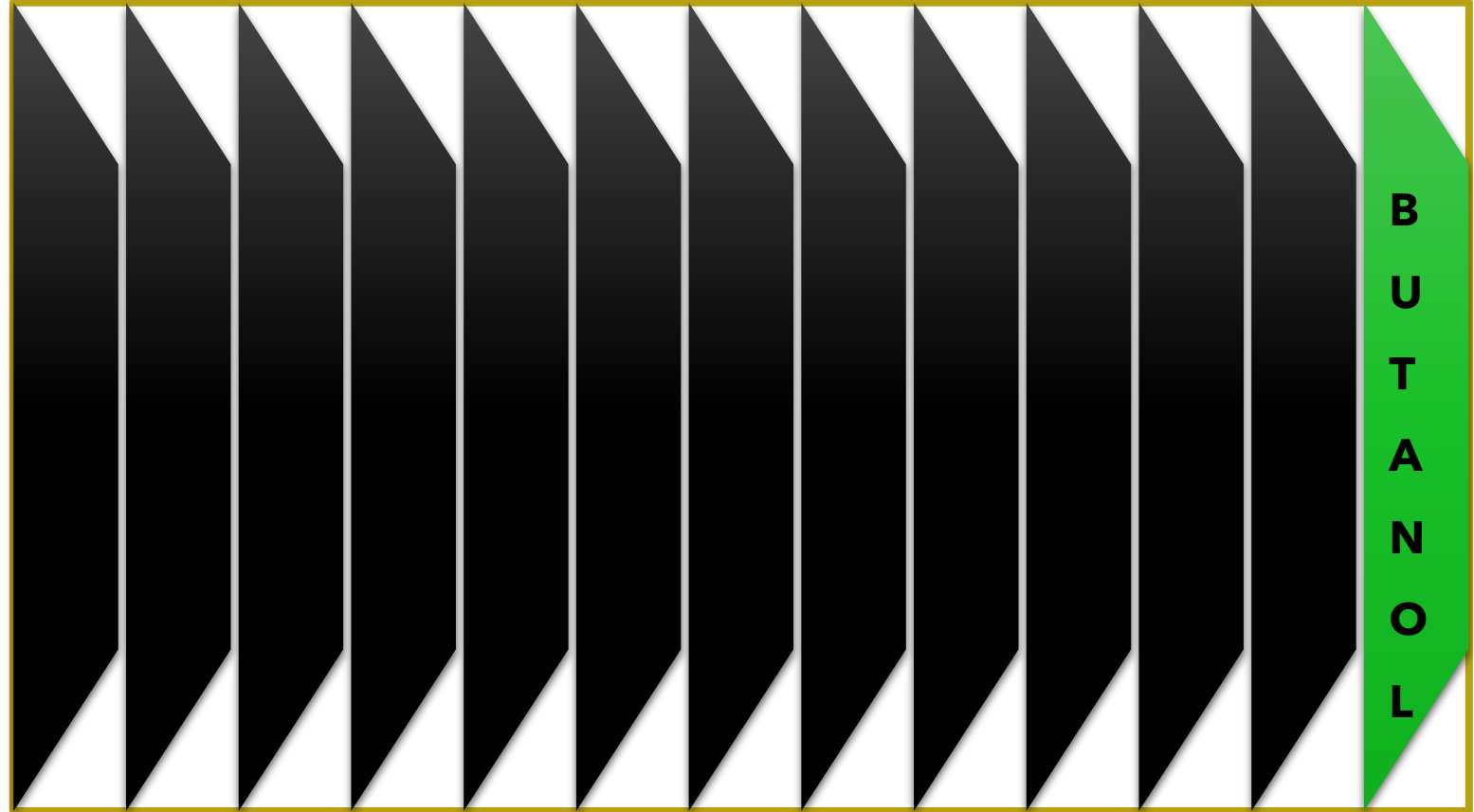
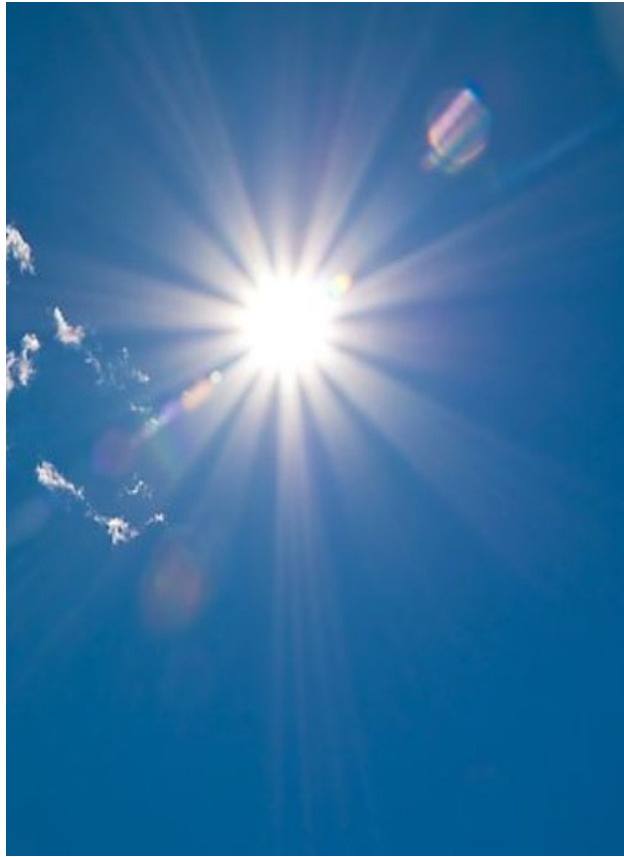
About 10-20 biocatalytic steps in microbes may convert glucose to butanol. These enzymes, if immobilized on substrates, may be arranged sequentially. If functional, the cascade may convert glucose to butanol in a butanol battery!

Even bigger ??

Capture NATURE

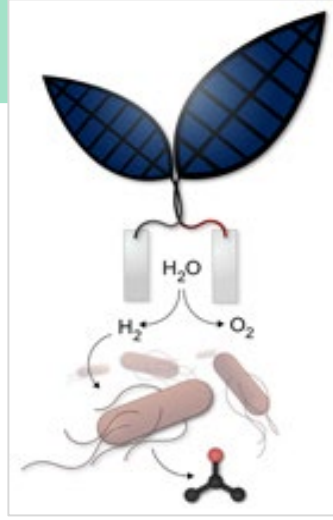
Hypothetical Immobilized Enzymatic Catalysis in Nano-Chloroplasts

2100 AD ??



Light-dependent (photosystem I and II) and light-independent reactions of photosynthesis may be difficult (not impossible) to immobilize (*cartoon*). Many integral proteins in thylakoids in chloroplasts makes it immensely complex.





Bohr,
to Pauli and Heisenberg



“We are all agreed that your theory is crazy. The question that divides us is whether it is crazy enough to have a chance of being correct.”



Wright Flyer in 1903

Heavier-than-air flying
machines are
impossible.

Lord Kelvin



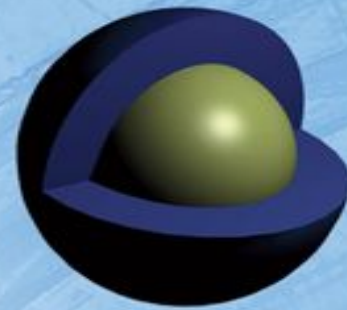
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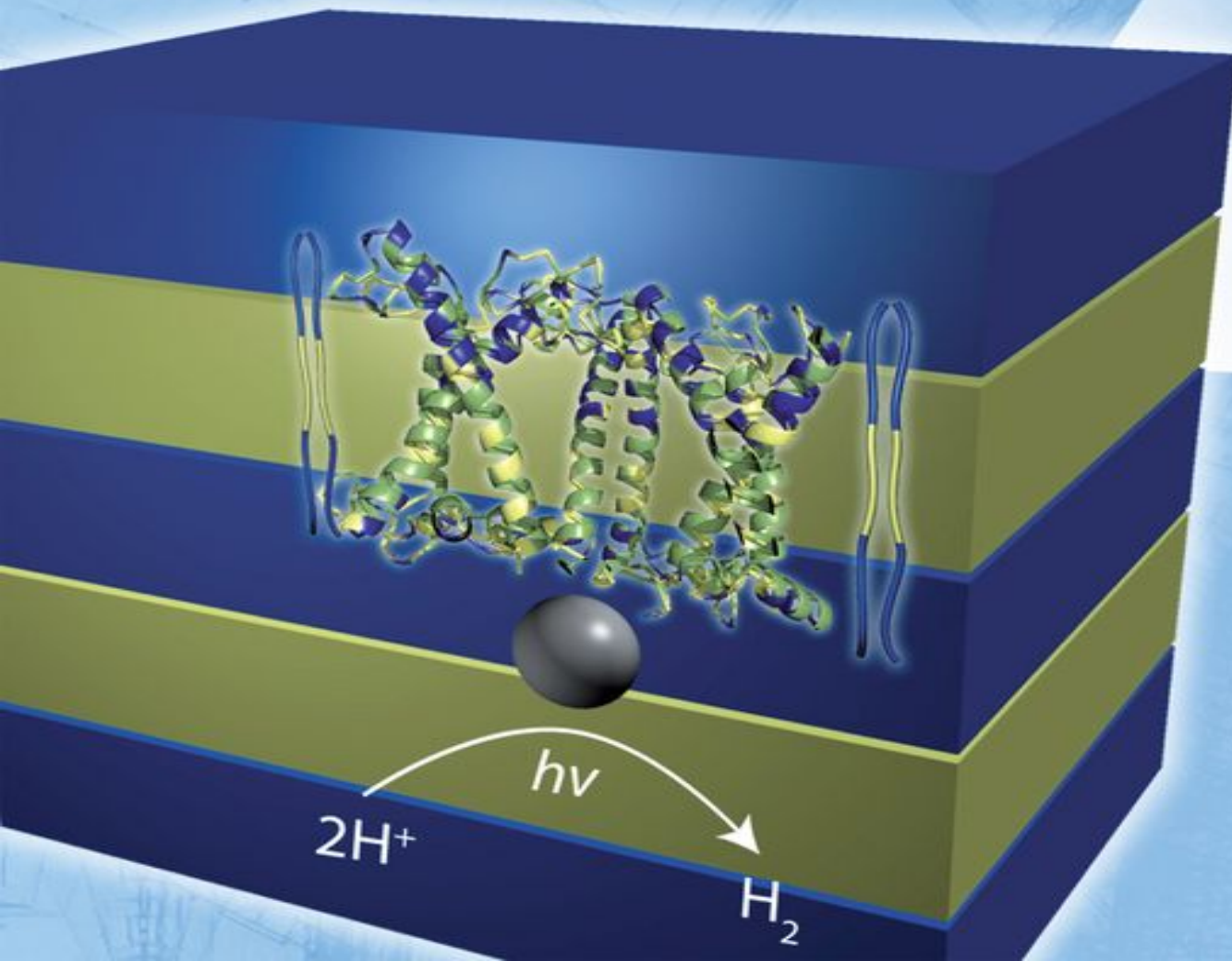
Lord Kelvin

THE PERSON WHO
SAY IT CANNOT BE
DONE SHOULD
NOT INTERRUPT
THE PERSON WHO
IS DOING IT

Supramolecular Assembly of Biohybrid Photo-conversion Systems (2011) Mateus B. Cardoso, Dmitriy Smolensky, William T. Heller, Kunlun Hong & Hugh O'Neill. Energy & Environmental Science (2011) 4 181-188. DOI: 10.1039/C0EE00369G



**Synthetic
photo-bio
Hydrogen
??**



Dr Hugh O'Neill *et al* at the ORNL Center for Structural Molecular Biology and Center for Nanophase Materials Sciences (Oak Ridge National Lab) have developed a bio-hybrid photo-conversion system based on the interaction of photo-synthetic plant proteins with synthetic polymers which can convert visible light into hydrogen fuel. What's next?

In the future, pH may also signify ...

Powered by pH (portable Hydrogen)

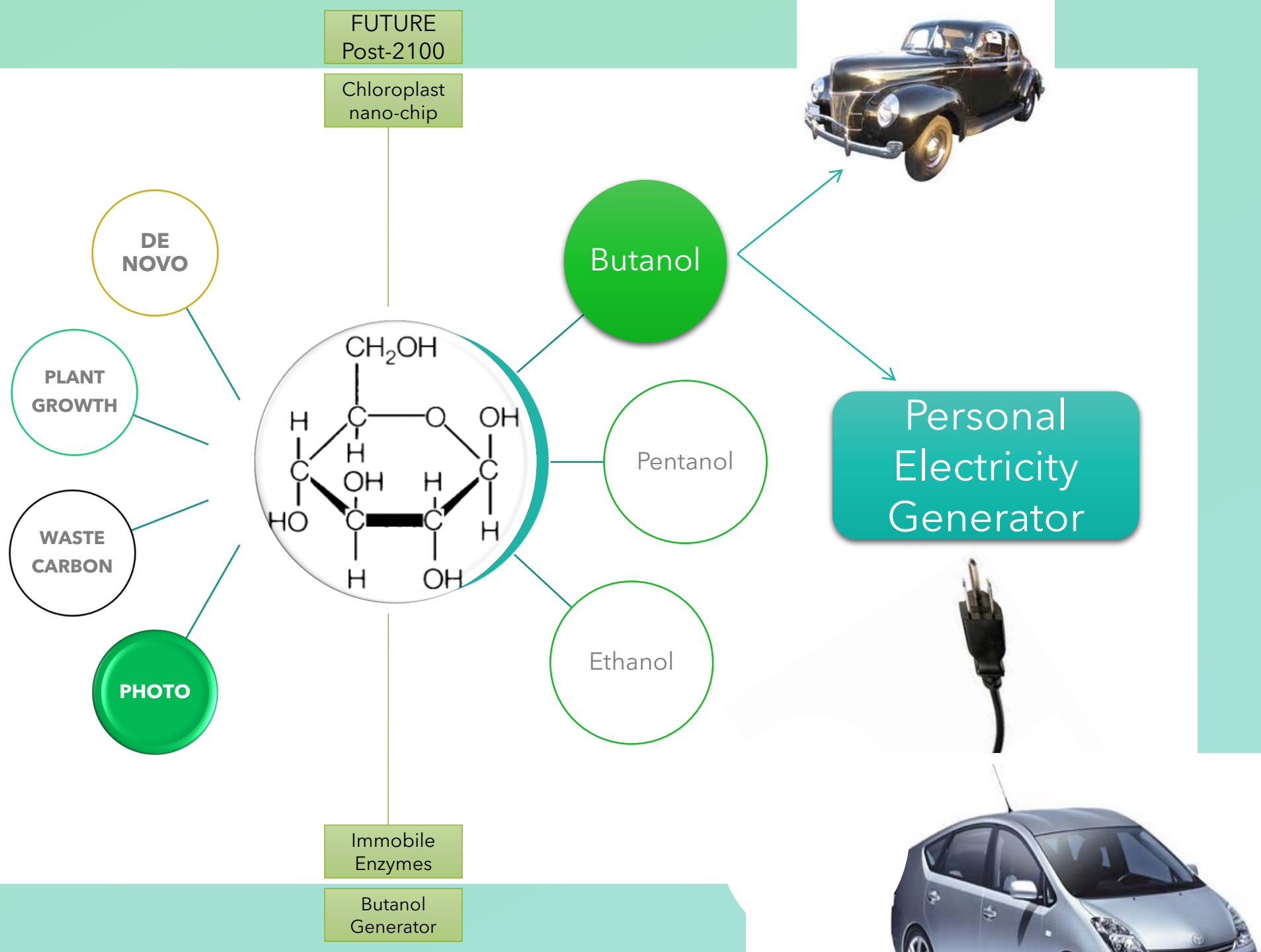
You can help to transform
these ideas into reality.

Can't you?

portable Hydrogen (pH)

Glucose

A grand challenge that can lift many boats but first we must unlock the science. Society in need of scientists.



Simplest things we don't know

DE NOVO (Latin for “new”) synthesis of Glucose is still beyond current knowledge of science and scientists. We do not know how to create glucose molecules from elements (C, carbon; H, Hydrogen; O, oxygen) or common compounds such as water (H₂O) and carbon dioxide (CO₂). What the world needs urgently is a “glucose” version of the chemical synthesis of Penicillin (which saved billions of lives) created in 1957 at MIT by John C. Sheehan and Kenneth R. Henery-Logan. An alternative approach may be a version of the Haber-Bosch process for glucose. Haber-Bosch process uses nitrogen (N) from air and hydrogen (H) from natural gas to synthesize ammonia (NH₃), a fertilizer, which has made it possible to feed billions of people.

But plants do



Photosynthesis



Carbon dioxide

+ Water

Light



Glucose + Oxygen

Chlorophyll



$6\text{CO}_2 + 6\text{H}_2\text{O}$

Light



$\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2$

Chlorophyll

Grand Challenge – Can immobilized enzymatic catalysis (nano-chloroplasts) capture photosynthesis *in silico* ??

At least, can we synthesize glucose from carbon dioxide and water if we cannot capture photosynthesis *in silico* ??

Scientists – we need synthetic glucose

Glucose (sugar) is easily transported in bags and packs. It is energy. We use sugar (glucose) to obtain our energy inside our bodies. What if we can use glucose for energy for cars (power for batteries) and homes (power for batteries). Just like ammonia, “glucose” plants can produce massive amounts of glucose. We can use the glucose (anywhere in the world) to feed the bacteria (in small domestic use equipment or large commercial fermenters) to produce fuel in the form of butanol and/or pentanol which can replace petroleum fossil fuel (petrol). Every household in the world can buy glucose from the grocery store and can produce their own liquid fuel (butanol, pentanol) in their home. The liquid fuel can be used in a generator (replaces petrol, kerosene, gasoline) to power homes and batteries. The batteries can power cars, scooters, vans and when they run out of charge (power) they can be swapped (swappable atoms). We will have power without the shining sun, if it is raining (Cherrapunji, India) or if it is Arctic Cold (Karasjok, Norway). Glucose is a low-cost solution for world’s energy. We need chemists, biologists, and other scientists/engineers to invent/discover how to make synthetic glucose.

What will happen if
all of us produces
C4 and C6
liquid fuels?

Anastomosis of sunlight-dependent C4 production with sunlight-agnostic production of C5

Renewable liquid butanol (C4) can be produced by micro-organisms using energy from sunlight and carbon dioxide from air. Because sunlight is not sufficiently available in parts of the world, butanol can be made in the ABSENCE OF SUNLIGHT if microorganisms are supplied with another source of primary energy, for example, glucose. At present many good sources of glucose are from food items (sugar cane, corn). It has ignited the food v fuel debate due to increasing cost of food items. We can avoid depleting food sources for glucose. Instead of food we can use cyanobacteria which can directly (auto-trophic) produce glucose from sunlight & atmospheric carbon dioxide. Thus, glucose may be viewed as a cash crop and commodity which can create new lines of global business and serve as a novel ingredient in the emerging supply chain of micro-scale renewable energy manufacturing futures. Any country with sufficient sunlight can manufacture glucose. Glucose can be used in the ABSENCE OF SUNLIGHT by other micro-organisms which can use glucose as the primary energy source (and carbon dioxide from air) to produce butanol in an appliance which may function indoors. Hence, butanol can be produced WITHOUT DEPLETING FOOD sources and is agnostic of sunlight (insolation independent). The anastomosis of sunlight-dependent glucose production (as a new commodity in the energy supply chain) with sunlight-agnostic production of butanol may usher microscale energy manufacturing platform as a tool for global economic development and job growth.

<http://dspace.mit.edu/handle/1721.1/59804>

Temporary Questions ?

Is it feasible to partially reduce green house gas (GHG) emissions by manufacturing vegetation-independent non-fossil carbon-neutral C4-C5 renewable liquid fuel from cyano-bacteria (micro-algae) using sunlight and carbon dioxide?

The risk in this manufacturing process is scalability of production volume to make a sufficient contribution as fuel source for global use. The risk may also be a reward. If cost or technology for scalability is unsuitable then production volume may remain low. The low volume product may be suitable and affordable for domestic use or small businesses. If each home or small business owned its independent energy manufacturing appliance (liquid fuel generator), it may reduce demand for grid distributed power. 80% of the global population benefits from low volume even if the affluent nations find it limiting.

Fuel (four-Carbon C4, five-Carbon C5) produced in high insolation (plenty of sun shine) zones will be useful locally but transportation is costly. Hence, the emergence of glucose (six-Carbon C6) as a driver of the future liquid energy supply chain. High insolation zones in developing nations can produce C6 and sell the product to industrialized nations in low insolation zones (less sun shine). Glucose may be converted by a variety of microbial or other methods to C4,C5 fuels without sunlight or the need to source vegetation or waste. Inventory of glucose may provide nations with energy security and partially reduce the uncertainty from energy prices which triggers volatility in economic development and socio-economic stability.

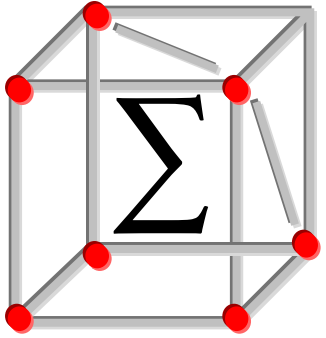
Production of C6 from embedded photosynthetic enzymatic components immobilized on chips is a possible extension of the convergence of bio and nano-technology for renewable energy. In a manner similar to present-day solar panels, 22nd Century may expect “nano-chloroplast” panels for manufacturing glucose-on-a-chip or C4/C5 chips. The latter may harness solar energy in chemical bonds. It may be used on-demand rather than directly generating electricity from photo-voltaic cells where energy may rapidly perish, if unused (unless storage technology significantly improves the life of energy in batteries). In the interim, glucose from microbes may become an important energy commodity and lift many nations out of poverty.

Distributed Energy Production

Energy Manufacturing as a Cottage Industry ??

Hypothetical Proposal by Shoumen Palit Austin Datta, 2009-2010 ♦ <http://dspace.mit.edu/handle/1721.1/59804>

Nobel Prize winner (chemistry) Robert F. Curl vehemently **disagreed** with this hypothetical proposal by the author (Shoumen Palit Austin Datta).



MICRO-SCALE

ENERGY

MANUFACTURING

Photo Bio C₄(C₅) Reactor



C4 PRODUCT
DEVELOPMENT

SOLAR DEPENDENT
PHOTO BIO C4
REACTOR



INSIDE BIO-REACTOR

ROTARY SHAKER

AERATION FOR
GROWTH

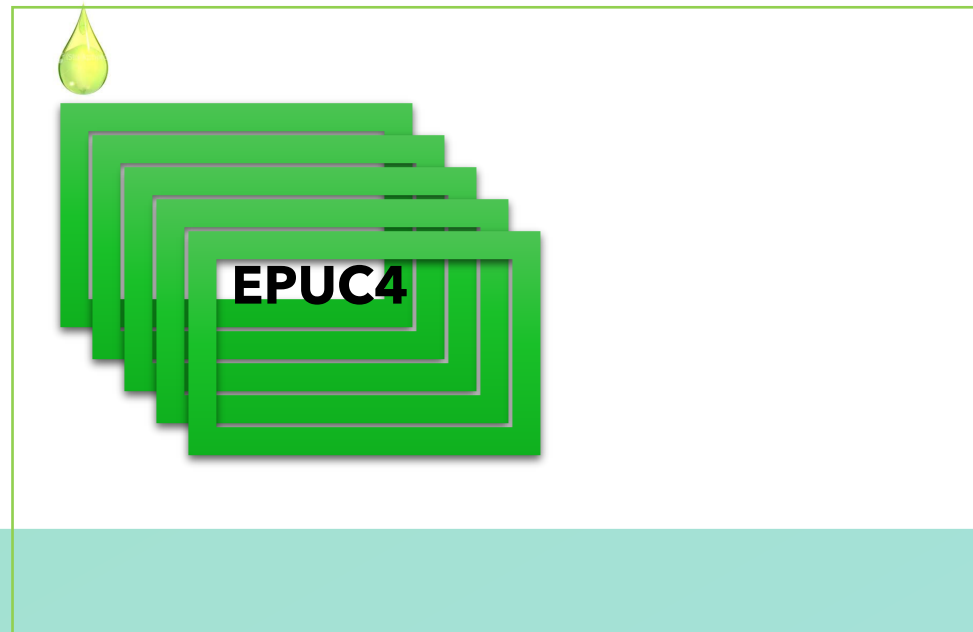


INPUT
MICRO-ORGANISMS
+ MINIMAL MEDIA

EXPOSE TO
SUNLIGHT

**OUTDOOR
APPLIANCE**

Microbes use sunlight for photo-catalytic conversion of nutrients to glucose (or other saccharides) and then convert the glucose (C₆) to butanol (C₄) liquid fuel. If we add glucose as the primary nutrient then the process is **agnostic** of sunlight.



OUTPUT

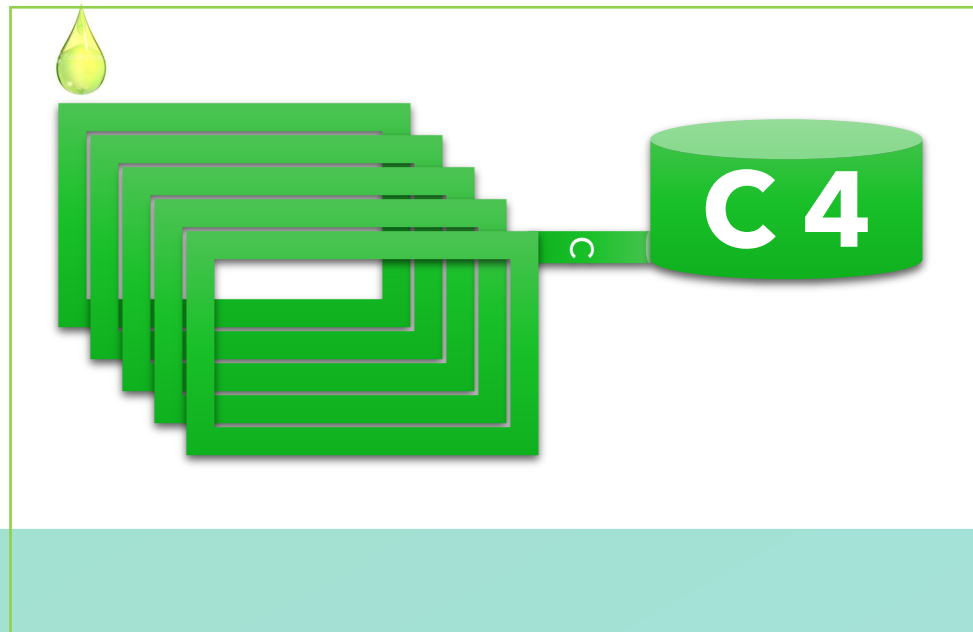
DILUTE BUTANOL ?
PURIFIED BUTANOL ?
BUTANOL MIXTURE ?

EPUC4 - C4
EXTRACTION
PURIFICATION UNIT

*This is a stumbling block.
Purifying C4 Butanol from
this mix needs innovation.*



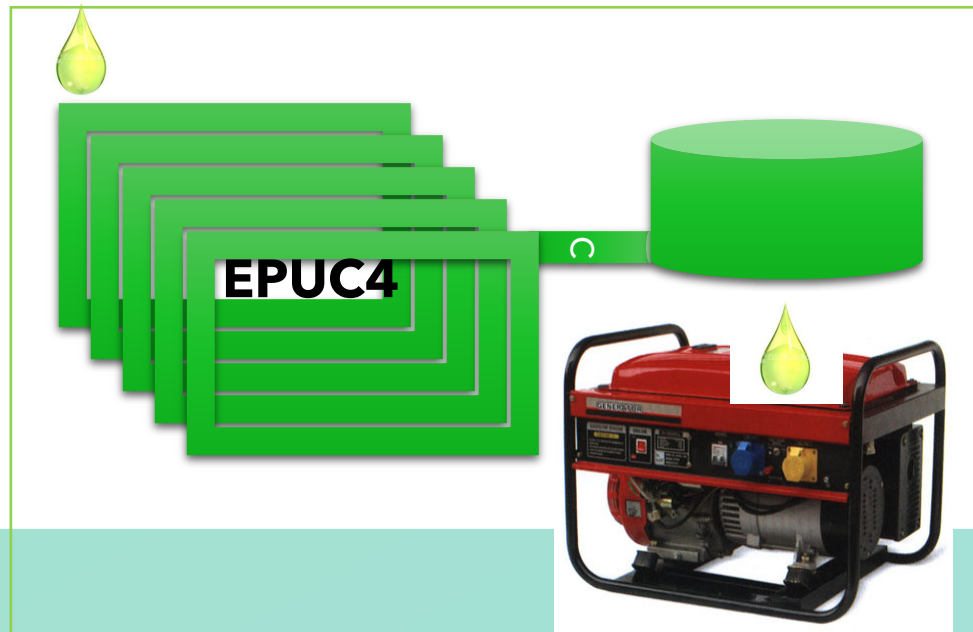
FUEL ? GRADE C4
BUTANOL



*How "fuel grade" is required?
Think kerosene: not quite pure!
Can we still use low grade C4?*

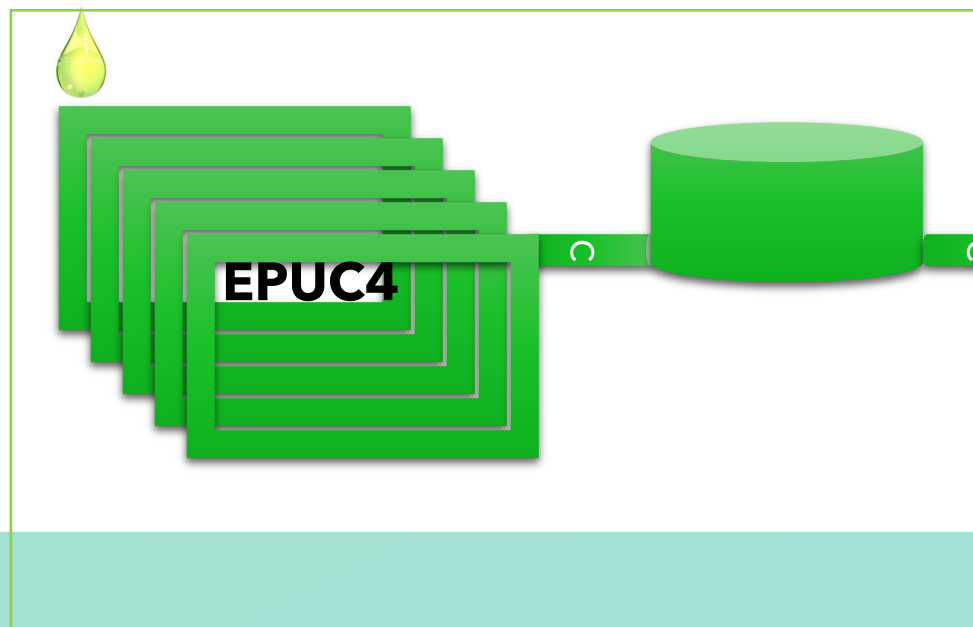


C4 - BUTANOL
low efficiency conversion
➔ ELECTRICITY
using commercial
GENERATOR



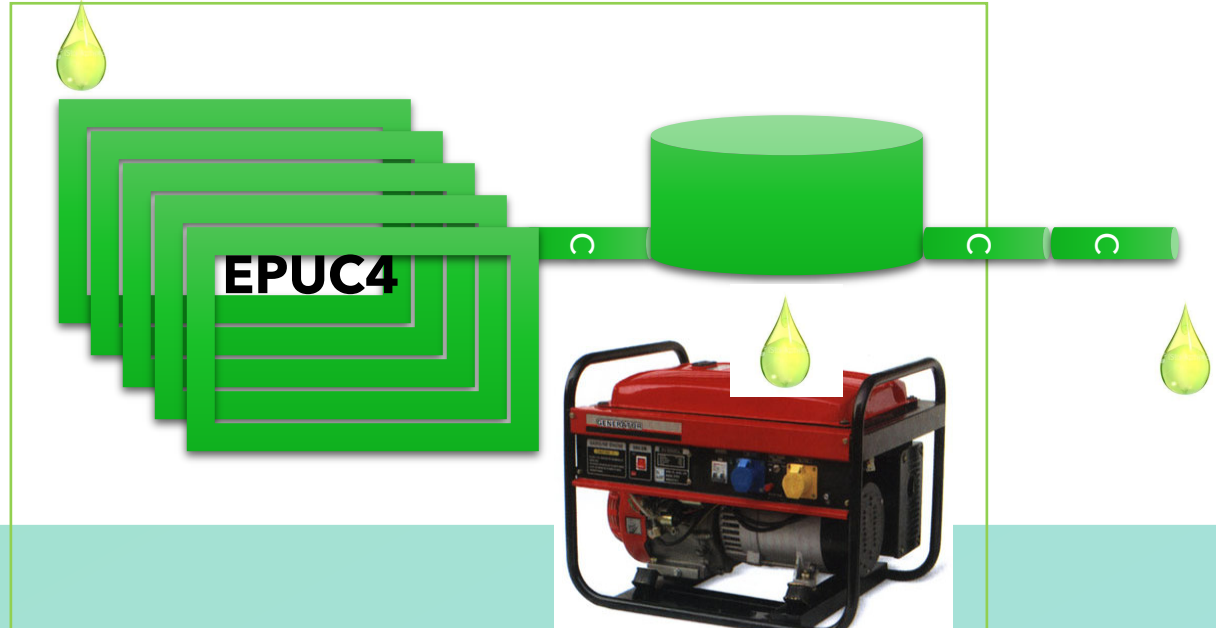


BUTANOL
DIRECT USE AS
COMBUSTION FUEL
TRANSPORTATION





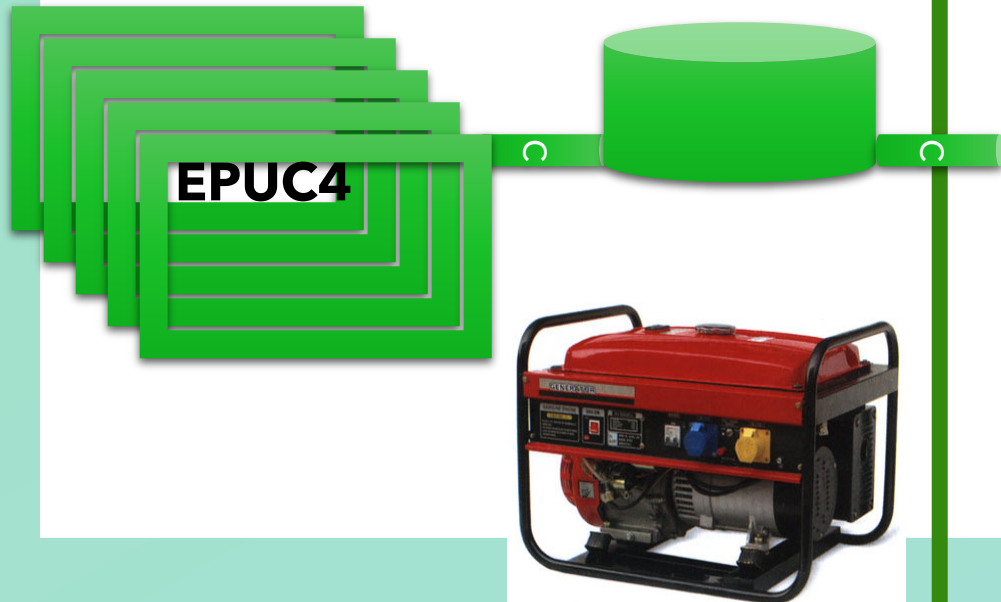
BUTANOL 
ELECTRICITY
for
DOMESTIC USE
ELECTRIC VEHICLES
SELL BACK TO GRID





SOLAR DEPENDENT
PHOTO BIO C4
BUTANOL REACTOR

**OUTDOOR
APPLIANCE**



**INDOOR
GARAGE UNIT**


FOR
ELECTRICITY
GENERATION

SOLAR DEPENDENT
PHOTO BIO C4
BUTANOL REACTOR

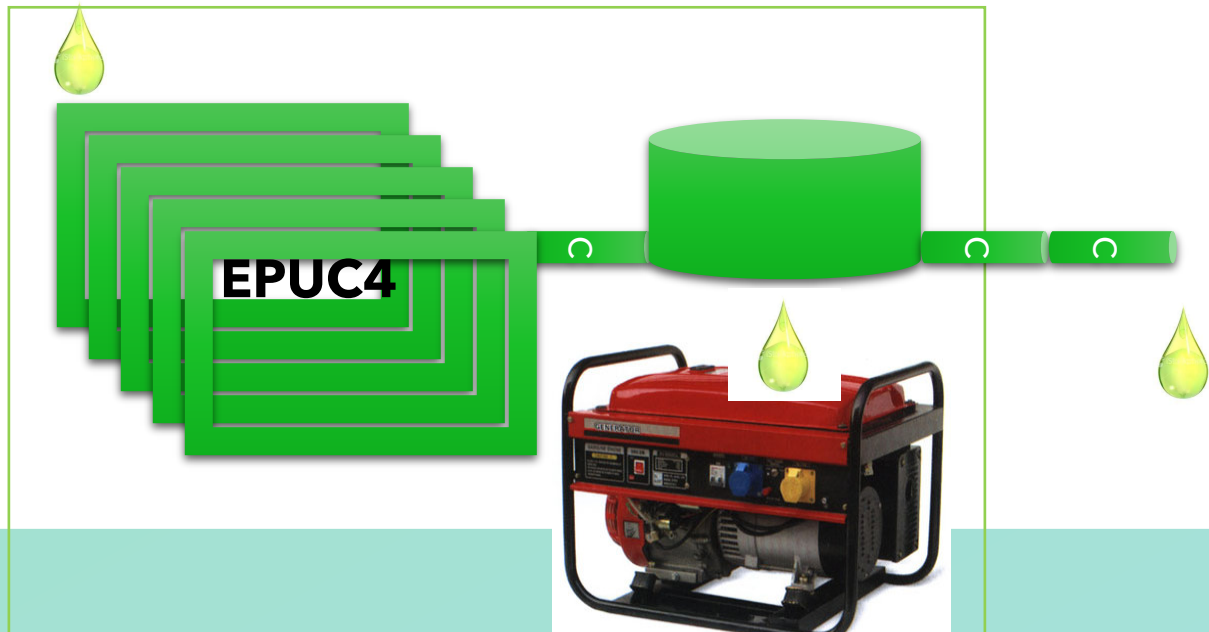
TWO-COMPONENT
ELECTRICITY
GENERATION





BUTANOL 
PENTANOL 
for ELECTRICITY

DOMESTIC USE
ELECTRIC VEHICLES
SELL BACK TO GRID



While we wait for scientists to chemically synthesize glucose from carbon dioxide and water ...

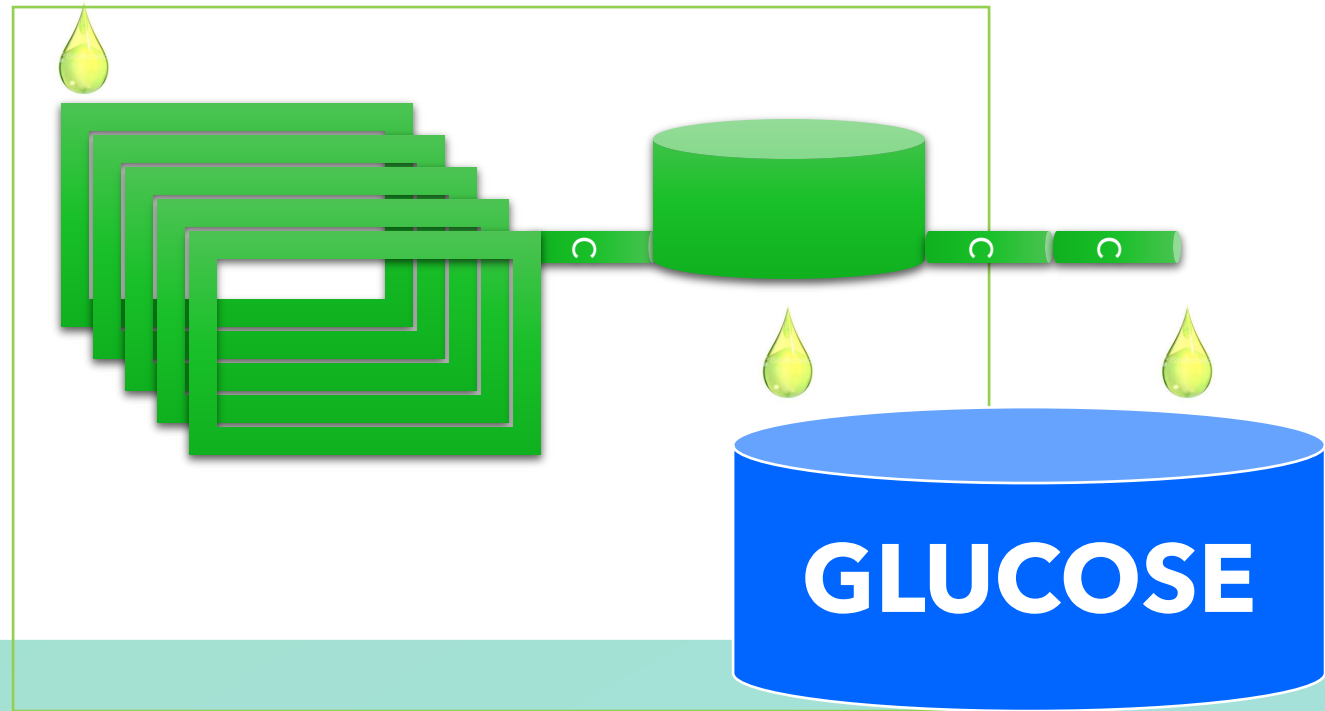
Very important fork in the road ...

Instead of photo-bio C4/C5, can we use this two-component system to create microbial **GLUCOSE**?
What if the microbial growth solution was partially dehydrated to form glucose paste (think molasses)?



SOLAR DEPENDENT
PHOTO BIO C6
GLUCOSE REACTOR

TWO-COMPONENT
GLUCOSE
PRODUCTION



GLUCOSE

Why create glucose paste ?

Glucose paste can be transported easily as a “feed” or nutrient. Microbes can use glucose directly to synthesize butanol (C4) or pentanol (C5) **WITHOUT SUNLIGHT** for insolation-independent (**indoor**) bio-C4/C5 production (anywhere). The Sahara Desert, The Thar Desert, The Gobi Desert, The Atacama Desert and other high insolation arid regions can be the **GLUCOSE FACTORIES** of the world to spur energy manufacturing in any garage, in any **cottage**.

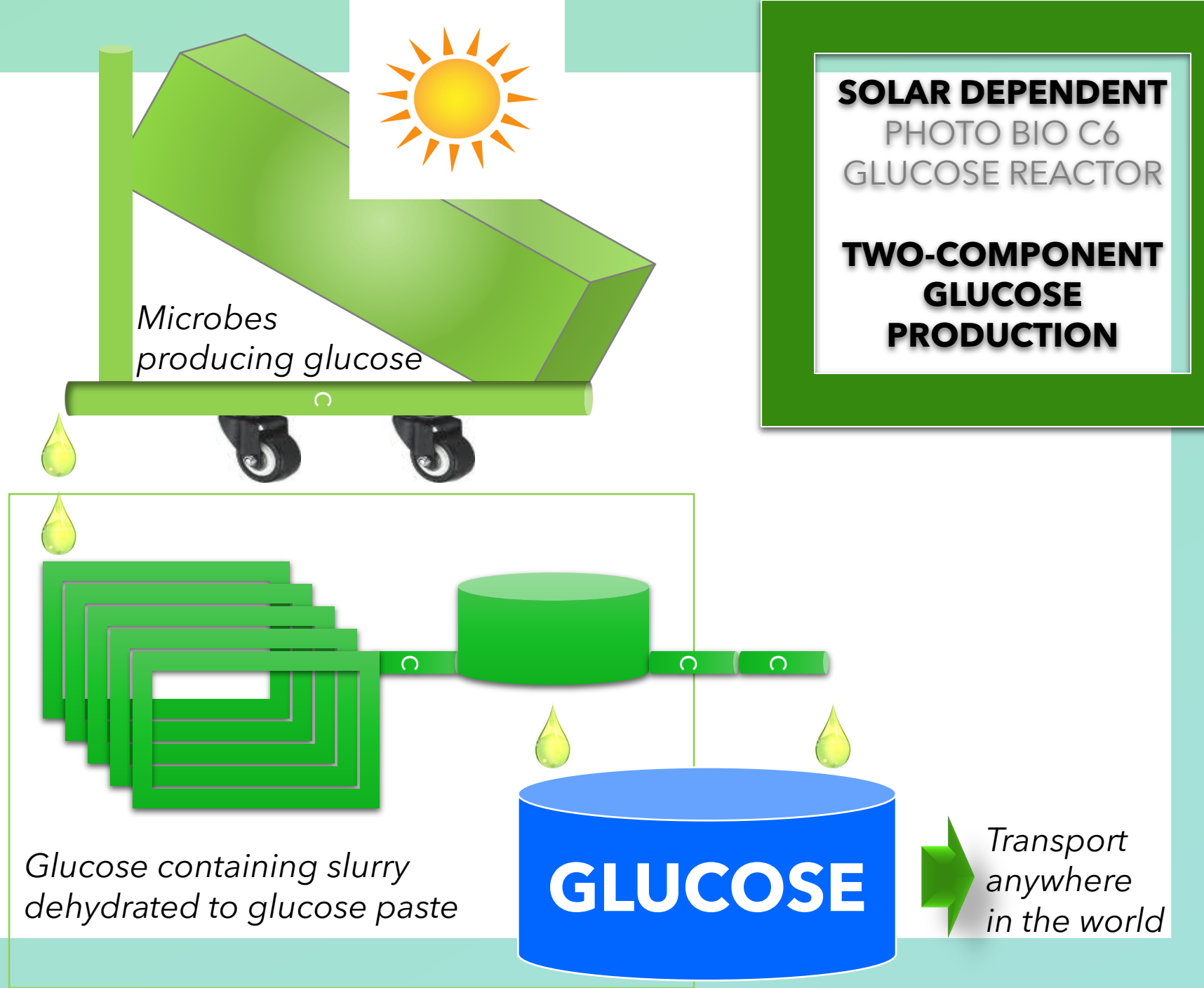
Photo-Bio Glucose [C6] Production

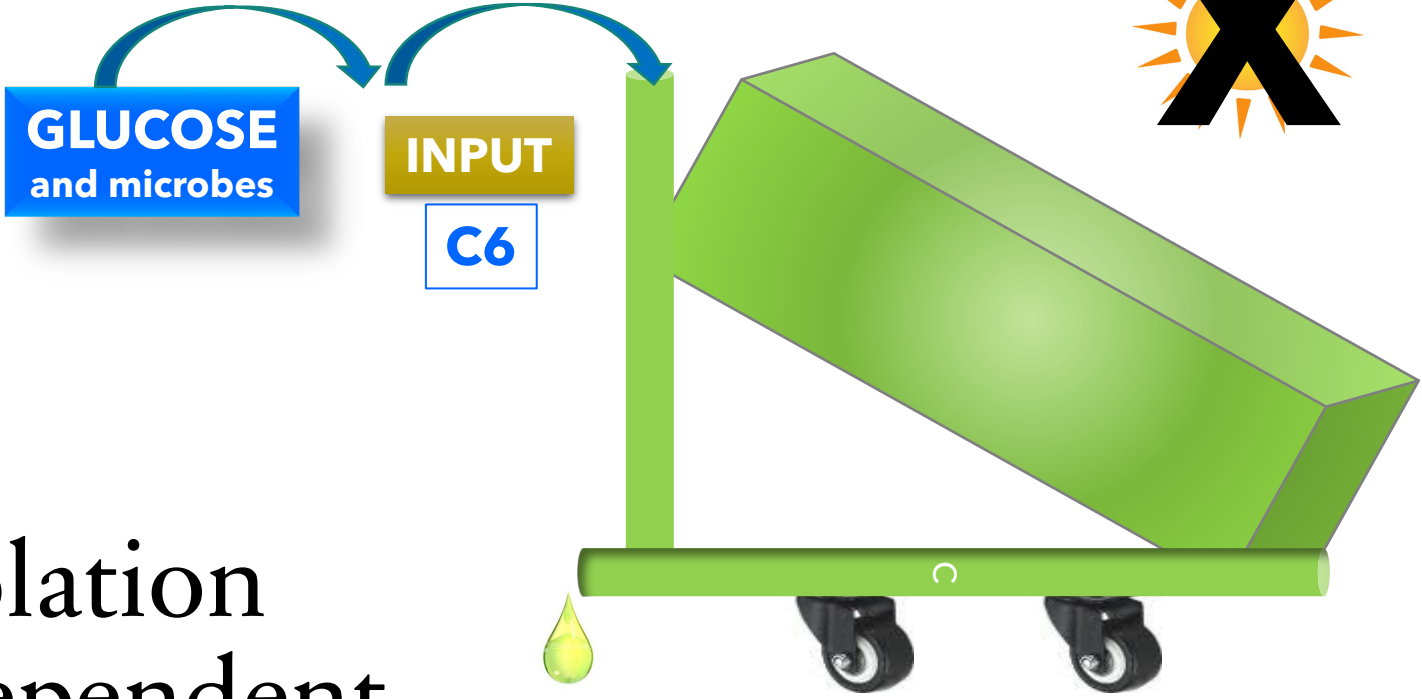
New Line of Global Manufacturing Business.

New Business. New Jobs. New Economic Growth.

New Commodity in the Renewable Energy Supply Chain.

Photo-Bio Glucose [C6] Production

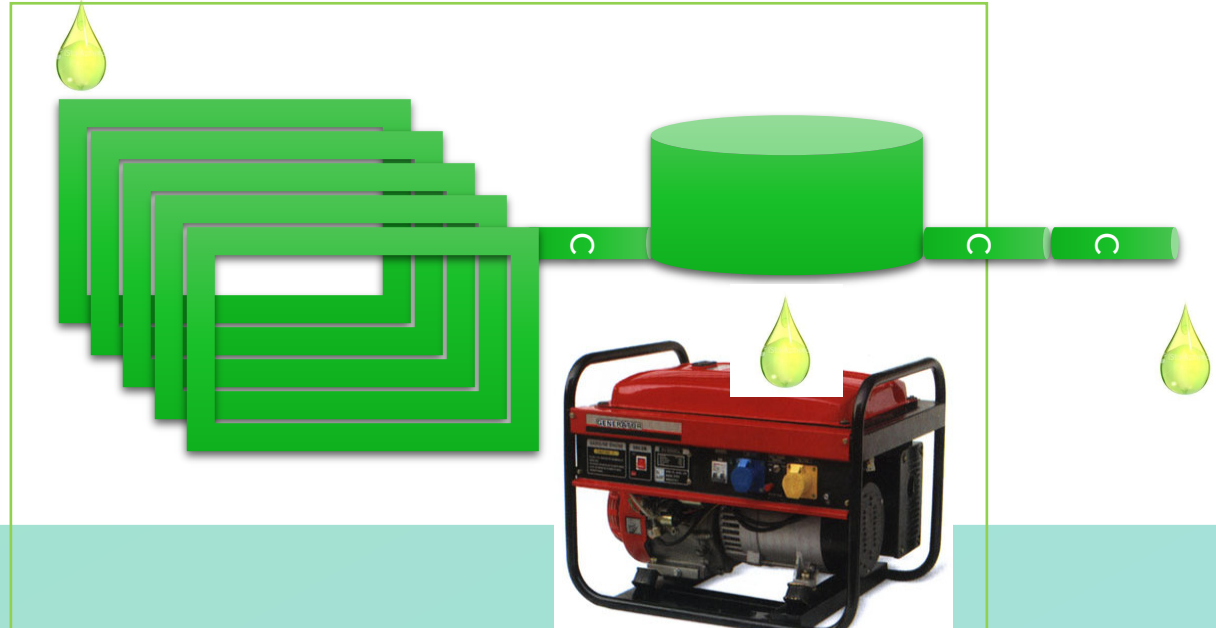




SUNLIGHT AGNOSTIC

- BUTANOL
- PENTANOL
- ELECTRICITY for DOMESTIC USE
- ELECTRIC VEHICLES
- SELL BACK TO GRID

Insolation
Independent
(Sunlight-Free)
Butanol
Pentanol
Production
Anywhere!



Insolation-Independent (Sunlight Agnostic) Photo-Bio C6-Dependent C4/C5 Bio-Reactor Electricity

Easy to propose, in principle, in a cartoon.

Very difficult to accomplish as a global practice.

Will change the global economy, if accomplished.

Insolation-Independent (Sunlight Agnostic) Photo-Bio C6-Dependent C4/C5 Bio-Reactor Electricity

“With willing hearts and skillful hands, the difficult we do at once; the impossible takes a bit longer.”

“The impossible we do at once; the miraculous takes a little longer.”

Distributed Energy Production

Energy Manufacturing as a Cottage Industry ??

Hypothetical Proposal by Shoumen Palit Austin Datta, 2009-2010 ♦ <http://dspace.mit.edu/handle/1721.1/59804>

Nobel Prize winner (chemistry) Robert F. Curl vehemently **disagreed** with this hypothetical proposal by the author (Shoumen Palit Austin Datta).

Comment by Nobel Prize winner Robert F Curl with respect to the hypothetical proposal by Shoumen Datta (distributed energy production involving potential manufacturing of liquid fuel as energy cottage industry).

“I cannot believe that it may ever make economic sense for an individual/home to make the capital expenditure for their own electric generation unless they can't connect to the grid. I do not believe in the assumptions about the future that your (energy) paper is based upon.”

– *Robert F Curl (10th November 2010)*

Robert F Curl co-discovered the field of nanotechnology & was awarded the Nobel Prize in Chemistry, 1996

<https://www.nobelprize.org/prizes/chemistry/1996/curl/facts/>

"I have traveled the length and breadth of this country and talked with the best people, and I can assure you that data processing is a fad that won't last out the year." -- *The editor in charge of business books for Prentice Hall, 1957.*

"There is no reason anyone would want a computer in their home." -- *Ken Olson, president, chairman and founder of Digital Equipment Corp., 1977.*

"This 'telephone' has too many shortcomings to be considered as a means of communication. Device is inherently of no value." -- *Western Union 1876*

"The Americans have need of the telephone, but we do not. We have plenty of messenger boys." -- *Sir William Preece, chief engineer, British Post, 1876.*

"Radio has no future." -- *William Thomson, Lord Kelvin, British scientist, 1899.*

"The wireless music box has no imaginable commercial value. Who would pay for a message sent to nobody in particular?" -- *David Sarnoff's associates in response to his urgings for investment in the radio in the 1920s.*

"The concept is interesting and well-formed, but in order to earn better than a 'C', the idea must be feasible." -- *A Yale University management professor in response to Fred Smith's paper proposing reliable overnight delivery service. (Smith went on to found Federal Express Corp, aka FedEx)*

"Who the hell wants to hear actors talk?" -- *H. M. Warner, Warner Brothers, 1927.*

"We don't like their sound, and guitar music is on the way out." -- *Decca Recording Co. rejecting the Beatles, 1962.*

"Stocks have reached what looks like a permanently high plateau." -- *Irving Fisher, Professor of Economics, Yale University, 1929.*

"There is not a slightest indication that nuclear energy will be obtainable. It would mean the atom would have to be shattered at will." -- *Einstein, 1932.*



KEEP CALM

AND

CARRY ON

Bob (Robert F Curl) is correct per
conventional wisdom as relates to
economics of technology.

Can science, engineering and
technology change economics?

YES

Robert Merton Solow

MIT

Nobel Prize in Economics, 1987

*demonstrated that technology could
alter the rate of economic growth.*



Left - Bob Solow
Right - SD
MIT, 2009

Left - Bob (Robert F Curl)
with Rebecca Jane Austin,
my wife. In our home, 2013.



Bob Curl vs Bob Solow

Who is correct?

Bob Curl vs Bob Solow

Who is correct?

I think both. It doesn't matter. What matters most is that in science it is imperative that we respect disagreements, especially if the person is a giant intellectual or is eminently qualified to comment on the matter. Debate and disagreement must be invited to maintain scientific clarity of thought and actions. Even though Bob Curl is a friend (and Bob Solow), he had no problem in providing his unvarnished remark in 2010. Even though we disagreed, Bob Curl visited us at our home in 2013 because he wanted me to cook him dinner. In 1995, while making a strenuous professional decision, I called Bob (Solow) and asked him for guidance. What he (Bob Solow) said to me and his wisdom, changed the trajectory of my life's path.

Distributed Energy Production

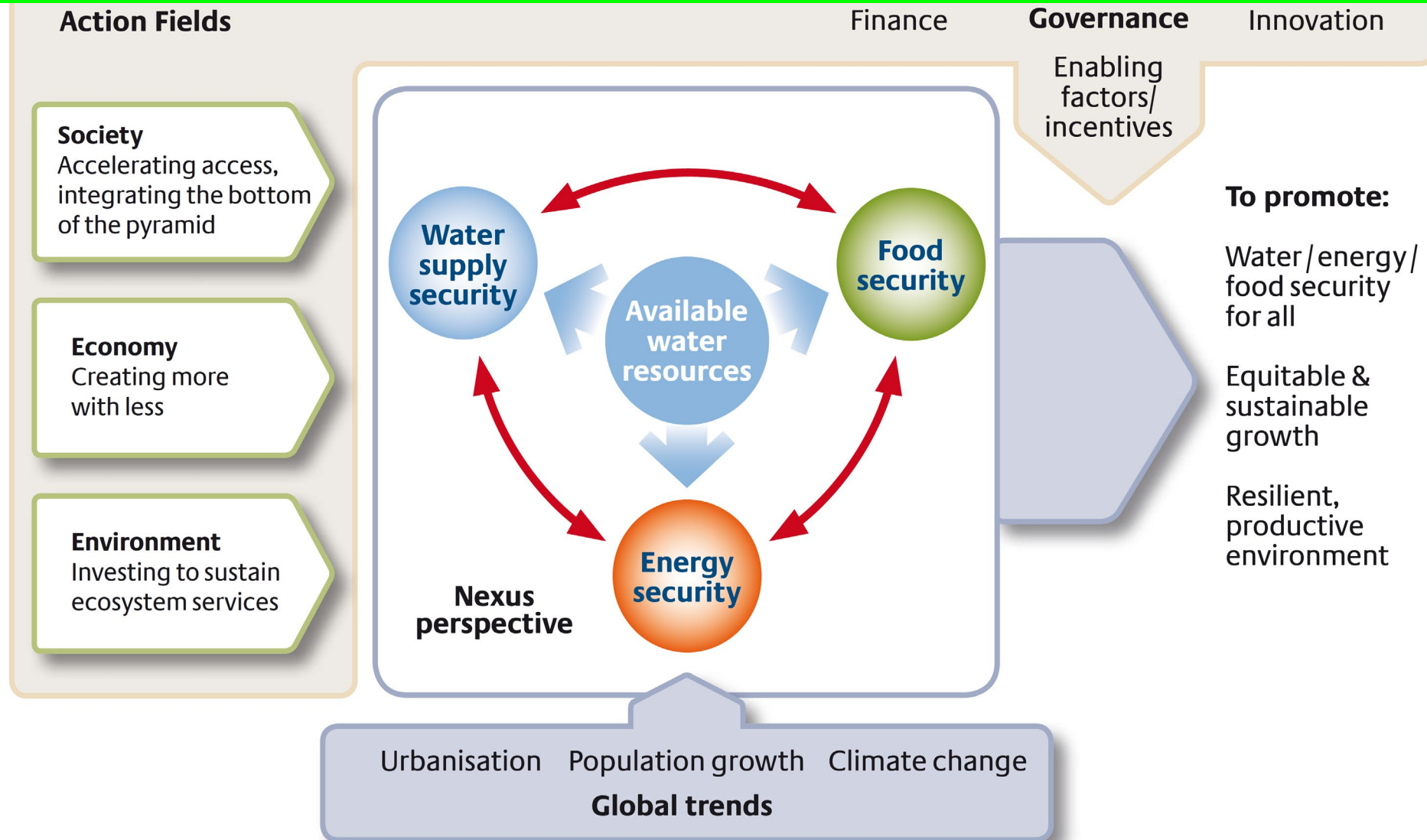
Energy Manufacturing as a Cottage Industry ??

Don't ask 'Why', ask instead, 'Why not'.

John F. Kennedy

Why energy is
the “glue” in
any economy

Food-Energy-Water Nexus



Lot more for energy innovation ...

Distributed Energy Production



Distributed Energy Production

We may be on the brink of a new paradigm for nuclear power, a group of nuclear specialists suggested in The Bridge (June, 2021) the journal of the US National Academy of Engineering. Much as large, expensive, and centralized computers gave way to distributed PCs of today, a new generation of relatively tiny and inexpensive factory-built reactors, designed for autonomous plug-and-play operation, similar to plugging in an oversized battery, is on the horizon.

www.nae.edu/255810/A-Strategy-to-Unlock-the-Potential-of-Nuclear-Energy-for-a-New-and-Resilient-Global-Energy-Industrial-Paradigm

My op-ed prediction on this topic in 2007-2008 <https://dspace.mit.edu/handle/1721.1/41897>
“WiFi Meet FuFi: Disruptive Innovation in Logistics Catalysed by Energy” by S. Datta, MIT

3Q: Why “nuclear batteries” offer a new approach to carbon-free energy

Jacopo Buongiorno and others say factory-built microreactors trucked to usage sites could be a safe, efficient option for decarbonizing electricity systems.

David L. Chandler | MIT News Office
June 25, 2021

▼ [PRESS INQUIRIES](#)



This cut-away rendering of the MIT nuclear battery concept shows important components such as the instrumentation and control module, the reactor, and the power module.

Courtesy of the researchers

MIT News

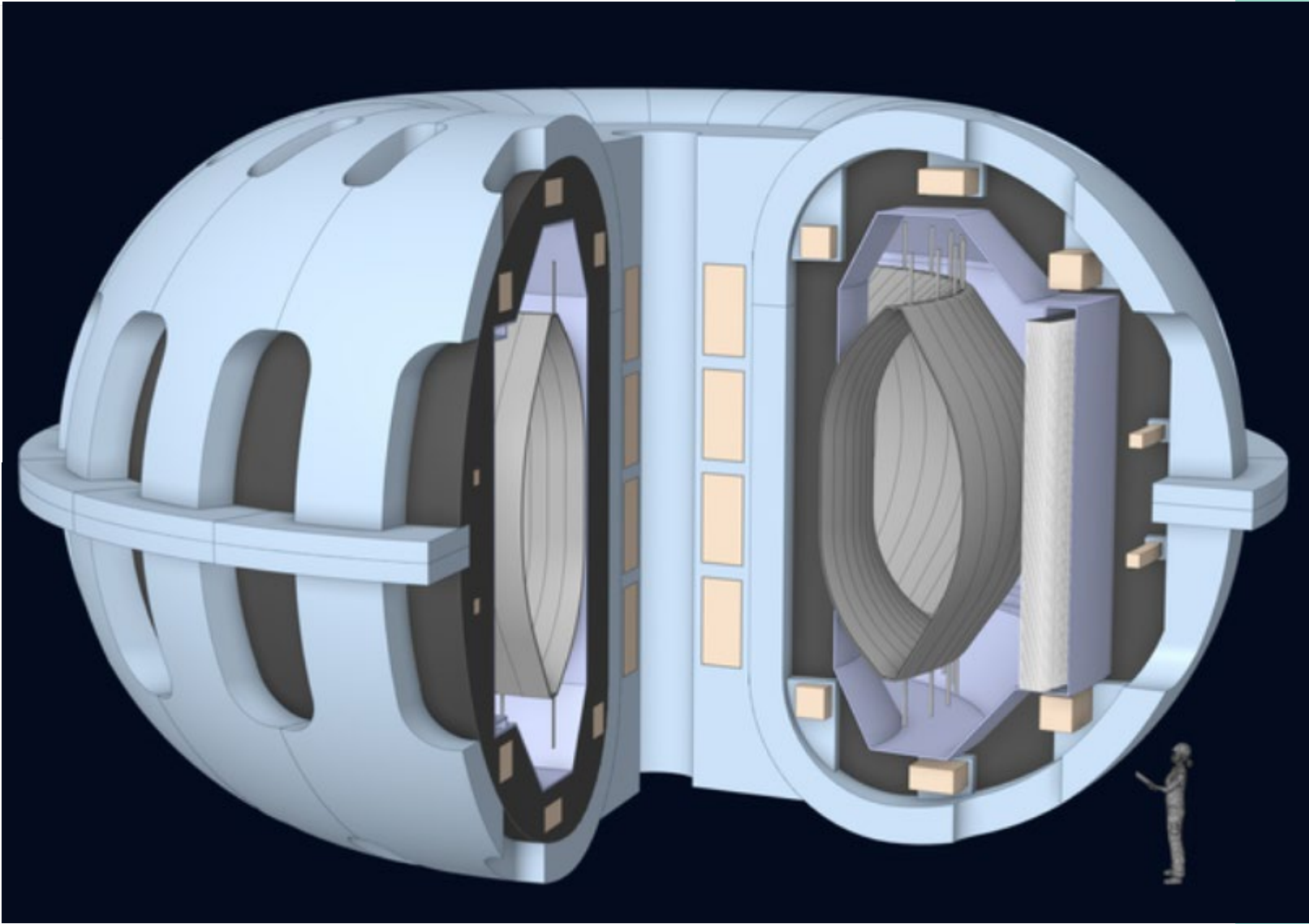
ON CAMPUS AND AROUND THE WORLD

On course to create a fusion power plant

How an MIT engineering course became an incubator for fusion design innovations.

Paul Rivenberg | Plasma Science and Fusion Center
April 29, 2021

ARCH is a design for an onboard fusion device capable of generating ammonia fuel for ship engines.



Distributed Energy Production appears easy in a cartoon

Commercial scale fusion reactor for power grids

Ambient temperature superconductor to reduce waste

High density material films for batteries to store remote energy



MIT News

ON CAMPUS AND AROUND THE WORLD

On course to create a fusion power plant

How an MIT engineering course became an incubator for fusion design innovations.

Paul Rivenberg | Plasma Science and Fusion Center

April 29, 2021

FUSION POWER –

THE HOLY GRAIL

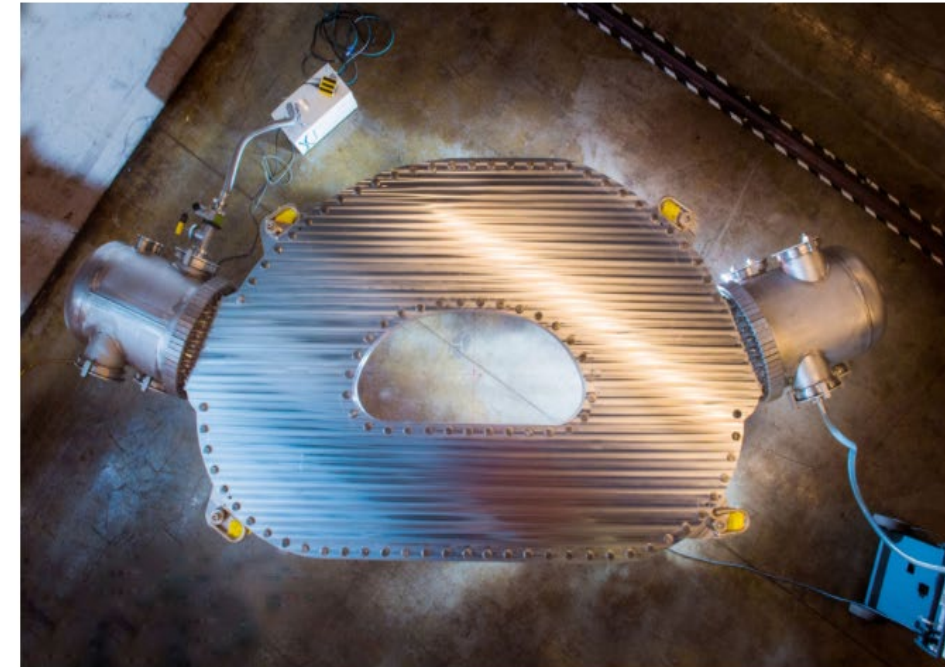
Large-bore, full-scale high-temperature superconducting magnet designed and built by CFS (Commonwealth Fusion Systems) and MIT's Plasma Science and Fusion Center (PSFC) demonstrated a record-breaking 20 tesla magnetic field.

MIT-designed project achieves major advance toward fusion energy

New superconducting magnet breaks magnetic field strength records, paving the way for practical, commercial, carbon-free power.

Watch Video

David Chandler | MIT News Office
September 8, 2021



It was a moment three years in the making, based on intensive research and design work: On Sept. 5, for the first time, a large high-temperature superconducting electromagnet was ramped up to a field strength of 20 tesla, the most powerful magnetic field of its kind ever created on Earth. That successful demonstration helps resolve the greatest uncertainty in the quest to build the world's first fusion power plant that can produce more power than it consumes, according to the project's leaders at MIT and startup company Commonwealth Fusion Systems

Discussion: Snippets of Examples

Number 3



W

Water

Your contribution to society matters.

Science and Scientists for Society

About 0.5% of the earth's water is available fresh water

usbr.gov/mp/arwec/water-facts-ww-water-sup.html	
Oceans	97.2%
Ice Caps/Glaciers	2.0%
Groundwater*	0.62%
Freshwater Lakes	0.009%
Inland seas/salt lakes	0.008%
Atmosphere	0.001%
Rivers	0.0001%
TOTAL	99.8381%

NO WATER



NO FOOD

Simplest things we don't know

DE NOVO (Latin for “new”) synthesis of water (dihydrogen monoxide) in amounts feasible for mass consumption is beyond the current capabilities of science and scientists. However, we can create a few water molecules but only on a laboratory bench.

About 0.5% of the earth's water is available fresh water

Oceans	97.2%
Ice Caps/Glaciers	2.0%
Groundwater*	0.62%
Freshwater Lakes	0.009%
Inland seas/salt lakes	0.008%
Atmosphere	0.001%
Rivers	0.0001%
TOTAL	99.8381%



We have 326 million cubic miles of water on the planet but 320 million cubic miles of water is **unusable** salt water in oceans (usable for cooling).

Solution: Remove Salt

Commercial Desalination



MIT News

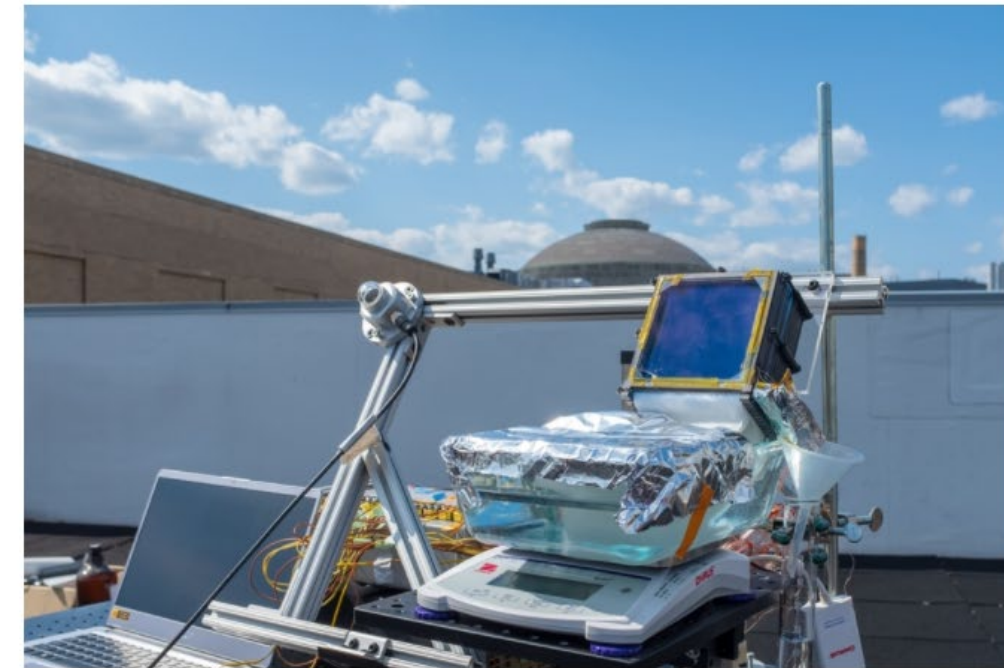
ON CAMPUS AND AROUND THE WORLD

Simple, solar-powered water desalination

System achieves new level of efficiency in harnessing sunlight to make fresh potable water from seawater.

David L. Chandler | MIT News Office

February 6, 2020



A completely passive solar-powered desalination system developed by researchers at MIT and in China could provide more than 1.5 gallons of fresh drinking water per hour for every square meter of solar collecting area. Such systems could potentially serve off-grid arid coastal areas

Tests on an MIT building rooftop showed that a simple proof-of-concept desalination device could produce clean, drinkable water at a rate of about 1.5 gallons (5.6 liters) per hour for each square meter of solar collecting area.



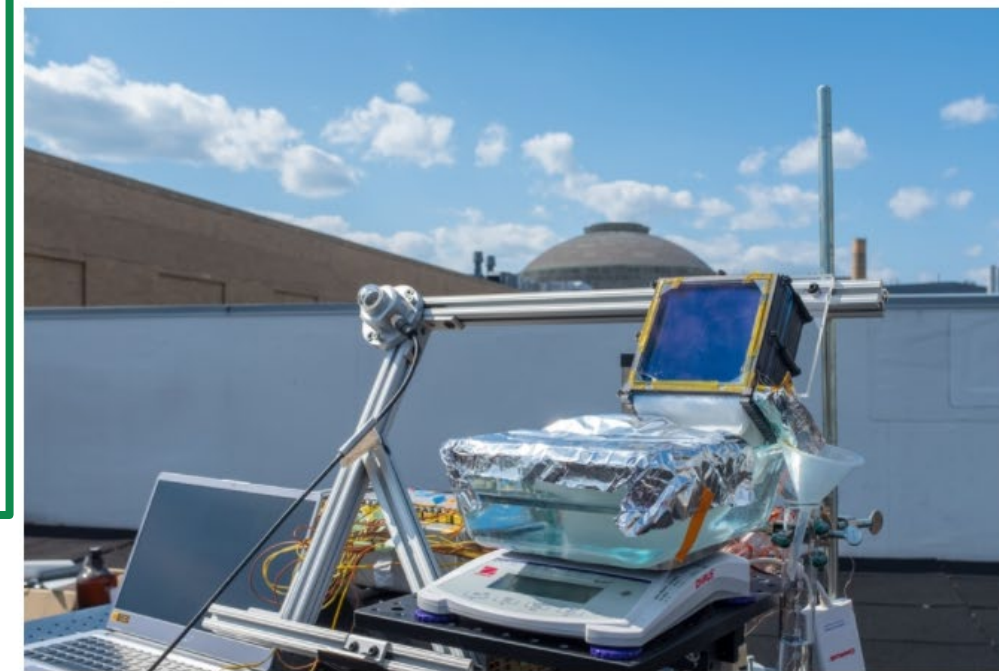
MIT News

ON CAMPUS AND AROUND THE WORLD

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ROYAL SOCIETY
OF CHEMISTRY

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COMMUNICATION

Ultrahigh-efficiency desalination *via* a thermally-localized multistage solar still†

Zhenyuan Xu, [‡]^{ab} Lenan Zhang, [‡]^b Lin Zhao, [‡]^b Bangjun Li, [‡]^a Bikram Bhatia, ^b Chenxi Wang, ^a Kyle L. Wilke, ^b Youngsup Song, ^b Omar Labban, ^b John H. Lienhard, ^b Ruzhu Wang ^{*a} and Evelyn N. Wang ^{*b}

Check for updates

Cite this: *Energy Environ. Sci.*, 2020, 13, 830

Received 21st December 2019,
Accepted 15th January 2020

DOI: 10.1039/c9ee04122b

The critical and most
expensive barrier for
commercial desalination is

ENERGY



Energy & Environment > Energy

Household electricity consumption per capita in India

(in kilowatt hours)

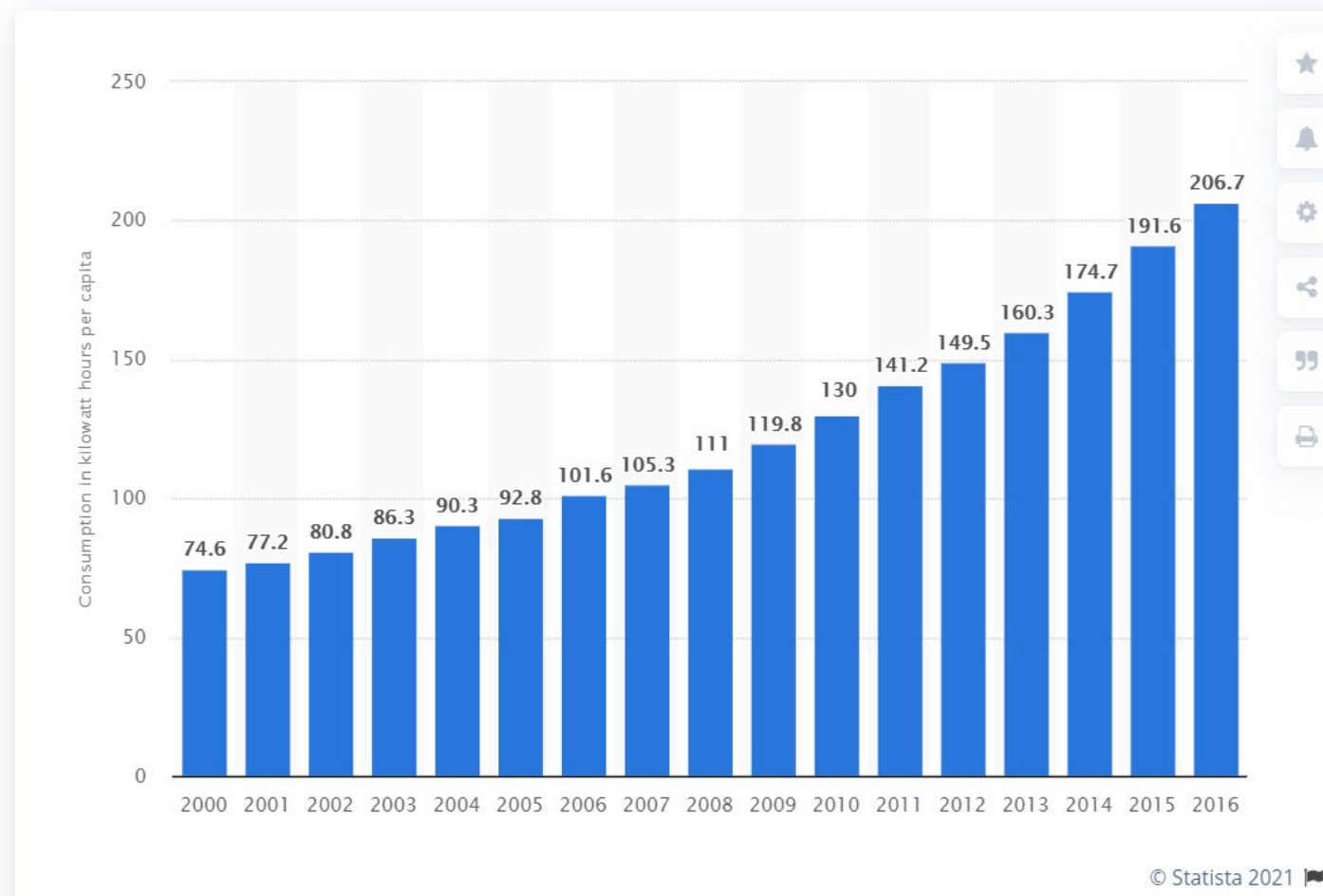

















Table 1. Energy requirements for different water sources.

Water Source	Energy (kWh/m ³)
Seawater	2.58–8.5
Wastewater reuse	1.0–2.5
Wastewater treatment	0.62–0.87
Groundwater	0.48

Table 2. Typical total electrical energy consumptions in different desalination technologies.

Desalination Technology	Specific Energy Requirements
Multi-Effect Distillation	14–21 kWh/m ³
Multi-Stage Flash	20–27 kWh/m ³
Mechanical Vapor Compression	7–12 kWh/m ³
Thermal Vapor Compression	16.26 kWh/m ³
Seawater Reverse Osmosis	4–6 kWh/m ³

Commercial Thermal Technologies for Desalination of Water from Renewable Energies: State of the Art Review

by  Jhon Jairo Feria-Díaz ^{1,2,*}  ,  María Cristina López-Méndez ¹  ,  Juan Pablo Rodríguez-Miranda ³  ,  Luis Carlos Sandoval-Herazo ¹   and  Felipe Correa-Mahecha ⁴  

206.7 kWh

Average per capita electricity used in India

0.135 m³

Average household water used in India

About 0.5% of the earth's water is available fresh water



How Much Water Does it Take to Produce Your Food?

Food	Portion	Gallons of Water
Orange Juice	1 cup	49
Orange	1 medium	14
Cantaloupe	1 melon	160
Broccoli	2 cups	11
Catsup	1 ounce	3
Corn	1 ear	80
Lettuce	1 cup	3
Tomato	1 small	8
Tomato Sauce	4 ounces	13
Butter	1 pat	46
Cheese	1 ounce	56
Milk	1 cup	48
Yogurt	1 cup	88
Beef Steak	8 ounces	1,232
Chicken	8 ounces	330
Egg	1 each	50
Hamburger	4 ounces	616
Tofu	2 cups	61
Almonds	1 ounce	80
Sugar	1 Tablespoon	7
White Rice	2 cups	25
Brown Rice	2 cups	16
Wheat Bread	1 slice	7
White Bread	1 slice	11
Pasta	2 ounces	36

Will the world run dry without the science/engineering of desalination?

Can bio-mimicry help desalination?

Water channel proteins used by cells/organisms to regulate salt.

The best way to do almost anything
is to look for something similar in
our natural environment

Desalination naturally?

Yes! Water channel proteins: Aquaporin.

Molecular Cloning, Overexpression and Characterization of a Novel Water Channel Protein from *Rhodobacter sphaeroides*

Mustafa Erbakan¹, Yue-xiao Shen², Mariusz Grzelakowski³, Peter J. Butler¹, Manish Kumar^{2*}, Wayne R. Curtis^{1,2*}

¹ Department of Biomedical Engineering, Pennsylvania State University, University Park, Pennsylvania, United States of America, ² Department of Chemical Engineering, Pennsylvania State University, University Park, Pennsylvania, United States of America, ³ AquaZ Inc, Cincinnati, Ohio, United States of America

Abstract

Aquaporins are highly selective water channel proteins integrated into plasma membranes of single cell organisms; plant roots and stromae; eye lenses, renal and red blood cells in vertebrates. To date, only a few microbial aquaporins have been characterized and their physiological importance is not well understood. Here we report on the cloning, expression and characterization of a novel aquaporin, RsAqpZ, from a purple photosynthetic bacterium, *Rhodobacter sphaeroides* ATCC 17023. The protein was expressed homologously at a high yield (~20 mg/L culture) under anaerobic photoheterotrophic growth conditions. Stopped-flow light scattering experiments demonstrated its high water permeability (0.17 ± 0.05 cm/s) and low energy of activation for water transport (2.93 ± 0.60 kcal/mol) in reconstituted proteoliposomes at a protein to lipid ratio (w/w) of 0.04. We developed a fluorescence correlation spectroscopy based technique and utilized a fluorescent protein fusion of RsAqpZ, to estimate the single channel water permeability of RsAqpZ as $1.24 (\pm 0.41) \times 10^{-12}$ cm³/s or $4.17 (\pm 1.38) \times 10^{10}$ H₂O molecules/s, which is among the highest single channel permeability reported for aquaporins. Towards application to water purification technologies, we also demonstrated functional incorporation of RsAqpZ in amphiphilic block copolymer membranes.

<https://pubmed.ncbi.nlm.nih.gov/24497982/>

Citation: Erbakan M, Shen Y-x, Grzelakowski M, Butler PJ, Kumar M, et al. (2014) Molecular Cloning, Overexpression and Characterization of a Novel Water Channel Protein from *Rhodobacter sphaeroides*. PLoS ONE 9(1): e86830. doi:10.1371/journal.pone.0086830

Artificial water channels enable fast and selective water permeation through water-wire networks

Woochul Song^{1,10}, Himanshu Joshi², Ratul Chowdhury¹, Joseph S. Najem^{3,11}, Yue-xiao Shen⁴, Chao Lang¹, Codey B. Henderson⁵, Yu-Ming Tu^{1,10}, Megan Farrell¹, Megan E. Pitz³, Costas D. Maranas¹, Paul S. Cremer⁵, Robert J. Hickey⁶, Stephen A. Sarles³, Jun-li Hou⁷, Aleksei Aksimentiev² and Manish Kumar^{1,8,9,12*}

Artificial water channels are synthetic molecules that aim to mimic the structural and functional features of biological water channels (aquaporins). Here we report on a cluster-forming organic nanoarchitecture, peptide-appended hybrid[4]arene (PAH[4]), as a new class of artificial water channels. Fluorescence experiments and simulations demonstrated that PAH[4]s can form, through lateral diffusion, clusters in lipid membranes that provide synergistic membrane-spanning paths for a rapid and selective water permeation through water-wire networks. Quantitative transport studies revealed that PAH[4]s can transport $>10^9$ water molecules per second per molecule, which is comparable to aquaporin water channels. The performance of these channels exceeds the upper bound limit of current desalination membranes by a factor of $\sim 10^4$, as illustrated by the water/NaCl permeability-selectivity trade-off curve. PAH[4]'s unique properties of a high water/solute permselectivity via cooperative water-wire formation could usher in an alternative design paradigm for permeable membrane materials in separations, energy production and barrier applications.

WATER CHANNEL PROTEINS used for Water Desalination

Water-channel protein, Aquaporin Z, RsAqpZ, from the purple photosynthetic bacterium, *Rhodobacter sphaeroides* ATCC 17023.

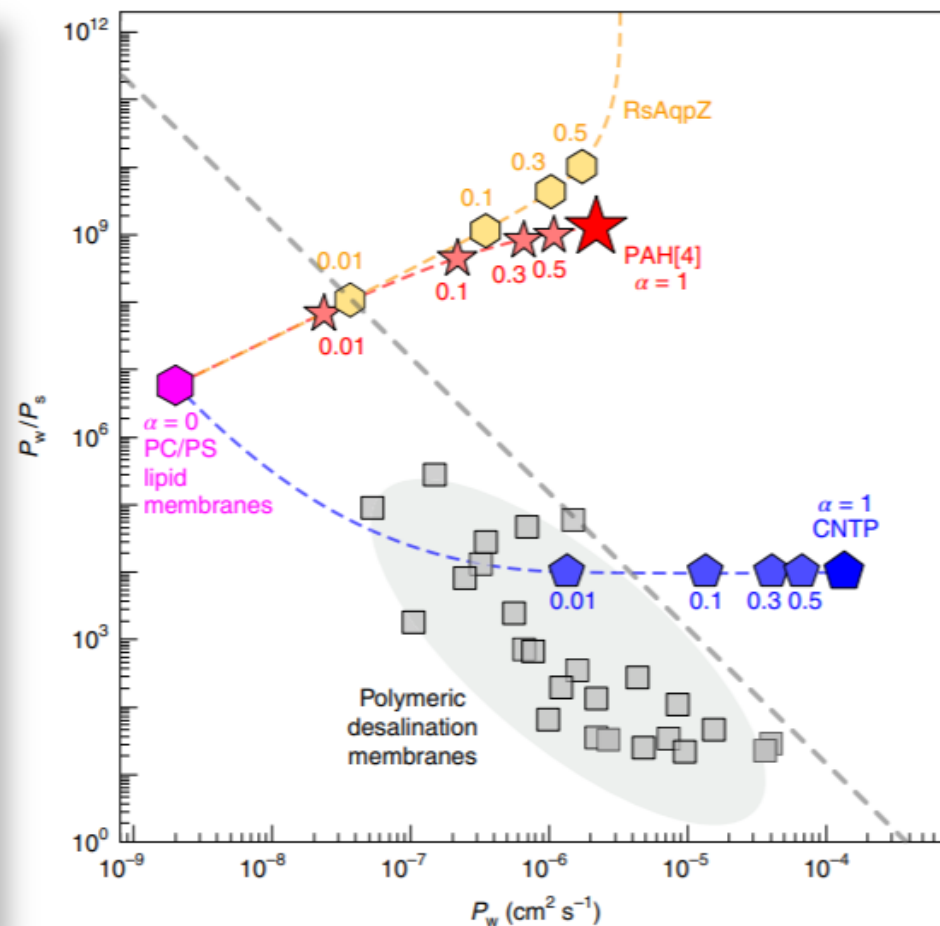


Fig. 3 | Intrinsic water/NaCl selectivity (P_w/P_s) versus P_w of PAH[4]-, CNTP- and RsAqpZ-based biomimetic membranes.

Kumar *et al* (2020) reports that cluster-forming organic nanoarchitecture, peptide-appended hybrid[4]arene (PAH[4]) is a new class of artificial water channel (**RED STAR**) which is orders of magnitude superior for water desalination compared to carbon nanotube porins (CNTP, **blue**). For PAH[4] the ratio of water vs salt (y-axis) is one part of salt in a billion (10^9) part of desalinated water (CNTP ratio 1: 10^4). That is an improvement of 5 orders of magnitude. While promising, it is still a very long way from commercial implementation.

Water-channel protein, Aquaporin Z, RsAqpZ, from the purple photosynthetic bacterium, *Rhodobacter sphaeroides* ATCC 17023.

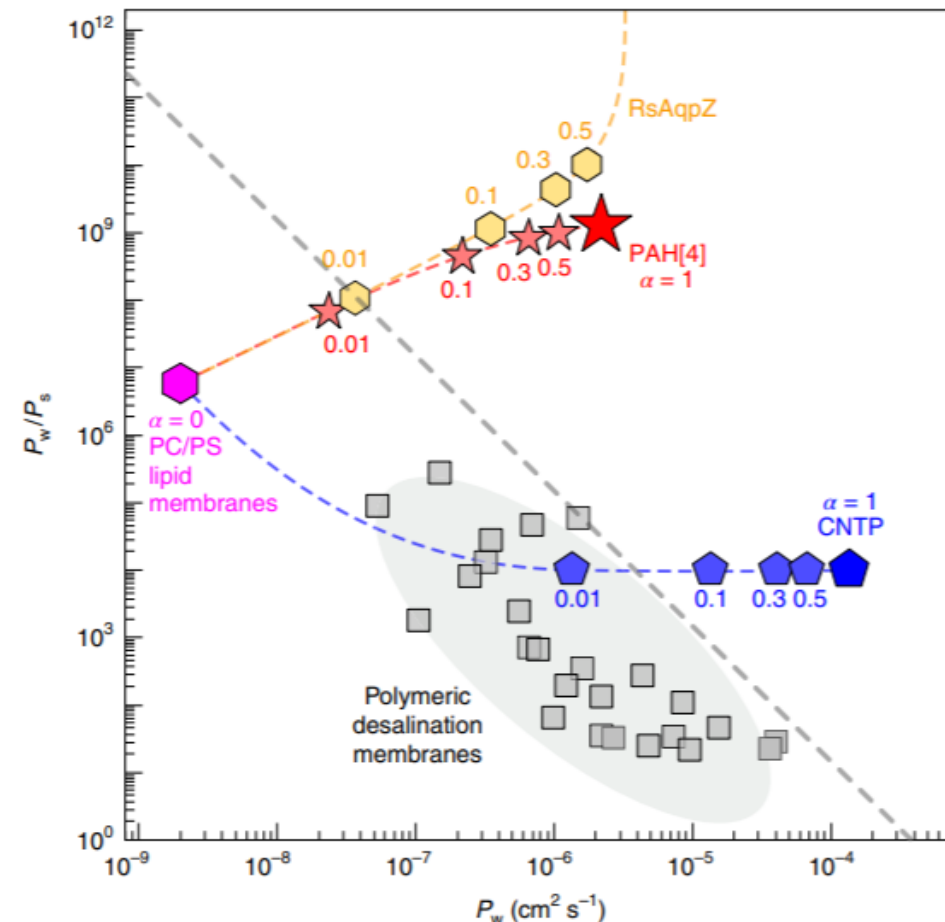
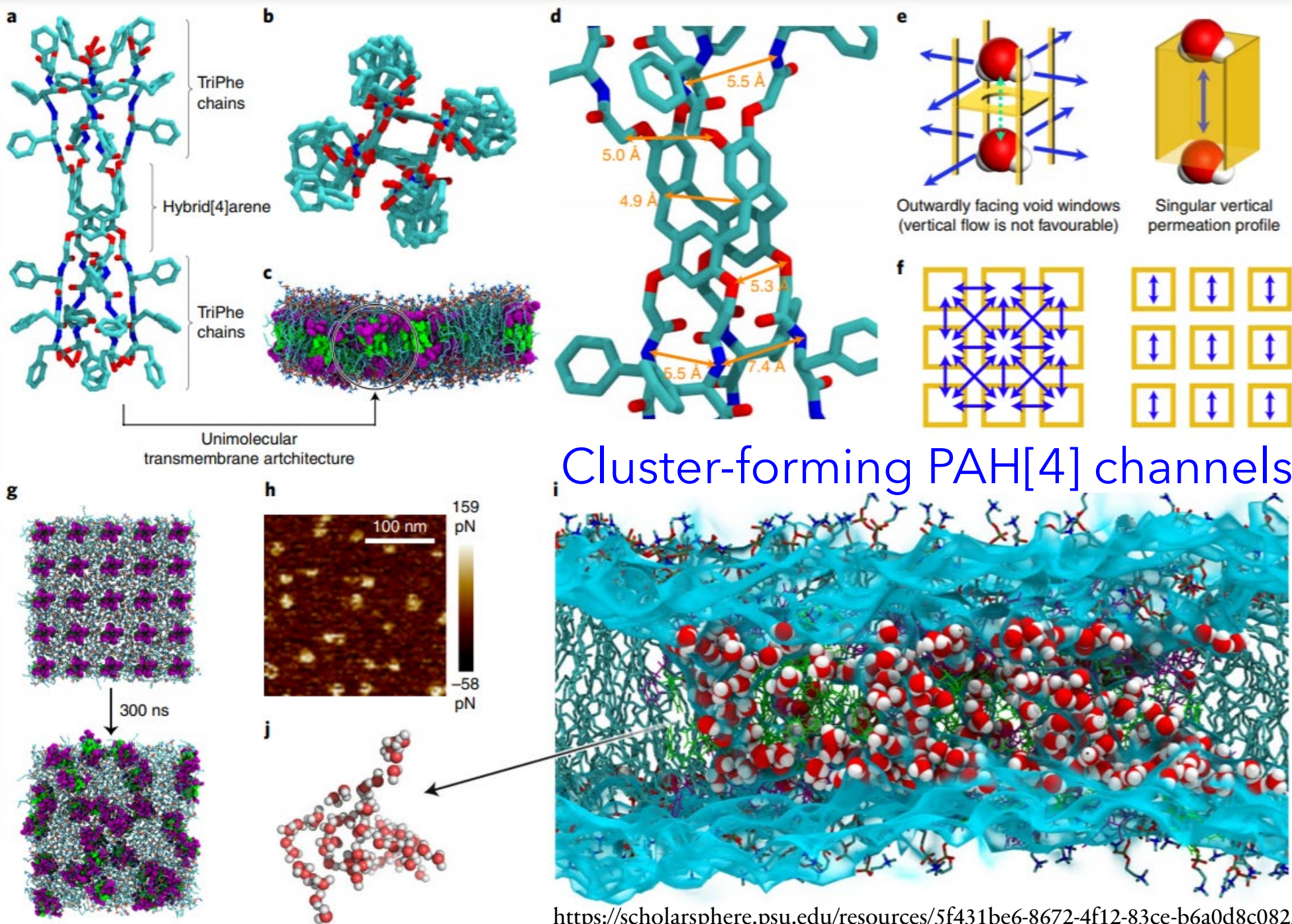


Fig. 3 | Intrinsic water/NaCl selectivity (P_w/P_s) versus P_w of PAH[4]-, CNTP- and RsAqpZ-based biomimetic membranes.

The road to desalination runs through nano-chemistry



Domestic Water Purification

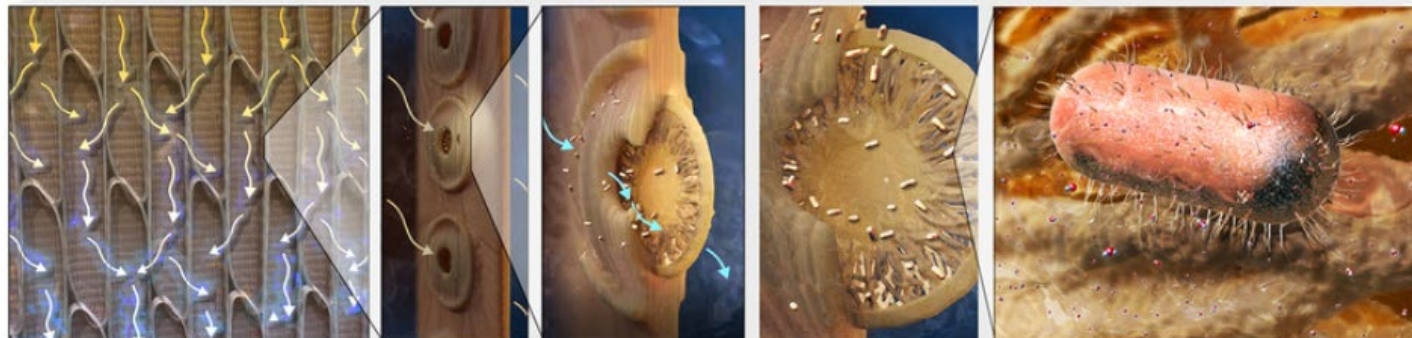
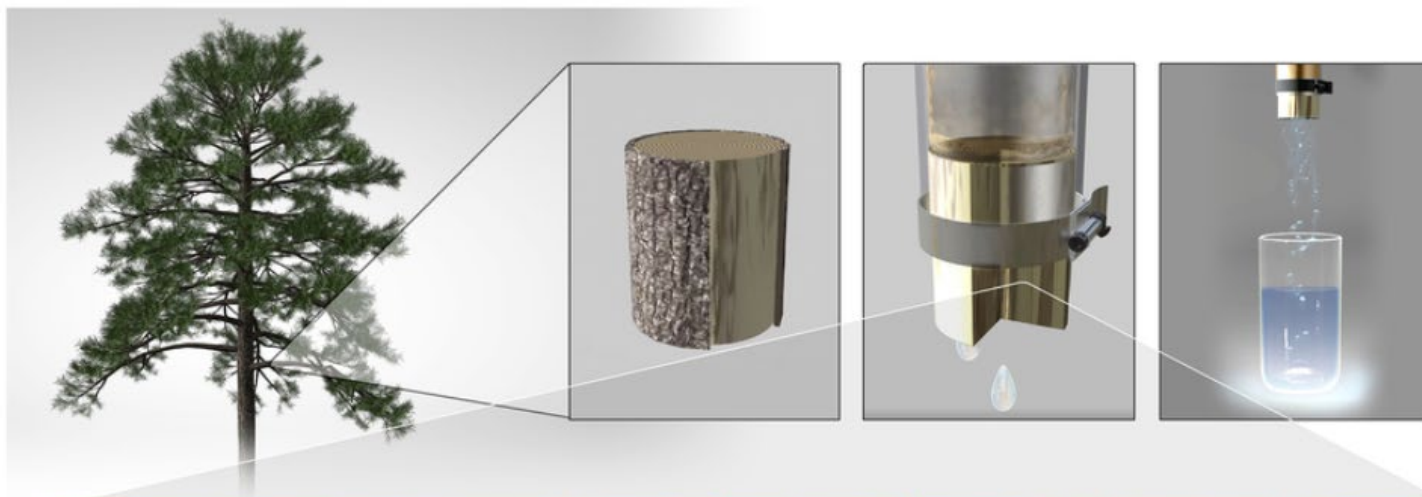
Low cost, small scale, purifiers may reduce risk of diseases

MIT engineers make filters from tree branches to purify drinking water

Prototypes tested in India show promise as a low-cost, natural filtration option.

Watch Video

Jennifer Chu | MIT News Office
March 25, 2021



Professor
Rohit Karnik

Professor of Mechanical Engineering; Associate Department Head
Education

INTERESTS

- 1 Microfluidic and nanofluidic transport
- 2 Graphene and nanostructured membranes
- 3 BioMEMS and lab-on-a-chip devices

- [Biomass Fuels & Cookstoves](#)
- [Energy](#)
- [Evaporative Cooling for Vegetable Preservation](#)
- [Lean Research](#)
- [Local Innovation](#)
- [MIT D-Lab | CITE](#)
- [Xylem Water Filter](#)

Xylem Water Filter



Women holding prototype of xylem water filter, India, 2018.

Xylem in gymnosperm sapwood can be used for water filtration. Xylem is comprised of conduits that are interconnected by membranes that filter out contaminants present in water, e.g., microbes.

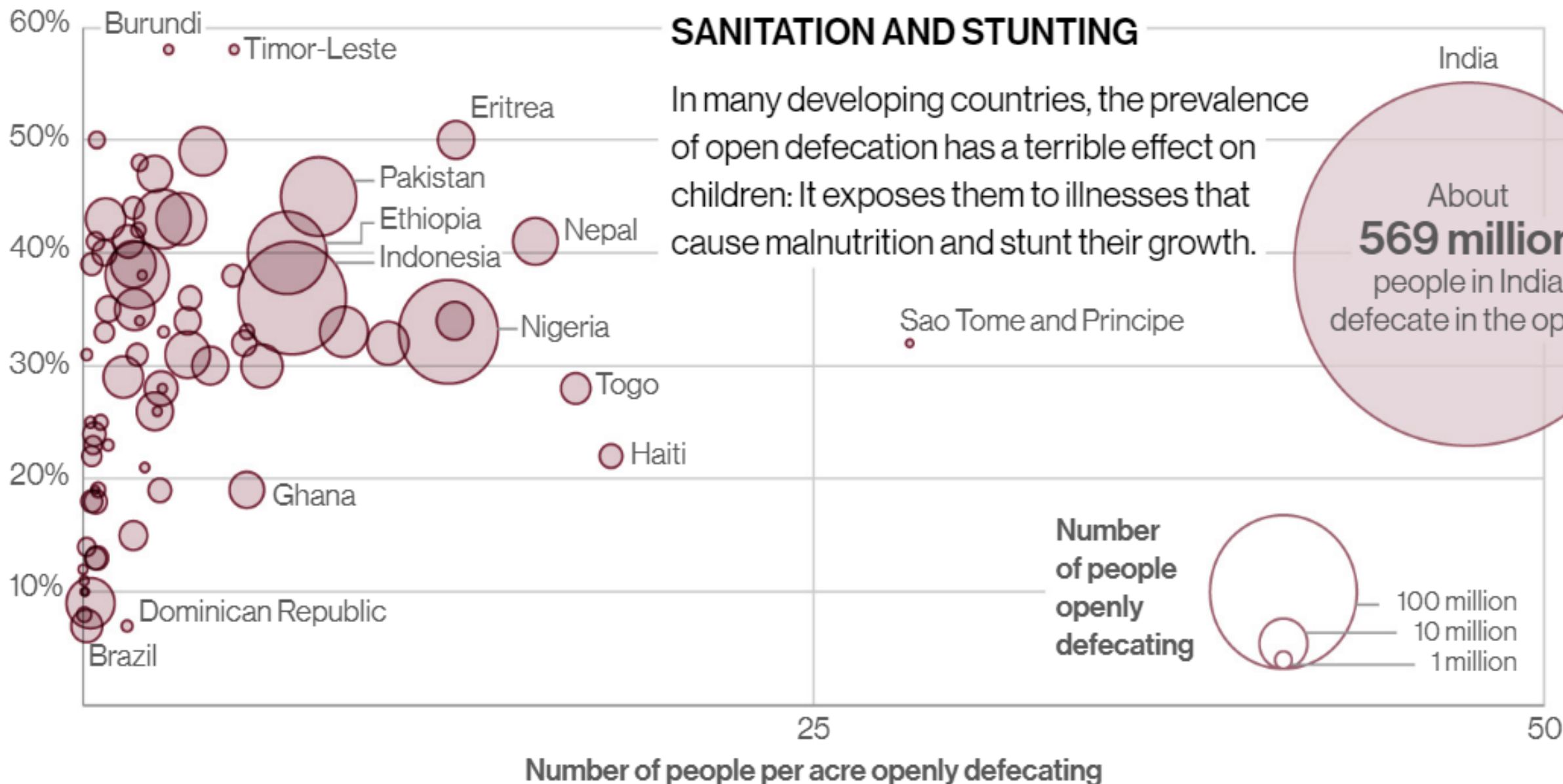
Developing low-cost water filters that exploit the natural filtration capabilities of xylem tissue in wood.

Stunting, death and malnutrition: why contaminated water has far more serious effects than the odd bout of diarrhoea



▲ Eight year olds in Monze District, Zambia beneath a chalk line indicating the global average height 40% of children in Zambia suffer from stunted growth, the 10th highest rate in Africa. Photograph: WaterAid/Chileshe Chanda

Percentage of children under five who are stunted





中文

Français

Русский

Español

1 in 3 people globally do not have access to safe drinking water – UNICEF, WHO

New report on inequalities in access to water, sanitation and hygiene also reveals more than half of the world does not have access to safe sanitation services.

18 June 2019 | News release | New York, Geneva

Billions of people around the world are continuing to suffer from poor access to water, sanitation and hygiene, according to a new report by UNICEF and the World Health Organization. Some 2.2 billion people around the world do not have safely managed* drinking water services, 4.2 billion people do not have safely managed sanitation services, and 3 billion lack basic** handwashing facilities.



Nada Osseiran

Communications Officer
WHO

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1624

Plumbum (Latin for Lead) – Lead Pipes are used for plumbing water





HHS Public Access

Author manuscript

J Public Health Manag Pract. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

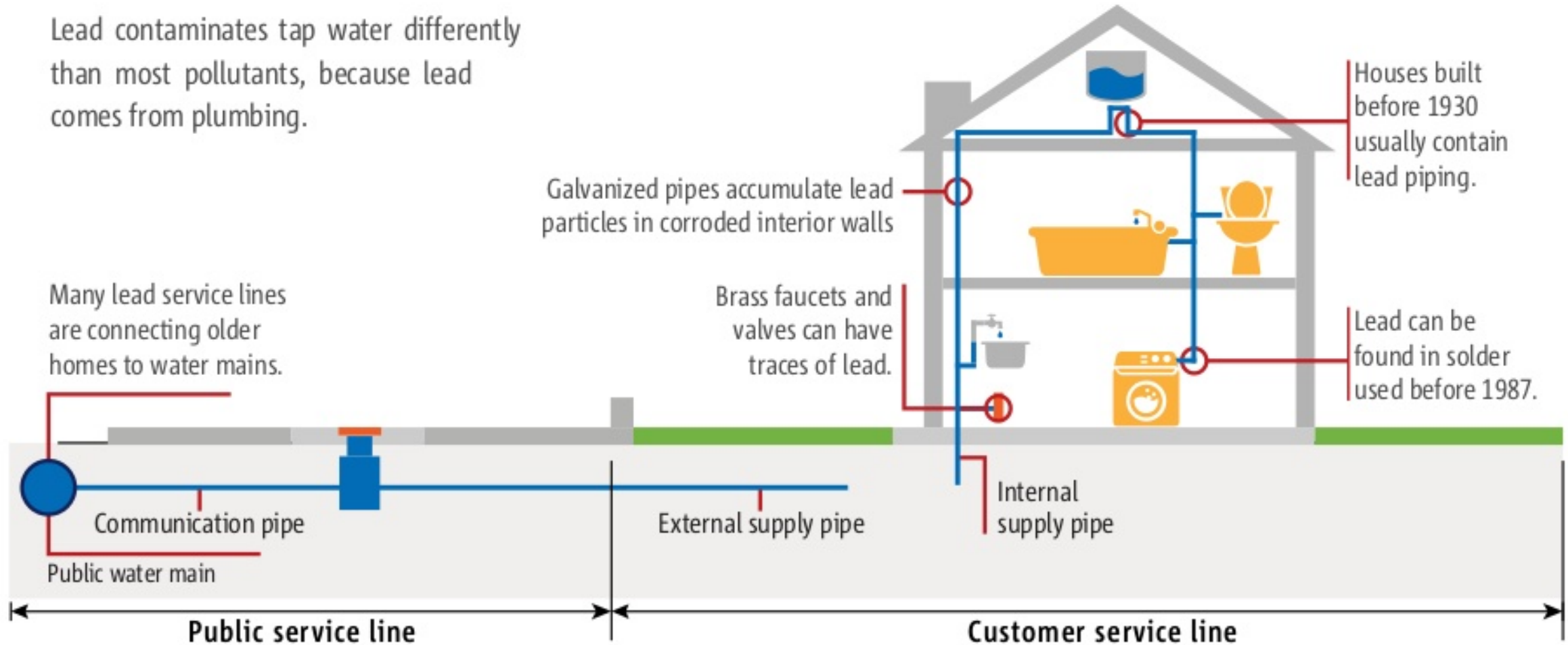
J Public Health Manag Pract. 2019 ; 25(Suppl 1 LEAD POISONING PREVENTION): S84–S90. doi:
10.1097/PHH.0000000000000871.

The Flint Water Crisis: A Coordinated Public Health Emergency Response and Recovery Initiative



THE PIPES

Lead contaminates tap water differently than most pollutants, because lead comes from plumbing.

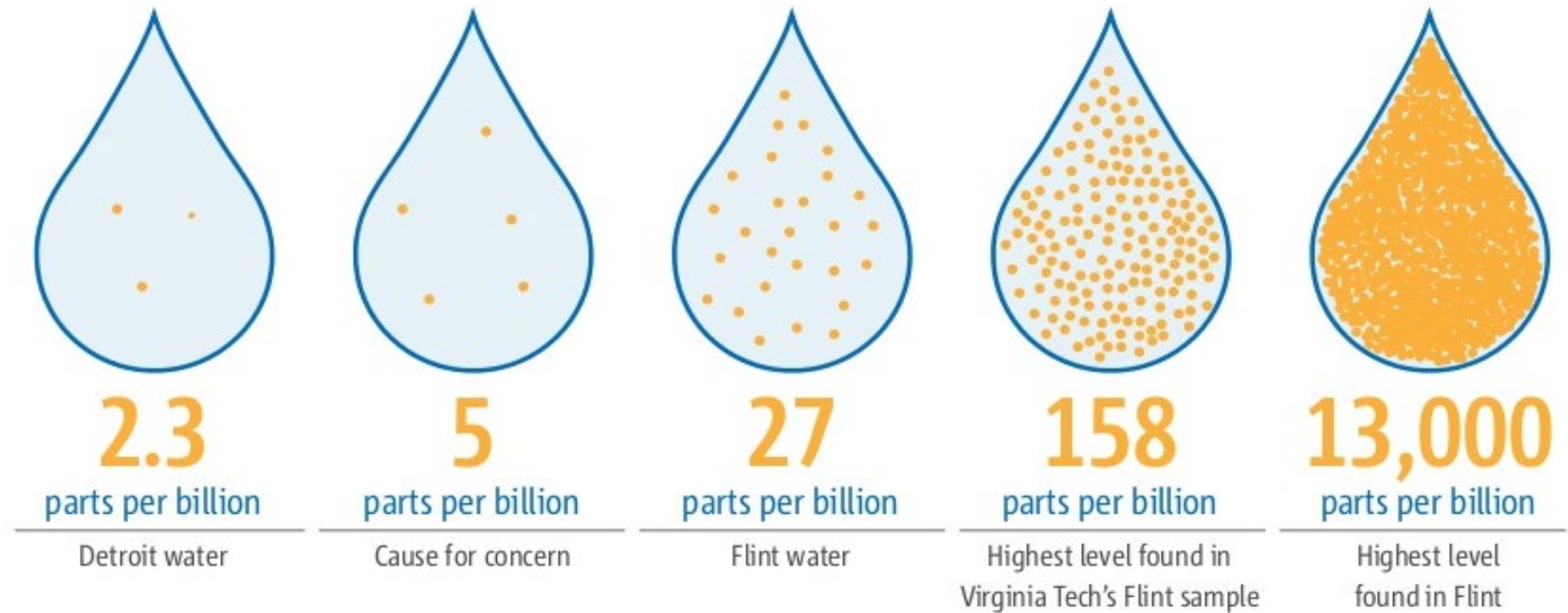


Summing up: water from Flint River moved through lead pipes, picking up the toxin as it went, and spread it throughout the population.

<https://www.slideshare.net/lbuckfire/the-flint-michigan-water-crisis-causes-effects>

THE KEY PROBLEM

Water from the Flint River is highly corrosive (its water has about 8 times more chloride (Cl⁻) in it than Detroit water) to iron and lead. Unfortunately, these pipe materials are widely used throughout Flint.

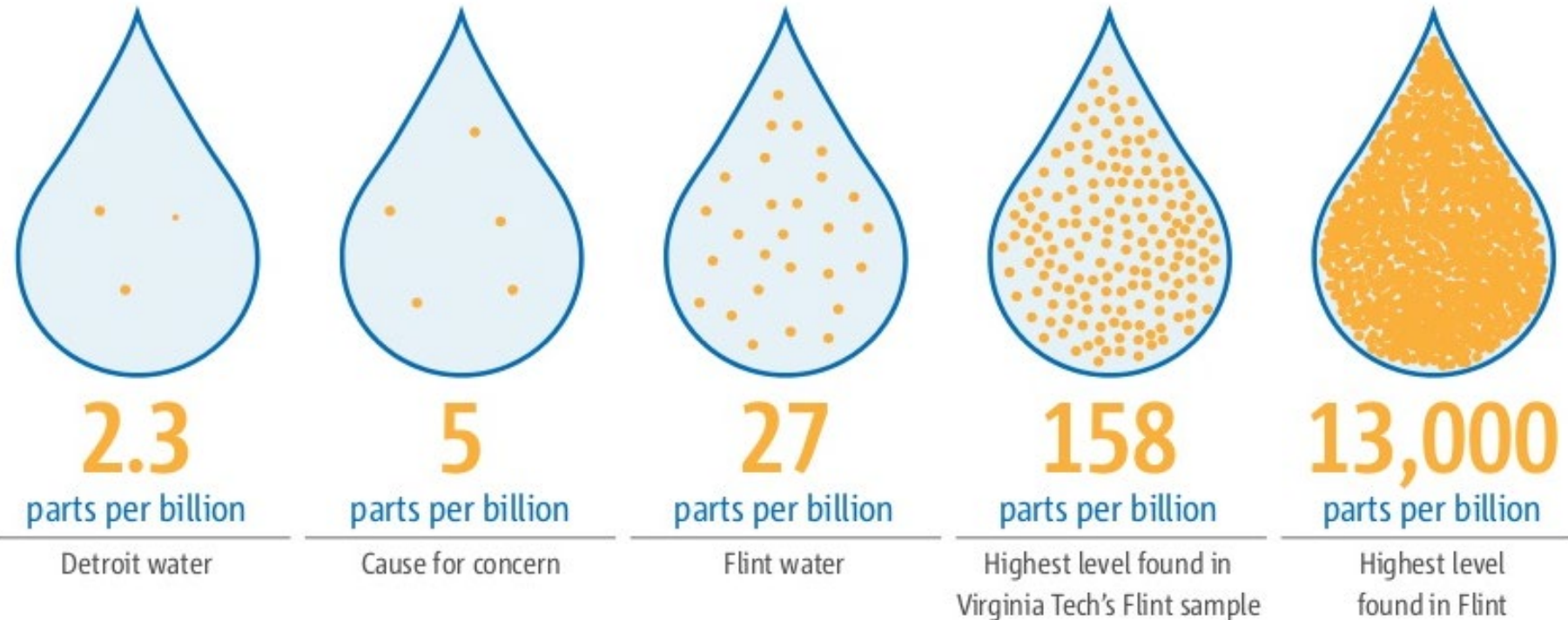


And, if these pipes are exposed to corrosive water, or if water sits too long inside them, the lead could be released and may end up coming out of the tap.

FLINT, MICHIGAN WATER CRISIS - LEAD POISONING FACTS AND FIGURES

THE KEY PROBLEM

Water from the Flint River is highly corrosive (its water has about 8 times more chloride (Cl⁻) in it than Detroit water) to iron and lead. Unfortunately, these pipe materials are widely used throughout Flint.



And, if these pipes are exposed to corrosive water, or if water sits too long inside them, the lead could be released and may end up coming out of the tap.

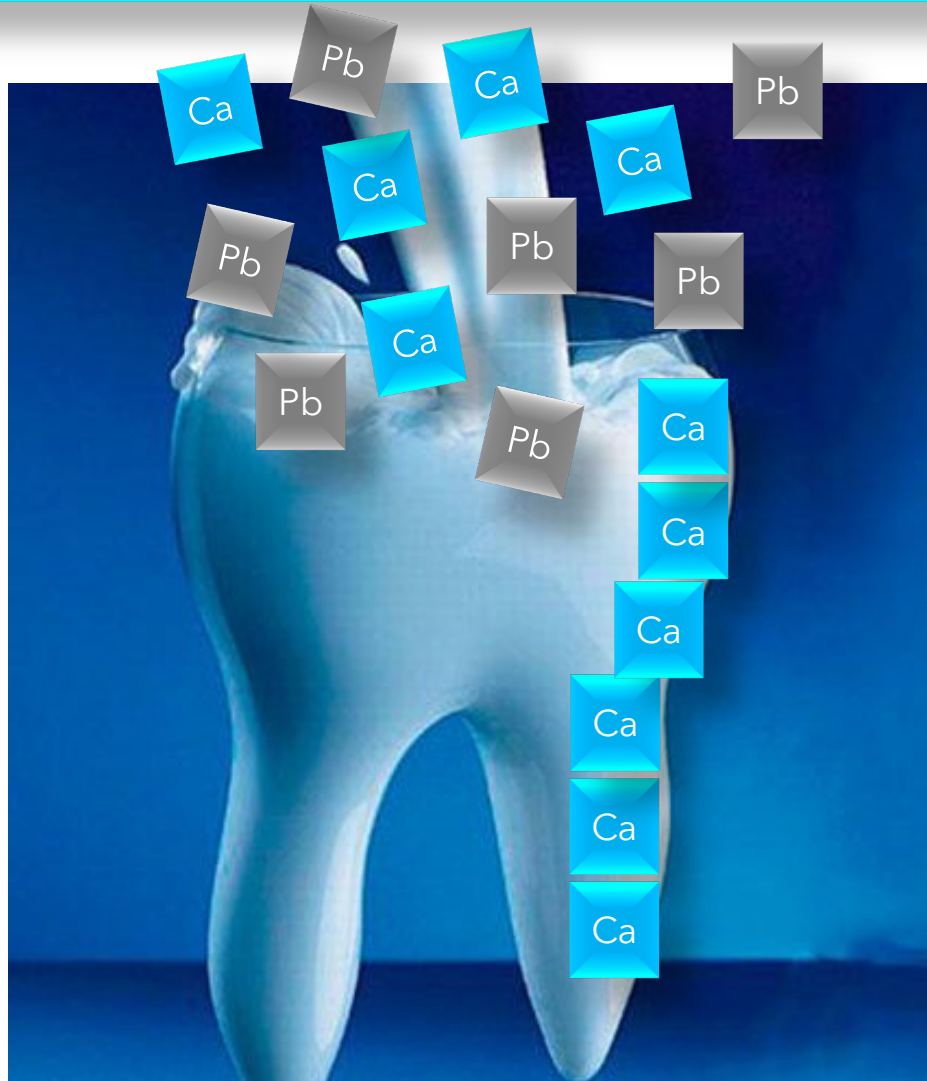
<https://www.slideshare.net/lbuckfire/the-flint-michigan-water-crisis-causes-effects>

THE FLINT'S WATER AND THE POISONED AMERICAN URBAN TRAGEDY CITY

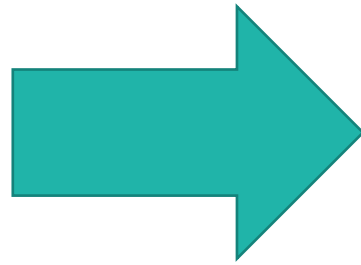
ANNA CLARK

Copyrighted Material

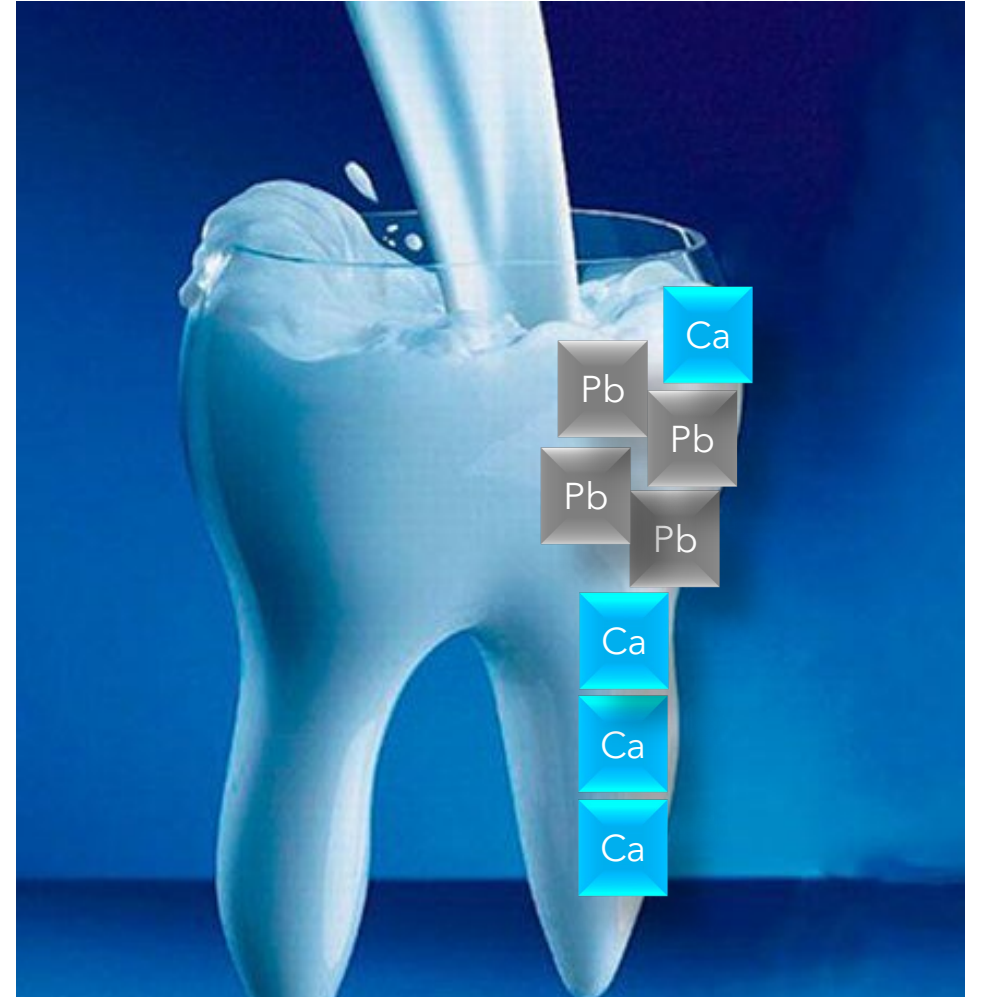
Lead (Pb) accumulates in teeth and bones



More lead exposure



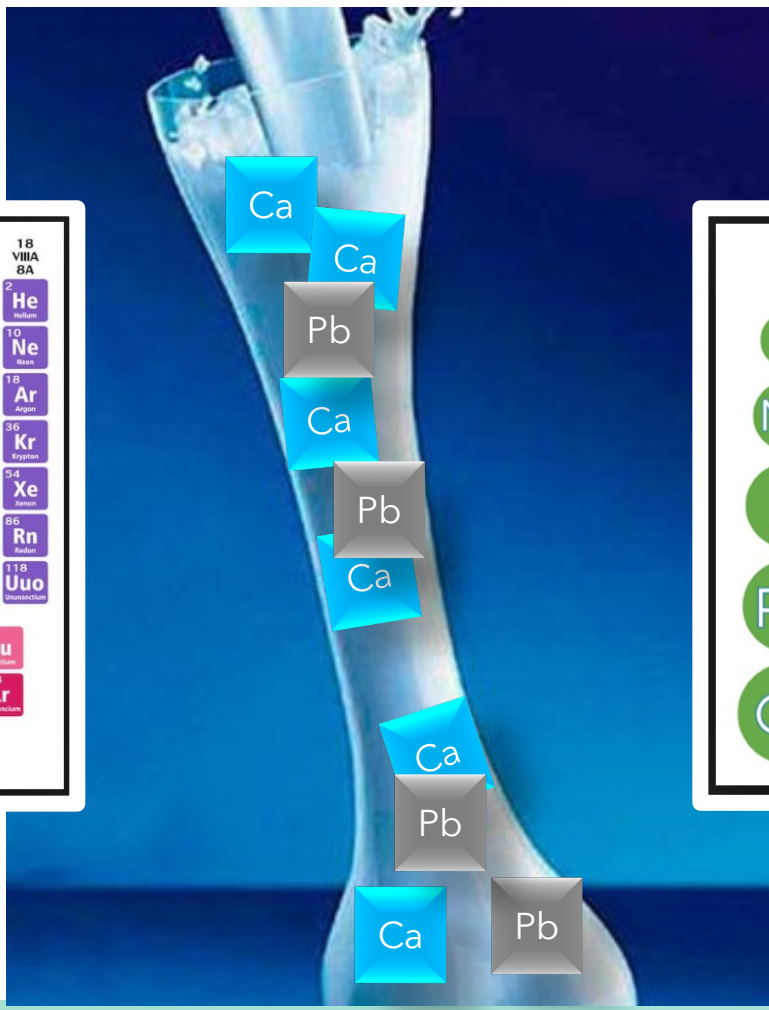
More lead is stored



Lead (Pb) accumulates in teeth and bones

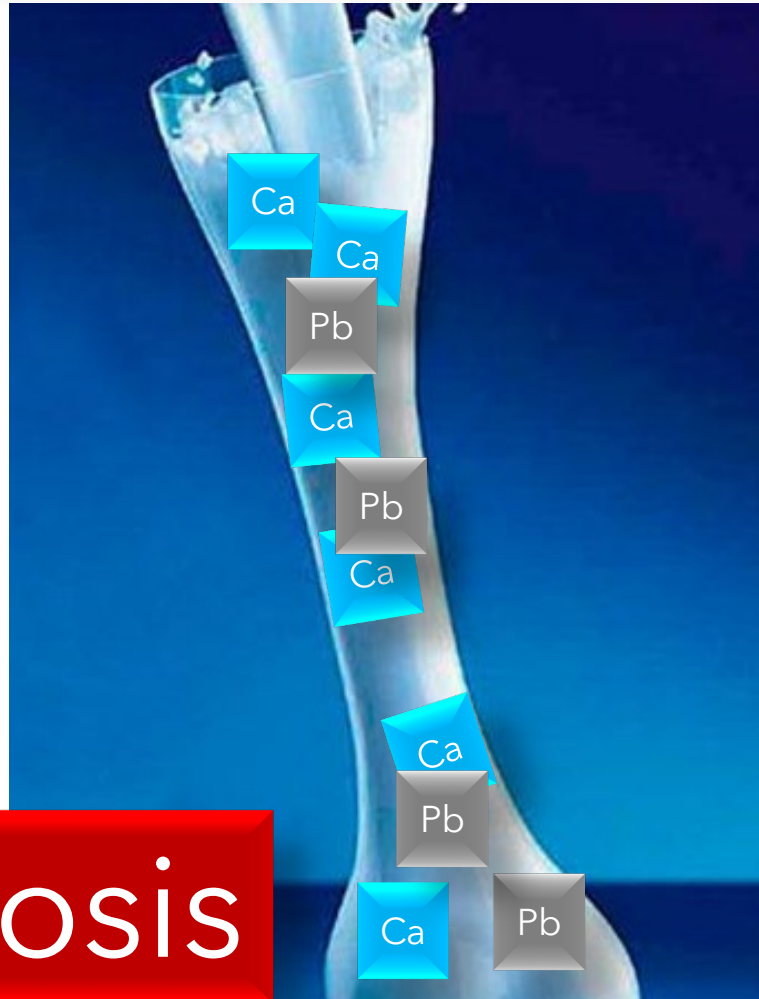
Periodic Table of The Elements

The periodic table shows elements from Hydrogen (H) to Oganesson (Og). It includes the Lanthanide Series (La-Lu) and Actinide Series (Ac-Lr). A legend indicates element types: Alkali Metal, Alkaline Earth, Transition Metal, Basic Metal, Semimetal, Nonmetal, Halogen, Noble Gas, Lanthanide, and Actinide.



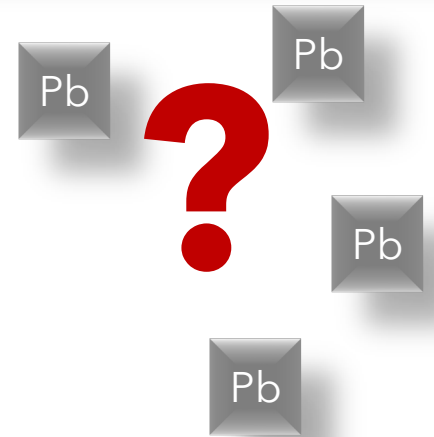
The simplified periodic table shows elements represented by colored circles. A vertical zigzag line separates the transition metals from the main group elements. The elements are arranged in rows and columns, with their symbols and names written inside the circles.

Lead (Pb) accumulates in teeth and bones

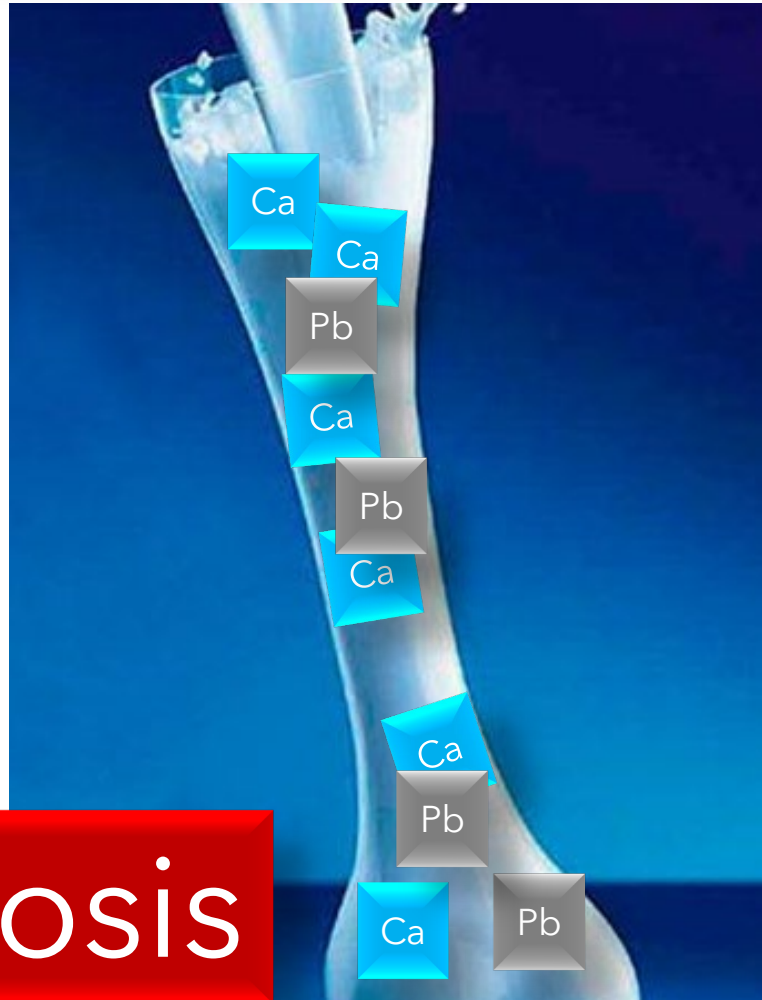


Osteoporosis

What happens to the **Pb** in the bones?

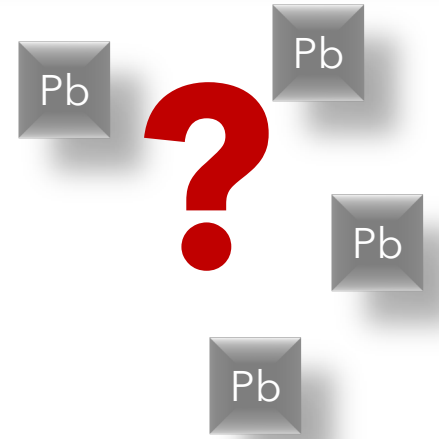


Lead (Pb) concentration increases in the blood



Osteoporosis

What
happens
to the **Pb**
in the bones?



Childhood Lead Poisoning
causes dementia in adults



The Association between Blood Lead Levels and Osteoporosis Adults—Results from the Third National Health and Nutrition Examination Survey (NHANES III)

James R. Campbell and Peggy Auinger

Published: 1 July 2007 | <https://doi.org/10.1289/ehp.9716> | Cited by: 35

78% of the U.S. population (1970s) had blood lead levels $\geq 10 \mu\text{g/dL}$. Bone is a repository for 90–95% of the total body burden of lead and harbors it for years after initial exposure. Thus, a high proportion of adult Americans may currently have elevated bone lead levels. With this many who were exposed to lead when younger, and the morbidity associated with osteoporosis, it is important to investigate whether an association exists between lead exposure and osteoporosis in humans. Our objective was to conduct a secondary analysis to explore an association between lead exposure and osteoporosis in U.S. adults.

Pb from water accumulates in teeth and bones. When Pb leaches out of bones, it may contribute to osteoporosis in adult life. Increased amount of Pb in blood may also contribute to dementia, Alzheimer's and neurotoxicity.

www.ncbi.nlm.nih.gov/pmc/articles/PMC3567843/pdf/nihms367232.pdf

Published in final edited form as:

Curr Alzheimer Res. 2012 June ; 9(5): 563–573.

Alzheimer's Disease and Environmental Exposure to Lead: The Epidemiologic Evidence and Potential Role of Epigenetics

Kelly M. Bakulski¹, Laura S. Rozek^{1,2}, Dana C. Dolinoy¹, Henry L. Paulson³, and Howard Hu^{1,4,5,*}

¹University of Michigan, School of Public Health, Department of Environmental Health Sciences

²University of Michigan, Medical School, Department of Otolaryngology

³University of Michigan, Department of Neurology

⁴University of Michigan, Department of Epidemiology

⁵University of Michigan, Medical School, Department of Internal Medicine

Abstract

Several lines of evidence indicate that the etiology of late-onset Alzheimer's disease (LOAD) is complex, with significant contributions from both genes and environmental factors. Recent research suggests the importance of epigenetic mechanisms in defining the relationship between environmental exposures and LOAD. In epidemiologic studies of adults, cumulative lifetime lead (Pb) exposure has been associated with accelerated declines in cognition. In addition, research in animal models suggests a causal association between Pb exposure during early life, epigenetics, and LOAD. There are multiple challenges to human epidemiologic research evaluating the relationship between epigenetics, LOAD, and Pb exposure. Epidemiologic studies are not well-suited to accommodate the long latency period between exposures during early life and onset of Alzheimer's disease. There is also a lack of validated circulating epigenetics biomarkers and retrospective biomarkers of Pb exposure. Members of our research group have shown bone Pb is an accurate measurement of historical Pb exposure in adults, offering an avenue for future epidemiologic studies. However, this would not address the risk of LOAD attributable to early-life Pb exposures. Future studies that use a cohort design to measure both Pb exposure and validated epigenetic biomarkers of LOAD will be useful to clarify this important relationship.

Do you know what is in your drinking water?

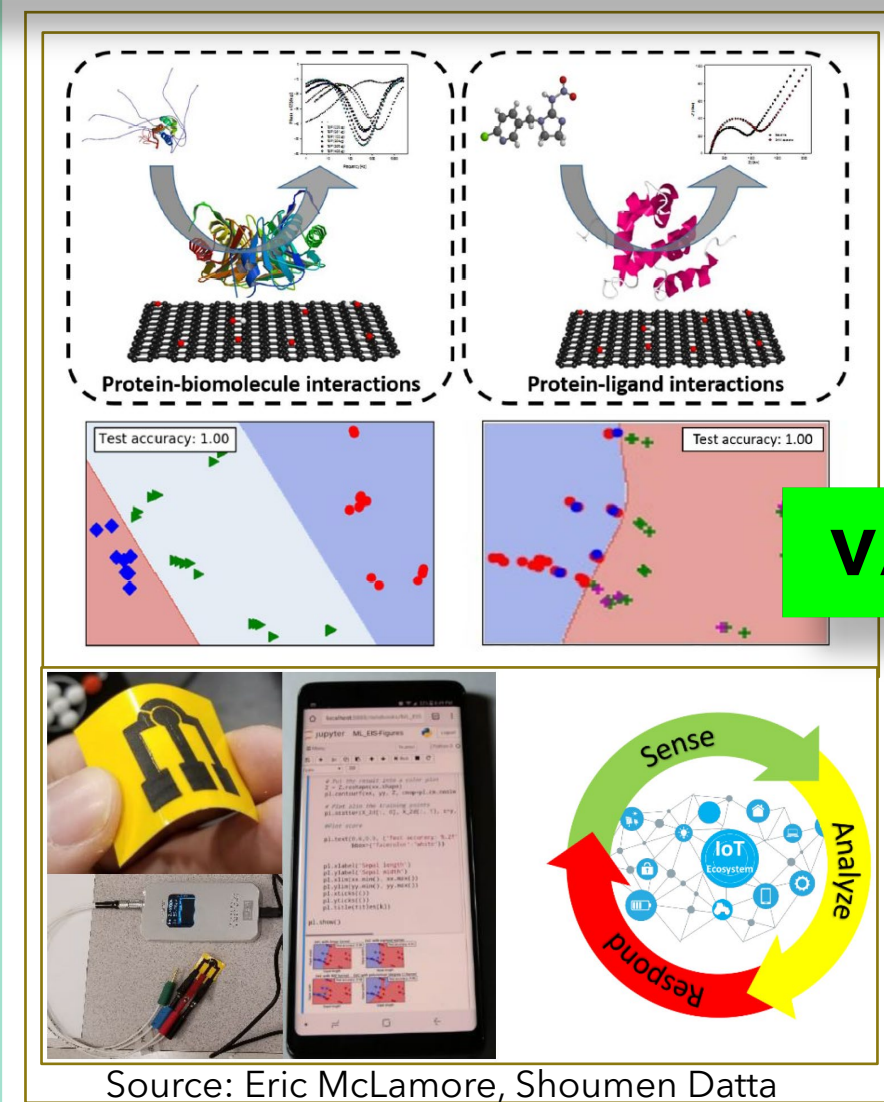
The Impact

535,000

U. S. children ages 1 to 5 years
have blood lead levels high
enough to damage their health.



WATER: science, engineering, technology, data



Flint, Michigan
Fes, Morocco

Fatehpur, India
Fuzhou, China

What can the user do with this data ??

World needs advanced tools and technologies to use the mobile data platform of smartphones for safety of people.

More than 1 billion people worldwide lack access to water, and almost 3 billion find water scarce for at least one month of the year. Inadequate sanitation is also a problem for more than 2 billion people, which exposes them to diseases, such as cholera and typhoid fever, and other water-borne illnesses. 2 million children die each year from diarrheal diseases alone, which is eminently preventable.

~ ~ ~ WATER ~ ~ ~

Immensely important global topic deserves intensely focused science and engineering research to alleviate human suffering.

Discussion: Snippets of Examples

Number 4



S

Sanitation

Your contribution to society matters.

Science and Scientists for Society

Mary-Ann Ochota

 @MaryAnnOchota

Tue 22 Nov 2016 07.48 EST



At the start of this year, the UN recognised sanitation as a universal human right. The Sustainable Development Goals aim to achieve global sanitation by 2030. But despite these grand ambitions, and a hard-working WASH (Water, Sanitation and Hygiene) development sector, 2.4 billion people around the world still don't have access to a proper toilet.

Mary-Ann Ochota

🐦 @MaryAnnOchota

Tue 22 Nov 2016 07.48 EST



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Lippenbekenntnis GERMAN

English translation of 'Lippenbekenntnis'

Lippenbekenntnis

NEUTER NOUN

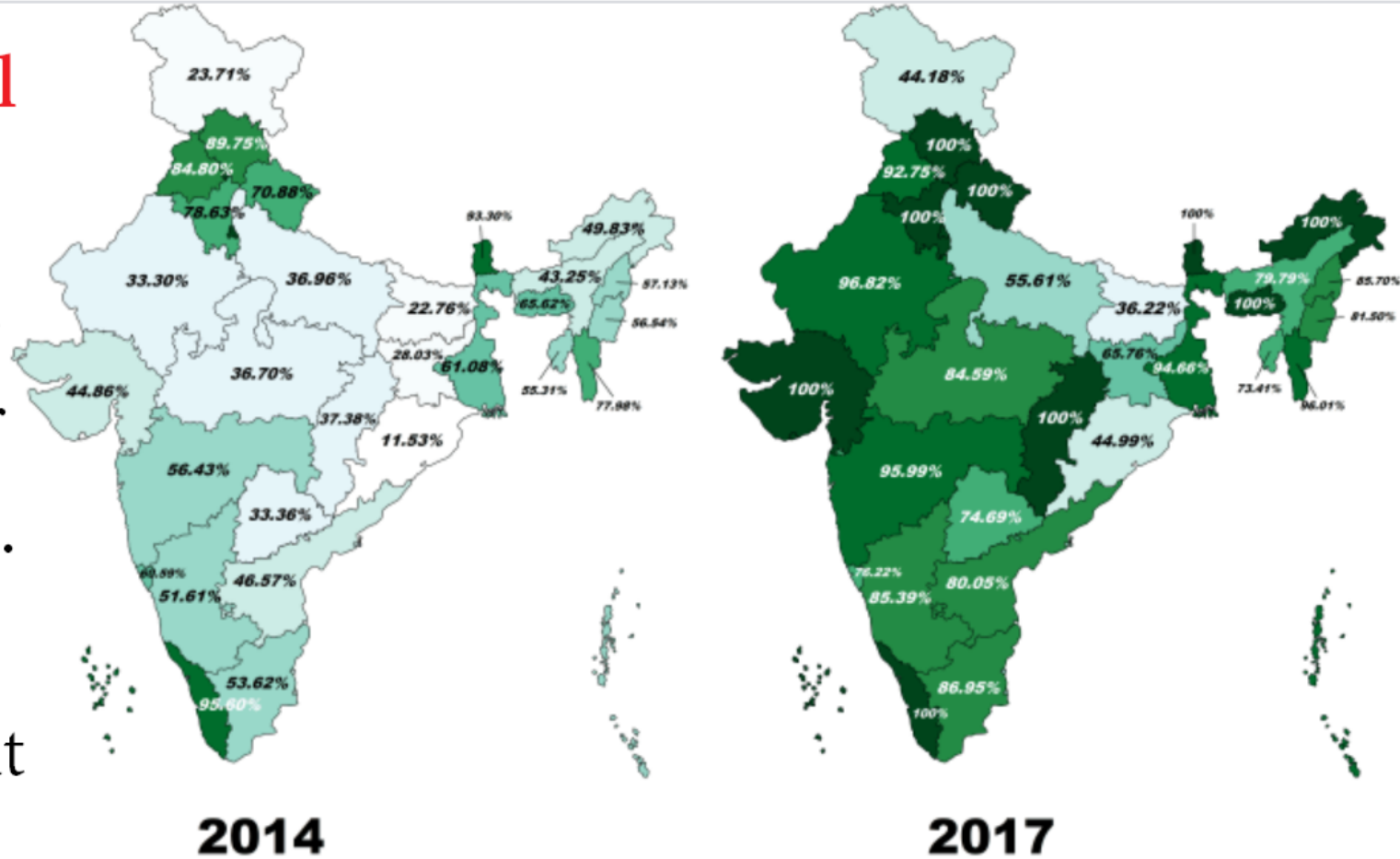
lip service

ein Lippenbekenntnis ablegen to pay lip service (to one's ideals etc)

Theoretical Change:

Household
with their
own toilets.

What about
those that
do not have
a house?



Map created by [Reddit user brahminthrowaway9460](#)

The map above shows the theoretical change in the percentage of Indian Households with their own toilets between 2014 and 2017.

35.5 Crore Women Don't Have Access To Toilet In India: Report

The Logical Indian

20 Nov 2017

Editor : The Logical Indian

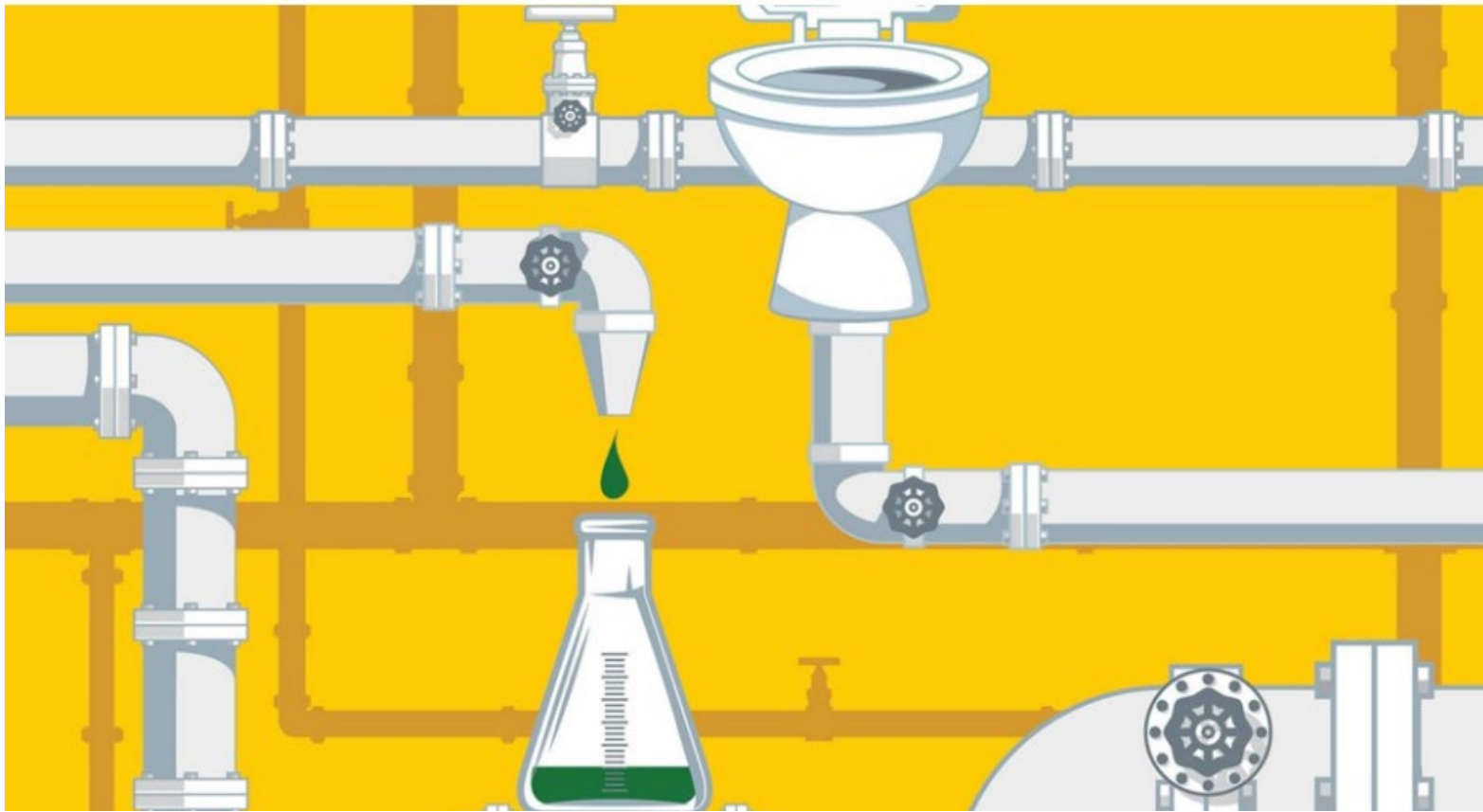


**732 Million Indians Defecate
In The Open**

Wastewater-based Epidemiology

In India?

It is akin to telling a hair-raising story to a bald-headed man!





Countries that account for almost open defecation:

1. India (626 million)
2. Indonesia (63 million)
3. Pakistan (40 million)
4. Ethiopia (38 million)
5. Nigeria (34 million)
6. Sudan (19 million)
7. Nepal (15 million)
8. China (14 million)
9. Niger (12 million)
10. Burkina Faso (9.7 million)
11. Mozambique (9.5 million)
12. Cambodia (8.6 million).

Percentage of population that defecates in the open

- More than 40
- 25 to 39.9
- 10 to 24.9
- 1 to 9.9
- Less than 1
- No data

Countries with highest rates

1. Eritrea
2. South Sudan
3. Niger
4. Chad
5. Burkina Faso
6. Sao Tome and Principe
7. Solomon Islands
8. Benin
9. Togo
10. Namibia

A gargantuan infrastructure problem compounded by lack of adequate energy and water

Is it mostly an infrastructure engineering problem?

Water-free nano-membrane toilet is indeed a good idea but is this high-maintenance system feasible?

→ cranfield.ac.uk/people/dr-alison-parker-734615



Watch on YouTube

<https://www.youtube.com/watch?v=jGPpXF7y9Rg>

<https://www.youtube.com/watch?v=x2gjipWubs0>



Home /

Dr Alison Parker

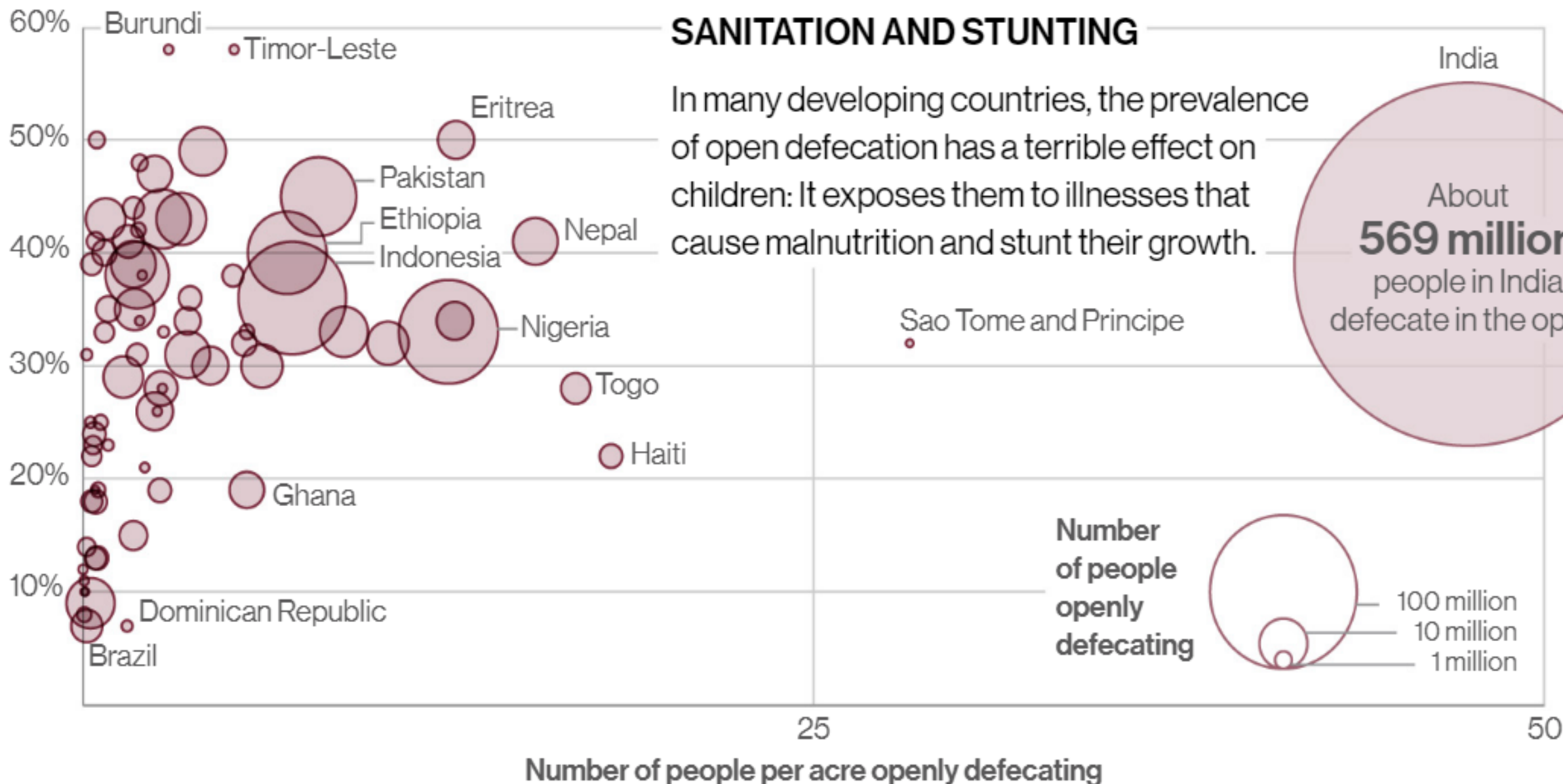
FGS, FHEA

Senior Lecturer in International Water and Sanitation
Cranfield Water Science Institute

Sanitation



May provide clues for
health and healthcare

Percentage of children under five who are stunted



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7566278/pdf/mSystems.00614-20.pdf>

SARS-CoV-2 Titers in Wastewater Are Higher than Expected from Clinically Confirmed Cases

 Fuqing Wu,^{a,n,o} Jianbo Zhang,^{a,n} Amy Xiao,^{a,n,o} Xiaoyong Gu,^{b,m} Wei Lin Lee,^{b,m} Federica Armas,^{b,m} Kathryn Kauffman,^c William Hanage,^d Mariana Matus,^e Newsha Ghaeli,^e Noriko Endo,^e Claire Duvallet,^e Mathilde Poyet,^{a,n,o} Katya Moniz,^{a,n,o} Alex D. Washburne,^p Timothy B. Erickson,^{f,g} Peter R. Choi,^{f,h,i} Janelle Thompson,^{j,k,m}  Eric J. Alm^{a,b,e,l,m,n,o}

^aCenter for Microbiome Informatics and Therapeutics, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

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^cUniversity at Buffalo, The State University of New York, Buffalo, New York, USA

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^kAsian School of the Environment, Nanyang Technological University, Singapore

^lBroad Institute of MIT and Harvard, Cambridge, Massachusetts, USA

^mCampus for Research Excellence and Technological Enterprise, Singapore

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^pSelva Analytics, LLC, Bozeman, Montana, USA

Jianbo Zhang and Amy Xiao contributed equally.

ABSTRACT Wastewater surveillance represents a complementary approach to clinical surveillance to measure the presence and prevalence of emerging infectious diseases like the novel coronavirus SARS-CoV-2. This innovative data source can improve the precision of epidemiological modeling to understand the penetrance of SARS-CoV-2 in specific vulnerable communities.

INFECTIOUS DISEASE

Novel coronavirus found in surprisingly high levels in sewage

Viral levels higher than expected based on confirmed COVID-19 cases

by *Celia Henry Arnaud*

APRIL 16, 2020 | APPEARED IN **VOLUME 98, ISSUE 15**



In a
Post-COVID
World:

New
Metaphors?
Paradigms?

CITCOM
Canaries in the
Coal Mine

SENSEW
Sensors in the
Sewer
Seawater
Wastewater



VIDEO

LIVE

SHOWS

2020 ELECTIONS

CORONAVIRUS



As the US struggles with lack of coronavirus testing, researchers look to our sewage for clues

Coronavirus may be tracked by where it shows up in wastewater.

By Dr. Nancy A. Anoruo

April 6, 2020, 2:24 PM • 6 min read



MIT begins testing wastewater to help detect Covid-19 on campus

The pilot project is designed to determine if wastewater testing can provide early signals about the spread of the virus.

[Watch Video](#)

Zach Winn | MIT News Office
October 2, 2020



Answers to urban health problems are right under our feet. Sewers carry a reservoir of information on human health and behavior. Scientists and engineers at MIT are on a mission to create real-time public health profiles of urban areas by sampling sewer/wastewater using tools from bio-chemistry, genomics, robotics, data analytics.



<https://www.biobot.io/>

Biobot Labs



Newsha Ghaeli



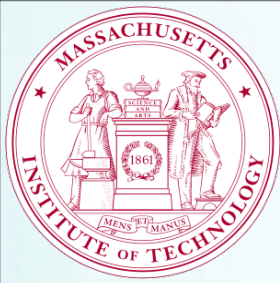
Mariana G. Matus



Carlo Ratti



Eric Alm



30,200 active
companies



4.6 million people
employed



\$1.9 trillion in
annual revenues



<http://web.mit.edu/innovate/entrepreneurship2015.pdf>

A new report estimates that, as of 2014, MIT alumni have launched 30,200 active companies, employing roughly 4.6 million people, and generating roughly \$1.9 trillion in annual revenues.



Katie Jennings Forbes Staff

Healthcare

I am a staff writer covering health care. Email me at kjennings@forbes.com.



forbes.com/sites/katiejennings/2020/04/24/mit-spinoff-raises-42-million-to-estimate-scope

Forbes

EDITORS' PICK | 4,558 views | Apr 24, 2020, 04:25pm EDT

MIT Spinoff Raises \$4.2 Million To Estimate Scope Of Coronavirus Cases By Analyzing Poop



Biobot Analytics co-founders Mariana Matus (L) and Newsha Ghaeli (R) in their lab in Somerville, MA. BIOBOT ANALYTICS

Mariana Matus says she learned firsthand what it meant not to have access to healthcare services



Katie Jennings Forbes Staff

Healthcare

I am a staff writer covering health care. Email me at kjennings@forbes.com.

Your Poop Might Be Key For Predicting End of the Pandemic

Looking for the new coronavirus in wastewater could give us a heads up about where the outbreak is spreading – and when it has started to dissipate.

By [Shayla Love](#)

Apr 8 2020, 4:55pm [Share](#) [Tweet](#) [Snap](#)



PAOLO CORDONI / EYEEH | GETTY

On March 5, there had not yet been a clinical diagnosis of COVID-19 in Amersfoort, a Dutch city of more than 150,000 people to the east of Amsterdam. But underneath Amersfoort's streets, dotted with Medieval buildings, the sewage pipes containing people's fecal matter told another story.

www.newsweek.com/coronavirus-traces-massachusetts-wastewater-levels-higher-expected-1497141

In a Post-COVID World: New lines of business – pay per pee healthcare

medrxiv.org/content/10.1101/2020.04.05.20051540v1.full.pdf

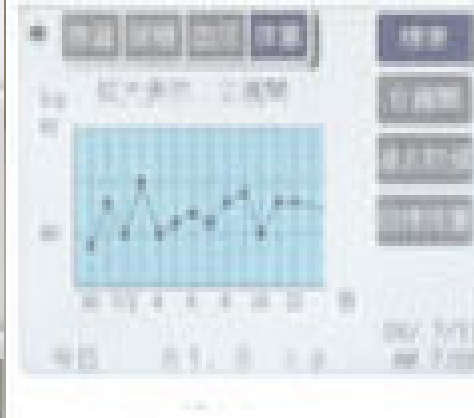
Title: SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases

Authors: Wu FQ(1); Xiao A(1); Zhang JB(1); Gu XQ(2); Lee WL(2); Kauffman K (3); Hanage WP(4); Matus M (5); Ghaeli N(5); Endo N(5); Duvallet C(5); Moniz K(1); Erickson TB(6); Chai PR (6); Thompson J(7); Alm EJ(1,2,5)

- 1: Center for Microbiome Informatics and Therapeutics, Departments of Biological Engineering and Civil & Environmental Engineering, Massachusetts Institute of Technology
- 2: Singapore-MIT Alliance for Research and Technology, National University of Singapore
- 3: University at Buffalo, The State University of New York
- 4: Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston
- 5: Biobot Analytics, Cambridge MA
- 6: Division of Medical Toxicology, Department of Emergency Medicine, Brigham and Women's Hospital
- 7: Singapore Center for Environmental Life Sciences Engineering, Asian School of the Environment, Nanyang Technological University, Singapore

Abstract. Wastewater surveillance may represent a complementary approach to measure the presence and even prevalence of infectious diseases when the capacity for clinical testing is limited. Moreover, aggregate, population-wide data can help inform modeling efforts. We tested wastewater collected at a major urban treatment facility in Massachusetts and found the presence of SARS-CoV-2 at high titers in the period from March 18 - 25 using RT-qPCR. We then confirmed the identity of the PCR product by direct DNA sequencing. Viral titers observed were significantly higher than expected

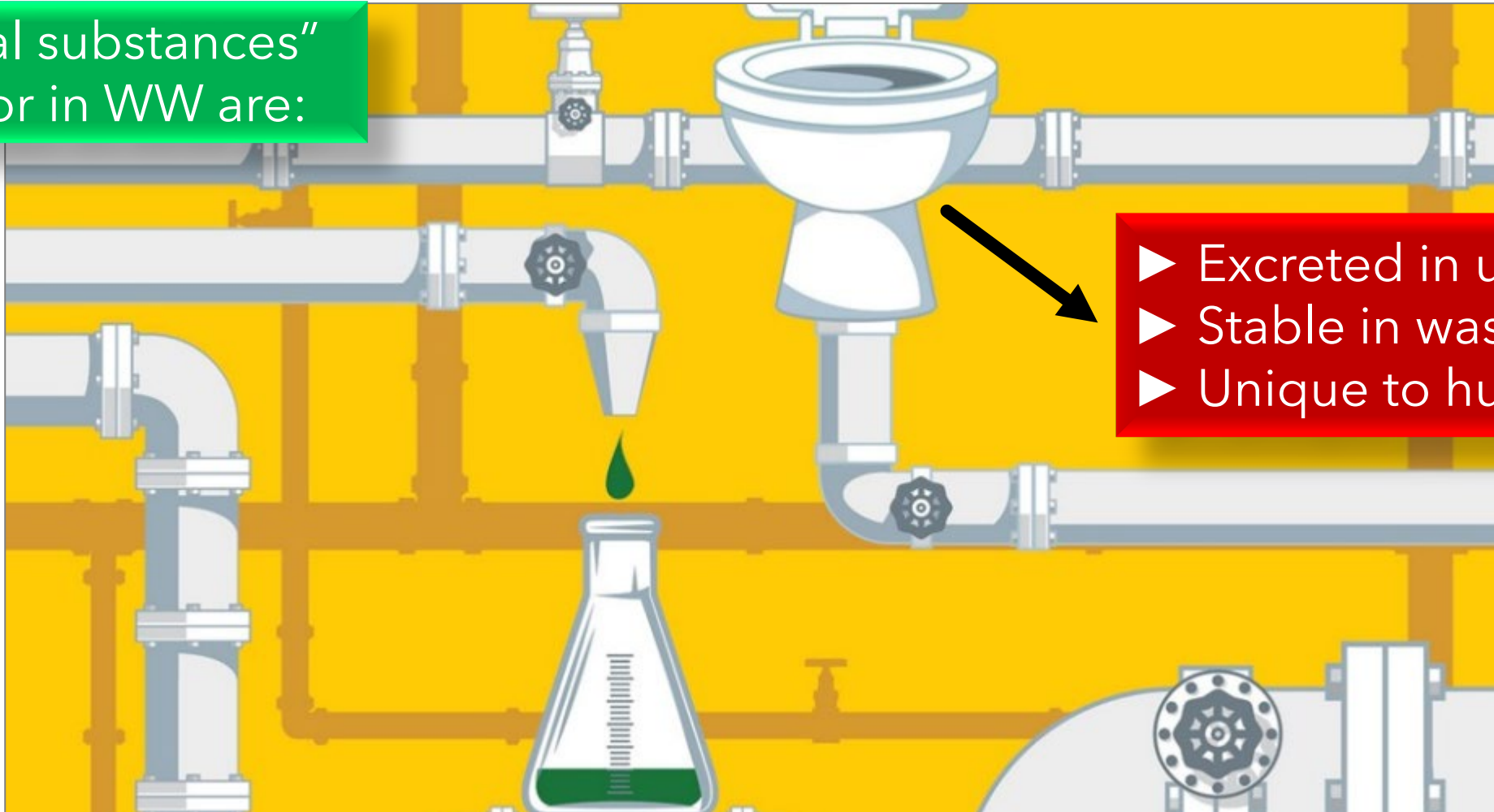
Pay-Per-Pee Home Health IoT Wireless Toilet Bowl Connected to Precision Public Health IT



Weigh-scale, BMI, FOBT, urine analysis, fecal matter (microbe), sugar, ketone body analysis, blood pressure monitor, pulse oximeter, networked to phone via WiFi and/or Bluetooth with biometrics and face recognition for secure communication with physician and hospital.

Wastewater based Epidemiology

The "ideal substances" to monitor in WW are:



- ▶ Excreted in urine/feces
- ▶ Stable in wastewater
- ▶ Unique to human

Sanitation & Healthcare

INEXTRICABLY

LINKED ??

Discussion: Snippets of Examples

Number 5



H

Healthcare

Your contribution to society matters.

Science and Scientists for Society

The division between “rich” versus “poor” may be less applicable to healthcare because human welfare and practices which may alleviate human suffering, diseases and morbidity may benefit all humans

But there are exceptions ...

Diseases neglected by the affluent world

The World Health Organization has established a list of 17 “official” neglected tropical diseases (NTDs): Buruli ulcer, Chagas disease, cysticercosis, dengue, dracunculiasis, echinococcosis, endemic treponematoses, foodborne trematode infections, human African trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, rabies, schistosomiasis, soil-transmitted helminthiases, and trachoma. These 17 diseases were chosen because of their adverse impact, relative obscurity, and the lack of availability of tools to combat them (because they are uncommon in the affluent world).

<https://www.ncbi.nlm.nih.gov/books/NBK62516/>

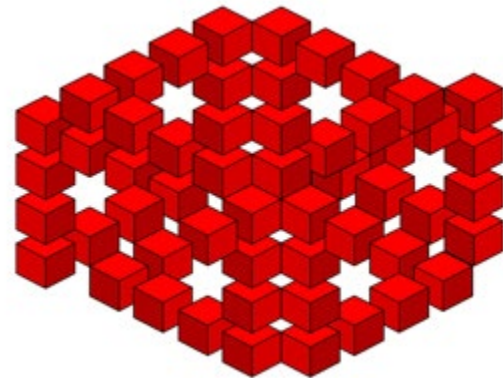
Diseases neglected by the affluent world

*The good news is that the **science** and **engineering** expertise we need in order to address the neglected diseases are similar in terms of their **foundation**, for almost any disease, neglected or not.*

Therefore, our discussion in the healthcare segment will address healthcare in general.

<https://dspace.mit.edu/handle/1721.1/107893>

HEALTHCARE ISSUES



Dr Shoumen Palit Austin Datta

Research Affiliate, MIT Auto-ID Labs, Department of Mechanical Engineering, School of Engineering, Massachusetts Institute of Technology shoumen@mit.edu

Senior Scientist, MDPnP Lab, Medical Device Interoperability & Cybersecurity Program, Department of Anesthesiology, Massachusetts General Hospital, Harvard Medical School sdatta8@mgh.harvard.edu



Dr JLarry Jameson MD PhD Molecular Endocrinology / Neuro-Endocrinology Dr Ann Klibanski MD

One decade ago, my research group at the University of Tokyo created a flexible electronic mesh and wrapped it around the mechanical bones of a robotic hand. We had dreamed of making an electronic skin, embedded with temperature and pressure sensors, that could be worn by a robot. If a robotic health aide shook hands with a human patient, we thought, this sensor-clad e-skin would be able to measure some of the person's vital signs at the same time.

Today we're still working intensively on e-skin, but our focus is now on applying it directly to the human body. Such a bionic skin could be used to monitor medical conditions or to provide more sensitive and lifelike prosthetics.

<http://spectrum.ieee.org/biomedical/bionics/bionic-skin-for-a-cyborg-you>

Where does this fit in your future?

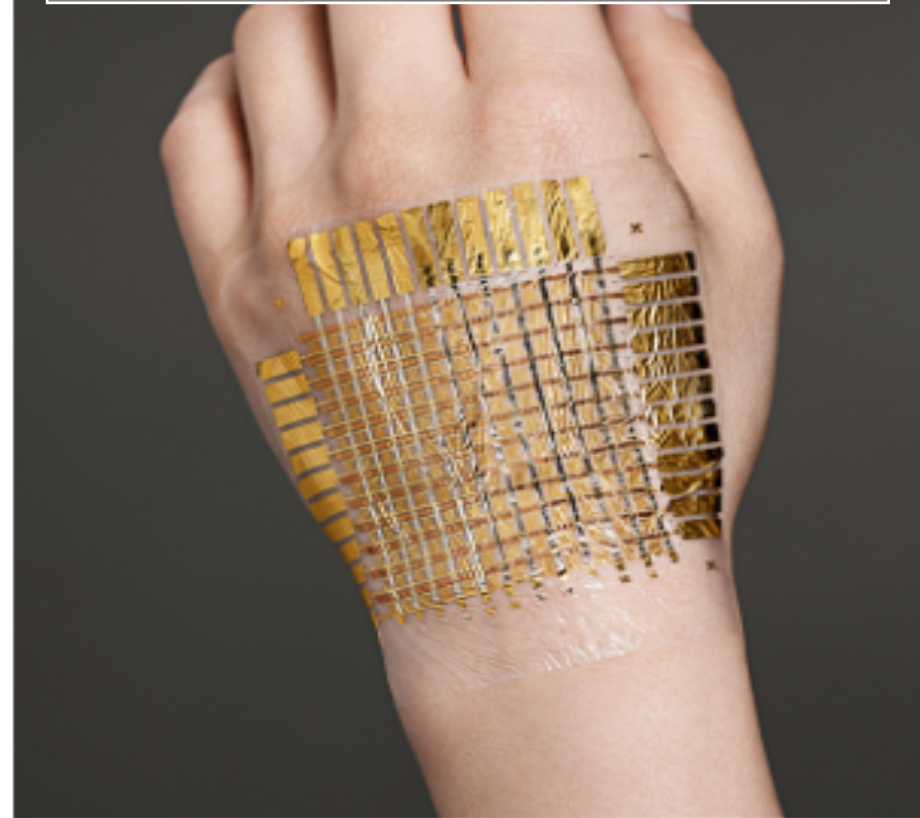


Photo: Someya-Sekitani Group

Gilded skin: Takao Someya's latest e-skin material is one-tenth the thickness of plastic kitchen wrap, and it can conform to any body shape.

Electronic Nose Sniffs Out Ovarian Cancer in Exhaled Breath

OCTOBER 6TH, 2015



EDITORS

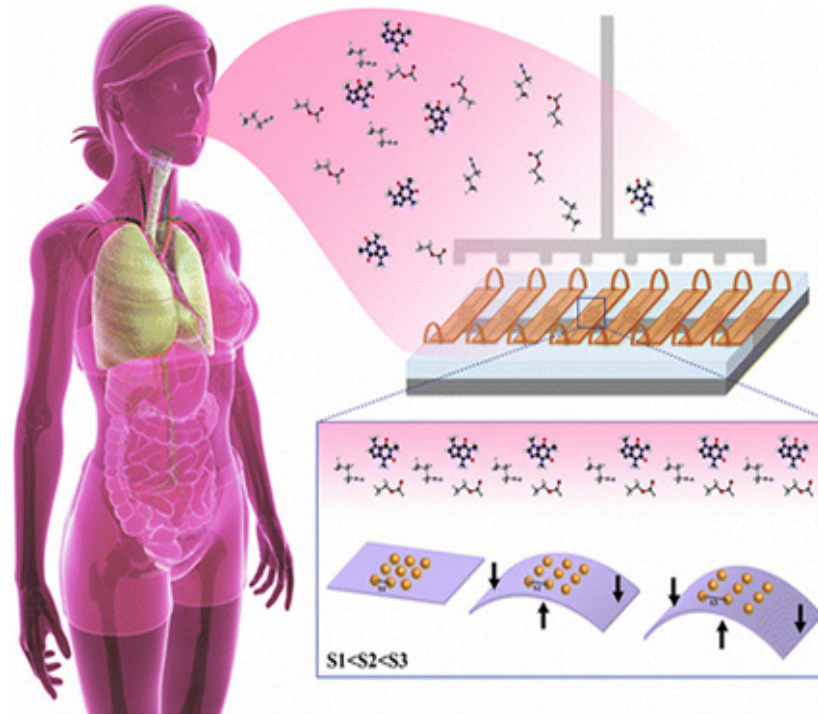


NANOMEDICINE, ONCOLOGY

Where does this fit in your future?

We know that exhaled breath contains biomarkers that point to presence of existing disease, including cancer, but their detection is challenging without bulky and expensive equipment. Building specialized devices that detect volatile organic compounds linked to disease requires large sensor arrays, a limitation that has made them currently impractical. Now researchers at Technion -Israel Institute of Technology and Carmel Medical Center in Haifa, Israel have developed tiny flexible sensors that are each able to replicate the work of many. In a study testing the breath of 43 volunteers that included 17 ovarian cancer patients, their sensors achieved an 82% accuracy of detection.

The sensors are flexible and are made of gold nanoparticles that have molecules onto which volatile organic compounds (VOCs) attach to. When captured, the different VOCs bend the sensors at different angles depending on their nature and provide more information than simply whether they're there or not.



Dynamic Nanoparticle-Based Flexible Sensors: Diagnosis of Ovarian Carcinoma from Exhaled Breath

Nicole Kahnt[†], Ofer Lavi[‡], Moran Paz[‡], Yaki Segev[‡], and Hossam Haick^{‡*}

[†] Department of Chemical Engineering and Russell Berrie Nanotechnology Institute, Technion-Israel Institute of Technology, Haifa 3200003, Israel

[‡] Gynecological Oncology and Surgery Unit, Carmel Medical Center, Haifa 3436212, Israel

Nano Lett., Article ASAP

DOI: 10.1021/acs.nanolett.5b03052

Publication Date (Web): September 9, 2015

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Malaria Diagnosis Using a Mobile Phone Polarized Microscope

Casey W. Pirnstill  & Gerard L. Côté

Scientific Reports 5, Article number: 13368

(2015)

doi:10.1038/srep13368

Received: 19 March 2015

Accepted: 14 July 2015

Published online: 25 August 2015

Poverty magnifies the need for health care while shrinking the capacity to finance it. Low-income countries face 56 percent of the global disease burden but account for only 2 percent of global health spending (World Bank 2005; Mathers, Lopez, and Murray, forthcoming). With spending levels of some \$30 per capita on average, over half of it out of pocket, low-income countries face severe challenges in providing their

The Leapfrog Opportunity In The World's Underserved Health Care Markets



President Uhuru Kenyatta of Kenya

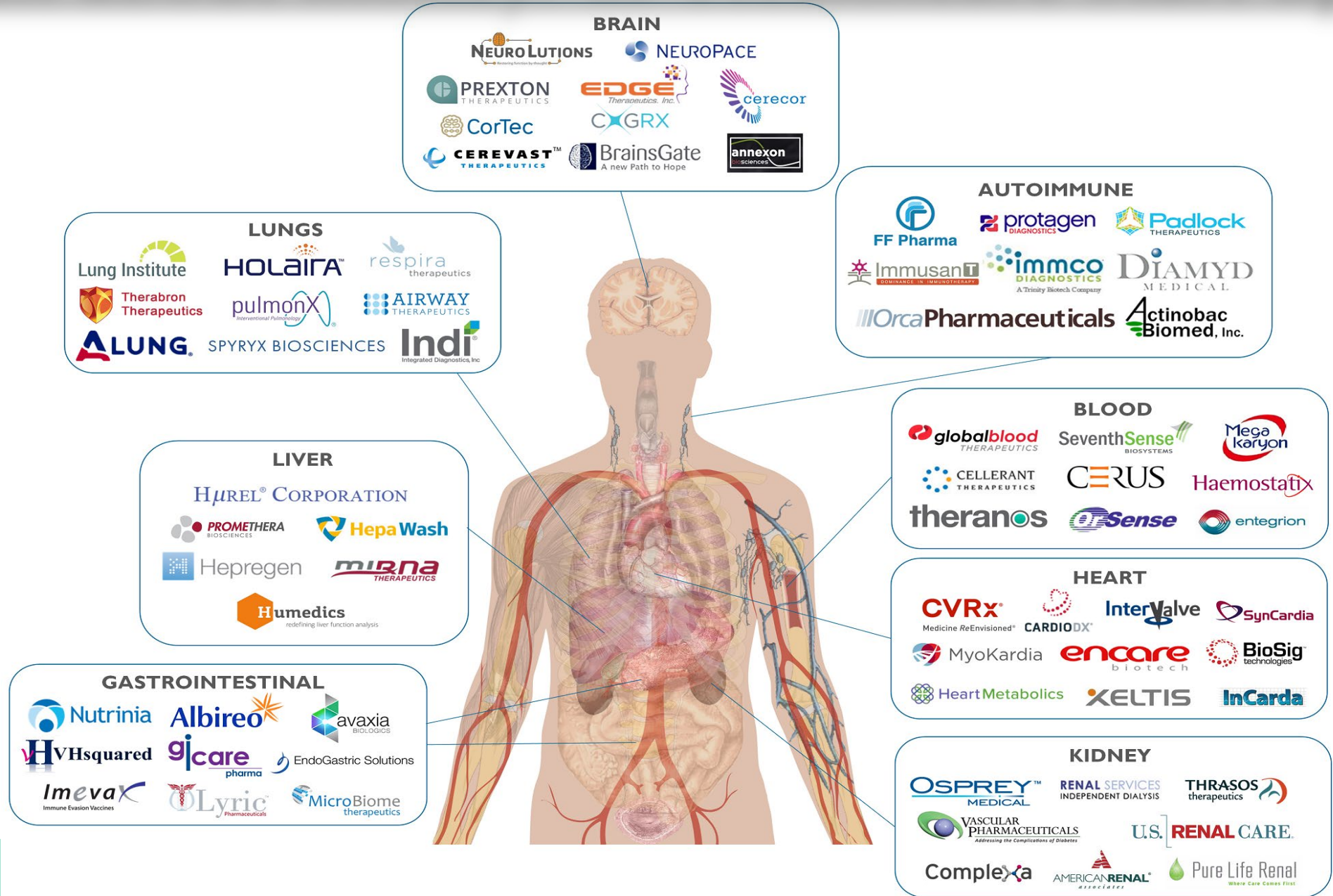
[+ Comment Now](#)

In Sub-Saharan Africa, traditional banking infrastructure has never quite gained a foothold. That's because instead of brick and mortar vaults, the region has seen sweeping use of mobile banking. Microfinancing and transfers, all from your cell phone, offered simplified, safer banking solutions for a fraction of the cost.

This is an example of “leapfrog” innovation and the same paradigm is beginning to emerge in [health](#) care in Africa, [Asia](#) and Latin America, creating a global opportunity for health innovators.

This past week President Obama was in Africa at the Global Entrepreneurship Summit [calling on entrepreneurs and industry leaders to ignite growth on that continent](#) and beyond. The question is will the leaders in today's largest health care [markets](#) seize the moment? Or will upstarts leap over them by bringing radically less expensive and more accessible healthcare options to the rest of the world?

Is it all about money? 69 Healthcare Start-ups (Yes)



Does US Abhor Low-Cost Healthcare?

How the healthcare system discourages creating low-cost solutions

<http://jama.jamanetwork.com/article.aspx?articleid=2429454>

The U.S. leads the world in creating new drugs and healthcare tech, but the system discourages inventors from creating cost-lowering technologies in favor of ones with a healthy return on investment, according to an [article](#) at the *Journal of the American Medical Association*.

"In the United States, the surest way to generate a healthy return on investment is to increase health care spending, not reduce it," says the authors, from the Uniformed Services University of the Health Sciences and Yale School of Medicine.

They use as an example a low-cost, once-a-day pill to treat cardiovascular disease, with the estimated potential to reduce the incidence of myocardial infarction and stroke by more than 80 percent.

When curing a disease with gene therapy is bad business

A drug giant turns over its pipeline of miracle drugs to a startup.

by **Antonio Regalado**

April 12, 2018

An analyst at Goldman Sachs asked a troubling question this week about gene therapy.

“Is curing patients a sustainable business model?”

In social media, reactions were quick and sharp. “Cold and immoral.”

→ ↻ cnbc.com/2018/04/11/goldman-asks-is-curing-patients-a-sustainable-business-model.html



MARKETS

BUSINESS

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POLITICS

CNBC TV

Goldman Sachs asks in biotech research report: 'Is curing patients sustainable business model?'

PUBLISHED WED, APR 11 2018•3:15 PM EDT | UPDATED WED, APR 11 2018•7:20 PM EDT

“medicine developers looking for sustained cash flow”

[cnbc.com/2018/04/11/goldman-asks-is-curing-patients-a-sustainable-business-model.html](https://www.cnbc.com/2018/04/11/goldman-asks-is-curing-patients-a-sustainable-business-model.html)



Goldman Sachs asks in biotech research report: ‘Is curing patients a sustainable

Goldman Sachs analysts attempted to address a touchy subject for biotech companies, especially those involved in the pioneering “gene therapy” treatment: cures could be bad for business in the long run.

“Is curing patients a sustainable business model?” analysts ask in an April 10 report entitled “The Genome Revolution.”

“The potential to deliver ‘one shot cures’ is one of the most attractive aspects of gene therapy, genetically-engineered cell therapy and gene editing. However, such treatments offer a very different outlook with regard to recurring revenue versus chronic therapies,” analyst Salveen Richter wrote in the note to clients Tuesday. “While this proposition carries tremendous value for patients and society, it could represent a challenge for genome medicine developers looking for sustained cash flow.”

Transaction Cost

Ronald Coase (Nobel Prize in Economics, 1991)



This \$153,000 rattlesnake bite is everything wrong with

American Healthcare

<http://bit.ly/US-MEDICAL-WASTE>

Statement Date	July 13, 2015	
Your payment is due:	July 27, 2015	Please send contact Med contact our status of y
Your balance due is:	\$153,161.25	
SUMMARY OF PATIENT SERVICES		
PHARMACY	\$83,341.25	
LABORATORY SERVICES	\$22,433.00	
INTERMEDIATE CARE ROOM	\$21,225.00	
INTENSIVE CARE ROOM	\$17,766.00	
EMERGENCY CARE SERVICES	\$5,564.00	
THERAPY SERVICES	\$1,423.00	
RADIOLOGY	\$947.00	
SPECIAL SERVICES	\$462.00	
TOTAL CHARGES	\$153,161.25	
ACCOUNT SUMMARY		
Service Date	07/04/15 to 07/09/15	
Type of Service	EMERGENCY-IP	
Account #	11-82728390	
Billed/Total Charges	\$153,161.25	
Adjustments	\$0.00	
Insurance Payments	\$0.00	
Patient Payments	\$0.00	
Due From Insurance	\$0.00	
This is your balance	\$153,161.25	
PLEASE RETAIN THIS PORT		

\$153,161.25

US Hospital charges for

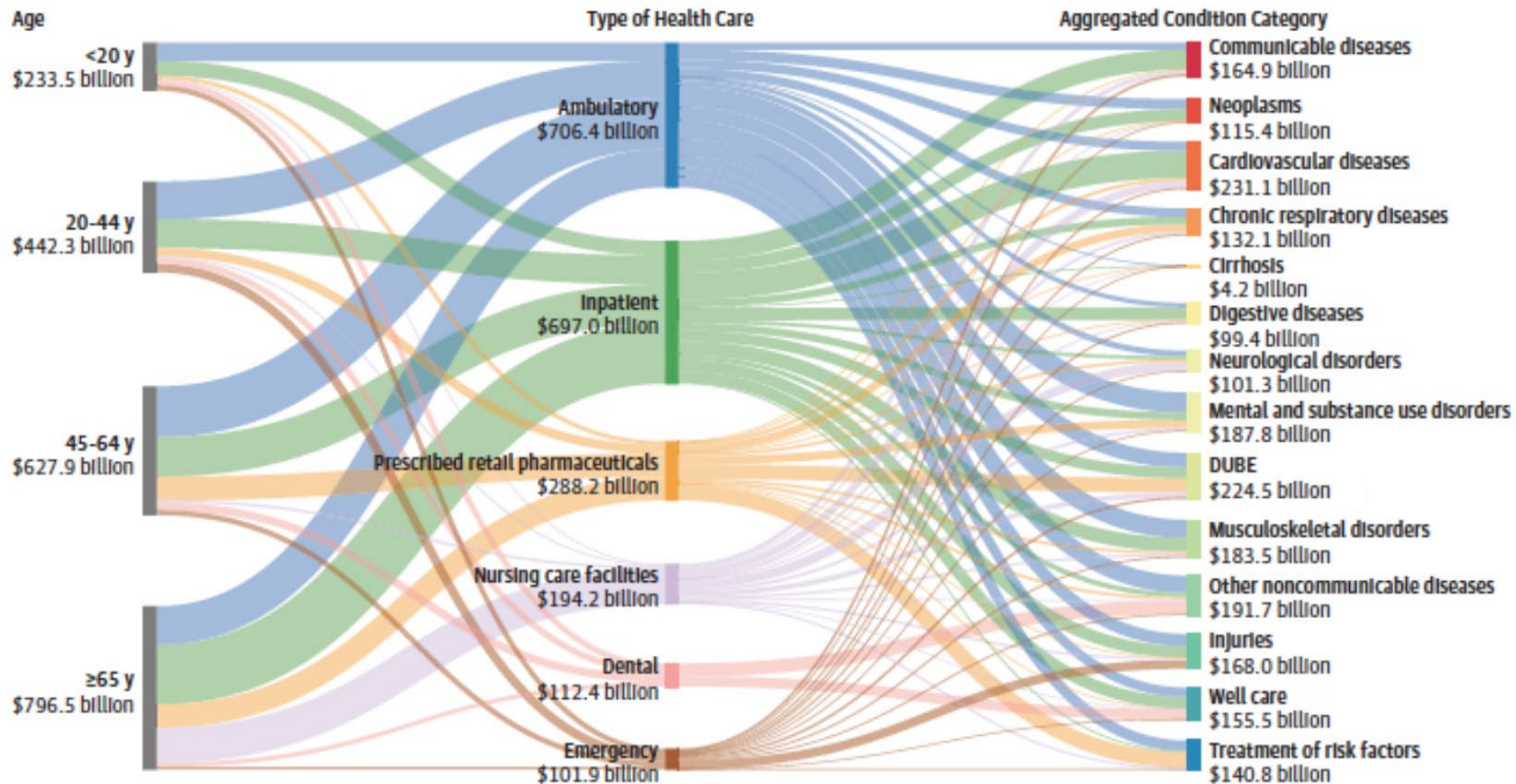
Treatment of Snake Bite



Dan Haggerty @10NewsHaggerty

US AV PER CAPITA INCOME <\$55,000

Personal Health Care Spending in the United States by Age Group, Aggregated Condition Category, and Type of Health Care, 2013

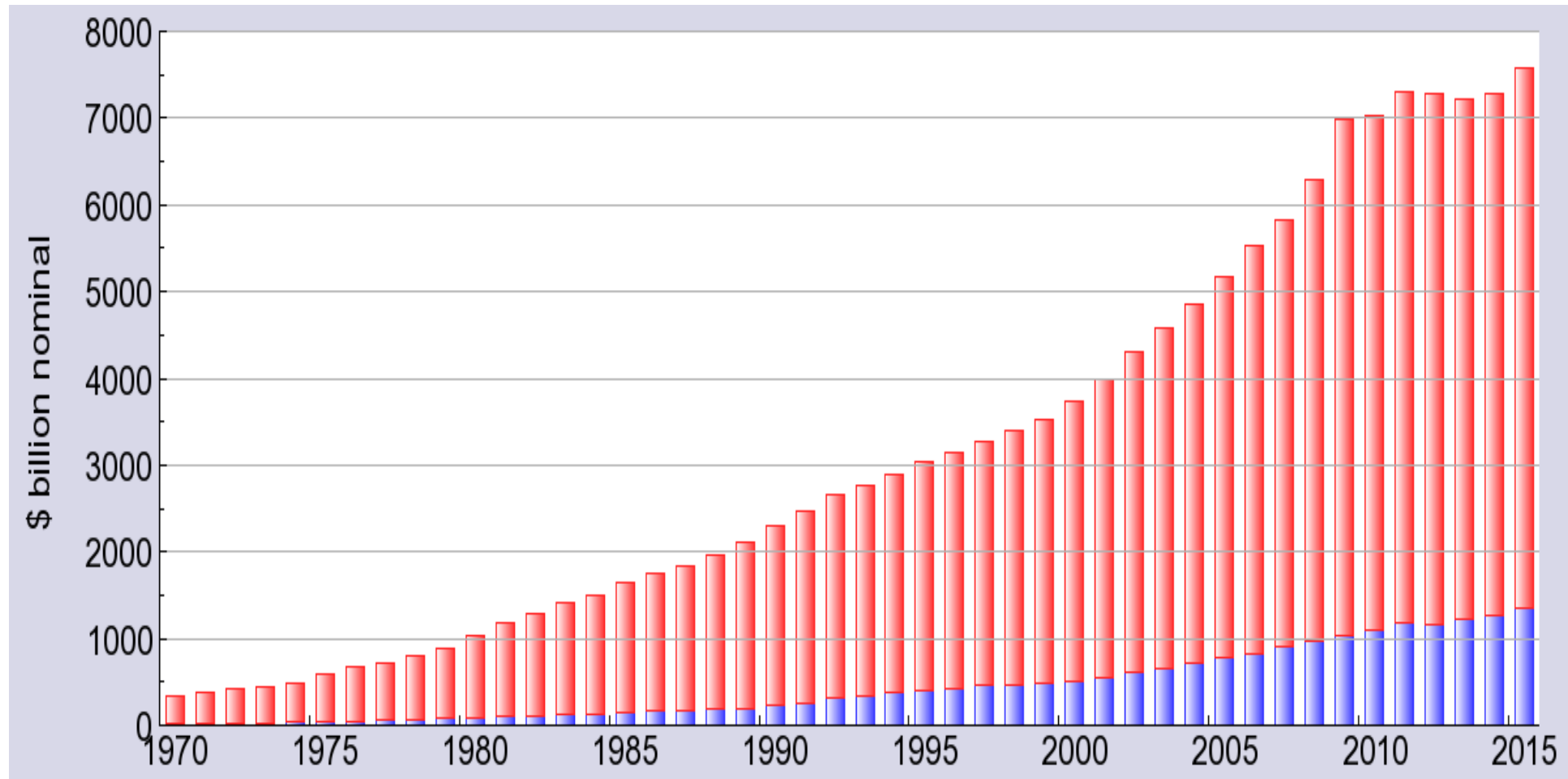


<http://jamanetwork.com/journals/jama/fullarticle/2594716>
<https://image-store.slidesharecdn.com/8250a975-308d-40a7-a573-e4c1ab8d791b-original.png>

DUBE indicates diabetes, urogenital, blood, and endocrine diseases. Reported in 2015 US dollars. Each of the 3 columns sums to the \$2.1 trillion of 2013 spending disaggregated in this study. The length of each bar reflects the relative share of the \$2.1 trillion attributed to that age group, condition

category, or type of care. Communicable diseases included nutrition and maternal disorders. Table 3 lists the aggregated condition category in which each condition was classified.

TOTAL US HEALTHCARE SPENDING 1970-2015



BUSINESS 6/18/2012 @ 7:59AM | 98,482 views

The Staggering Cost Of An Epic Electronic Health Record Might Not Be Worth It

[Judy Faulkner](#) once walked into a roomful of hospital CIOs, tossed her macramé handbag on a table, and announced she came to decide who she wanted as customers. Faulkner doesn't do marketing. The formidable founder of electronic health records Epic Systems boasts an enviable roster of customers made up of prestigious hospitals and academic centers. She has quietly convinced them that her product is best: a single, seamless database—the fruit of a company that has grown organically, and shunned acquisitions. And, because it is no small task to deploy, she is there all the way to hand-hold jittery CIOs, and help them get millions of dollars in government subsidies by showing meaningful use of her EHR.

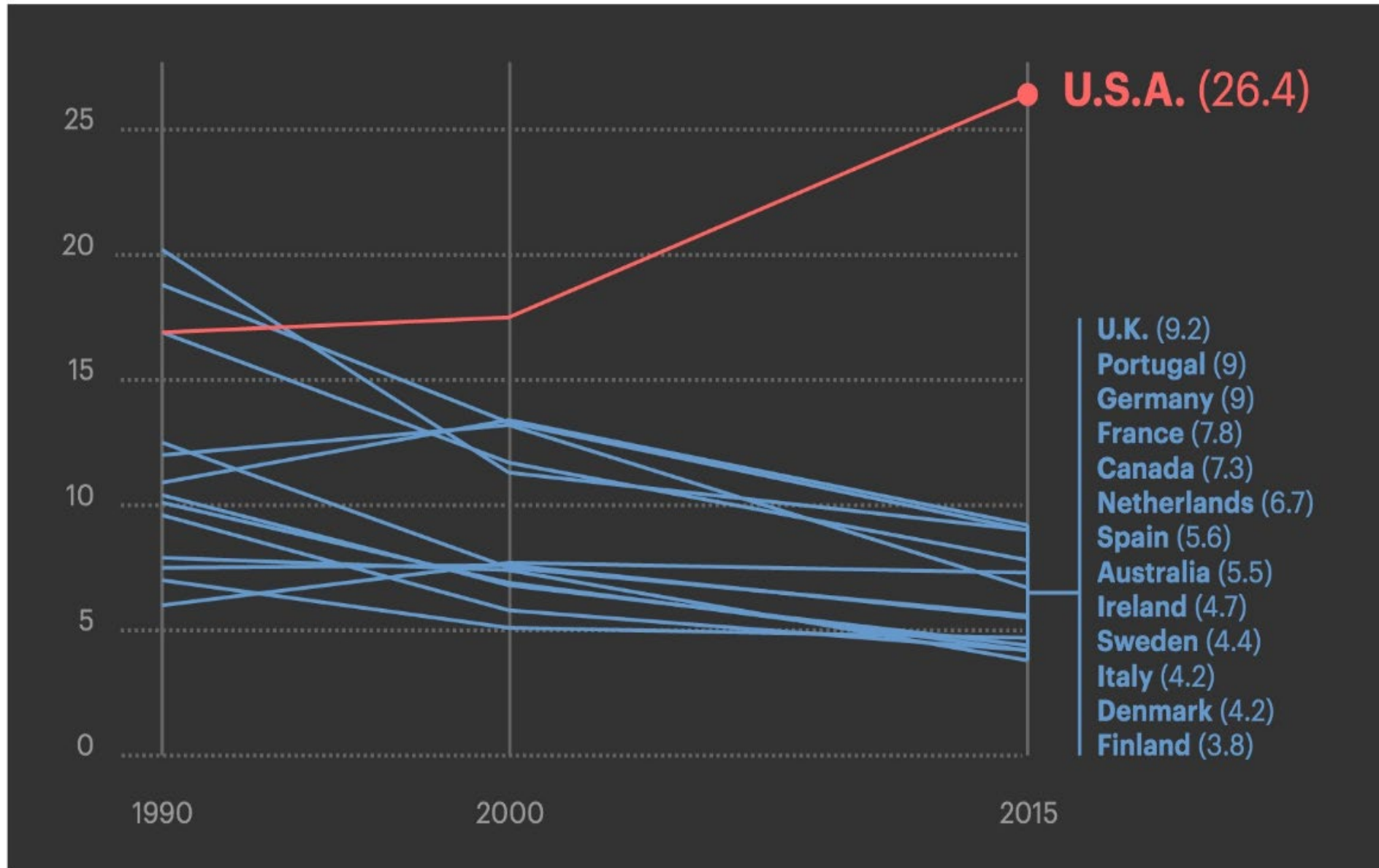
Her not-for-profit clientèle will need every penny of those taxpayers' dollars, but they won't cover anywhere near the staggering cost of an Epic EHR. [Duke University Health System](#) will shell out \$700 million, so will [Boston](#)-based Partners HealthCare; University of California, [San Francisco](#) will pay \$150 million.

\$700
million

The “care” in healthcare

Where is it ??

Maternal Mortality Is Rising in the U.S. As It Declines Elsewhere



Per 100,000 live births. Source: "Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015," *The Lancet*. Note: Only data for 1990, 2000 and 2015 was made available in the journal.

Leading causes of death in the USA (annual data)

1. 597,689 Heart Disease
2. 574,743 Cancer
3. 138,080 Chronic lower respiratory diseases
4. 129,476 Stroke
5. 120,859 Accidents
6. 83,494 Alzheimer's disease
7. 69,071 Diabetes
8. 56,979 Influenza & Pneumonia
9. 47,112 Kidney diseases
10. 41,149 Suicide



• 2010 • OIG HHS bad hospital care deaths ~180,000 patients in Medicare alone (in 1 year).

Patient Safety 2013

Exploring Quality of Care in the U.S.

How Many Die From Medical Mistakes in U.S. Hospitals?



A New, Evidence-based Estimate of Patient Harms Associated with Hospital Care

John T. James, PhD



98,000
deaths due to error

210,000 – 440,000 deaths

400,000 deaths due to medical mistakes – shared with the US Senate

Deaths by medical mistakes hit records



Tejal Gandhi, MD, president of the National Patient Safety Foundation and associate professor of medicine, Harvard Medical School, spoke at the hearing.

The way IT is designed remains part of the problem

WASHINGTON | July 18, 2014

It's a chilling reality – one often overlooked in annual mortality statistics: Preventable medical errors persist as the No. 3 killer in the U.S. – third only to heart disease and cancer – claiming the lives of some **400,000 people** each year. At a Senate hearing Thursday, patient safety officials put their best ideas forward on how to solve the crisis, with IT often at the center of discussions.

Hearing members, who spoke before the Subcommittee on Primary Health and Aging, not only underscored the devastating loss of human life – more than 1,000 people each day – but also called attention to the

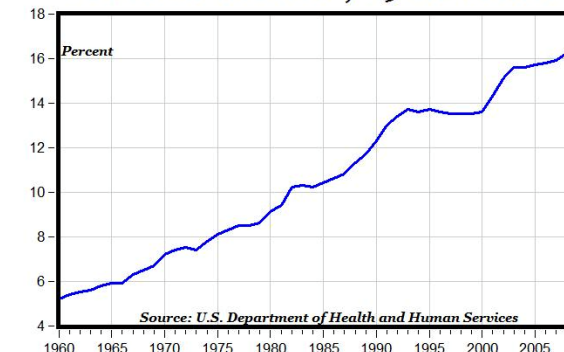
fact that these medical errors cost the nation a colossal **\$1 trillion each year**.

"The tragedy that we're talking about here (is) deaths taking place that should not be taking place," said subcommittee Chair Sen. Bernie Sanders, I-Vt., in his opening remarks.

3rd Leading cause of death in the USA ?

1. 597,689 Heart Disease
2. 574,743 Cancer
3. **Deaths Due to Medical Errors (180,000 - 210,000 - 440,000)**
4. 138,080 Chronic lower respiratory diseases
5. 129,476 Stroke
6. 120,859 Accidents
7. 83,494 Alzheimer's disease
8. 69,071 Diabetes
9. 56,979 Influenza & Pneumonia
10. 47,112 Kidney diseases
11. 41,149 Suicide

**Total Health Care Expenditures
Percent of GDP, 1960-2008**



Equivalent to at least one 747 Jumbo Jet airplane crash every day

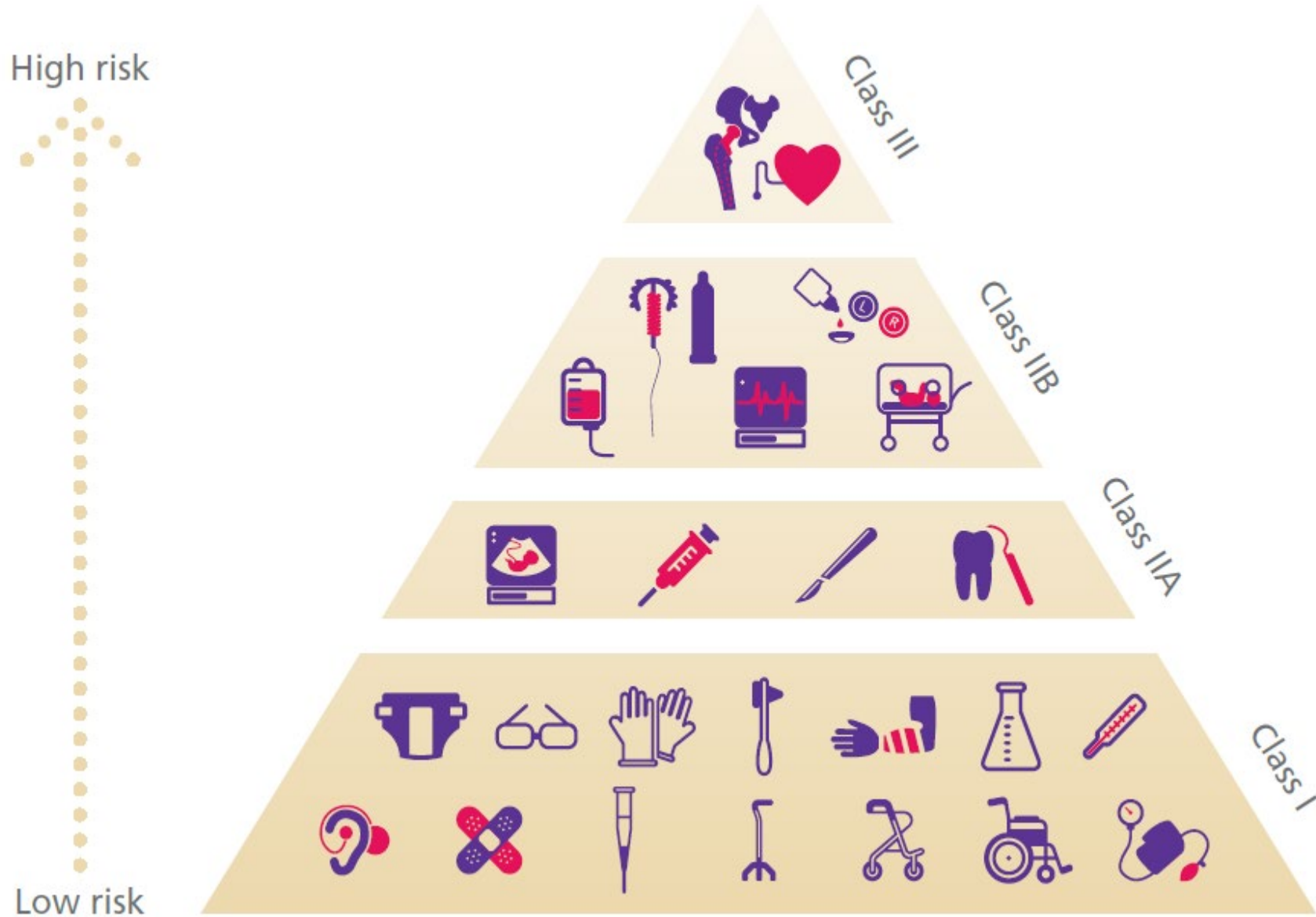
Medical Devices Today

stand alone, unintegrated, not patient-centric, proprietary data

- Philips Intellivue Series Monitors
- GE Solar 8000x / Dash 4/5000
- Dräger Apollo / EvitaXL / V500
- Nonin Bluetooth OnyxII 9650 / WristOx 3150
- Oridion Capnostream20
- Ivy 450C
- Nellcor N-595
- Masimo Radical-7



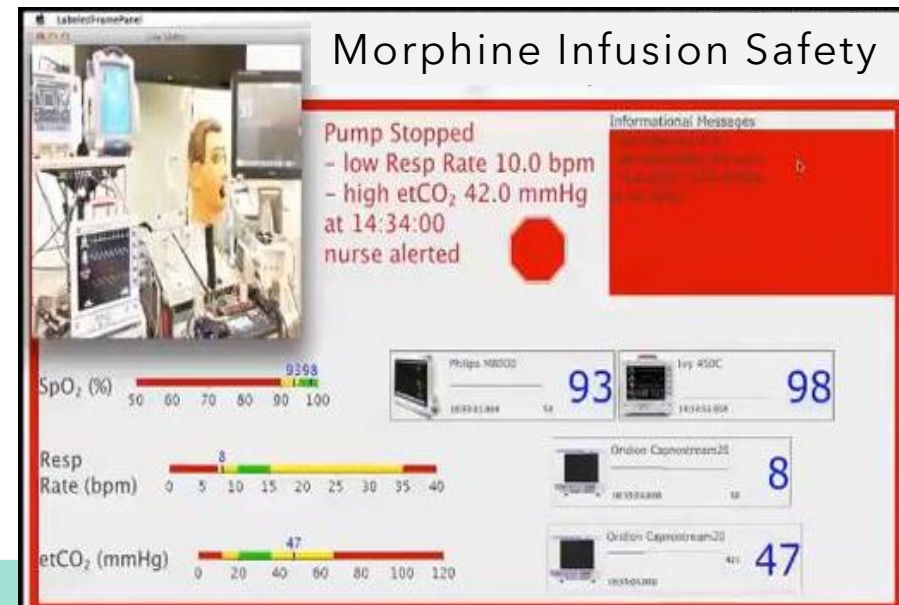
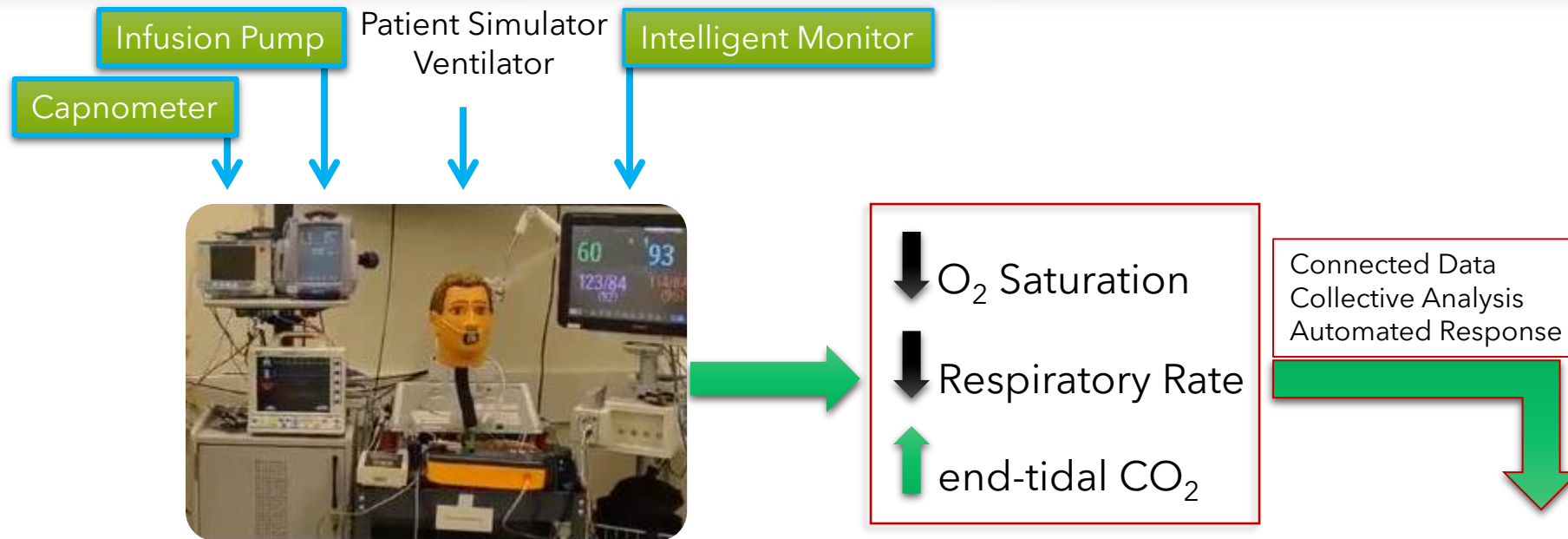
Device Manufacturers Builds Things – not Patient Care Systems



SOLUTIONS APPROACH

Devices that can talk to each other and synthesize data to present an integrated physiological status that is patient centric and updates patient medical records without locking raw data.

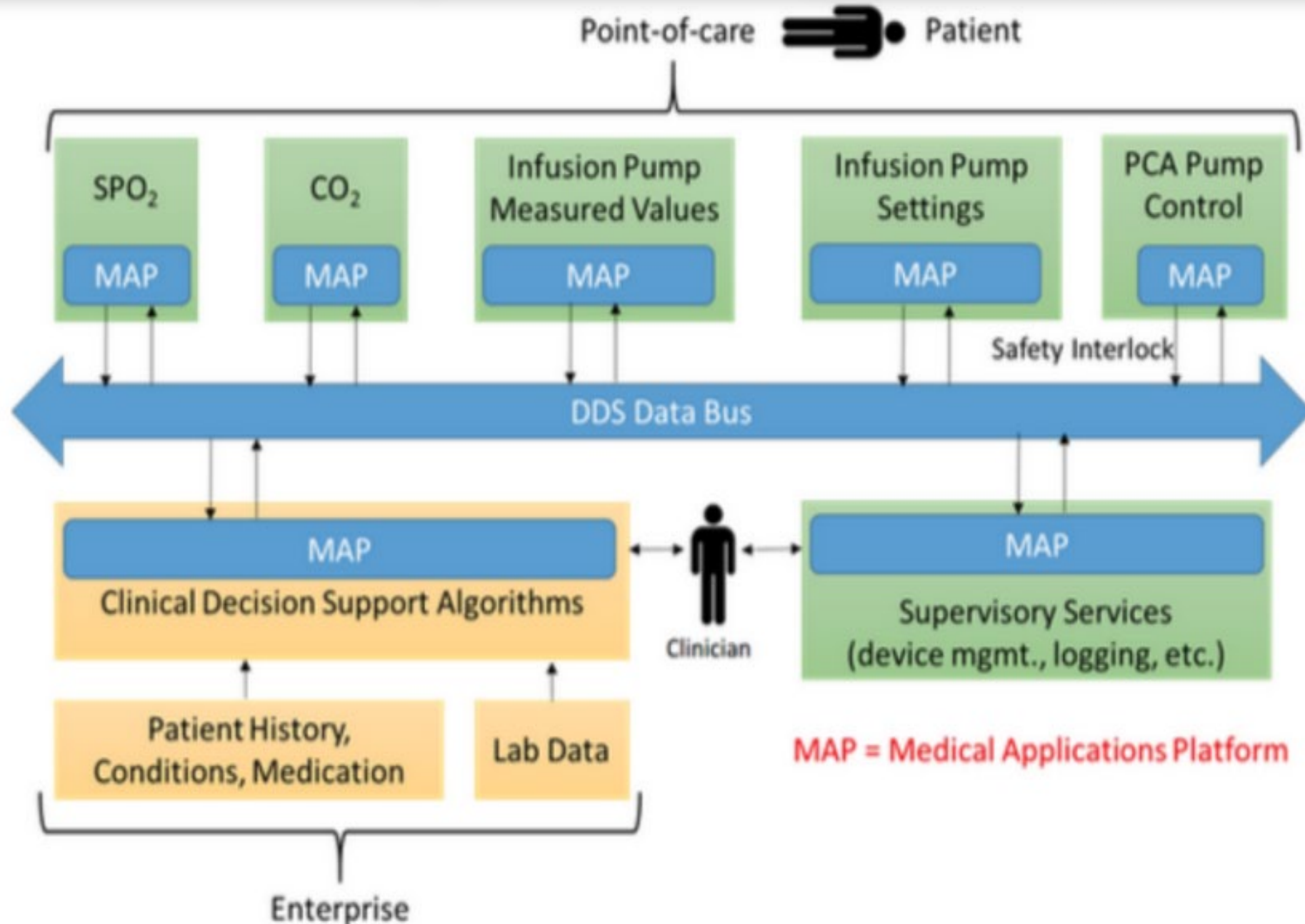
Autonomous Control of Morphine Infusion Pump – Medical Device Integration Model



Julian Goldman MD (MDPnP.org and Partners.org)
Massachusetts General Hospital, Harvard Medical School
Harvard - MIT Center for Integrative Medicine and Information Technology

Patient Controlled Analgesia Safety Application

Autonomous Control of Morphine Infusion Pump – Medical Device Data Integration



PROOF OF CONCEPT

Response to White House Call for Ebola Management

<https://vimeo.com/111314176>

Is there a need for Integrated Healthcare Platforms?

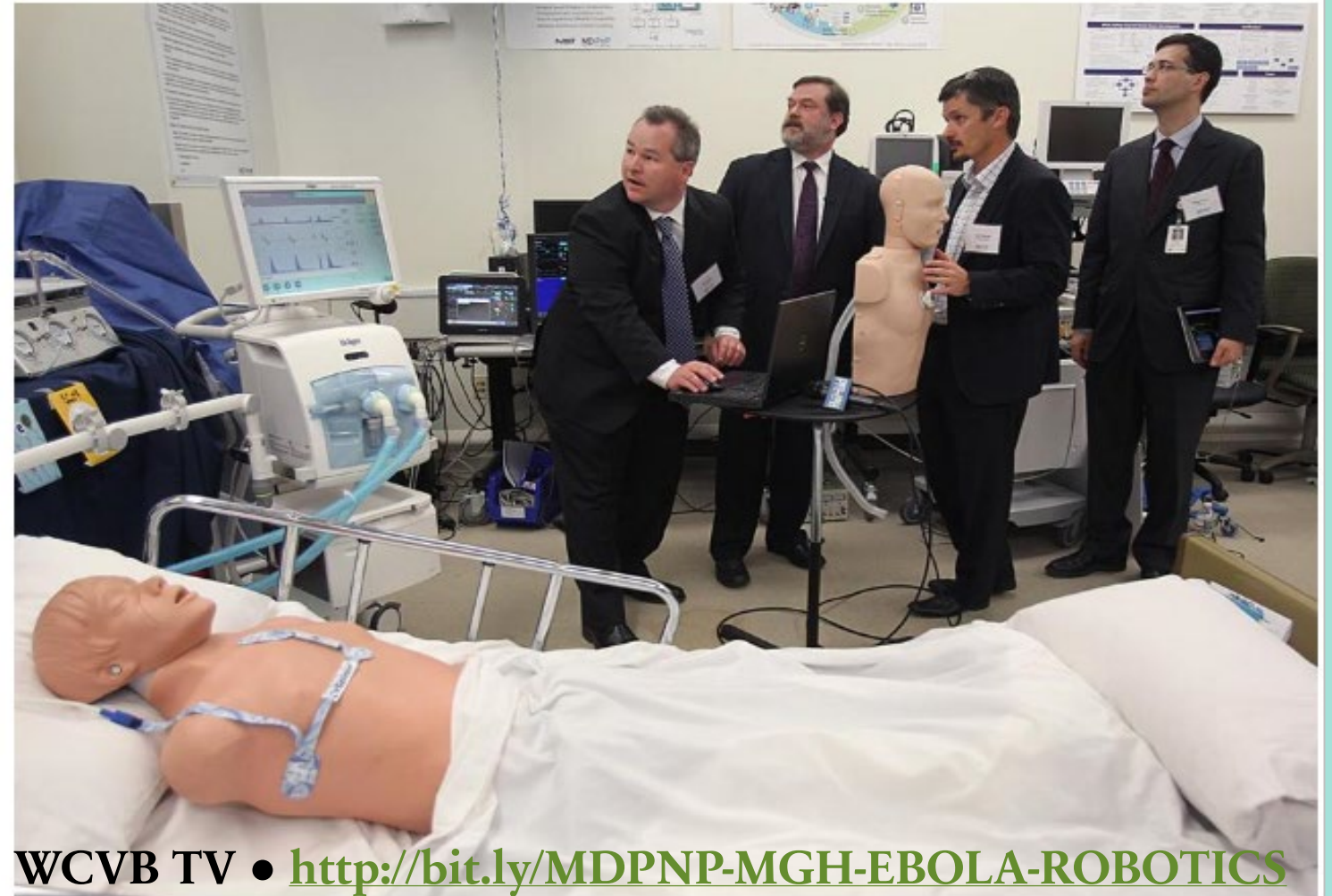


Ebola spurs rethinking of devices at MGH

By Carolyn Y. Johnson

| GLOBE STAFF NOVEMBER 07, 2014

You cannot buy a TV without a remote. You cannot buy a medical device with a remote. Dr Julian M Goldman, MGH



WCVB TV • <http://bit.ly/MDPNP-MGH-EBOLA-ROBOTICS>

SUZANNE KREITER/GLOBE STAFF

Health officials demonstrated treating an Ebola patient remotely in a mock ICU. Pictured, left to right: Eric Lynn, Julian M. Goldman, Brian Russell, and Dave Arney.

Robotic Tools in Infectious Diseases Management Need for Medical Device Interoperability Platform



COLLABORATORS



FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL
AND MASSACHUSETTS GENERAL HOSPITAL



HARVARD
MEDICAL
SCHOOL



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A



MD PnP MedTech Hackathon Open Medical Device and Data Integration Platforms to Support the Management of Ebola

Will FDA drown medical device interoperability efforts through conventional regulatory acts?

Yes ? No ?

Dr. Shuren received his B.S. and M.D. degrees from Northwestern University under its Honors Program in Medical Education. He completed his medical internship at Beth Israel Hospital in Boston, his neurology residency at Tufts New England Medical Center, and a fellowship in behavioral neurology and neuropsychology at the University of Florida. He received his J.D. from the University of Michigan.

Participation of the US FDA
CDRH was a powerful
incentive for medical device
manufacturers to explore
innovative medical
technology solutions,
especially those benefiting
from interoperability
between manufacturers



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Room 5447, Building 66
Silver Spring, MD 20993-0002

November 3, 2014

Julian M. Goldman, MD
Director, Medical Device Interoperability Program
65 Landsdowne Street
Cambridge, MA 02139

Dear Dr. Goldman,

Thank you for reaching out to the Center for Devices and Radiological Health (CDRH) via our Emergency Preparedness/Operations and Medical Countermeasures (EMCM) Program.

We understand that The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program, under your coordination, has been asked by the White House Office of Science and Technology Program to mobilize resources among medical device manufacturers and the clinical community, so as to design and demonstrate proof of concept for an interoperable platform that would enable critical care of Ebola-infected patients in an isolation environment with reduced exposure to health care workers.

FDA recognizes the importance of implementing strategies that minimize direct exposure of clinical personnel to patients infected with Ebola virus. We understand that MDPNP, along with its collaborators, are developing potential approaches that would include comprehensive data access and potential remote control of medical devices in the isolation environment, thereby reducing the risk of healthcare worker exposure to the virus.

CDRH recognizes the importance of these efforts and is ready and willing to collaborate with you, the clinical community and your industry partners to demonstrate the potential of this technology in serving this particular public health emergency. We are eager to observe the demonstration taking place Friday November 7th for OSTP, and we look forward to participating in the development of next steps with MDPNP and your medical device partners so as to do our part in enabling advancement of technology that can protect our healthcare workers who put themselves on the front line to promote the public health mission.

Sincerely,

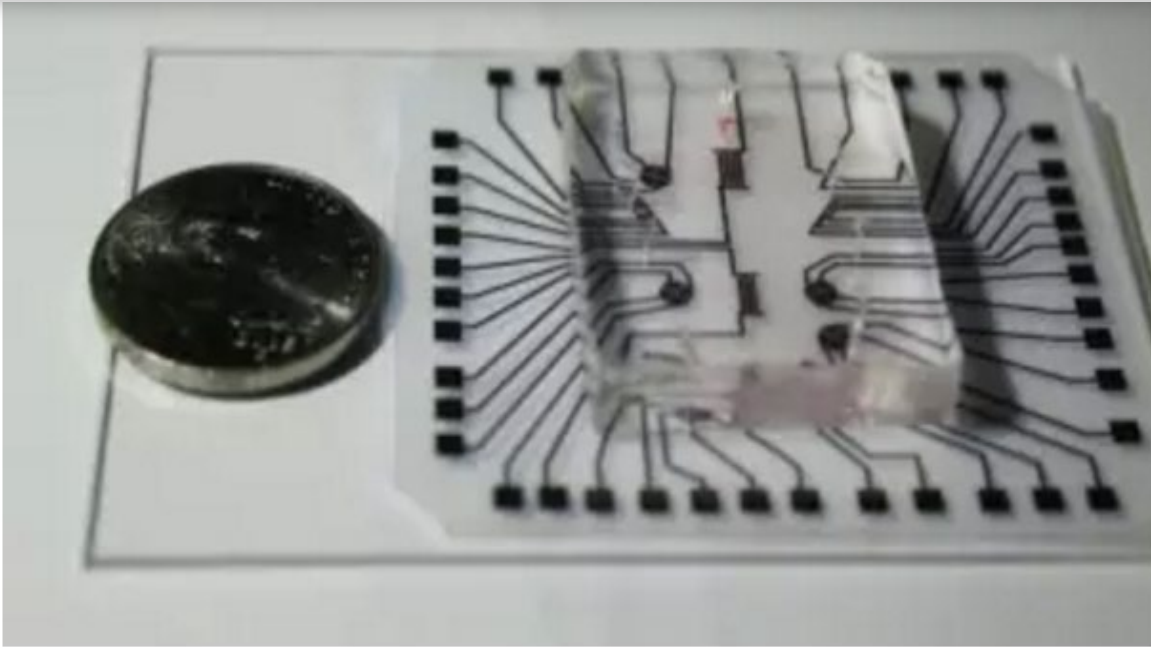
A handwritten signature in black ink that reads 'Jeffrey Shuren'.

Jeffrey Shuren, M.D., J.D.
Director
Center for Devices and
Radiological Health

Plethora of healthcare tools

What's stopping them from providing services for humanity?

IS HEALTHCARE A HUMAN RIGHT? IS IT FOR THE BILLIONS?



This device costs one cent to make and could help deliver critical diagnostic care to remote, impoverished areas of the globe. (Image courtesy of Stanford.)

Multifunctional, inexpensive, and reusable nanoparticle-printed biochip for cell manipulation and diagnosis

Rahim Esfandyarpour^{a,b}, Matthew J. DiDonato^c, Yuxin Yang^d, Naside Gozde Durmus^{a,b}, James S. Harris^d, and Ronald W. Davis^{a,b,1}

Stanford | MEDICINE



Gozde
Durmus

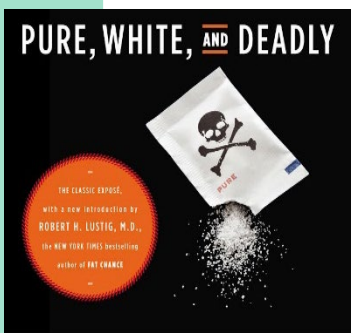
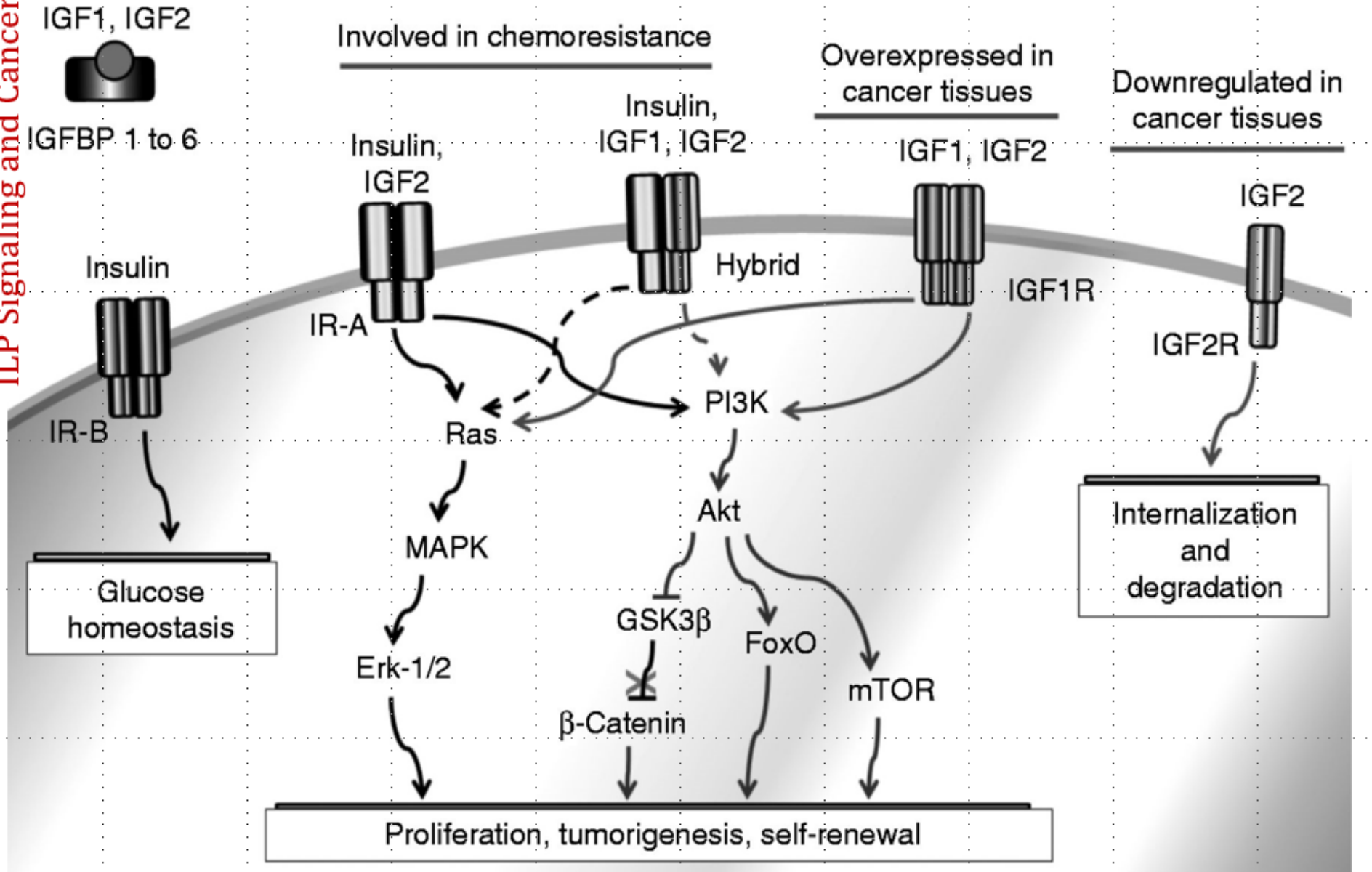
Insulin Resistance and Cancer

ILP Signaling and Cancer

IGF1, IGF2



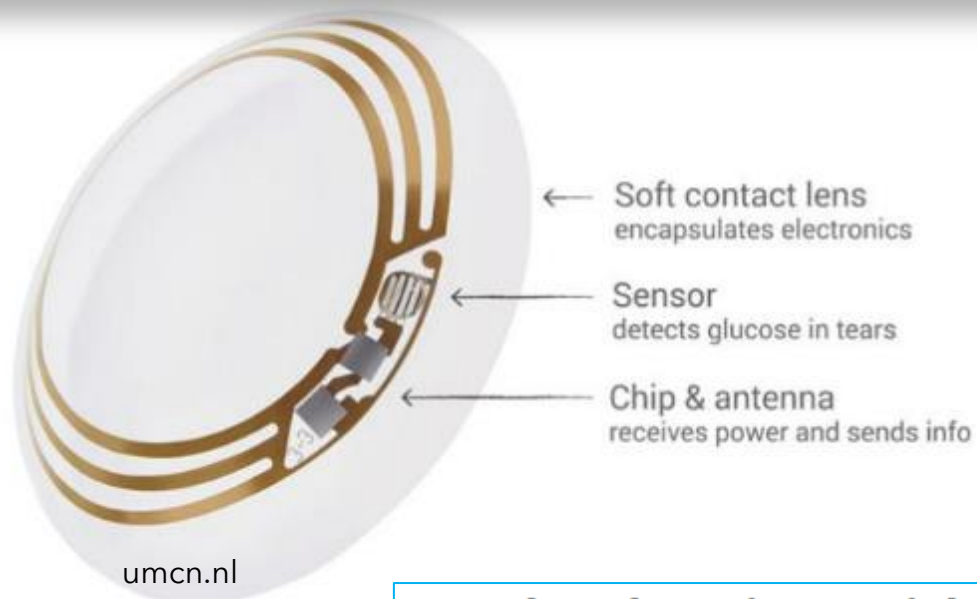
IGFBP 1 to 6



How Sugar Is Killing Us and What We Can Do to Stop It
John Yudkin

How Sugar is Killing Us www.ncbi.nlm.nih.gov/pubmed/23207292

DIABETES - The next pandemic?



Google, DexCom to Make Glucose Monitoring Devices for Diabetes Patients

by Robin Sinha, 13 August 2015



Soon after the announcement of its new CEO Sundar Pichai and a holding company called Alphabet, the Google Life Sciences team has teamed up with a healthcare firm DexCom to build blood glucose monitoring devices for diabetes patients that are smaller and less expensive than current technologies.

Google Takes Aim at Diabetes with Big Data, Internet of Things

By Jennifer Bresnick on August 31, 2015



Freshly revitalized after Google's much-discussed reorganization under the **Alphabet** umbrella, the tech giant's life science team is once again **planning to tackle diabetes** with the help of big data analytics and innovative Internet of Things technologies.

With the formation of a new partnership that enlists the aid of the **Joslin Diabetes Center** and Sanofi, a multinational pharmaceutical developer, Google hopes to reduce the burden of Type 1 and Type 2 diabetes on both patients and providers.



ABOUT HMS

EDUCATION

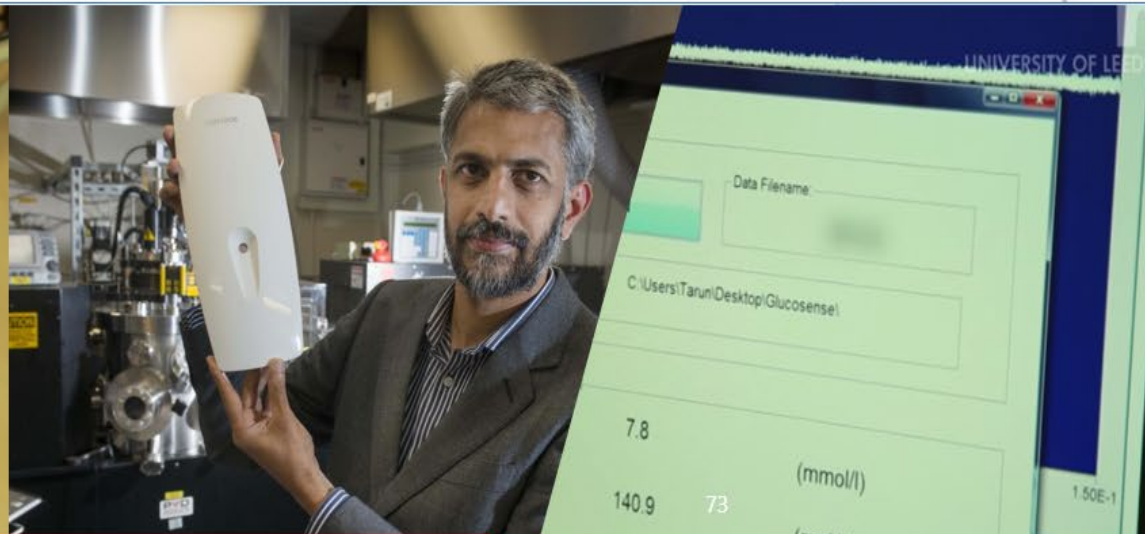
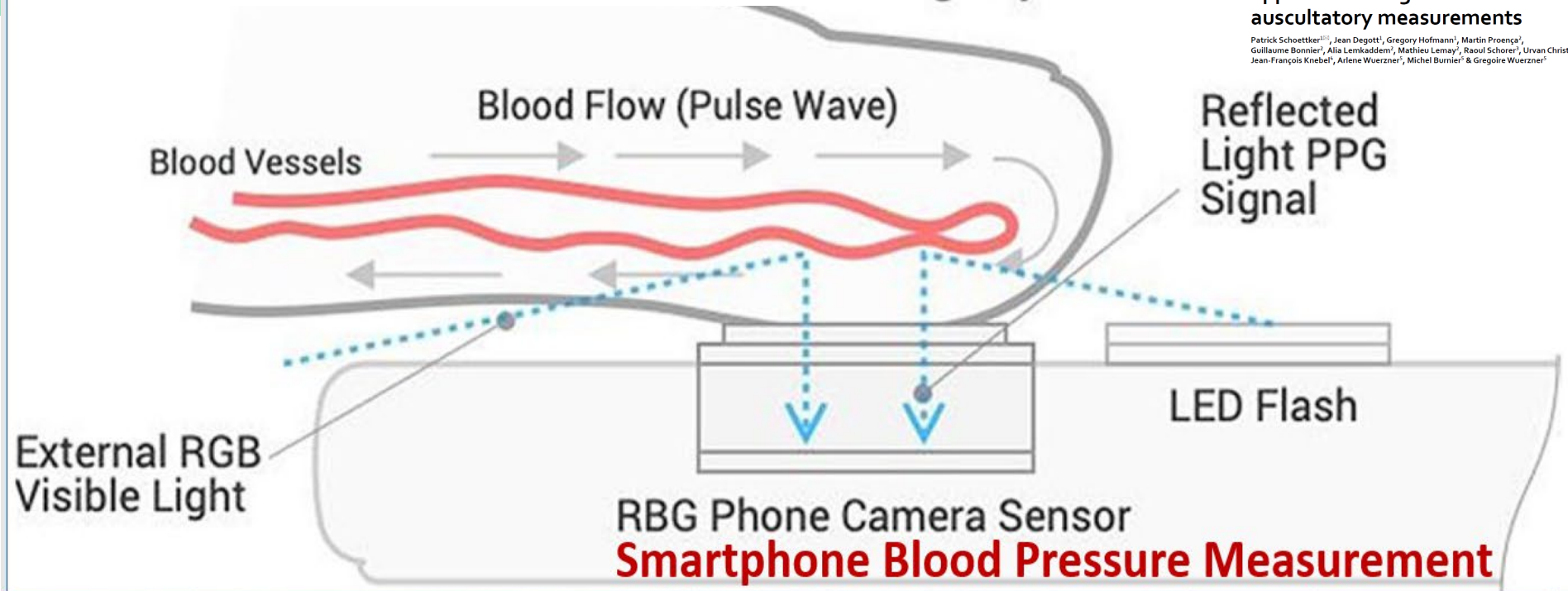
Joslin Diabetes Center

<https://doi.org/10.1038/s41598-020-74955-4>

Fingertip

Blood pressure measurements with the OptiBP smartphone app validated against reference auscultatory measurements

Patrick Schoettker¹, Jean Degott¹, Gregory Hofmann¹, Martin Proença¹, Guillaume Bomnier¹, Aïta Lemkaddem¹, Matthieu Lemay¹, Raoul Schorer¹, Urvan Christen¹, Jean-François Knebel¹, Arlene Wuerzner¹, Michel Burnier¹ & Gregoire Wuerzner¹



Non-invasive Blood Glucose Monitoring

BLOOD-FREE NON-INVASIVE BLOOD HEMOGLOBIN ??

Laser excitation of oxy-hemoglobin generates highly specific resonance (Raman spectra) which could be exploited in the development of non-invasive tool.



This statement is made by the author. It is merely a suggestion.

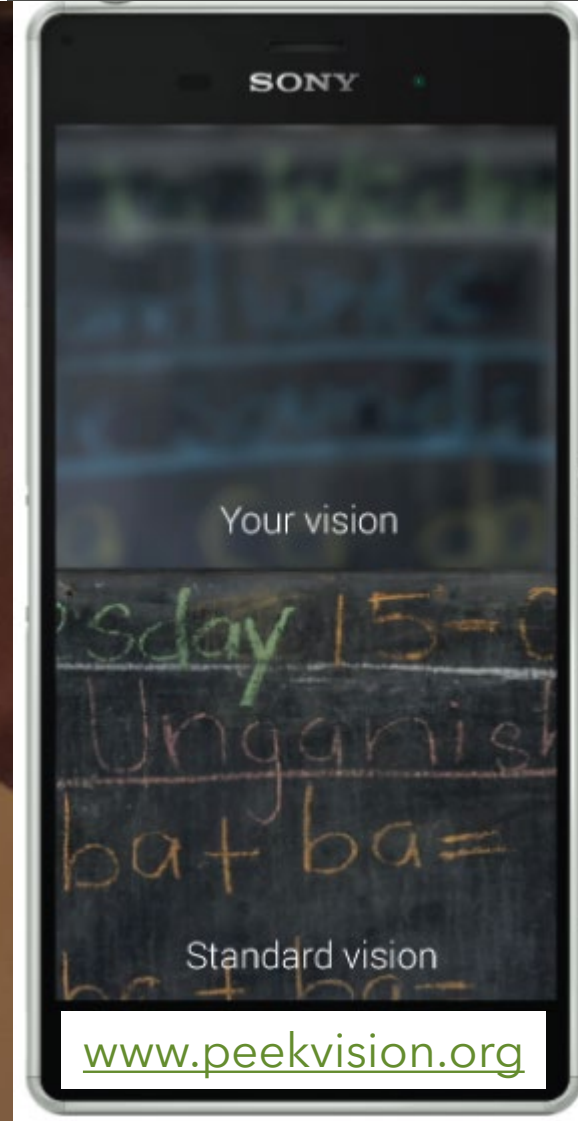
Wrig Nanosystems, a medical technology startup company which develops and markets a hemoglobin measurement device, has attracted financial interest from different investors in the product. The company has made an investment of up to 15 cr to commercialise and further develop the product and Avendus Wealth Management acted as the advisor to Wrig on this deal.

The list of investors includes Flipkart co-founders Sachin and Binny Bansal, Malvinder and Shivinder Singh (former Ranbaxy and Fortis promoters), Gurpreet Singh (Round Glass Partners) and others.

Optics for the Masses

The Peek Retina adapter is being developed through a collaboration between the University of Strathclyde, where Dr Mario Giardini heads the engineering design; the London School of Hygiene & Tropical Medicine; and the Glasgow Centre for Ophthalmic Research of NHS Greater Glasgow and Clyde.

- View the retina with high quality imaging
- See cataracts clearly for classification
- Simulates a patient's eyesight on screen
- Visual acuity tests for eyesight
- Colour and contrast tests



OPTICIAN'S CLINIC-IN-A-POCKET

www.bbc.com/news/health-22553730



A woman from Nakuru, Kenya, having a cataract scan with the Peek smartphone tool. This portable eye testing kit can diagnose eye problems in remote areas, where access to clinics is limited. ©Peek

What we hope is that it will provide eye care for those who are the poorest of the poor

Dr Andrew Bastawrous, London School of Hygiene and Tropical Medicine

What the phone app can do for eyes

Peek can diagnose a vast range of eye problems, blindness and vision impairments,

- [Glaucoma](#)
- Cataracts
- Macular degeneration
- [Diabetic retinopathy](#)
- Other retinal and optic nerve diseases.

MIT News

ON CAMPUS AND AROUND THE WORLD

<https://news.mit.edu/2017/cardiio-app-screens-arrhythmia-smartphone-camera-0329>



MIT Media Lab spinout Cardio has developed a mobile app that uses a smartphone camera to detect facial signs of a heart arrhythmia associated with strokes.

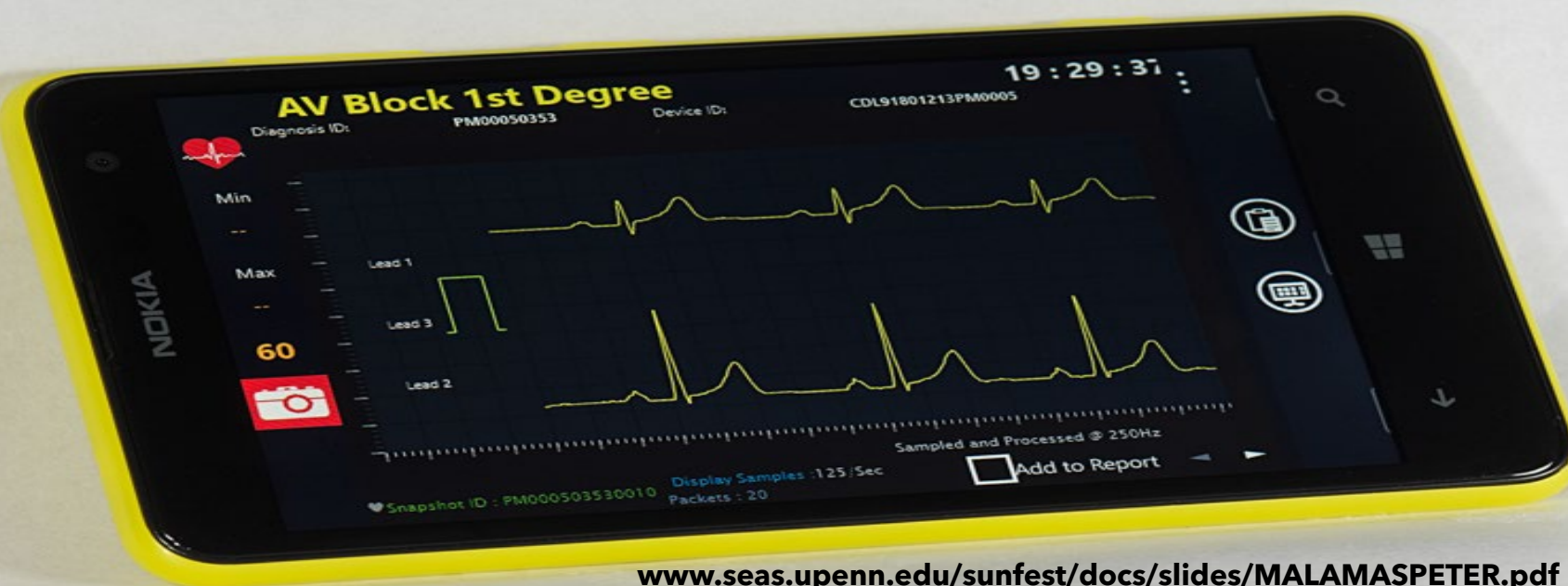
Courtesy of Cardio

App screens for arrhythmia using smartphone

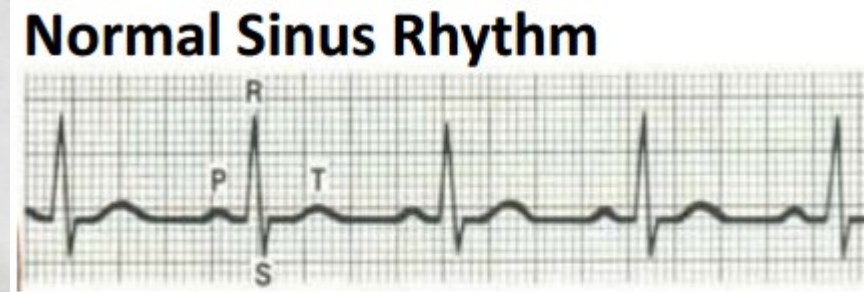


Dr Leslie Saxon, University of Southern California

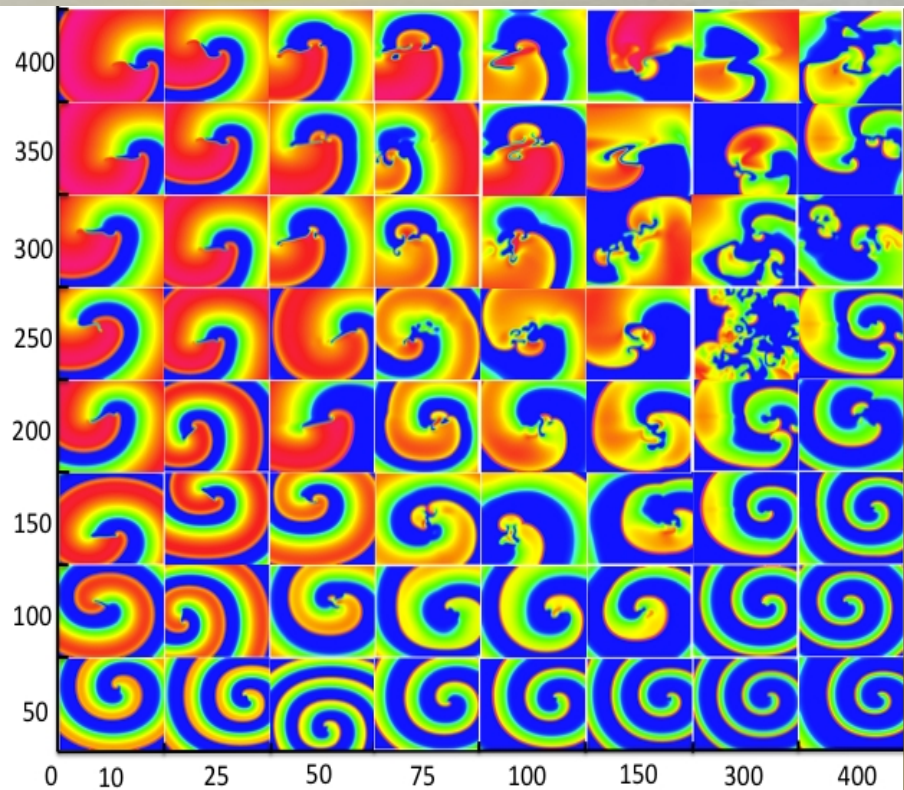
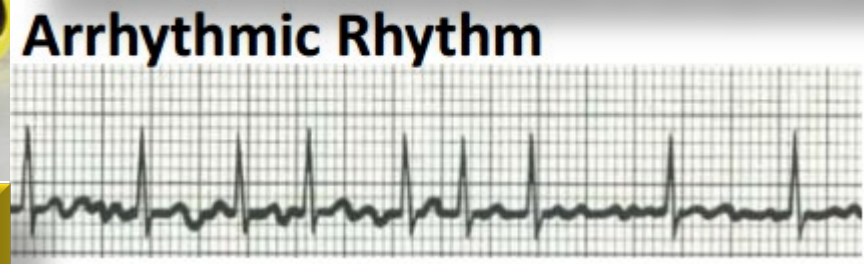
PHONE ECG DETECTS
IRREGULAR HEARTBEAT



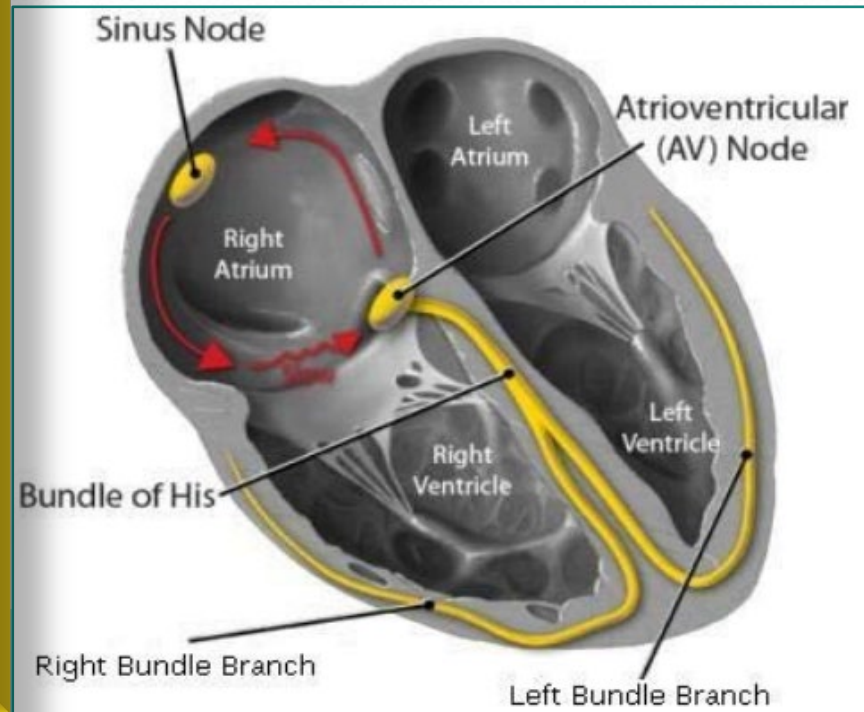
www.seas.upenn.edu/sunfest/docs/slides/MALAMASPETER.pdf



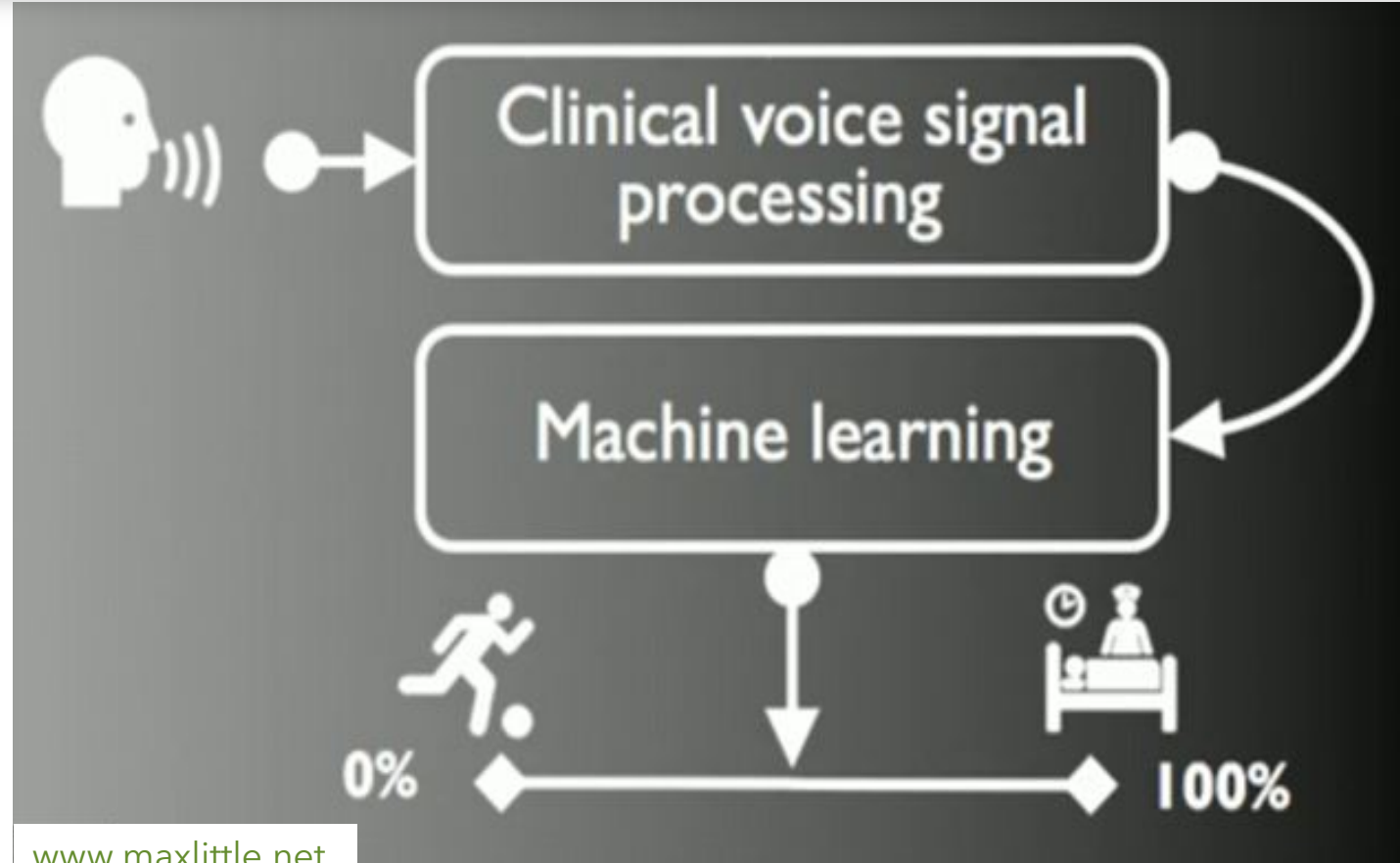
Circular pathways in the heart conduction system is a common cause of arrhythmias



CARDIAC ARRHYTHMIA
 DIAGNOSIS & REPORTING
 CARDIOLOGIST-in-a-POCKET

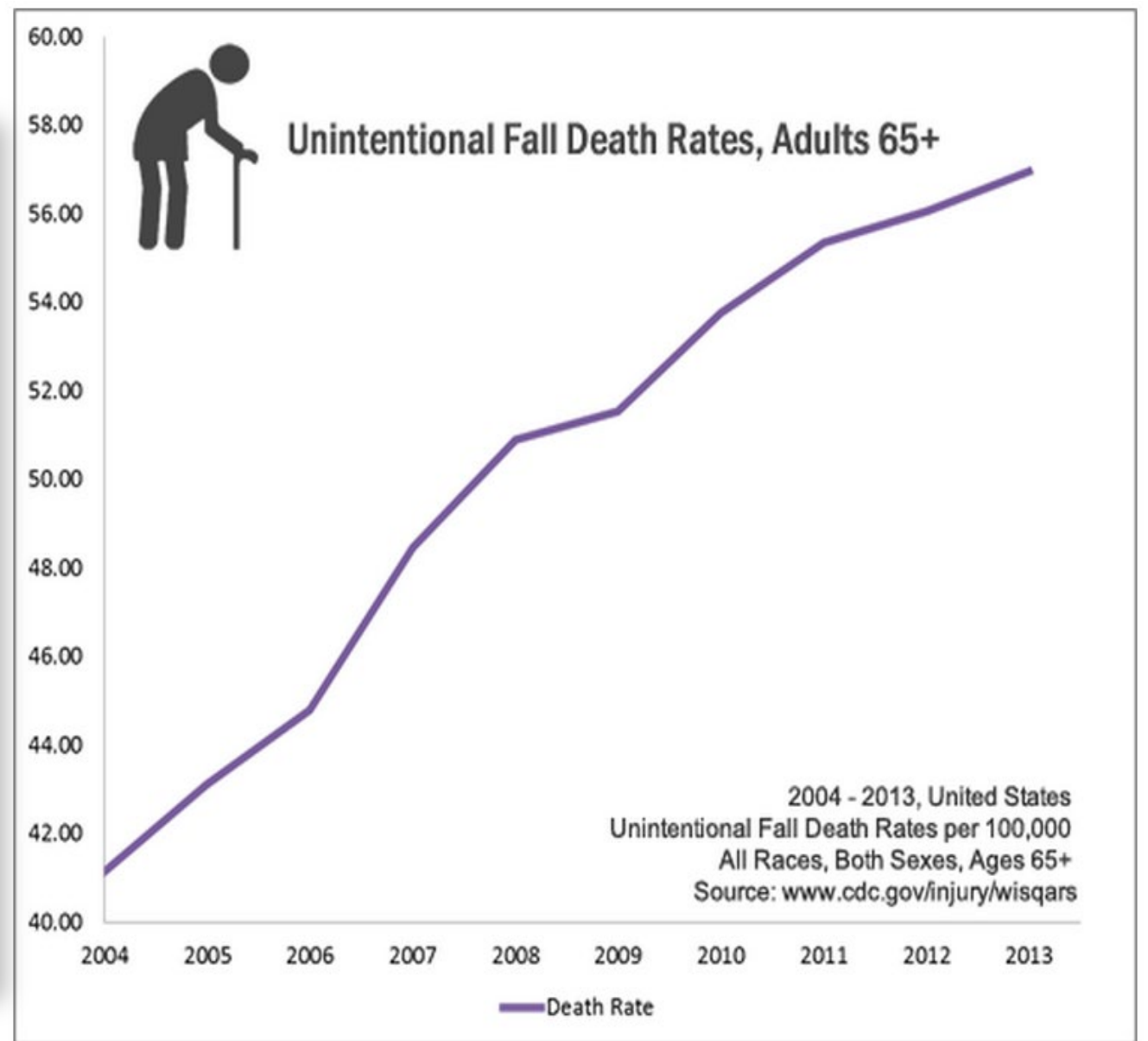


How reliable is the detection of Parkinson's Disease using a smartphone?



Acoustic signal processing data may be used to detect Parkinson's Disease with a smartphone or predict torrential rainfall or used in hydrogeomorphology apps.

2.5 million falls, 2013
734,000 hospitalized
25,500 died from fall
\$34 billion direct cost



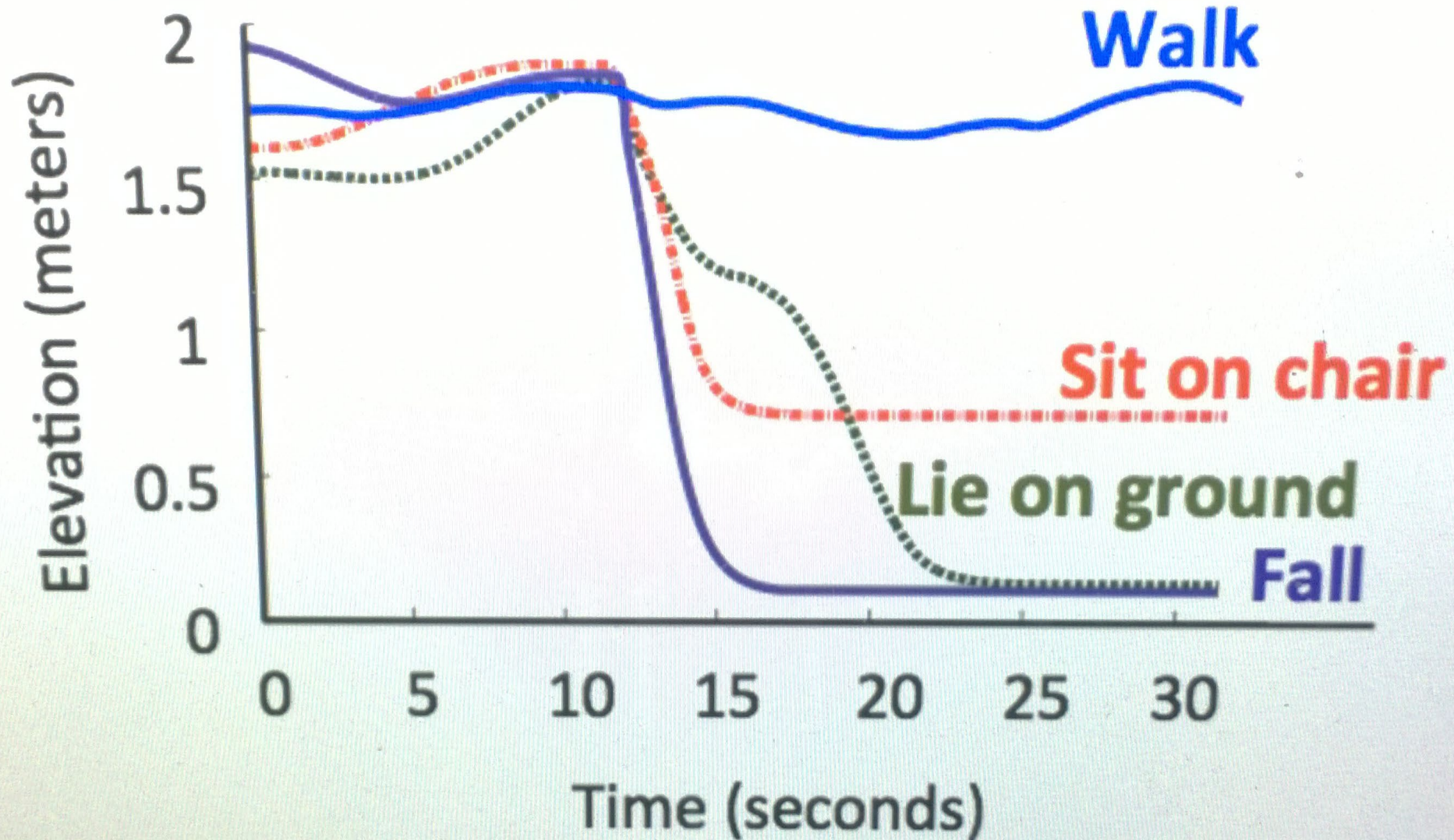
Professor Dina Katabi (MIT) presenting RF Reflection to President Obama at the White House (4 August 2015)



President Obama invites MIT entrepreneurs to give demo at the White House <http://bit.ly/President-Obama-with-Dina-Katabi>

Fall Detection – Wire less, Sensor less, Without any Wearable

RF Reflection Data from Prof Dina Katabi, Wireless Center, CSAIL, MIT

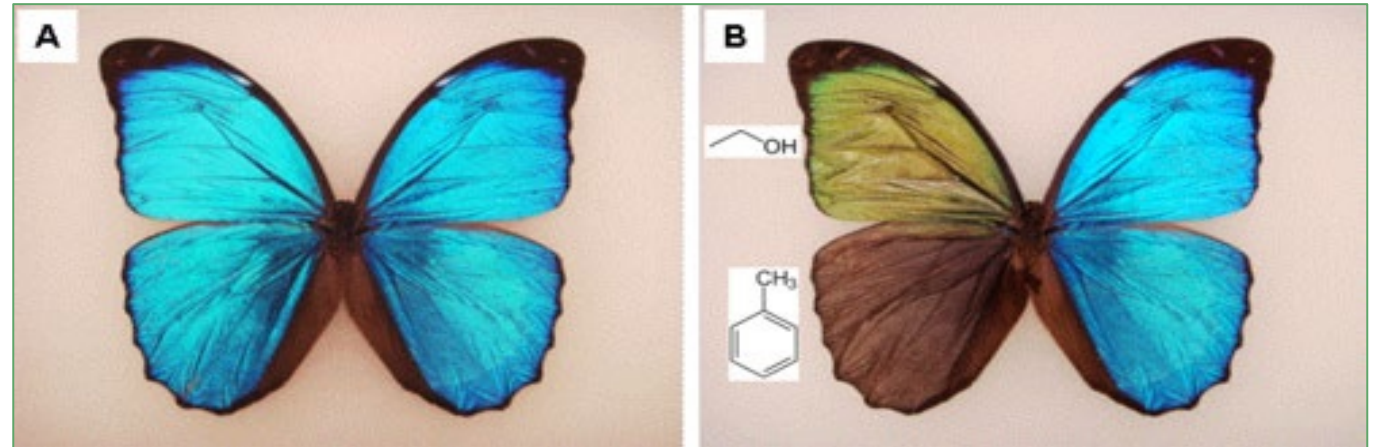
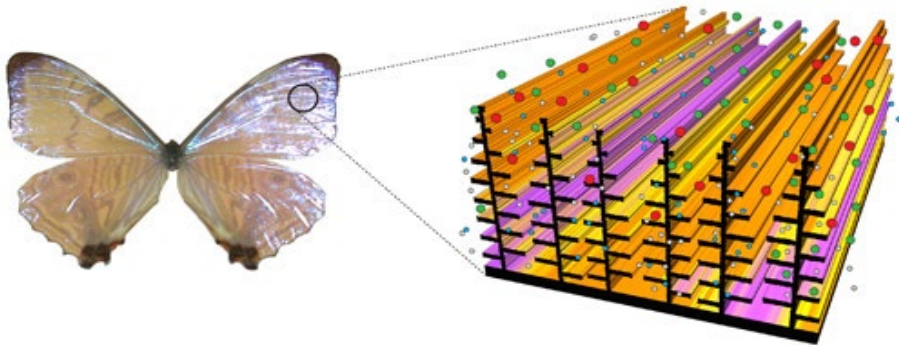


Digital Health and Advances in Diagnostic Tools / Systems

How relevant is it for the less affluent world?

Preventive Medicine • Diagnostic Devices with High Performance Sensitive Nano-Sensors

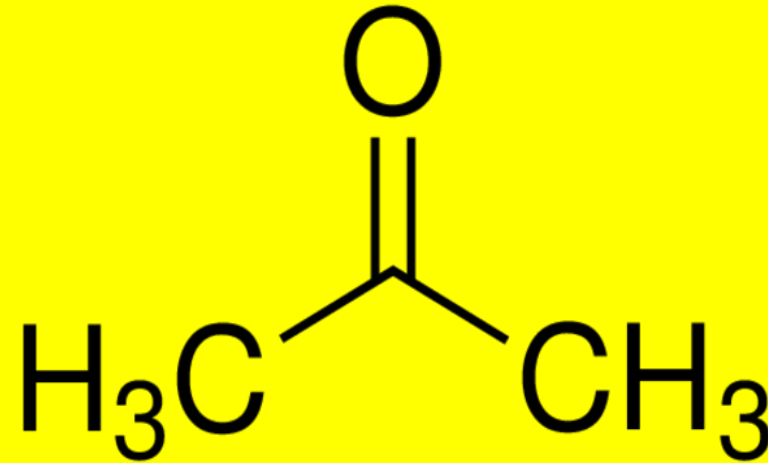
Swiss engineer George de Mestro invented Velcro after his dog came home covered with thistle burrs, Speedo learned from sharkskin to make faster swimsuits, and chemical companies designed self-cleaning paint after studying lotus leaves.



GE scientists observed that *Morpho* wings change their color when they come into contact with heat, gases and chemicals. The normal iridescent blue color of butterfly wings (A) changes when exposed to ethanol (panel B top) or toluene (panel B bottom). These findings may lead to the development of fast, ultra-sensitive thermal and chemical imaging sensors for applications in night vision goggles, super-sensitive surveillance cameras, handheld or wearable medical diagnostic devices.

Can Butterflies Help Prevent Diabetes?

This is a suggestion by the author (Shoumen Datta) and not a fact or system which is under investigation or is available at present.



Dual Acetone Sensors on a single chip may differentiate between acetone in the environment vs acetone in the blood, breath or urine of diabetics. Subtractive analysis alerts to blood ketones. Occurs when body uses fat instead of glucose. It signals insulin dysfunction. If undiagnosed, it may lead to diabetic ketoacidosis (DKA) which may result in diabetic coma and may be fatal. The acetone (ketone bodies) sensors may be able to detect trace levels (nano milli moles eq) and may help preventive care to stem the clinical onset of type II diabetes mellitus (glucose >120 mg/dl).



Michael S. Strano

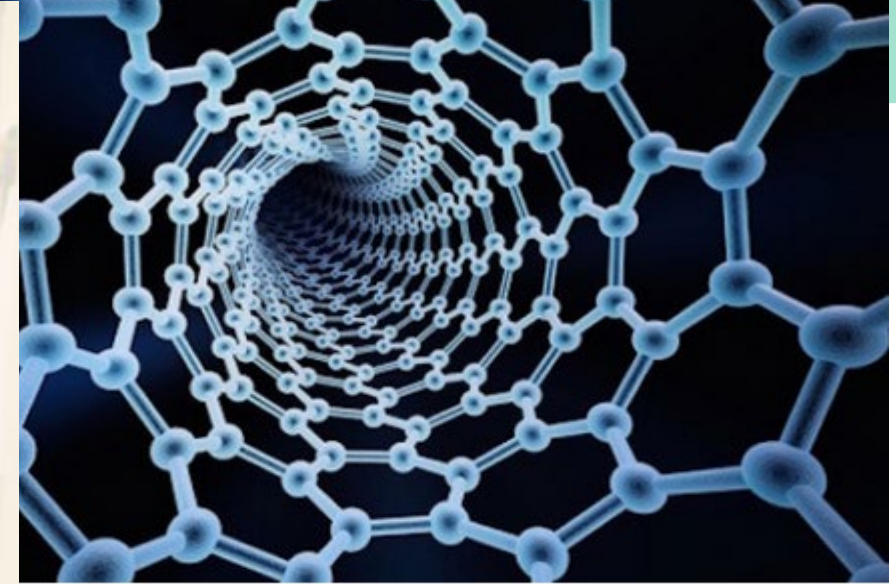
Carbon P. Dubbs Professor of Chemical Engineering

Department of Chemical Engineering
Massachusetts Institute of Technology

Room 66-570B

77 Massachusetts Ave

Cambridge MA 02139 USA



Embedded nano-sensors and nano-radios will transmit data from inside the body using ad hoc mesh networks (nano-com). They may coordinate actions of nano-bots and nano-drones introduced through nasal inhalation or epidermal patches to optimize time-dependent drug delivery, radio/laser ablation, magnetic monitoring or surgically remove abnormal growth. Real-time internal data will help manage external support, such as printed stem cell therapy or assembly of pre-synthetic peptides to form active proteins (think printed insulin in your medicine cabinet).

NANOTUBES

IMPLANTED NANOTUBE SENSOR DIAGNOSTICS

🕒 AUGUST 24, 2015 👤 LISAWEINER

MIT researchers are developing tiny devices made from polymer wrapped carbon nanotubes that detect insulin, nitric oxide and fibrinogen — simplifying and automating diagnostic tests.

Past efforts to develop implantable sensors have failed, due to the body's inclination to protect itself and recycle biological material. Devices can become wrapped in scar tissue, or their components can be broken down. The team believes that the nanotube sensors can be effective for the long term.

Peptoid nanosheets exhibit a new secondary-structure motif

Ranjan V. Mannige, Thomas K. Haxton, Caroline Proulx, Ellen J. Robertson, Alessia Battigelli, Glenn L. Butterfoss, Ronald N. Zuckermann & Stephen Whitelam

[Affiliations](#) | [Contributions](#) | [Corresponding authors](#)

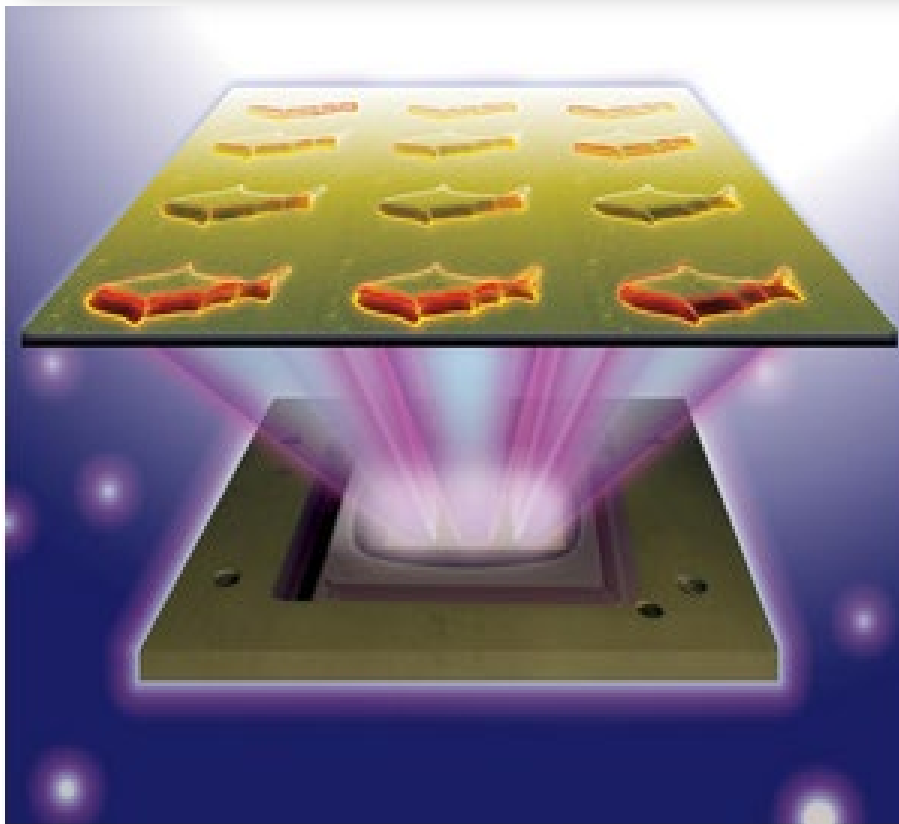
Nature (2015) | doi:10.1038/nature15363

Received 20 April 2015 | Accepted 27 July 2015 | Published online 07 October 2015

A promising route to the synthesis of protein-mimetic materials that are capable of complex functions, such as molecular recognition and catalysis, is provided by sequence-defined peptoid polymers^{1, 2}—structural relatives of biologically occurring polypeptides. Peptoids, which are relatively non-toxic and resistant to degradation³, can fold into defined structures through a combination of sequence-dependent interactions^{3, 4, 5, 6, 7, 8}. However, the range of possible structures that are accessible to peptoids and other biological mimetics is unknown, and our ability to design protein-like architectures from these polymer classes is limited⁹. Here we use molecular-dynamics simulations, together with scattering and microscopy data, to determine the atomic-resolution structure of the recently discovered peptoid nanosheet, an ordered supramolecular assembly that extends macroscopically in only two dimensions. Our simulations show that nanosheets are structurally and dynamically heterogeneous, can be formed only from peptoids of certain lengths, and are potentially porous to water and ions. Moreover, their formation is enabled by the peptoids' adoption of a secondary structure that is not seen in the natural world. This structure, a zigzag pattern that we call a Σ ('sigma')-strand, results from the ability of adjacent backbone monomers to adopt opposed rotational states, thereby allowing the backbone to remain linear and untwisted. Linear backbones tiled in a brick-like way form an extended two-dimensional nanostructure, the Σ -sheet. The binary rotational-state motif of the Σ -strand is not seen in regular protein structures, which are usually built from one type of rotational state. We also show that the concept of building regular structures from multiple rotational states can be generalized beyond the peptoid nanosheet system.

Printed Proteins ? Insulin ?

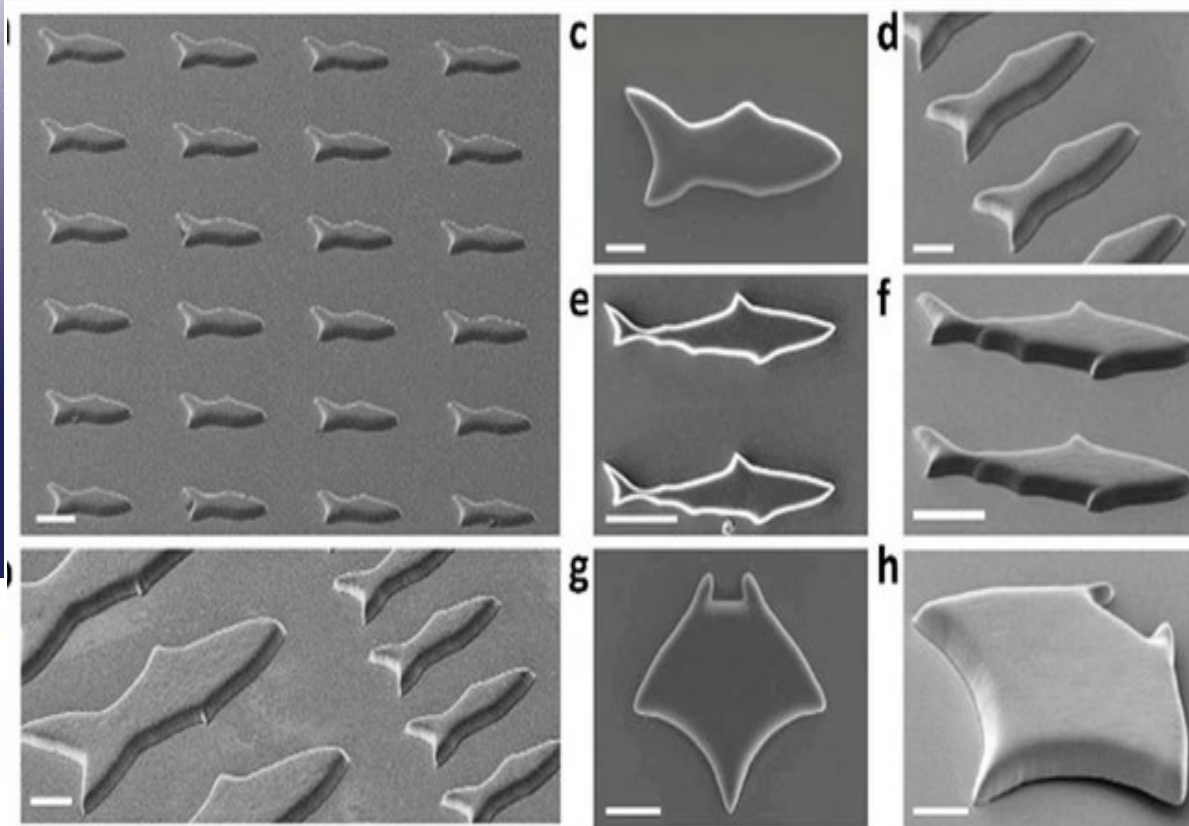
Conceptual Convergence of Material Genome with the Human Genome?



3D-printed microfish contain functional nanoparticles that enable them to be self-propelled, chemically powered and magnetically steered. The microfish are also capable of removing and sensing toxins. Image

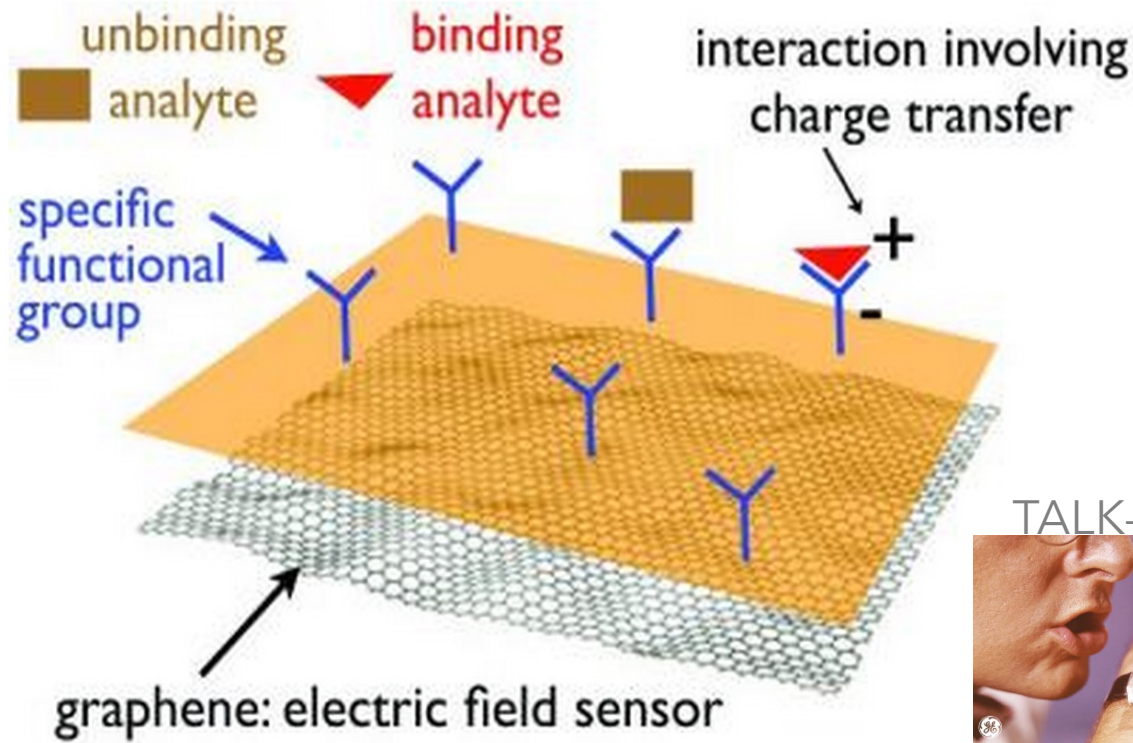
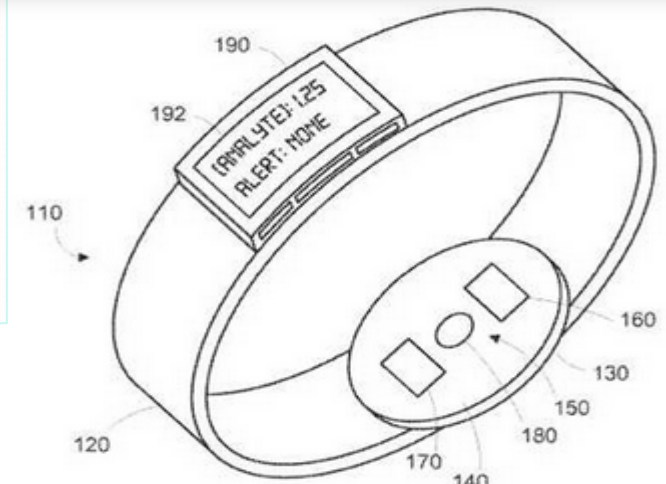
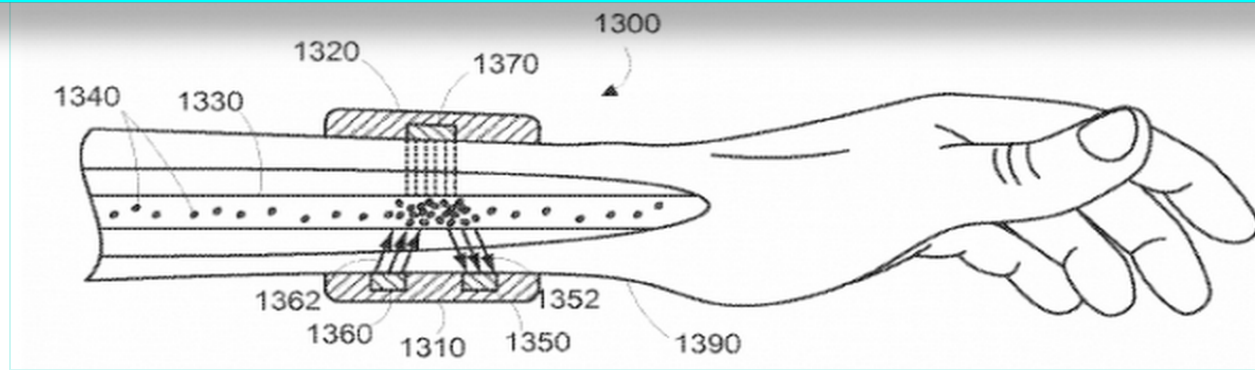
“With our 3D printing technology, we are not limited to just fish shapes. We can rapidly build micro-robots inspired by other biological organisms such as birds,” said Zhu.

Professor Shaochen Chen & Joseph Wang, NanoEngineering Dept, UCSD



3D printed robots from iron oxide, which can be magnetically guided; platinum, which can be chemically guided; and polydiacetylene (PDA) which can be used for neutralising harmful toxins.

Target Specific Analytes in Detection, Monitoring and Treatment



New test can predict cancer up to 13 years before disease develops

People who develop cancer have shorter telomeres, the caps at the end of chromosomes which protect the DNA

Target Specific Analytes in Detection, Monitoring & Treatment



ANALYTES ??

Cohesin ?

Shelterin ?

Condensin ?

<http://bit.ly/SHELTERIN-ANALYTE-FOR-TELOMERE>

Cancer Treatment

\$2,900 HCG Oncology, India

\$22,000 U.S. average

Kidney Dialysis

\$12,000 Deccan Hospital, India

\$66,750 U.S. average

Fast Forward FEWSH → Pay A Penny Per Use (PAPPU)

\$1 - Bone density

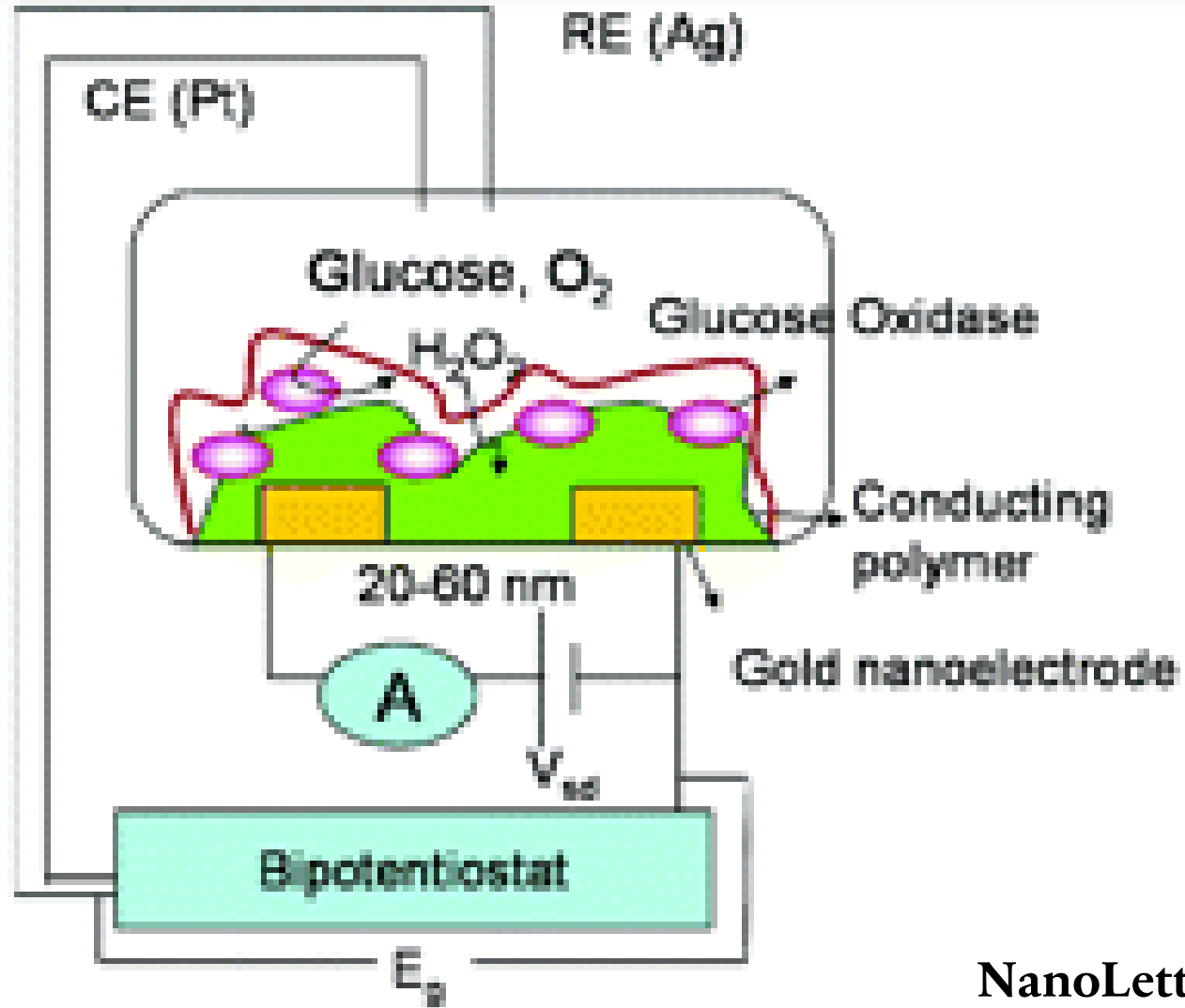
\$1 - Mammogram

at the corner of Happy and Healthy in every zip code in India, China, Indonesia

data transmitted to specialists and reports sent to individuals, doctor and clinic

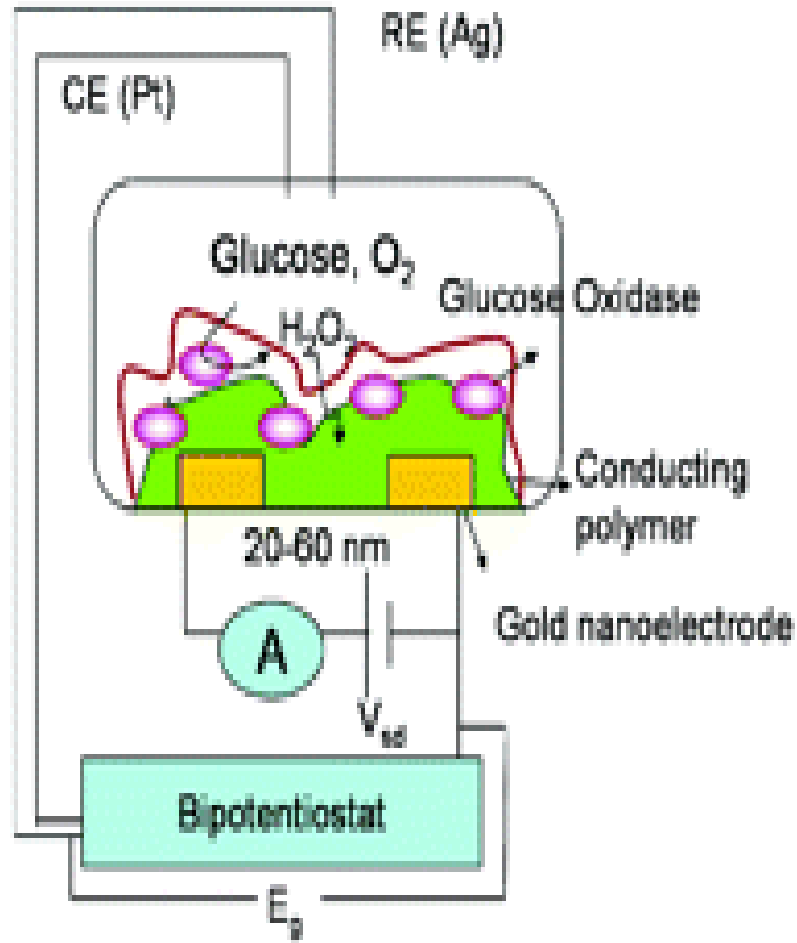
A very old idea

Glucose NanoSensor



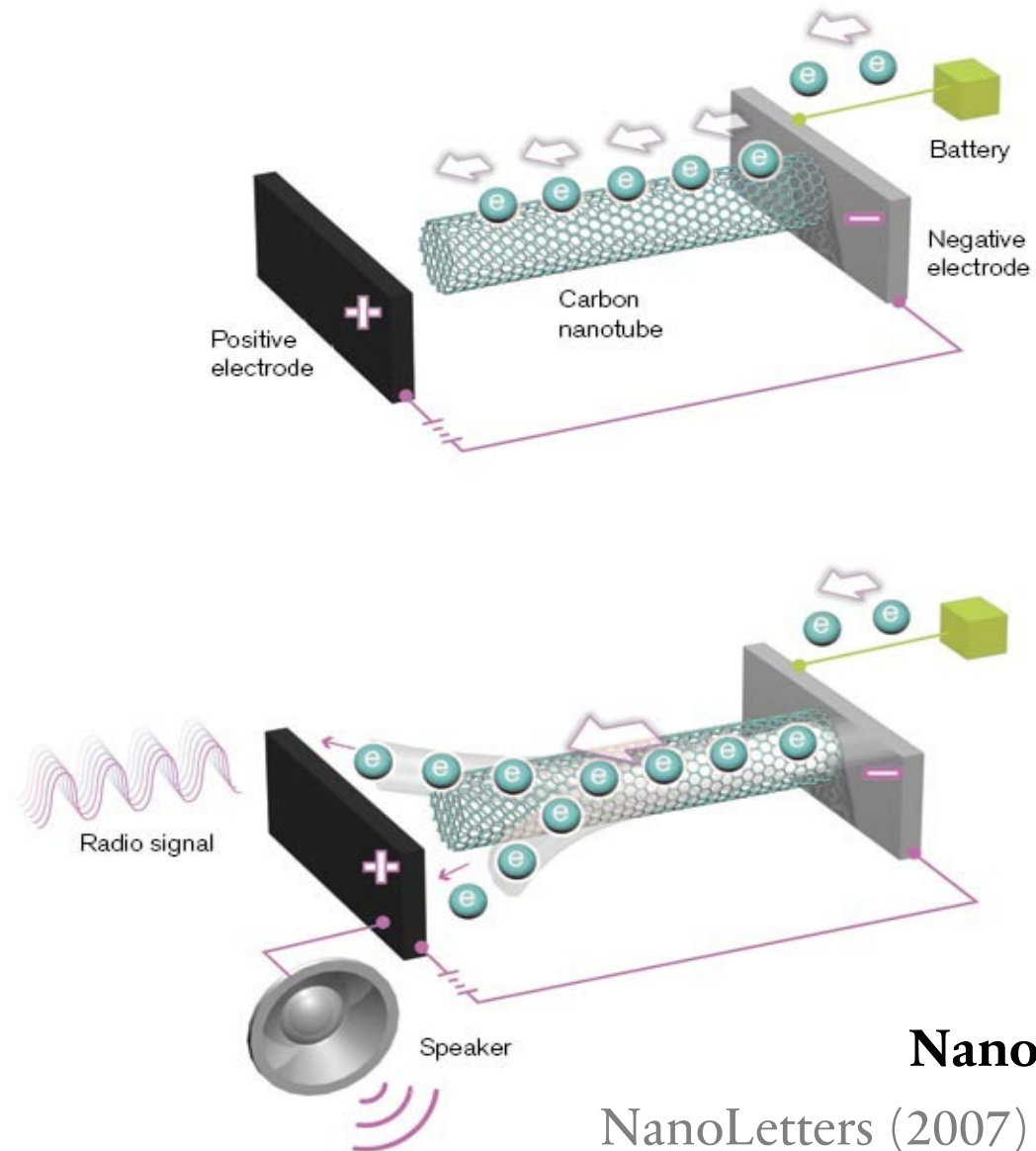
NanoLetters (2004) 4 1785-1788

Convergence ?



Blood Glucose Nano-sensor

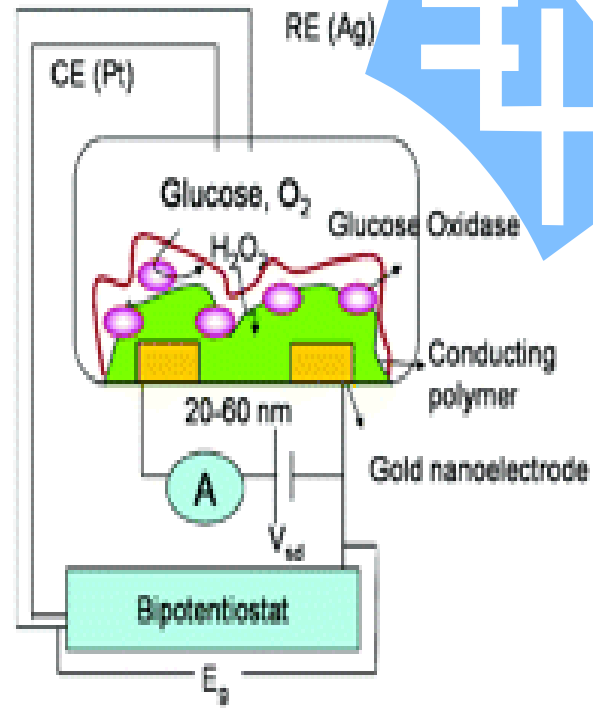
NanoLetters (2004) 4 1785-1788



Nanotube Radio

NanoLetters (2007) 7 3508-3511

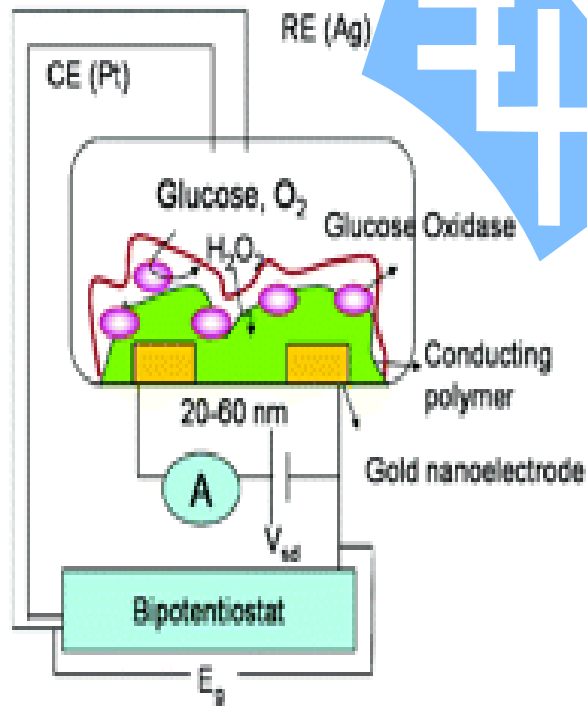
Integrated Glucose NanoSensor NanoRadio



www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf

Diabetes - Remote Health Monitoring ?

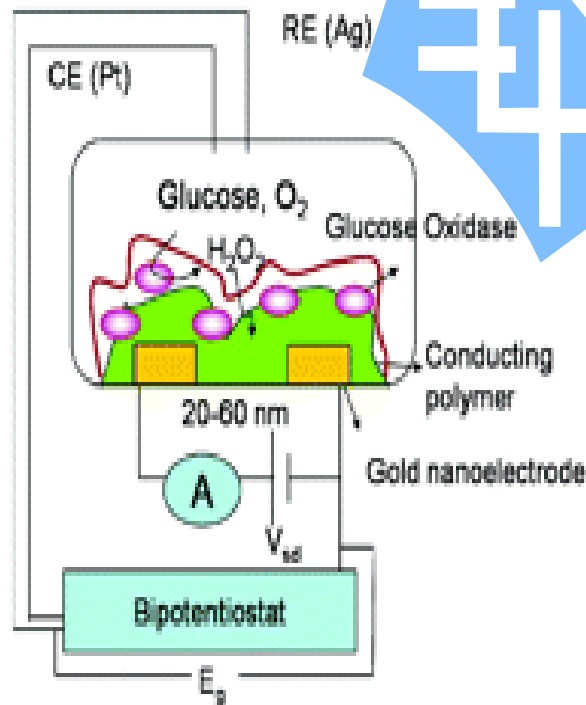
May I implant a glucose nano-sensor nano-radio chip on your shoulder? Are you an obese diabetic?



Prime Minister Bertie Ahern (Taoiseach)
Prime Minister of Ireland, 2005 Trinity College

Glucose NanoSensor NanoRadio: Ecosystem of healthcare monitoring?

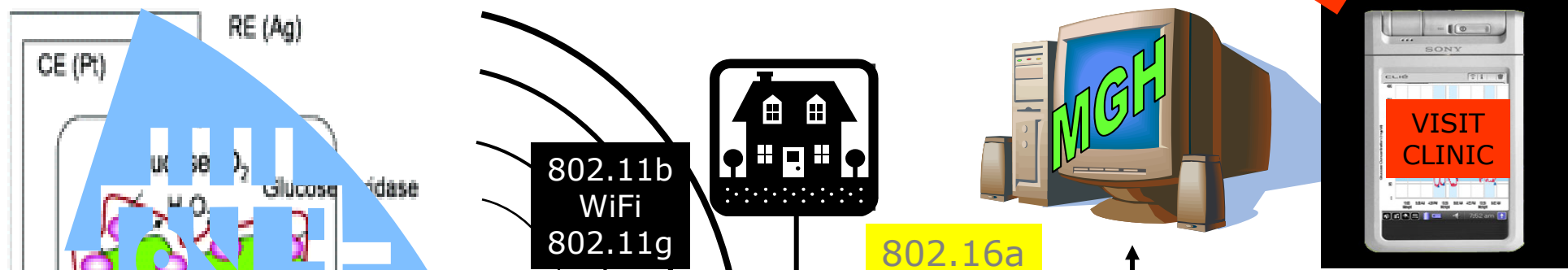
~30 million individuals in US affected by diabetes



www.cdc.gov/nchs/fastats/diabetes.htm



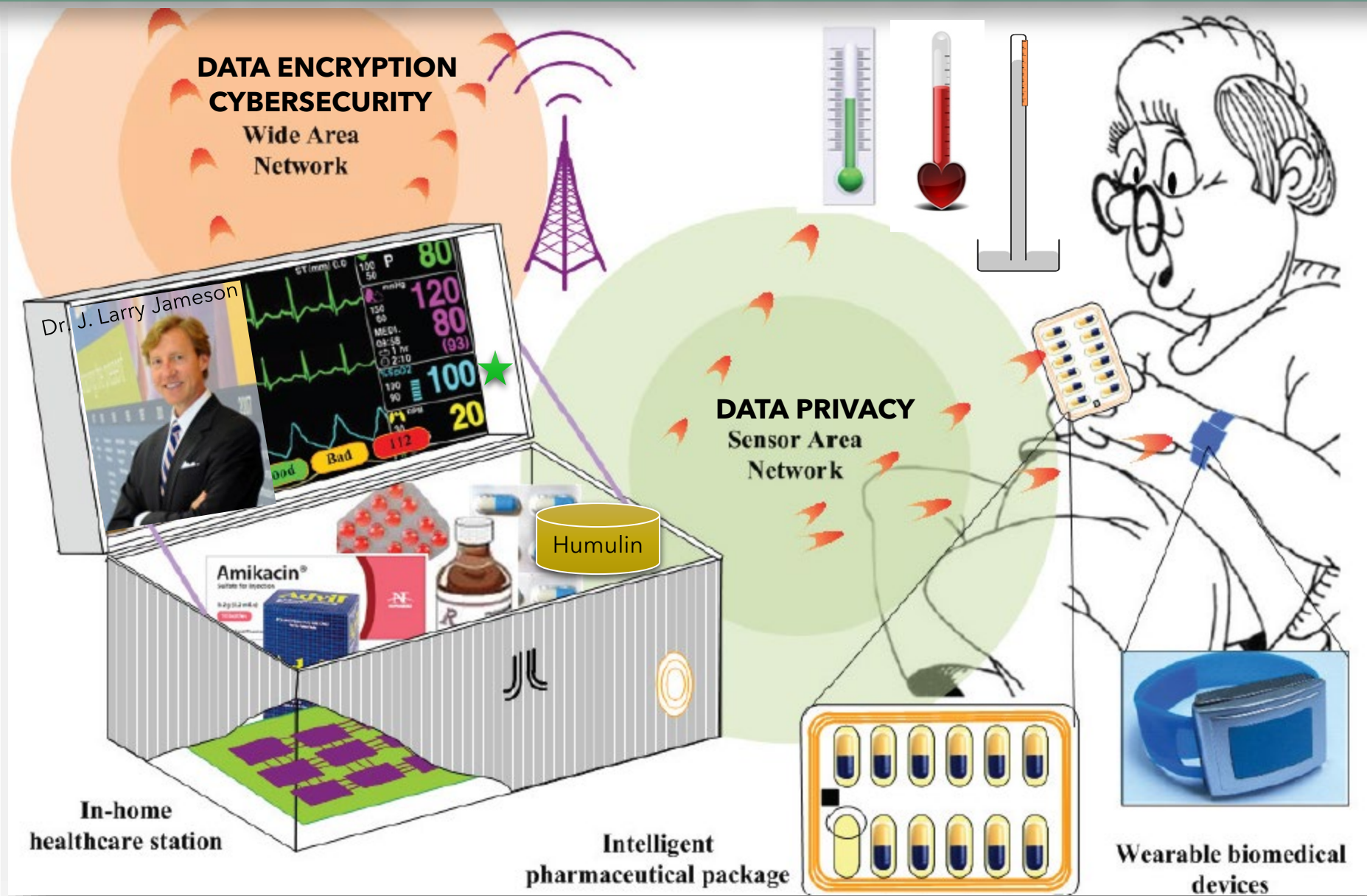
1. Implanted wireless sensor transmits blood glucose data from home or office or airport (WiFi/WAN/gateway)
2. Data travels from you to your hospital or clinic (MAN)
3. Blood glucose data updates risk and patient profile
4. If you need medical attention or insulin or other treatment then auto-responder sends message or calls



Improved healthcare services, savings, create jobs from new products, new services and potential to create as well as capture new emerging markets of billions (BRICS)

Metabolomics
Genetic Risk
EHR - EMR
RT Analytics
SNP Analysis

Larry Gold is at home with hypercholesterolemia: Hello Dr Jameson - Do I need Lipitor today?



Dr Larry Jameson: Avoid KFC. Your LDL-VLDL ratio looks good. No Lipitor.

Congestive Heart Failure (CHF)

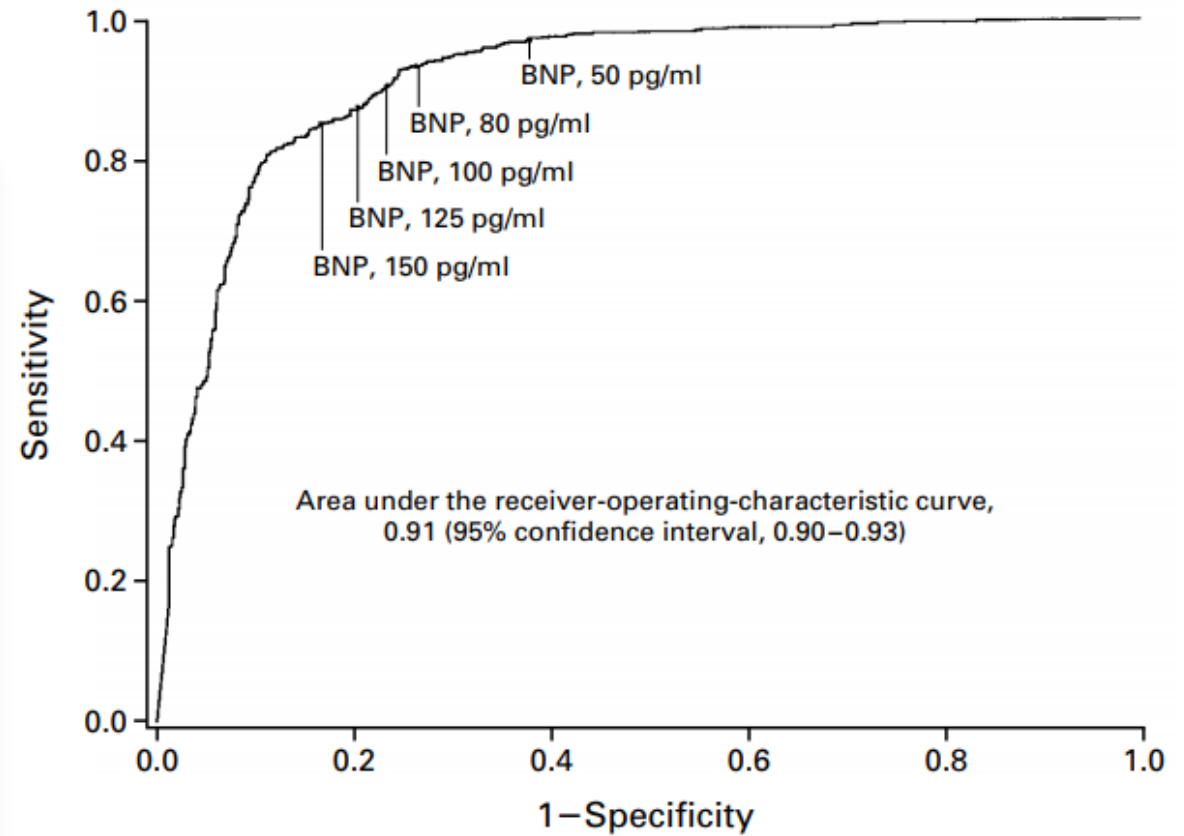
- About 5.1 million people in the United States have heart failure.
- About half of people with CHF die within 5 years of diagnosis.
- CHF costs the nation an estimated \$32 billion each year.

Abundance of prognostic biochemical markers -

- C-reactive protein (CRP5 / CRP6) - 1954 and Framingham Heart Study
- Tumour necrosis factor alpha (TNF α)
- Brain Natriuretic Peptide (1981) BNP <100 pg/ml unlikely & >400 pg/ml CHF likely
- N-terminal (NT) pro-BNP <300 pg/ml unlikely & >400-900 pg/ml CHF likely (age?)

48,629 patients of acute decompensated heart failure found linear correlation between BNP levels and in hospital mortality. Failure of BNP to decline during hospitalization predicts death and re-hospitalization while discharge levels of 250pg/ml or less predicts event free survival.

BNP as a key biochemical marker in coronary syndromes and congestive heart failure (CHF)



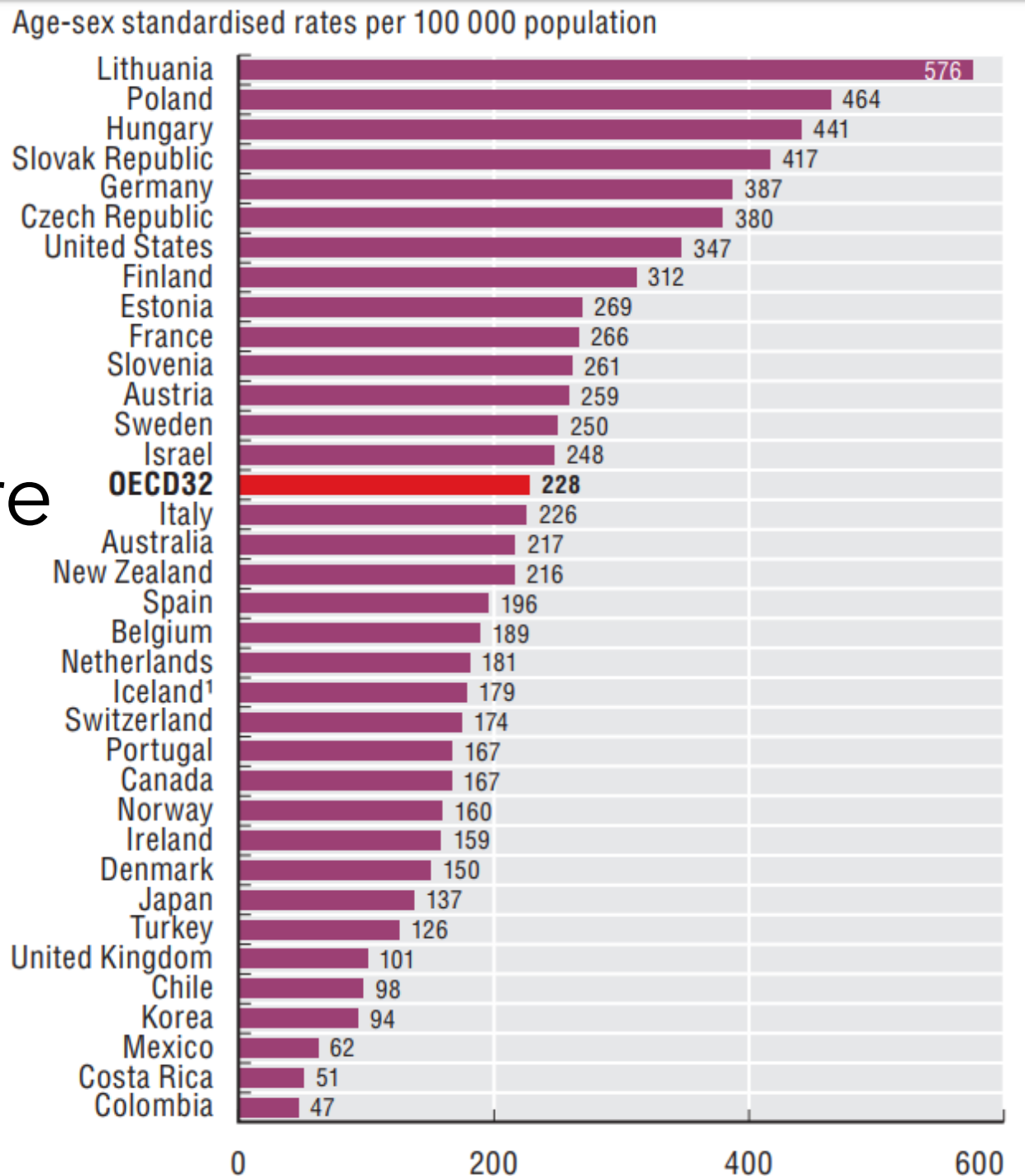
BNP pg/ml	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE	ACCURACY
	(95 percent confidence interval)				
50	97 (96-98)	62 (59-66)	71 (68-74)	96 (94-97)	79
80	93 (91-95)	74 (70-77)	77 (75-80)	92 (89-94)	83
100	90 (88-92)	76 (73-79)	79 (76-81)	89 (87-91)	83
125	87 (85-90)	79 (76-82)	80 (78-83)	87 (84-89)	83
150	85 (82-88)	83 (80-85)	83 (80-85)	85 (83-88)	84

Figure 3. Receiver-Operating-Characteristic Curve for Various Cutoff Levels of B-Type Natriuretic Peptide (BNP) in Differentiating between Dyspnea Due to Congestive Heart Failure and Dyspnea Due to Other Causes.

Congestive heart failure hospital admission (2015)

OECD Health Statistics 2017

<http://dx.doi.org/10.1787/888933603507>



Symptomatic Angina: The Tip of the Ischemic Iceberg

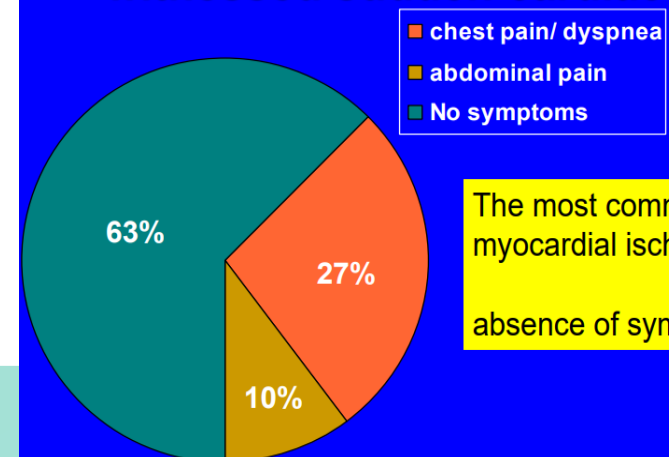
24% (symptomatic angina)

76% (silent ischemia)

Total Ischemic Burden

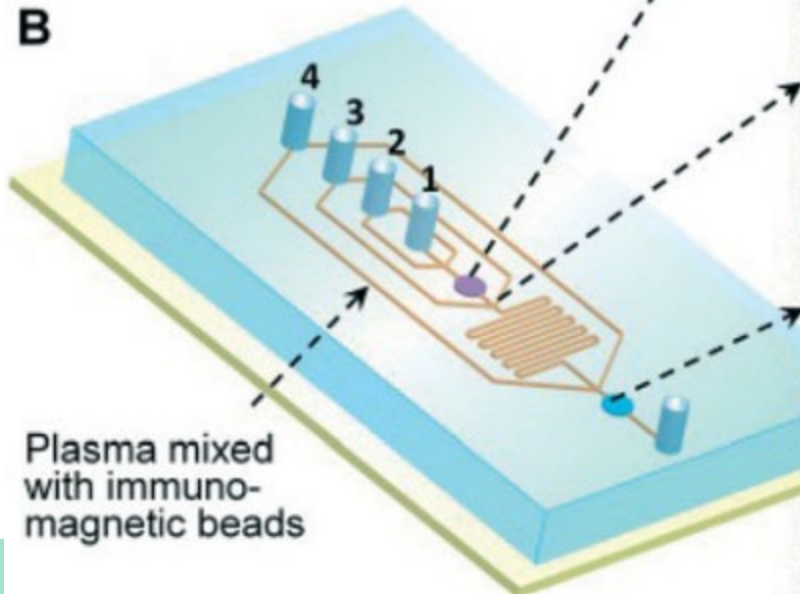
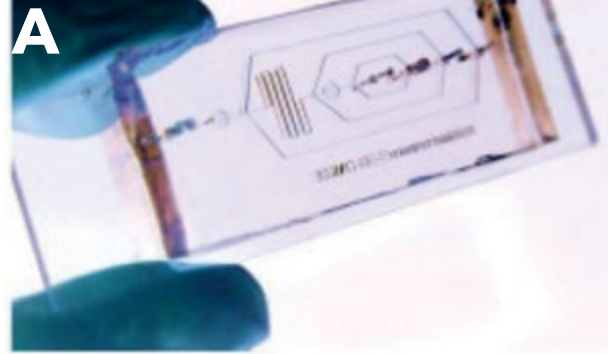
If you cannot sense, you cannot detect.
If you cannot predict, you cannot prevent.
If you cannot measure, you do not have metrics.
If you do not have data, you cannot take a decision.

<https://dspace.mit.edu/handle/1721.1/107893>



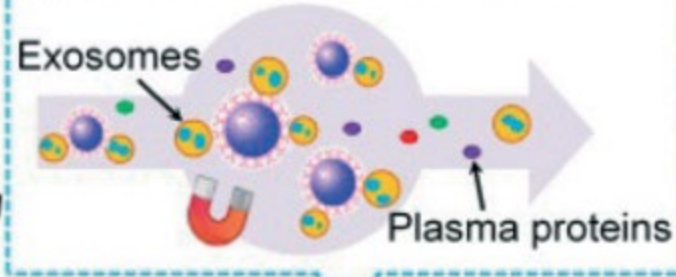
The most common symptom of myocardial ischemia:
absence of symptoms

Lab on a Chip - Detection of Non-Small Cell Lung Cancer (C) and Ovarian Cancer (D)

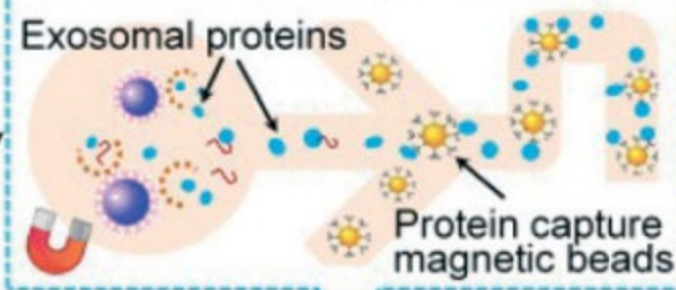


Total on-chip Assay Time: 1.5 hrs

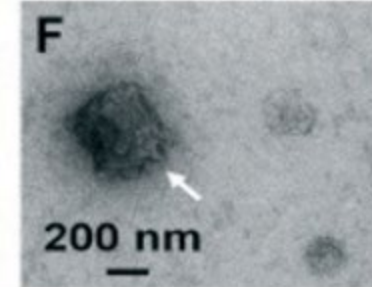
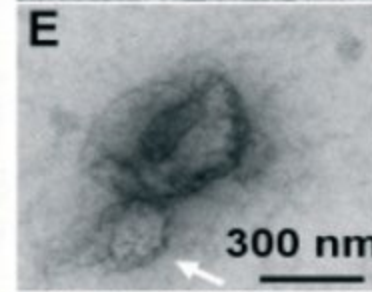
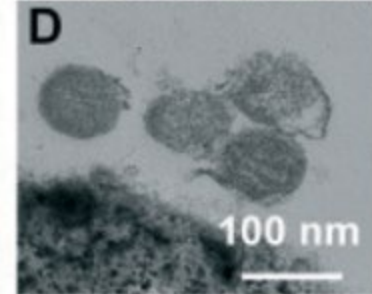
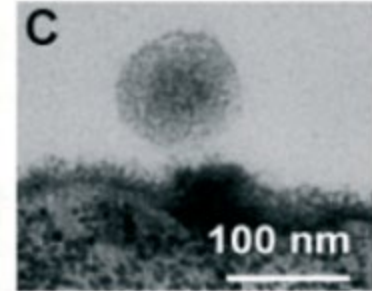
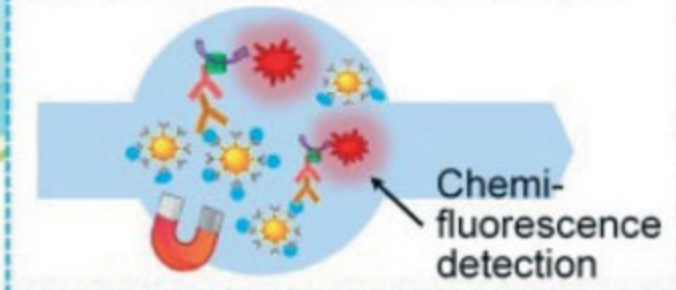
1) Immunomagnetic isolation



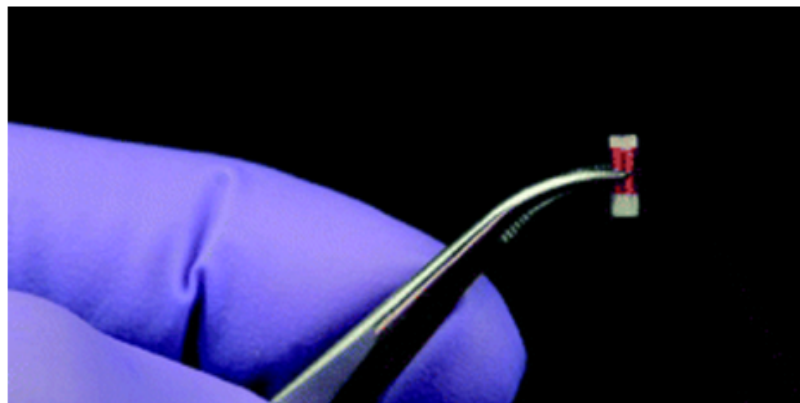
2) Exosome lysis & protein capture



3) Intravesicular protein analysis



Biopsy is an important diagnostic tool for a broad range of conditions. Cancer diagnoses, for example, are confirmed using tissue explanted with biopsy. Here we demonstrate a miniaturized wireless sensor that can be implanted during a biopsy procedure and return chemical information from within the body. Power and readout are wireless *via* weak magnetic resonant coupling to an external reader. The sensor is filled with responsive nuclear magnetic resonance (NMR) contrast agents for chemical sensitivity, and on-board circuitry constrains the NMR measurement to the contents. This sensor enables longitudinal monitoring of the same location, and its simple readout mechanism is ideal for applications not requiring the spatial information available through imaging techniques. We demonstrated the operation of this sensor by measuring two metabolic markers, both *in vitro* and *in vivo*: pH in flowing fluid for over 25 days and in a xenograft tumor model in mice, and oxygen in flowing gas and in a rat hind-limb constriction experiment. The results suggest that this *in vivo* sensing platform is generalizable to other available NMR contrast agents. These sensors have potential for use in biomedicine, environmental monitoring and quality control applications.



Miniaturized, biopsy-implantable chemical sensor with wireless, magnetic resonance readout

[C. C. Vassiliou](#),^{†ab} [V. H. Liu](#)^{ab} and [M. J. Cima](#)^{*ac}

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^c Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Single-molecule detection of protein efflux from microorganisms using fluorescent single-walled carbon nanotube sensor arrays

Markita Patricia Landry, Hiroki Ando, Allen Y. Chen, Jicong Cao, Vishal Isaac Kottadiel, Linda Chio, Darwin Yang, Juyao Dong, Timothy K. Lu & Michael S. Strano

Affiliations | **Contributions** Department of Chemical Engineering, Massachusetts Institute of Technology

Nature Nanotechnology (2017) | doi:10.1038/nnano.2016.284

Received 20 January 2016 | Accepted 01 December 2016 | Published online 23 January 2017

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Hiroki Ando, Allen Y. Chen, Jicong Cao & Timothy K. Lu

Biophysics Program, Harvard University, Cambridge, Massachusetts 02138, USA
Allen Y. Chen

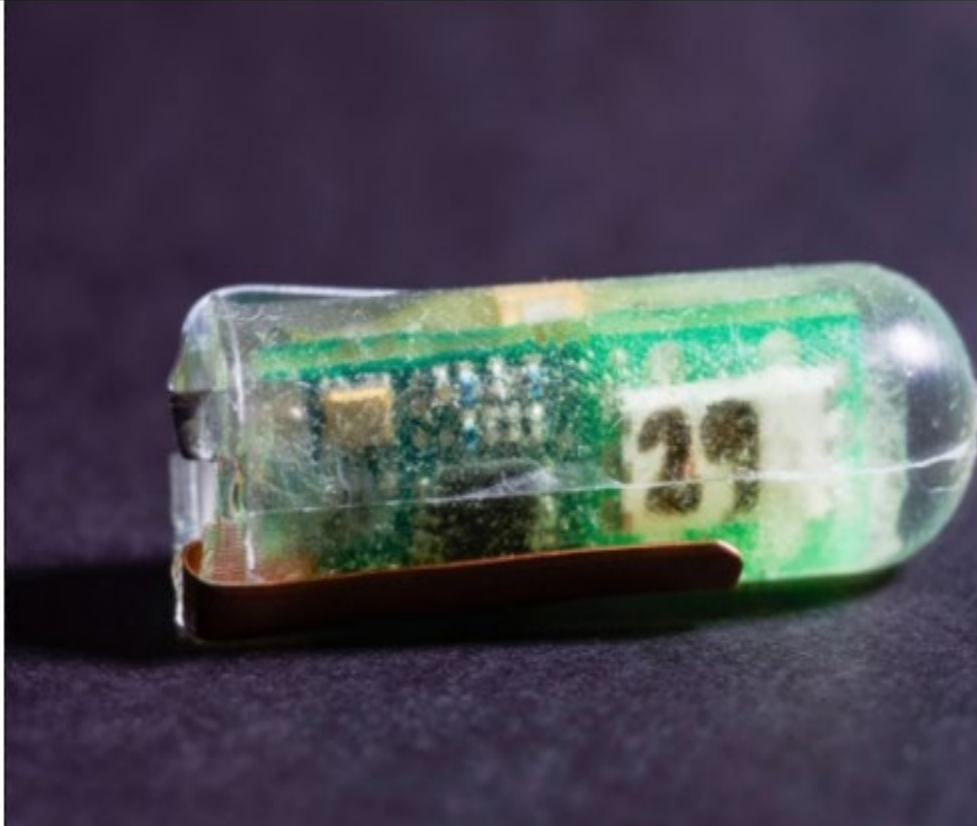
The Rowland Institute at Harvard University, Cambridge, Massachusetts 02142, USA
Vishal Isaac Kottadiel

A distinct advantage of nanosensor arrays is their ability to achieve ultralow detection limits in solution by proximity placement to an analyte. Here, we demonstrate label-free detection of individual proteins from *Escherichia coli* (bacteria) and *Pichia pastoris* (yeast) immobilized in a microfluidic chamber, measuring protein efflux from single organisms in real time.



STROKE DETECTOR – BIOSENSOR

i Nicholas Dale with his SMARTchip



Dr Phillip Nadeau with the "silver bullet" device, which could revolutionise medical treatment (Photo: Andrew)

Researchers at MIT and Brigham and Women's Hospital have designed and demonstrated a small, ingestible voltaic cell that is sustained by the acidic fluids in the stomach.

Photo: Diemut Strebe

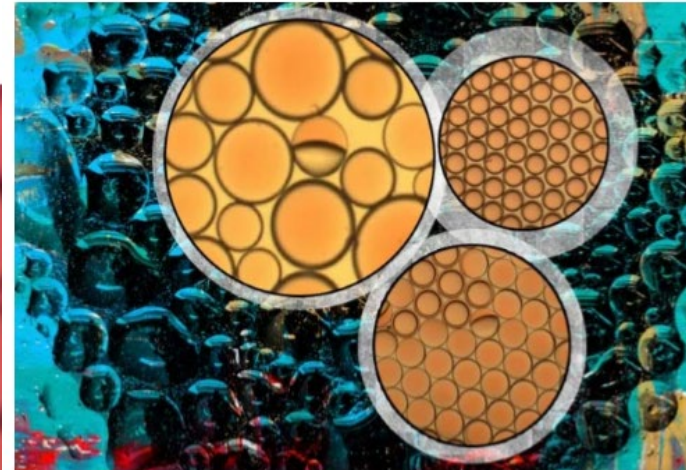
<http://news.mit.edu/2017/engineers-harness-stomach-acid-power-tiny-sensors-0206>

Engineers harness stomach acid to power tiny sensors

Ingestible electronic devices could monitor physiological conditions or deliver drug



Food Testing. Blood
Testing? Sputum?
Mucus? Fluids?



A simple way to make and reconfigure complex emulsions

Anne Trafton | MIT News Office
February 25, 2015

Janus Emulsions for the Detection of Bacteria

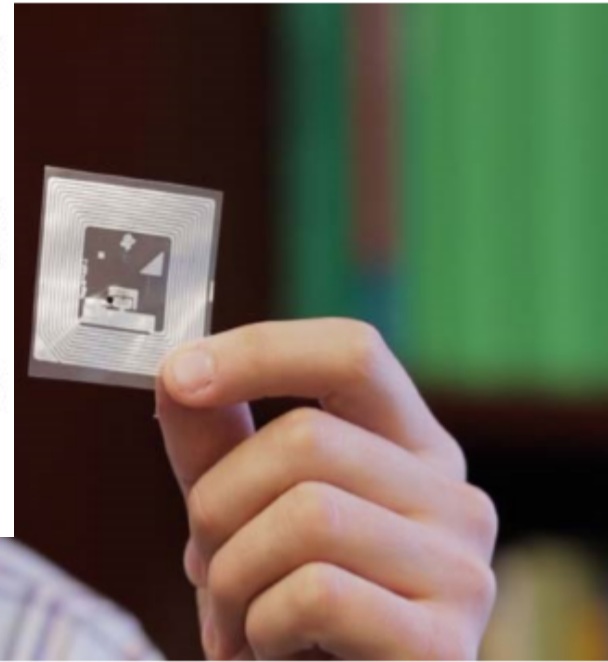
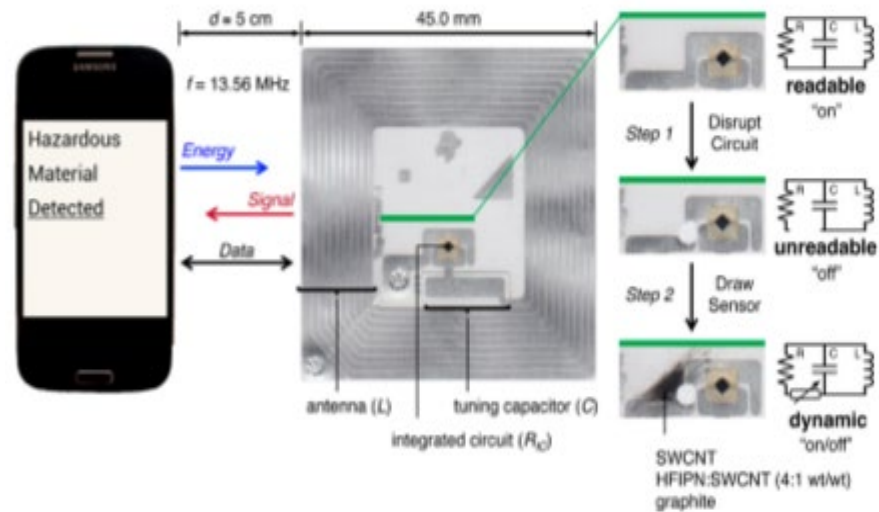
Qifan Zhang,[†] Suchol Savagatrup,[†] Paulina Kaplonek,^{‡,§} Peter H. Seeberger,^{*,†,§}
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[†]Department of Chemistry and Institute for Soldier Nanotechnologies, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, United States

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[§]Institute of Chemistry and Biochemistry, Free University Berlin, Arnimallee 22, 14195 Berlin, Germany

Specialized droplets interact with bacteria and can be analyzed using a smartphone.



The MIT researchers' wireless chemical sensor.

Photo: Melanie Gonick



Detecting gases wirelessly and cheaply

New sensor can transmit information on hazardous chemicals or food spoilage to a smartphone.

Wireless gas detection with a smartphone via rf communication

Joseph M. Azzarelli, Katherine A. Mirica, Jens B. Ravnsbæk¹, and Timothy M. Swager²

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139

Edited by Chad A. Mirkin, Northwestern University, Evanston, IL, and approved November 5, 2014 (received for review August 10, 2014)

Pay A Penny Per Use – PAPPU Analytics, Apps, Data Distribution Service



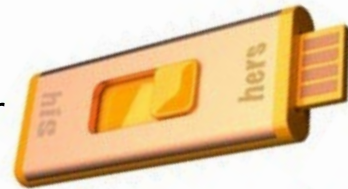
Glucose Sensor



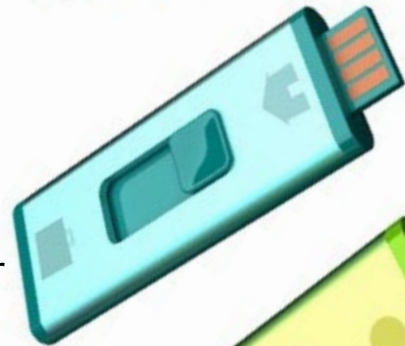
Cholesterol Sensor



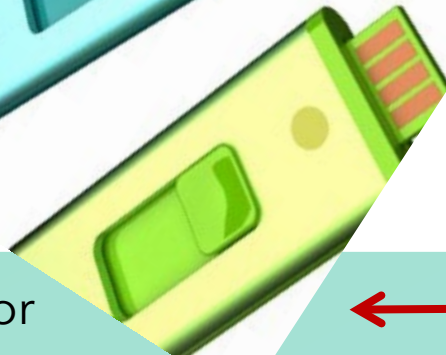
BNP Sensor



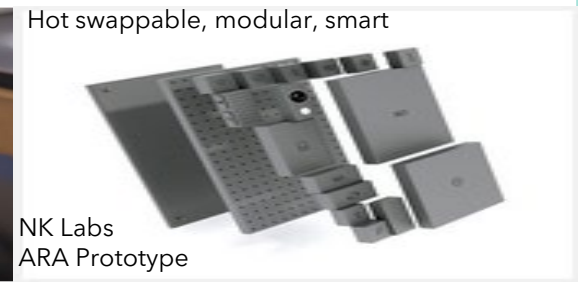
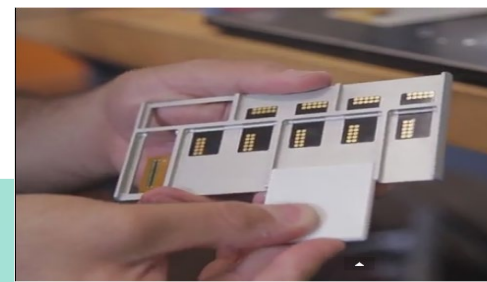
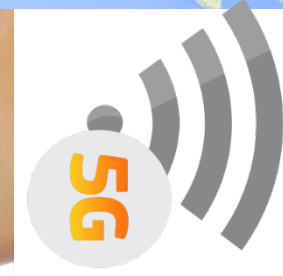
SARS-CoV-2 Sensor



Ebola Virus Sensor



What does the data suggest about my health?



Hot swappable, modular, smart

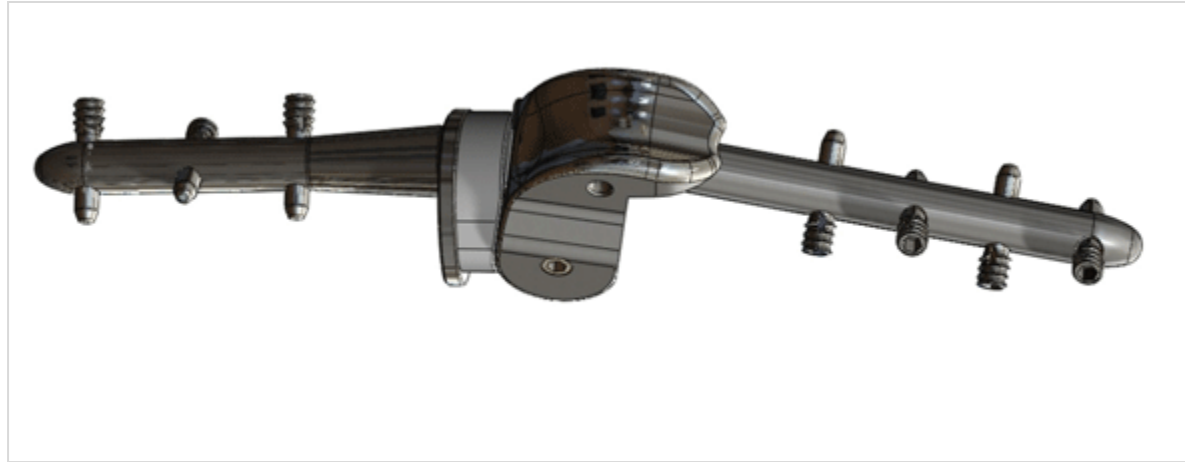
NK Labs ARA Prototype

Made-on-Demand ▪ Made-to-Design

3D Printed Spare Parts - specifically designed for each patient

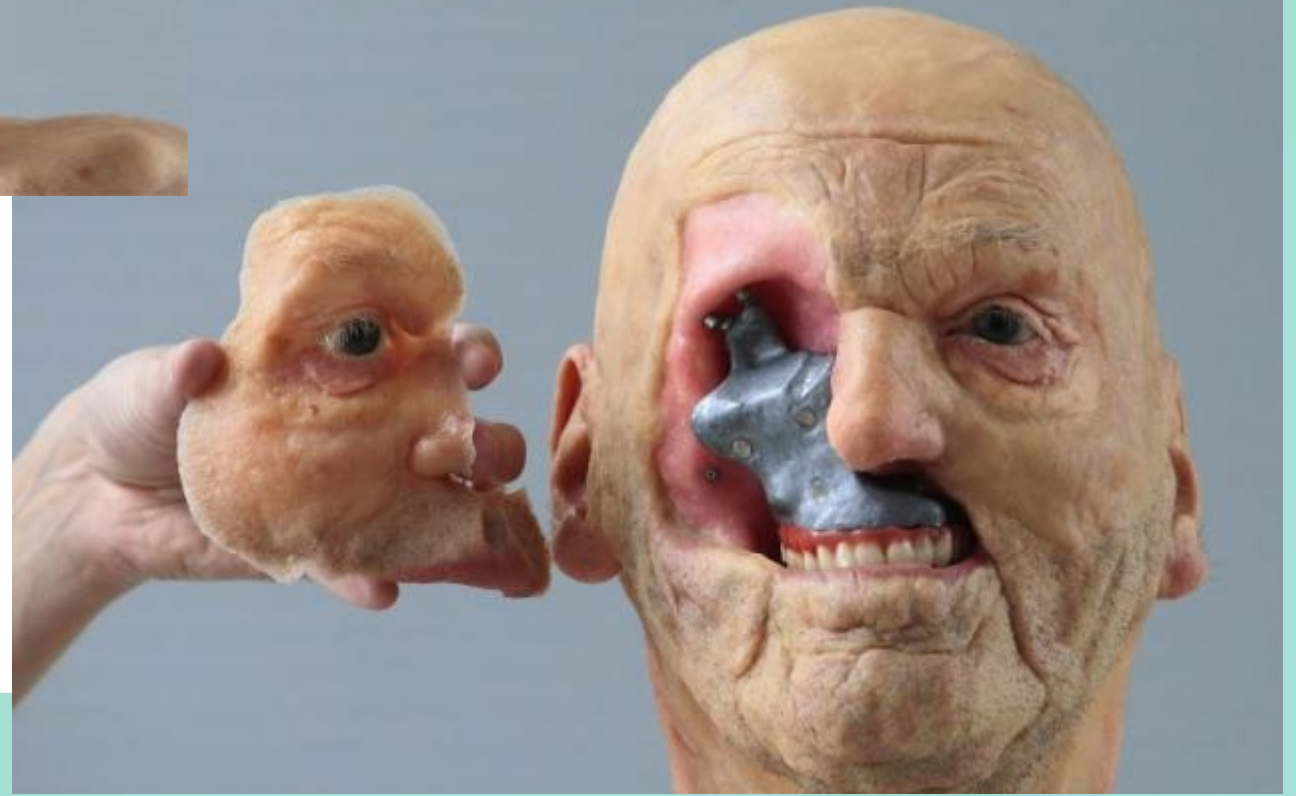
3-D Printing

Design of Prosthetics and Orthopedic Imaging

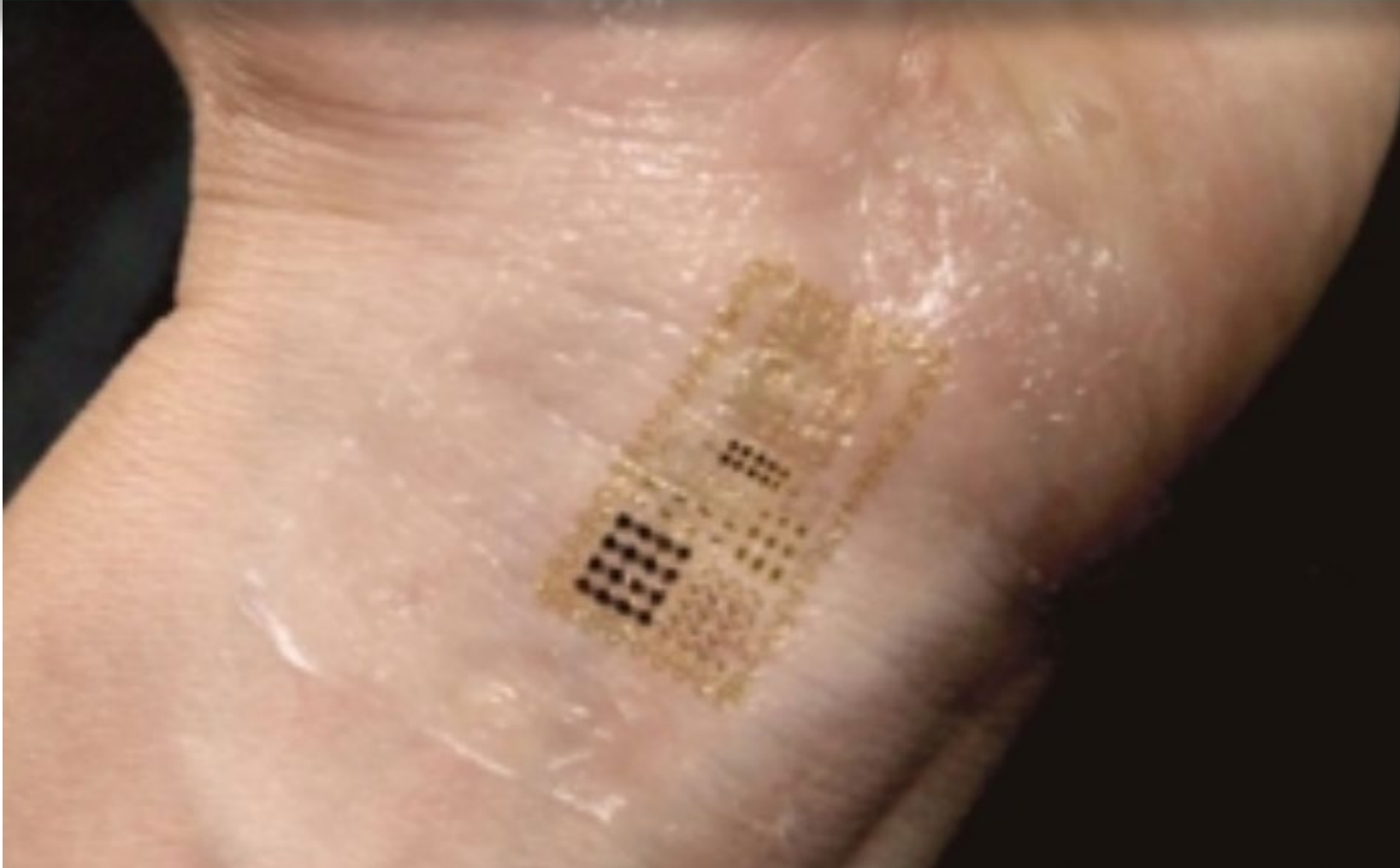


Cyrano L. Catte II (above) is the first feline to receive a total knee arthroplasty (TKA). Femoral and tibial components were created with direct metal laser sintering (EOS).

3-D Printing of Fitted Parts on Demand



Artificial Skin with embedded sensory surface talks to smart phone via capacitive sensing using Touchcode adapted for printed i-Skin

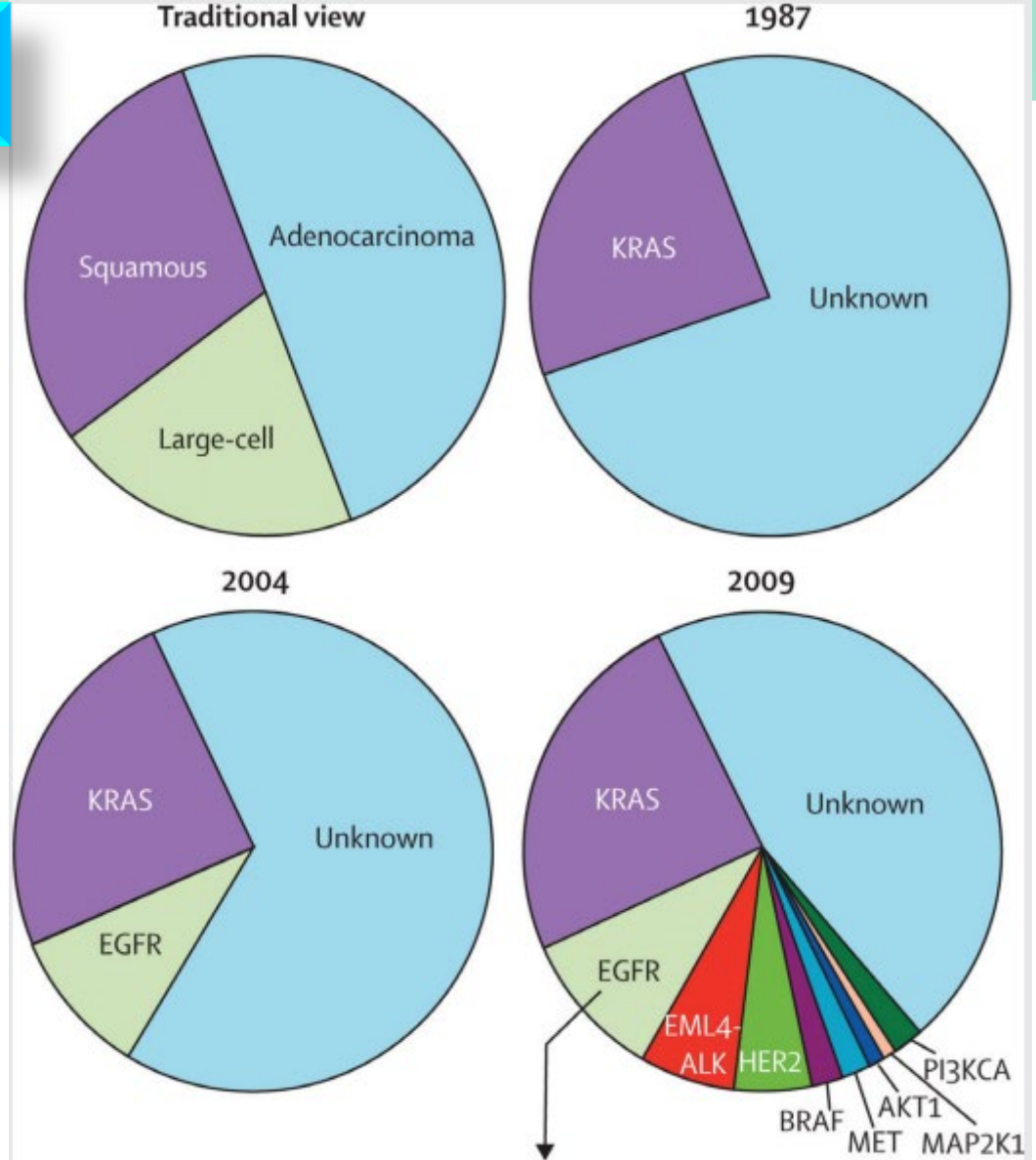


Your medicine can inform your doctor about its kinetics, bio-availability and side effects. It can alert your pharmacist about potential over-dose if multiple medications contain same or similar active ingredients. Your medicine can query your physician and even adjust dosage.

The Final Frontier or Excessive Greed ?

Precision Medicine

Non-Small Cell Lung Carcinoma



- **Mutations associated with drug sensitivity**
EGFR Gly719X, exon 19 deletion, Leu858Arg, Leu861Gln
- **Mutations associated with primary drug resistance**
EGFR exon 20 insertions
- **Mutations associated with acquired drug resistance**
EGFR Thr790Met, Asp761Tyr, Leu747Ser, Thr854Ala

Imprecision Medicine

new ones and identifying appropriate disease biomarkers, such as tumour DNA circulating in the bloodstream. It will also require a cultural shift on many levels — in regulatory agencies, in pharmaceutical companies and, most of all, in the clinic.

A WORLD OF DIFFERENCE

Discovering that an intervention works well in certain groups happens relatively rarely and often by chance. Researchers typically get disappointing results with a drug in large, population-based trials. This leads them to conduct ad hoc post-trial analyses, to try to identify the factors that cause some of the people in the trial to seem to be responsive³.

For instance, the drug Gleevec (imatinib) was found to double survival rates of leukaemia patients⁴ with a chromosomal abnormality in their tumours called the Philadelphia translocation. Similarly, it turns out that Erbitux (cetuximab) improves the survival of people with colorectal cancer whose tumour cells carry a mutated *EGFR* gene but not a mutated *KRAS* gene⁵.

This approach to discovery is inefficient at best. Conventional phase III trials involve thousands of people. The intervention being tested is often given at random to one group while another group receives a sham treatment, such as a sugar pill or the standard treatment that physicians would give such patients. Because scant data are collected on factors such as genetics, lifestyles and diets, the results of these trials often indicate the need for yet another study to validate the effectiveness of the intervention among the apparent responders and to establish the

1. ABILIFY (aripiprazole)
Schizophrenia



2. NEXIUM (esomeprazole)
Heartburn



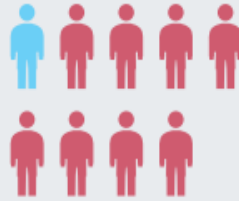
3. HUMIRA (adalimumab)
Arthritis



4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



9. COPAXONE (glatiramer acetate)
Multiple sclerosis



10. NEULASTA (pegfilgrastim)
Neutropenia



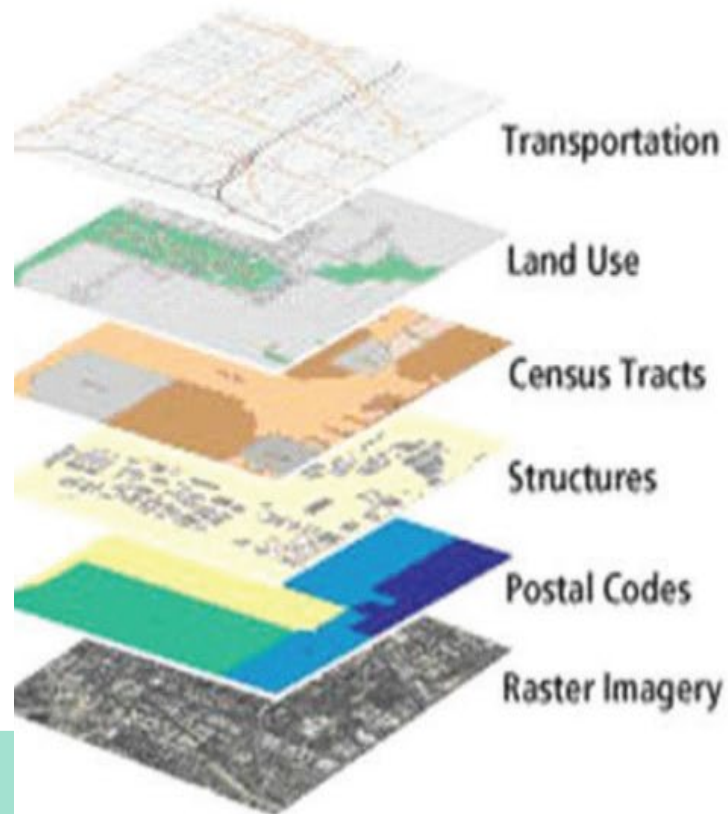
Precision Medicine – Drug Development

A successful example of the precision medicine approach to drug development involves the drug Crizotinib, an inhibitor of the MET and ALK kinases, which began clinical development in a broad population of patients with lung cancer (Kwak et al. 2010). During the early stages of the initial Crizotinib clinical trial conducted by pharmaceutical industry scientists, an independent group of academic scientists published their discovery that a particular chromosomal translocation involving the gene encoding ALK drives tumor growth in a subset of non-small cell lung cancer patients (Soda et al. 2007). Access to this knowledge allowed the pharmaceutical industry scientists to modify their clinical trial to look specifically at a cohort of patients with this translocation, and the results were dramatic. For those patients who had the translocation, the median disease-free survival with Crizotinib was a year, compared to just a few months with the standard of care. Thus, even in a trial that involved only a small number of patients that were compared to historical controls, it was obvious that the drug was active. In contrast, in an unselected patient population, most patients did not benefit from this drug and it was unclear whether the drug had any activity.

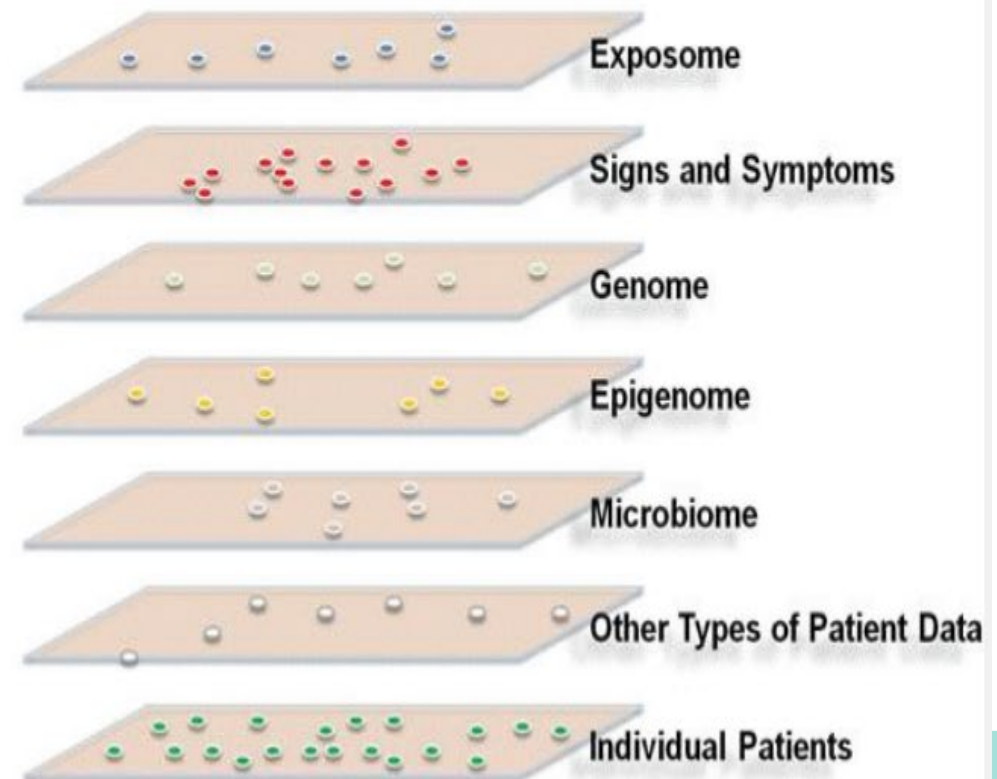
(Crizotinib is expected to receive regulatory approval for treatment of ALK translocation-positive lung cancer within the next year.)

The principle of GIS helped to organize patient-centric information layers

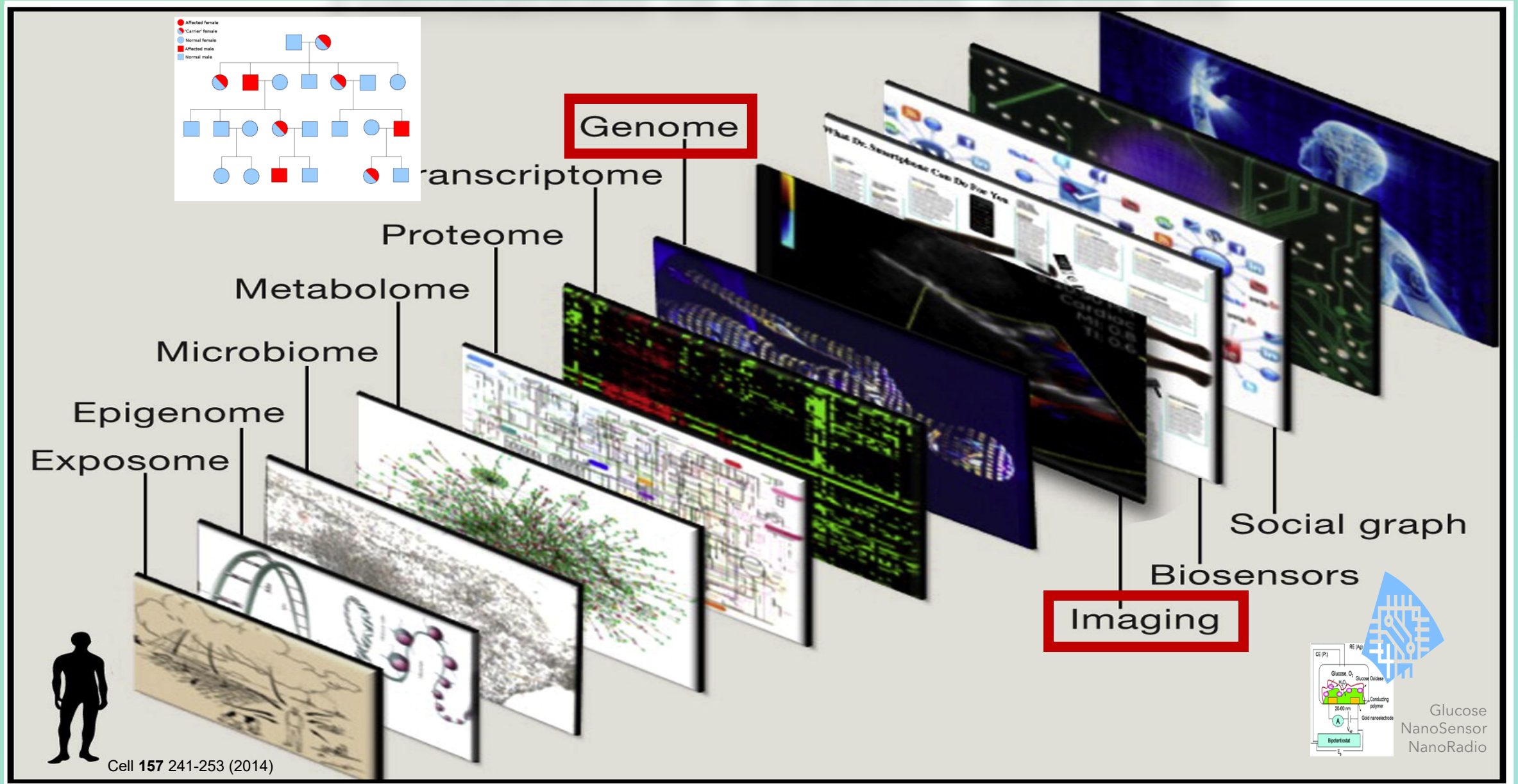
Google Maps: GIS layers
Organized by Geographical Positioning



Information Commons
Organized Around Individual Patients

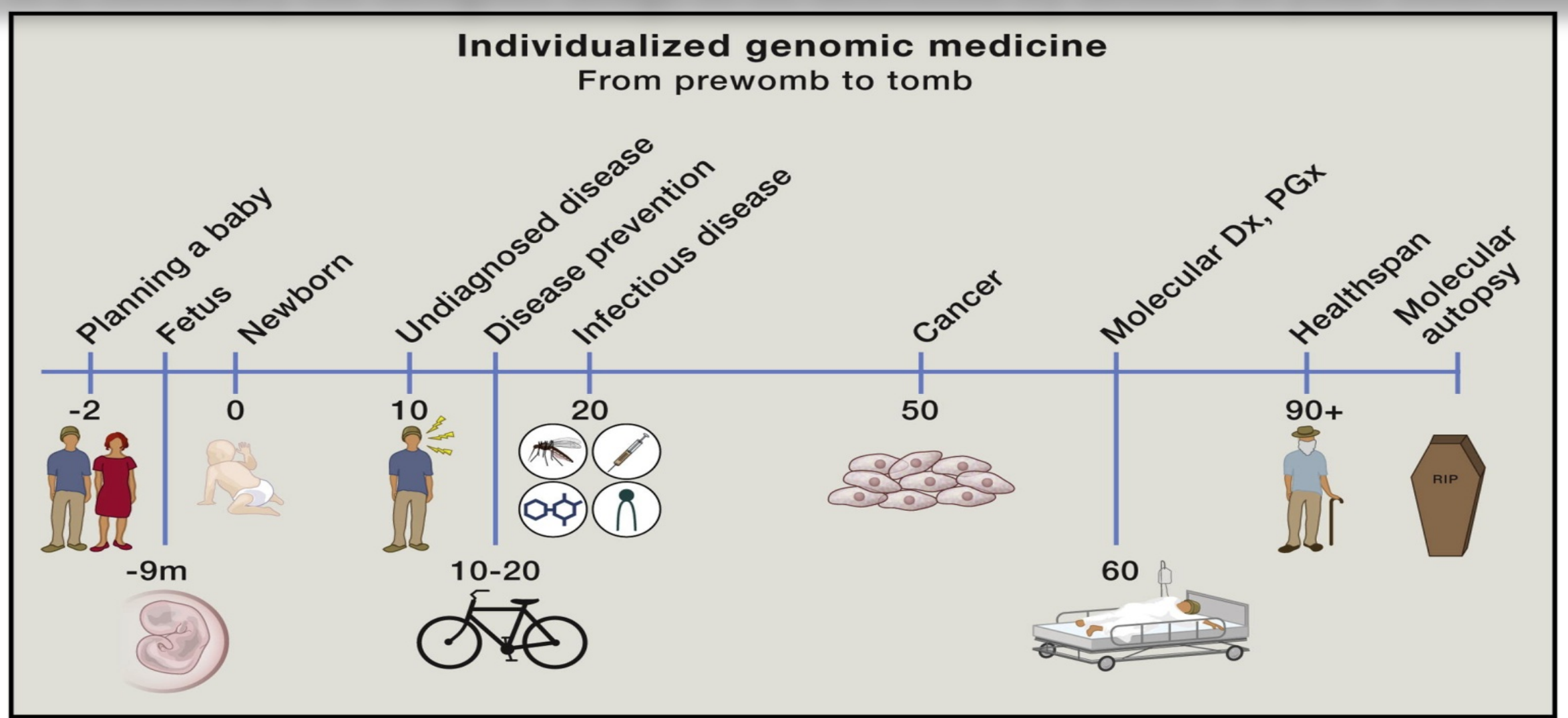


Foundations of Genomic Medicine

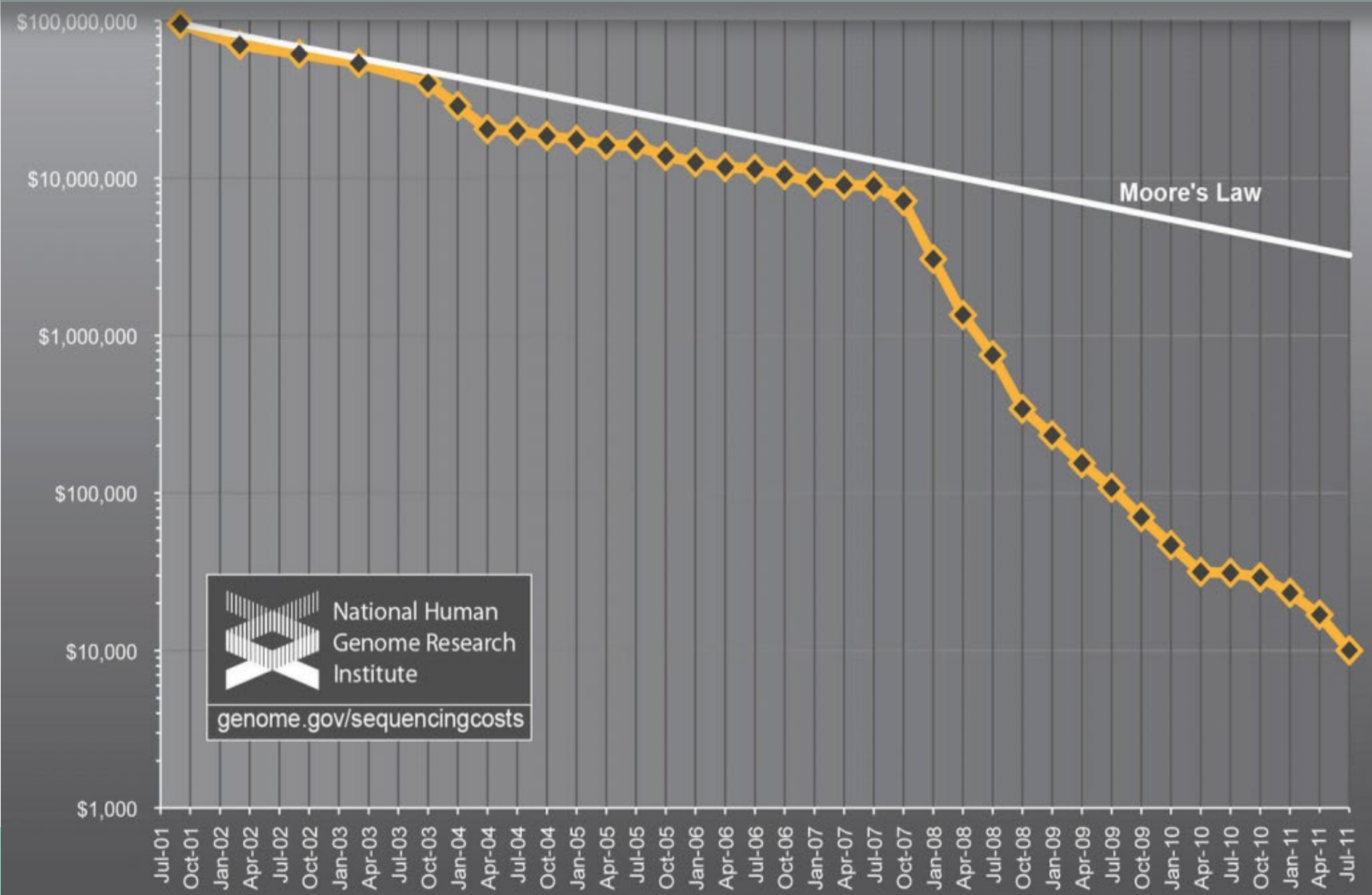


Human Genomics in the Age of Precision Medicine: Is it irrational exuberance?

Is it necessary for designer drugs to be delivered by drones to your bedroom?



Plummeting cost of complete genome sequencing – is there information of value in the data ?

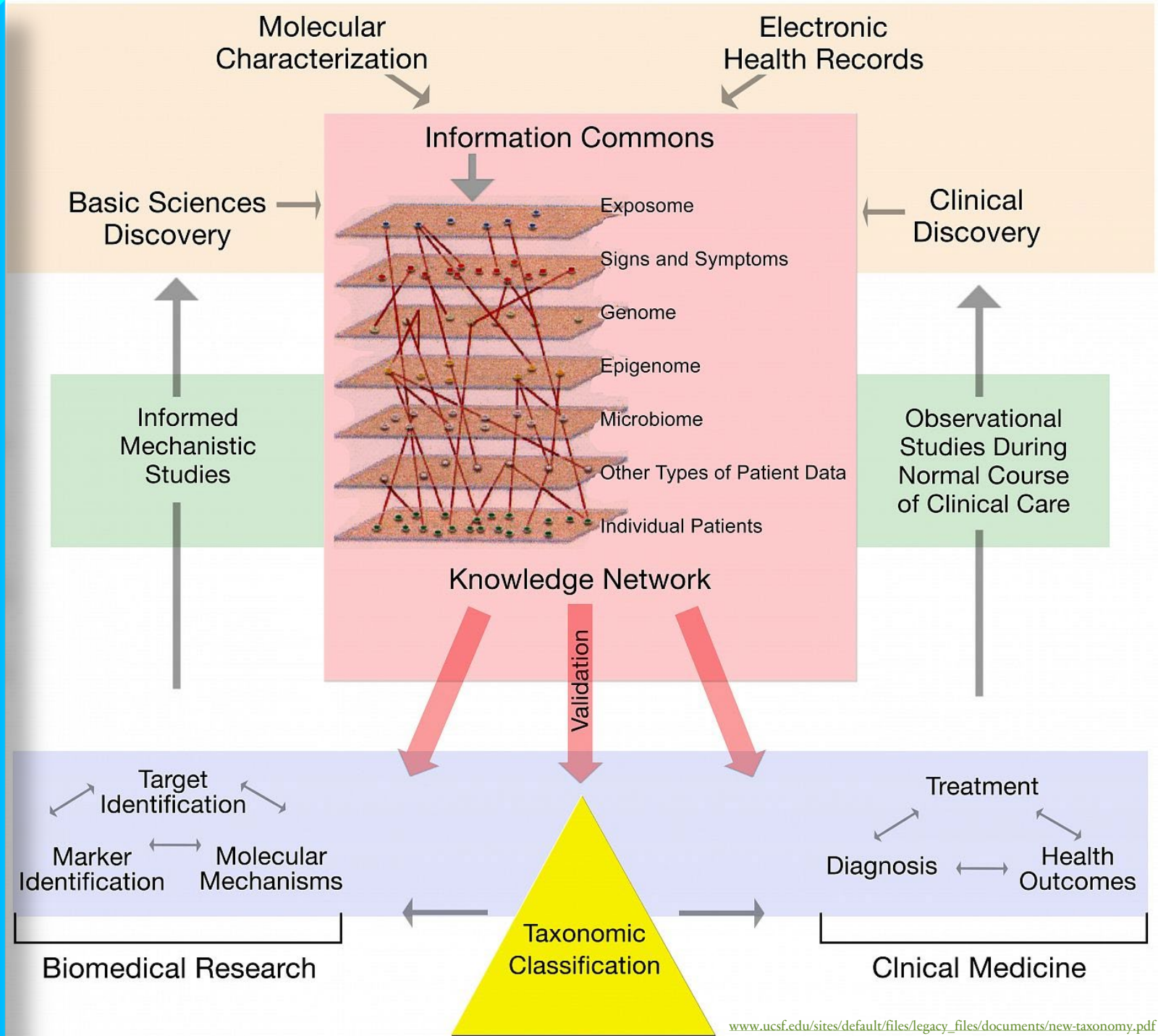


MinION USB stick gene sequencer finally comes to market

By John Hewitt (<http://www.extremetech.com/author/jhewitt>) on September 19, 2014 at 2:10 pm



How do we integrate data and information from these systems with diverse open source healthcare platforms?

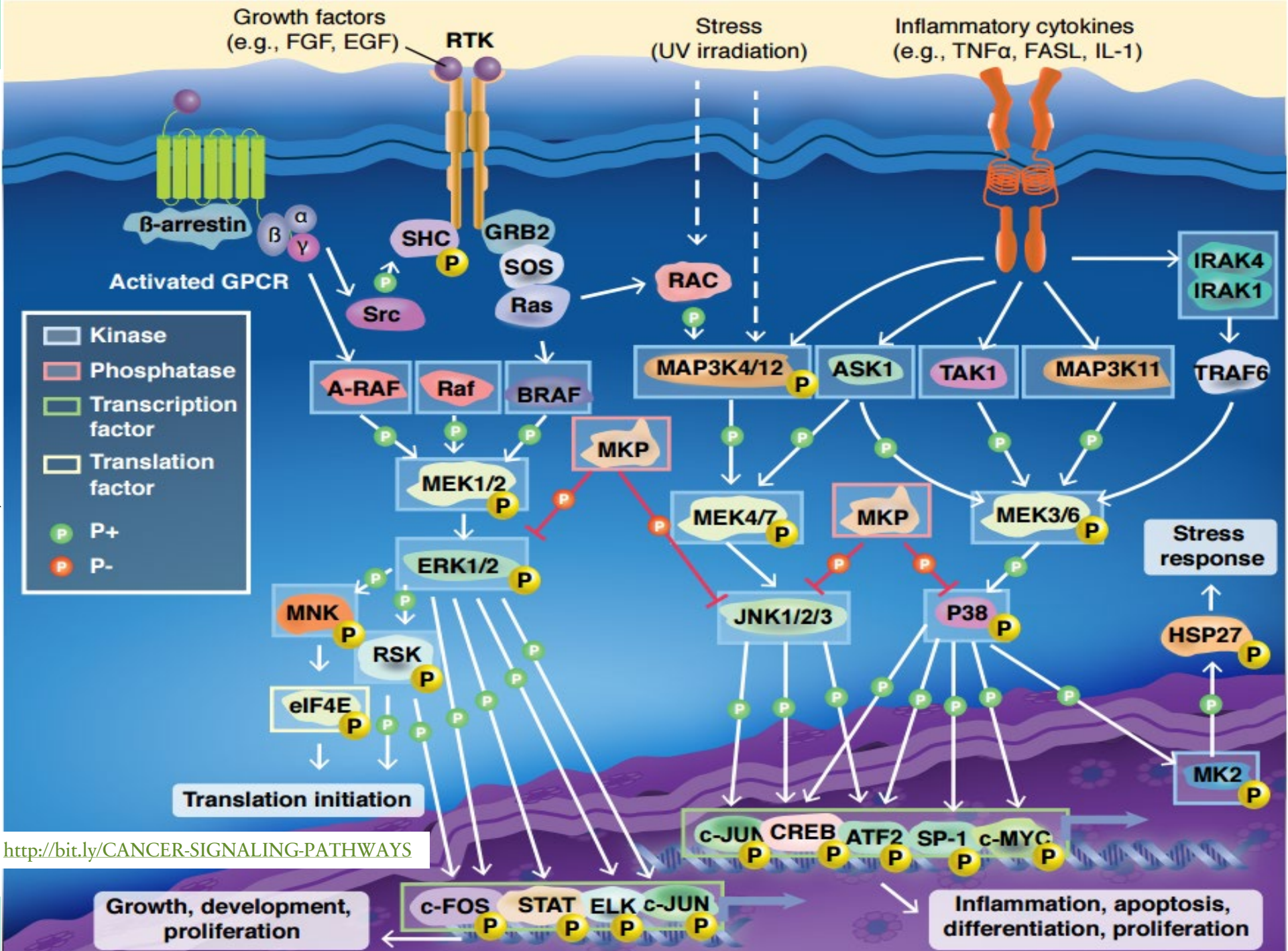


What is the challenge of
precision medicine?

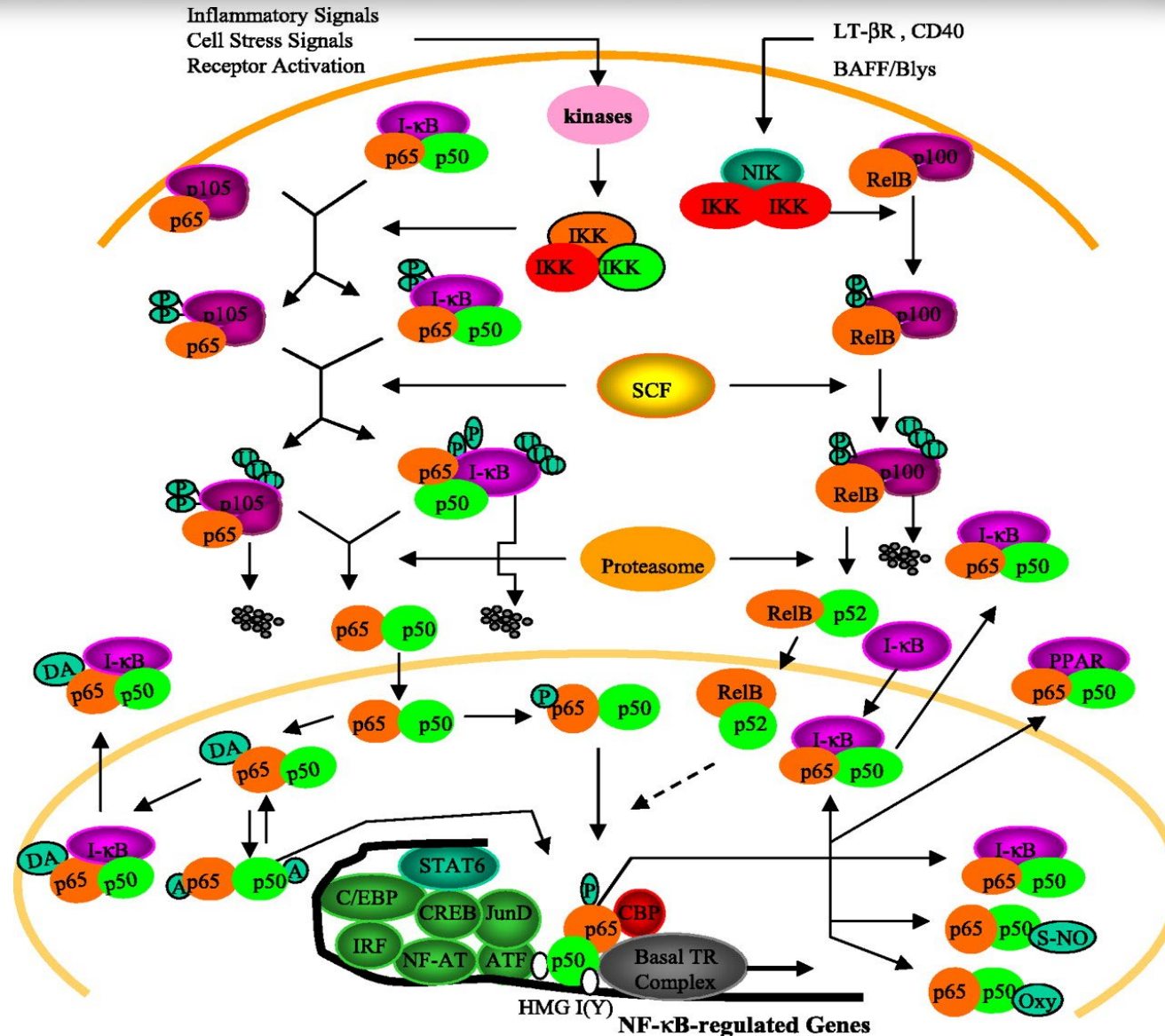
Avoid the hyperbole

How close are we to the
“knowledge network” of
biological/disease networks?

MAPK



NF- κ B activation cascade in the canonical pathways



How close are we to the “knowledge network” of biological/disease networks?

We know so little that only those who are egotistical, stupid and braggadocious will venture to claim knowledge about “knowledge networks” in biology and/or diseases.

Healthcare garbage from IBM and others. How tabloid fodder is promoted from rubbish to veritable truth.

"IBM **spun** a story about how Watson could improve cancer treatment that was superficially plausible."

--David Howard, Department of Health Policy and Management at Emory University

Far flung future frontier ...

NOVEMBER 9, 2015

C&EN

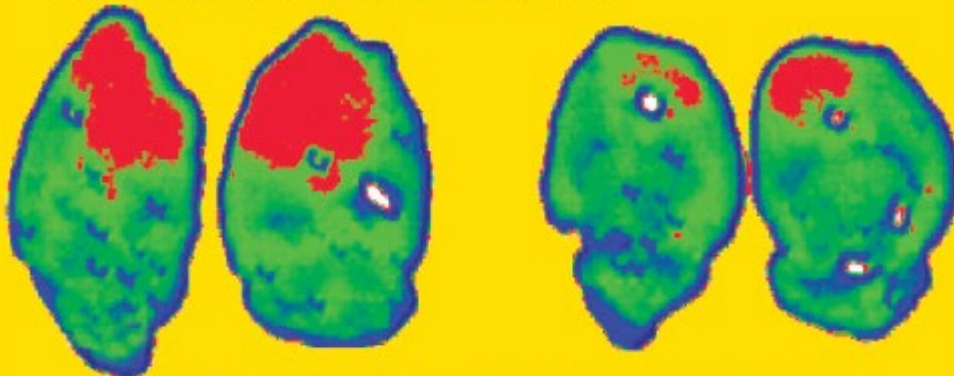
CHEMICAL & ENGINEERING NEWS

CPhI IN MADRID

Optimism unstoppable at
fine chemicals expo P.18

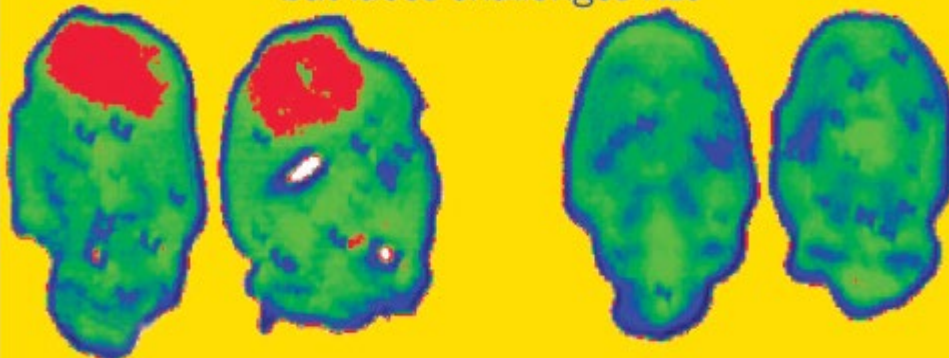
CHEMCENSUS TURNS 30

ACS member makeup and
earnings in review P.30



TERAHERTZ IMAGING

Technology could aid disease diagnosis
but faces challenges P.10



PUBLISHED BY THE AMERICAN CHEMICAL SOCIETY

<http://bit.ly/Terahertz-Imaging>

Proteins are Radios

We can detect, diagnose and correct RF radiation.

Can we?

Protein Electrodynamics

Nature Vol. 267 16 June 1977

articles

Dynamics of folded proteins

J. Andrew McCammon, Bruce R. Gelin & Martin Karplus

Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

The dynamics of a folded globular protein (bovine pancreatic trypsin inhibitor) have been studied by solving the equations of motion for the atoms with an empirical potential energy function. The results provide the magnitude, correlations and decay of fluctuations about the average structure. These suggest that the protein interior is fluid-like in that the local atom motions have a diffusional character.



The Nobel Prize in Chemistry 2013
Martin Karplus, Michael Levitt, Arieh Warshel

The Nobel Prize in Chemistry 2013



Photo: A. Mahmoud
Martin Karplus

Prize share: 1/3



Photo: A. Mahmoud
Michael Levitt

Prize share: 1/3



Photo: A. Mahmoud
Arieh Warshel

Prize share: 1/3

The Nobel Prize in Chemistry 2013 was awarded jointly to Martin Karplus, Michael Levitt and Arieh Warshel "for the development of multiscale models for complex chemical systems".

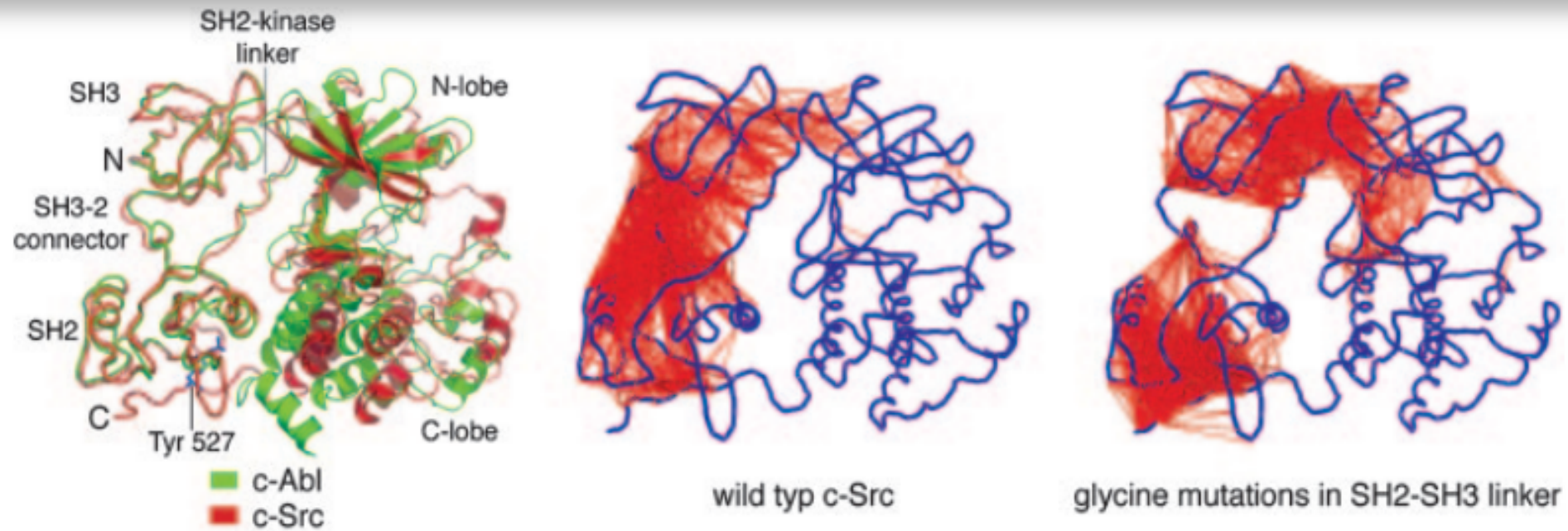
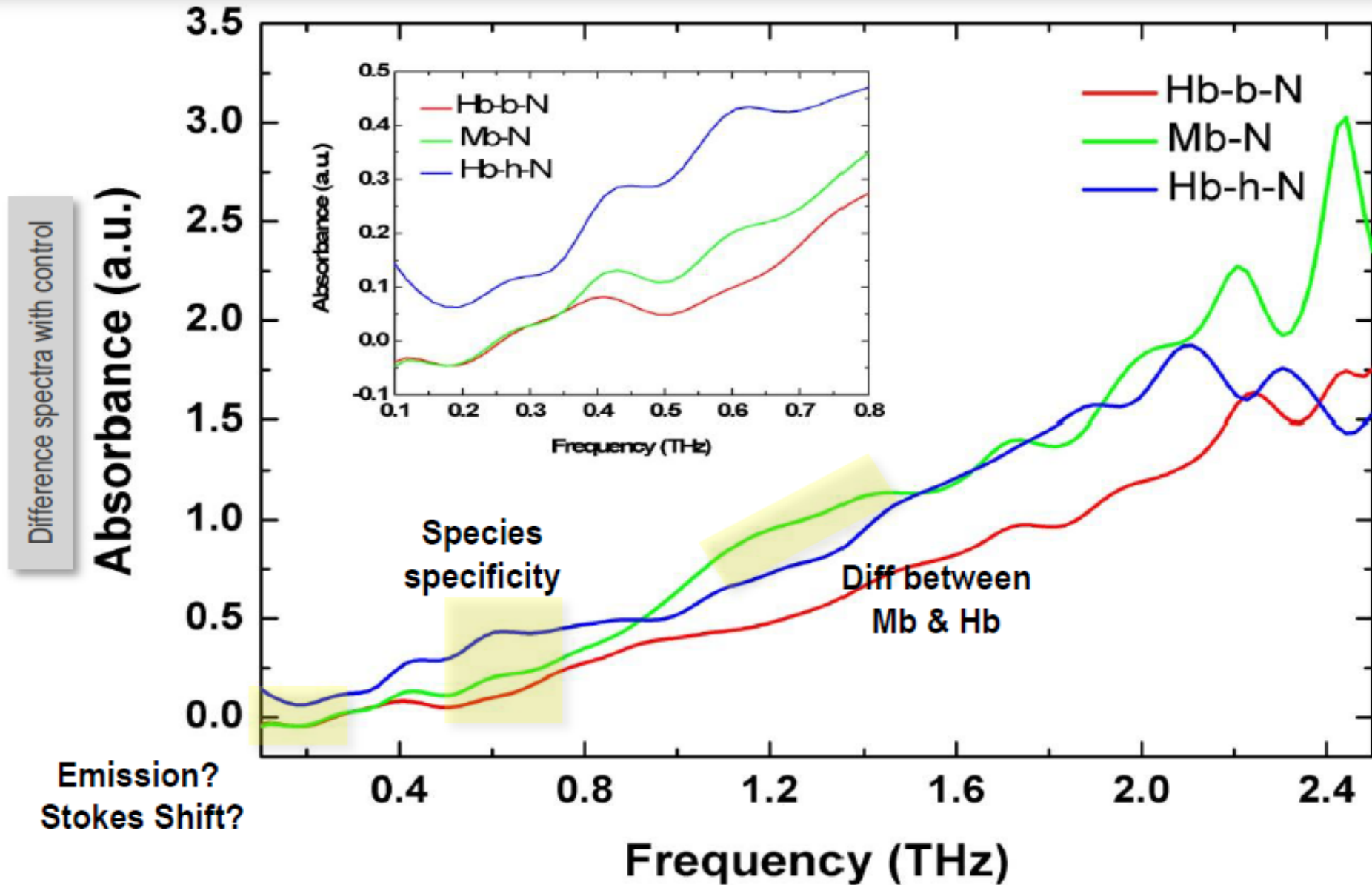


Fig. 5. Structure and dynamics of the Src and Abl kinases. (*Left*) The structures of c-Abl (green) and c-Src (red) are shown superimposed on their SH2 and SH3 domains (69, 70, 75). Note the dissimilarity in the conformation of the kinase domains. (*Center and Right*) The results of unbiased molecular dynamics simulations of c-Src. Residues in different domains that move in a correlated manner in the simulation are linked by a red line. These correlations were calculated by superimposing each instantaneous structure in the simulation on the C-terminal lobe of the kinase domain, and motions that are correlated to the C-terminal lobe are removed by this procedure. (*Right*) The mutation of residues in the SH2–SH3 linker to glycine reduces the correlation in the dynamics of these domains. Similar results were obtained for c-Abl. (Modified from refs. 8 and 75.)

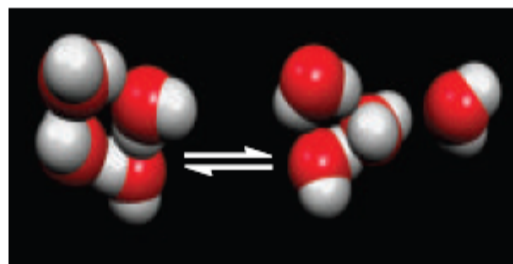
Proteins Absorb Radio Frequency (RF) at the TeraHertz (THz) Range



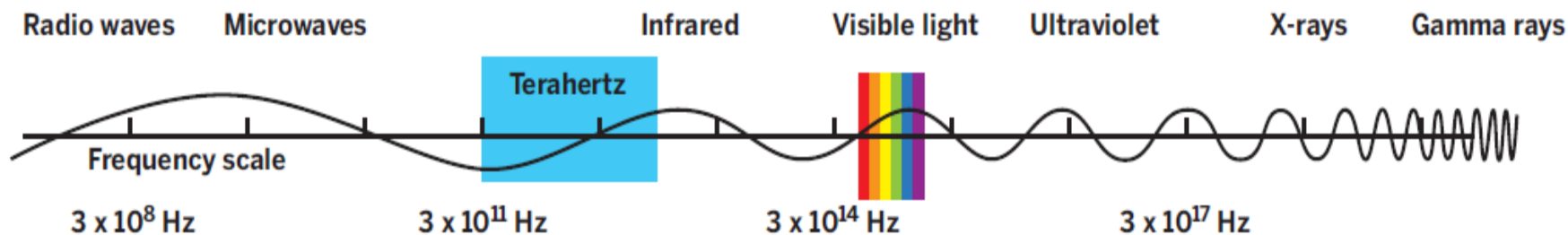
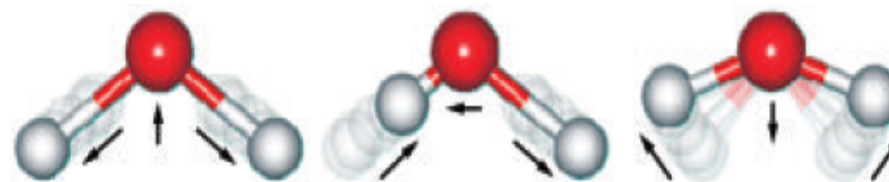
Terahertz Spectroscopy – A Tool ??

TERAHERTZ SPECTROSCOPY 101

Light with submillimeter wavelengths and a frequency range of roughly 0.1 to 10 THz, or 3 to 300 cm^{-1} , is known as terahertz radiation. It can penetrate plastics, paper, and textiles, but it is absorbed strongly by water, making it a sensitive probe of biological tissue.



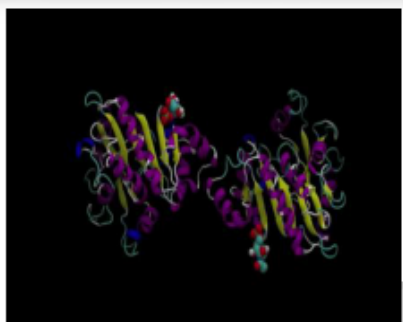
Unlike the relatively high-frequency stretching and bending motions that infrared light induces in individual water molecules (above), THz light causes groups of water molecules to coalesce and disassemble repeatedly (left).



MATTHIAS HEYDEN/
RUHR UNIVERSITY BOCHUM

MARTIN CHAPLIN/ LONDON
SOUTH BANK U.

Axioms of Protein Electrodynamics



1. Proteins Vibrate

2. Proteins Are Charged

The Poisson-Boltzmann Equation

The classical treatment of electrostatic interactions in solution is based on the Poisson-Boltzmann equation (PBE)

$$\nabla \cdot [\epsilon(r)\nabla \phi(r)] - \epsilon(r)\kappa(r)\sinh[\phi(r)] + 4\pi\rho(r)/kT = 0 \quad (1)$$

where $\phi(r)$ is the dimensionless electrostatic potential in units of kT/q (k is the Boltzmann constant, T is the absolute temperature, and q is the charge on a proton), ϵ is the dielectric constant, and ρ is the fixed charge density (in proton charge units). The term $\kappa^{-1} = 1/\lambda = 8\pi q^2 l / \epsilon kT$, where λ is the Debye length and l is the ionic strength of the bulk solution. The variables ϕ , ϵ , κ , and ρ are all functions of the position vector r .

Science

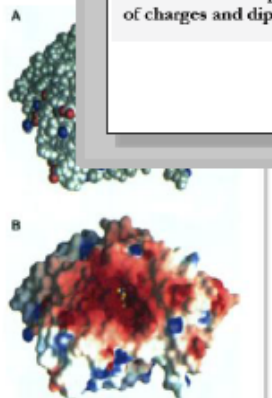
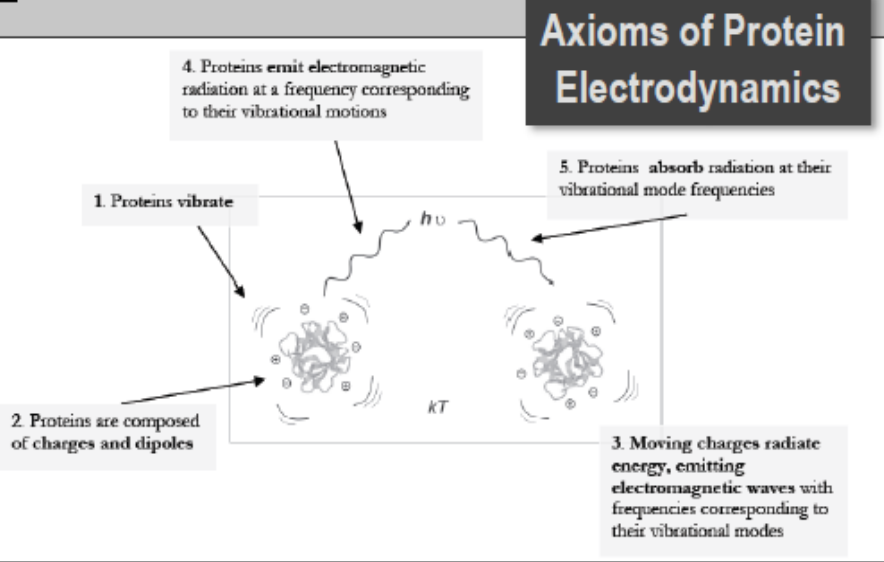


Fig. 1. Surface representations of acetylcholine esterase.



3. Maxwell's Equations

$$\begin{aligned} \nabla \cdot \mathbf{E} &= 0 & \nabla \times \mathbf{E} &= -\frac{\partial \mathbf{B}}{\partial t} \\ \nabla \cdot \mathbf{B} &= 0 & \nabla \times \mathbf{B} &= \frac{1}{c^2} \frac{\partial \mathbf{E}}{\partial t} \end{aligned}$$

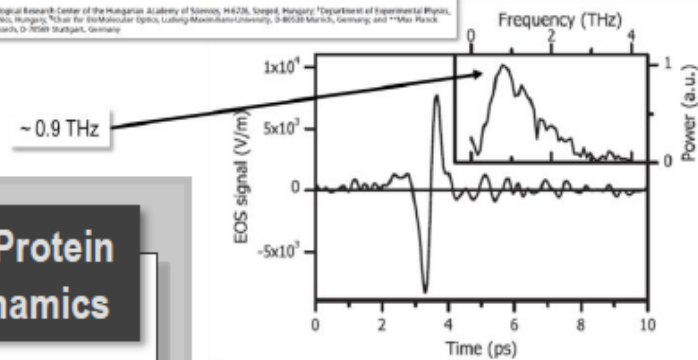
Terahertz radiation from bacteriorhodopsin reveals correlated primary electron and proton transfer processes

PNAS

PNAS | May 13, 2008 | vol. 105 | no. 19

G. I. Groma¹, J. Hebling², I. Z. Kozma³, G. Váró⁴, J. Hauer⁵, J. Kuhl⁶, and E. Riedle⁷

¹Institute of Biophysics, Biological Research Center of the Hungarian Academy of Sciences, H-6226, Szeged, Hungary; ²Department of Experimental Physics, University of Pecs, H-7624, Pecs, Hungary; ³Chair for FemtoMolecular Optics, Ludwig-Maximilians-University, D-80539 Munich, Germany; and ⁴Max Planck Institute for Solid State Research, D-70569 Stuttgart, Germany

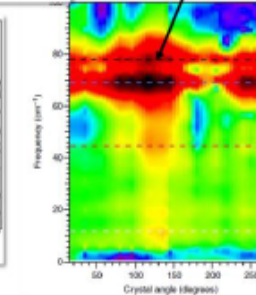
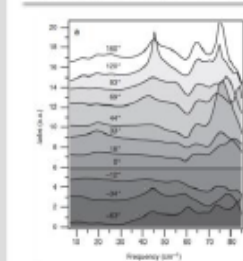


4. Proteins emit THz radiation

ARTICLE
Received 9 Jul 2005; Accepted 6 Dec 2005; Published 6 Jan 2006

Optical measurements of long-range protein vibrations

Shouqin Xiao¹, Katherine A. Nasser¹, Edward H. Snee¹ & A.G. Markes^{1,2}



nature

5. Proteins absorb THz radiation

Absence of Protein • Absence of Vibration

Concept of protein vibration as a signature

Police Tool Targets Guns

Kelly Says 'T-Ray' Can Indicate a Firearm Under Clothing

By TAMER EL-GHOBASHY

Jan. 23, 2013 9:20 p.m. ET

The New York Police Department is testing a new device it says can detect firearms concealed beneath layers of clothing, a high-tech crime-fighting tool seemingly torn from the pages of science fiction.

The so-called T-Ray machine detects terahertz radiation, a high-frequency electromagnetic natural energy that is emitted by people and can penetrate many materials, including clothing.

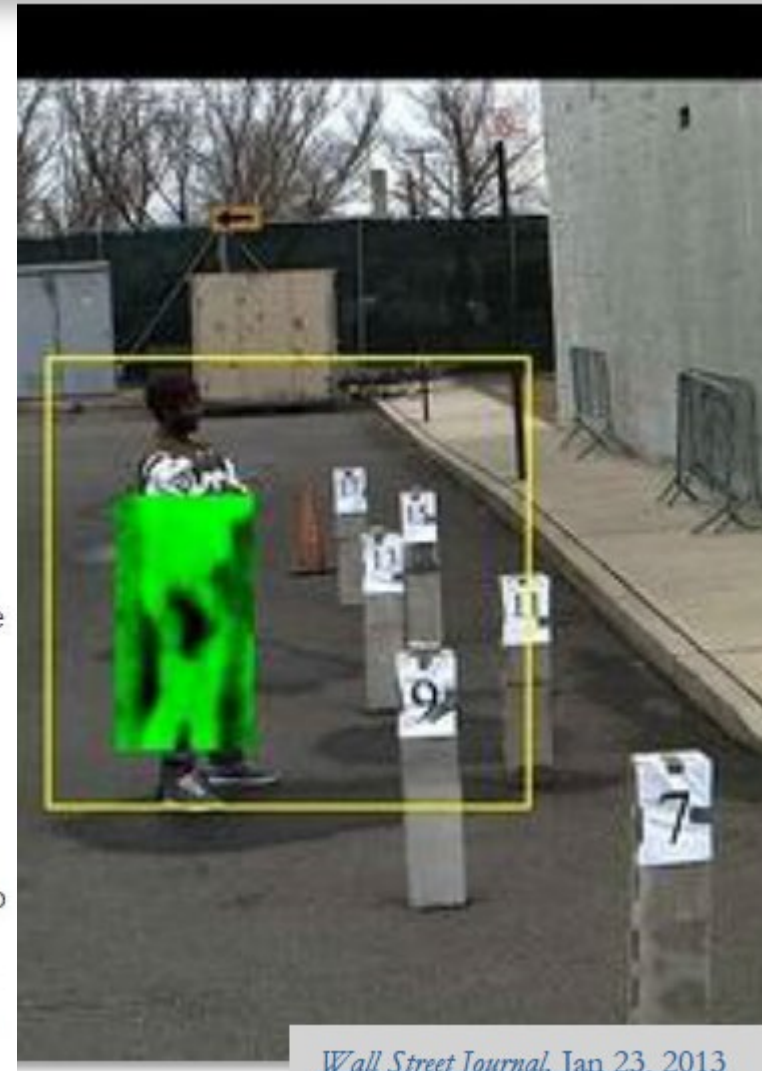


The T-Ray machine. NYPD

"If something is obstructing the flow of that radiation, for example a weapon, the device will highlight that object," said Commissioner Raymond Kelly, who described the device Wednesday in a speech at the Waldorf-Astoria Hotel.

News of the device prompted concerns from privacy advocates, though they also saw a potential benefit: It might render unnecessary the legally disputed police

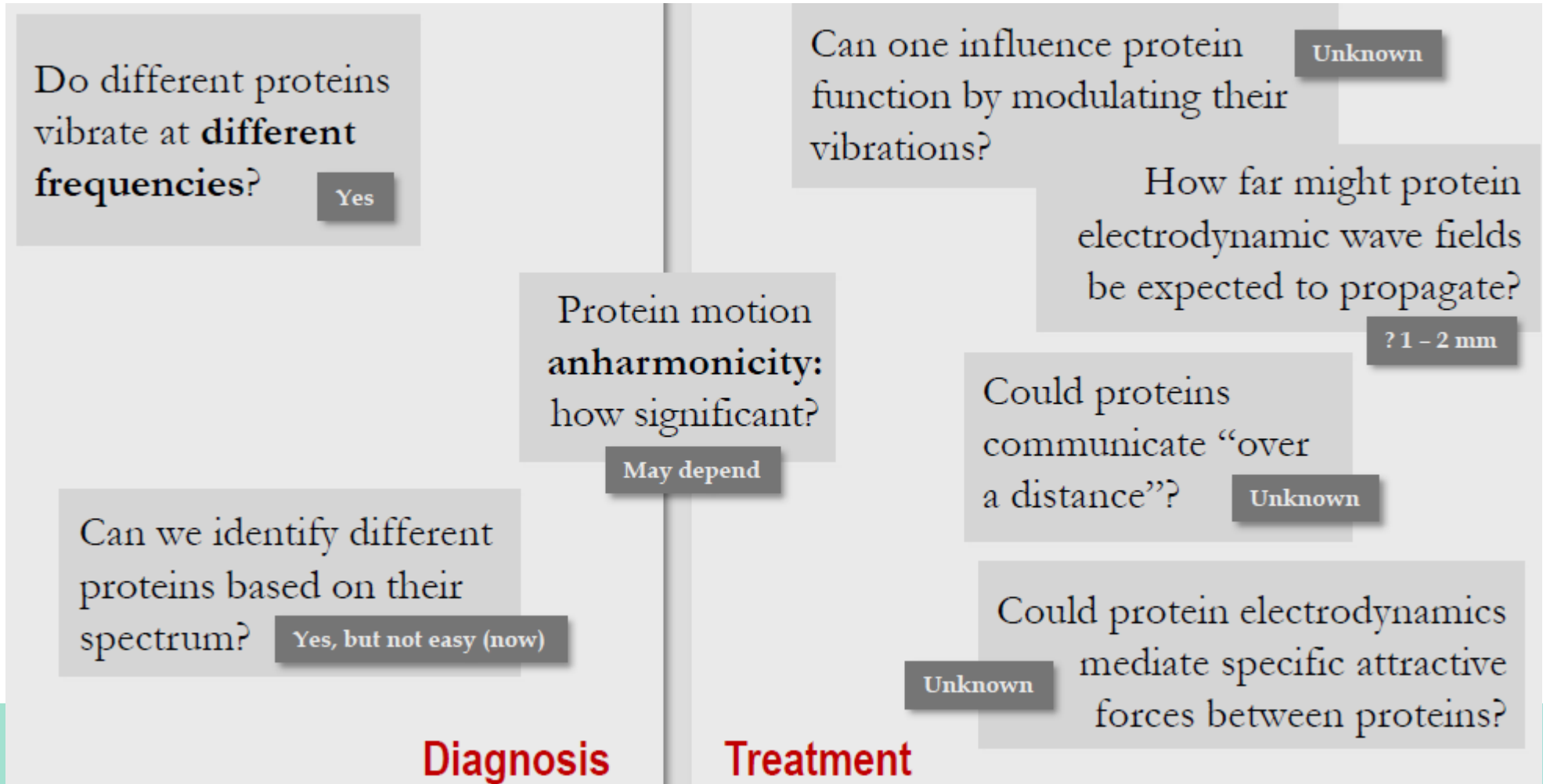
policy of stopping and frisking people who haven't been first identified as suspects in crimes.



TeraHertz Medicine

Concept of protein vibration as a signature

- Is the protein signature sufficiently specific as a tool for protein structure, conformation and configuration?
- Can it be used for diagnosis to differentiate between normal and mutant proteins or degraded products/peptides?
- Can RF modulation reconfig protein structure to activate normal function or detect/deactivate harmful proteins?



Key technical challenges in TeraHertz Medicine

Concept of protein vibration as a signature is clouded by water

The “noise” from RF vibration of water molecules may significantly distort the TeraHertz profile.

How do we correct the error due to this (Shannon) “noisy channel” related to water?

Is this a signal processing issue? Can novel algorithms subtract the “noise” due to water?

What about the application of the principles of (Shannon, Kalman-Bucy) error correcting algorithms?

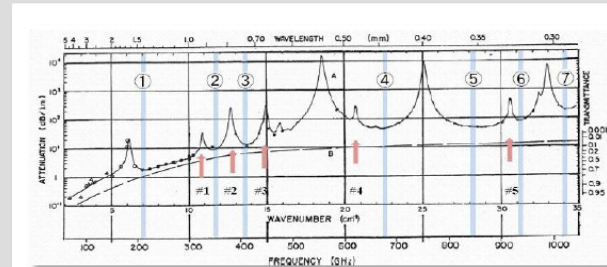
https://en.wikipedia.org/wiki/Kalman_filter

<http://news.mit.edu/2010/explained-shannon-0115>

<http://www.cs.cmu.edu/~guyb/realworld/errorcorrecting.html>

<http://www.cs.cmu.edu/~aarti/Class/10704/lec16-shannonnoisythrm.pdf>

- **Range: 0.2 – 1THz** for biomedical applications (e.g. proteins)
- **Tunability: cw** spectroscopy (water windows)
- **Pulsed: (~ 10 ps)**
Minimize water relaxation effects
- **High power:**
Beer-Lambert, etc.



Optics Express (2011), 19(9)

Data Curation Concepts from Laminar Flow in TeraHertz Medicine? Can we subtract RF vibration due to water from protein vibration?

The data (TeraHertz profile) is a mix of RF due to water and protein (which needs to be separated).

Is this a data curation problem? Are we observing related signal/noise issues in data analytics?

Are there any concepts related to data curation which may be triggered by laminar flow?

<http://bit.ly/LAMINAR-FLOW-DATA-CURATION-CONCEPT>





www.eecs.berkeley.edu/~christos/classics/shannon-report.pdf

www.princeton.edu/~verdu/reprints/IT44.6.2057-2078.pdf

<http://web.mit.edu/6.933/www/Fall2001/Shannon1.pdf>

<http://web.mit.edu/6.933/www/Fall2001/Shannon2.pdf>

<http://home.ustc.edu.cn/~zhanghan/cs/Gallager01.pdf>

www.pnas.org/cgi/doi/10.1073/pnas.1517384113

www.pnas.org/cgi/doi/10.1073/pnas.1013529108

A Mathematical Theory of Communication

By C. E. SHANNON

INTRODUCTION

THE recent development of various methods of modulation such as PCM and PPM which exchange bandwidth for signal-to-noise ratio has intensified the interest in a general theory of communication. A basis for such a theory is contained in the important papers of Nyquist¹ and Hartley² on this subject. In the present paper we will extend the theory to include a number of new factors, in particular the effect of noise in the channel, and the savings possible due to the statistical structure of the original message and due to the nature of the final destination of the information.

The fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point. Frequently the messages have *meaning*; that is they refer to or are correlated according to some system with certain physical or conceptual entities. These semantic aspects of communication are irrelevant to the engineering problem. The significant aspect is that the actual message is one *selected from a set* of possible messages. The system must be designed to operate for each possible selection, not just the one which will actually be chosen since this is unknown at the time of design.

If the number of messages in the set is finite then this number or any monotonic function of this number can be regarded as a measure of the information produced when one message is chosen from the set, all choices being equally likely. As was pointed out by Hartley the most natural choice is the logarithmic function. Although this definition must be generalized considerably when we consider the influence of the statistics of the message and when we have a continuous range of messages, we will in all cases use an essentially logarithmic measure.

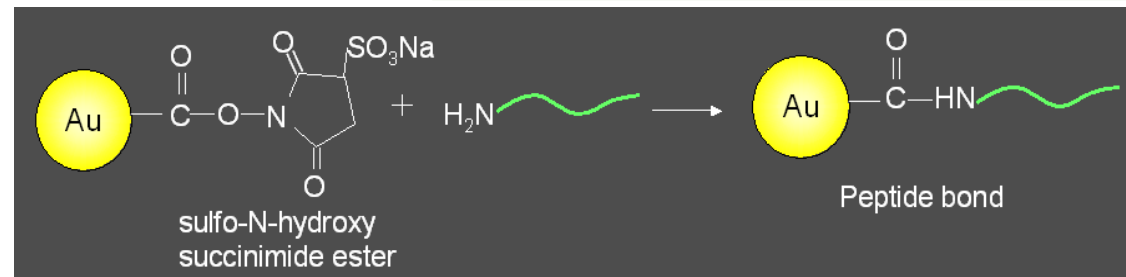
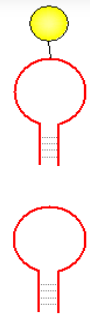
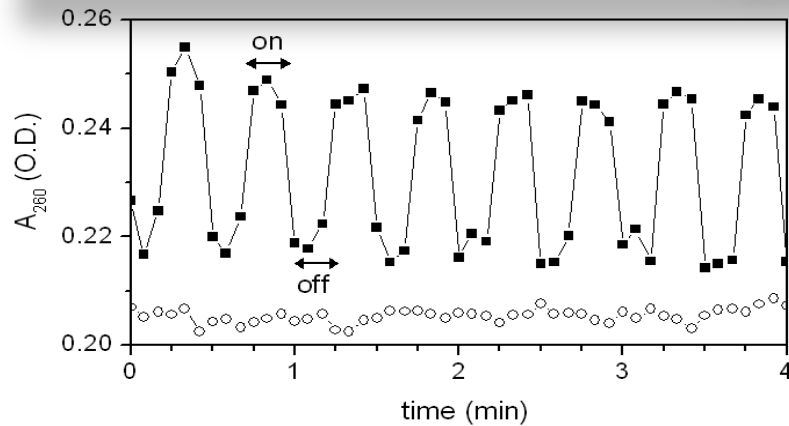
The logarithmic measure is more convenient for various reasons:

1. It is practically more useful. Parameters of engineering importance

¹Nyquist, H., "Certain Factors Affecting Telegraph Speed," *Bell System Technical Journal*, April 1924, p. 324; "Certain Topics in Telegraph Transmission Theory," *A. I. E. E. Trans.*, v. 47, April 1928, p. 617.

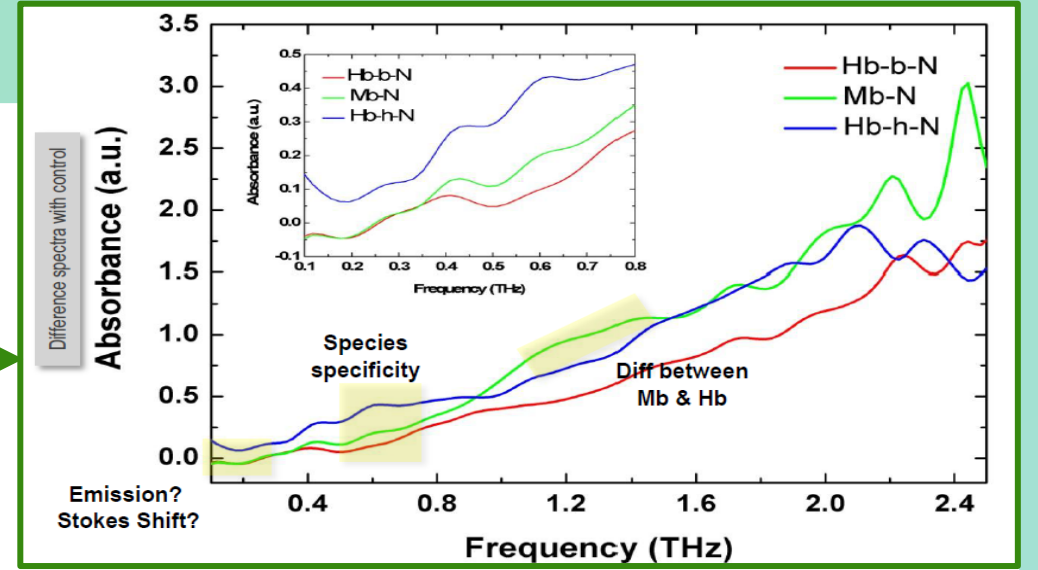
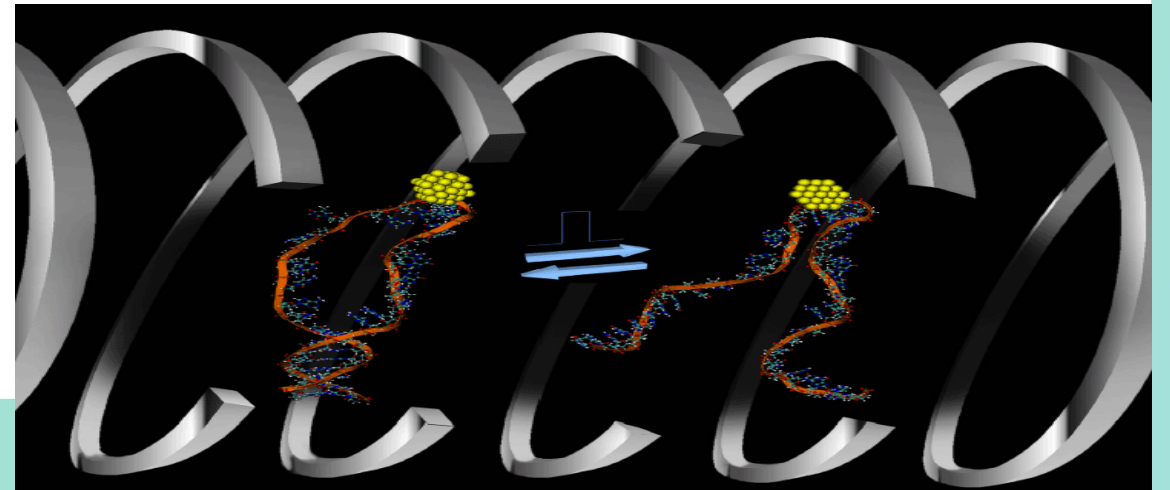
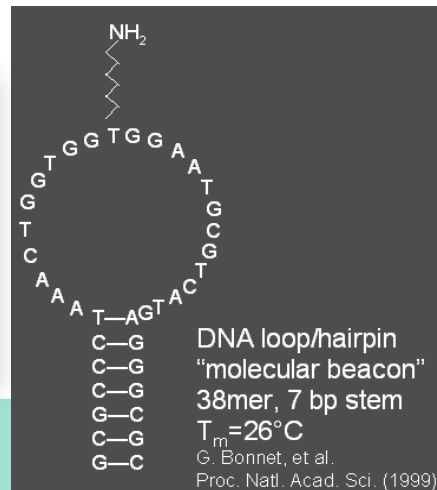
²Hartley, R. V. L., "Transmission of Information," *Bell System Technical Journal*, July 1928, p. 535.

Convergence (?) of TeraHertz Medicine (proteins are radios) & RF Nano Biology?



Remote Electronic Control of DNA Hybridization Through Inductive Coupling to an Attached Metal Nanocrystal Antenna
Kimberly Hamad-Schifferli, J J Schwartz, A T Santos, S G Zhang and J M Jacobson [Nature (415) 152-155, 2002]

Beyond the horizon ?
Close at hand ?



Leapfrogging healthcare ??

In at least one vein of healthcare ... hip and knee replacements

*Due to my ignorance,
this is an US-centric
scenario but it can be
Implemented, anywhere.*



Smash hit by Hayden. Body by milk.

You don't have to be a hero to feel invincible. That's why I drink milk. The protein helps build muscle and some studies suggest teens who choose it tend to be leaner. Cheers to that.

got milk?



Sections



The mysterious case of America's plummeting milk consumption

Americans, on average, drink 37 percent less milk today than they did in 1970, according to data from the USDA. Forty years ago, per capita consumption was nearly one and a half cups per day; now it's nearer to 0.8. While the fallout spans every type of cow's milk—whole, low fat, and skim—it's been most unkind to the full fat variety. Whole milk per capita consumption has tumbled by 78 percent since 1970 (from more than 1.1 cups per day to fewer than .24).

<http://bit.ly/GOT-MILK>

Whole milk consumption plummets since 1970

Whole and skim milk consumption, cups per day

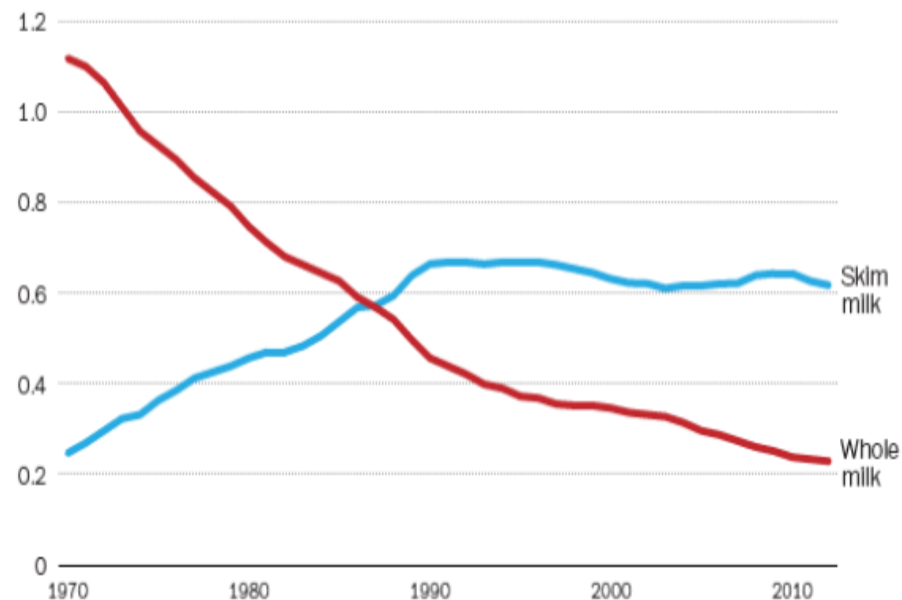
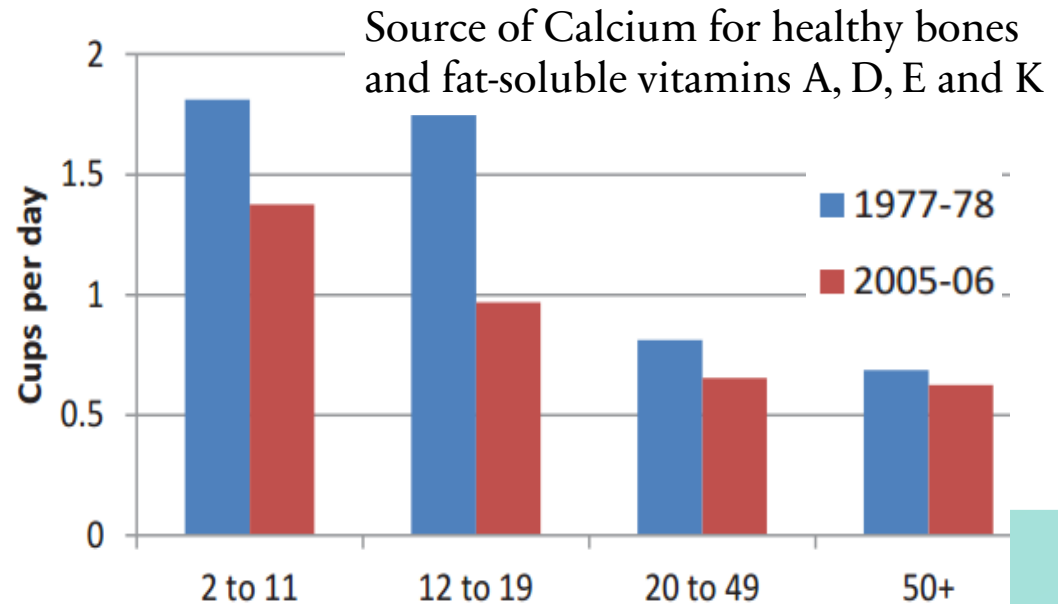


Figure 2: Mean Intake of Fluid Milk

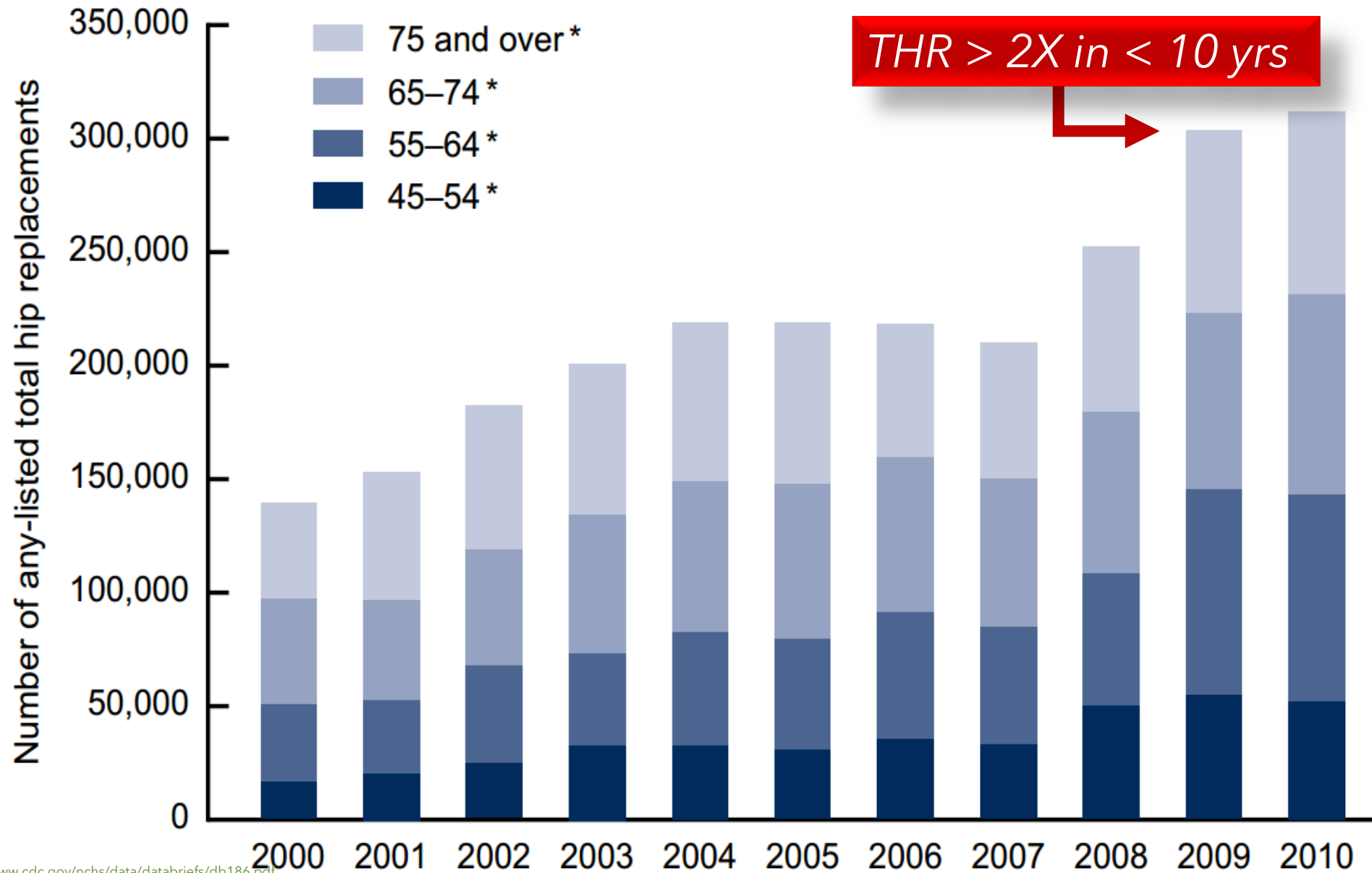


Causality

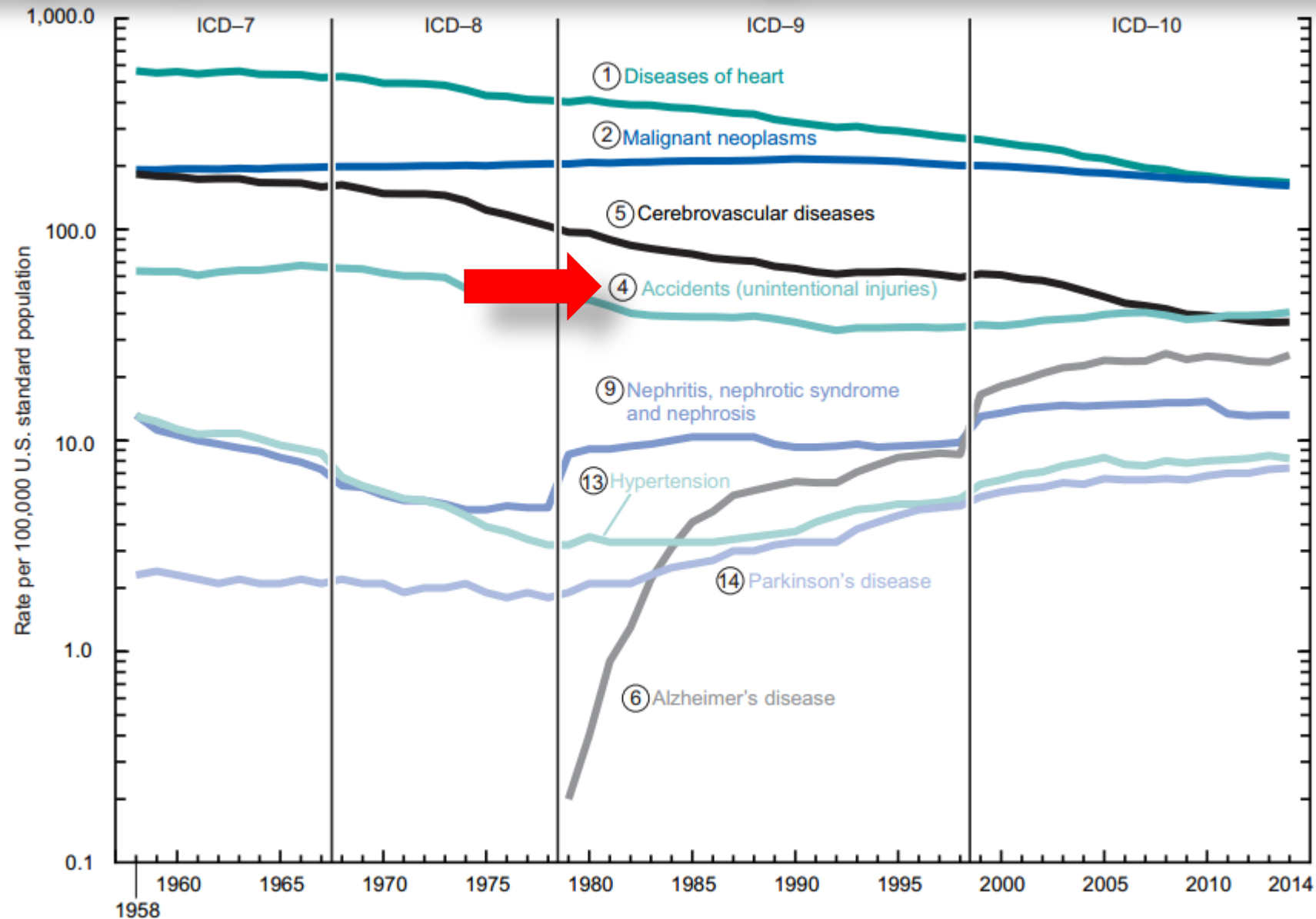
significant correlation?

326,100 total hip replacements (US, 2010) 95% cases age 45+

www.cdc.gov/nchs/data/databriefs/db186.pdf

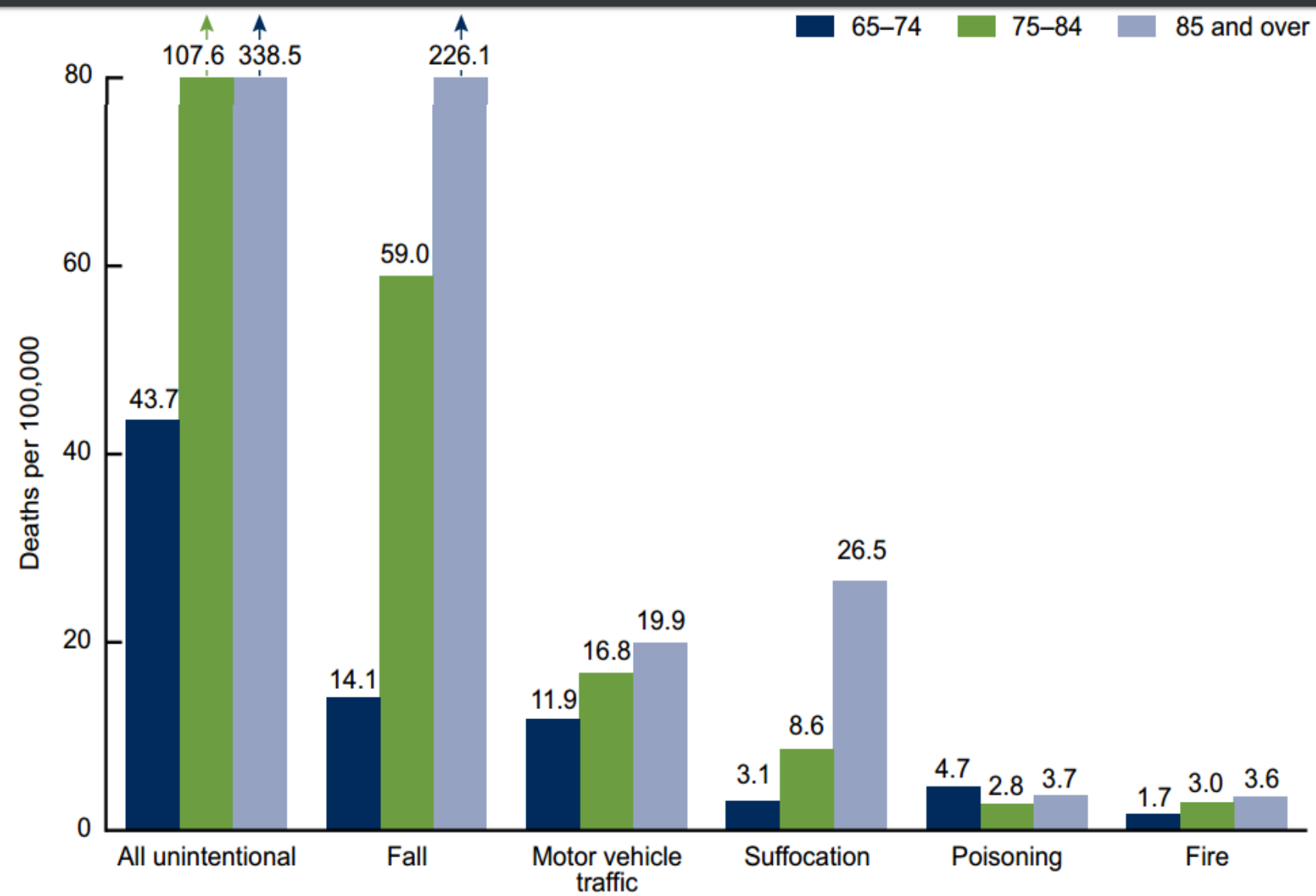


Age-adjusted rates for leading causes of death in US



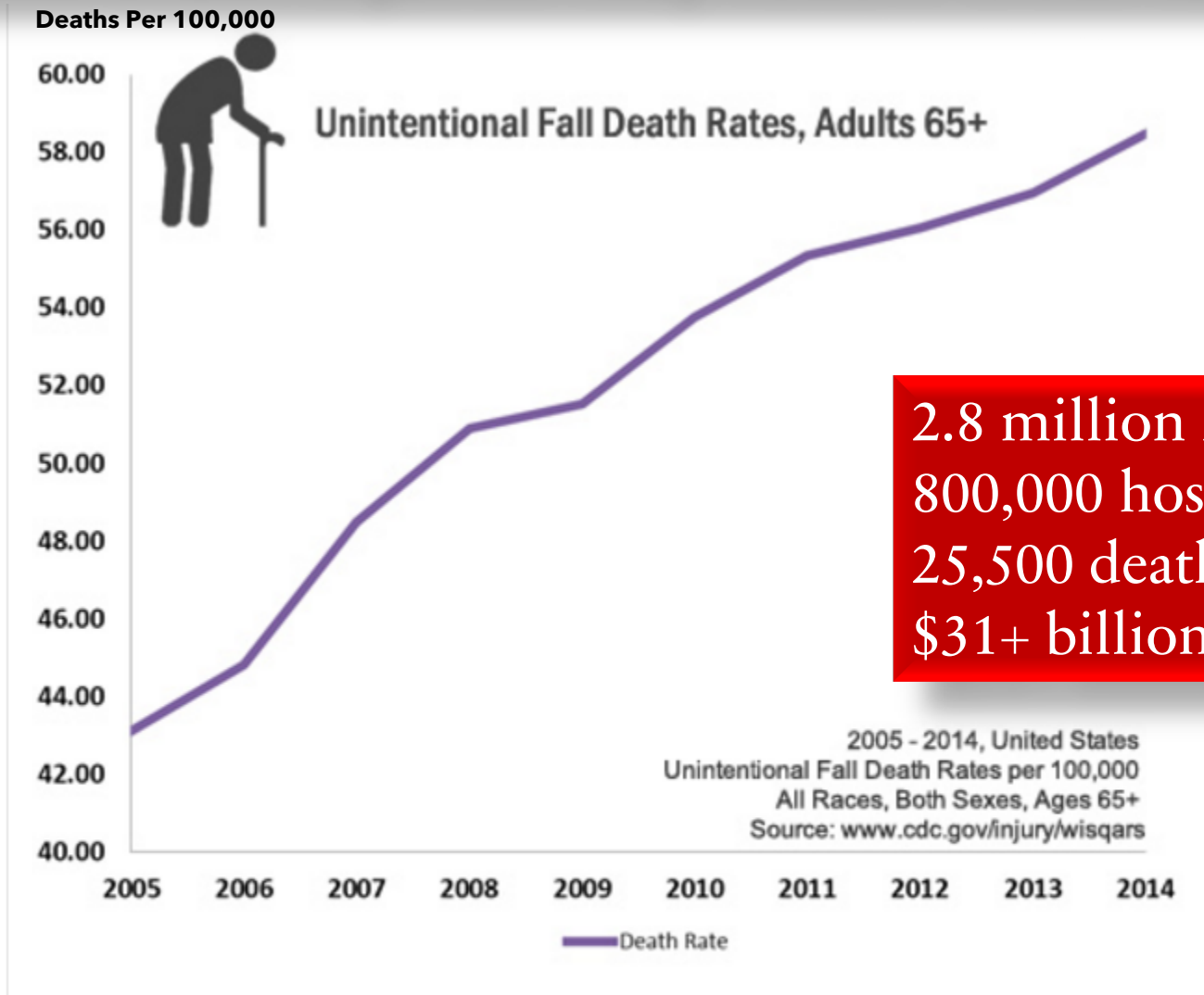
NOTES: ICD is the *International Classification of Diseases*. Circled numbers indicate ranking of conditions as leading causes of death in 2014.
SOURCE: NCHS, National Vital Statistics System, Mortality. http://www.cdc.gov/nchs/data/nvsr/nvsr65/nvsr65_04.pdf

Cause of death for US adults aged 65+ (2012–2013)



Hip fractures and brain injuries may follow from fall

- One out of five falls causes a serious injury such as broken bones or a head injury.^{3,4}
- Each year, 2.8 million older people are treated in emergency departments for fall injuries.⁵
- Over 800,000 patients a year are hospitalized because of a fall injury, most often because of a head injury or hip fracture.⁵
- Each year at least 300,000 older people are hospitalized for hip fractures.⁶
- More than 95% of hip fractures are caused by falling,⁷ usually by falling sideways.⁸
- Falls are the most common cause of traumatic brain injuries (TBI).⁹
- Adjusted for inflation, the direct medical costs for fall injuries are \$31 billion annually.¹⁰ Hospital costs account for two-thirds of the total.



2.8 million falls in 2014
800,000 hospitalized
25,500 deaths due to fall
\$31+ billion direct costs

After the fall ...

More than 30 million+ people may need implants

TKA and THA Replacement Potential	USA 325,000,000 population	EU-28 505,000,000 population	India 1.333 billion population	China 1.384 billion population
1% prevalence Knee and Hip combined	3,250,000	5,050,000	13,330,000	13,840,000
Total US folks TKA or THA	6.7 + 4.5 million 11,200,000			



<http://www.ors.org/Transactions/56/0214.pdf>

- EU Ageing <http://ec.europa.eu/eurostat>
- Prevalence <http://bit.ly/AAOS-2014>

Total Knee Replacement (TKR)



Age group	Female	Male
<50	0.1%	0.1%
50-59	1.8%	1.2%
60-69	5.5%	3.6%
70-79	10.1%	7.3%
80-89	11.0%	8.8%
90+	7.4%	7.4%

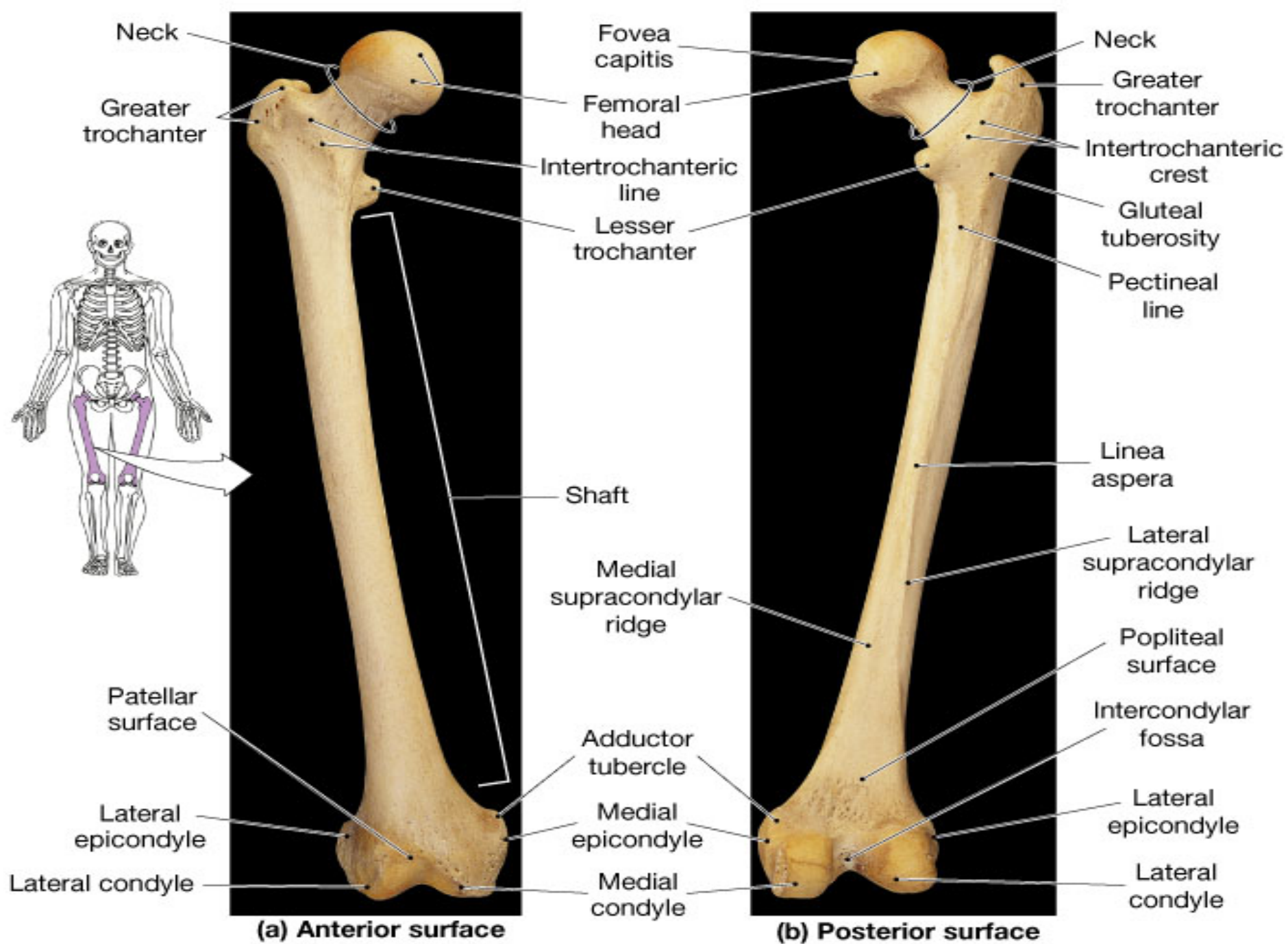
- 4.7 million (3.0 million women, 1.7 million men) individuals with total knee replacement in 2010

Total Hip Replacement (THR)

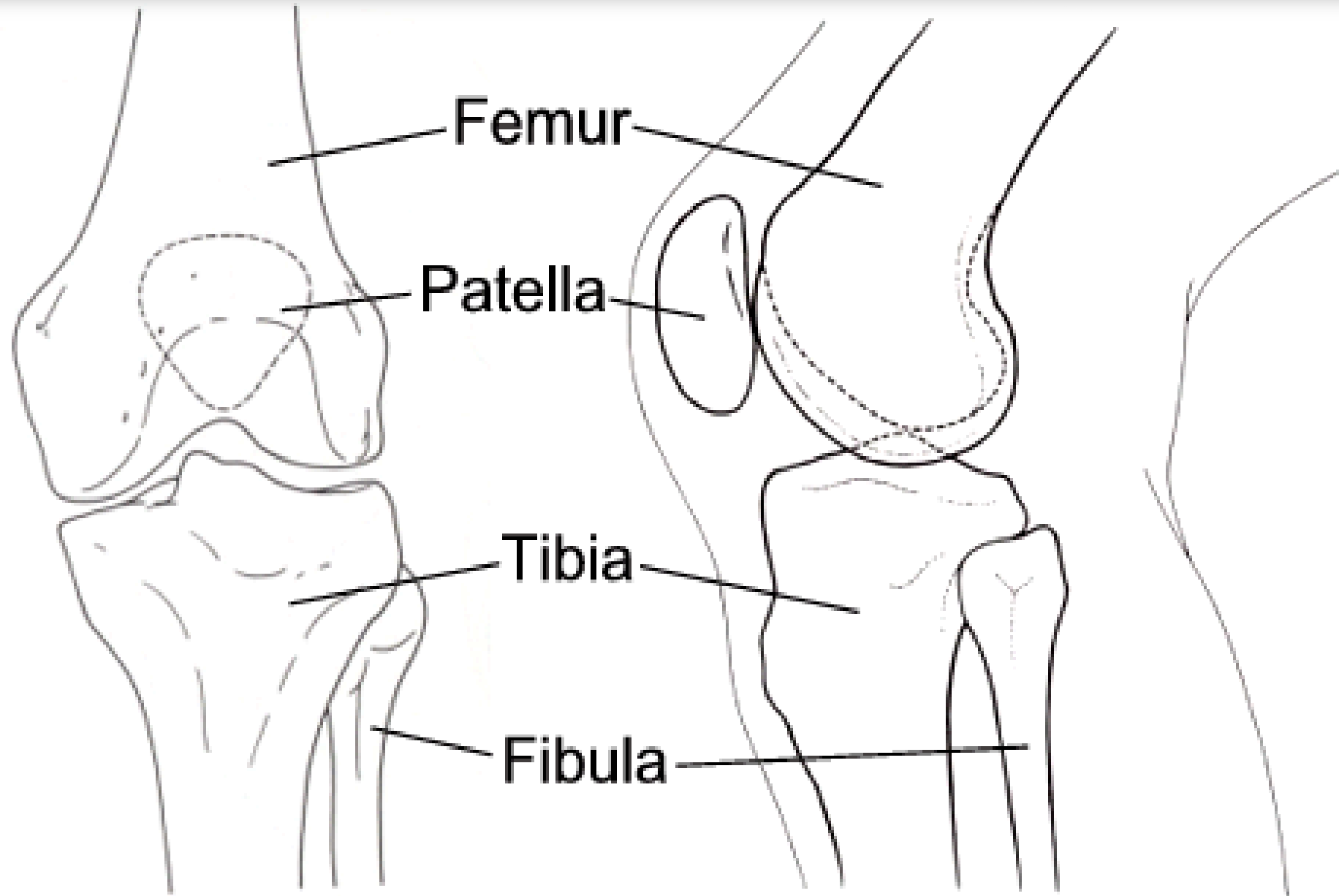


Age group	Female	Male
<50	0.1%	0.1%
50-59	0.8%	1.0%
60-69	2.1%	2.1%
70-79	4.4%	3.8%
80-89	6.3%	4.8%
90+	6.1%	4.8%

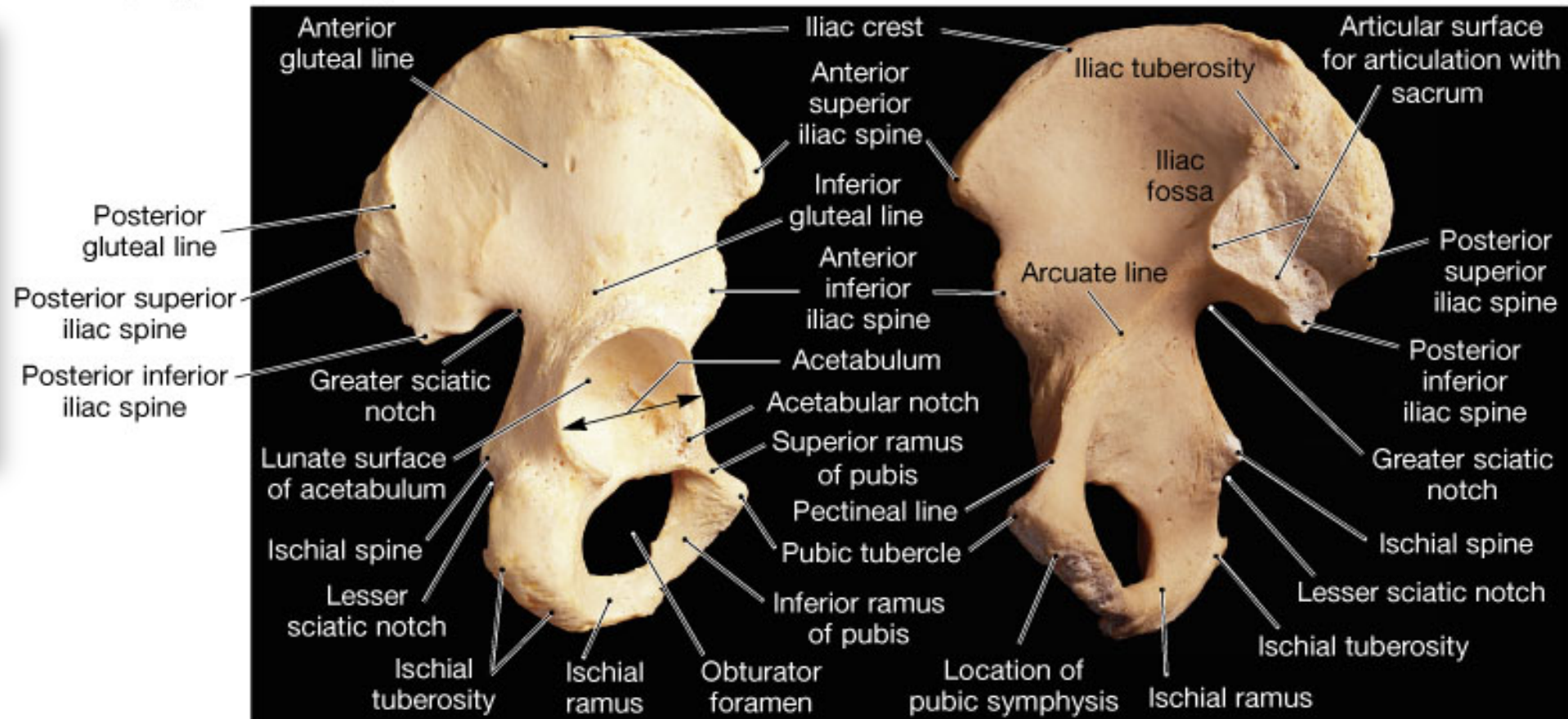
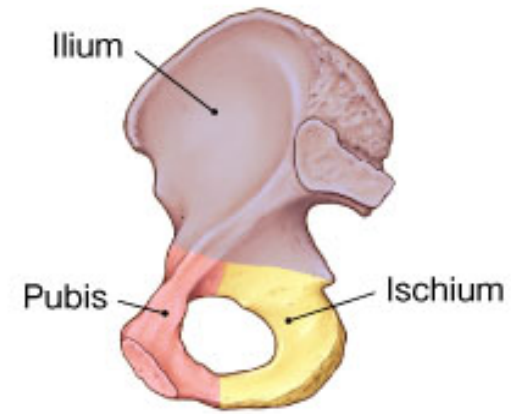
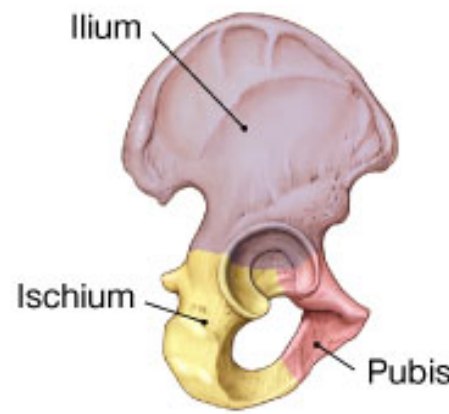
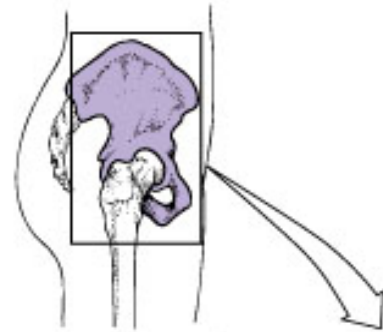
- 2.5 million (1.4 million women, 1.1 million men) individuals with total hip replacement in 2010



Anatomy of Knee Joint



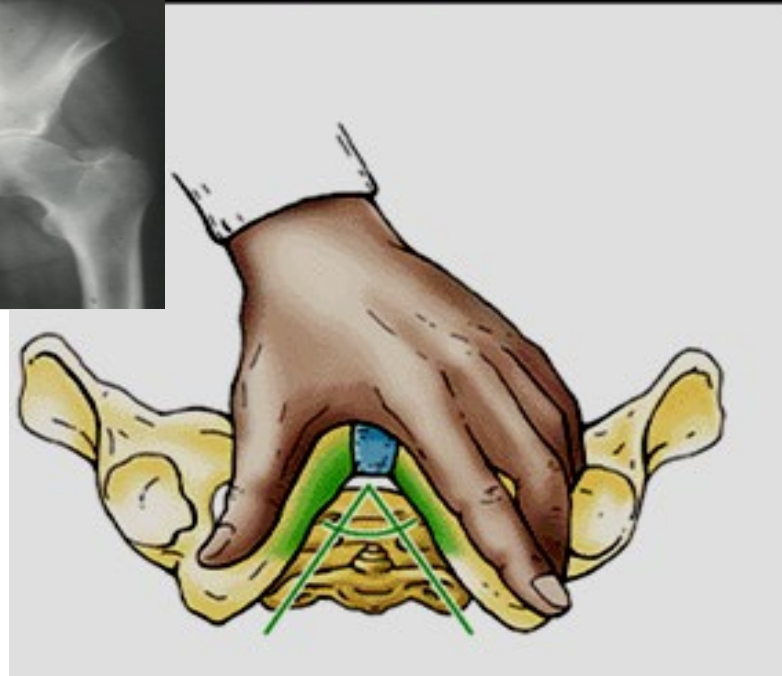
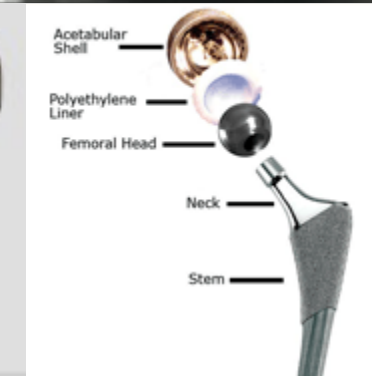
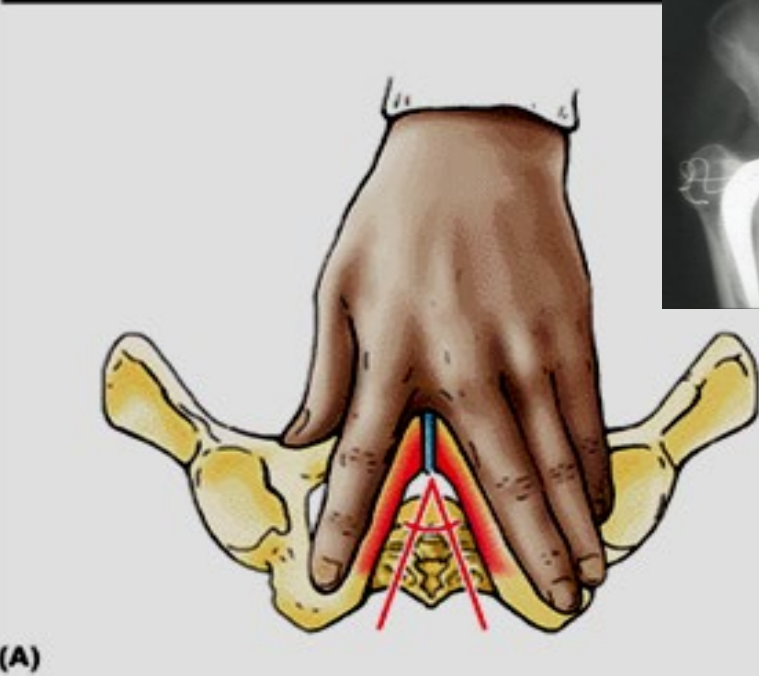
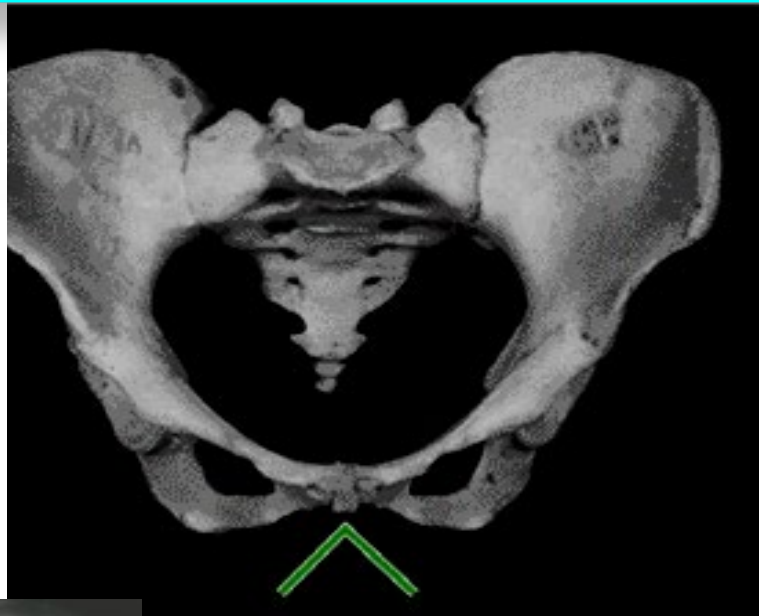
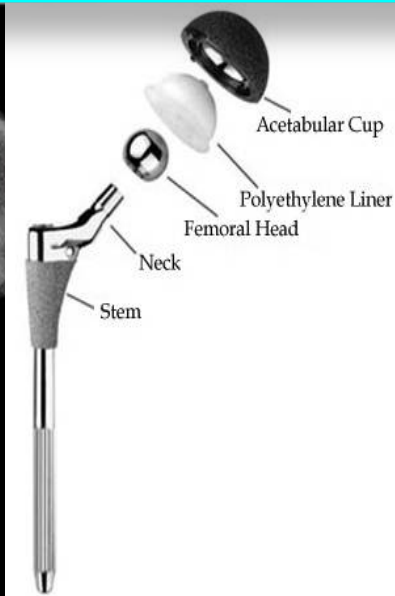
Anatomy of Hip Joint



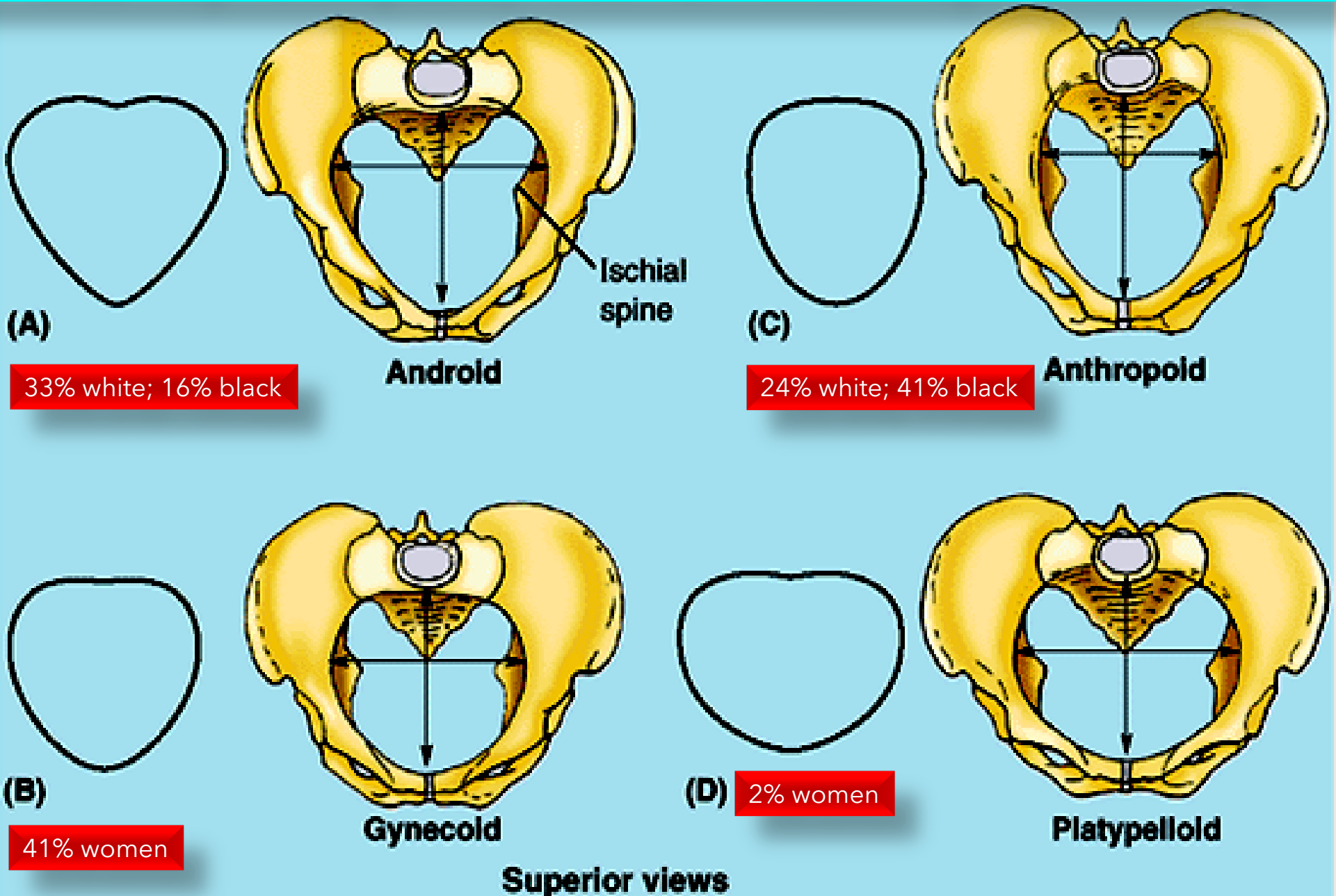
(a) Right os coxae, lateral view

(b) Right os coxae, medial view

Total Hip Arthroplasty - Are All Acetabular Caps Created Equal?



Total Hip Arthroplasty - Are All Female Hips Created Equal ?



One shoe doesn't fit all !!

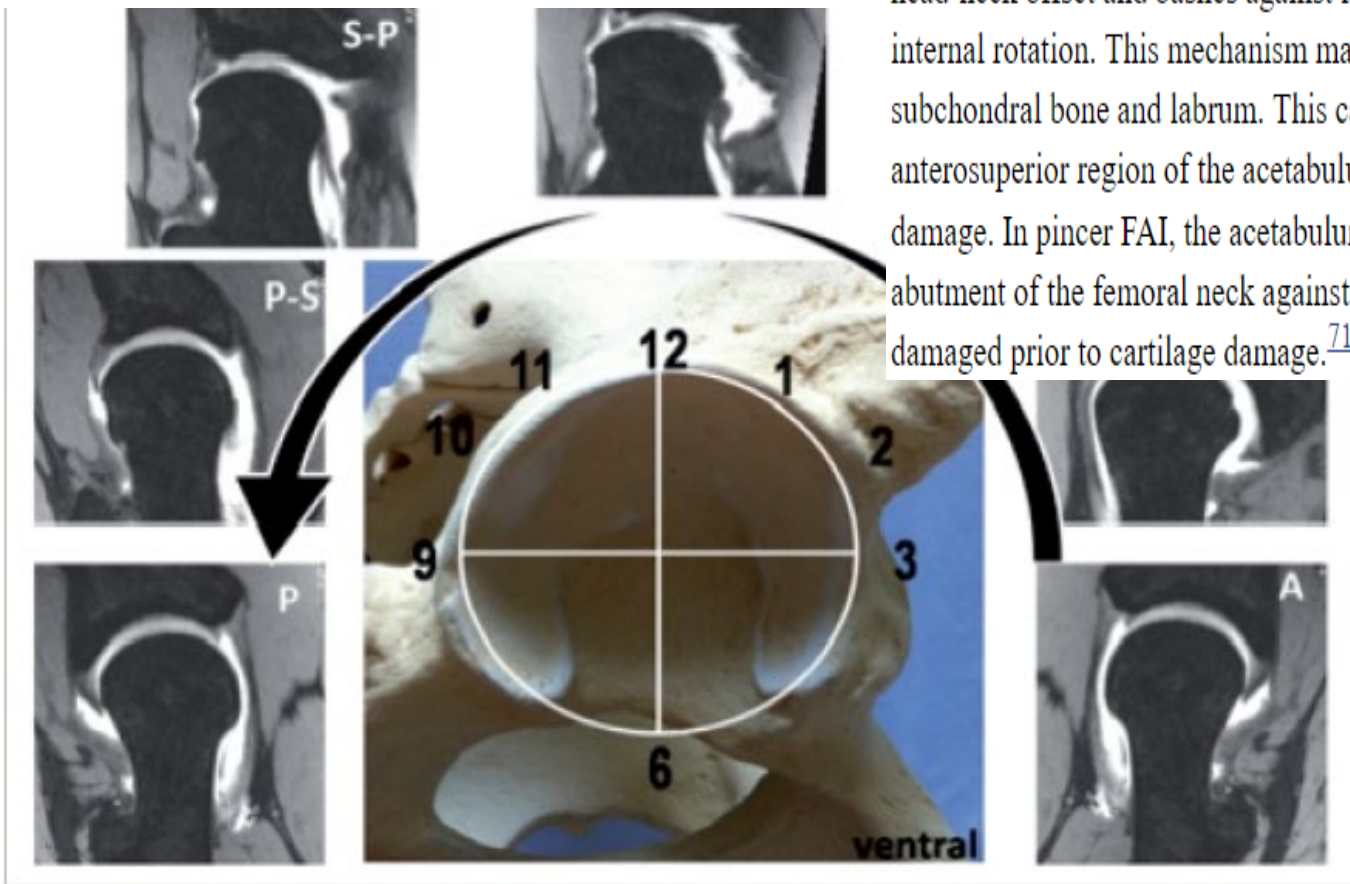
FEMOROACETABULUM

Femoroacetabular Impingement

The concept of femoroacetabular impingement (FAI) as a major contributor to the development of premature hip OA has been recognized and accepted all over the world. Table 2 demonstrates the remarkable number of publications in PUBMED concerning *femoroacetabular impingement* within the past decade. The cam-lesion is the reduced head-neck offset and bashes against labrum and acetabular cartilage during flexion and internal rotation. This mechanism may cause cartilage delamination from the subchondral bone and labrum. This carpet phenomenon is located mostly in the anterosuperior region of the acetabulum.⁶⁸⁻⁷⁰ as well as causing intraarticular cartilage damage. In pincer FAI, the acetabulum might be too deep globally or locally, causing an abutment of the femoral neck against the acetabulum so that the labrum might be damaged prior to cartilage damage.⁷¹⁻⁷⁵ Further causes for FAI are rotational anomalies

tev (Pavia)

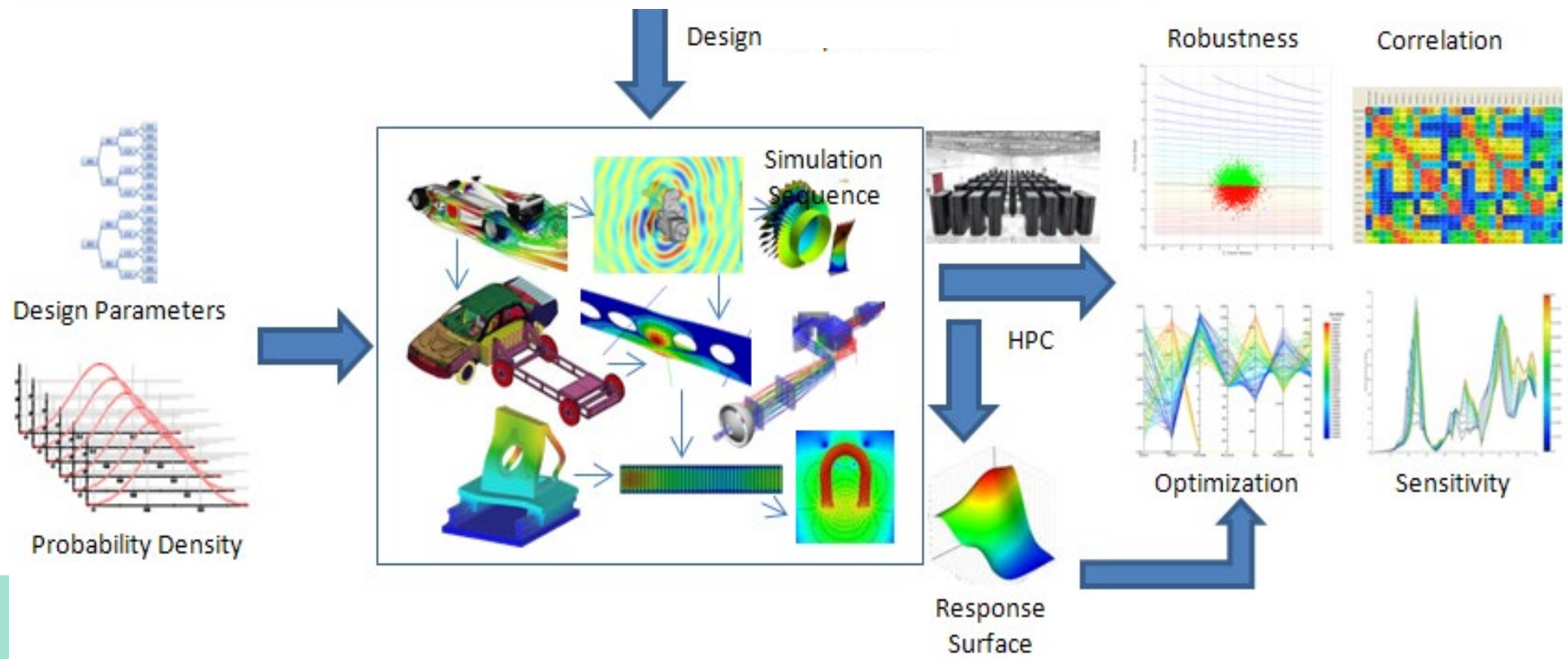
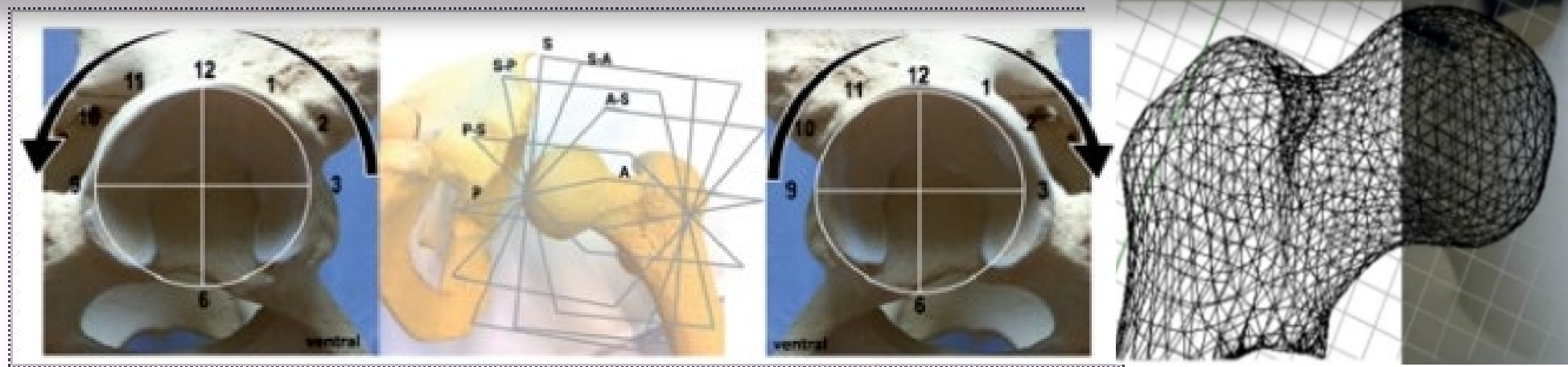
Orthop Rev (Pavia)



Radial images in a hip dysplasia patient.

Connect \Rightarrow Converge \Rightarrow Compile

Hip arthroplasty (MRI/MRA) data integrated design & 3D Print

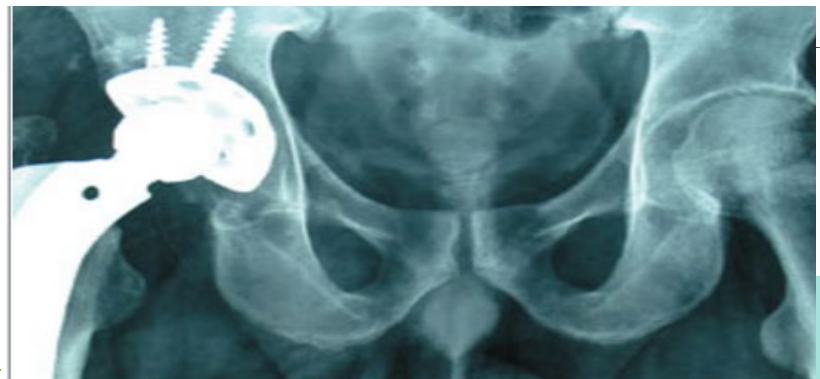
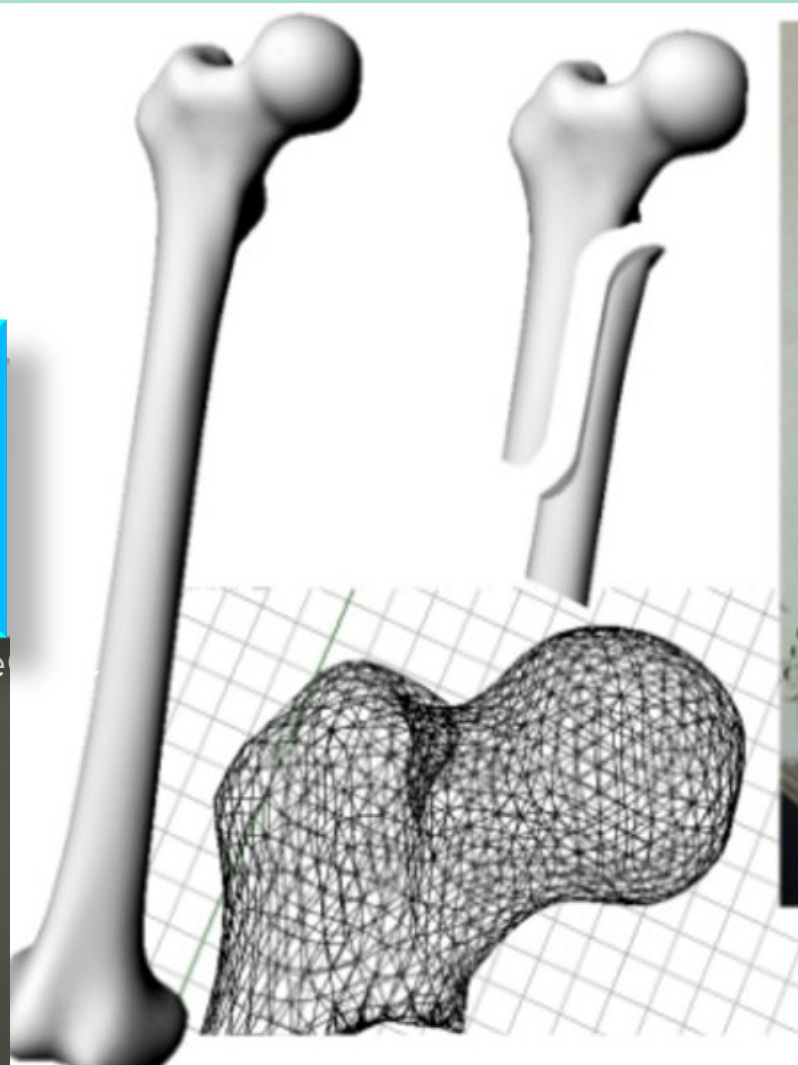
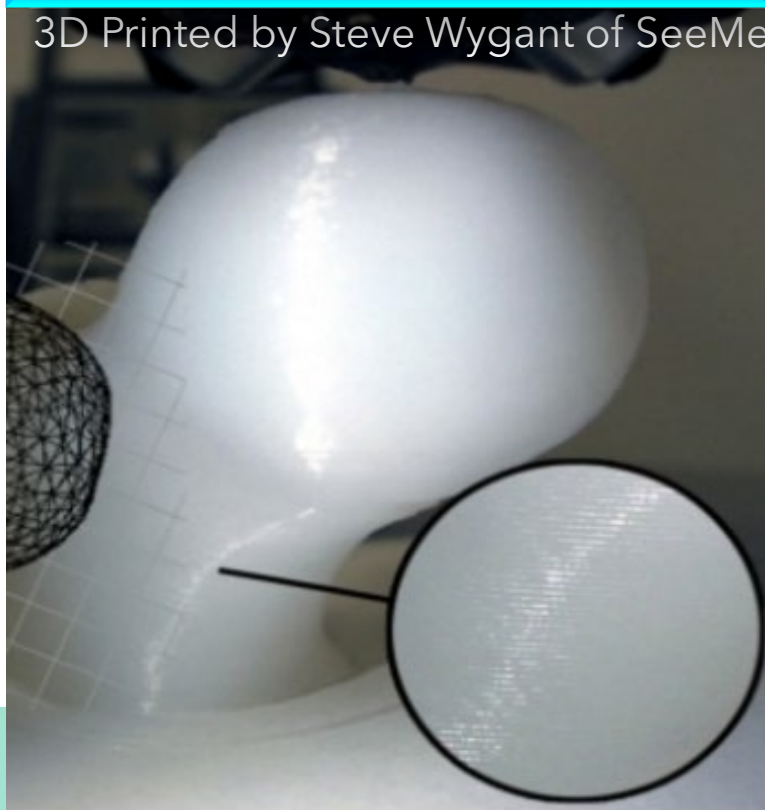


Connect ➔ Converge ➔ Communicate to 3D Printer

Upper Femur

3D Printed with 9572 psi tensile strength 618 nylon co-polymer

3D Printed by Steve Wygant of SeeMe



<http://bit.ly/AAOS-2014>

Can it happen in *Asia, Africa* ?

Can it happen in *Asia, Africa* ?





Margrit Harting, Maresa Harting-Hertz, Dietmar Harting, Chancellor, President, Philip Harting



Figure 2. Suman Das shows an investment casting mold (right) fabricated by large-area maskless photopolymerization and a turbine blade casting (left).



Make ceramic cores and integral-cored shell molds for precision investment castings and intricate engineered ceramic components without hard tooling and at a fraction of conventional cost and lead-time using our patented LAMP™ Large Area Maskless Photopolymerization technology platform.

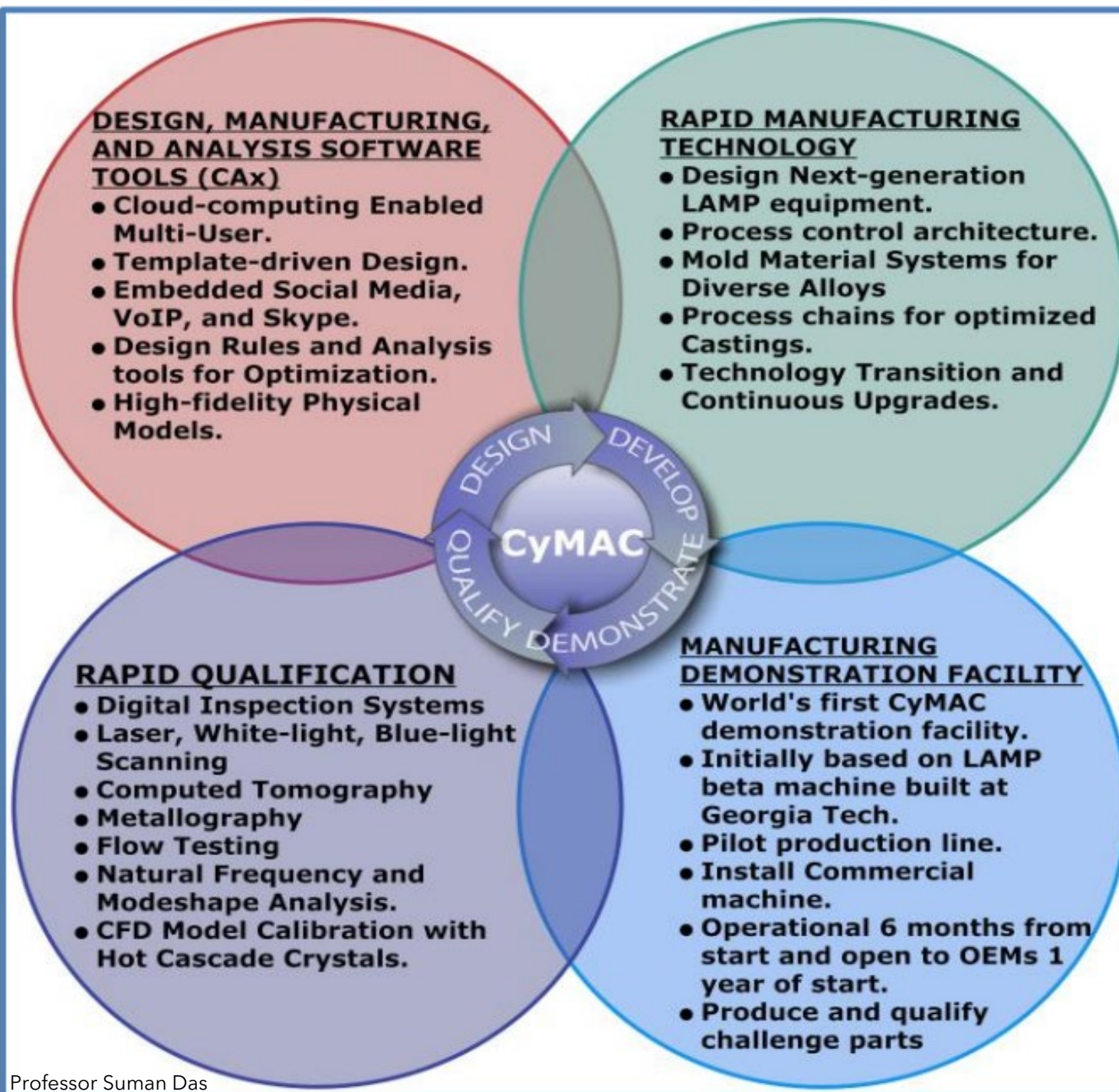


Can it happen in Asia, Africa ?

CYMAC

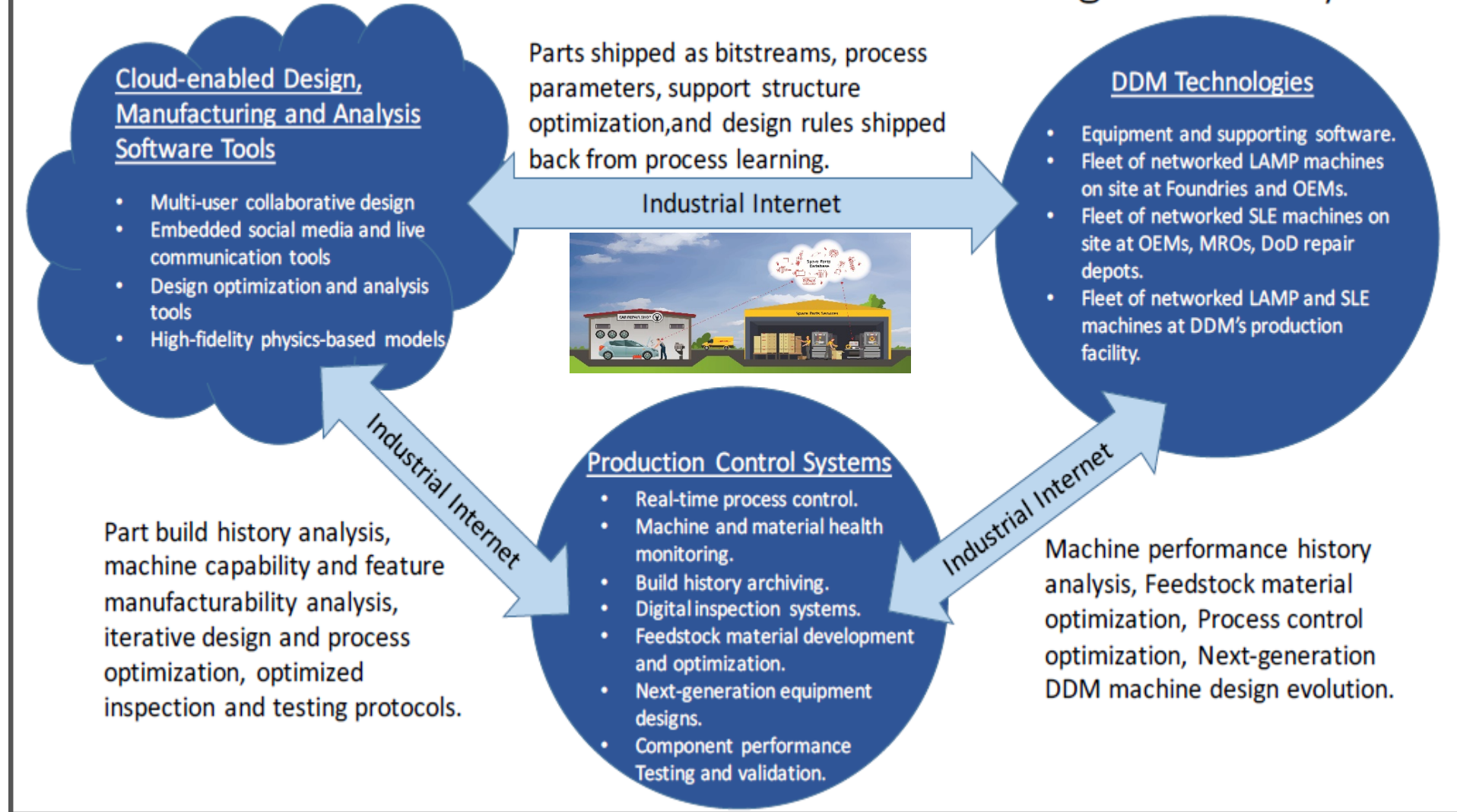
CyberManufacturing of Orthopedic Parts and Prosthetic Joints

It can happen anywhere, with a little bit of effort and enthusiasm



CYMAC

The Future Vision of a CeMS-DDM based Digital Factory



Down to earth, present reality ...

After [#covid19](#), thankfully we can shift from BS innovation to BB (Back to Basics) innovation that really serves humanity.

Juicero offering refunds to all customers after people realize \$400 juicer is totally unnecessary



« The best brains in the world are busy solving the problems of the rich, who really don't have problems »

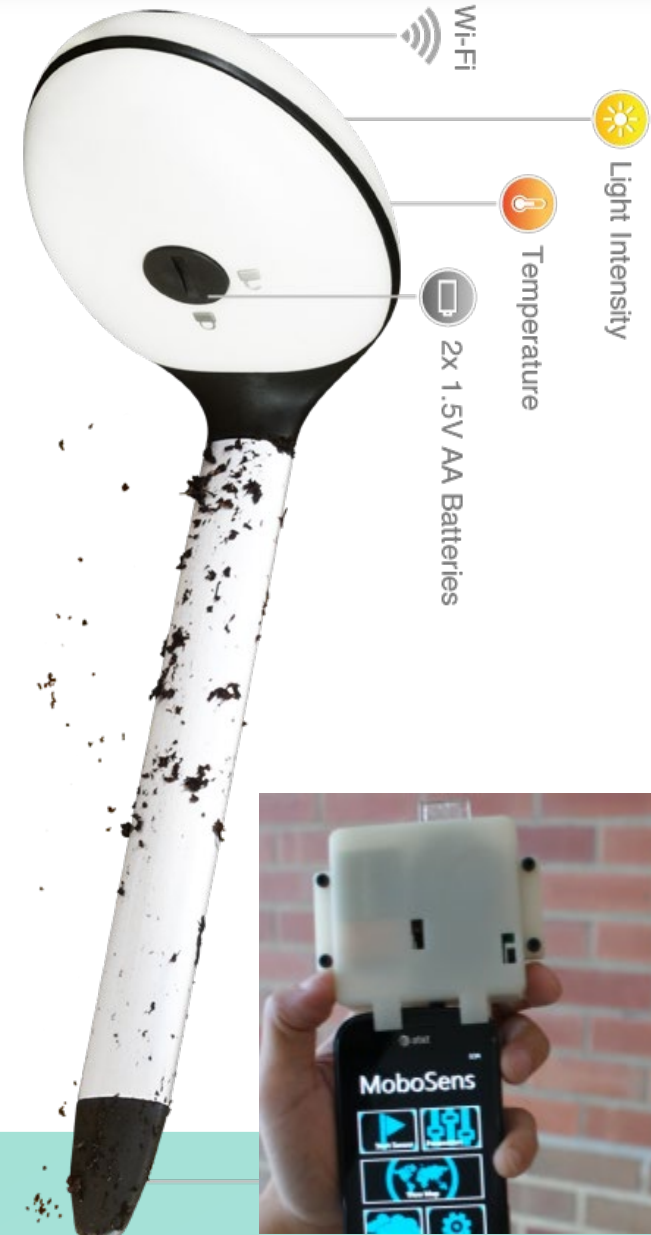


Solve real problems

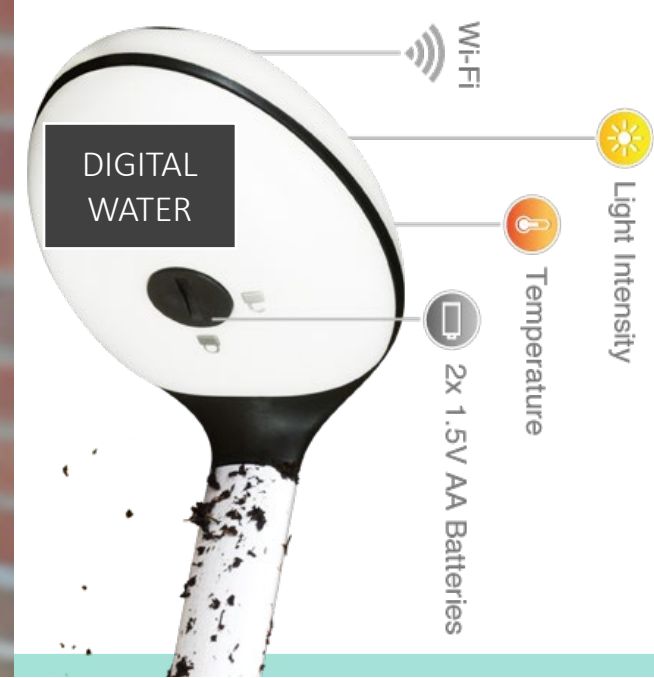
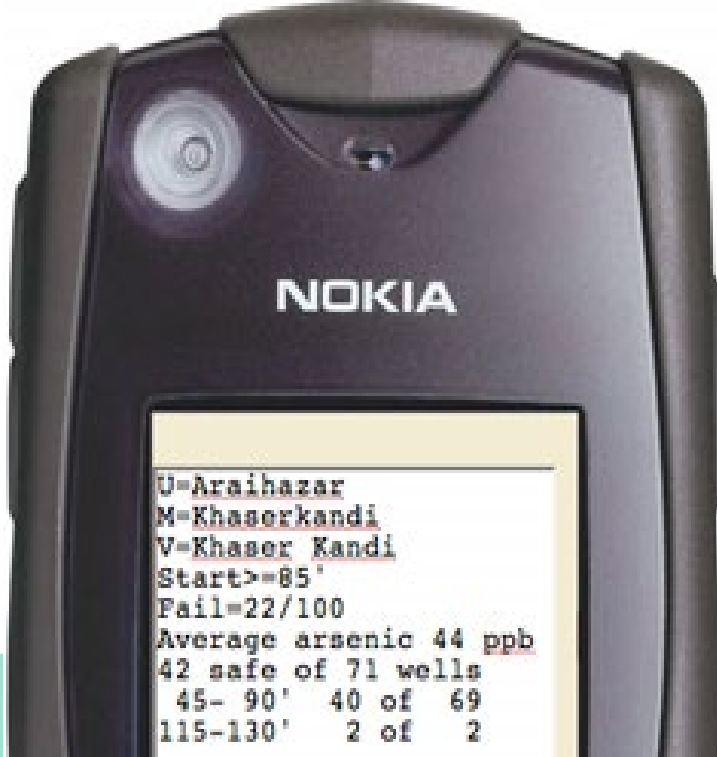
Reality Check Arsenic in Water (Bangladesh)



Healthcare Internet of Things - Impact of Clean Water



Nokia 'sensor as a service' can improve lives ☑ Internet of Things (IoT) Tool - Arsenic in water



<http://news.mit.edu/2016/faculty-profile-rohit-karnik-0901>

Can't conclude HEALTHCARE without discussing SARS-CoV-2/CoVID-19

Please refer to these discussions (see PDFs).
Please download PDFs from the MIT Library.

PDF from May 19th, 2021

◆ <https://bit.ly/PART-ONE-MAY-19>

PDF from May 21st, 2021

◆ <https://bit.ly/PART-TWO-MAY-21>

Articles and essays from the MIT Library

◆ <https://dspace.mit.edu/handle/1721.1/128017>

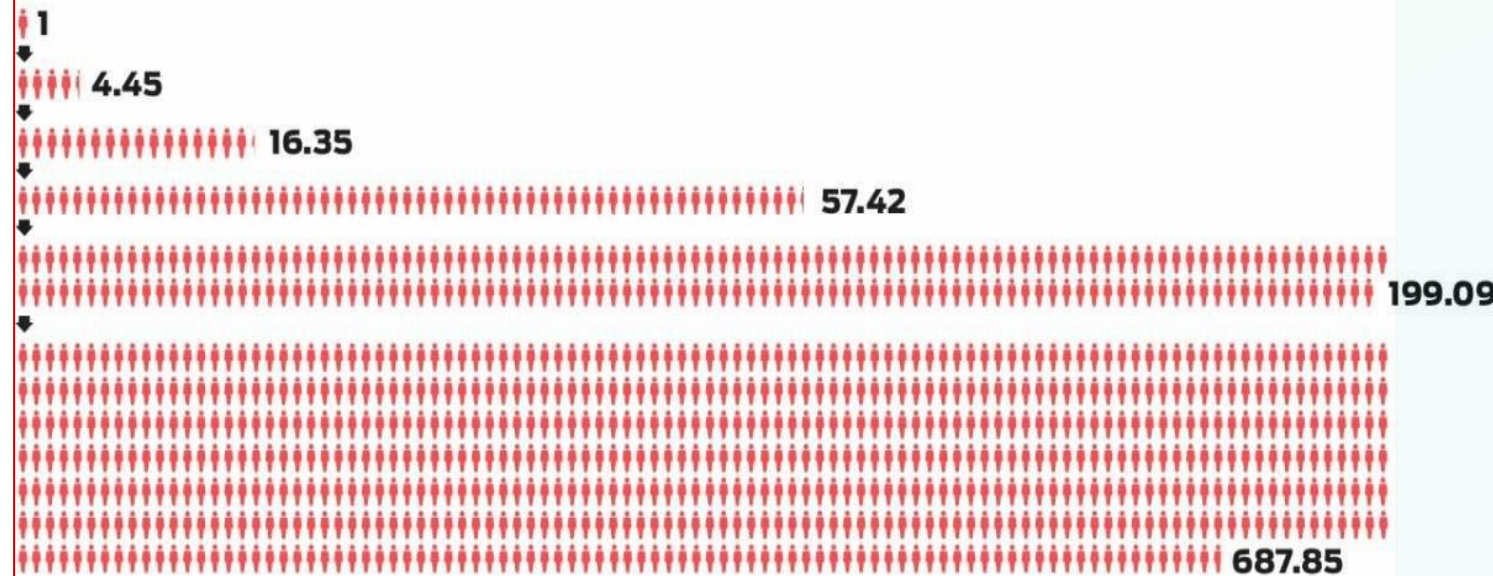
How vaccines can slow community transmission

This diagram depicts how the original virus and the highly contagious delta variant could spread from one infected person to others in the community, based on data pertaining to vaccination rates, vaccination efficacy and the reproductive number.

50% VACCINATION RATE

Delta variant

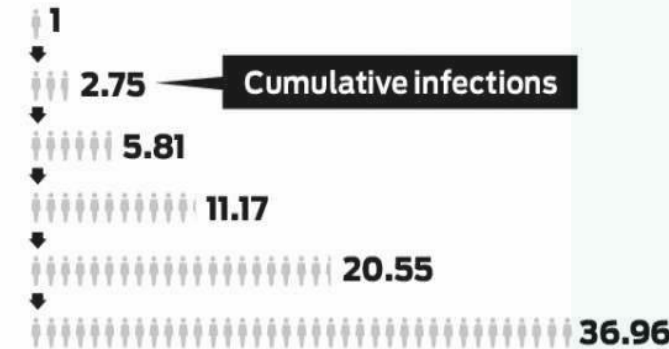
Each person gives it to 3.45 other people



50% VACCINATION RATE

Original virus

Each person gives it to 1.75 other people



Long way to go ...

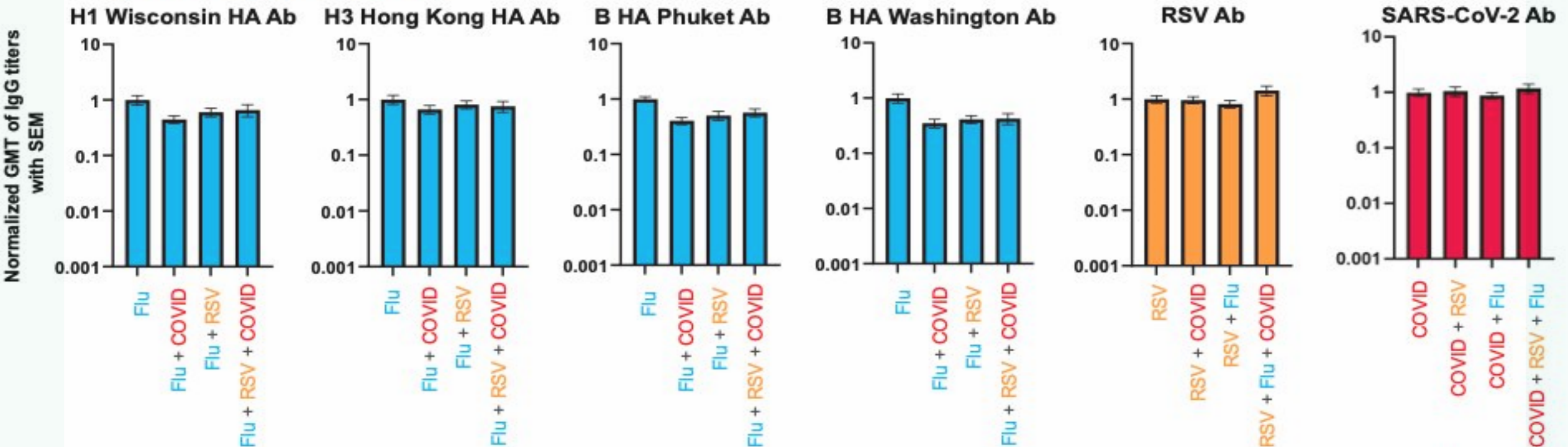
A Flu, RSV and SARS-CoV-2 combo vaccine induces robust antibody responses to all components in mice

Flu vaccine (mRNA-1010) encodes for **4 antigens** (HA)

COVID-19 vaccine (mRNA-1273) encodes for **1 antigen** (spike protein)

RSV vaccine (mRNA-1345) encodes for **1 antigen** (prefusion F protein)

or mRNA-1010 + mRNA-1345 + mRNA-1273



*Resist Tweeter-ionic
disinformation*



Élysée 
@Elysee

 Follow

.@fhollande rencontre plusieurs personnalités indiennes francophiles, dont l'actrice Aishwarya Rai #IndePR

2:10 AM - 26 Jan 2016

The latest US influenza season is more severe and has caused more deaths than usual.

EPIDEMIOLOGY

When Google got flu wrong

US outbreak foxes a leading web-based method for tracking seasonal flu.

BY DECLAN BUTLER

When influenza hit early and hard in the United States this year, it quietly claimed an unacknowledged victim: one of the cutting-edge techniques being used to monitor the outbreak. A comparison with traditional surveillance data showed that Google Flu Trends, which estimates prevalence from flu-related Internet searches, had drastically overestimated peak flu levels. The glitch is no more than a temporary setback for a promising strategy, experts say, and Google is sure to refine its algorithms. But as flu-tracking techniques based on mining of web data and on social media proliferate, the episode is a reminder that they will

complement, but not substitute for, traditional epidemiological surveillance networks.

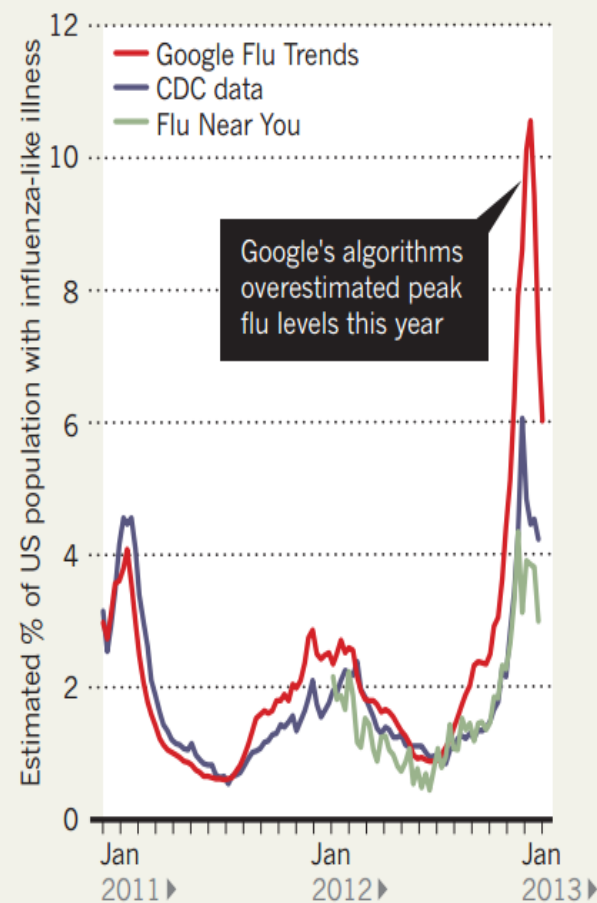
“It is hard to think today that one can provide disease surveillance without existing systems,” says Alain-Jacques Valleron, an epidemiologist at the Pierre and Marie Curie University in Paris, and founder of France’s Sentinelles monitoring network. “The new systems depend too much on old existing ones to be able to live without them,” he adds.

This year’s US flu season started around November and seems to have peaked just after Christmas, making it the earliest flu season since 2003. It is also causing more serious illness and deaths than usual, particularly among the elderly, because, just as in 2003, the predominant strain this year is H3N2 — the most

nologies could open the way to easier, faster estimates of ILI, spanning larger populations.

FEVER PEAKS

A comparison of three different methods of measuring the proportion of the US population with an influenza-like illness.



Raison d'être

Tackling gender inequality could add \$12tn to world economy, study finds

Researchers say extra GDP output could come from reforms, such as allowing more women in workforce in countries where they currently face restrictions



📷 A woman working at a salt pan in Mumbai. Due to gender inequality, only 17% of India's GDP comes from women. The figure is 40% in the US and western Europe. Photograph: Divyakant Solanki/EPA

Tackling gender inequality and boosting women's opportunities in the labour market could add \$12tn (£7.8tn) to annual global GDP over the next decade, according to new research. <http://bit.ly/GENDER-INEQUALITY>

Take time to peruse, read and reflect

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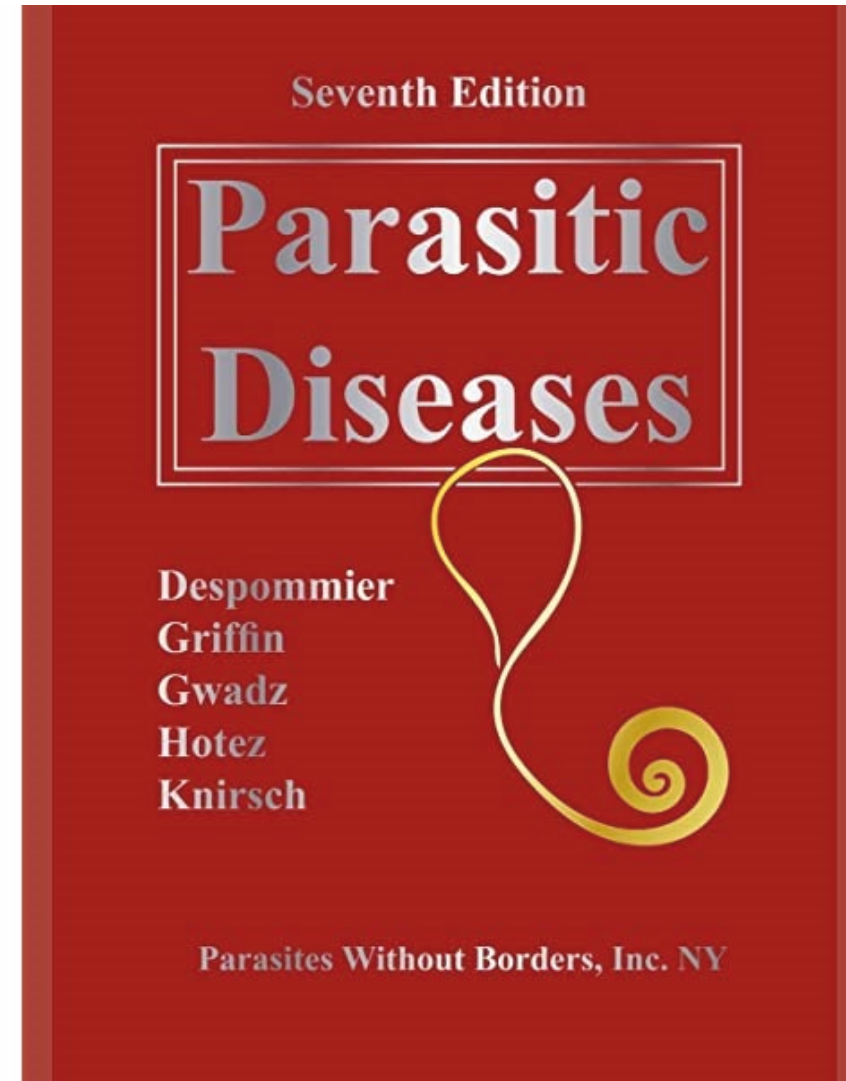
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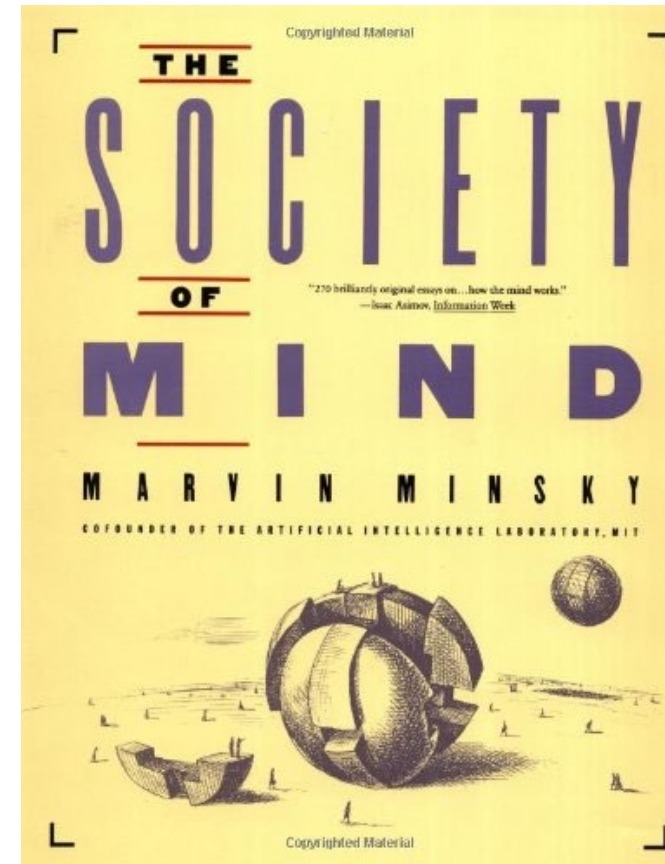
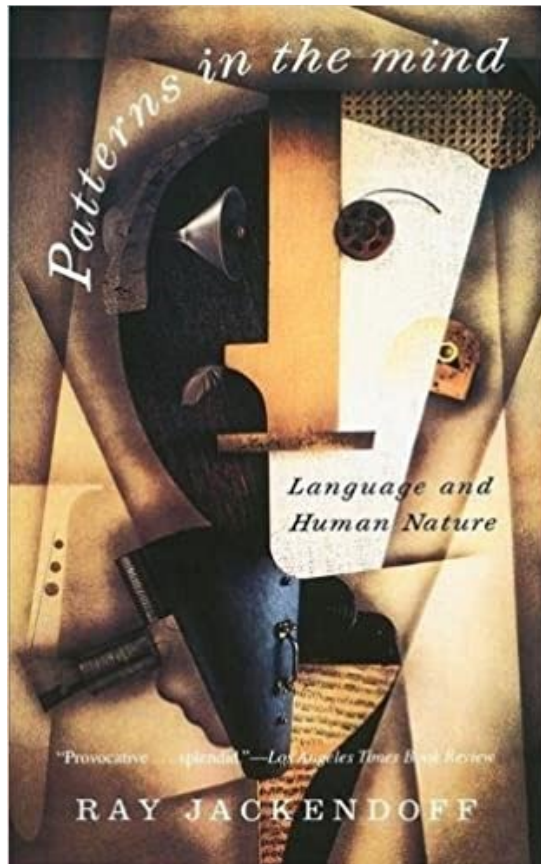
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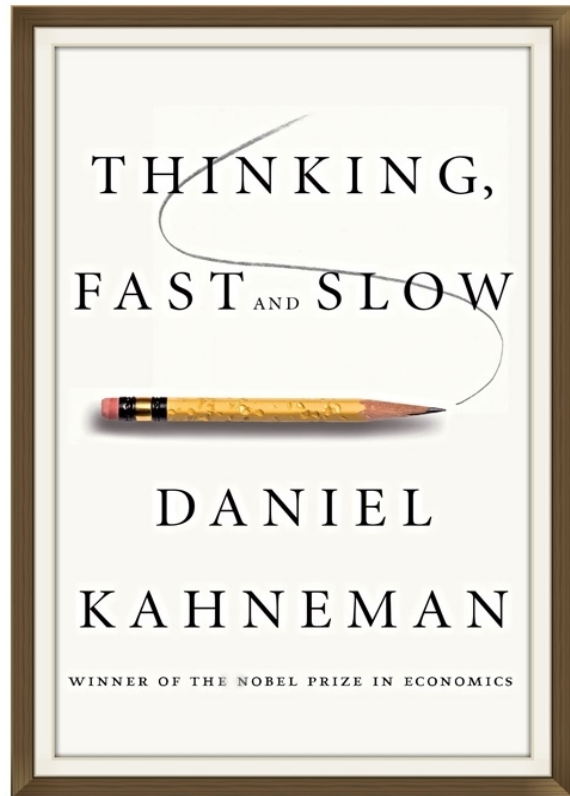
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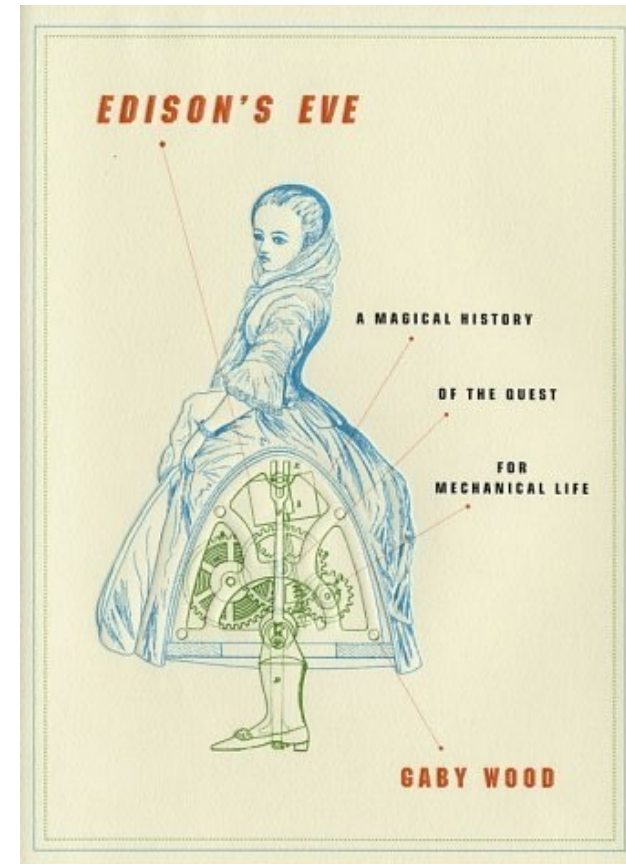
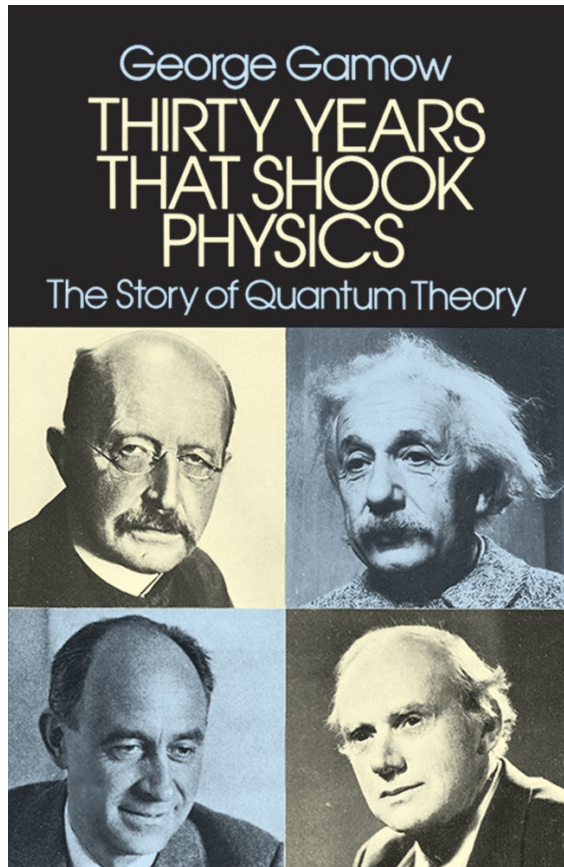
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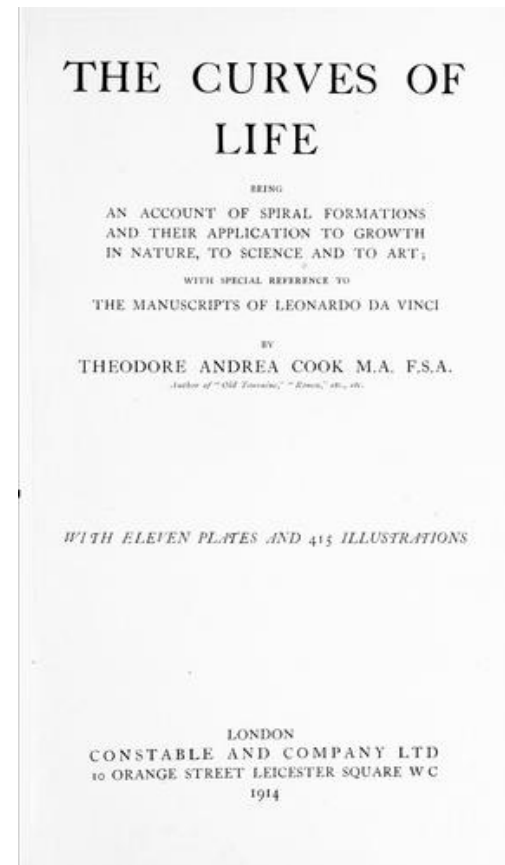
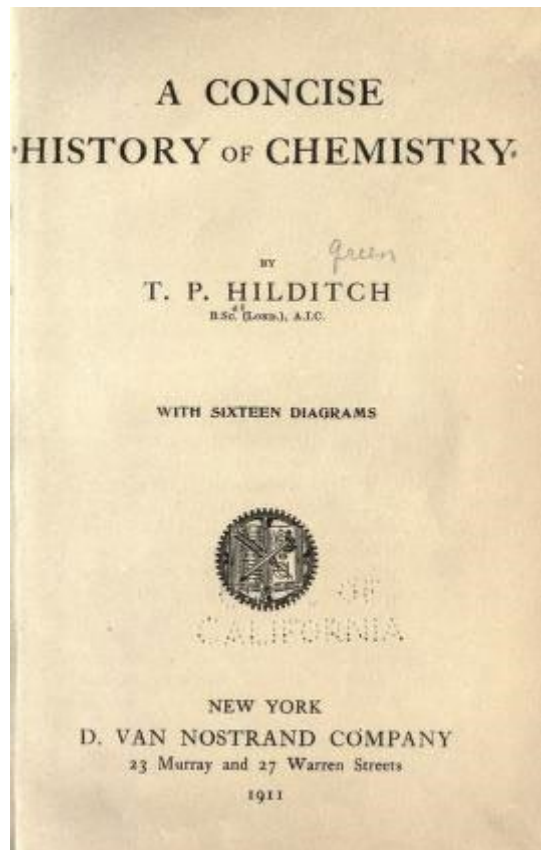


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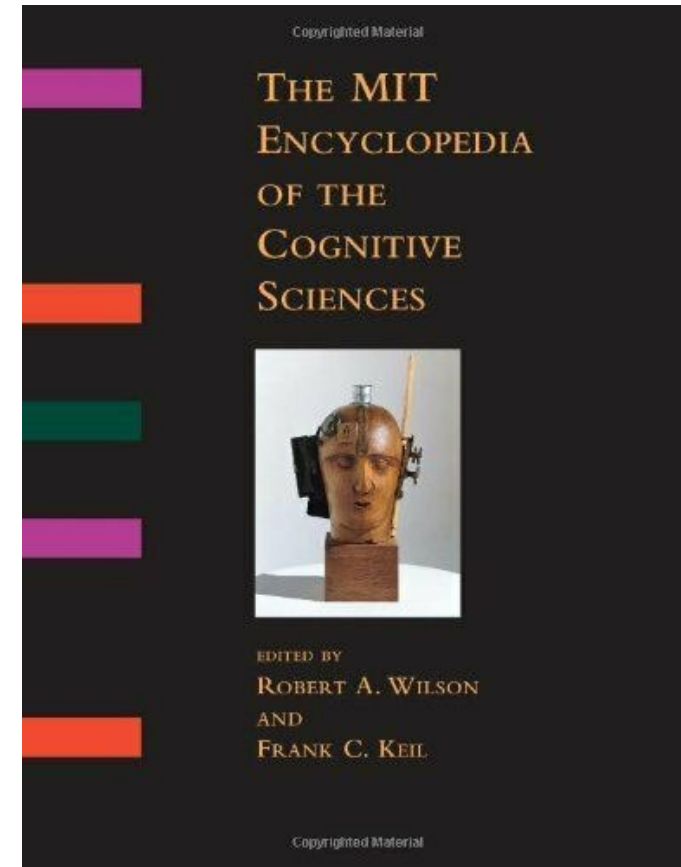
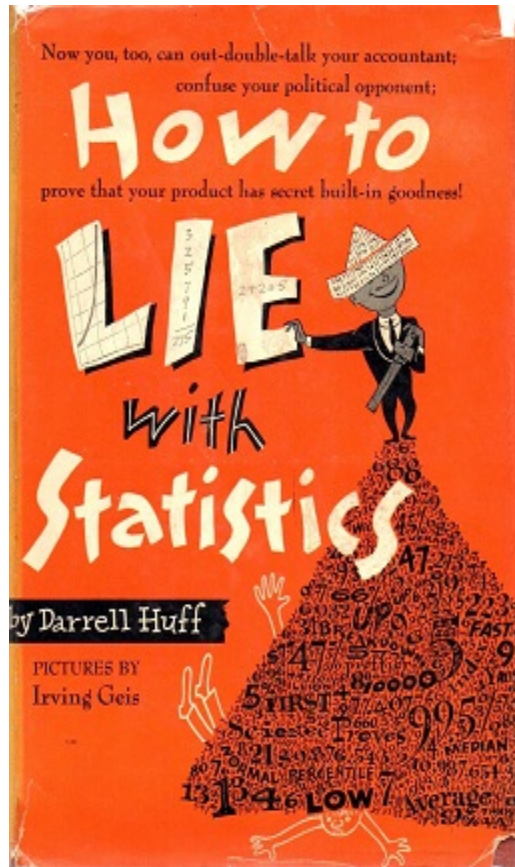
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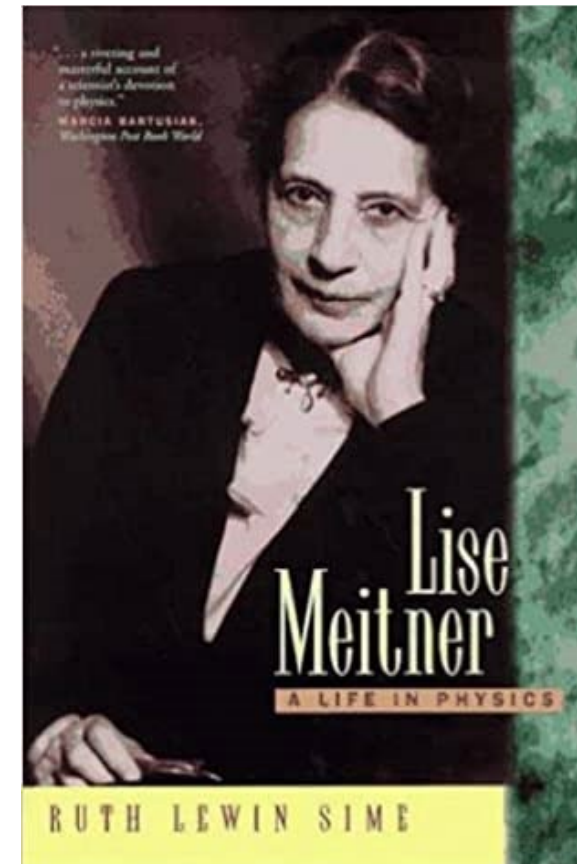
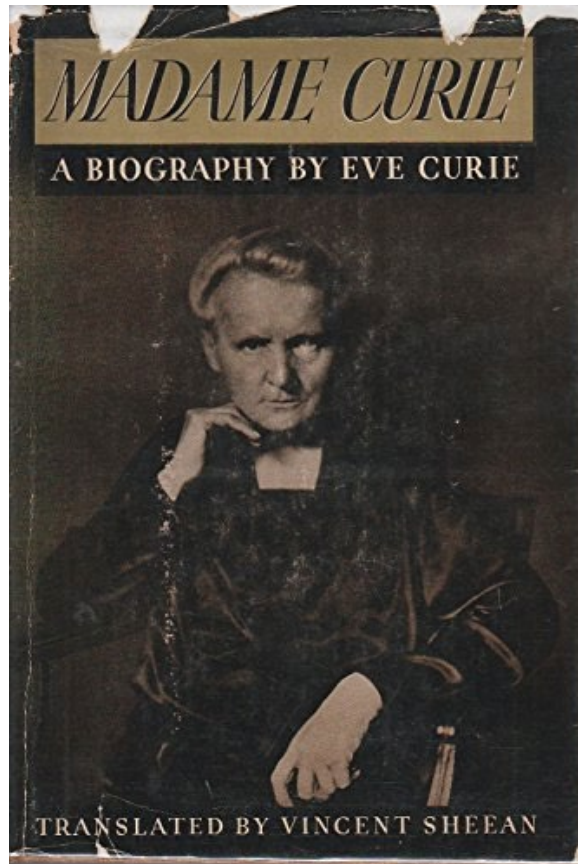


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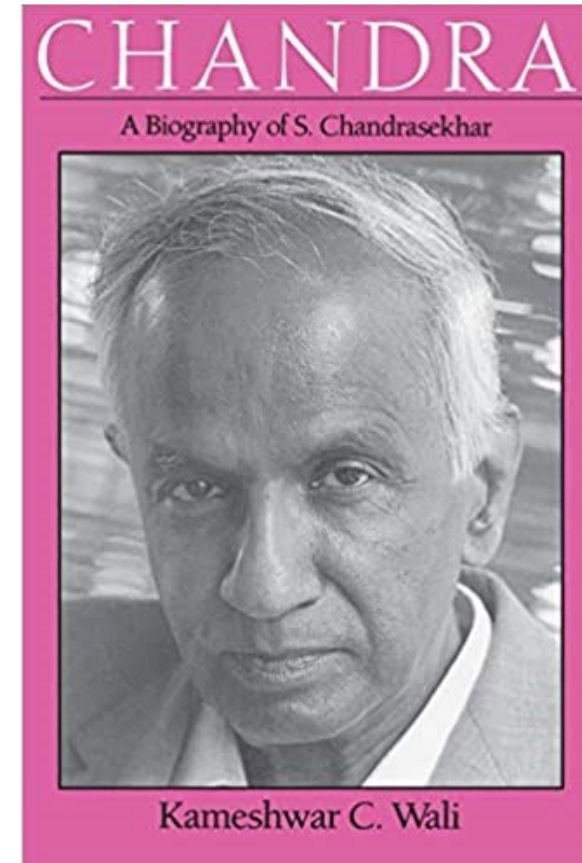
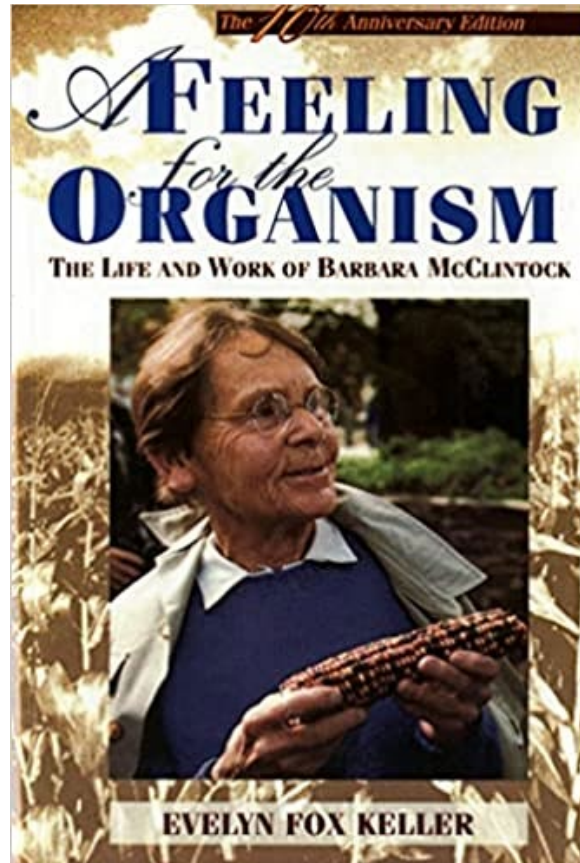


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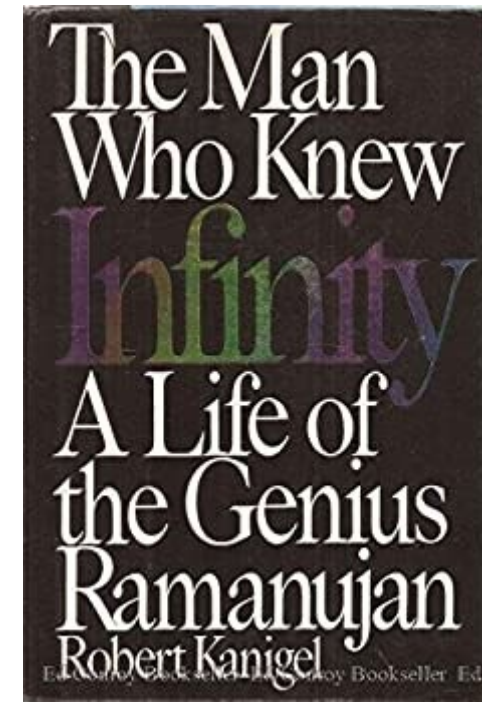
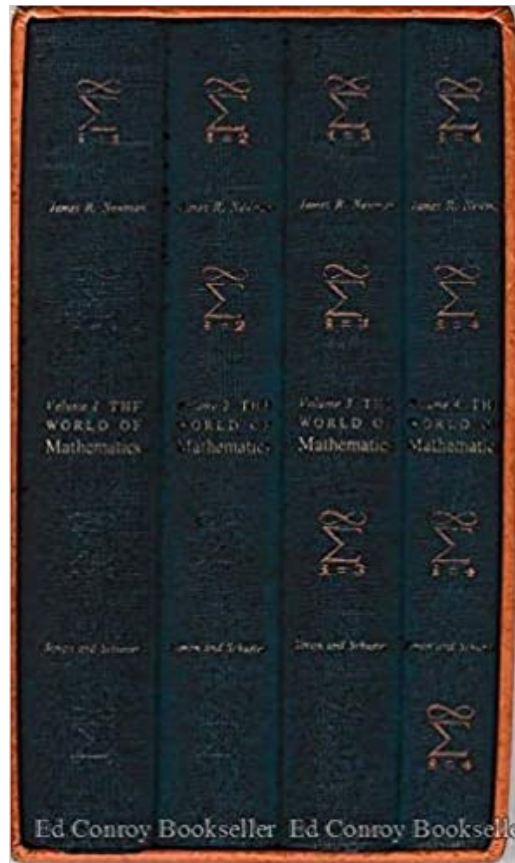
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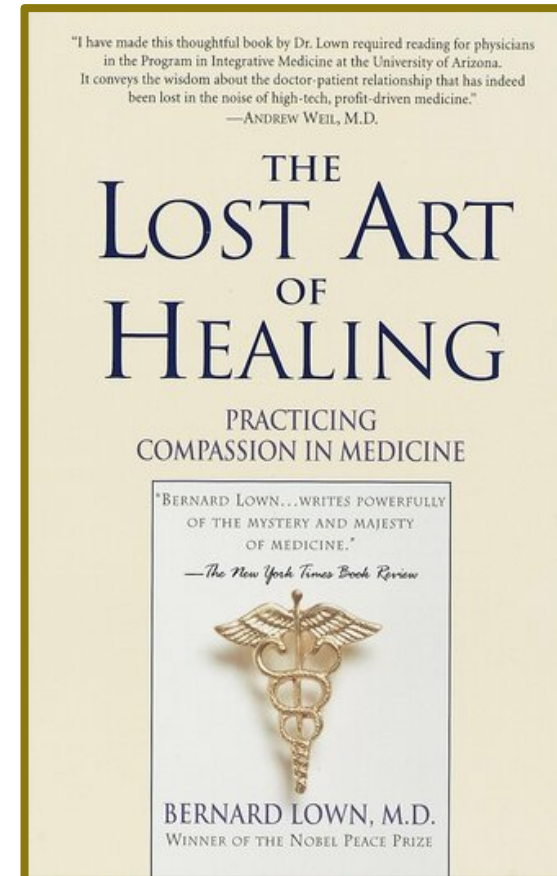
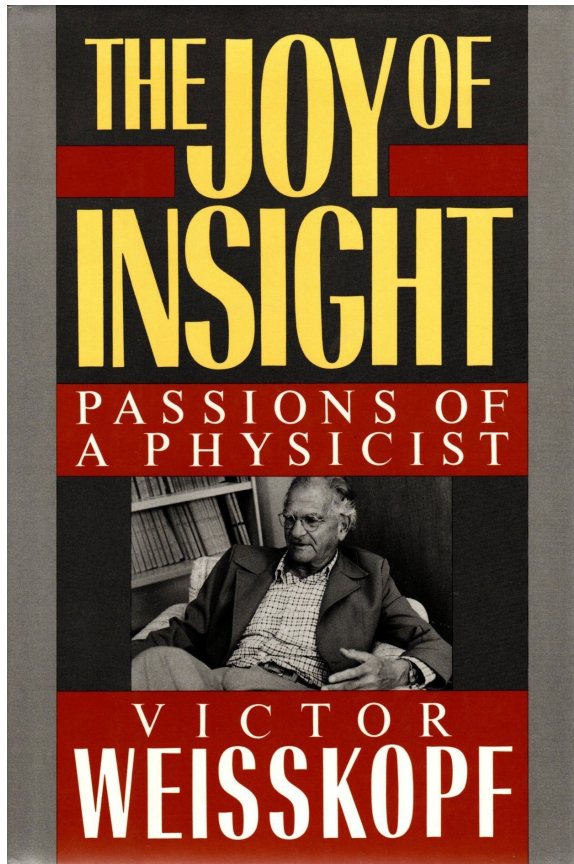
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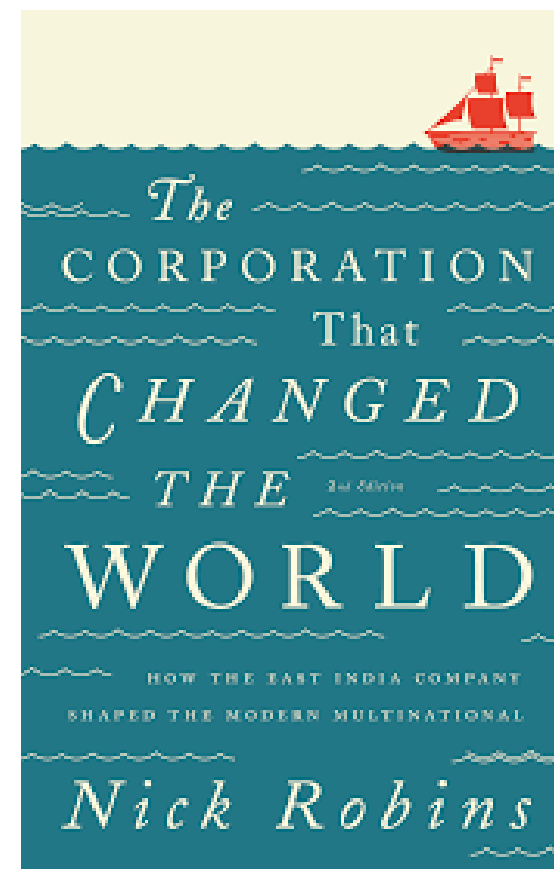
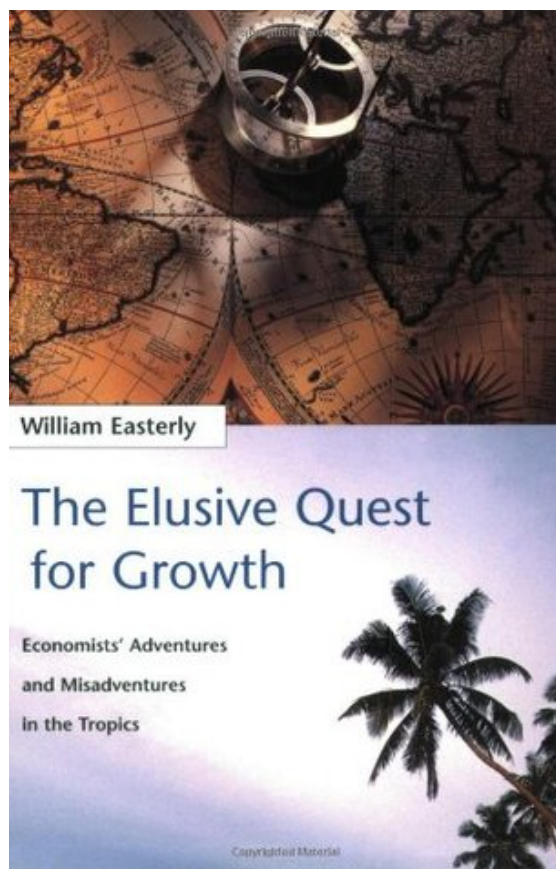
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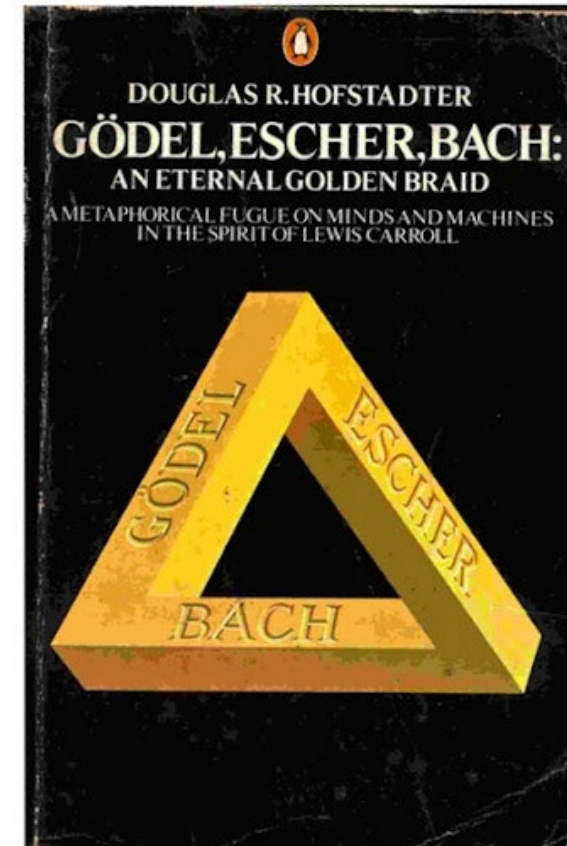
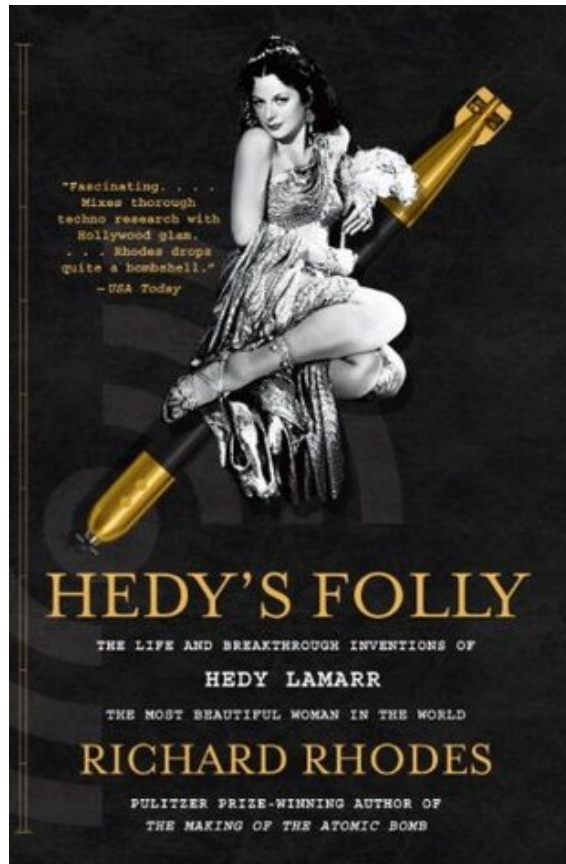
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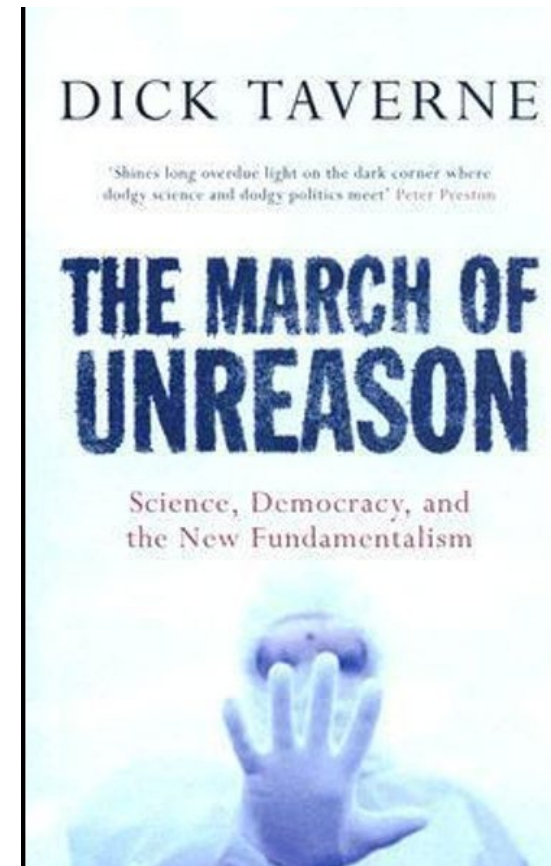
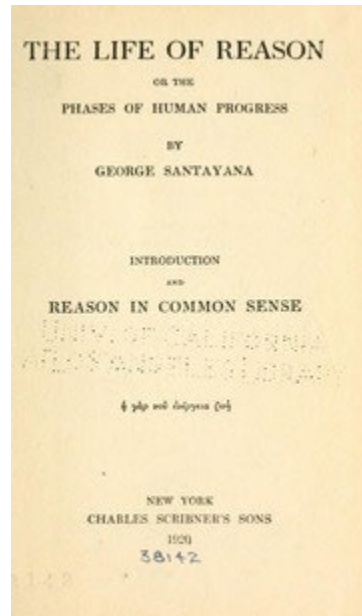


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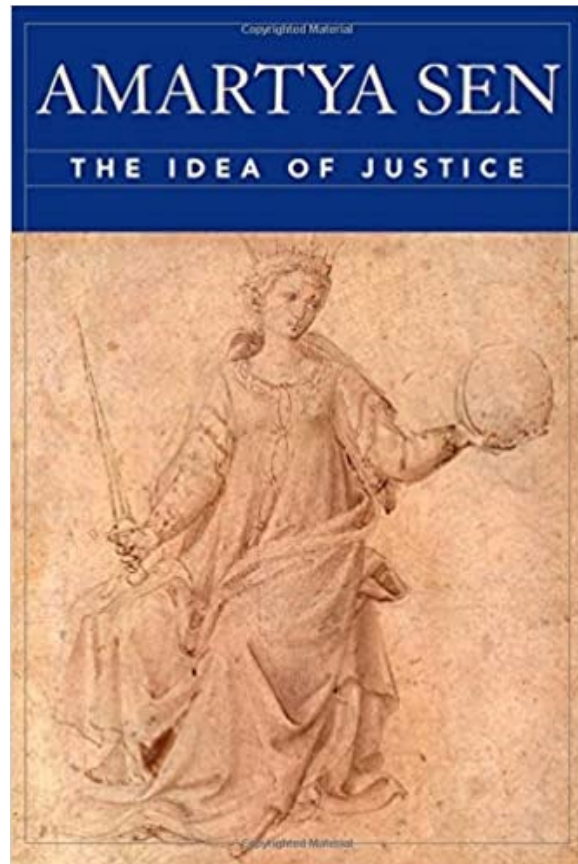
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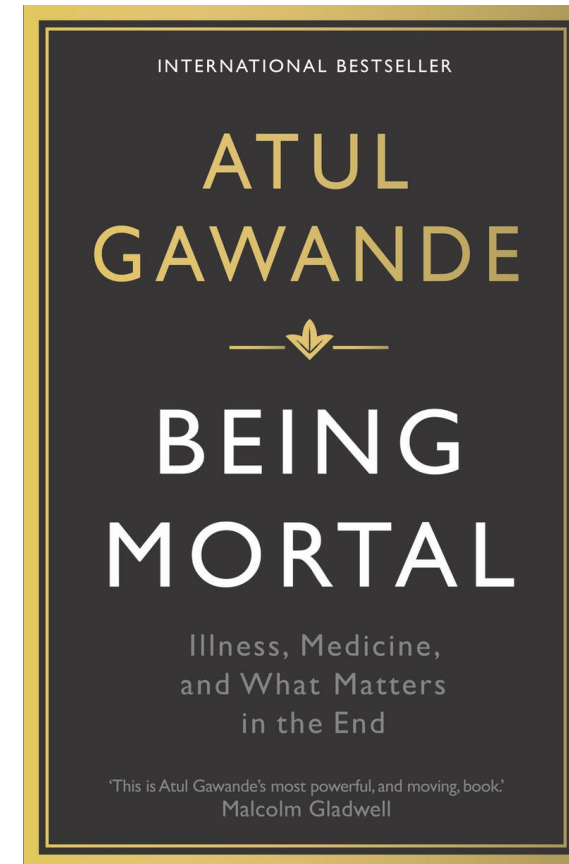
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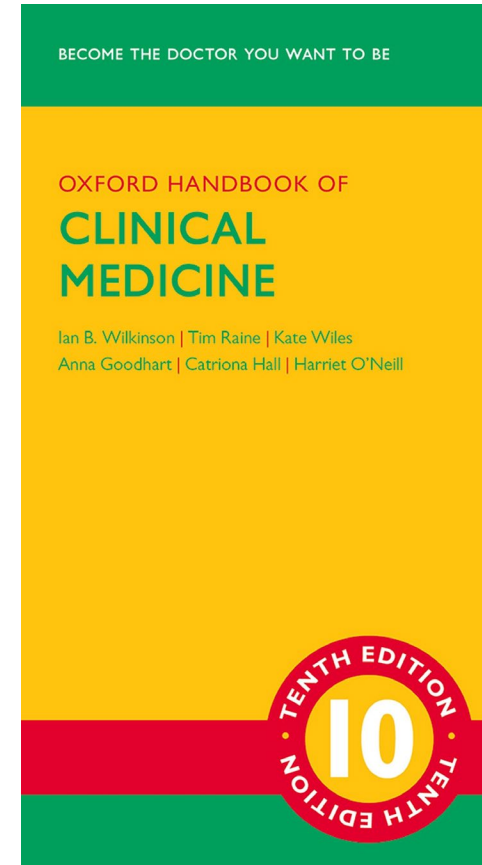
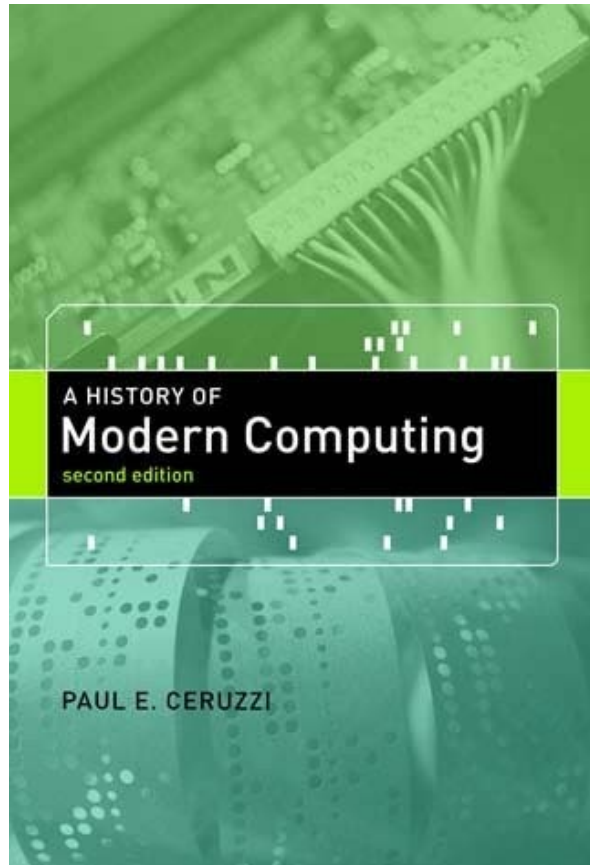
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Temporary Conclusion ...

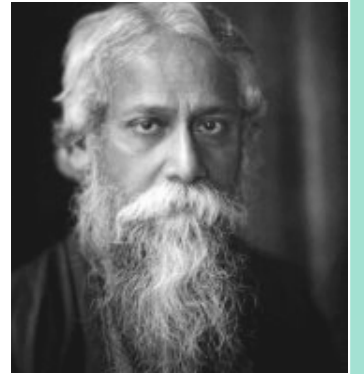
Did I bore you to sleep ?



Your contribution to society matters. Enabling engineering and science to serve society requires preparation. The road ahead is not a bed of roses. You can complain that rose bushes have thorns or rejoice because thorny bushes also grow roses. In *your* design of *your* sense of the future, the “rose” is a metaphor for sign-posts you are likely to encounter on this long journey. Finding your mental compass to navigate your direction is quintessential. Your family, friends, teachers and academia are your sources of values, virtues and vices. Yet, ultimately, it is your aspiration, ambition and your courage to discover not only knowledge, but the wisdom you must inculcate, to re-shape your destiny.

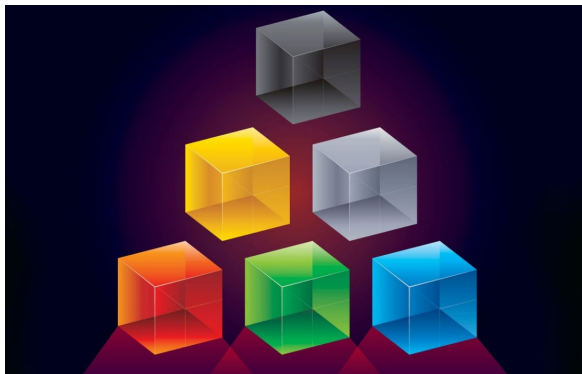
This talk is just a **tiny** point in the pragmatic philosophical fabric of life, whose quality depends on what you are weaving. I aim to mention a few elements of scientific significance pertaining to 5 strands (FEWSH) of global public goods which acts as purveyors of civilization. We are not indulging in the hubris, extravagance and waste which is in abundance in the West. We aim to discuss how the fruits of science may lift lives of people who are down-trodden, forgotten or misbegotten. What can you do to help 80% of the world’s population? Does your plight include lifting many boats or just a few yachts?

“What we do in life echoes in eternity” (Attributed to Maximus Decimus Meridius)



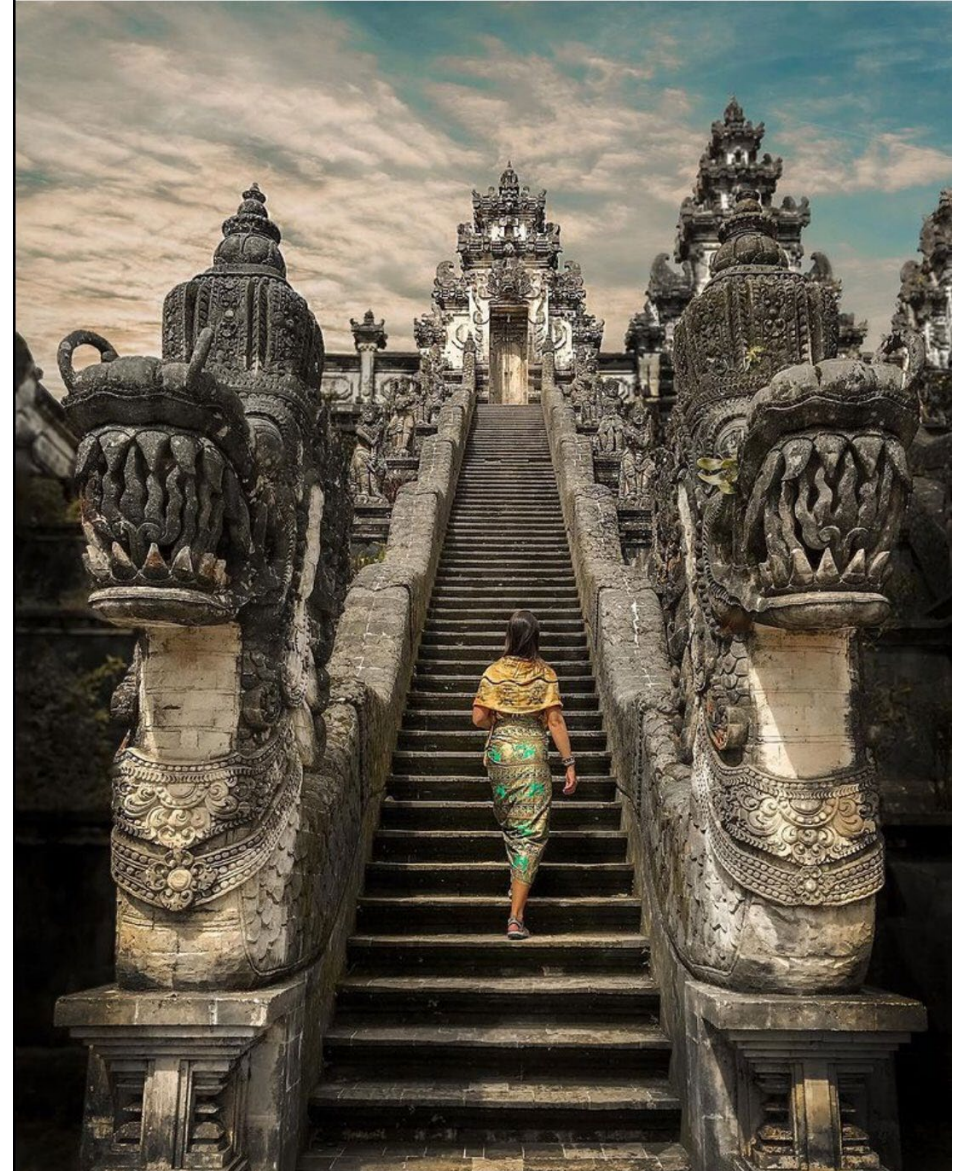
The child ever dwells in the mystery
of an ageless time
unobscured by the dust of history.

"Nobody has the power to take two steps together; you can take only one step at a time."



Build back better

Shoumen Palit Austin Datta



<https://www.youtube.com/watch?v=fvM34feO7P0>