HEALTHCARE

Principles and Practice of

P_3

Extracting Entrepreneurial Innovation Opportunities for Social Businesses Pursuing Ethical Profitability

Shoumen Palit Austin Datta

Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

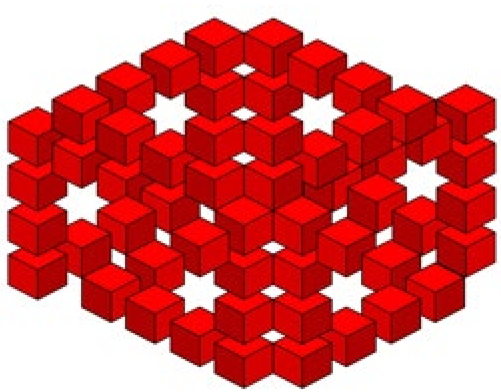
A new report estimates that, as of 2014, MIT alumni have launched 30,200 active companies, employing roughly 4.6 million people, and generating roughly $1.9 trillion in annual revenues.

1989 ● (Department of Medicine) Massachusetts General Hospital, Harvard Medical School

Dr J Larry Jameson MD PhD Molecular Endocrinology & Neuro-Endocrinology Dr Anne Klibanski MD https://dspace.mit.edu/handle/1721.1/111021

Review "IoT is a Metaphor"

Medical IoT



Dr Shoumen Palit Austin Datta

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

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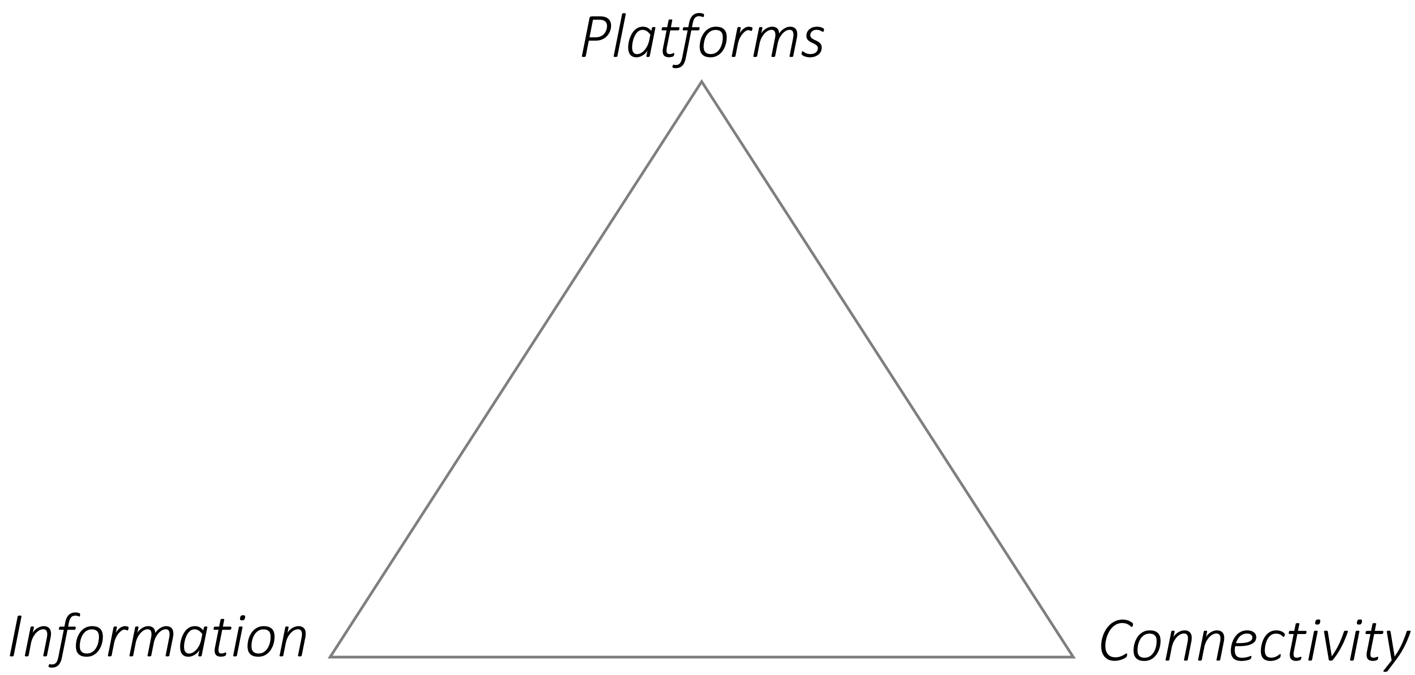
Platforms are indivisible but better understood if discussed as

Platform as a Principle = Information

Platform as a Practice = Connectivity



Information

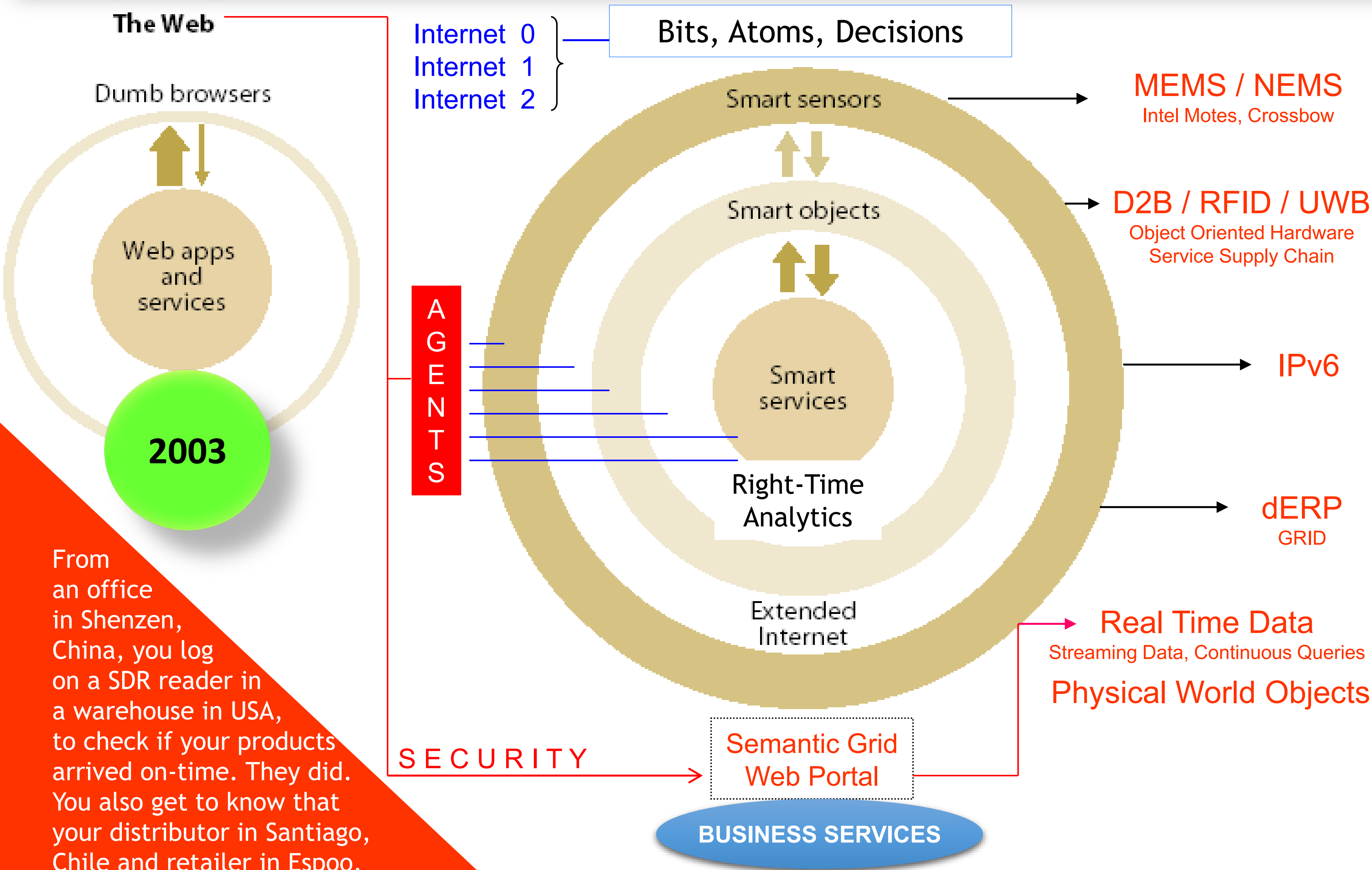
The Information Age is not over. It started with the Big Bang which created the Solar System and it may persist *ad infinitum* as long as the Solar System continues its physical existence. It is the mother of all platforms and the most fundamental fabric of connectivity. Our understanding of the difference 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 which died prematurely vs the almost identical Palm Pilot that once climbed the luminous summit. Information changes when the car you are driving is suddenly crushed in a collision with a truck. 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. Information has grown. 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.

Platform as a Practice

Connectivity

Is it a new theme? Isn't it fundamentally pervasive in every entity – physical, metaphysical and cyberphysical? Doesn't it transcend 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 neuromorphic quantum dots are 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 which is hiding in plain sight. This series highlights some of these old ideas.

Integrating Ubiquitous Analytics in Real-Time with Data, Information, Application



From an office in Shenzen, China, you log on a SDR reader in a warehouse in USA, to check if your products arrived on-time. They did. You also get to know that your distributor in Santiago, Chile and retailer in Espoo, Finland also checked the delivery status, moments before you logged on.

SDR Data Interrogators as Ubiquitous Internet Appliances in IoT (2003)

Industrial Internet vs Consumer Internet

Jeff Immelt, GE Minds & Machines conference, San Francisco, Nov. 2012

Tim Cook, Apple Special Event, San Francisco, Sept 2014

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.

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.

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

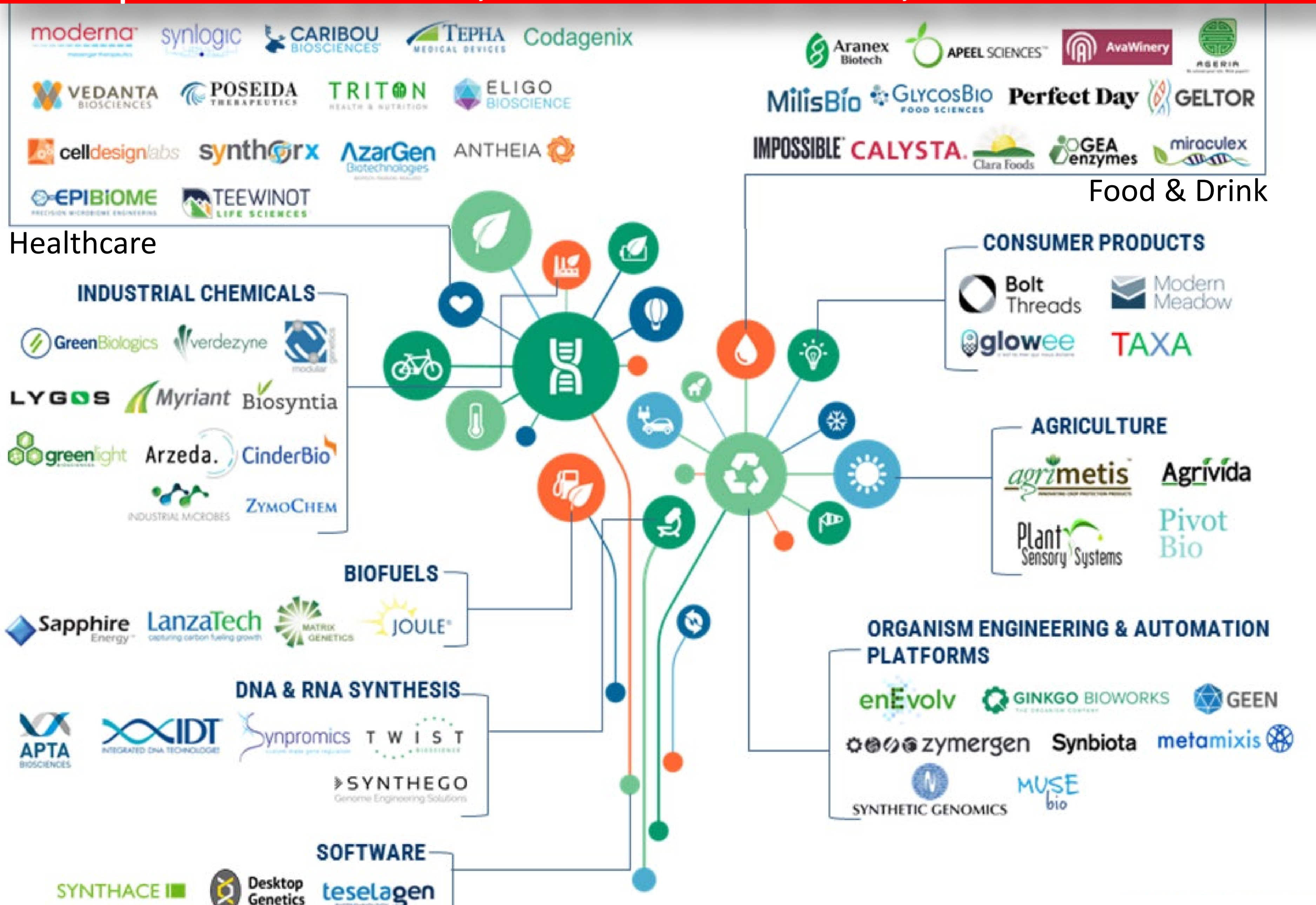
Entirely Different Outcome

Medical IoT

Internet of Systems for Healthcare

MIoT
IoSH

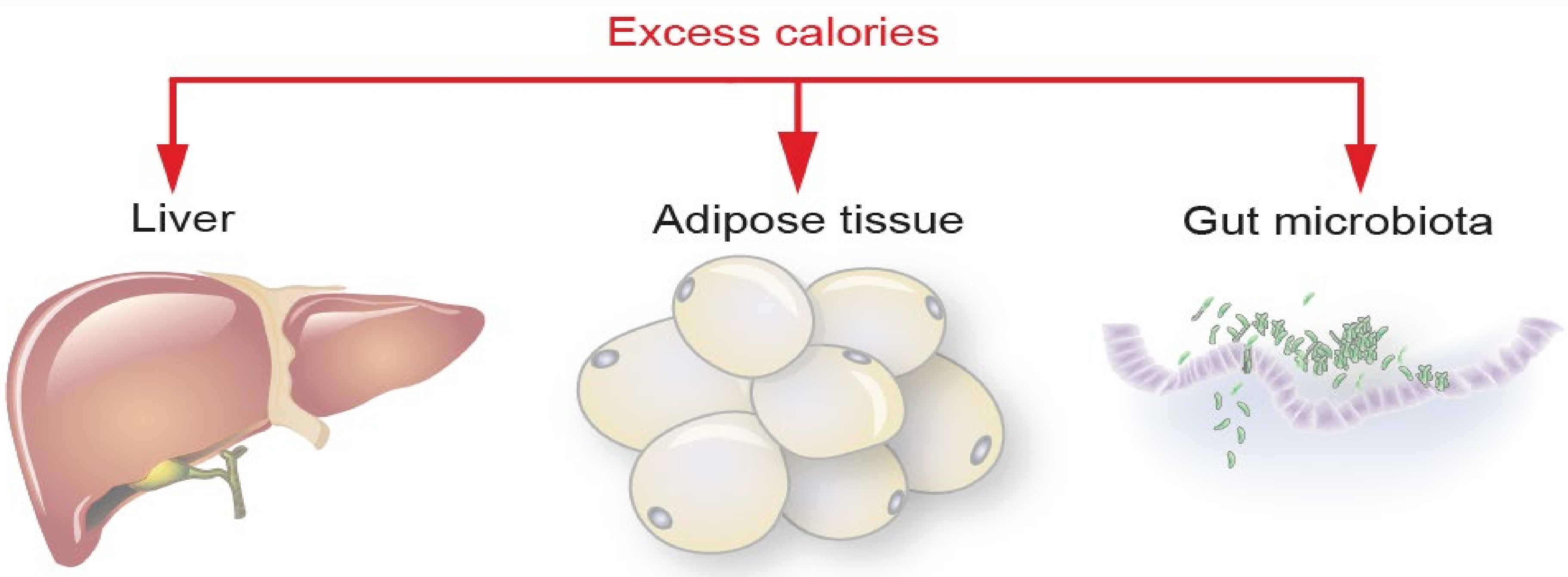
Grapeless Wine, Cowless Milk, Gasless Fuel



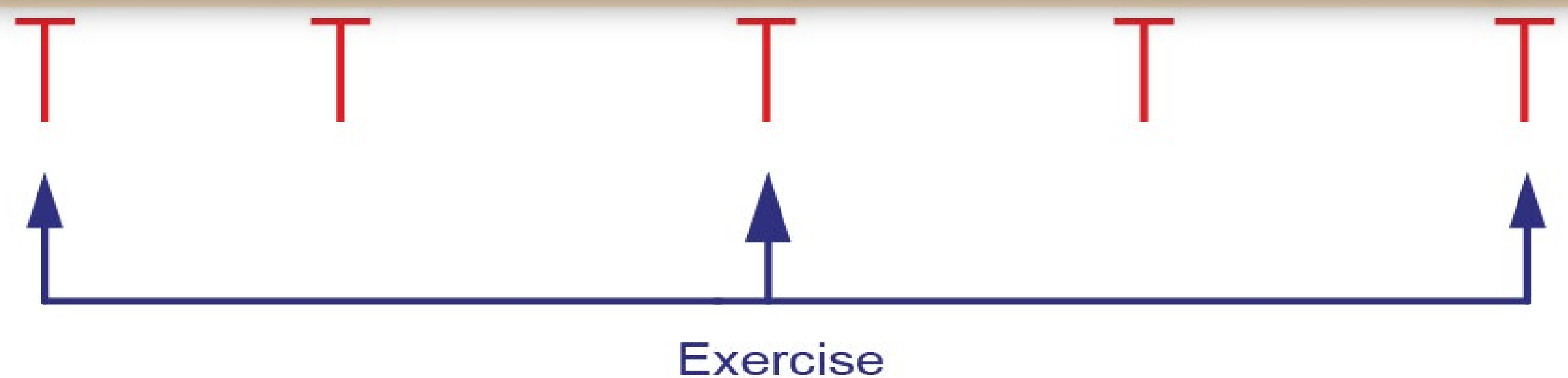
https://www.cbinsights.com/blog/synthetic-biology-startup-market-map fitbit

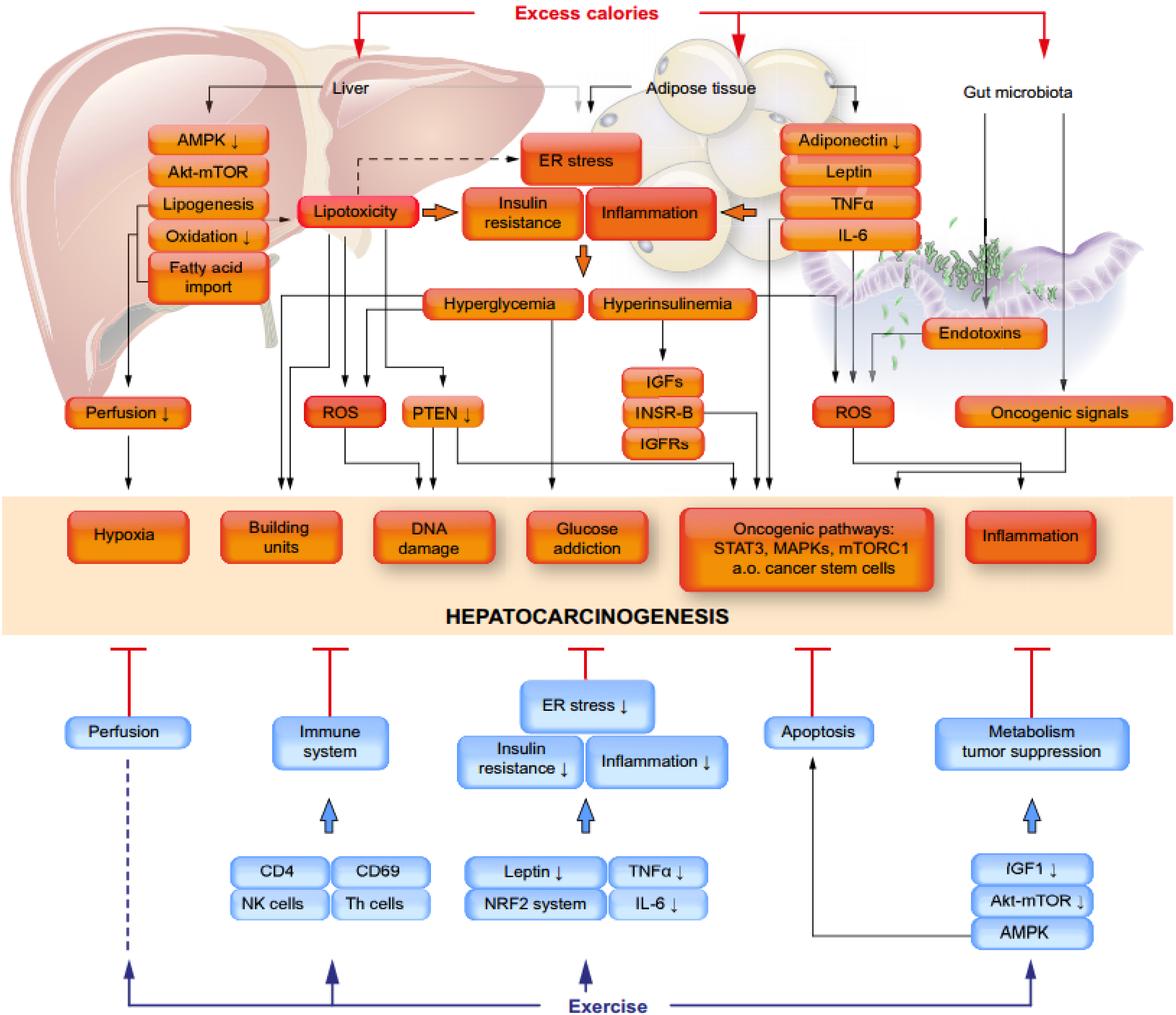
prevents cancer

FitBit's Claim in Cancer Prevention



Cirrhosis-independent effects of exercise in Hepatocarcinogenesis





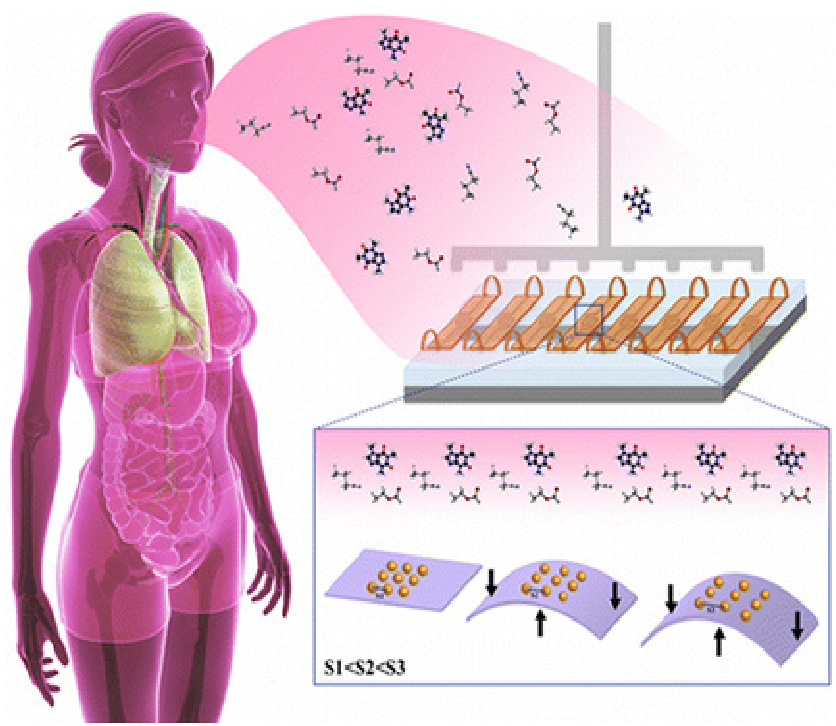
www.journal-of-hepatology.eu/article/S0168-8278(15)00600-5/pdf

Electronic Nose Sniffs Out Ovarian Cancer in Exhaled Breath

OCTOBER 6TH, 2015 EDITORS NANOMEDICINE, ONCOLOGY

MIoT
IoSH

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 Kahn†, Ofer Lavie‡, Moran Paz‡, Yakir 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

*E-mail: hhossam@technion.ac.il.

Malaria Diagnosis Using a Mobile Phone Polarized Microscope

Casey W. Pirnstill & Gerard L. Coté

Scientific Reports **5**, Article number: 13368 (2015)
doi:10.1038/srep13368

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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

http://siteresources.worldbank.org/INTHSD/Resources/topics/Health-Financing/HFRChap7.pdf

ENTREPRENEURS 8/01/2015 @ 7:00AM | 1,215 views

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

President Uhuru Kenyatta of Kenya

+ Comment Now

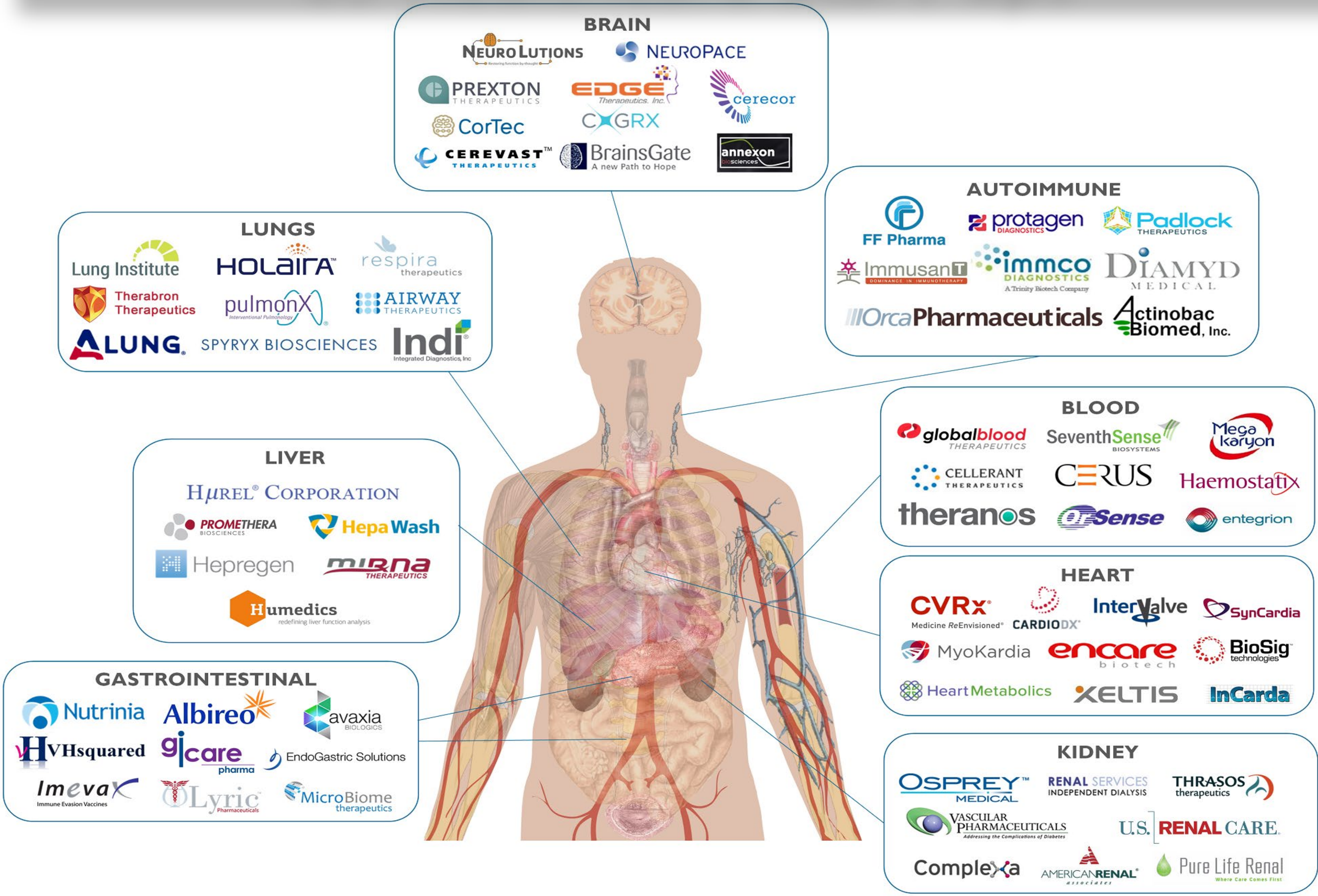
In Sub-Saharan Africa, traditional banking infrastructure has never quite gained a foothold. That's because instead of brick and mortar vaults, the region has seen sweeping use of mobile banking. Microfinancing and transfers, all from your cell phone, offered simplified, safer banking solutions for a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

http://onforb.es/1IQ1pSQ

69 Healthcare Start-ups



80/20

US consumes 40% (approx) of the world's total financial resources for healthcare. The remaining OECD nations consume 40%.

Total global expenditure for health[1]	US$ 6.5 trillion
Total global expenditure for health per person per year	US$ 948
Country with highest total spending per person per year on health	United States (US$ 8362)
Country with lowest total spending per person per year on health	Eritrea (US$ 12)
Country with highest government spending per person per year on health	Luxembourg (US$ 6906)
Country with lowest government spending per person per year on health	Myanmar (US$ 2)
Country with highest annual out-of-pocket household spending on health	Switzerland (US$ 2412)
Country with lowest annual out-of-pocket household spending on health	Kiribati (US$ 0.2)
Average amount spent per person per year on health in countries belonging to the Organisation for Economic Co-operation and Development (OECD)	US$ 4380
Percentage of the world's population living in OECD countries	18% ← 20
Percentage of the world's total financial resources devoted to health currently spent	84% ← 80

www.who.int/mediacentre/factsheets/fs319/en/

US Abhors Low Cost Healthcare Alternatives

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*.

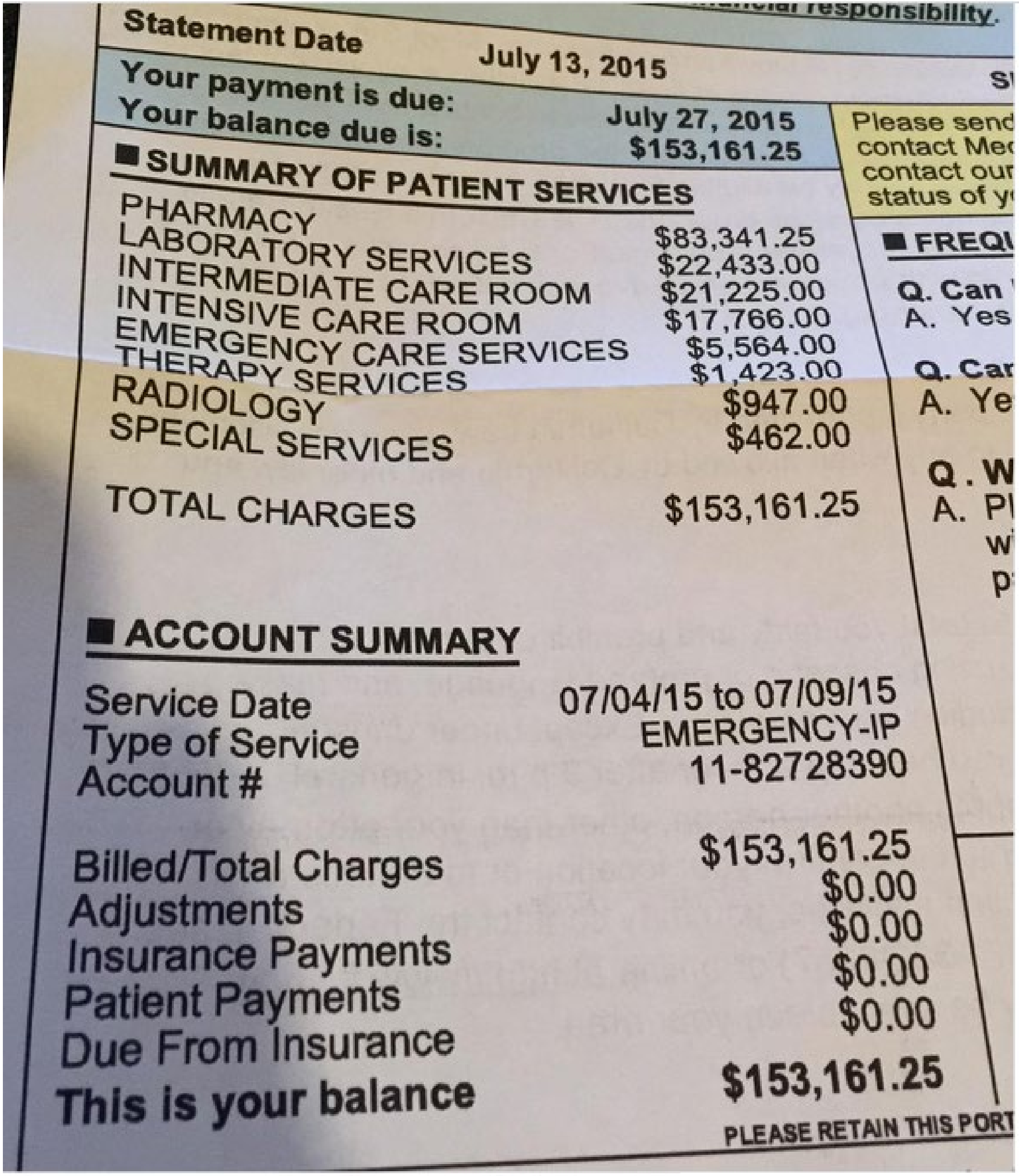
"In the United States, the surest way to generate a healthy return on investment is to increase health care spending, not reduce it," says the authors, from the Uniformed Services University of the Health Sciences and Yale School of Medicine.

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.

This $153,000 rattlesnake bite is everything wrong with

American Healthcare

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



...responsibility.

Statement Date July 13, 2015

Your payment is due: July 27, 2015

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...

Dan Haggerty
@10NewsHaggerty

US AV PER CAPITA INCOME <$55,000

$153,161.25

US Hospital charges for

Treatment Of Snake Bite

$8,694

Median monthly cost in the US of eight cancer drugs

$2,587

Median monthly cost in the UK of the same eight drugs

$2,741

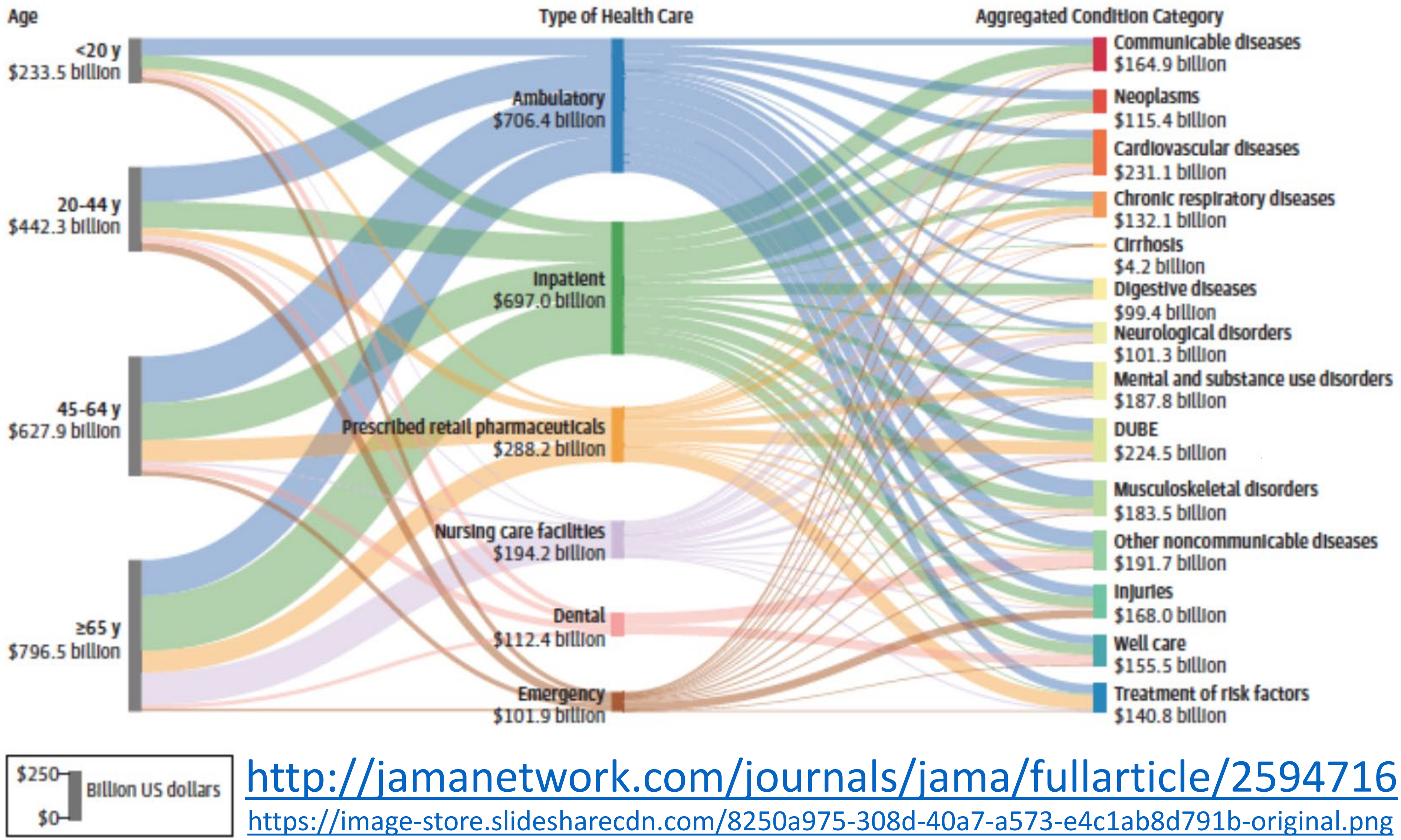
Median monthly cost in Australia of the same drugs

FT

Transaction Cost

example of yet another dimension from Yale Law School

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



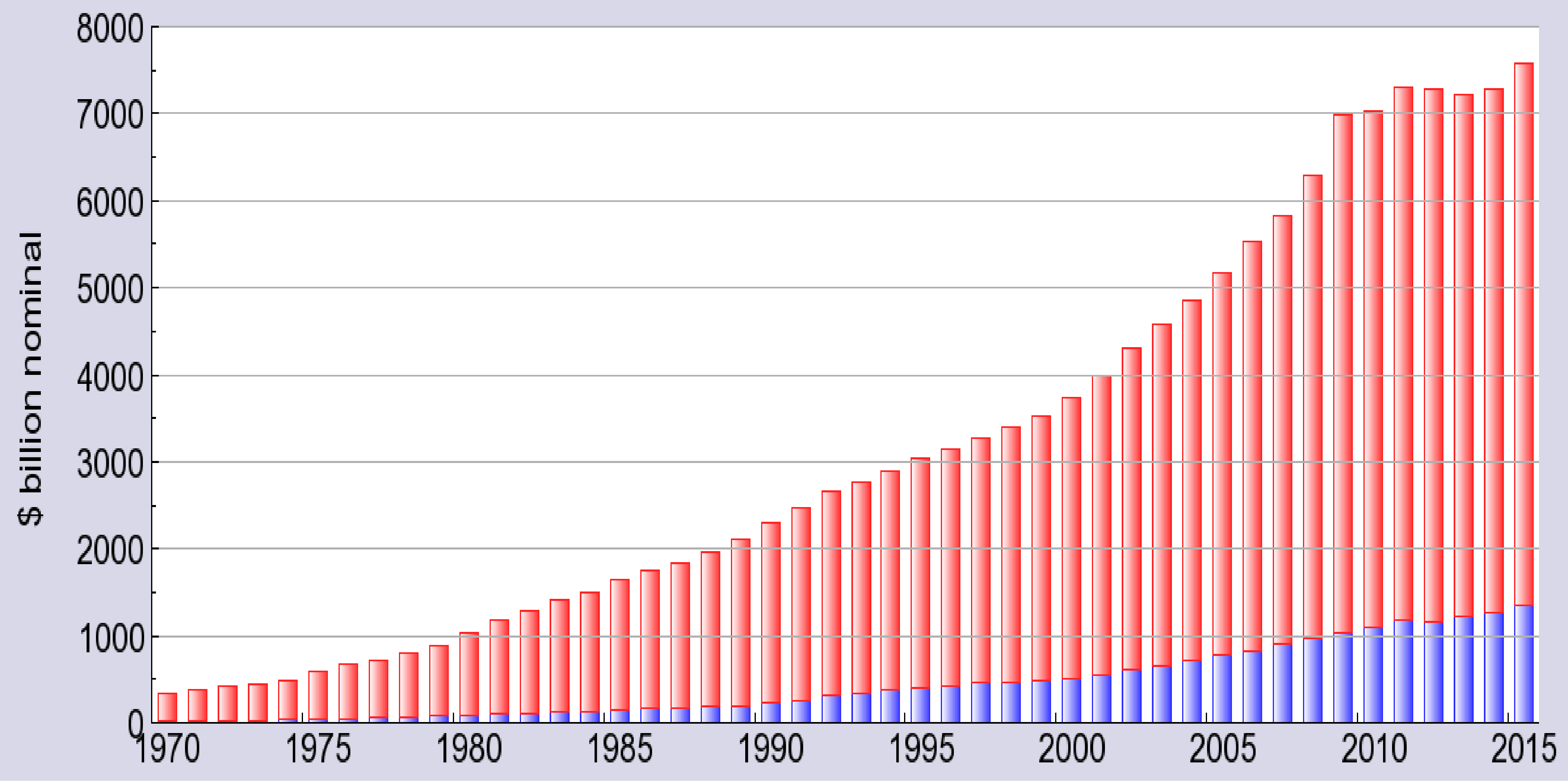
http://jamanetwork.com/journals/jama/fullarticle/2594716

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.

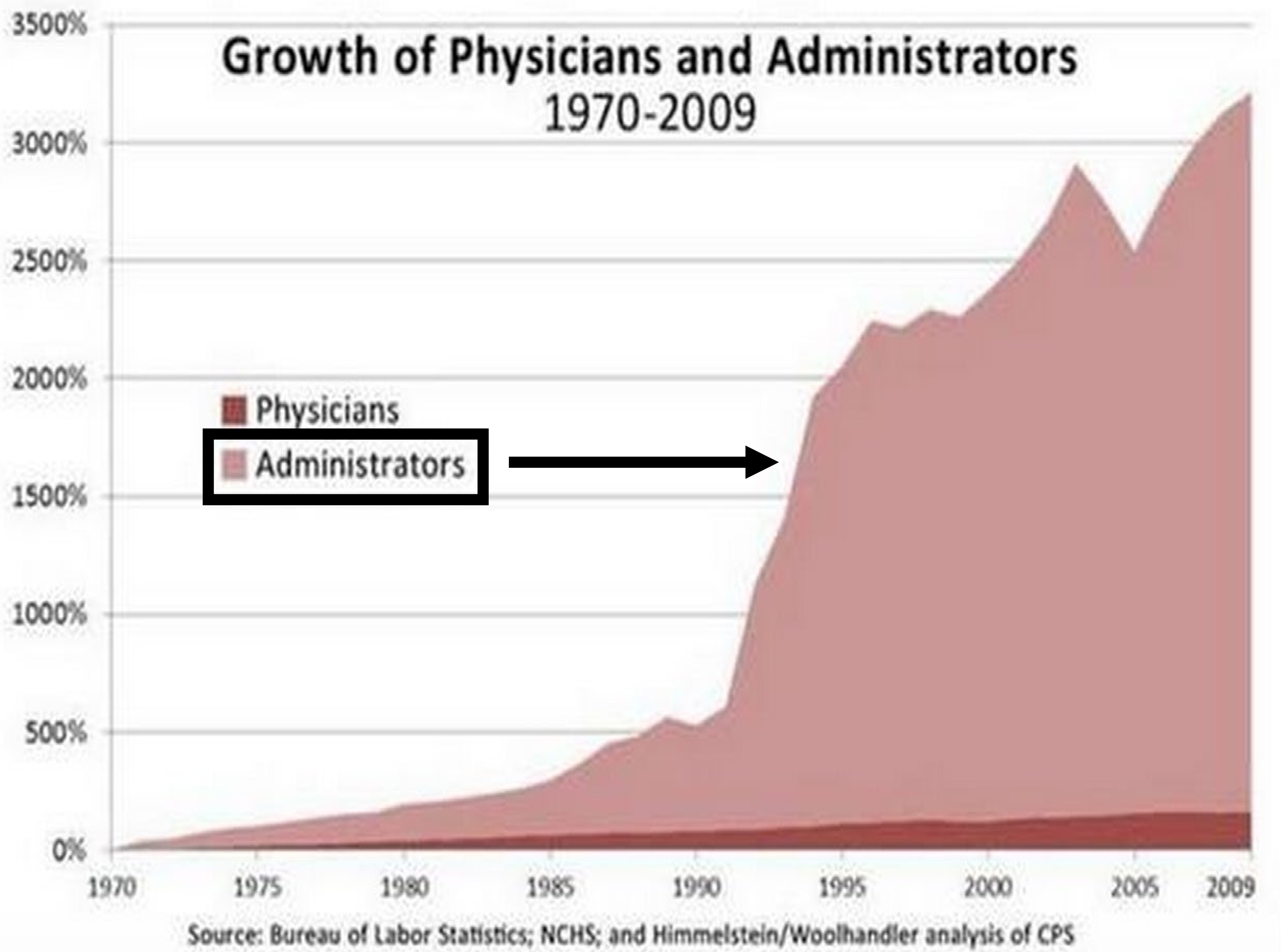
Joseph L. Dieleman, PhD[1]; Ranju Baral, PhD[2]; Maxwell Birger,

TOTAL US HEALTHCARE SPENDING 1970-2015



www.usgovernmentspending.com/spending_chart_1970_2015USb_16s2li111mcn_00tF0t

US healthcare spending explained by **one** word?


Growth of Physicians and Administrators
1970-2009
3500%
3000%
2500%
2000%
1500%
1000%
500%
0%
Physicians
Administrators
1970
1975
1980
1985
1990
1995
2000
2005
2009
Source: Bureau of Labor Statistics; NCHS; and Himmelstein/Woolhandler analysis of CPS


English - detected
Japanese
the greatest good
最大の良いです
Saidai no yoidesu
Open in Google Translate


English - detected
Japanese
the greatest greed
最大の欲
Saidai no yoku
Open in Google Translate

Forbes

EPIC GREED

http://onforb.es/KWJHJF

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.

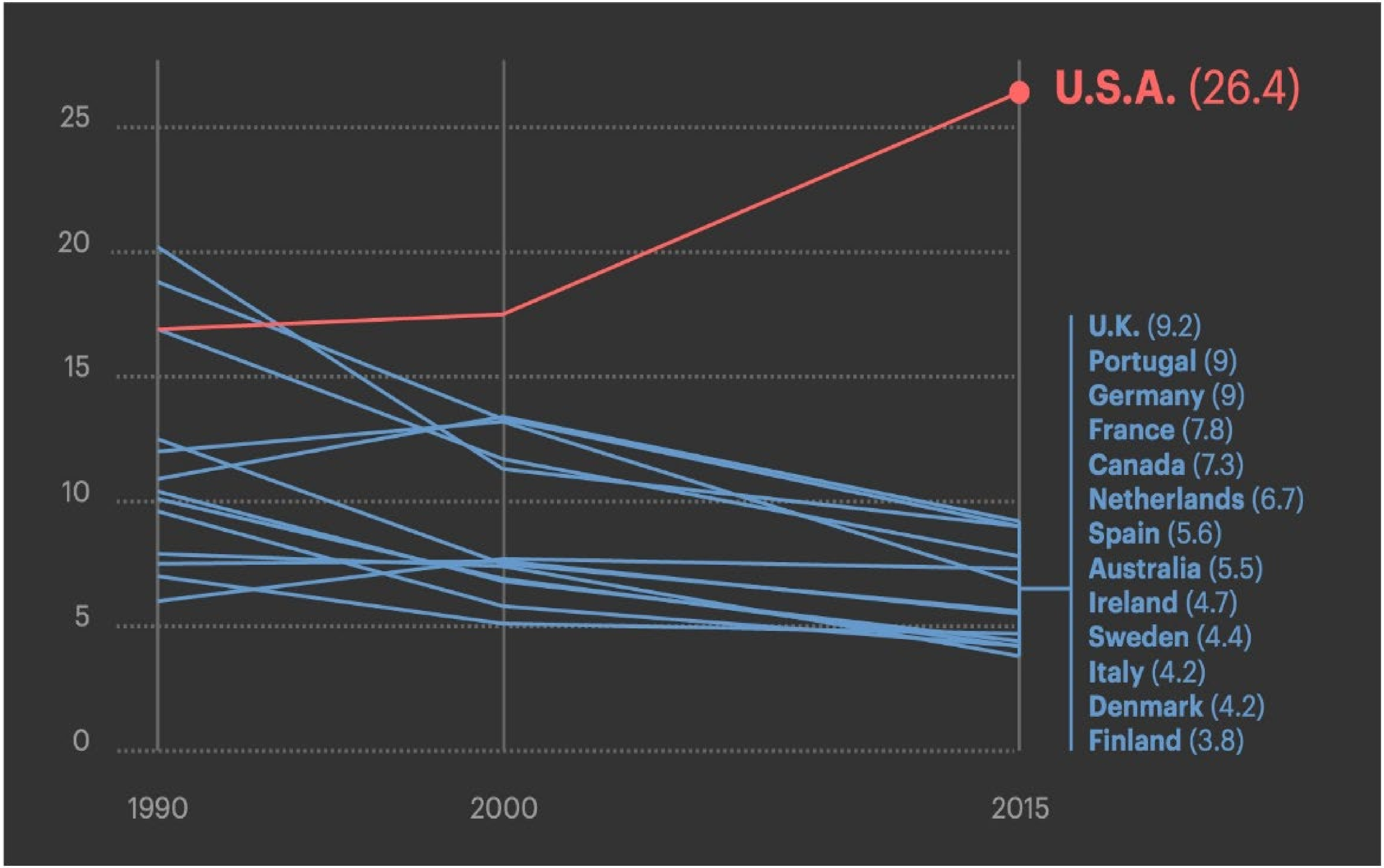
Her not-for-profit clientèle will need every penny of those taxpayers' dollars, but they won't cover anywhere near the staggering cost of an Epic EHR. Duke University Health System will shell out $700 million, so will Boston-based Partners HealthCare; University of California, San Francisco will pay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

$700 million

Healthcare

Let us look elsewhere

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

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

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

CDC

● 2010 ● OIG HHS bad hospital care deaths about <u>180,000</u> patients in Medicare alone in a year

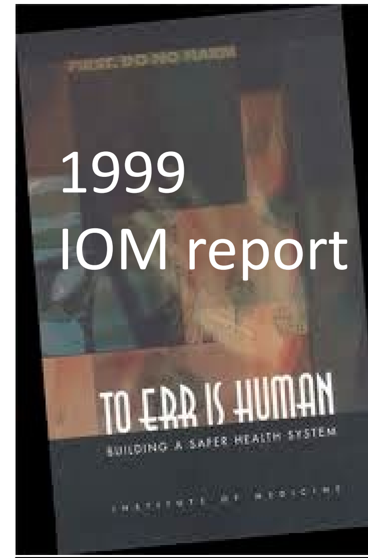
Patient Safety 2013
Exploring Quality of Care in the U.S.

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

Dr Julian Goldman



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

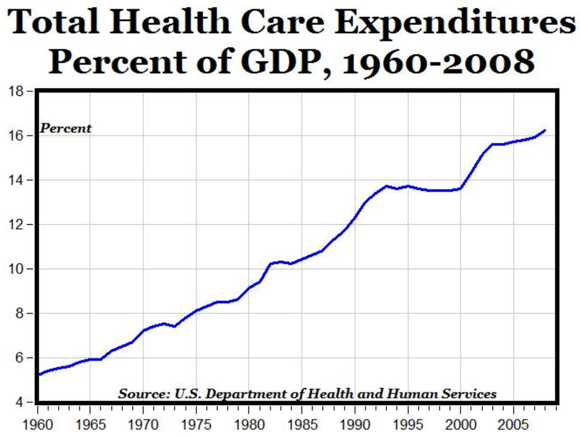
It's a chilling reality – one often overlooked in annual mortality statistics: Preventable medical errors persist as the No. 3 killer in the U.S. – third only to heart disease and cancer – claiming the lives of some 400,000 people each year. At a Senate hearing Thursday, patient safety officials put 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.

Third 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



Equivalent to at least one 747 airplane crash every day

Nurses blame interoperability woes for medical errors

$30B could be saved each year from better device coordination

March 16, 2015

Each year, a staggering 400,000 people are estimated to have died due to medical errors. What's more, each day there's also 10,000 serious complications resulting from medical mistakes. Part of the blame, nurses are saying, can be attributed to the lack of interoperability among medical devices.

MD PnP™

Getting Connected for Patient Safety™

Change Expectations > Change Technology > Change Healthcare

The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program is promoting innovation in patient safety and clinical care by leading the adoption of patient-centric integration of medical devices and IT systems in clinical environments.

Search

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Medical Device "Plug-and-Play" Interoperability Program working on "safe interoperability™" to improve patient safety

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

Most Medical Devices Today
stand alone, unintegrated, not patient-centric

- 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



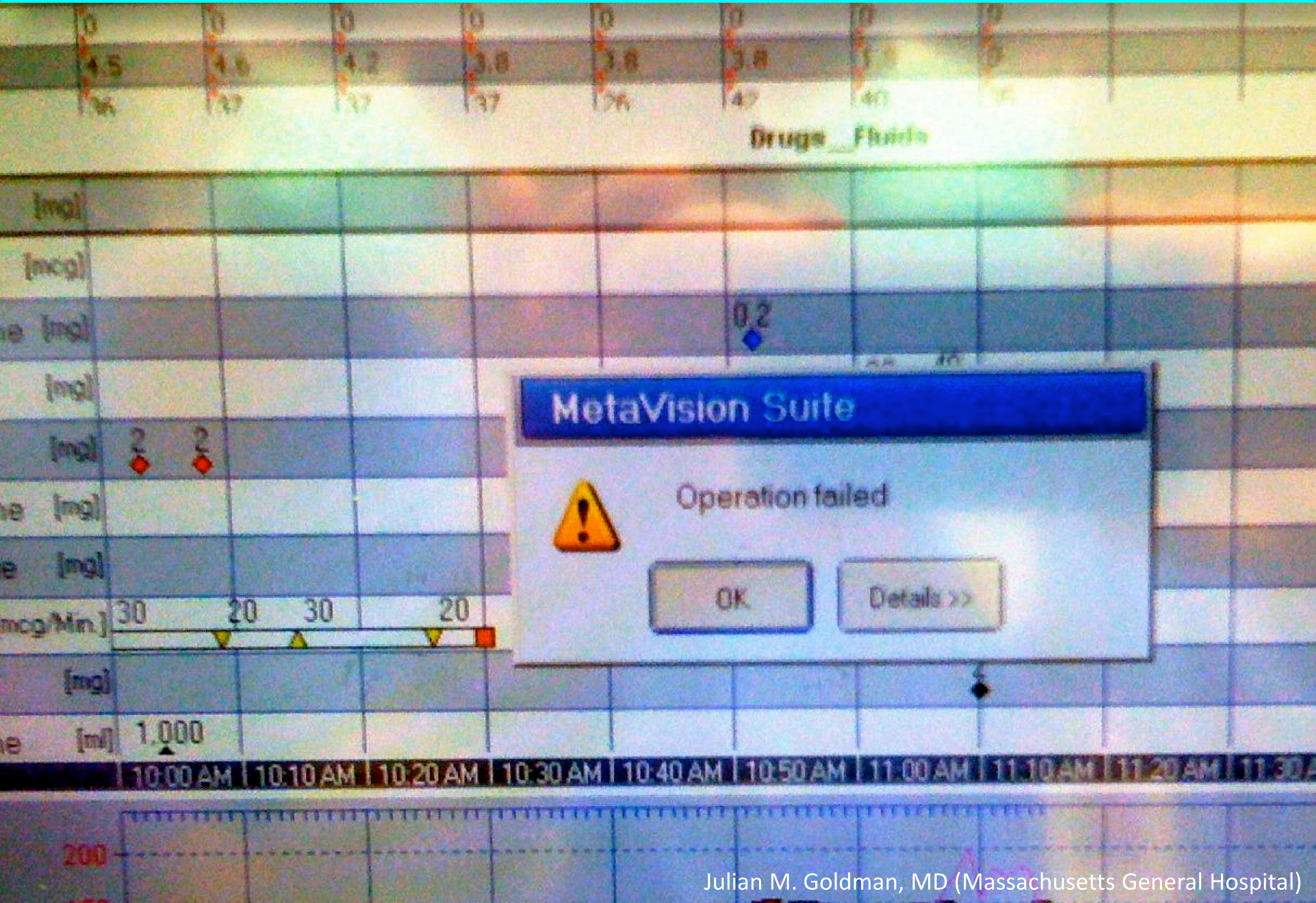






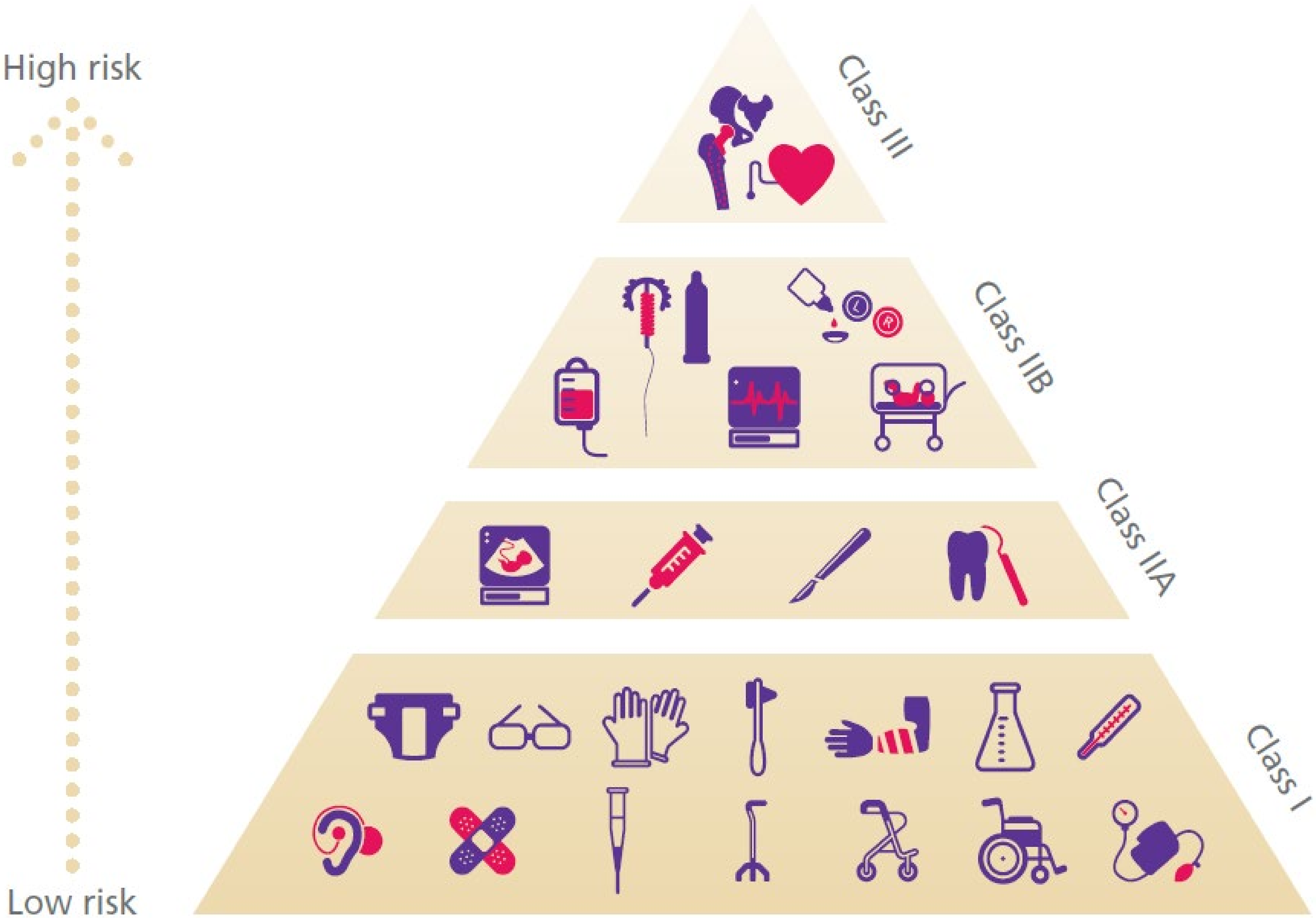


Screen capture from intra-operative EMR during surgery



Julian M. Goldman, MD (Massachusetts General Hospital)

Device Manufacturers Builds Things, not Systems



ONE ? 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

Autonomous Control of Morphine Infusion Pump – Medical Device Integration Model

Infusion Pump

Capnometer

Patient Simulator Ventilator

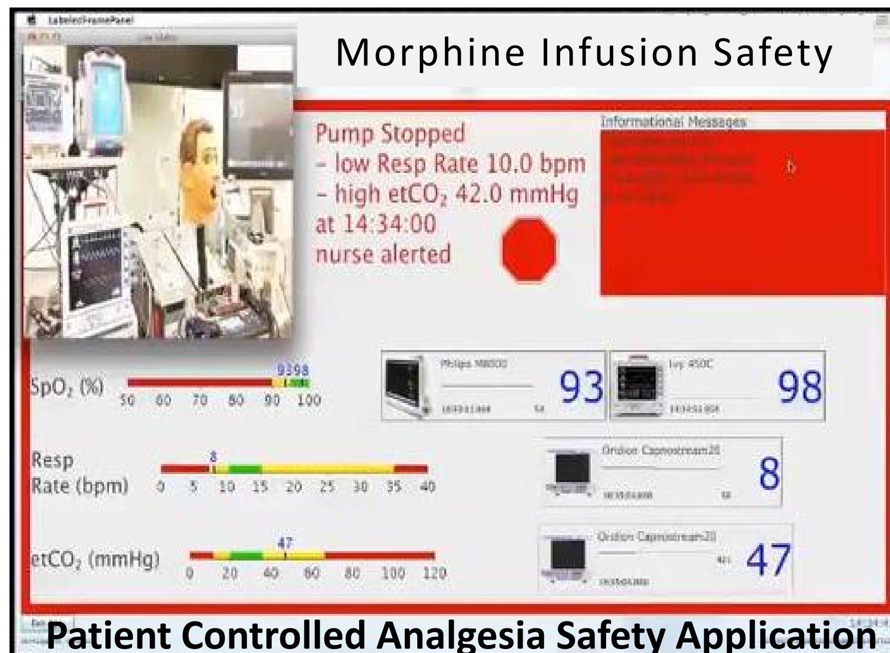
Intelligent Monitor

↓ O_2 Saturation

↓ Respiratory Rate

↑ end-tidal CO_2

Connected Data
Collective Analysis
Automated Response



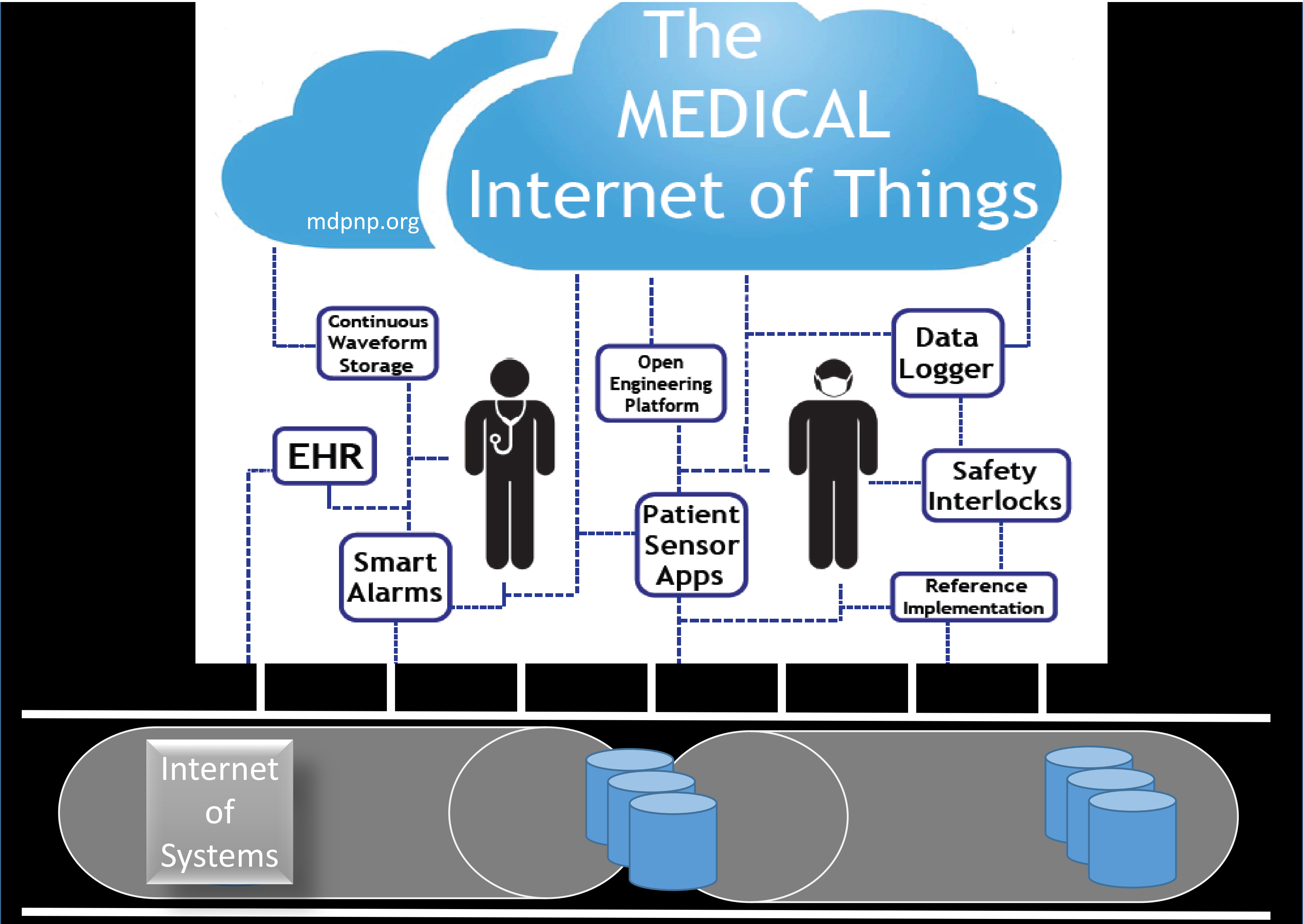
Vital Signs Monitor

Simulator connected to vital signs monitor

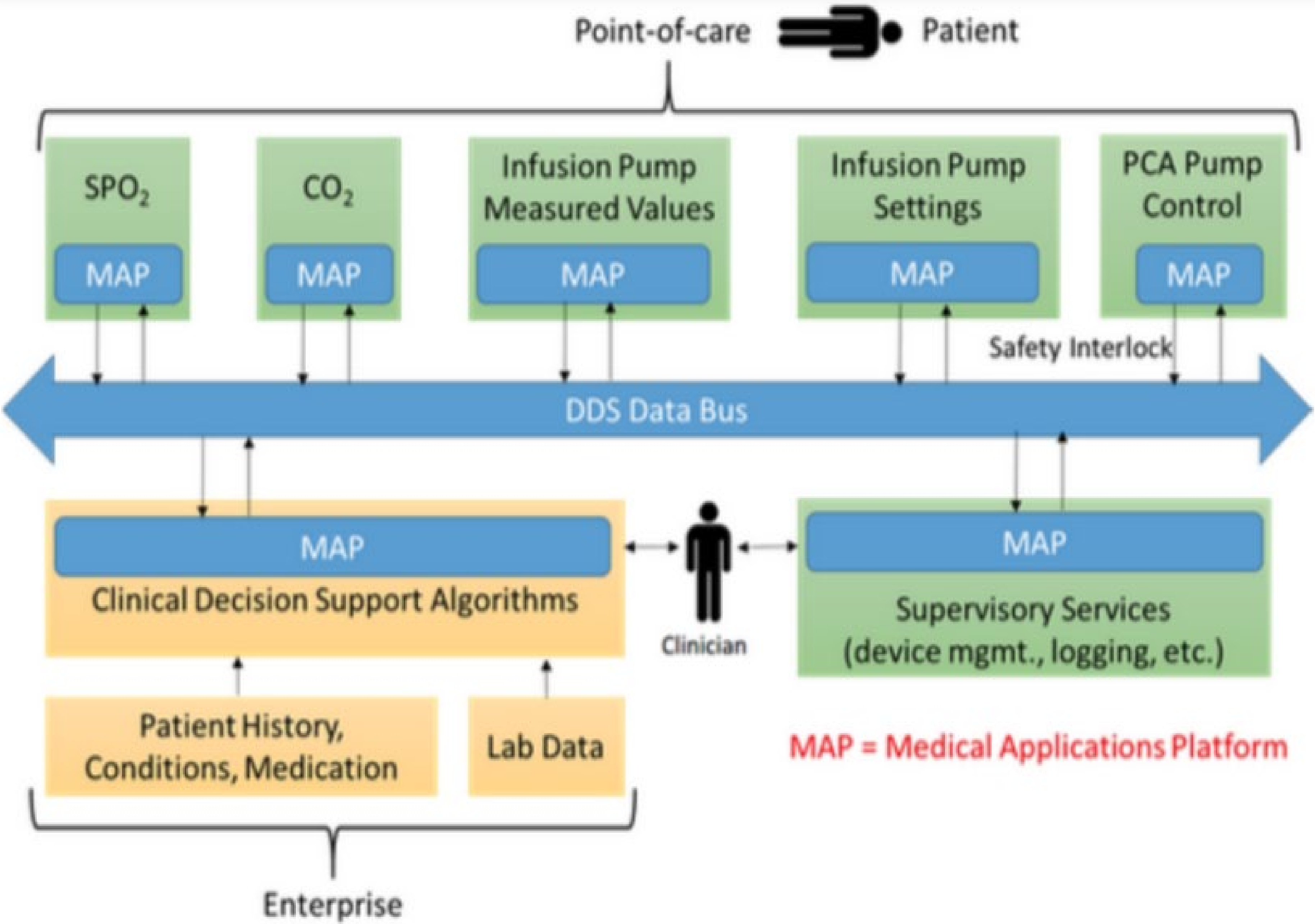
Fluke ProSim 8 connected to intelligent monitor

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

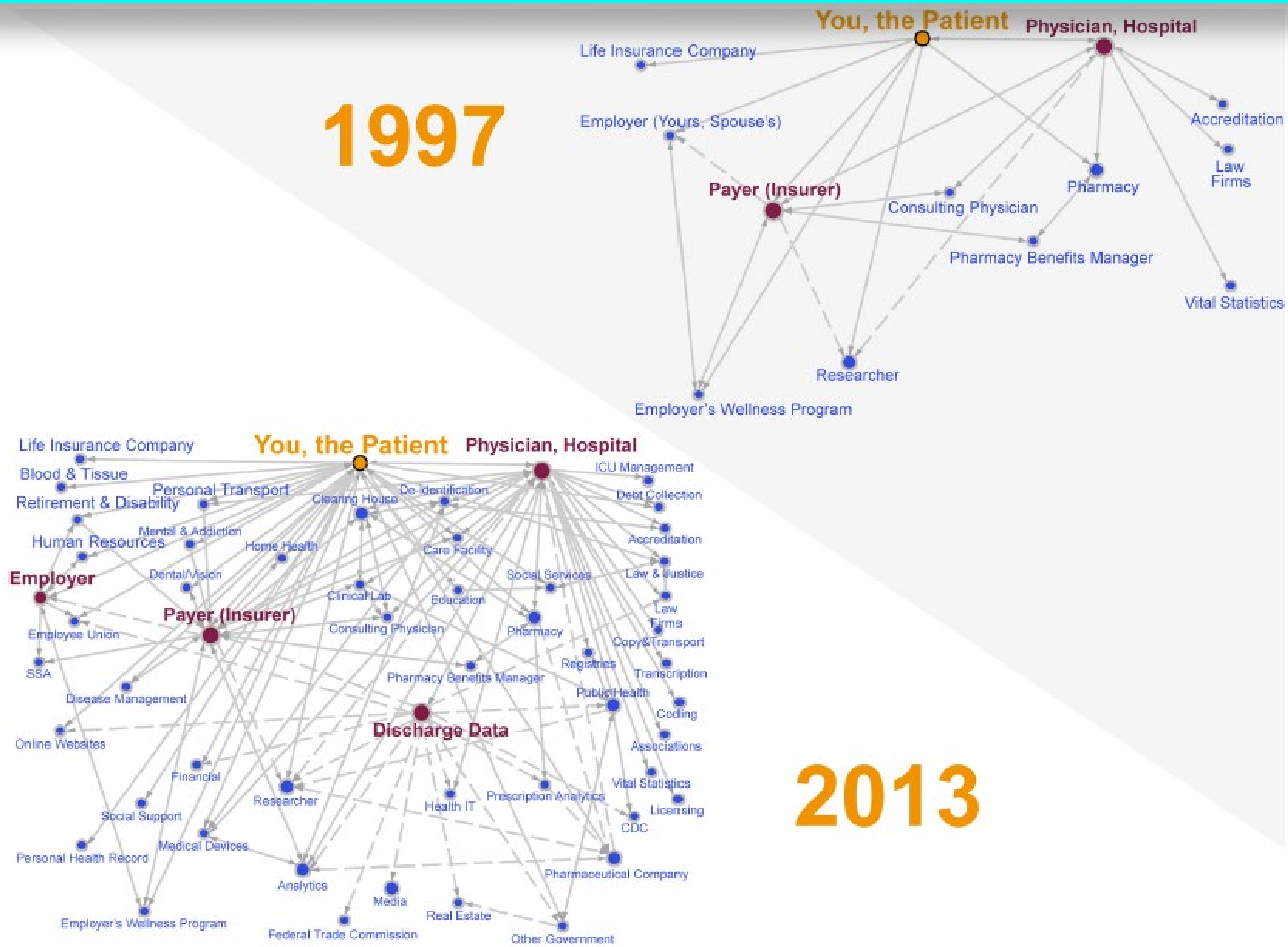
http://pulse.embs.org/november-2014/solving-interoperability-challenge/



Autonomous Control of Morphine Infusion Pump – Medical Device Data Integration



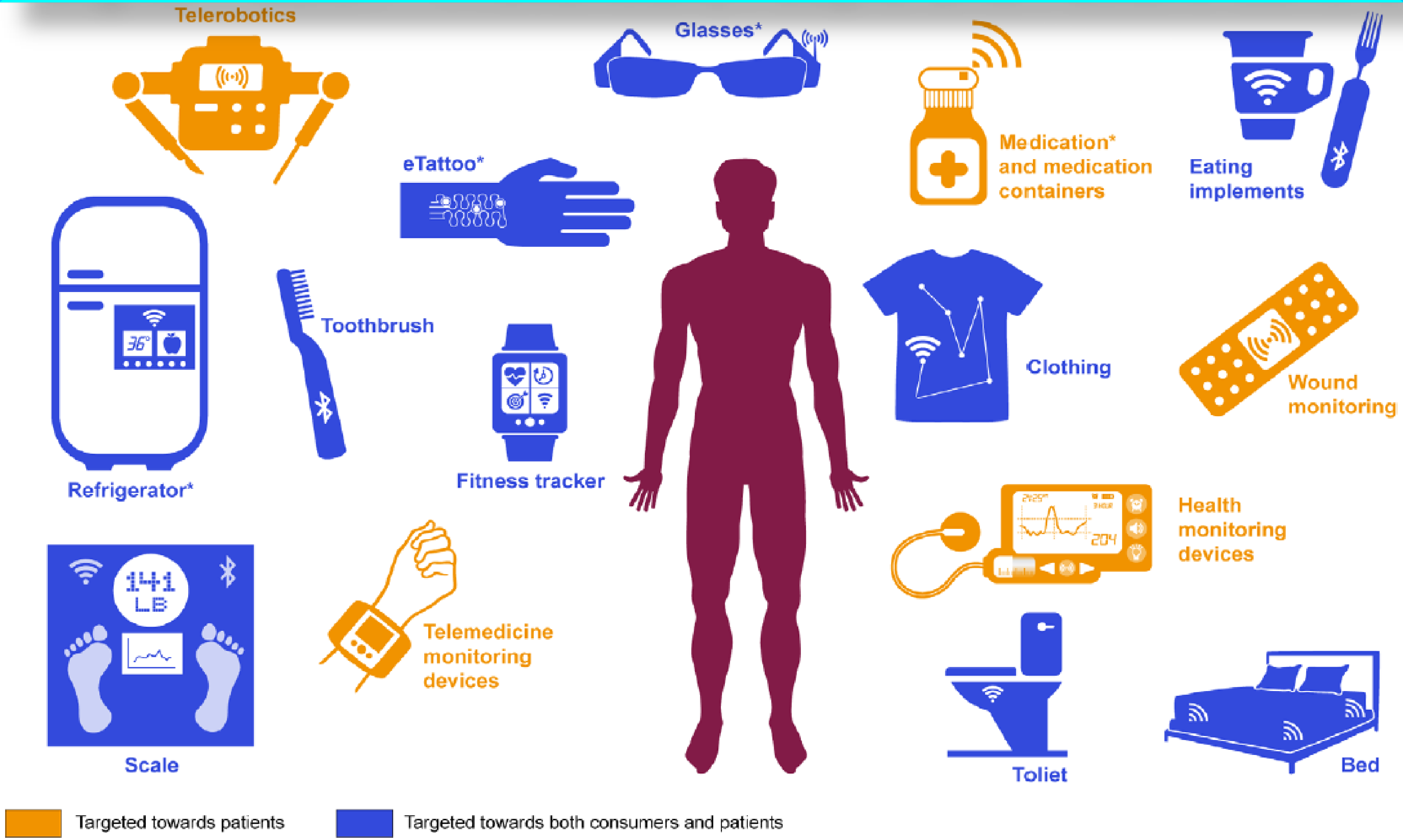
Digital Transformation in Healthcare Data 1997-2013



Source: Adapted from Sweeney, L. 2014. theDataMap. http://thedatamap.org. | GAO-16-659SP

Improve Quality of Care and Reduce Transaction Cost?

Digital Health – Prevention, People and Patient-centric



Critical need in healthcare to reduce transaction cost

Digital Transformation ↑ Patient-centric Healthcare

Healthcare Category	Key drivers of	Potential savings (Dollars in billions)
Innovation	• Accelerating discovery in research a • Improviding trial operations	$40 to $70
Care	• Alignment around proven pathways • Coordinated care across providers	$90 to $110
Provider	• Shifting volume to right care setting • Reducing emergency room/readmit	$50 to $70
Value	• Payment innovation and alignment • Provider-performance transparency	$50 to $100
Lifestyle	• Targeted disease prevention • Data-enabled adherence programs	$70 to $100

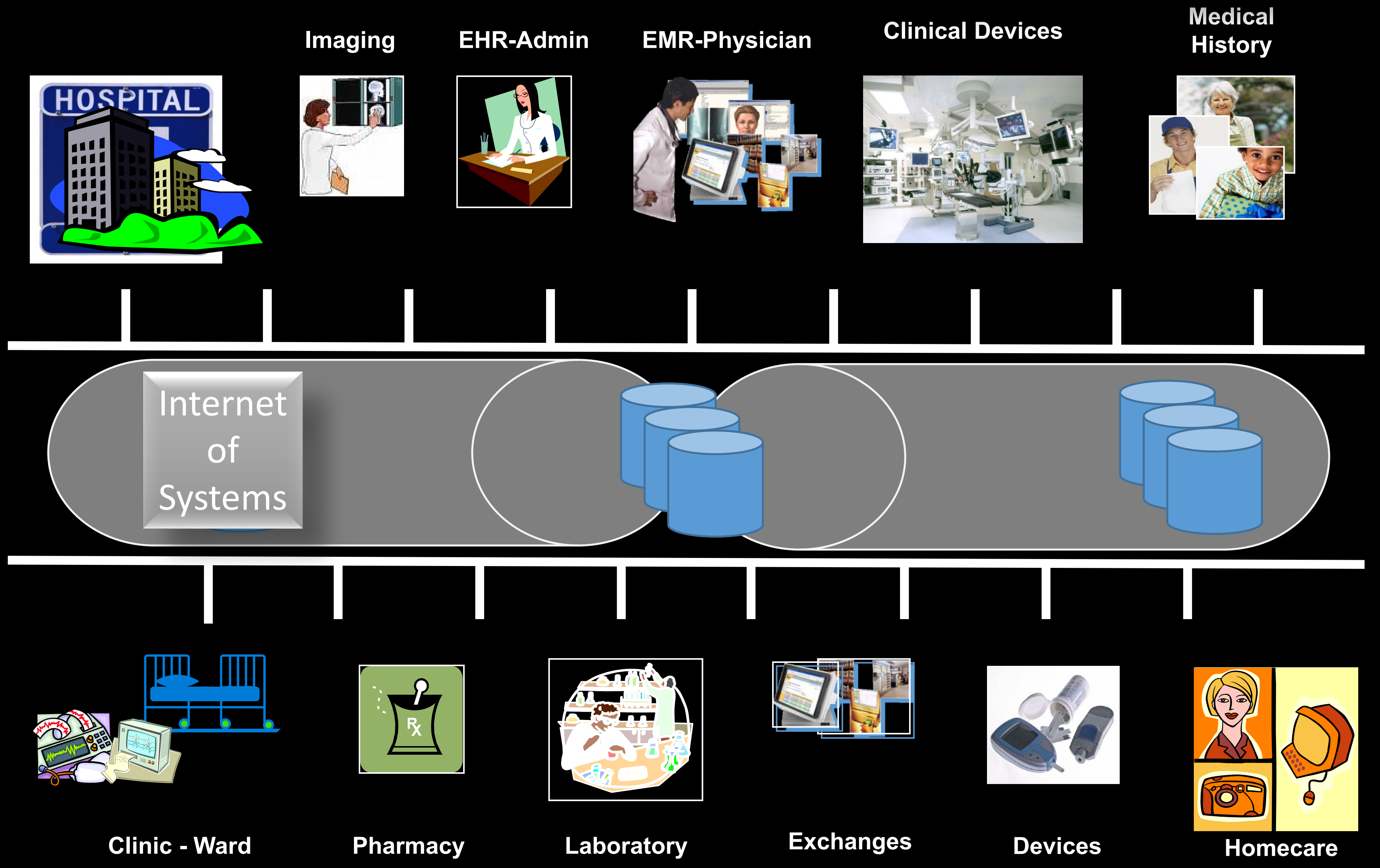
GAO-16-659SP

Potential for savings from reducing transaction costs?

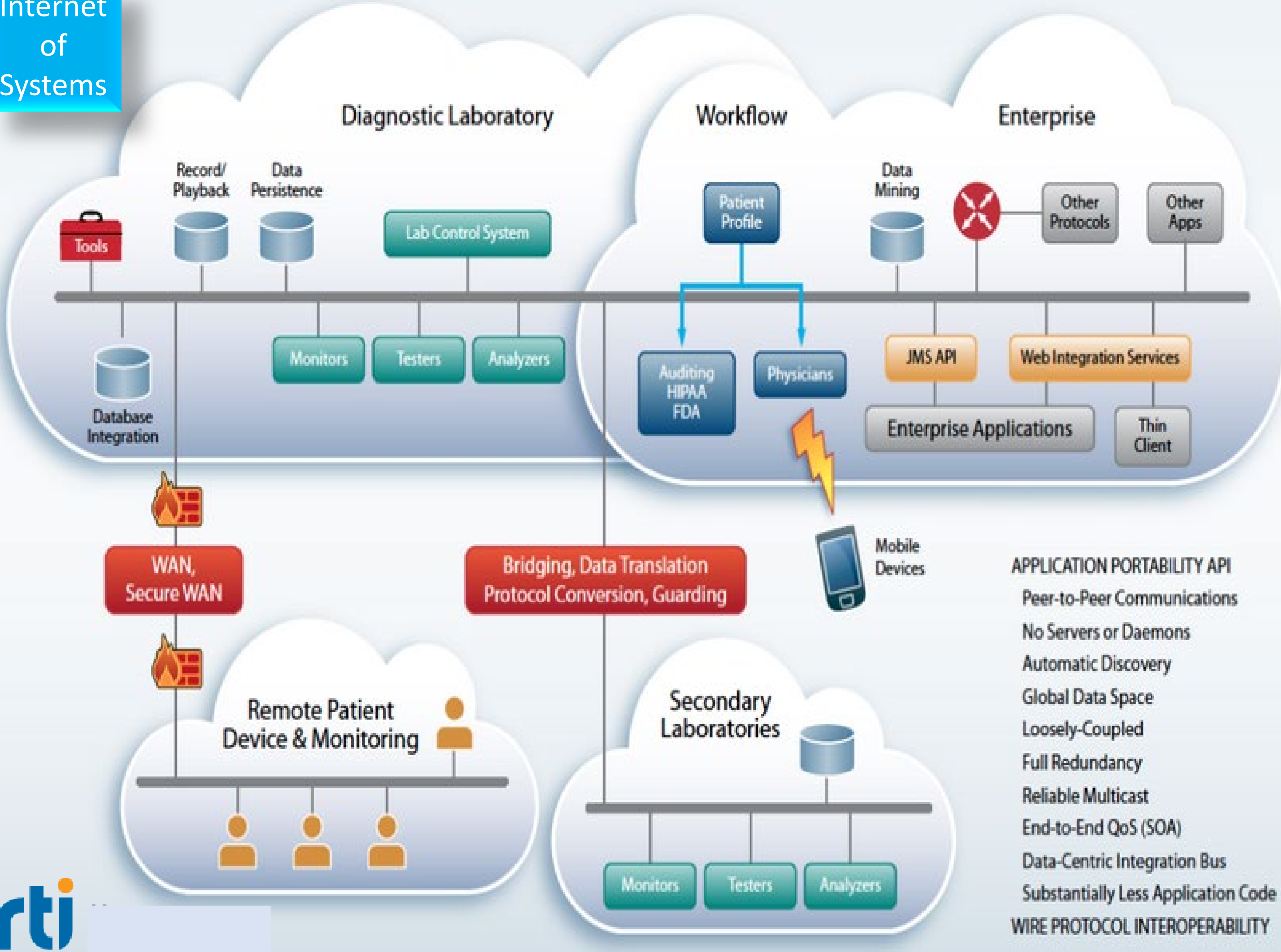
KEY REQUIREMENT

Devices that can serve the masses and an open yet secure platform for interoperability and data fusion

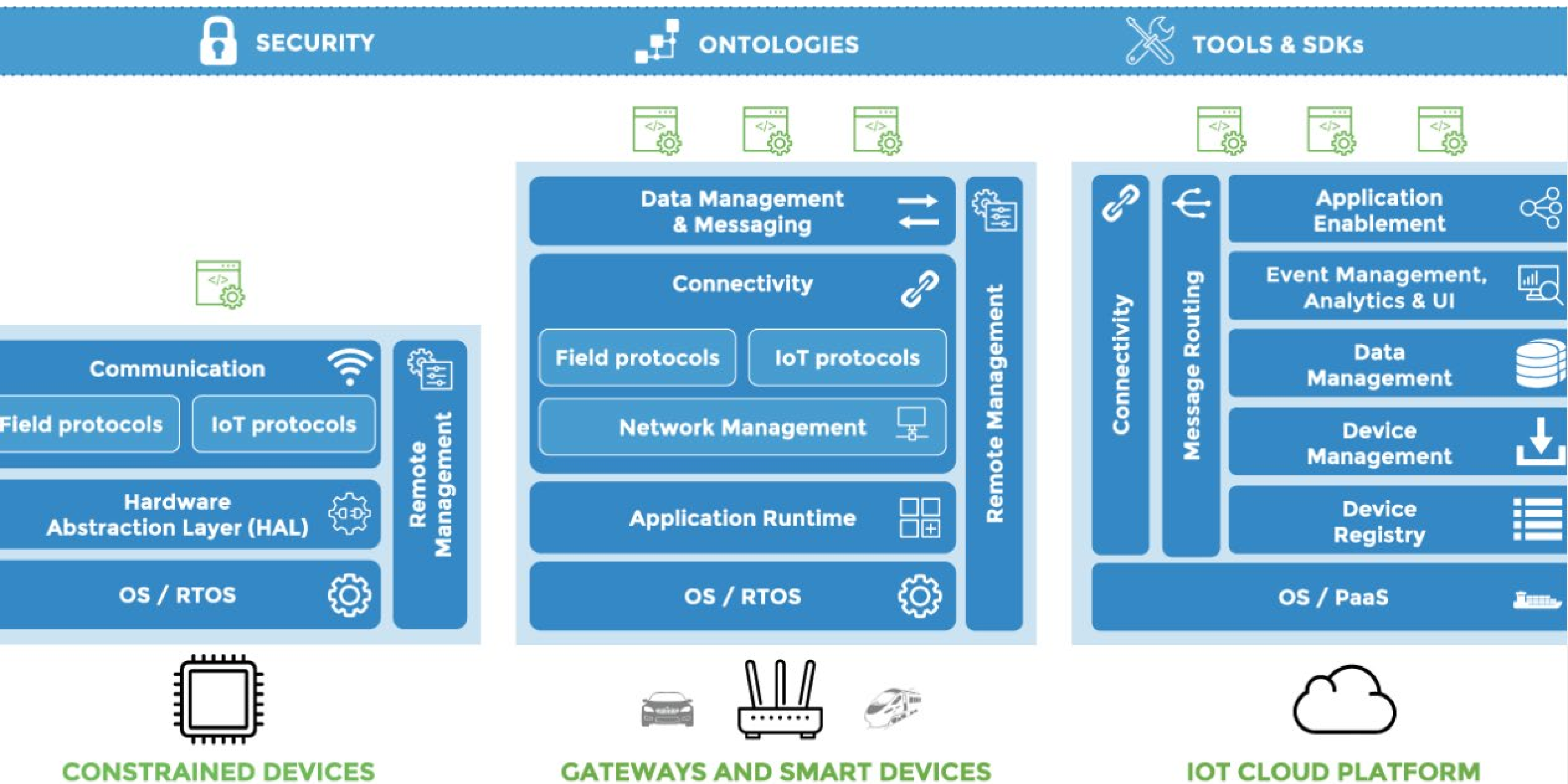
Healthcare Platforms – Integrated Clinical Environment Data Logging & Access via Secure Interoperable Standard



Internet of Systems



Healthcare Middleware – Integrated Clinical Environment
How can we (?) use Open Standard IoT Software as a model ?



PROOF OF CONCEPT

Response to White House Call for Ebola Management

https://vimeo.com/111314176

Need for Integrated Healthcare Platforms?

Ebola spurs rethinking of devices at MGH

By Carolyn Y. Johnson

| GLOBE STAFF NOVEMBER 07, 2014

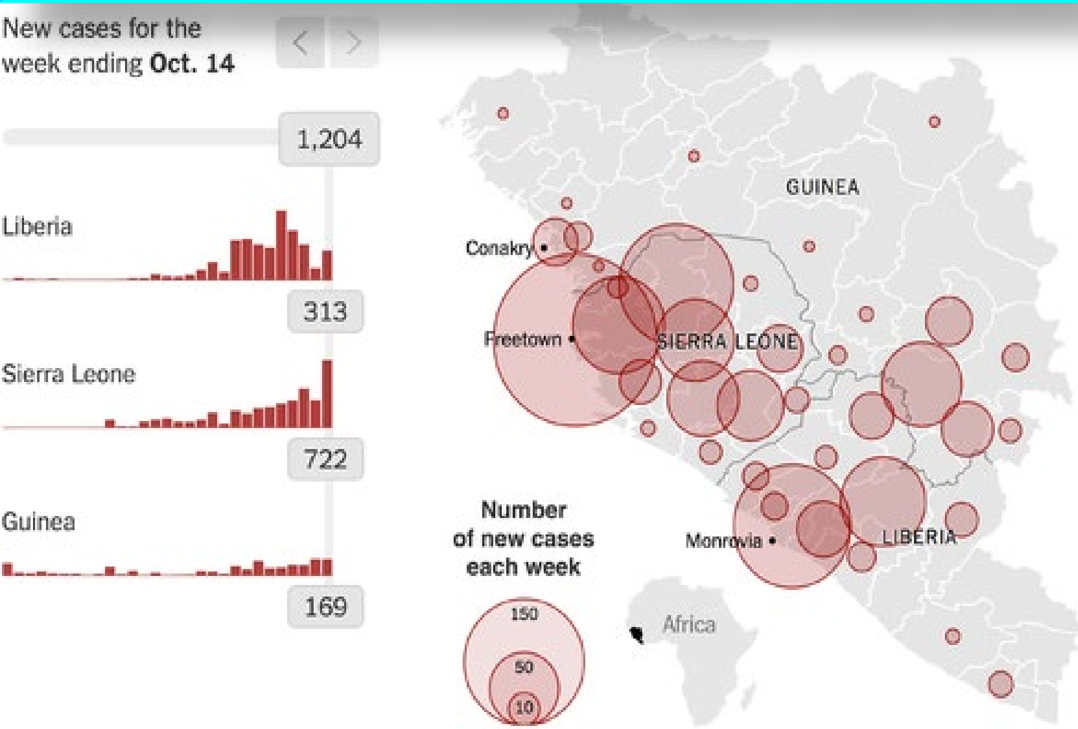
You cannot buy a TV without a remote. You cannot buy a medical device with a remote. Dr Julian M Goldman (MGH/HMS) MD PnP

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.

Robotics Community Responds to Safety of Ebola Workers



Bill and Gerry Brinton of Charles Creek Winery pose with Sonoma Valley Hospital (SVH, CA) CEO Kelly Mather to display the “Lisa” aka the Germ-Zapping Robot manufactured by Xenex (pulsed xenon UV disinfection technology to rapidly reduce germ loads). The Brintons donated the robot to the hospital (SVH).

www.nytimes.com/2014/10/23/science/scientists-consider-repurposing-robots-for-ebola.html?ref=technology

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

www.gereports.com/post/104422691785/hospital-hack-a-thon-attacks-ebola-with-robots

EBOLA

COLLABORATORS

PARTNERS. HEALTHCARE

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

MD PnP™
Getting Connected for Patient Safety™

MGH 1811

HARVARD MEDICAL SCHOOL

smiths medical
bringing technology to life

Lyntek

FCC

FDA
Center for Devices and Radiological Health

IEEE

DOCBOX

Zephyr

COVIDIEN

TATRC

GE Healthcare

RESPIRATORY MOTION INC.
INSPIRED INNOVATION

WPI

PHILIPS

Dräger

intel

IIC MEMBER
industrial internet CONSORTIUM

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~~ Julian,

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.

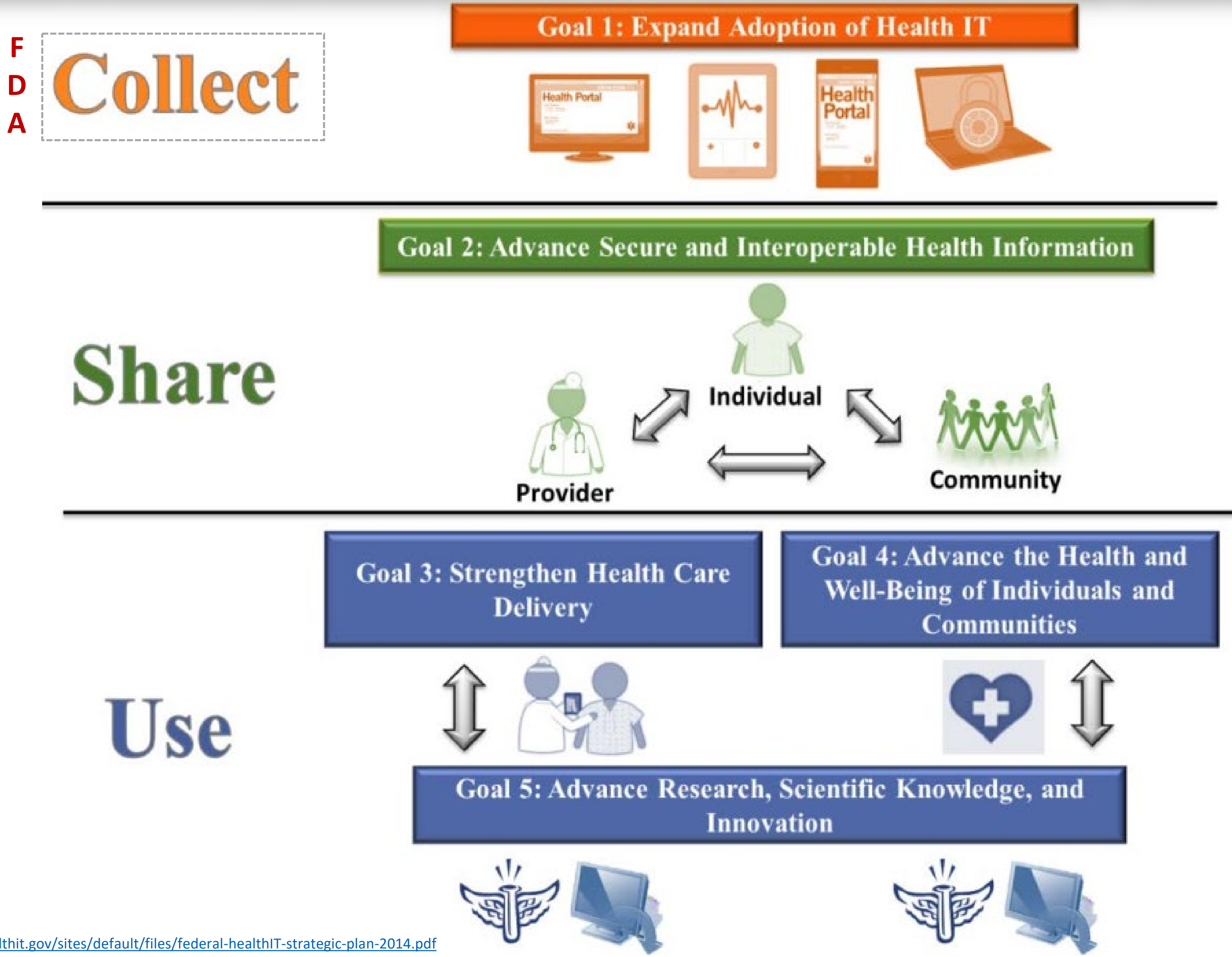
FDA recognizes the importance of implementing strategies that minimize direct exposure of clinical personnel to patients infected with Ebola virus. We understand that MDPNP, along with its collaborators, are developing potential approaches that would include comprehensive data access and potential remote 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,

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

US Federal HIT Goals from the ONC, US HHS



www.healthit.gov/sites/default/files/federal-healthIT-strategic-plan-2014.pdf

Device, data, diagnostics

The Quest for Convergence of Platform and Interoperable Standards

Emmanuelle Charpentier ▪ Jennifer Doudna

UC Berkeley

Berkeley News

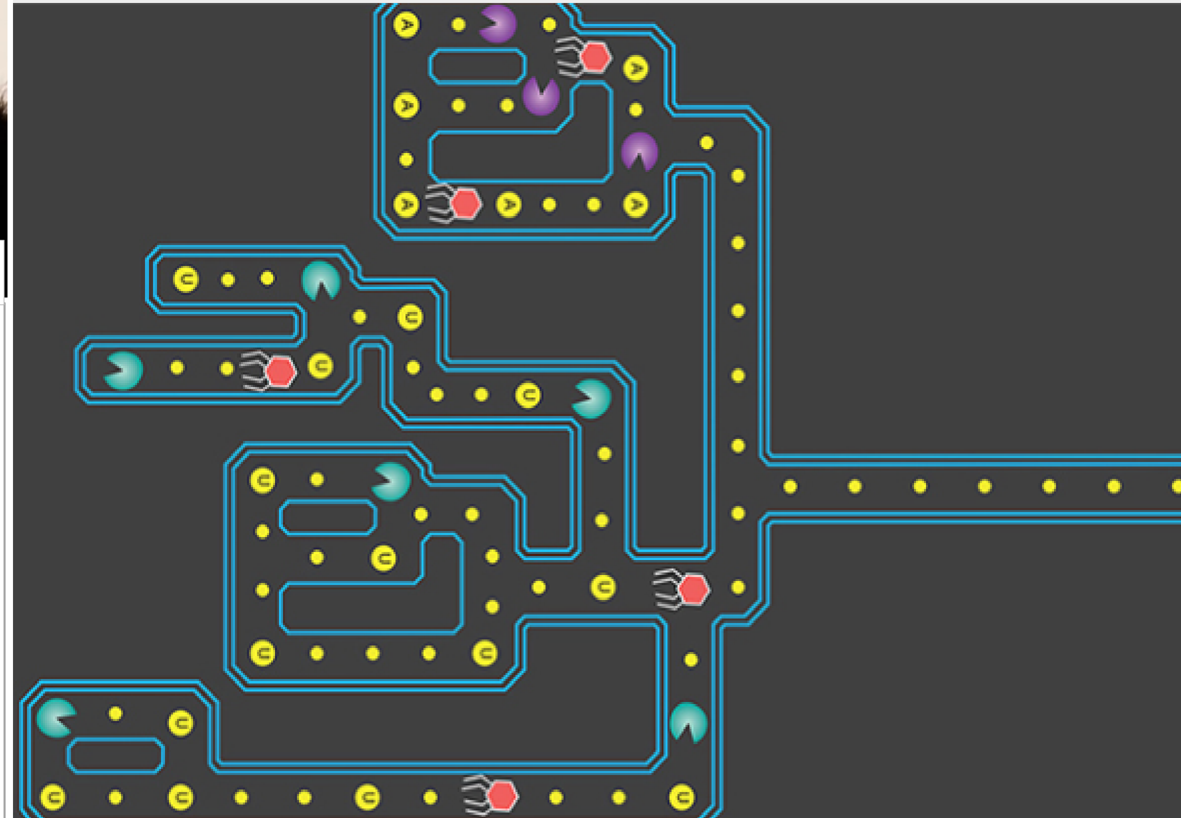
Research ▸ People ▸

AWARDS, PEOPLE

Doudna awarded Japan Prize for invention of CRISPR gene editing

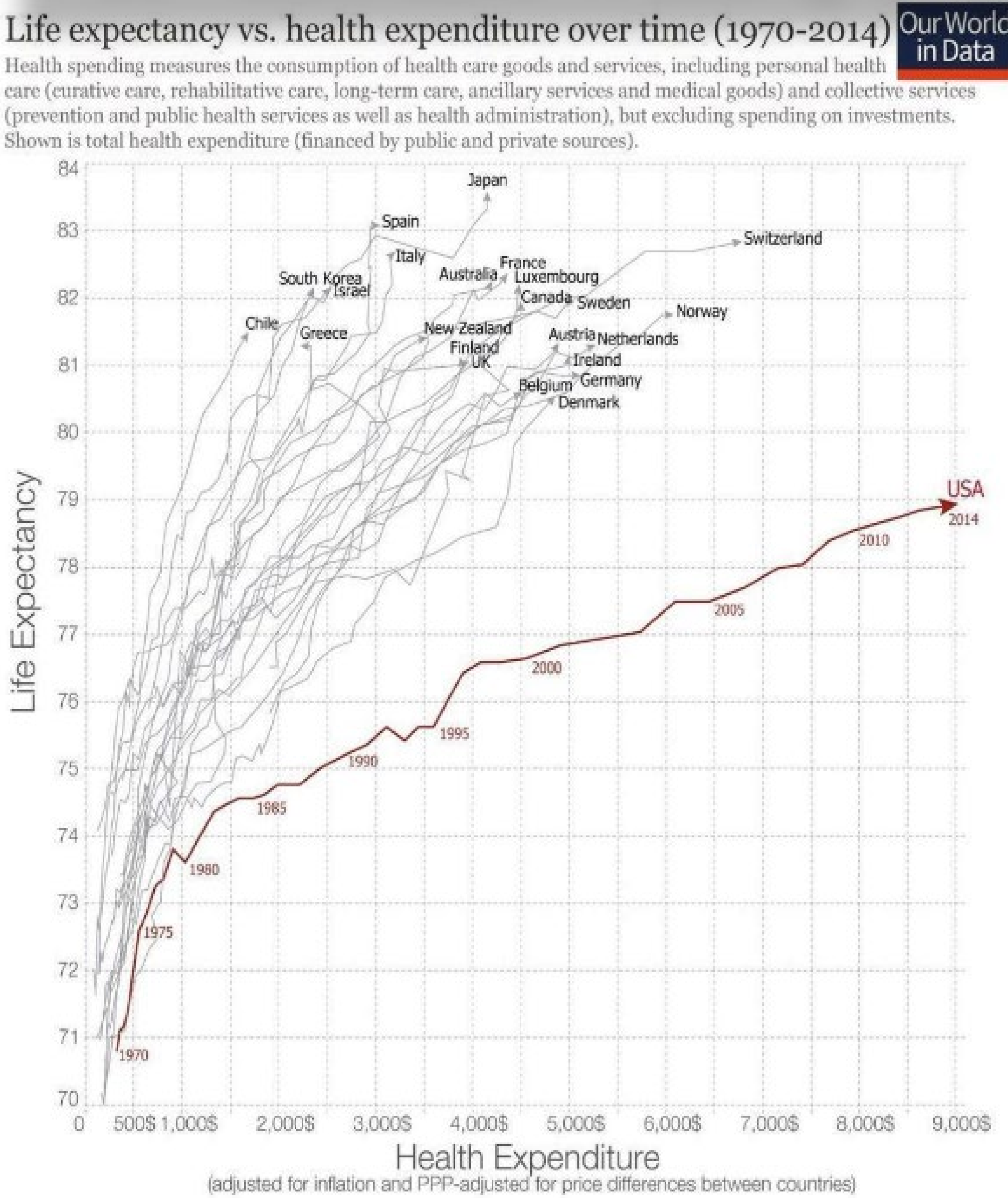
By Robert Sanders, Media relations | FEBRUARY 2, 2017

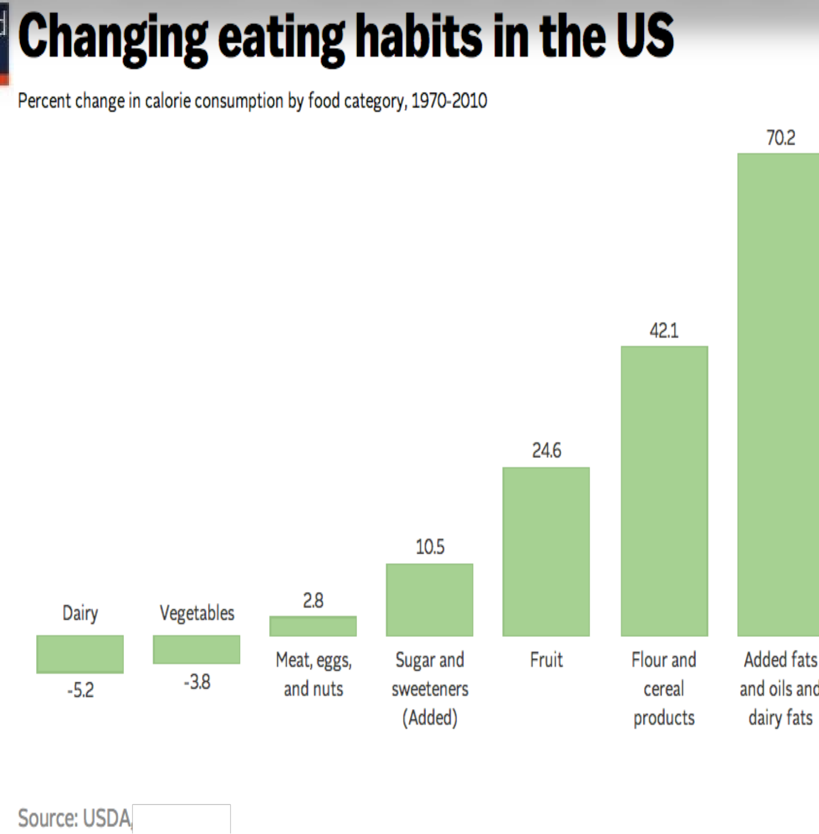
Pac-Man-like CRISPR enzymes have potential for disease diagnostics

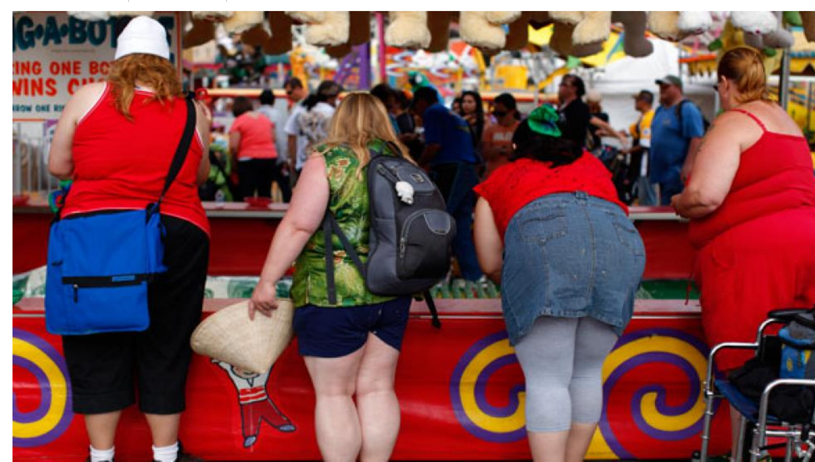


Researchers have described 10 new CRISPR enzymes that, once activated, behave like Pac-Man to chew up RNA in a way that could be used as sensitive detectors of infectious viruses. The new CRISPR enzymes are variants of a CRISPR protein, Cas13a, which could be used to detect specific sequences of RNA, such as from a virus. The researchers showed that once CRISPR-Cas13a binds to its target RNA, it begins to indiscriminately cut up all RNA, easily cutting RNA linked to a reporter molecule, making it fluoresce to allow signal detection. Such a system could be used to detect any type of RNA, including RNA distinctive of cancer cells.

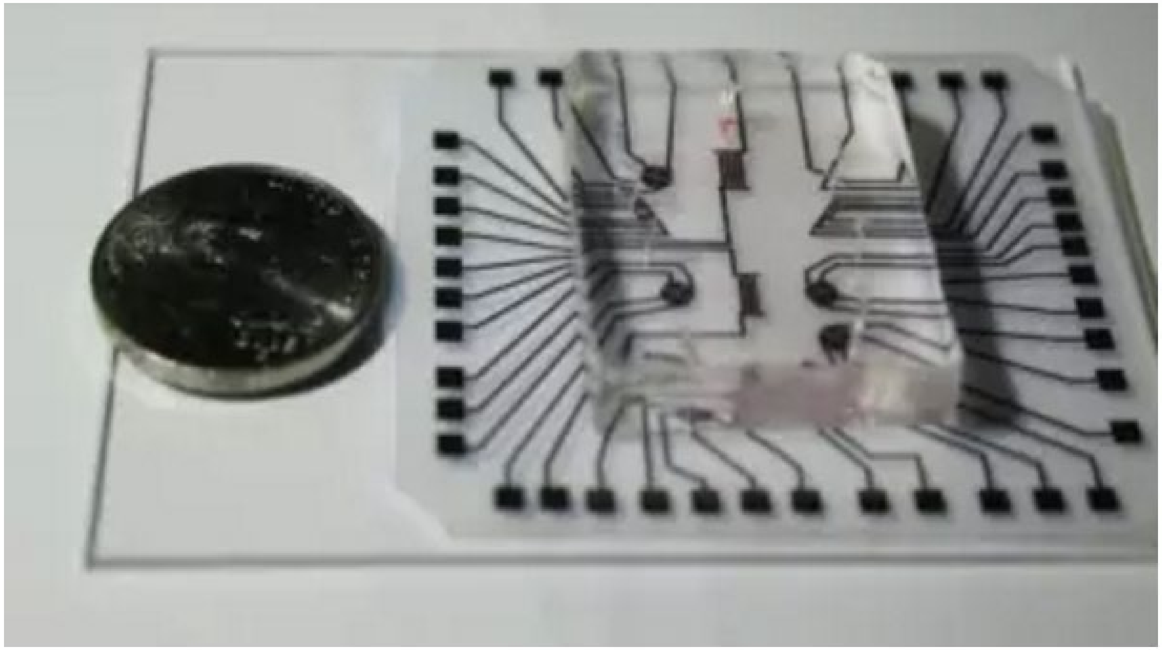
US Healthcare: A Losing Battle? Bad Habits Die Hard







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

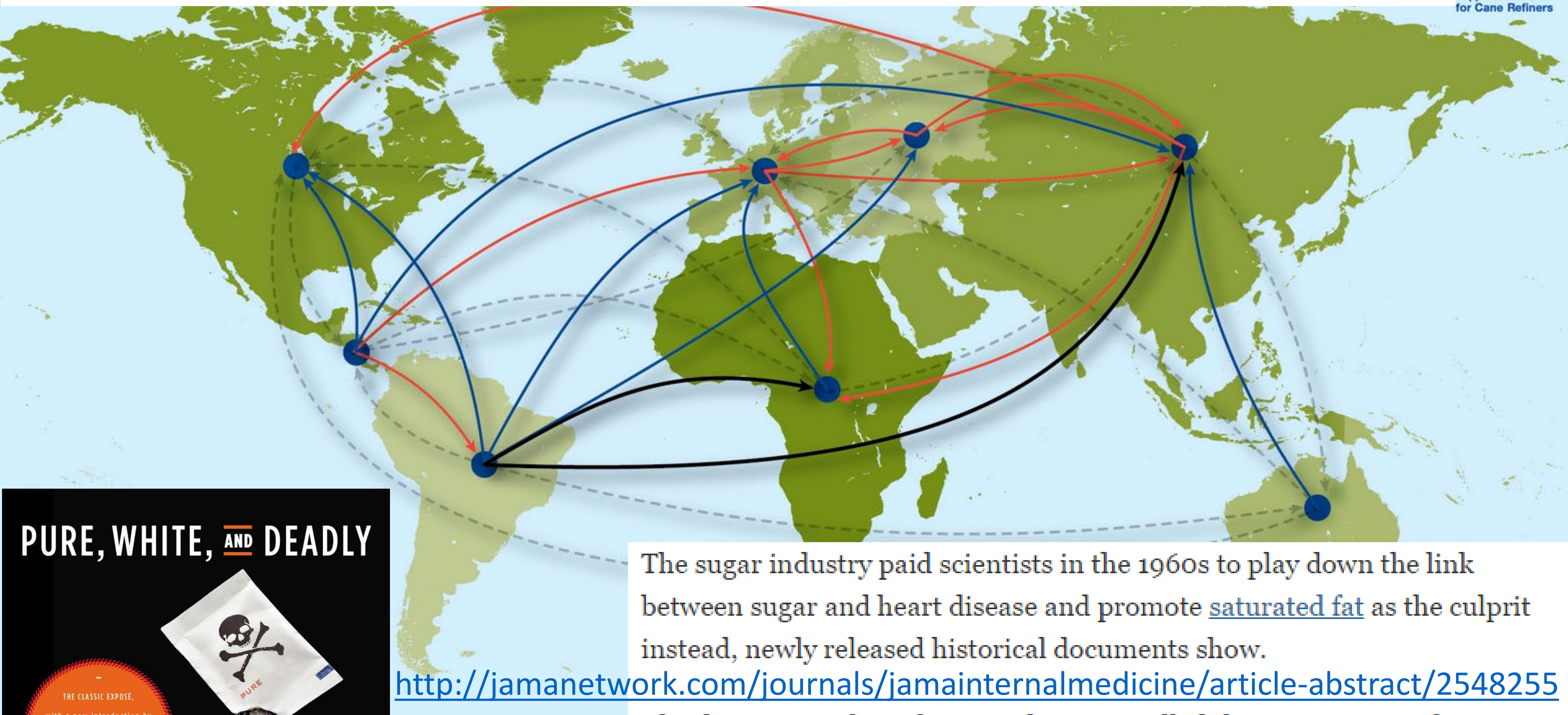
Rahim Esfandyarpour[a,b], Matthew J. DiDonato[c], Yuxin Yang[d], Naside Gozde Durmus[a,b], James S. Harris[d], and Ronald W. Davis[a,b,1]

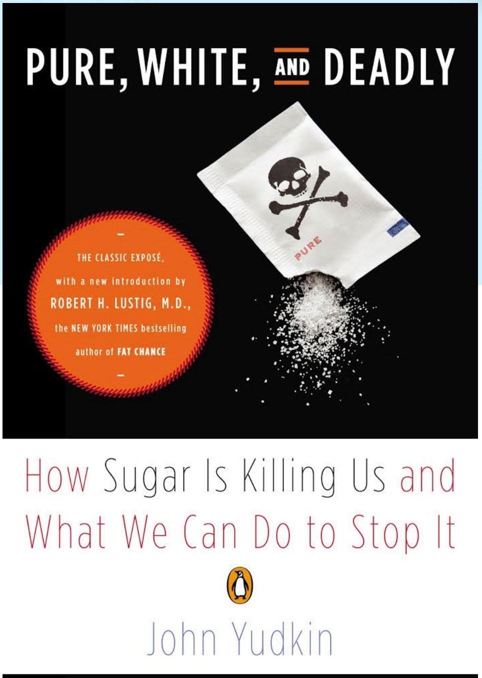
http://www.pnas.org/content/114/8/E1306.abstract

World Sugar Trade (2010/2011)

www.nytimes.com/2016/09/13/well/eat/how-the-sugar-industry-shifted-blame-to-fat.html?_r=0
www.npr.org/sections/thetwo-way/2016/09/13/493739074/50-years-ago-sugar-industry-quietly-paid-scientists-to-point-blame-at-fat

www.SAVEOURSUGAR.eu
SAVE OUR SUGAR
Support a Fair Deal for Cane Refiners





The sugar industry paid scientists in the 1960s to play down the link between sugar and heart disease and promote saturated fat as the culprit instead, newly released historical documents show.

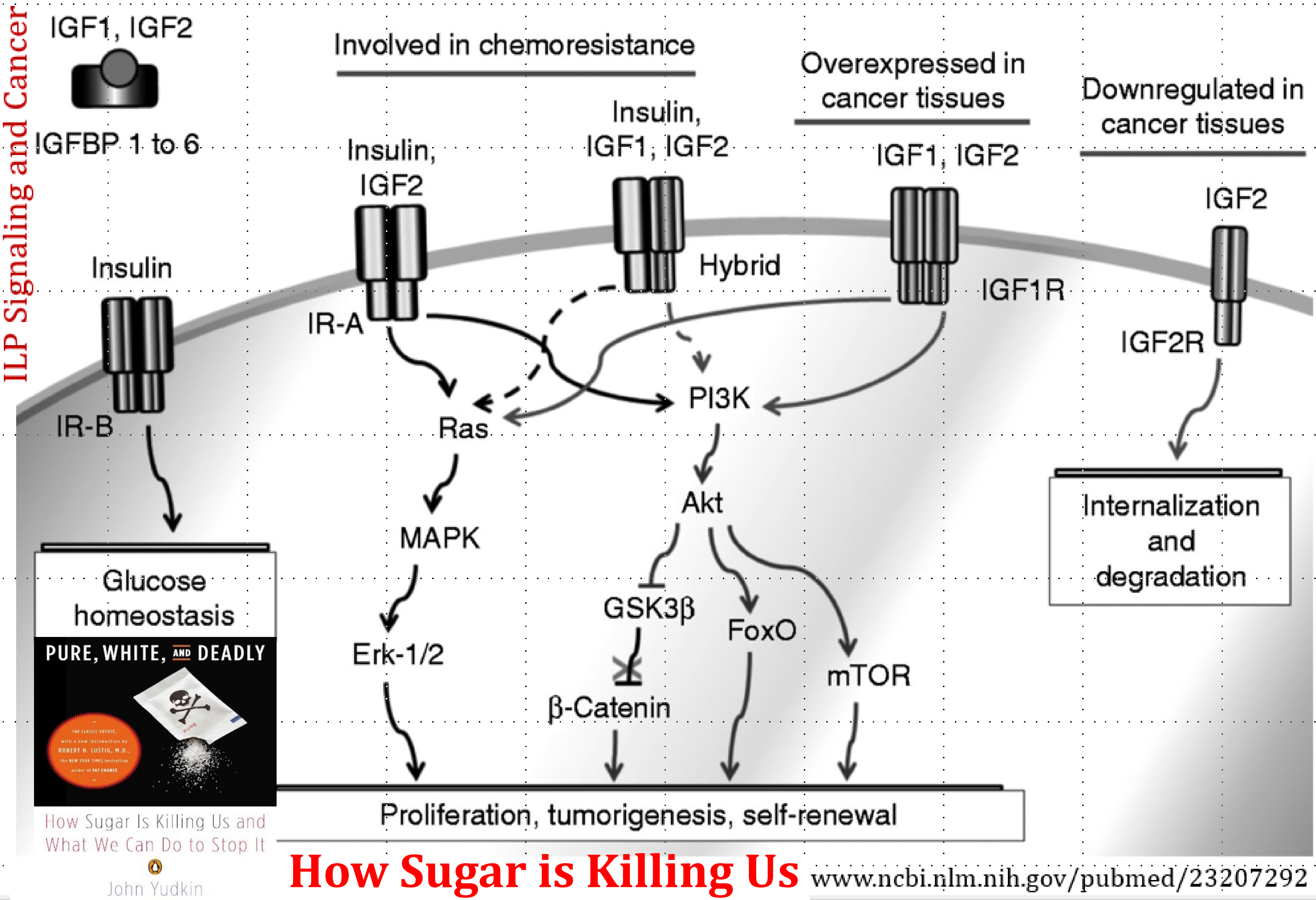
http://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2548255

The documents show that a trade group called the Sugar Research Foundation, known today as the Sugar Association, paid three Harvard scientists the equivalent of about $50,000 in today's dollars to publish a 1967 review of research on sugar, fat and heart disease. The studies used in the review were handpicked by the sugar group, and the article, which was published in the prestigious New England Journal of Medicine, minimized the link between sugar and heart health and cast aspersions on the role of saturated fat.

www.ncbi.nlm.nih.gov/pubmed/5339699

Insulin Resistance and Cancer

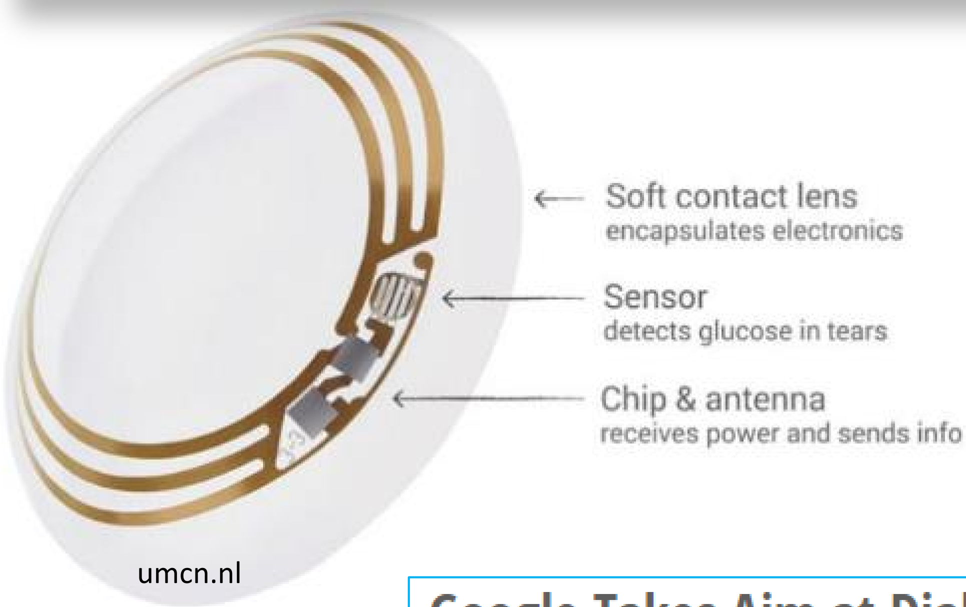
ILP Signaling and Cancer



How Sugar is Killing Us

www.ncbi.nlm.nih.gov/pubmed/23207292

DIABETES – The next medical IoT Focus



umcn.nl

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

SANOFI

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.

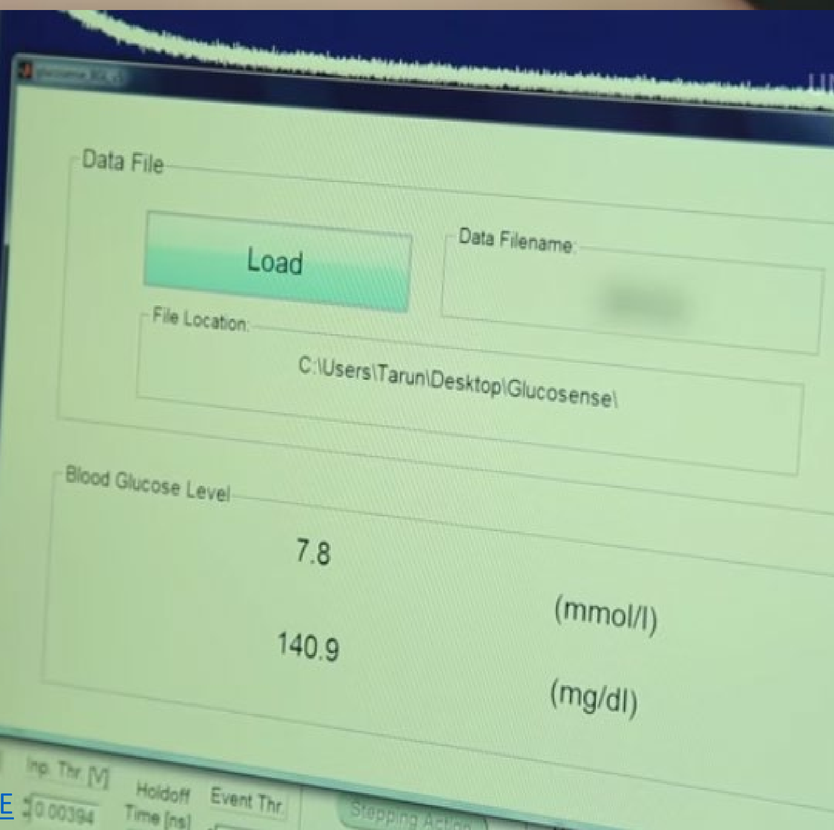
With the formation of a new partnership that enlists the aid of the Joslin Diabetes Center and Sanofi, a multinational pharmaceutical developer, Google hopes to reduce the burden of Type 1 and Type 2 diabetes on both patients and providers.

HARVARD MEDICAL SCHOOL

ABOUT HMS | EDUCATION

Joslin Diabetes Center

BLOOD-FREE NON-INVASIVE BLOOD GLUCOSE



Professor Gin Jose, University of Leeds ● http://bit.ly/BLOOD-FREE-BLOOD-GLUCOSE

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 to determine hemoglobin.

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

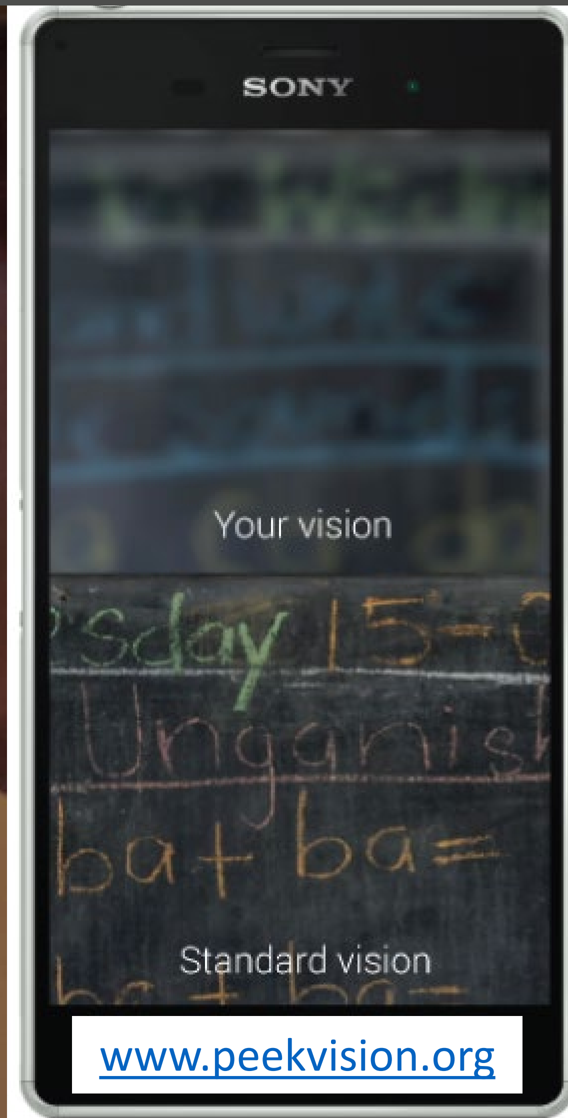
Wrig Nanosystems, a medical technology startup company which develops and markets a hemoglobin measurement device, has attracted financial interest from different investors in the product. The company has made an investment of up to 15 cr to commercialise and further develop the product and Avendus Wealth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

- 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

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.



OPTICIAN'S

CLINIC-IN-A-POCKET

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

www.bbc.com/news/health-22553730

What the phone app can do for eyes

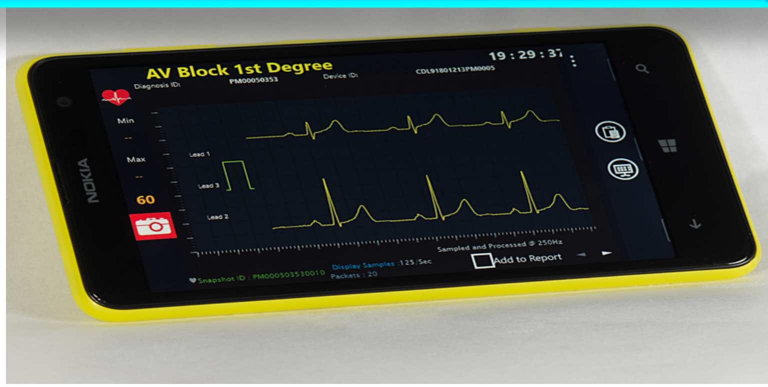
Peek can diagnose a vast range of eye problems, blindness and vision impairments,

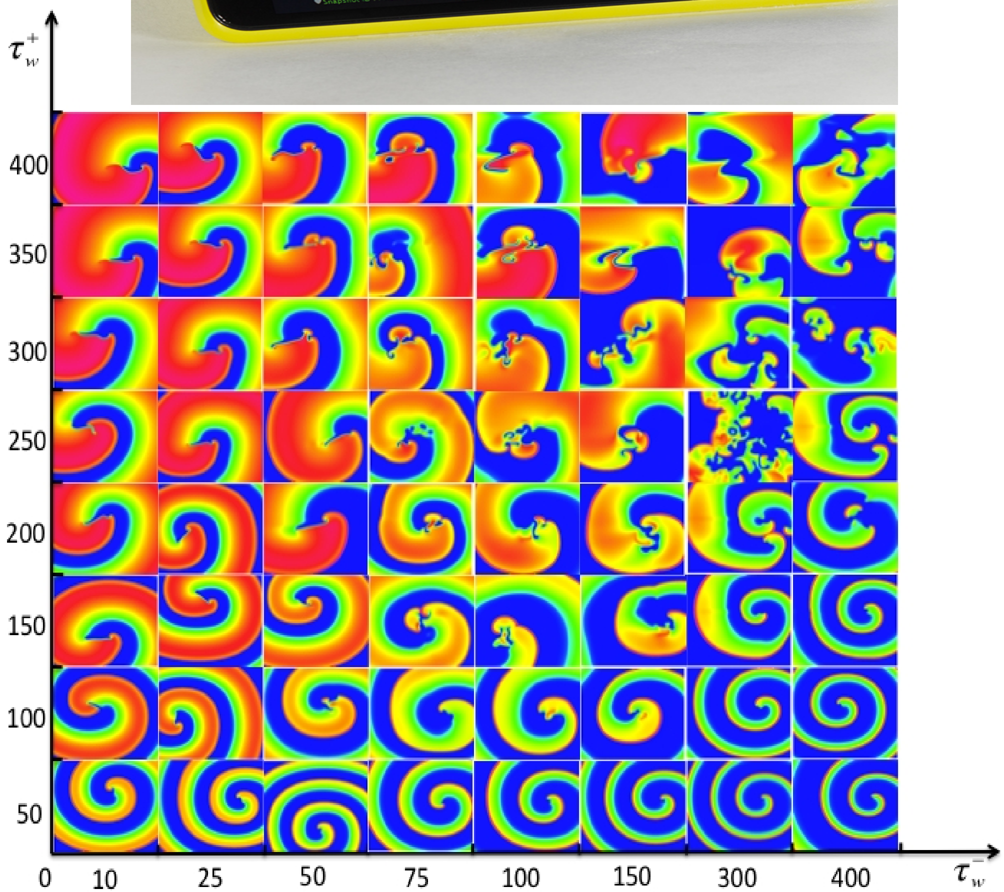
- Glaucoma
- Cataracts
- Macular degeneration
- Diabetic retinopathy
- Other retinal and optic nerve diseases.

Dr Leslie Saxon, University of Southern California

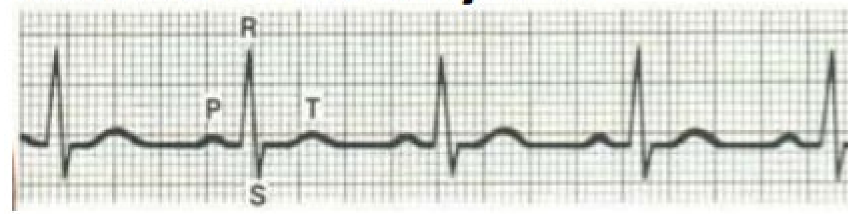
PHONE ECG DETECTS IRREGULAR HEARTBEAT

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



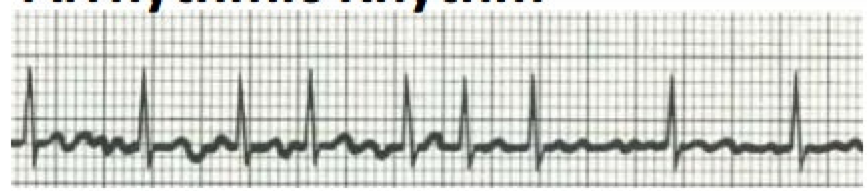


Normal Sinus Rhythm

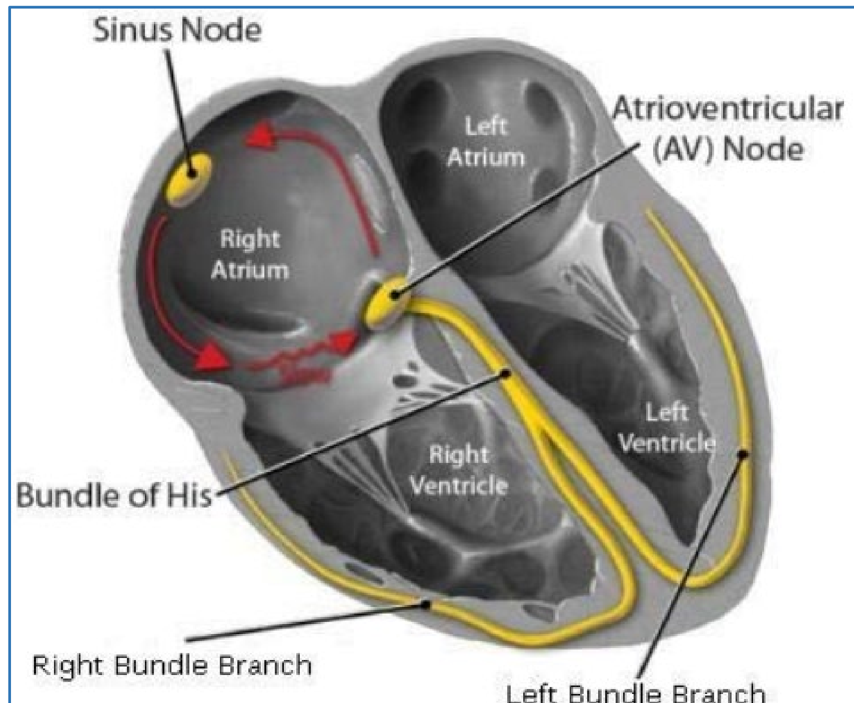


Circular pathways in the heart conduction system is a common cause of arrhythmias

Arrhythmic Rhythm



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



MIT News
ON CAMPUS AND AROUND THE WORLD

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

Courtesy of Cardiio

App screens for arrhythmia using smartphone

Samsung's NeuroLogica digital X-ray system

DISRUPTION

By Emily Wasserman

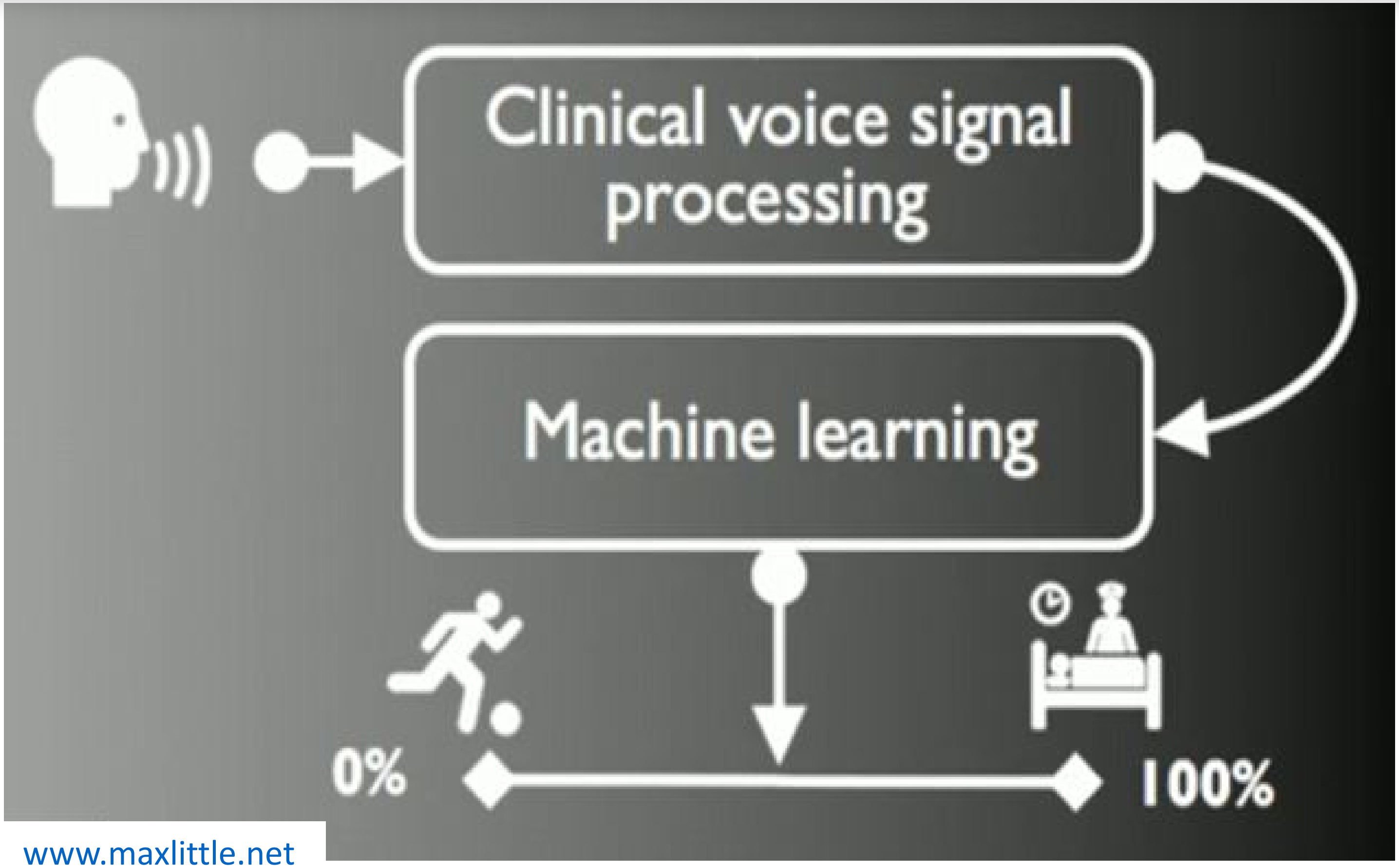
Samsung's NeuroLogica unit snagged an FDA OK for its digital radiography system, giving the company a boost as it aims for a top spot in the medical device imaging market.

Samsung's GC85A system--Courtesy of Samsung

The devicemaker's GC85A ceiling digital X-ray system adds to its expanding suite of products, which includes its mobile digital GM60A, the U-arm digital GU60A and the ceiling digital GC80. The device includes wireless, lightweight detectors, a portable grid, and smart features that allow operators to position the entire system with one touch and work with compatible Samsung equipment, the company said in a statement.

"The Samsung GC85A represents NeuroLogica's latest commitment to introducing user- and patient-centric innovation to healthcare to provide fast, easy and accurate diagnoses," David Webster, NeuroLogica's chief marketing officer and VP of global sales, said in a statement. "The system's superior image quality and ease of control will enable users to experience a new level of efficiency with a DR system designed for streamlined operation."

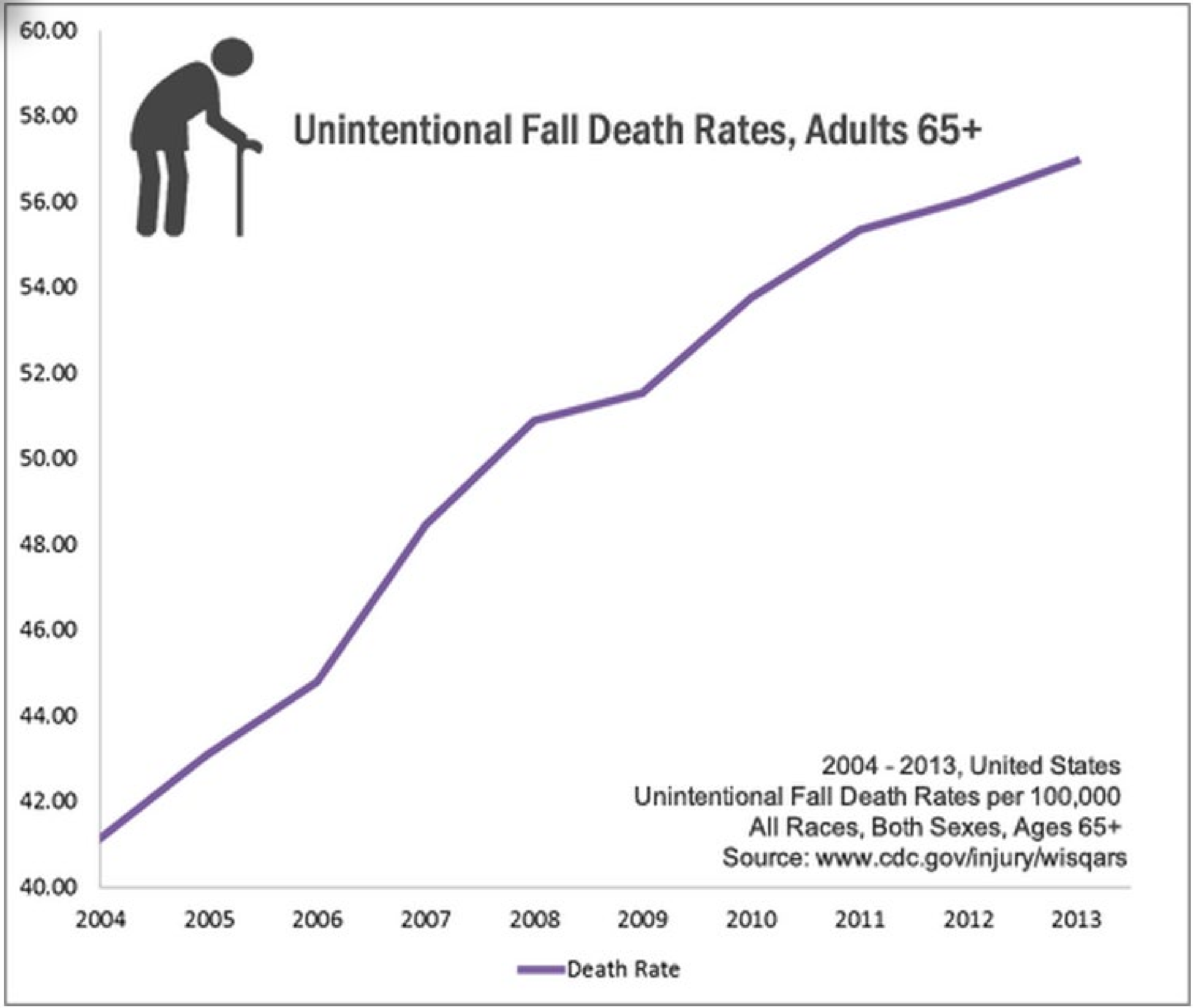
Detection of Parkinson's Disease using a Smart Phone



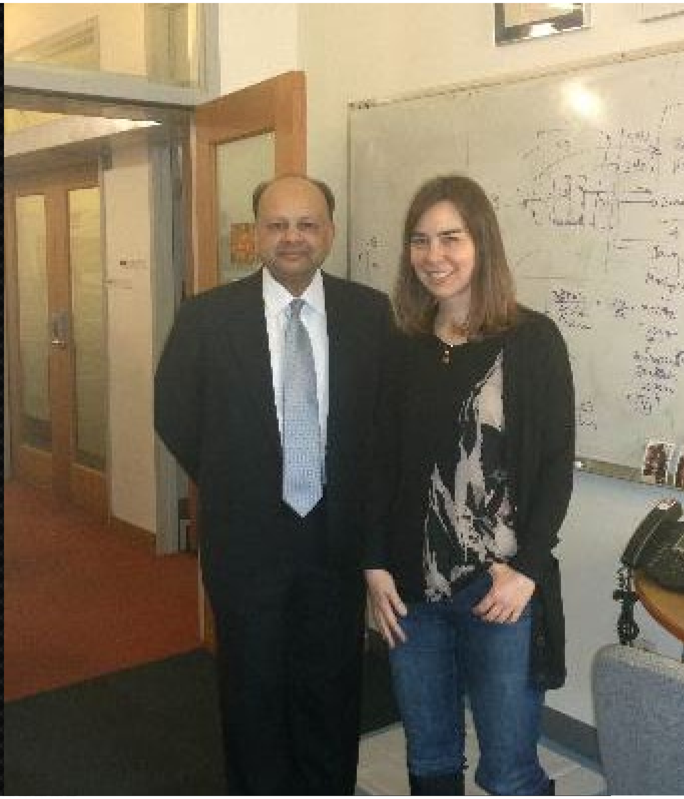
www.maxlittle.net

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



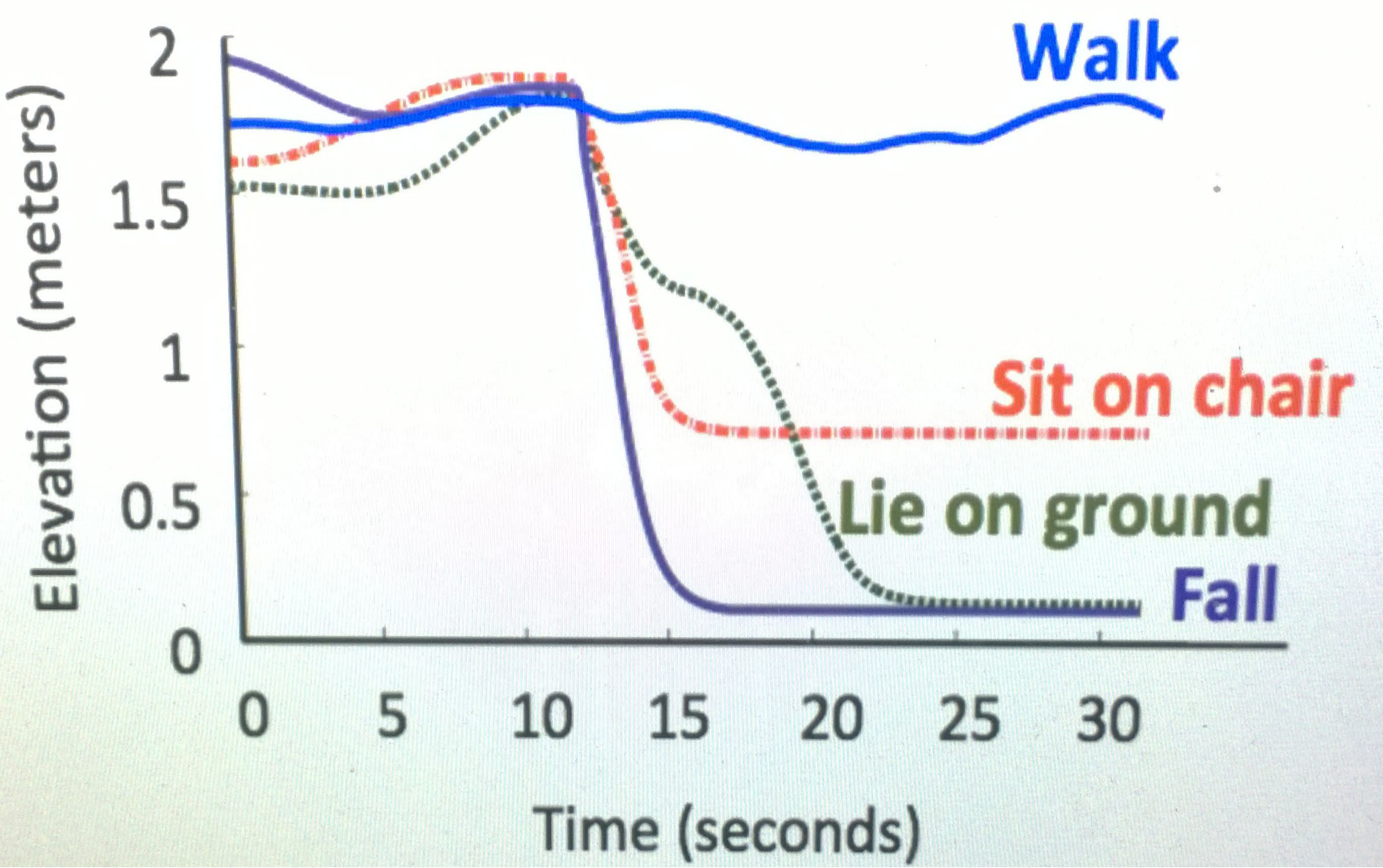
Professor Dina Katabi (MIT) presenting RF Reflection to President Obama (White House Demo, 4 August 2015)



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

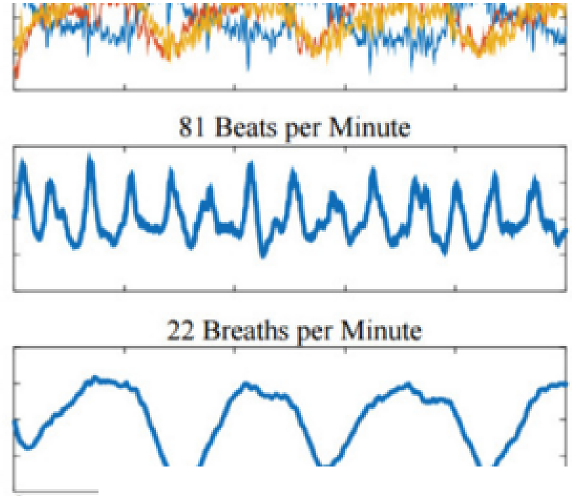
http://newsoffice.mit.edu/2015/president-obama-meets-mit-entrepreneurs-white-house-demo-day-0806

Fall Detection – Wire less, Sensor less, Without Wearables



RF Reflection Data - Professor Dina Katabi, Wireless Center, CSAIL, MIT ● IIC Member

Many more innovations are on the way …



HEART, MONITORING, RESPIRATORY

PHONE TRACKS HEALTH WITHOUT WEARABLE SENSORS

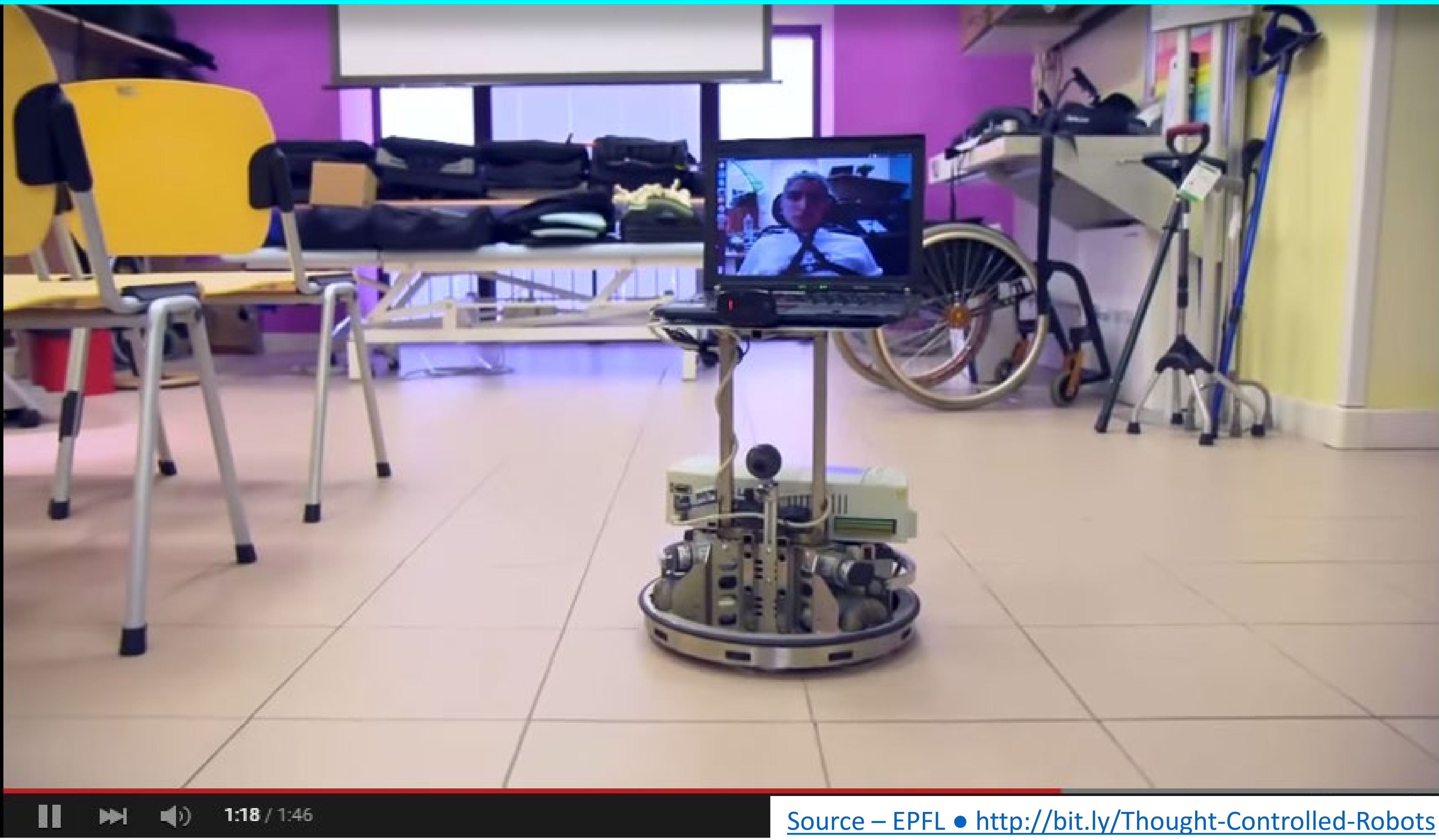
NOVEMBER 14, 2015 LISAWEINER

Javier Hernandez Rivera of Rosalind Picard's Affective Computing Group at MIT is developing a health monitoring phone that does not require a wearable. BioPhone derives biological signals from a phone's accelerometer, which the team says captures small body movements that result from one's heart beating and chest rising and falling.

Hernandez said that BioPhone is meant to gather data during still moments, simplifying the capture of small vibrations without having to account for many body movements. He believes that this can detect stress, which could trigger the phone to provide breathing exercises, or notify a loved one to call.

12 subjects sat, stood, and lied down, before and after pedaling a bike, with a smartphone in their pocket. To compare results, they wore sensors to capture heart and breathing rates. Heart rates reported by smartphone data alone were off by 1 beat per minute, and breathing rates were off by 1/4 of a breath per minute.

Remote Thought-Controlled Telepresence Robots directed by humans with motor neuron paralysis



Source – EPFL ● http://bit.ly/Thought-Controlled-Robots

This is not a new problem. It has been recognized for a couple decades.

Healthcare tools may need an open platform to curate and catalyze data interoperability between devices to better treat the patient, in real-time.

www.cimit.org/services-engineering-resources.html

www.mdpnp.org/uploads/PSQH_Article.pdf

CIMIT

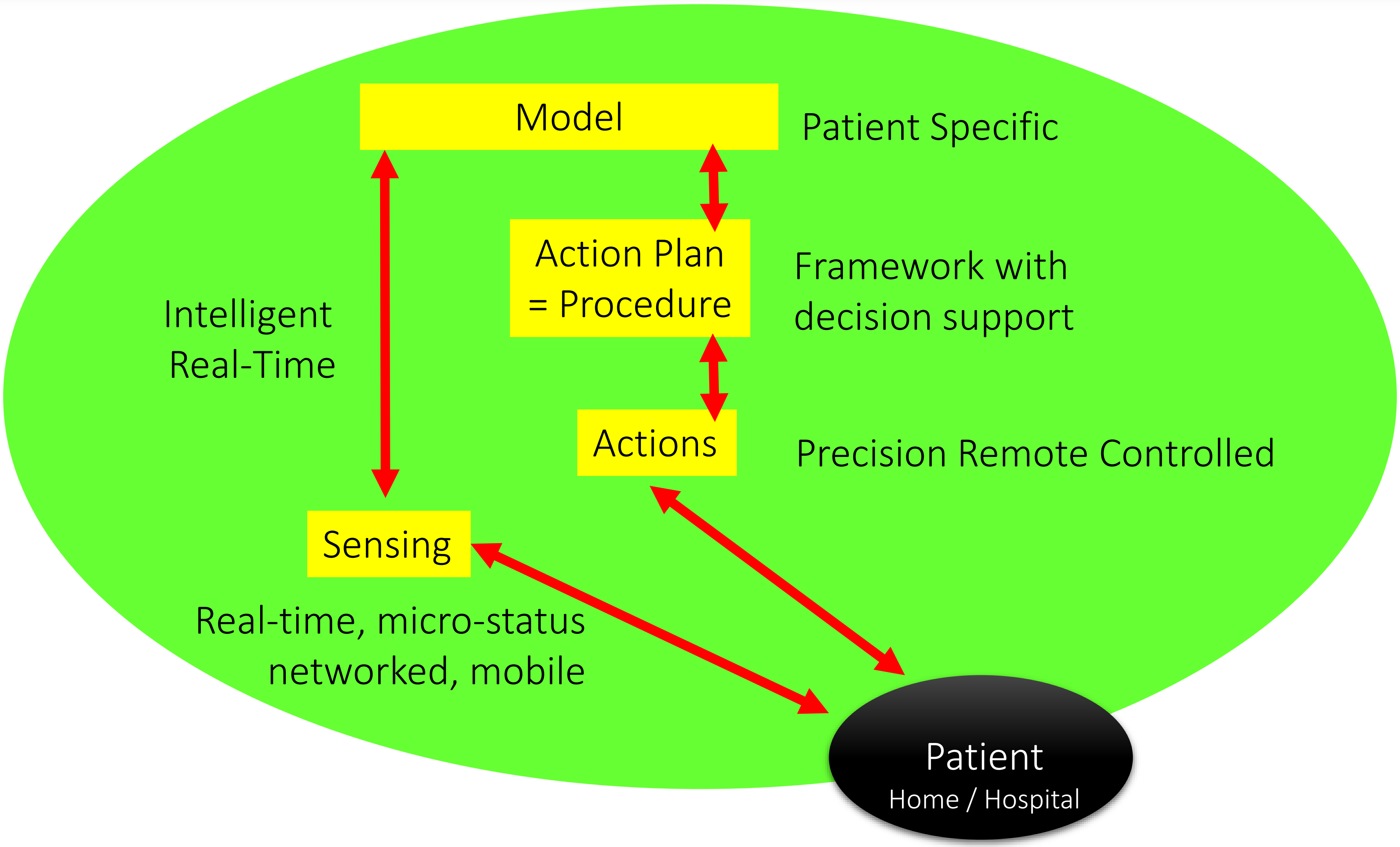
CIMIT Model

Clinical Impact

MIT is one of the four institutions that came together in 1998 to found CIMIT. In addition to the CIMIT-funded projects MIT researchers have pursued, CIMIT and MIT have been working together through guest faculty support of its Health Science and Technology Program to provide meaningful training in medical device development for graduate students.

The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program was established in 2004 to lead the adoption of open standards and technology for medical device interoperability to support clinical innovation. The term "PnP" was adopted because the required technology infrastructure has many elements in common with the plug-and-play approach used in other computer-based systems. The program is affiliated with Massachusetts General Hospital (MGH), CIMIT (Center for Integration of Medicine and Innovative Technology), and Partners HealthCare Information Systems, with additional support from TATRC (U.S. Army Telemedicine & Advanced Technology Research Center). Having evolved from the OR of the Future program at MGH, the MD PnP program remains clinically grounded.

Early Remit of CIMIT – Sense, *then*, Respond – Future Integrated Healthcare Monitoring



The distinction between healthcare and other industry is in differentiation of scalability. Patient centricity as a service is not scalable but patient centric infrastructure (architecture) is scalable.

MD PnP™

Getting Connected for Patient Safety™

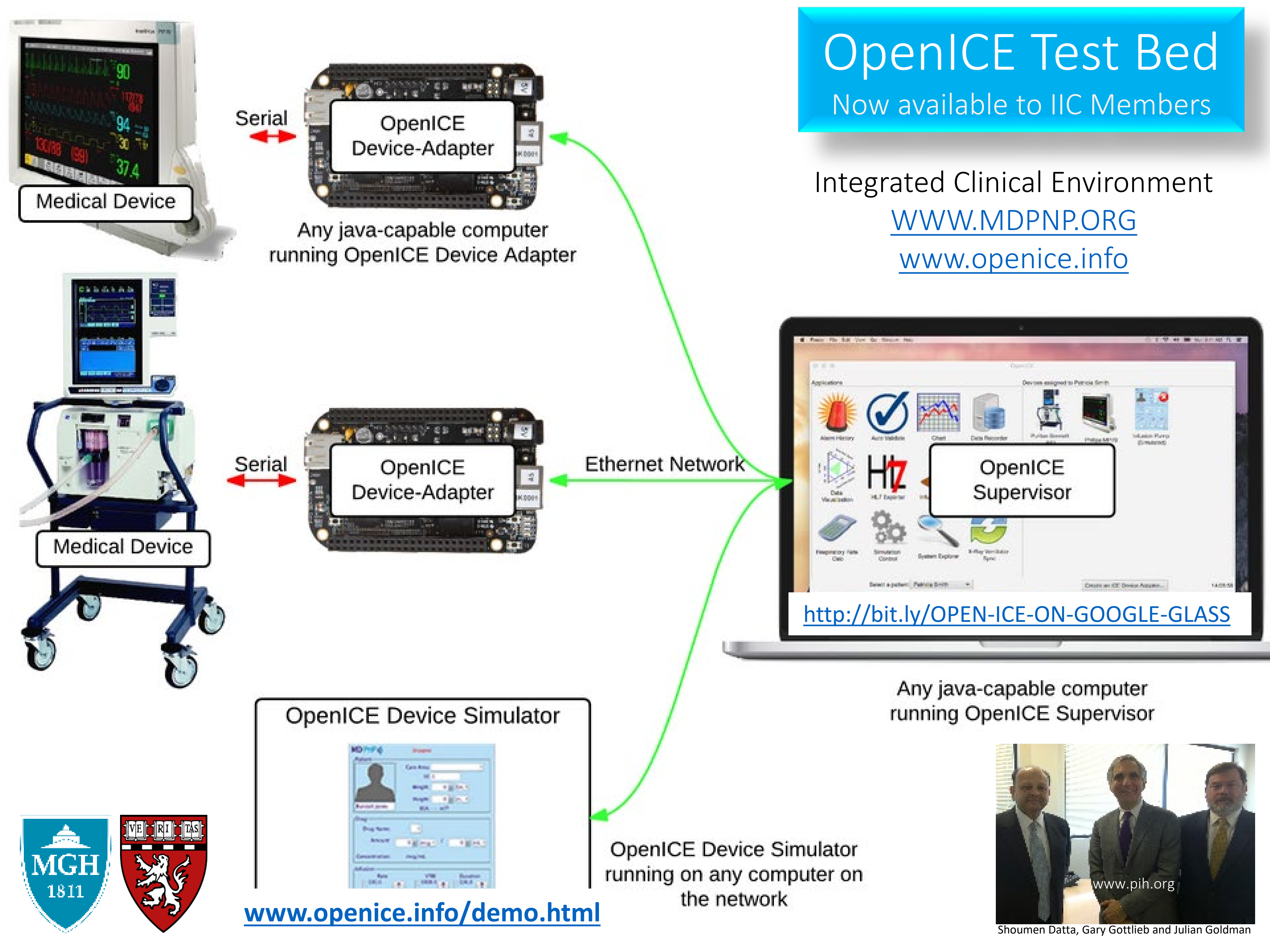
HOME | ABOUT PROGRAM | PROJECTS | NEWS | EVENTS | PUBLICATIONS & TALKS | OUR LAB

Sitemap

Medical Device "Plug-and-Play" Interoperability Program working on "safe interoperability™" to improve patient safety

The CIMIT MD PnP Lab opened in May 2006 to provide a vendor-neutral "sandbox" to evaluate the ability of candidate interoperability solutions to solve clinical problems, to model clinical use cases (in a simulation environment), to develop and test related network safety and security systems, and to support interoperability and standards conformance testing.

At the CIMIT Innovation Congress in November 2007, Dr. Julian Goldman demonstrated how patient safety could be improved by synchronization of the x-ray exposure with the ventilator during surgery.


OpenICE Test Bed
Now available to IIC Members
Integrated Clinical Environment
WWW.MDPNP.ORG
www.openice.info
Serial
OpenICE
Device-Adapter
Medical Device
Any java-capable computer
running OpenICE Device Adapter
Serial
OpenICE
Device-Adapter
Ethernet Network
Medical Device
OpenICE
Supervisor
http://bit.ly/OPEN-ICE-ON-GOOGLE-GLASS
Any java-capable computer
running OpenICE Supervisor
OpenICE Device Simulator
www.openice.info/demo.html
OpenICE Device Simulator
running on any computer on
the network
MGH
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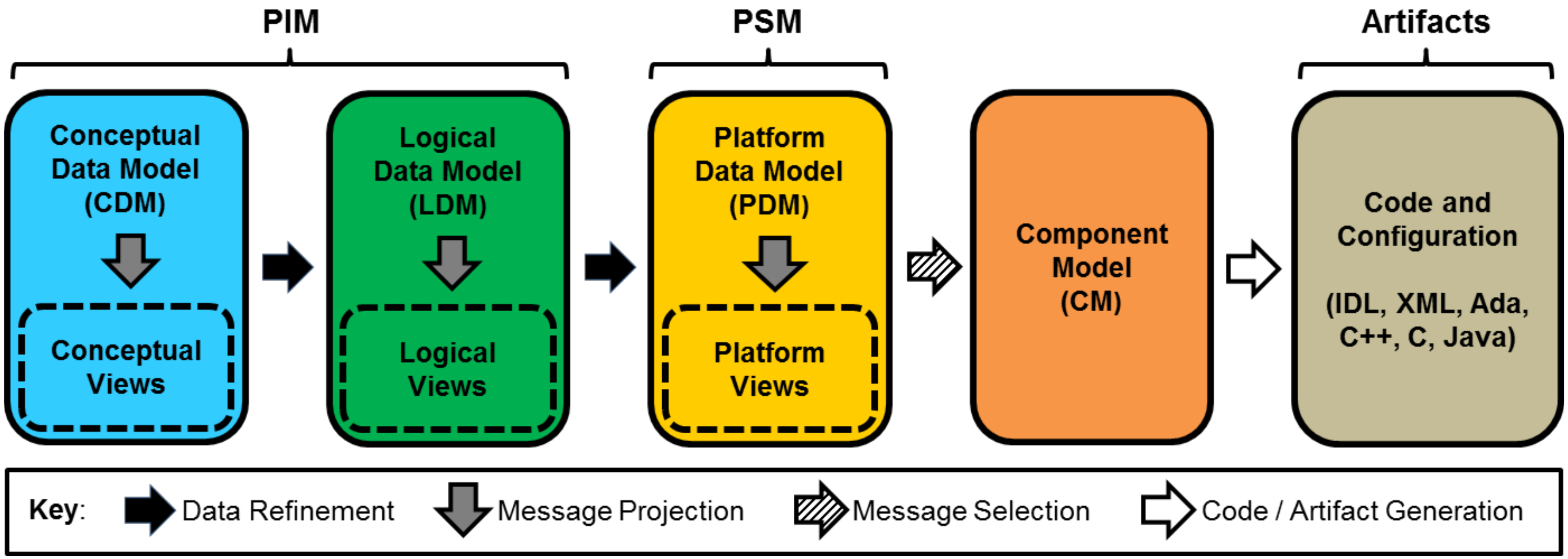
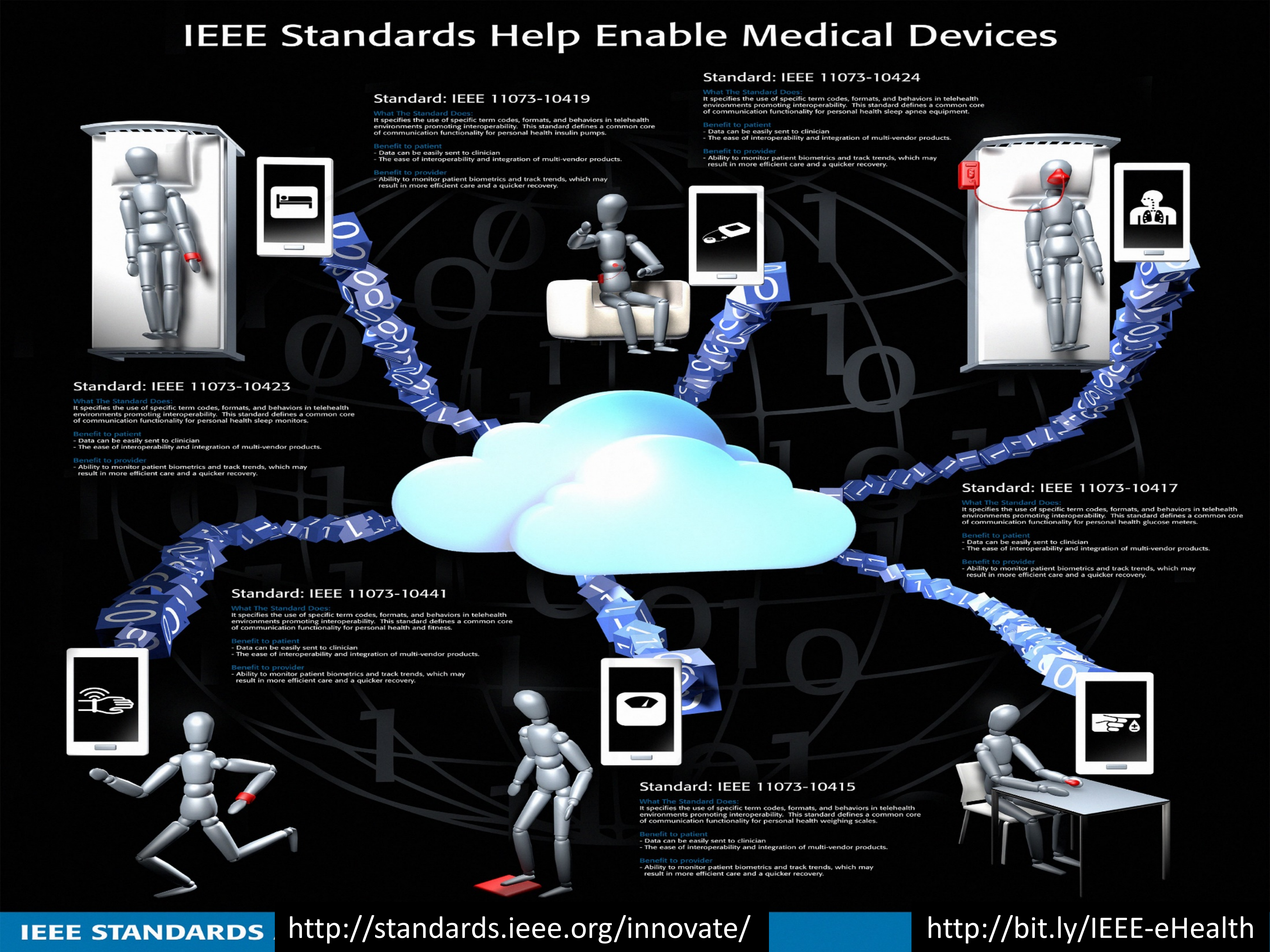
VE RI TAS
www.pih.org
Shoumen Datta, Gary Gottlieb and Julian Goldman

Is FACE a useful guide for healthcare platforms?

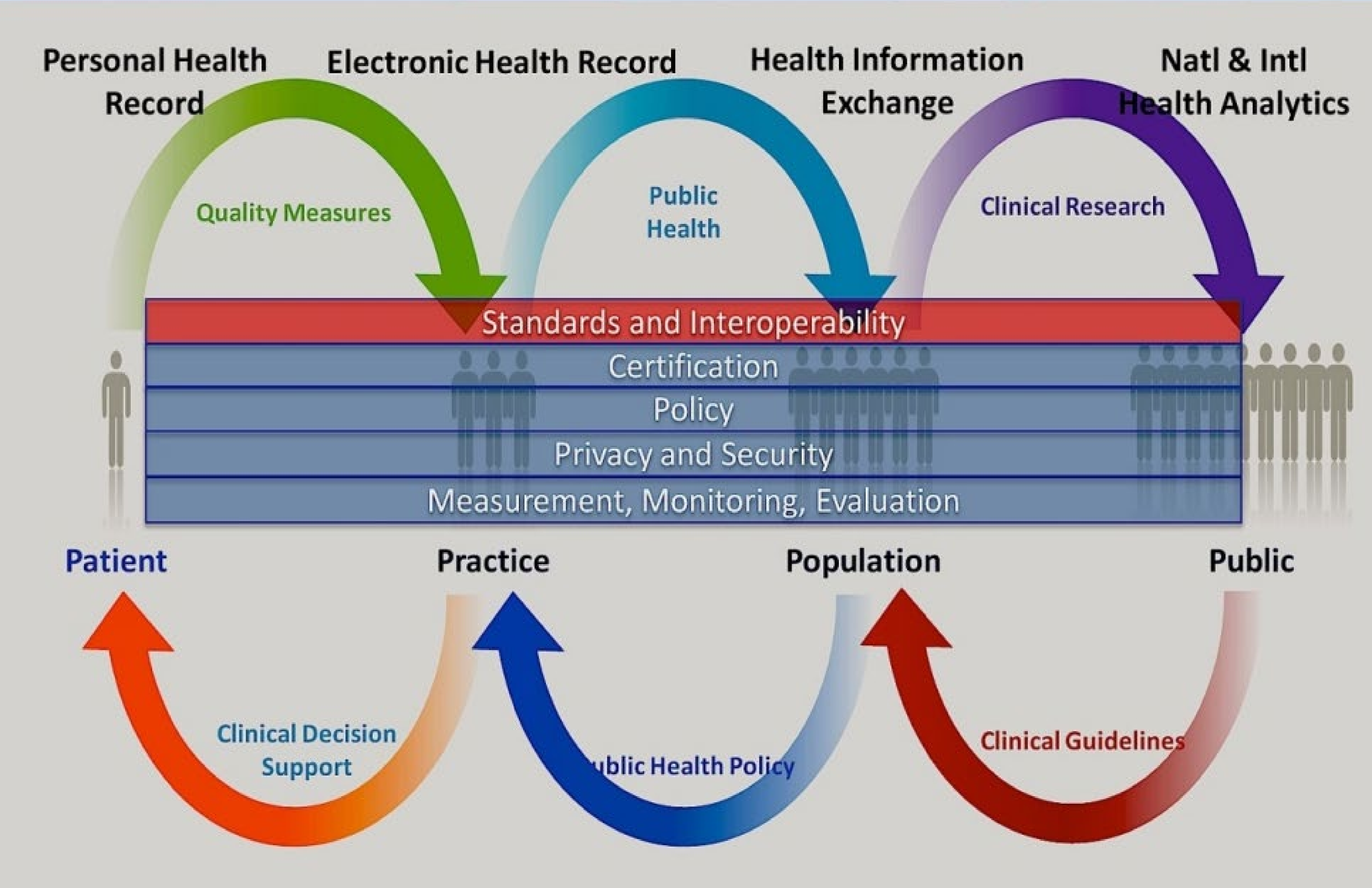


- Data and message models aligned with OMG Model Driven Architecture ™
- Addition of the Component (UoP) model allows component integration with messages and data elements in the Platform Model
- Supports definition and potentially auto-generation of code and other artifacts

Figure from FACE Technical Standard, edition 2.1 ● www.opengroup.org/face/tech-standard-2.1


IEEE Standards Help Enable Medical Devices
Standard: IEEE 11073-10424
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health sleep apnea equipment.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
Standard: IEEE 11073-10419
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health insulin pumps.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
Standard: IEEE 11073-10423
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health sleep monitors.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
Standard: IEEE 11073-10417
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health glucose meters.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
Standard: IEEE 11073-10441
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health and fitness.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
Standard: IEEE 11073-10415
What The Standard Does:
It specifies the use of specific term codes, formats, and behaviors in telehealth environments promoting interoperability. This standard defines a common core of communication functionality for personal health weighing scales.
Benefit to patient
- Data can be easily sent to clinician
- The ease of interoperability and integration of multi-vendor products.
Benefit to provider
- Ability to monitor patient biometrics and track trends, which may result in more efficient care and a quicker recovery.
IEEE STANDARDS
http://standards.ieee.org/innovate/
http://bit.ly/IEEE-eHealth

Platform for Trusted Data Access via Secure Standards and Interoperability



Healthcare Data Interoperability & Standards

… semantics, data dictionaries, billing codes

- Terminology
  - SNOMED, LOINC
- Classification Systems
  - ICD10, CPT
- Devices
  - IEEE 11073
- EHR-Related
  - DICOM, HL7 (CDA)
- Interoperability
  - DICOM, HL7 Messaging, HIPAA Transactions, NCPDP
- Language Formats
  - XML, X12

Increase in computational time may be compensated by a relaxed priority queue which allows throughput scaling for large number of threads. Hence, parallelizing common algorithms to work on multicore chips: ***The SprayList*** www.mit.edu/~jerryzli/SprayList-CR.pdf

DIAGNOSIS CODES for SPRAINED & STRAINED ANKLES

ICD-9

845.00 Sprain and strain of ankle unspecied site
845.01 Sprain and strain of ankle, Deltoid ligament/ Internal collateral ligament
845.02 Sprain and strain of ankle, Calcaneobular (ligament)
845.03 Sprain and strain of ankle, Tibiobular (ligament) distal

ICD-10

S93.401A Sprain of unspecied ligament of right ankle – initial encounter
S93.401D Sprain of unspecied ligament of right ankle – subsequent encounter
S93.401S Sprain of unspecied ligament of right ankle – sequela
S93.402A Sprain of unspecied ligament of left ankle – initial encounter
S93.402D Sprain of unspecied ligament of left ankle – subsequent encounter
S93.402S Sprain of unspecied ligament of left ankle – sequela
S93.409A Sprain of unspecied ligament of unspecied ankle – initial encounter
S93.409D Sprain of unspecied ligament of unspecied ankle - subsequent encounter
S93.409S Sprain of unspecied ligament of unspecied ankle – sequela
S93.412D Sprain of calcaneobular ligament of left ankle – subsequent encounter
S93.412S Sprain of calcaneobular ligament of left ankle – sequela
S93.419A Sprain of calcaneobular ligament of unspecied ankle – initial encounter
S93.419D Sprain of calcaneobular ligament of unspecied ankle – subsequent encounter
S93.419S Sprain of calcaneobular ligament of unspecied ankle
S93.431A Sprain of tibiobular ligament of right ankle – initial encounter
S93.431D Sprain of tibiobular ligament of right ankle – subsequent encounter
S93.431S Sprain of tibiobular ligament of right ankle – sequela
S93.432A Sprain of tibiobular ligament of left ankle – initial encounter
S93.432D Sprain of tibiobular ligament of left ankle – subsequent encounter
S93.432S Sprain of tibiobular ligament of left ankle – sequela
S93.439A Sprain of tibiobular ligament of unspecied ankle – initial encounter
S93.439D Sprain of tibiobular ligament of unspecied ankle – subsequent encounter
S93.439S Sprain of tibiobular ligament of unspecied ankle – sequela
S93.491A Sprain of other ligament of right ankle (Internal collateral/ talobular) initial encounter
S93.491D Sprain of other ligament of right ankle (Internal collateral/ talobular) subsequent encounter
S93.491S Sprain of other ligament of right ankle (Internal collateral/ talobular) sequela
S93.492A Sprain of other ligament of left ankle, initial encounter
S93.492D Sprain of other ligament of left ankle subsequent encounter
S93.492S Sprain of other ligament of left ankle sequela
S93.499A Sprain of other ligament of unspecied ankle initial encounter
S93.499D Sprain of other ligament of unspecied ankle subs encounter
S93.499S Sprain of other ligament of unspecied ankle (Internal collateral/talobular) sequela
S96.211A Strain of intrinsic muscle and tendon at right ankle and foot level initial encounter
S96.211D Strain of intrinsic muscle and tendon at right ankle and foot level subsequent encounter
S96.211S Strain of intrinsic muscle and tendon at right ankle and foot level sequela
S96.212A Strain of intrinsic muscle and tendon at left ankle and foot level initial encounter
S96.212D Strain of intrinsic muscle and tendon at left ankle and foot level subsequent encounter
S96.212S Strain of intrinsic muscle and tendon at left ankle and foot level sequela
S96.219A Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side initial encounter
S96.219D Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side subs encounter
S96.219S Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side
S96.811A Strain of other muscles and tendons at right ankle and foot level initial encounter
S96.811D Strain of other muscles and tendons at right ankle and foot level subsequent encounter
S96.811S Strain of other muscles and tendons at right ankle and foot level sequela
S96.812A Strain of other muscles and tendons at left ankle and foot level initial encounter
S96.812D Strain of other muscles and tendons at left ankle and foot level subsequent encounter
S96.812S Strain of other muscles and tendons at left ankle and foot level sequela
S96.819A Strain of other muscles and tendons at ankle and foot level, unspecied side initial encounter
S96.819D Strain of other muscles and tendons at ankle and foot level, unspecied side subs encounter
S96.819S Strain of other muscles and tendons at ankle and foot level, unspecied side sequela
S96.911A Strain of unspecied muscle and tendon at right ankle and foot level initial encounter
S96.911D Strain of unspecied muscle and tendon at right ankle and foot level subs encounter
S96.911S Strain of unspecied muscle and tendon at right ankle and foot level sequela
S96.912A Strain of unspecied muscle and tendon at left ankle and foot level initial encounter
S96.912D Strain of unspecied muscle and tendon at left ankle and foot level subs encounter
S96.912S Strain of unspecied muscle and tendon at left ankle and foot level sequela
S96.919A Strain of unspecied muscle and tendon at ankle and foot level, unspec. side initial encounter
S96.919D Strain of unspecied muscle and tendon at ankle and foot level, unspec. side subs encounter
S96.919S Strain of unspecied muscle and tendon at ankle and foot level, unspec. side sequela

CONVERGENCE : DIAGNOSIS CODE and SEMANTIC INTEROPERABILITY ?

ICD-9

845.00 Sprain and strain of ankle unspecied site
845.01 Sprain and strain of ankle, Deltoid ligament/ Internal collateral ligament
845.02 Sprain and strain of ankle, Calcaneobular (ligament)
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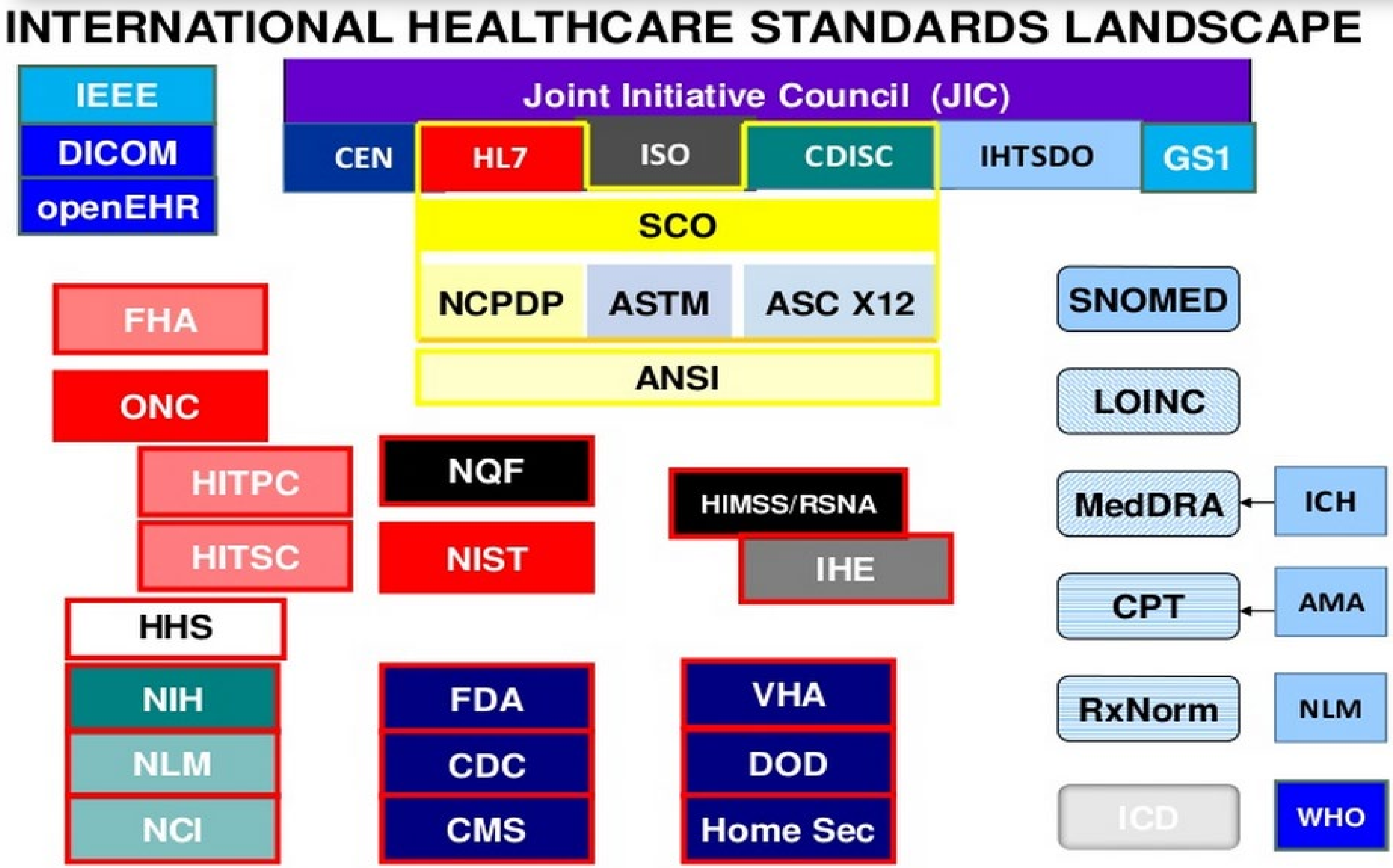
S93.409A Sprain of unspecied ligament of unspecied ankle – initial encounter
S93.409D Sprain of unspecied ligament of unspecied ankle - subsequent encounter
S93.409S Sprain of unspecied ligament of unspecied ankle – sequela
S93.412D Sprain of calcaneobular ligament of left ankle – subsequent encounter
S93.412S Sprain of calcaneobular ligament of left ankle – sequela
S93.419A Sprain of calcaneobular ligament of unspecied ankle – initial encounter

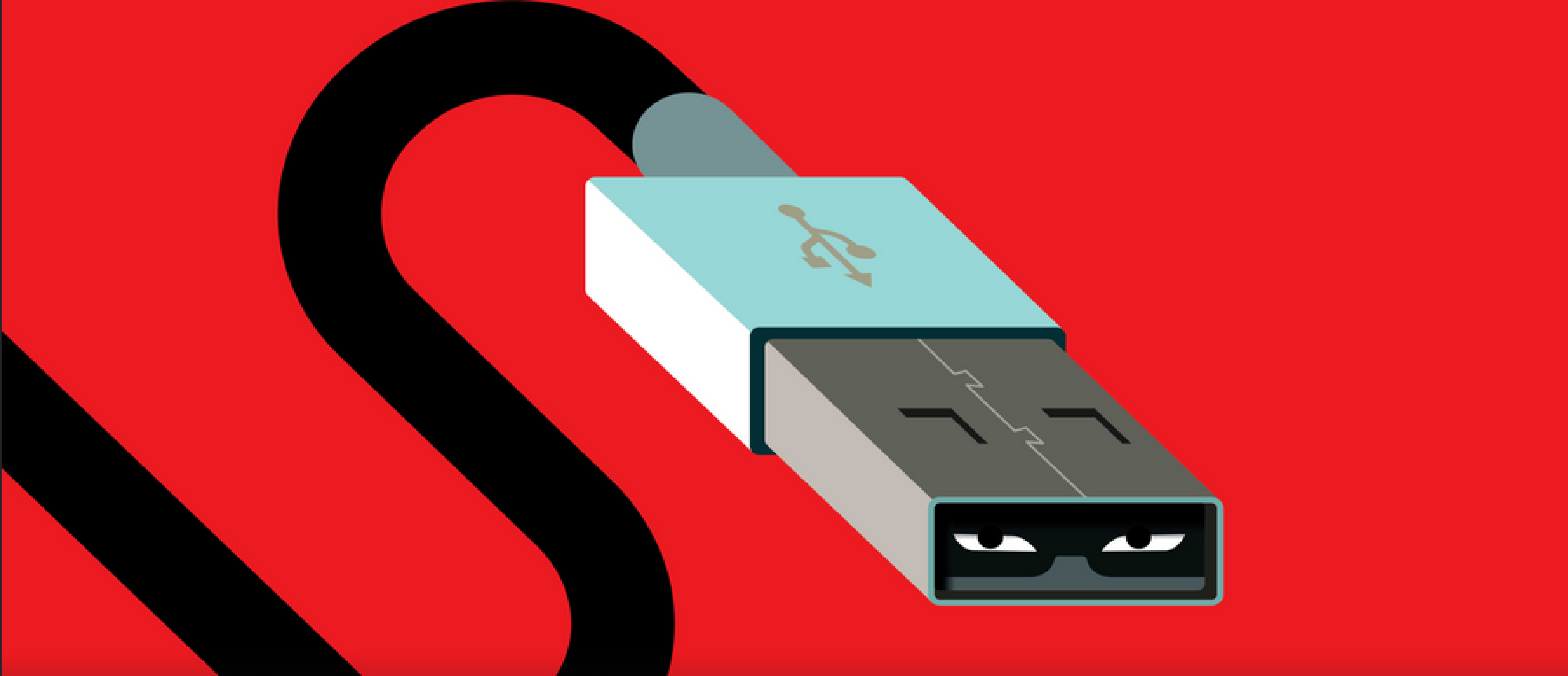
Proprietary closed semantic data dictionaries (EPIC) and heterogeneity of billing codes are contributors to lack of semantic interoperability and inhibitor for OS platforms

Barriers to Interoperability? Role of Ontology and Semantics in the Healthcare Standards Landscape



Digital Health Frameworks

Must address security, data integration, diagnostic platforms and tools with health IT interoperability



The Agenda
INTERNET OF THINGS

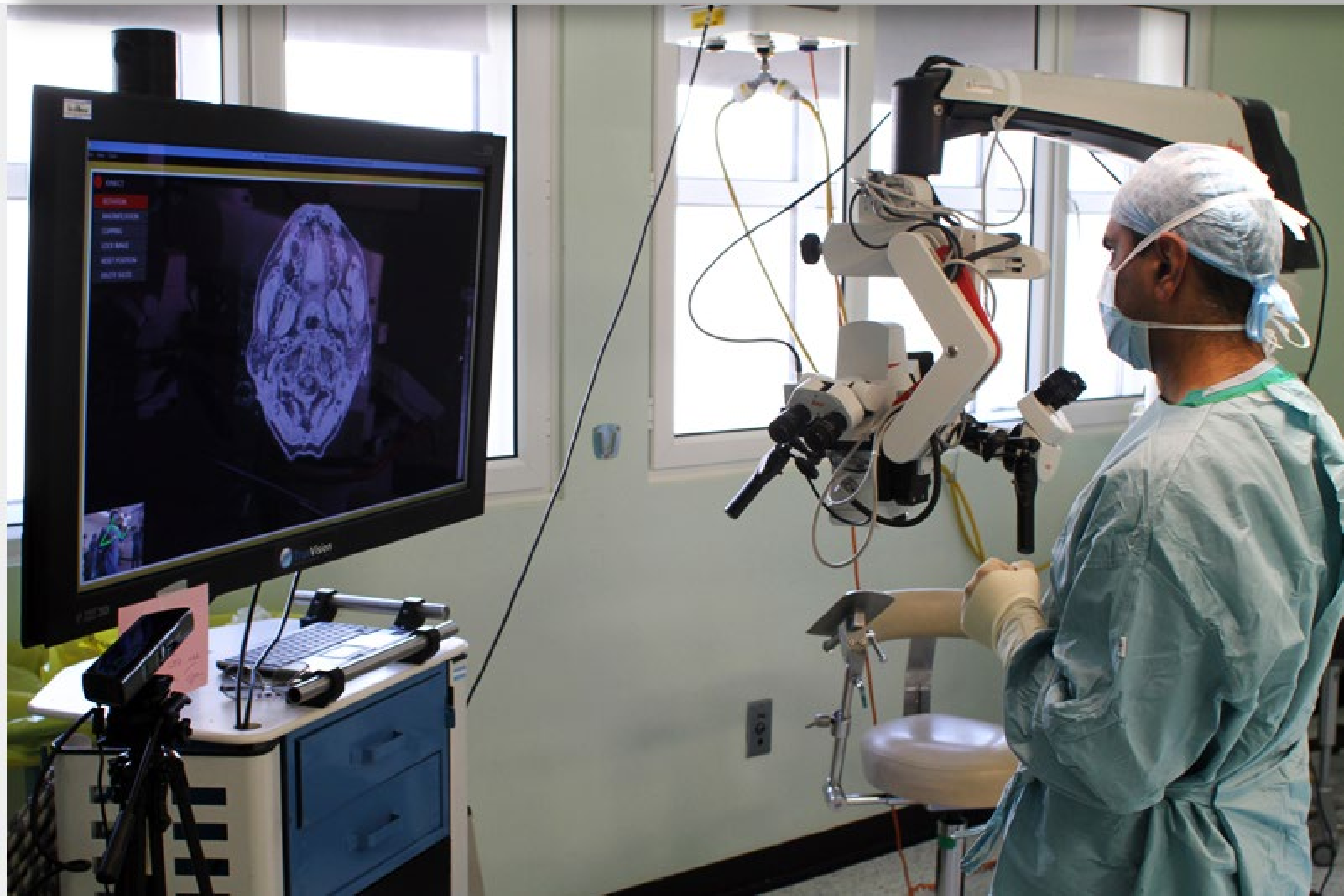
I helped invent the Internet of Things. Here's why I'm worried about how secure it is.

By SANJAY SARMA

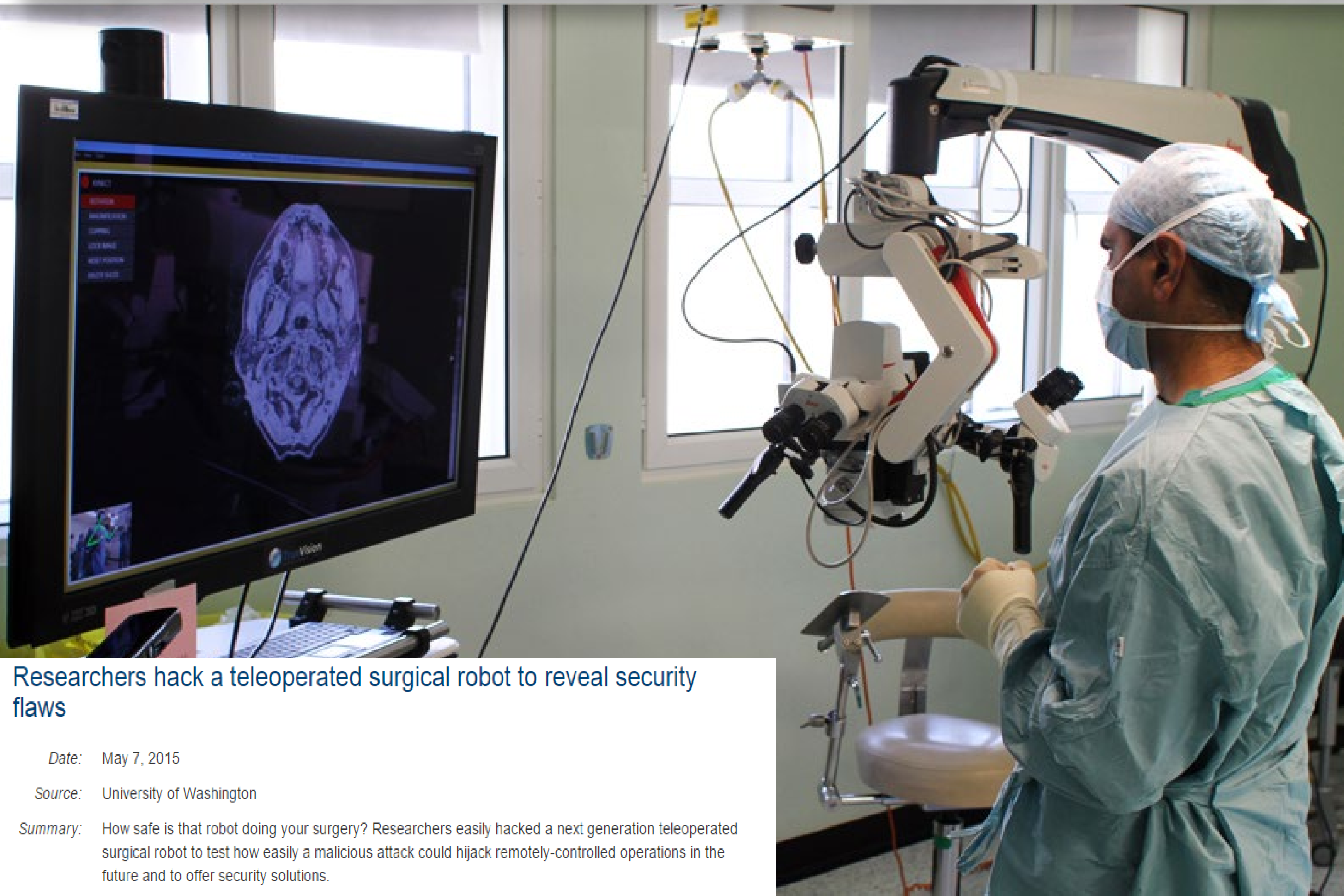
Peter Greenwood for POLITICO

I'm a mechanical engineering professor at MIT, and 17 years ago, with my colleagues David Brock, Kevin Ashton and Sunny Siu, I helped launch the research effort that laid some of the groundwork for the Internet of Things. As you might imagine, my life is pretty connected.

Remote Robotic Surgery – Operation Theatre of the Future



Operational Security of the Future ?



Researchers hack a teleoperated surgical robot to reveal security flaws

Date: May 7, 2015

Source: University of Washington

Summary: How safe is that robot doing your surgery? Researchers easily hacked a next generation teleoperated surgical robot to test how easily a malicious attack could hijack remotely-controlled operations in the future and to offer security solutions.

National Science Foundation
WHERE DISCOVERIES BEGIN

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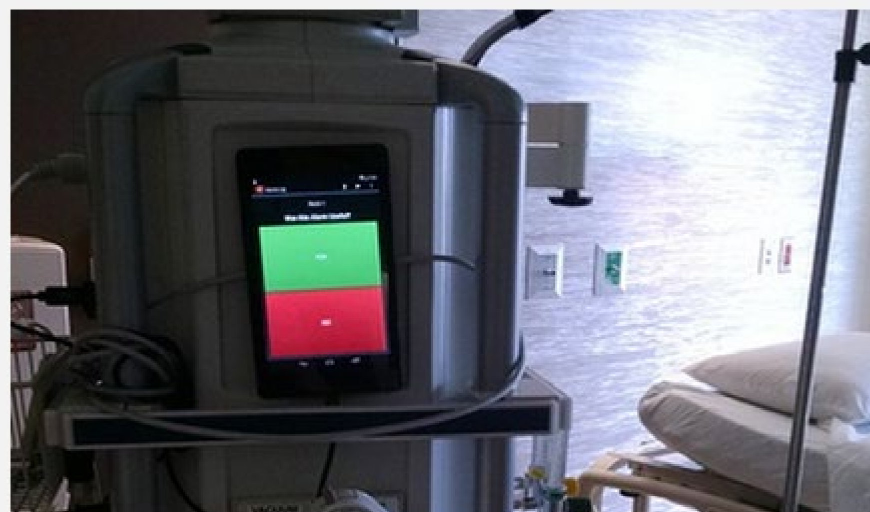
NSF CPS
MEDICAL
DEVICE
SECURITY

Press Release 15-096

A partnership to secure and protect the emerging Internet of Things

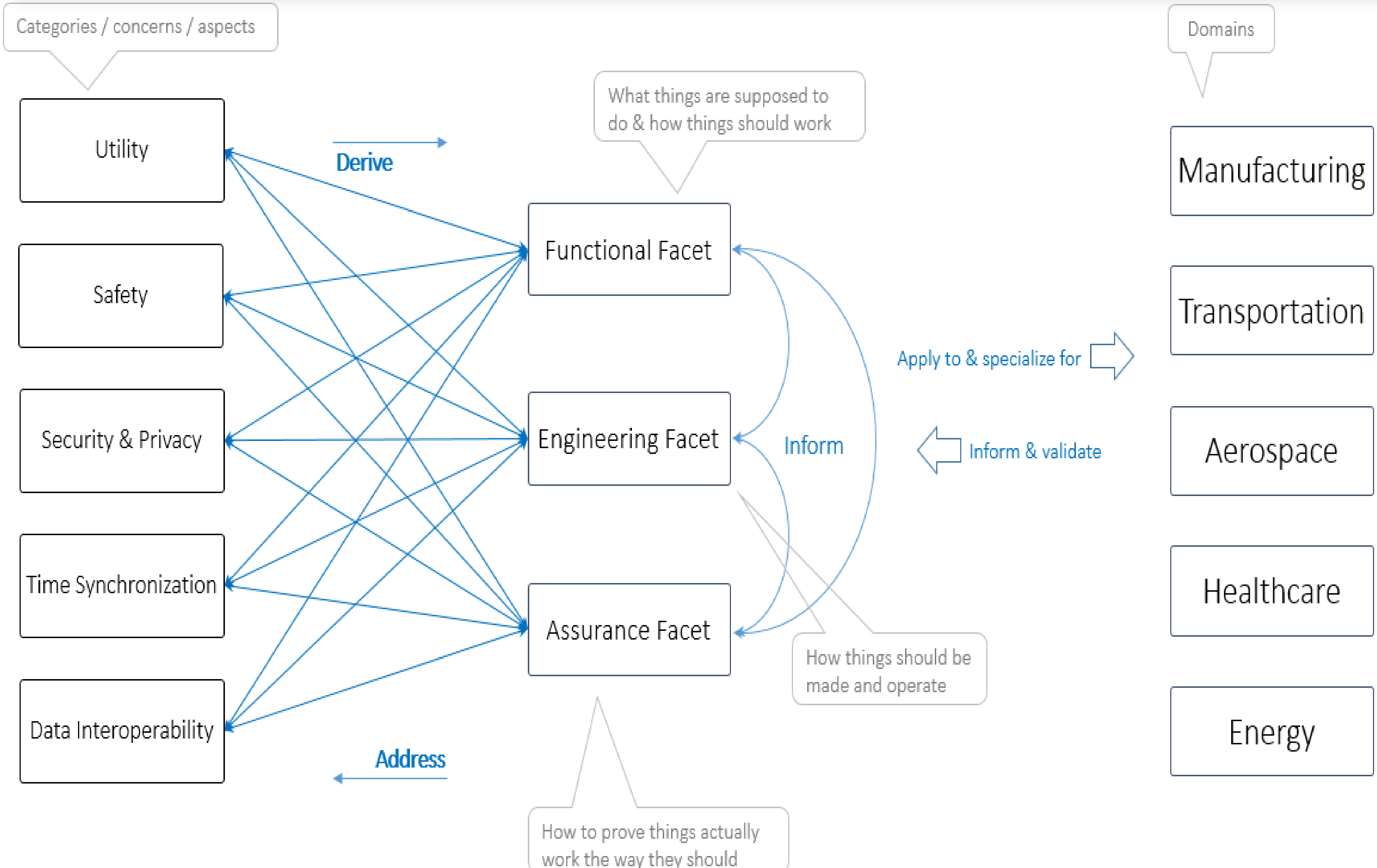
National Science Foundation and Intel Corporation team to improve the security and privacy of computing systems that interact with the physical world using a new cooperative research model



Researchers will adapt smart alarm research to detect and react to attacks on medical devices.

28 August 2015

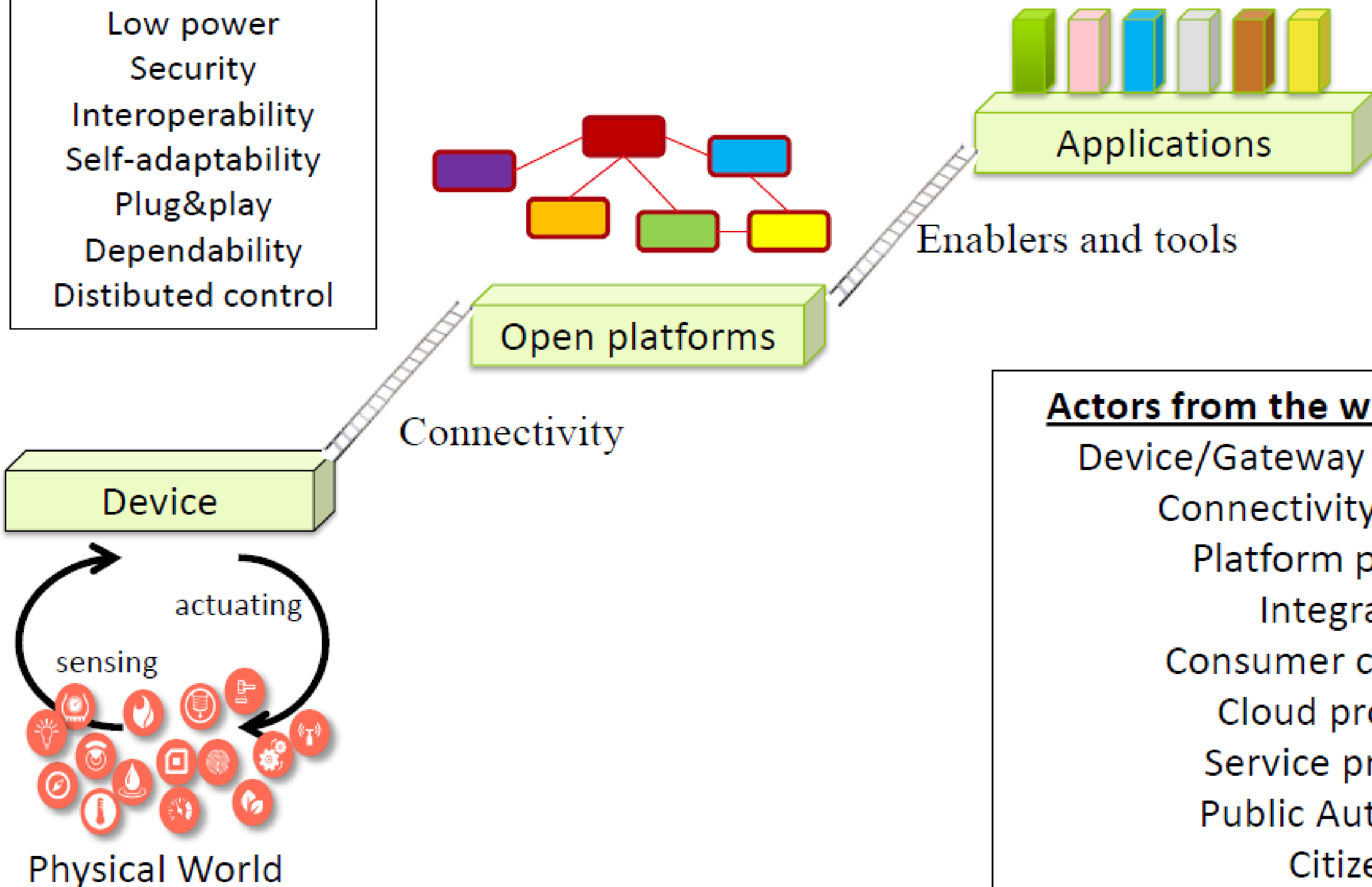
Apply Analytical Rigor of CPS to Health IT



General Abstraction ● Connectivity, Open Platforms and Broad Spectrum of Applications

Technical challenges

Heterogeneity
Integration
Low power
Security
Interoperability
Self-adaptability
Plug&play
Dependability
Distibuted control

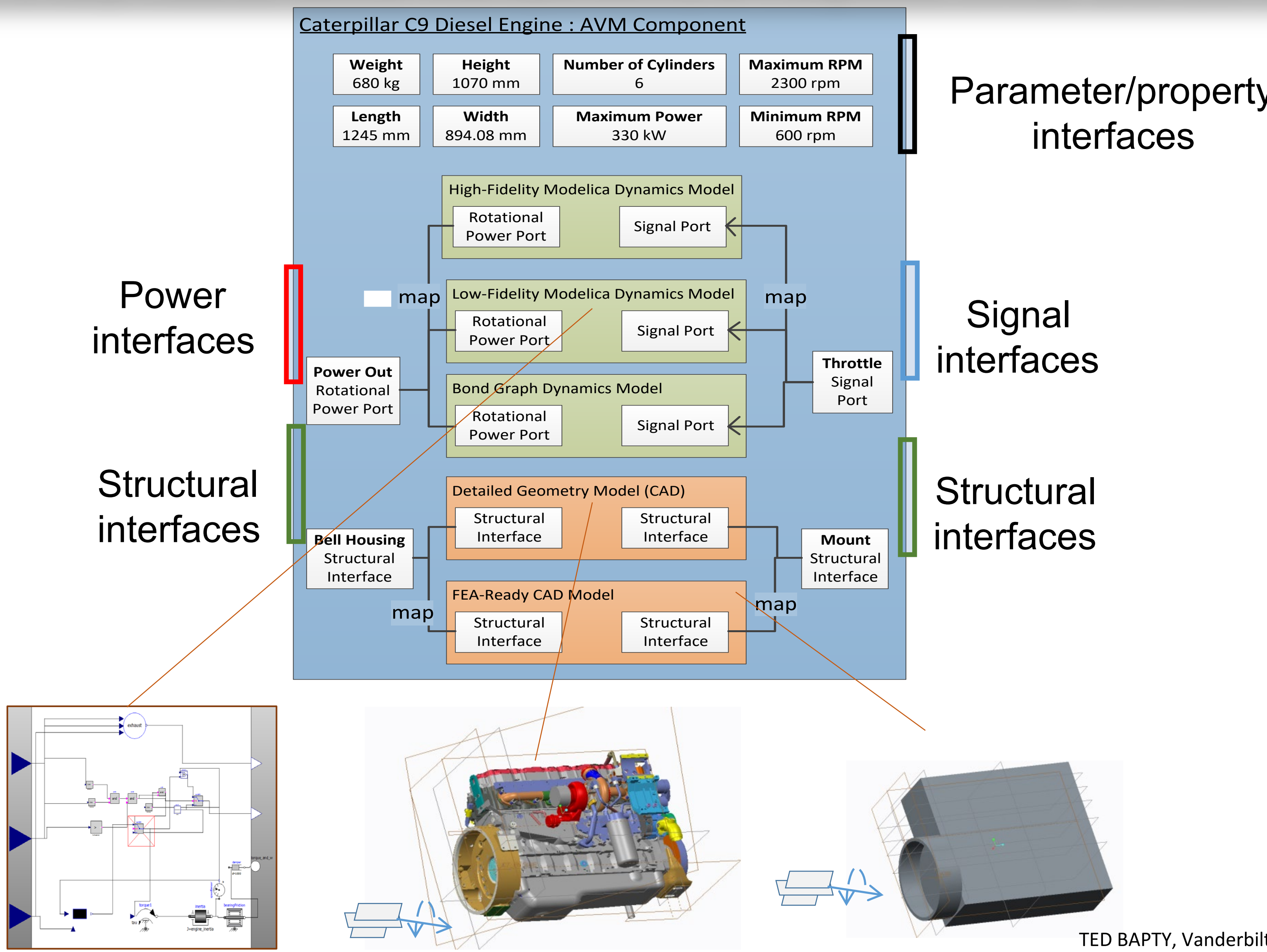


Actors from the whole value chain

Device/Gateway manufacturers
Connectivity providers
Platform providers
Integrators
Consumer companies
Cloud providers
Service providers
Public Authorities
Citizens

AVM Component Model

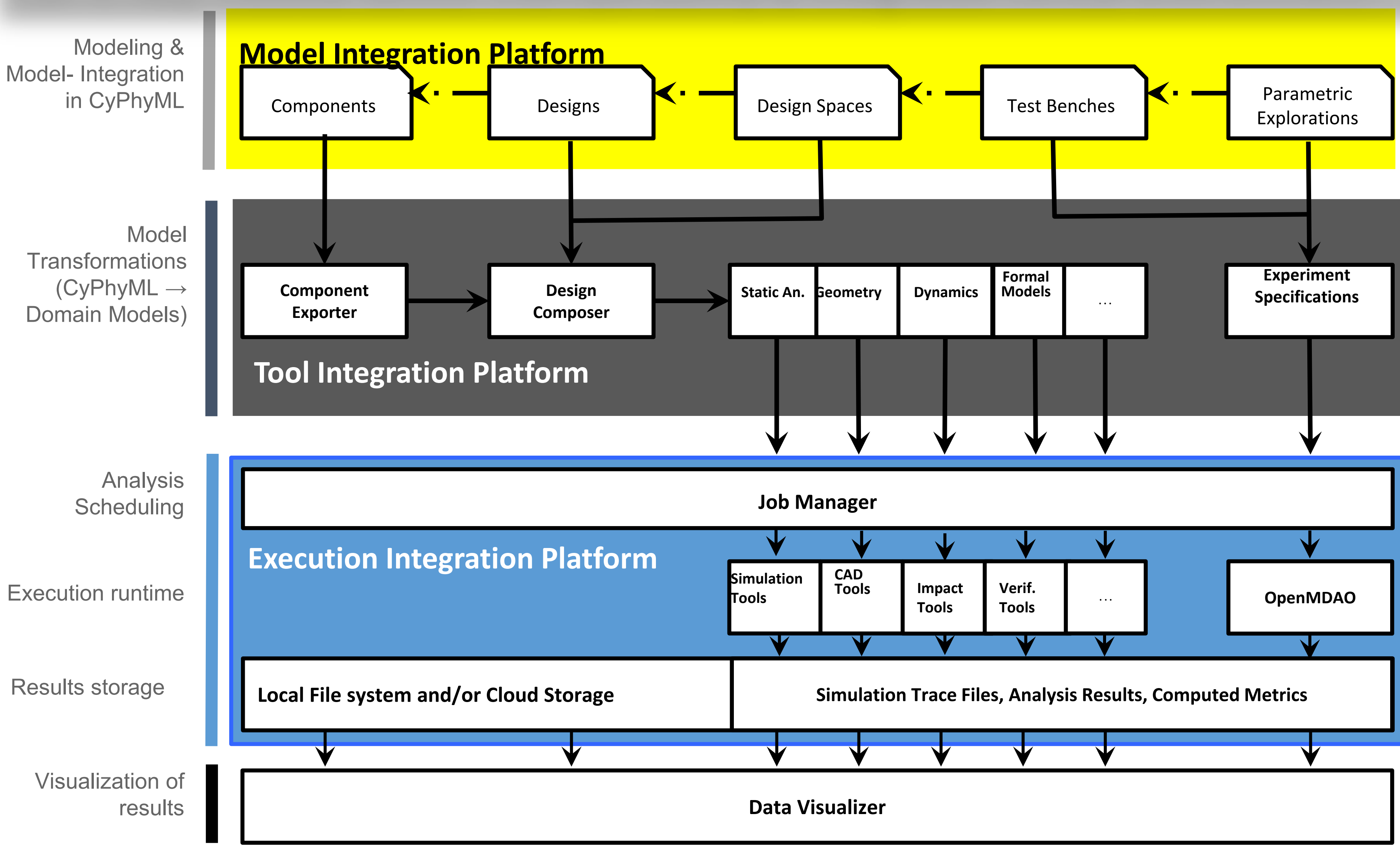
Can it help medical device interoperability & integrated clinical environment ?



TED BAPTY, Vanderbilt University

Meta Tool Suite Architecture

Can it help medical device interoperability & integrated clinical environment?



DR TED BAPTY ● www.isis.Vanderbilt.edu ● http://bit.ly/META-TOOL-SUITE

AVM Component Model

Can it help medical device interoperability and integrated clinical environment ?

If you combine the model and the tool suite can you create an exact digital representation of the dynamic clinical environment of the patient attached to various devices from ER to OR and from post-operative ICU to discharge?

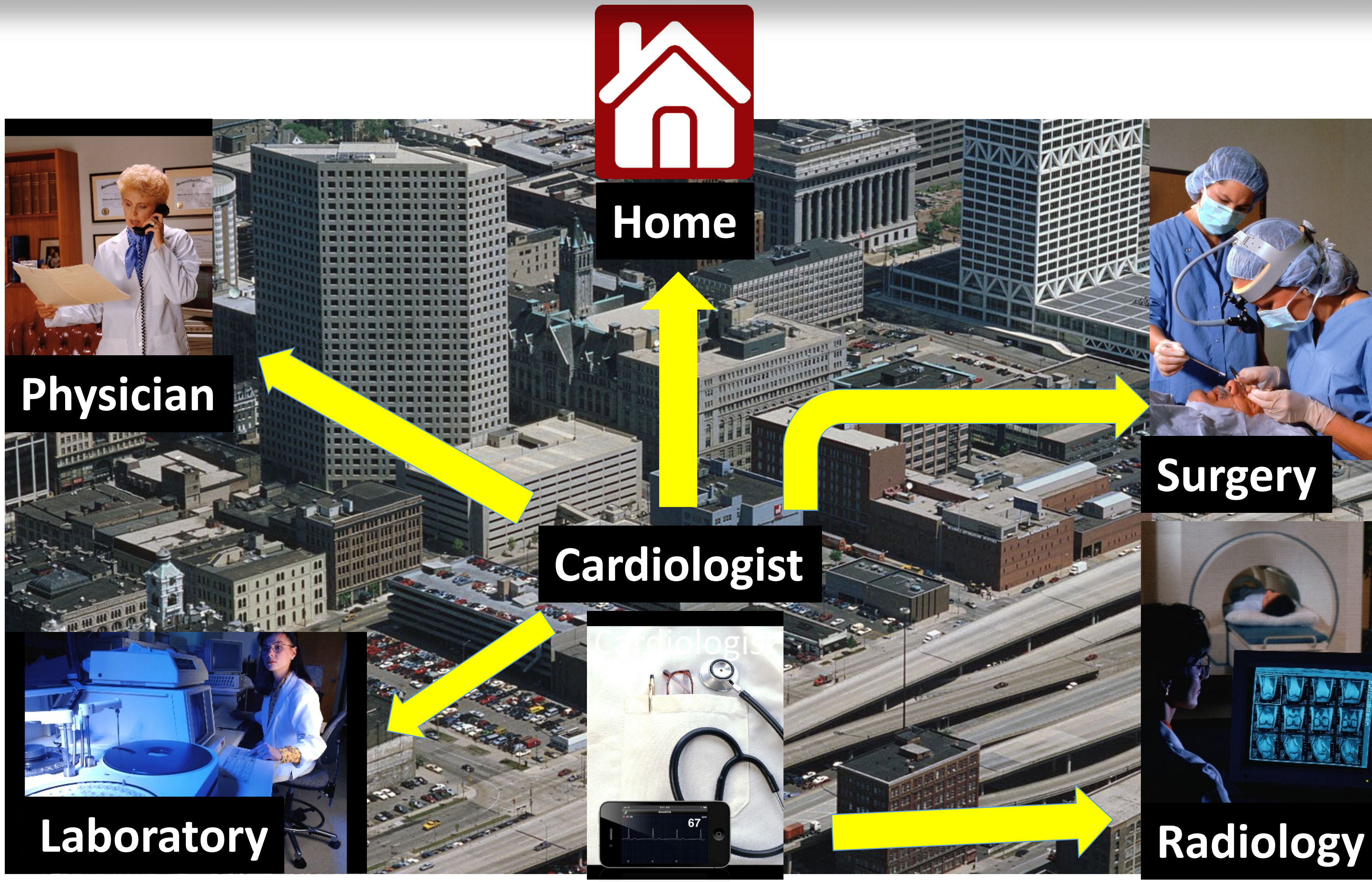
The creation of a digital duplicate as an entity level agent based model is essential to analytics and simulation of what-if scenarios (deterministic) to better prepare for the non-deterministic states (emergency). This approach is not limited to medicine but crucial for any "atom" with connected bits (data),

Digital duplication will be the underpinning of all most all elements in the context of connectivity (IoT, IIoT). Data from each individual node of this model (eg sensor data from each part in a machine with hundreds of parts) will feed the digital duplicate connected to algorithm engines in the cloud to drive real-time analytics, provide feedback to improve efficiency or precision of the machine or device or process or decision support system in a manner that is context-aware and delivers intelligence at the edge to boost autonomy.

Meta Tool Suite Architecture

Can it help medical device interoperability and integrated clinical environment?

Evolution of the Integrated Healthcare Platform(s)
n-Directional Data Access via Secure Interoperable Standards



Ubiquitous Remote Monitoring from Edge Devices
Potential Diagnostic Value in Digital Health IT

General Purpose In and Out – GPIO
CPU, Memory (16 GB), WiFi, Bluetooth

Edge Ambient Intelligence – Analytics in the Mist
Latency boundary unsuitable for fog or the cloud

Ubiquitous Remote Monitoring from Edge Devices EYERISS – real time analytics for Digital Health PoC

http://www.rle.mit.edu/eems/wp-content/uploads/2016/02/eyeriss_isscc_2016_slides.pdf

http://people.csail.mit.edu/emer/papers/2016.06.isca.eyeriss_architecture.pdf

https://dspace.mit.edu/handle/1721.1/101151

MIT introduced a new computer chip optimized for deep-learning, an approach to AI. The chip, dubbed "Eyeriss" could allow mobile devices to perform tasks like natural language processing and facial recognition without being connected to the internet. It's the latest attempt to make the complex operations of machine learning more portable. That means that our smartphones, wearables, robots, self-driving cars, and other IoT devices could begin performing complex deep learning processes, locally, with the aid of analytical engines at the edge (without cloud or fog).

How will sensor-enabled wearables integrate with the ecosystem of digital health IT ?

Hands-Free

- Voice / gesture control

Always-On

- Low power consumption
- Instant wake
- Background working / sensing

Environment -Aware

- GPS
- Accelerometer
- Compass
- Camera
- Microphone
- Other Sensors

Connected

- Wi-Fi
- 3G / 4G
- Bluetooth
- NFC

Attention-Getting

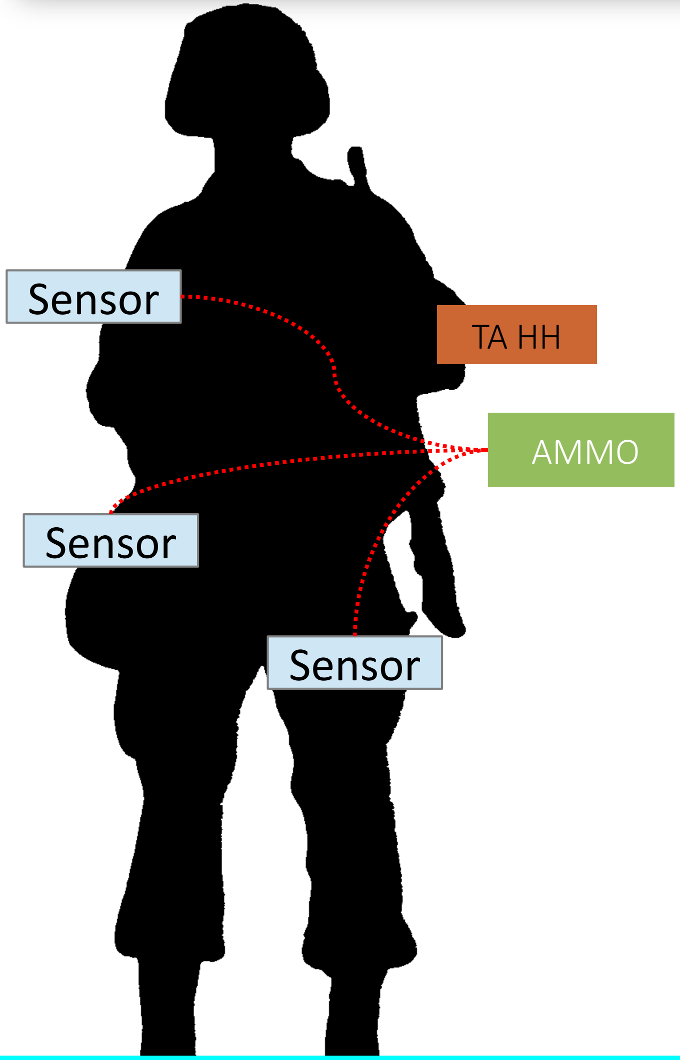
- Less distracting when receiving alerts / reminders / messages

Development Platform

- 3rd party apps
- API partners
- Accessories

MIT

BAN – Body Area Networks



- Bluetooth-enabled sensors / devices
- AMMO receives/uploads sensor data

- glucose
- heart rate
- pulse oximeter
- body temperature
- pedometer

- Soldier in desert (high temperature)
- Monitor health via sensor data / analytics
- Intervene before it is necessary / prevent A&E

POTENTIAL AMMO APPLICATIONS

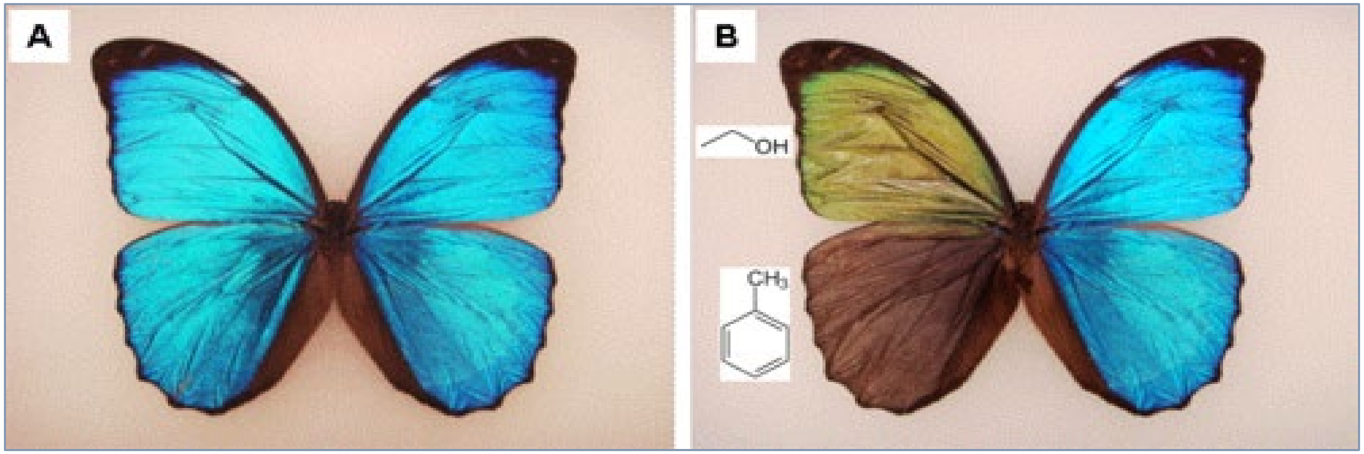
- Pre- and Post- surgery interactive care plan execution and monitoring
- Improved home-health & patient communication with social partners
- Remediate loss of HIV patients identified for anti-retro viral treatment
- Ebola Infection - patient, population and physician data / monitoring
- Adhoc mesh / zero configuration networking for search & rescue (A&E)
- Google Project Ara - integrated/on-platform tactical radio and SDR
- Novel nano-sensors with embedded sub-cutaneous radio/transmitters

Sandeep Neema

Android Mobile Middleware Objects

Emergence of IoS Preventive Medicine Era ● Wearable Diagnostic Devices with High Performance Ultra-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 have 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). Radislav Potyrailo's team at GE wants to use their findings to develop fast, ultra-sensitive thermal and chemical imaging sensors for applications in night vision goggles, super-sensitive surveillance cameras, handheld or wearable medical diagnostic devices. ☑ www.gereports.com/post/80985289914/like-a-butterfly-out-of-hell-the-next-wave-of

Digital Health Diagnostics

MIoT as a catalyst for preventative medicine?


DO ANY OF YOUR RELATIVES SUFFER FROM MENTAL ILLNESS?


DO ANY OF YOUR RELATIVES SUFFER FROM MENTAL ILLNESS?
NO.... THEY ALL SEEM TO ENJOY IT!!!

Michael S. Strano

Carbon P. Dubbs Professor of Chemical Engineering

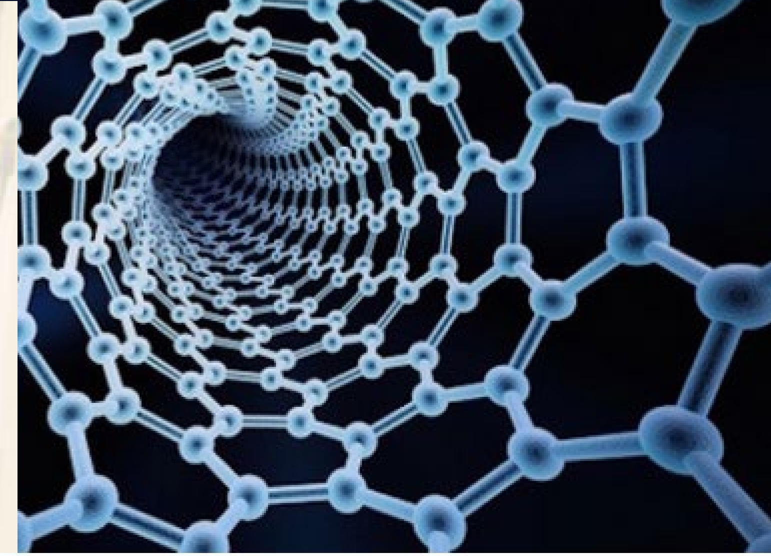
Department of Chemical Engineering

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

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

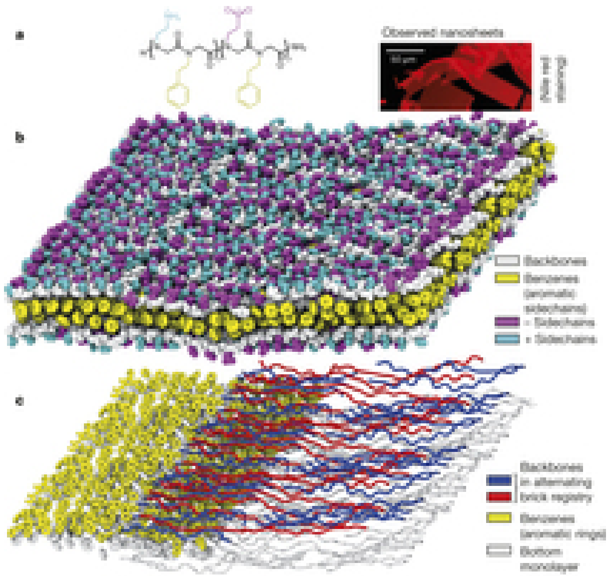
Past efforts to develop implantable sensors have failed, due to the body's inclination to protect itself and recycle biological material. Devices can become wrapped in scar tissue, or their components can be broken down. The team believes that the nanotube sensors can be effective for the long term.

Printed Proteins?

Printed Insulin? What about secondary structure?

Printed Proteins? It could happen …

Figure 1: Snapshot of a peptoid nanosheet obtained from molecular-dynamics simulations.



a, Left, an amphiphilic 28-residue peptoid, which assembles into extended nanosheets only two molecules thick[10], as shown in the fluorescent-microscopy image to the right. **b**, Snapshot of a bilayer, obtained from molecular-dynamics simul…

Peptoid nanosheets exhibit a new secondary-structure motif

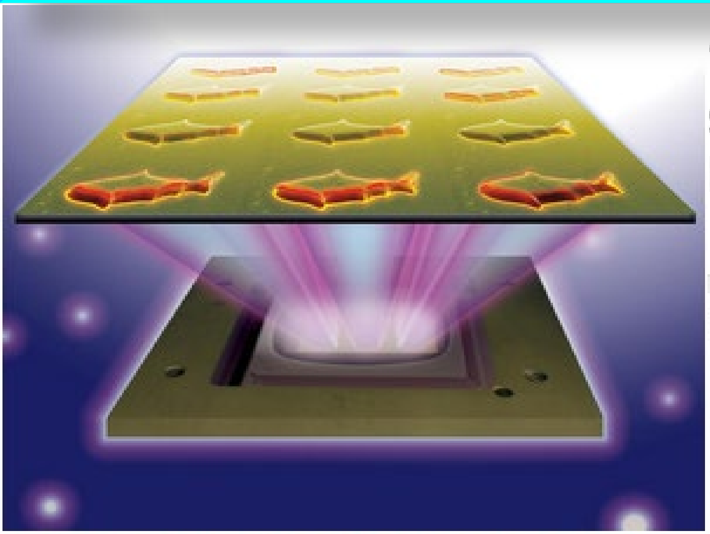
Ranjan V. Mannige, Thomas K. Haxton, Caroline Proulx, Ellen J. Robertson, Alessia Battigelli, Glenn L. Butterfoss, Ronald N. Zuckermann & Stephen Whitelam

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 degradation[3], 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 limited[9]. 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.

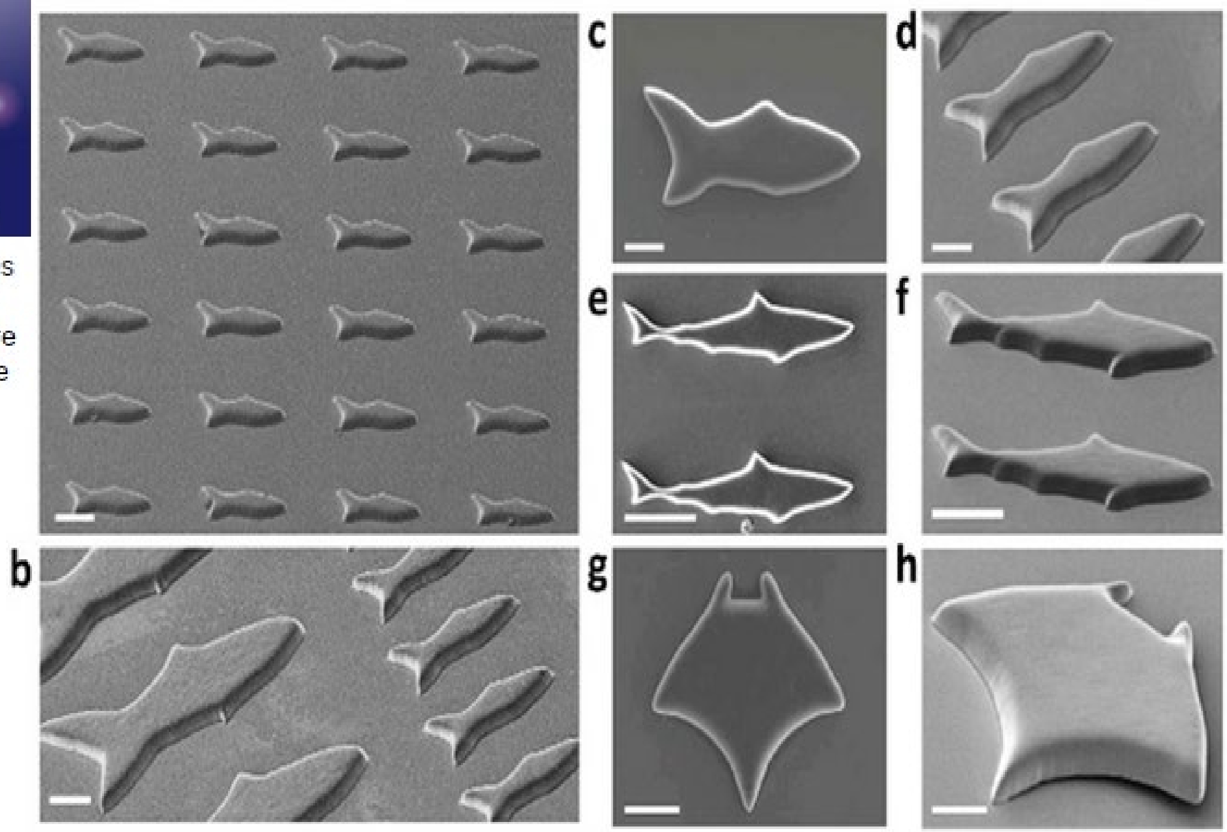
Conceptual Convergence of Material Genome with the Human Genome?



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.

Prof Shaochen Chen and Joseph Wang, NanoEngineering Dept, UC San Diego



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.

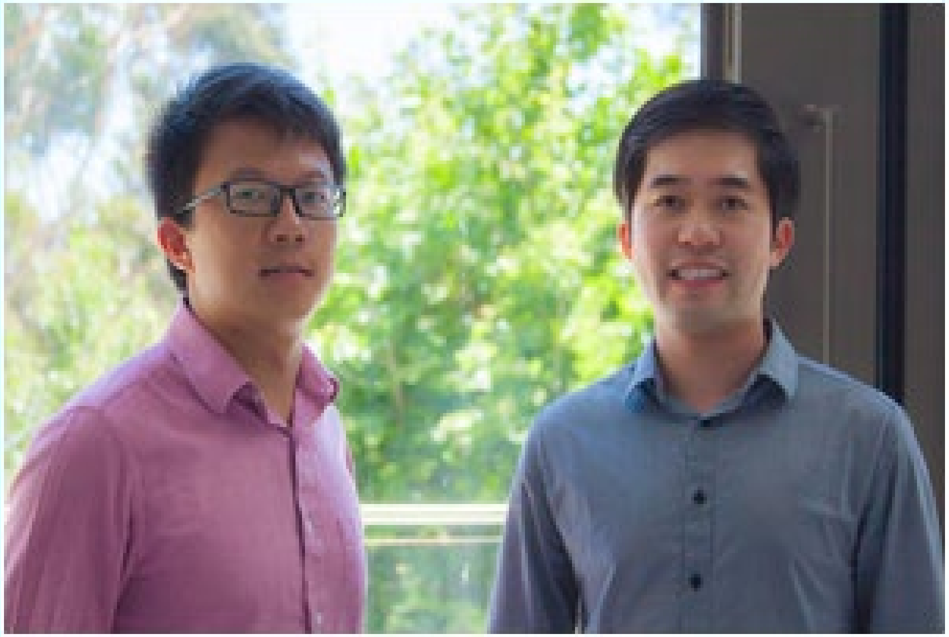
http://bit.ly/POTUS-REPORTS

Materials Views
www.MaterialsViews.com
http://onlinelibrary.wiley.com/doi/10.1002/adma.201501372/pdf
ADVANCED MATERIALS
www.advmat.de

3D-Printed Artificial Microfish

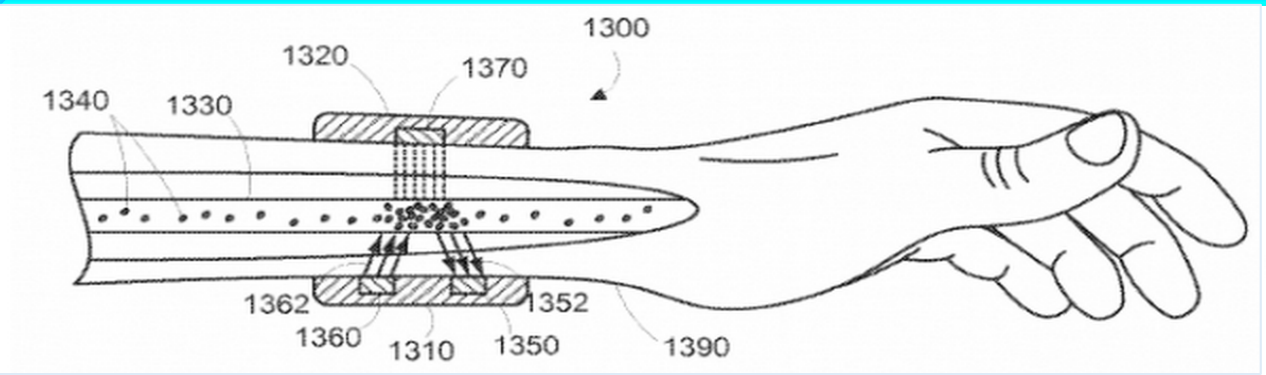
Wei Zhu, Jinxing Li, Yew J. Leong, Isaac Rozen, Xin Qu, Renfeng Dong, Zhiguang Wu, Wei Gao, Peter H. Chung, Joseph Wang , and Shaochen Chen**

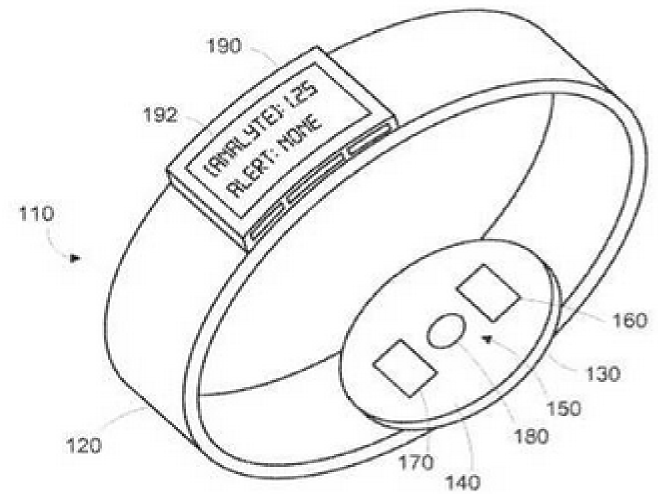
To maneuver within their environment, aquatic organisms employ a variety of locomotive strategies. These diverse mechanisms offer inspiration in designing artificial microswimmers for applications ranging from directed drug delivery to accelerated environmental decontamination.[1–6]One challenge in adapting naturally evolved designs for "smart" microswimmer systems lies in replicating their complex biomimetic form and function. Here, using a rapid 3D printing platform – microscale continuous optical printing (μCOP) – we engineered hydrogel microfish featuring biomimetic structures, locomotive capabilities, and functionalized nanoparticles. The μCOP system can print complex 3D structures within seconds at high resolution (≈1 μm) across multiple orders of magnitude in scale. The 3D-printed microfish exhibits propulsion that is highly efficient, chemically powered, and magnetically guidable. By incorporating polydiacetylene (PDA) nanoparticles, we demonstrate the microfish's utility in toxin-neutralization applications. The multiple capabilities integrated within these proof-of-concept microfish highlight the technical flexibility and broad applicability of our approach in engineering advanced functional biorobotics for actuation, sensing, and detoxification.

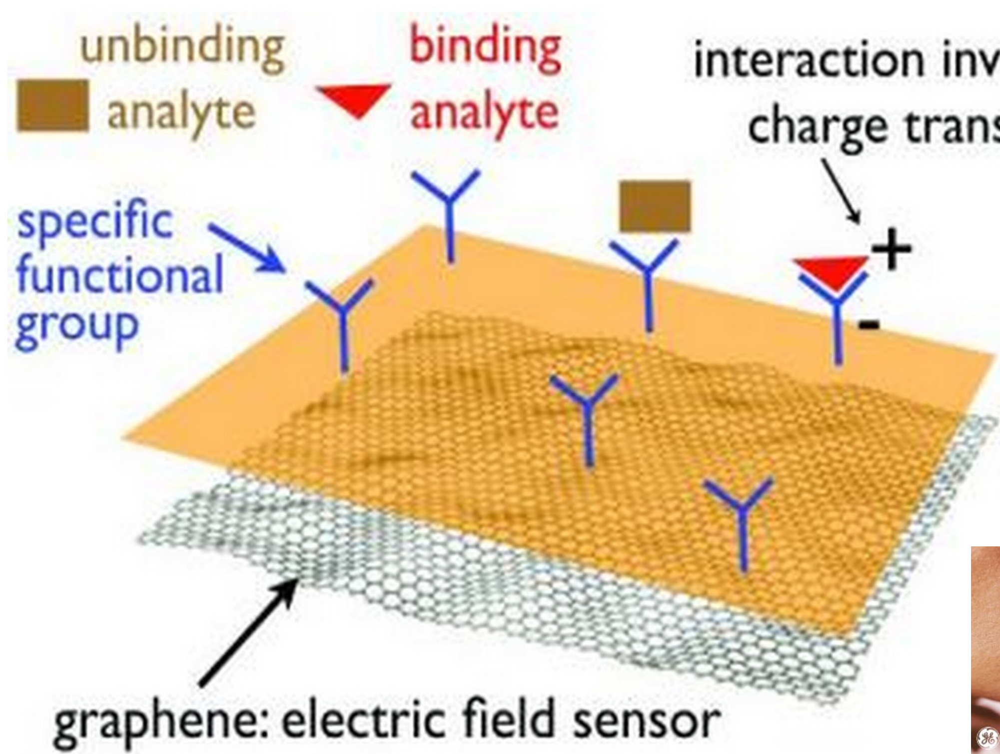


The co-first authors Jinxing Li (right) and Wei Zhu (left), both nanoengineering Ph.D. students at the UC San Diego Jacobs School of Engineering.

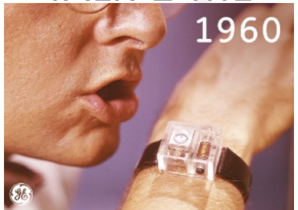
Target Specific Analytes in Detection, Monitoring & Treatment







TALK-2-ME



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

http://genesdev.cshlp.org/content/19/18/2100.full.pdf+html

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

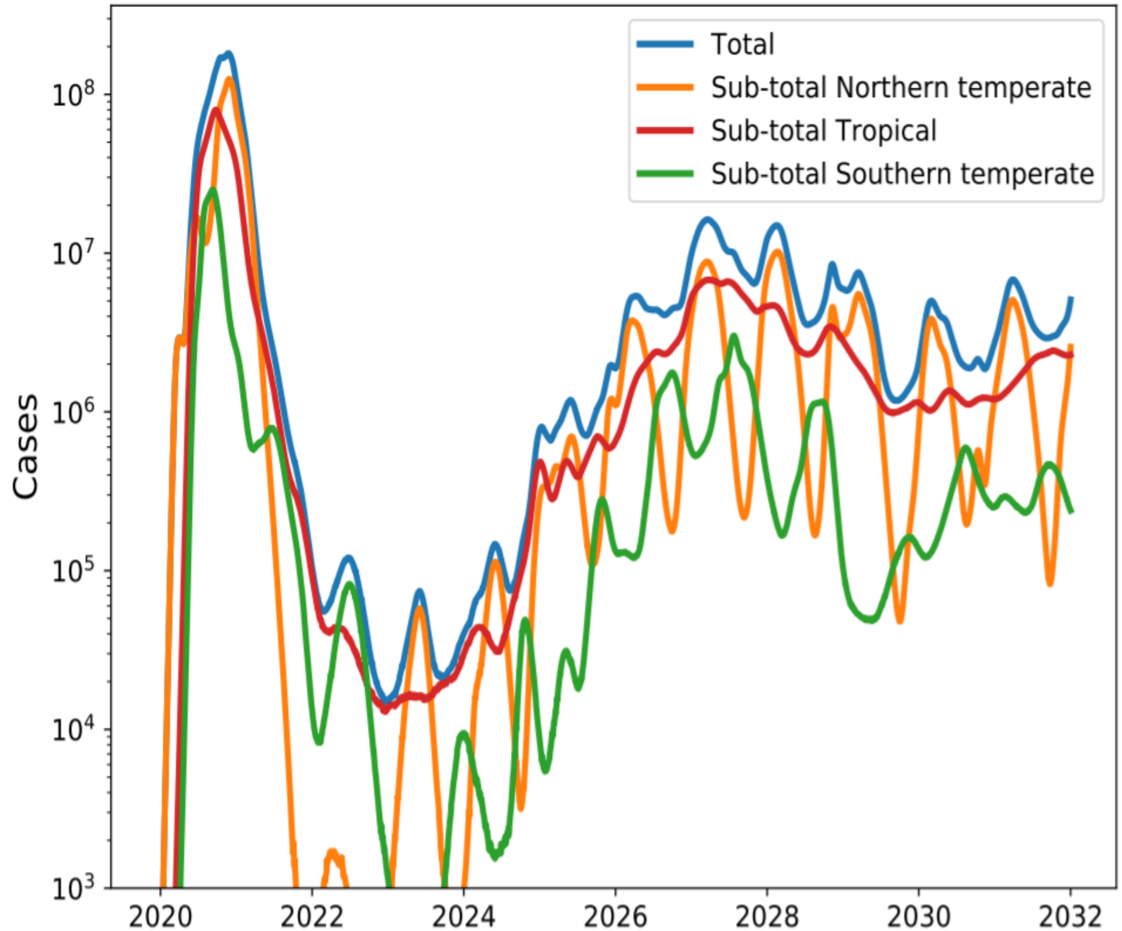
ANALYTES ??
Cohesin ?
Shelterin ?
Condensin ?

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

PAPPU

PAY A PENNY PER USE ◆ Pay-Per-Pee Home Health is a Human Right ?

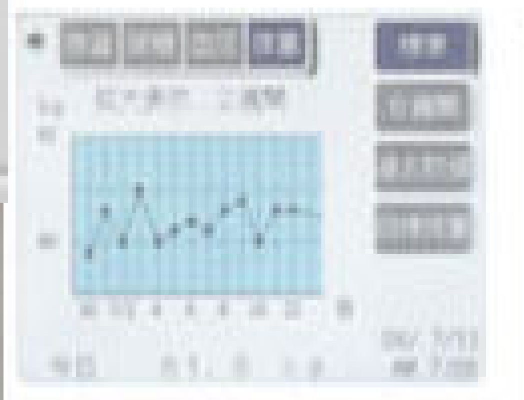
Why do entrepreneurial innovators ignore the social business opportunity for adopting simple 'boxes' at the edge concept to reduce falls due to osteoporosis or monitor metabolism to enable data fusion and analytics to predict / prescribe need for pro-active diagnosis / data-informed treatment?



www.medrxiv.org/content/10.1101/2020.02.13.20022806v1.full.pdf

FIG. 5 **Transition to an endemic seasonal virus.** If previously infected individuals can be reinfected after some time, as for example by seasonal influenza virus, SARS-CoV-2 could develop into a seasonal CoV that returns every winter. This would typically happen at much lower prevalence than peak pandemic levels. These simulations assume reinfection on average every 10 years.

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



Weigh-scale, BMI, FOBT, urine analysis, 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 or clinic, globally.

Walgreens Specials - $1.99 for 24-pack Diet Coke • $1.99 for Bone Density • $1.99 Mammogram

PDEXA SCAN
BONE MINERAL
DENSITY PROFILE

Value Network Ecosystem Testbed

Walgreens – Retail Healthcare
GE – Equipment
Cisco – IPv6 Routers
AT&T – Data Transmission
Intel – MIPS
IBM – Data Analytics
Samsung – Diagnostic Apps
Walmart – Grocery Supply Chain

PAPPU

Pay A Penny Per Use

Walgreens Specials - $1.99 for 24-pack Diet Coke • $1.99 for Bone Density • $1.99 Mammogram

PDEXA SCAN
BONE MINERAL
DENSITY PROFILE

Value Network Ecosystem Testbed

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Samsung – Diagnostic Apps
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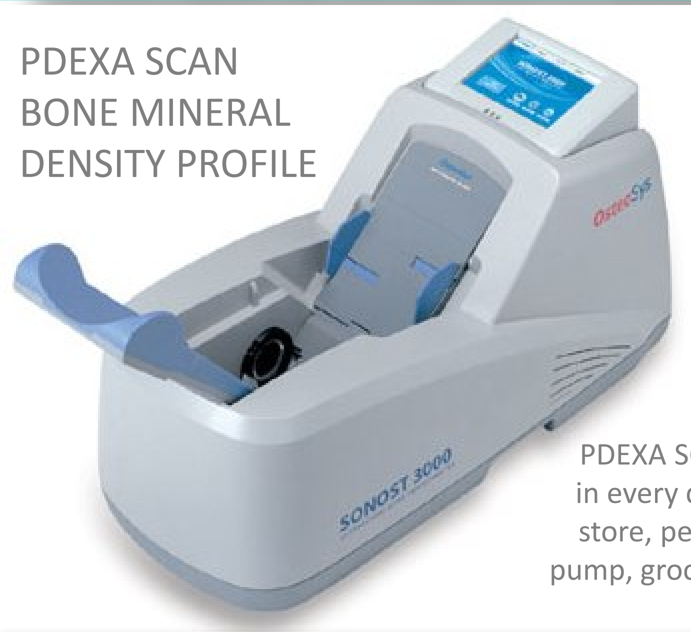
Why do entrepreneurial innovators ignore the social business opportunity for adopting simple 'boxes' at the edge concept to reduce falls due to osteoporosis & monitor metabolism to enable data fusion and analytics to prescribe need for pro-active diagnosis / data-informed treatment?

CVS Special $0.99 for 1-quart Milk • $1.99 for Bone Density • $2.99 Mammogram

PDEXA SCAN
BONE MINERAL
DENSITY PROFILE



PDEXA SCAN in every drug store, petrol pump, grocery

Osteoporosis

EU → 28 million in 2010 to 34 million in 2025 (increase of 23%)

US → 44 million (represents 55% of people aged 50+)

Brazil → 10 million (1 in every 17)

India → 36 million (2013)

China → 70 million (50+). Cost of treatment USD1.5 billion in 2006. Estimated US$12.5 billion in 2020 and US$265 billion in 2050.

In 2008, Indonesia had 34 DXA machines, half of them in Jakarta (population 237 million) which translates to 0.001 machine per 10,000 population. The equivalent recommended number for Europe is 0.11 (per 10,000)

http://bit.ly/BONE-HEALTH

Health data

CONNECT

GROCERY STORE PURCHASE LOG

Integrated system detects fall in bone density and correlates with reduced purchase of milk. Prevention for osteoporosis starts early. Avoids trauma and/or morbidity from broken bones. Connected healthcare data.

US Healthcare spending nears $4 trillion (2013)

Spending category	Costs estimated in NHEA categories (in billions)		Costs estimated with sources other than NHEA (in billions)			
	Direct Costs		Direct Costs		Indirect/ Imputed costs	
Hospital care	Hospital care	$814				
Professional services	Physician and clinical services	$516				
	Dental services	$105				
	Other professional services	$68				
	Other personal health care	$129				
			All other ambulatory	$19		
			CAM practitioner costs	$31		
			Weight-reducing centers	$2		
Long-term care (LTC)	Home health care	$70				
	Nursing home care	$143				
			Homes for the elderly	$17		
Prescription drugs	Prescription drugs	$259				
Retail products and services	Durable medical equipment	$38				
	Other non-durable medical products	$45				
			CAM products	$2		
			Health publications	$2		
			Nutrition/supplements	$56		
Direct administrative costs	Total non-personal health care	$408				
Supervisory care					Supervisory care	$492
Total		**$2,594**		**$129**		**$492**

Deloitte

Low Cost of Healthcare in India leaves billions in the dust without access to healthcare

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 → Penny Per Person Per Use Per Day

$1 - Bone density

$1 - Mammogram

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

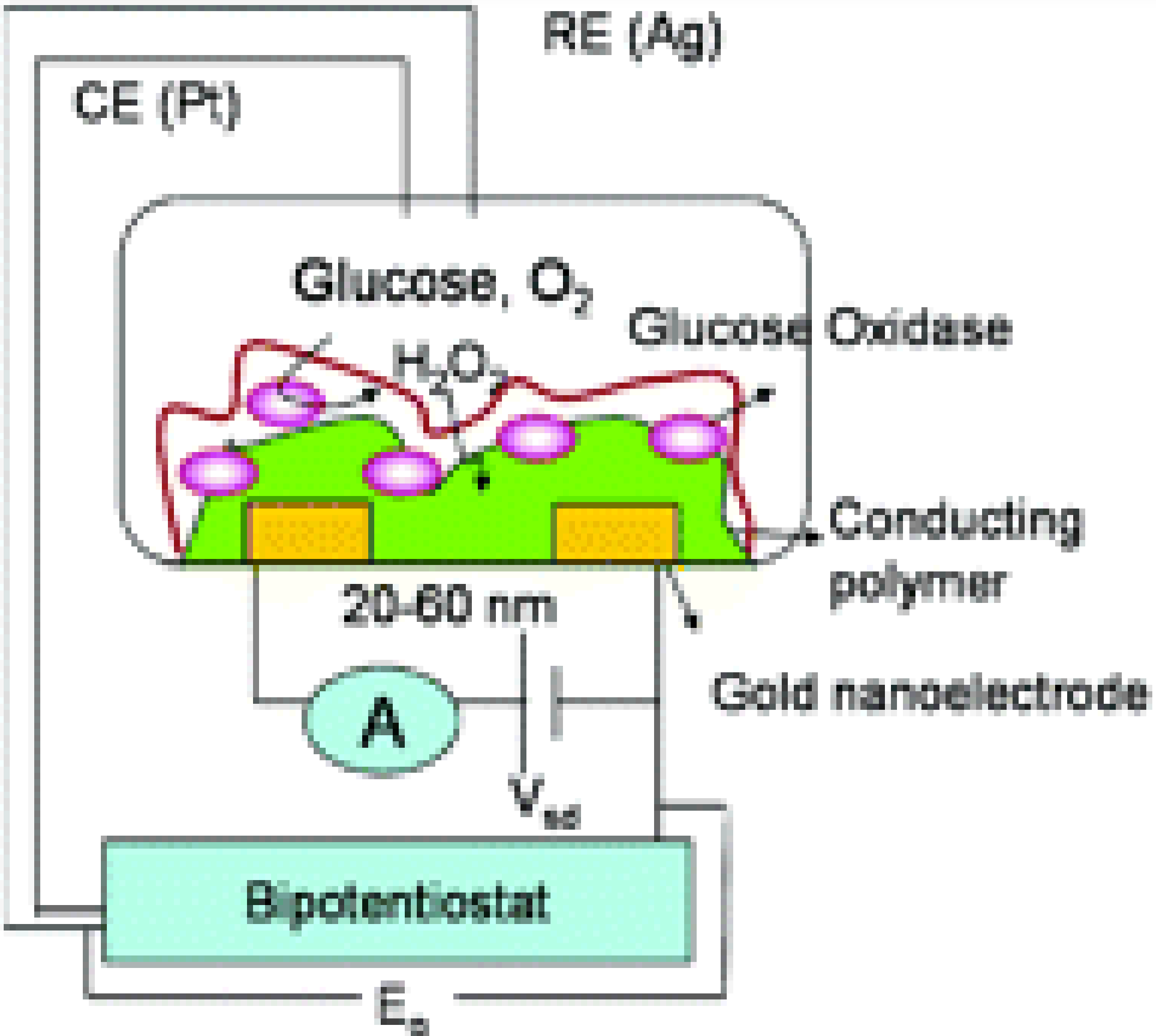
data transmitted to specialists and reports sent to individuals, doctor and clinic

The micro-revenue earnings potential with 10% penetration for population of 3+ billion & aging!

An old idea (2004)

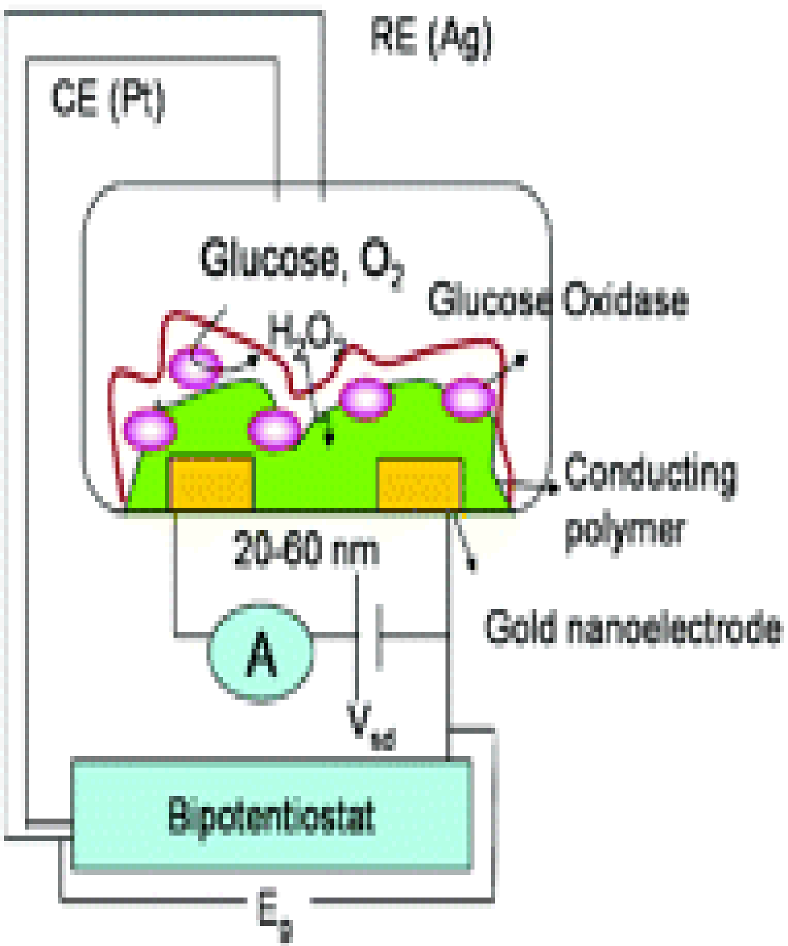
gets some new wings

Glucose NanoSensor



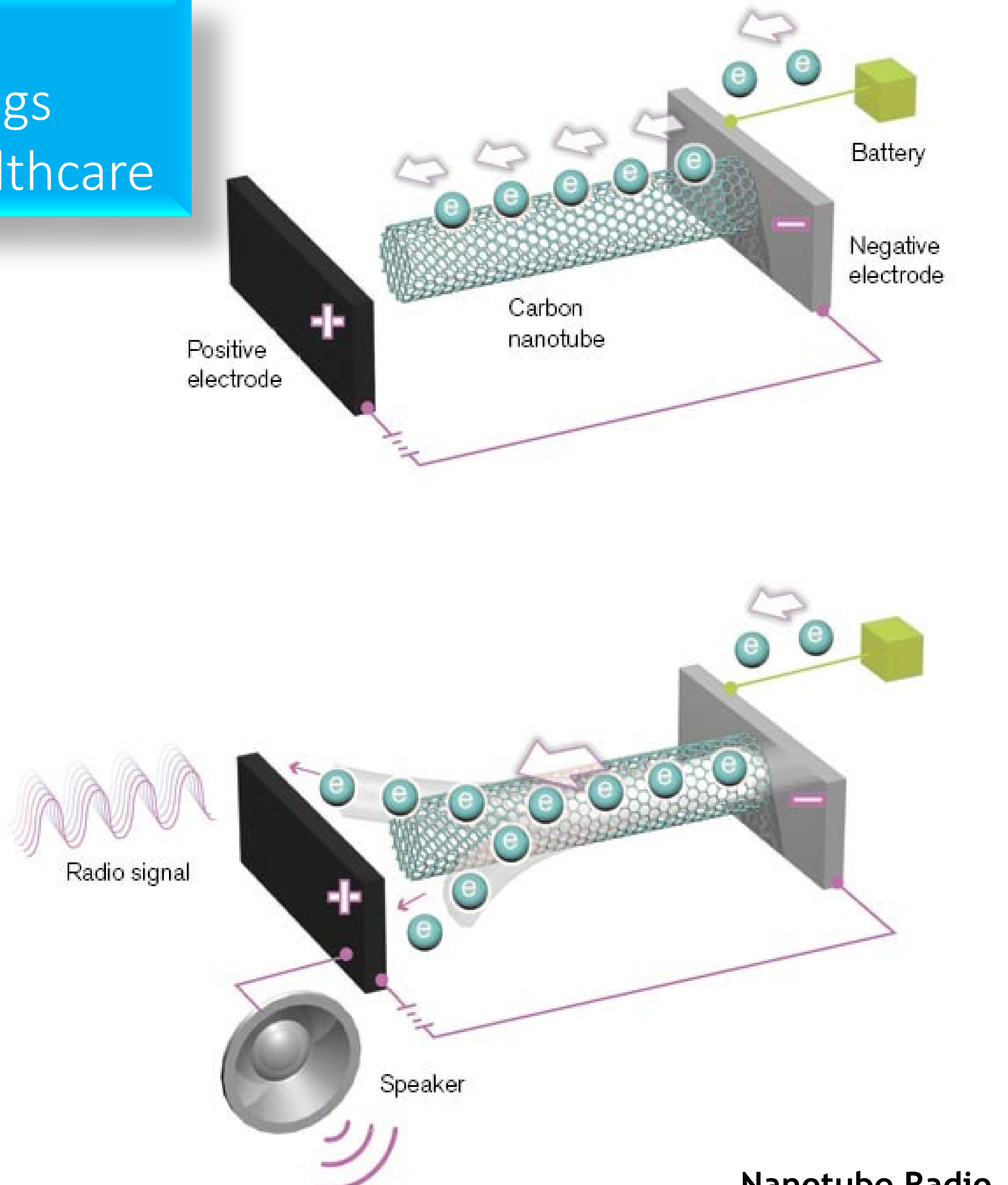
NanoLetters (2004) 4 1785-1788

The Industrial Internet
The Industrial Internet of Things
The Industrial Internet of Healthcare



Blood Glucose Nano-sensor

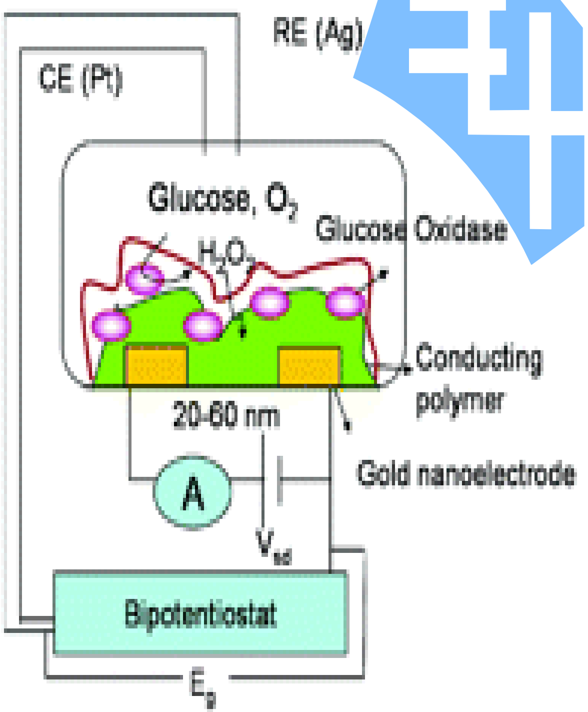
NanoLetters (2004) 4 1785-1788



Nanotube Radio

NanoLetters (2007) 7 3508-3511

Integrated Glucose NanoSensor NanoRadio



Hypothetical (S. Datta)

Diabetes affects 25.8 million people

8.3% of the U.S. population

DIAGNOSED

18.8 million people

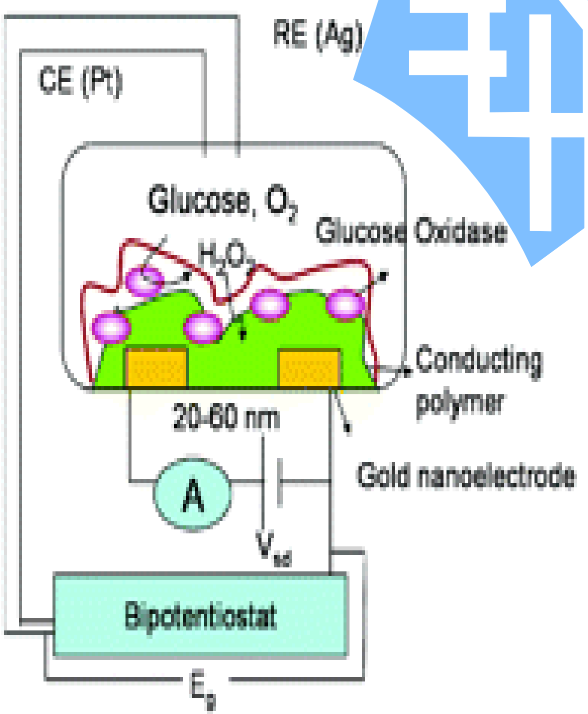
UNDIAGNOSED

7.0 million people

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

Industrial Internet of Remote Heath Monitoring

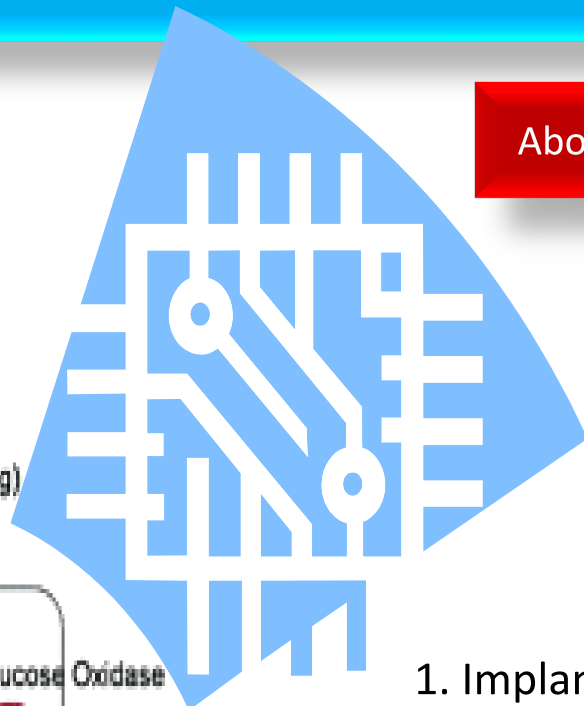
May I implant a glucose nano-sensor nano-radio chip on your shoulder? You are fat. You could become diabetic.

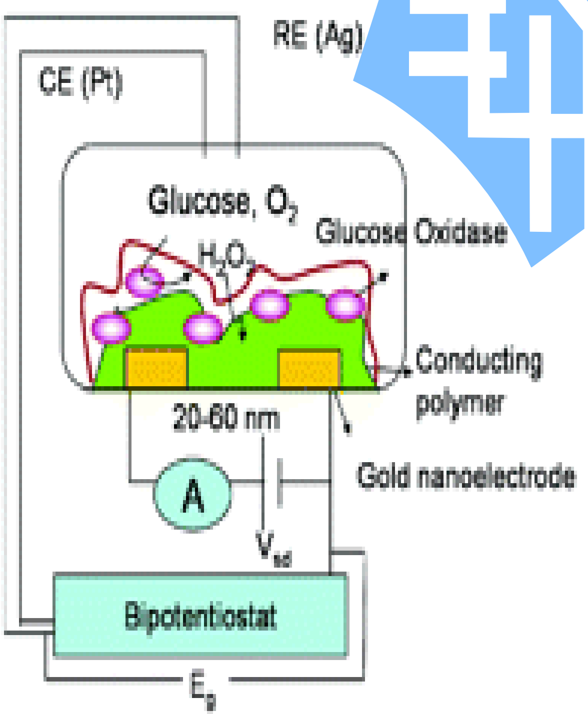


Prime Minister Bertie Ahern (Taoiseach) 2005 at TCD, IRL

Glucose NanoSensor NanoRadio ecosystem of health-care monitoring

About 30 million individuals in US affected by diabetes





1. Implanted wireless sensor transmits blood glucose data from home or office or airport (WiFi/WAN/gateway)

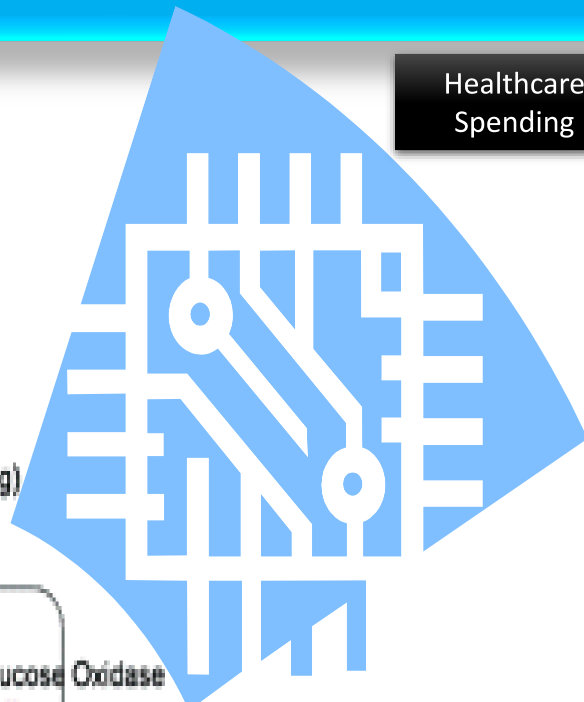
2. Data travels from you to your hospital or clinic (MAN)

3. Blood glucose data updates risk and patient profile

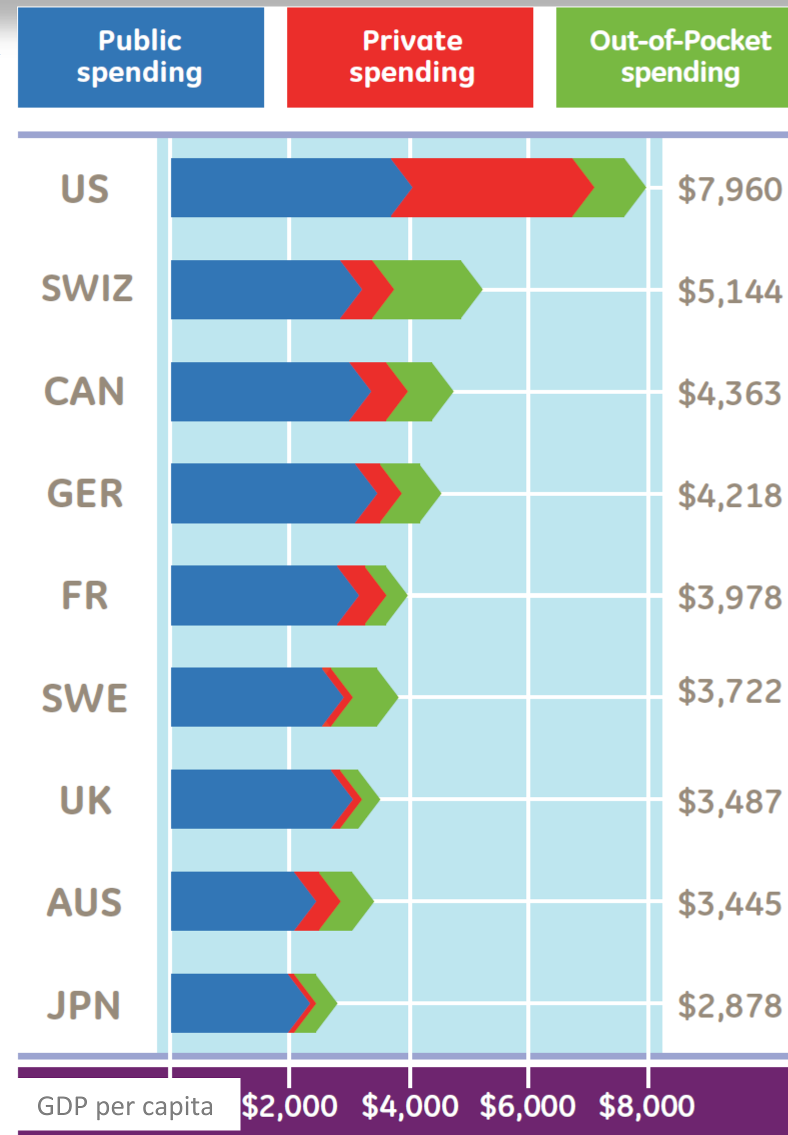
4. If you need medical attention or insulin or other treatment then auto-responder sends message or calls

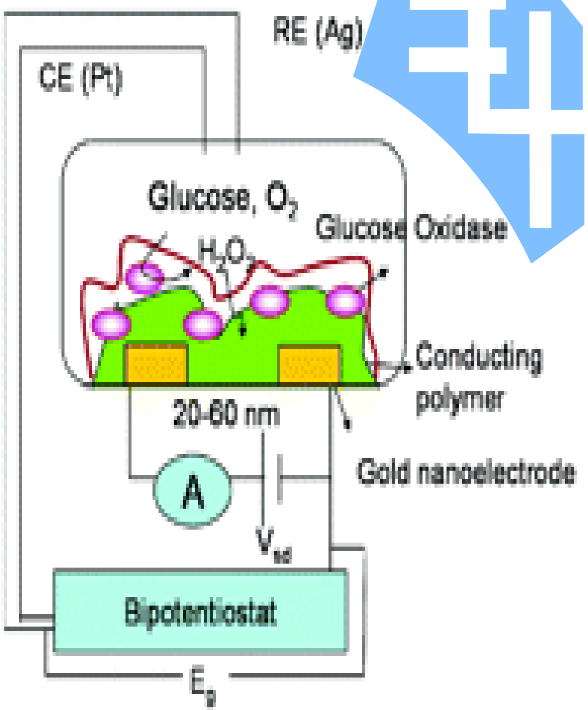
www.cdc.gov/nchs/fastats/diabetes.htm

Glucose NanoSensor NanoRadio ecosystem of health-care monitoring may have a minor economic impact

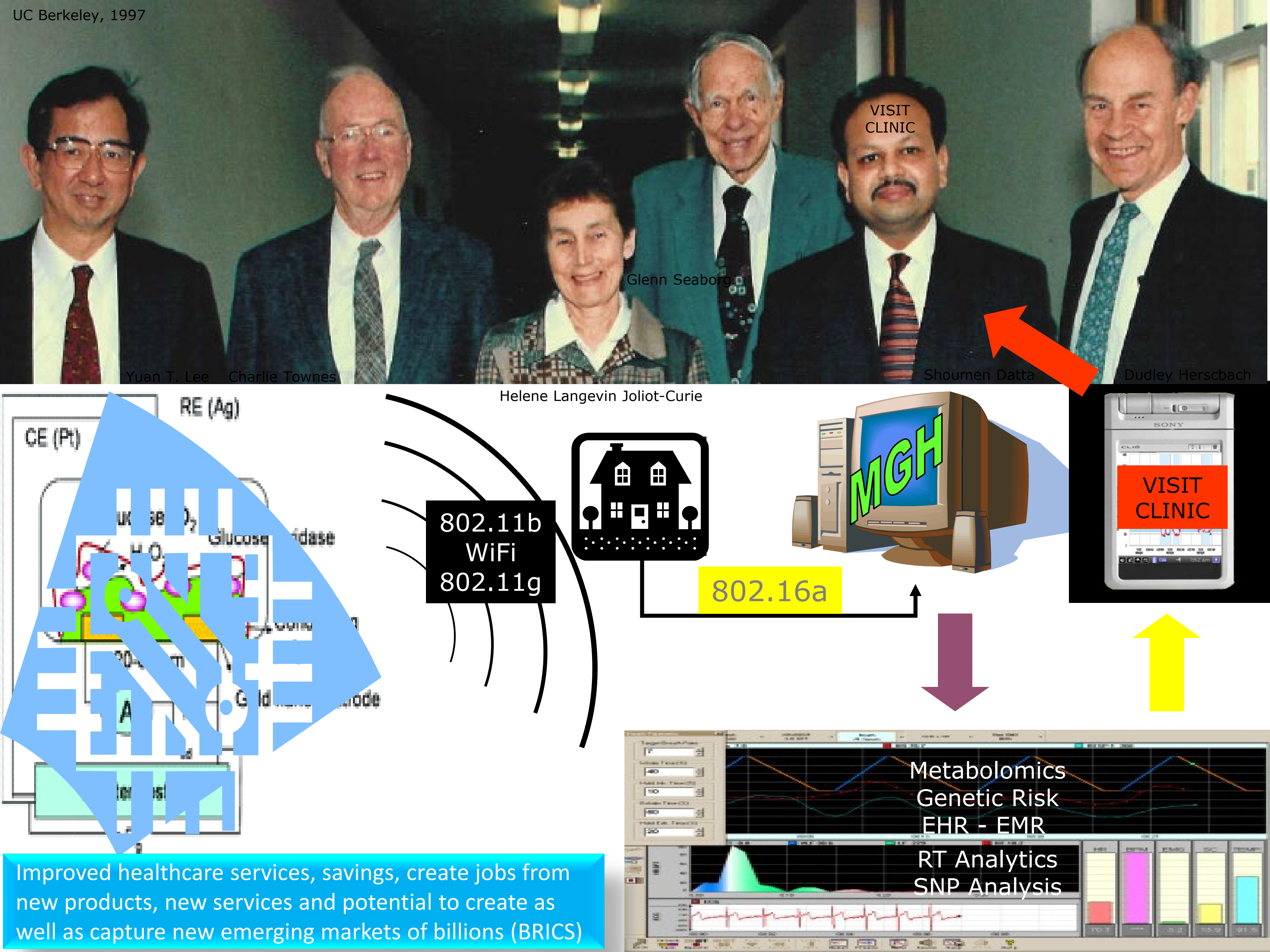


Healthcare Spending



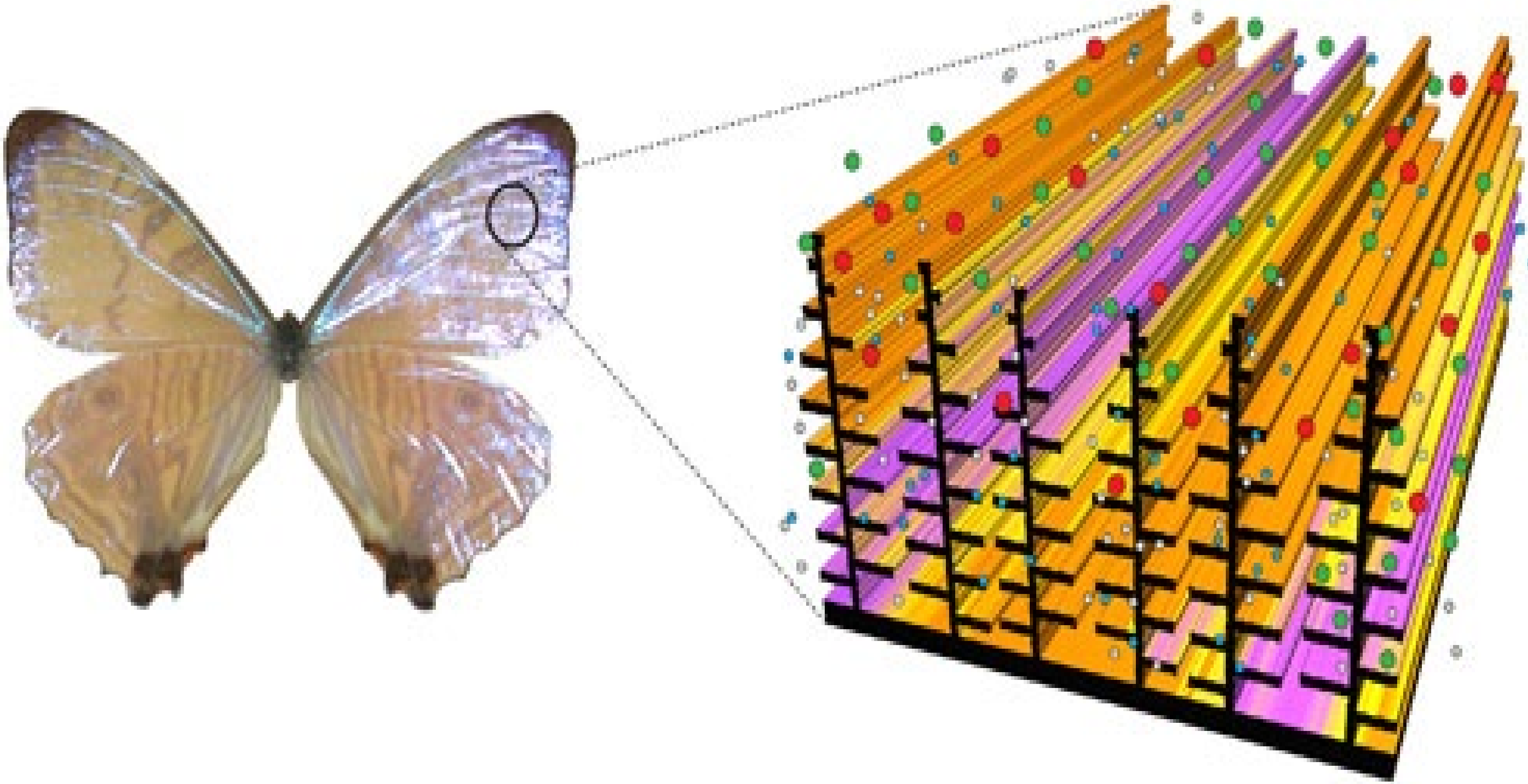


www.cdc.gov/nchs/fastats/diabetes.htm



UC Berkeley, 1997
VISIT CLINIC
Glenn Seaborg
Yuan T. Lee
Charlie Townes
Shoumen Datta
Dudley Herscbach
Helene Langevin Joliot-Curie
RE (Ag)
CE (Pt)
802.11b
WiFi
802.11g
802.16a
MGH
SONY
VISIT CLINIC
Metabolomics
Genetic Risk
EHR - EMR
RT Analytics
SNP Analysis
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)

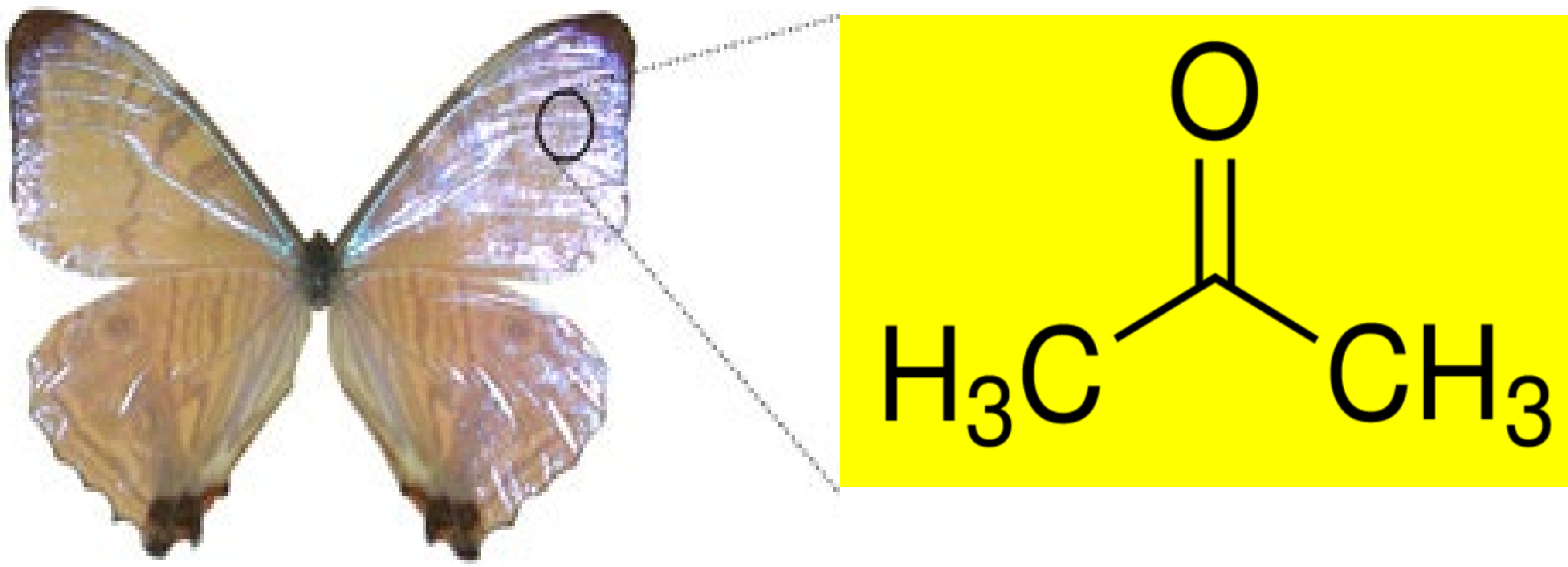
Changes to be ushered in by the connectivity potential from the IoS will shape the global economy in ways which could be limited only by our imagination



Scientists at GE Global Research discovered that the nanostructures on the wing scales of Morpho butterflies have excellent sensing capabilities. They could allow them to build sensors that can detect heat and also as many as 1,000 different chemicals. Image: GE Global Research

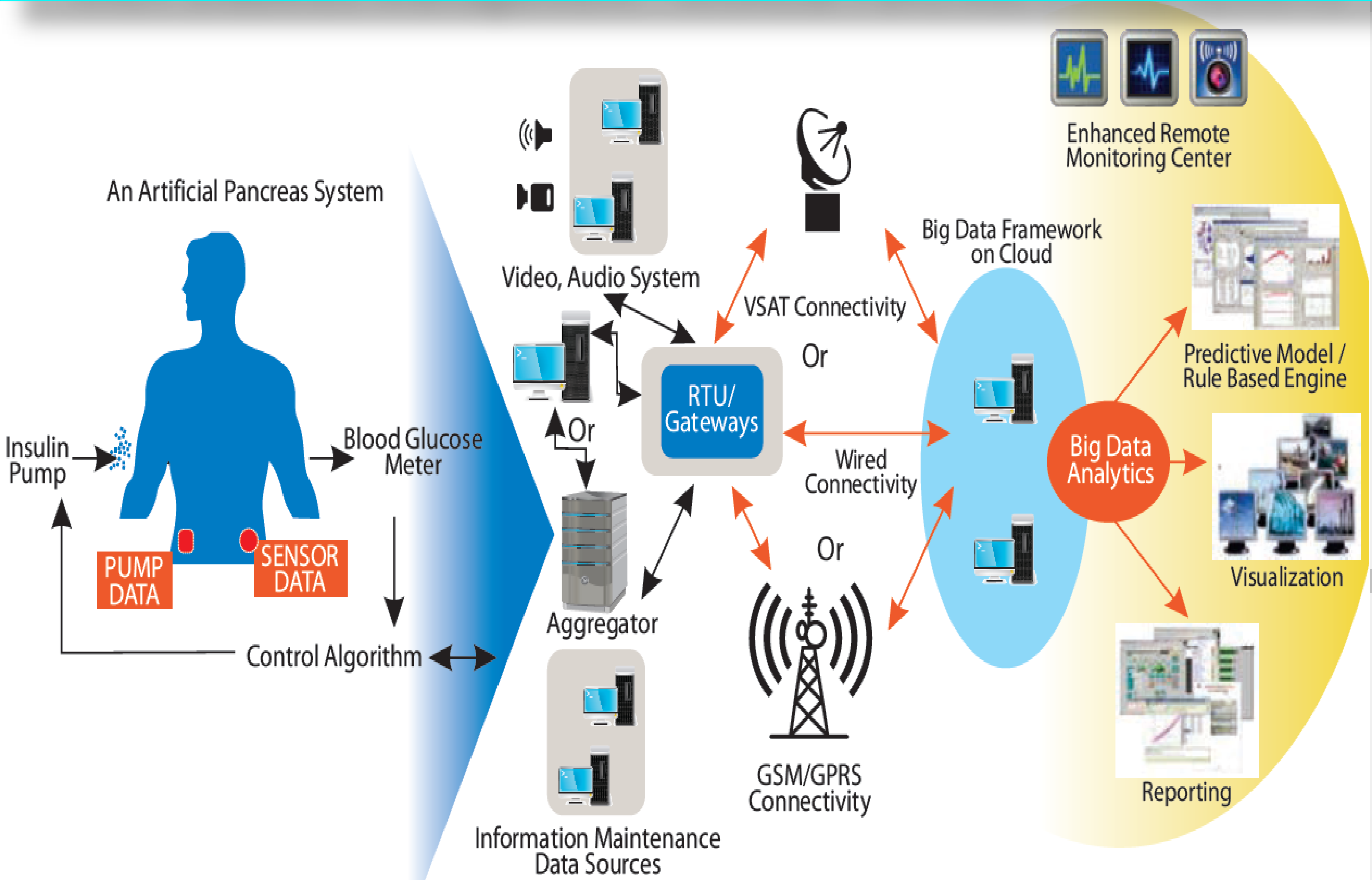
Can Butterflies Help Prevent Diabetes?

This is only a suggestion by the author and not a fact or system which is under investigation or is available at present.

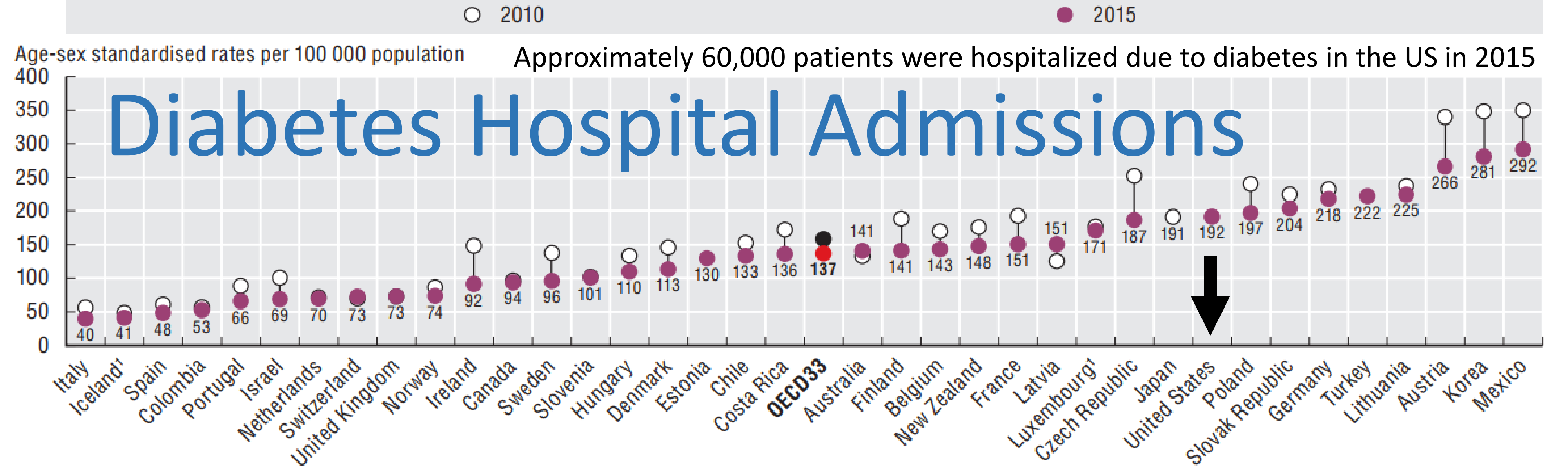


Dual Acetone Sensors on a single chip may differentiate between acetone in the environment vs acetone in the blood, breath or urine of diabetics. Subtractive analysis alerts to blood ketones. Occurs when body uses fat instead of glucose. It signals insulin dysfunction. If undiagnosed, it may lead to 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).

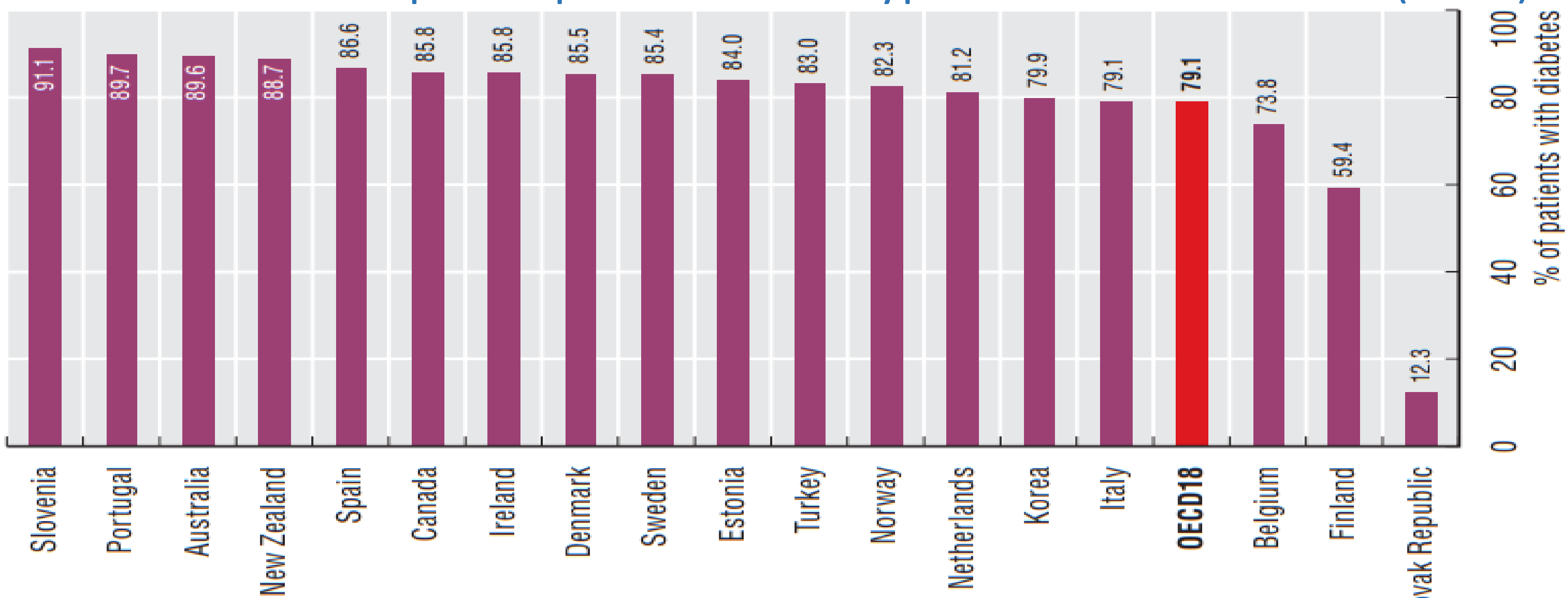
MIoT Diabetes Management - Artificial Pancreas Device Systems



www.tcs.com/SiteCollectionDocuments/White%20Papers/Personalized-Artificial-Pancreas-Device-Systems_1014-1.pdf



Diabetics with a prescription for anti-hypertensive medication (2015)



OECD Health Statistics 2017 ▪ http://dx.doi.org/10.1787/888933603545 ▪ http://dx.doi.org/10.1787/888933603564

Congestive Heart Failure

Why should CHF claim about 5 million lives in the US?

- 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.

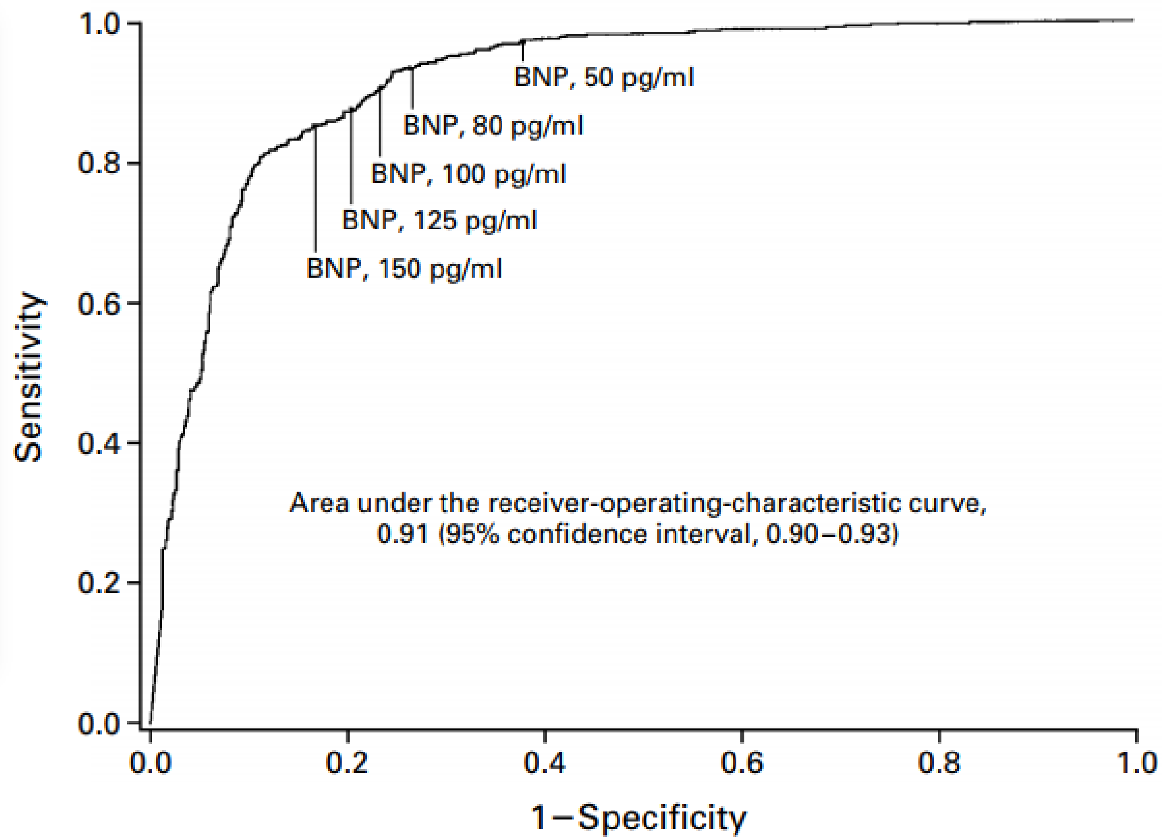
Abundance of prognostic biochemical markers –

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

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.

http://medind.nic.in/jac/t10/i4/jact10i4p282.pdf www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_failure.htm

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

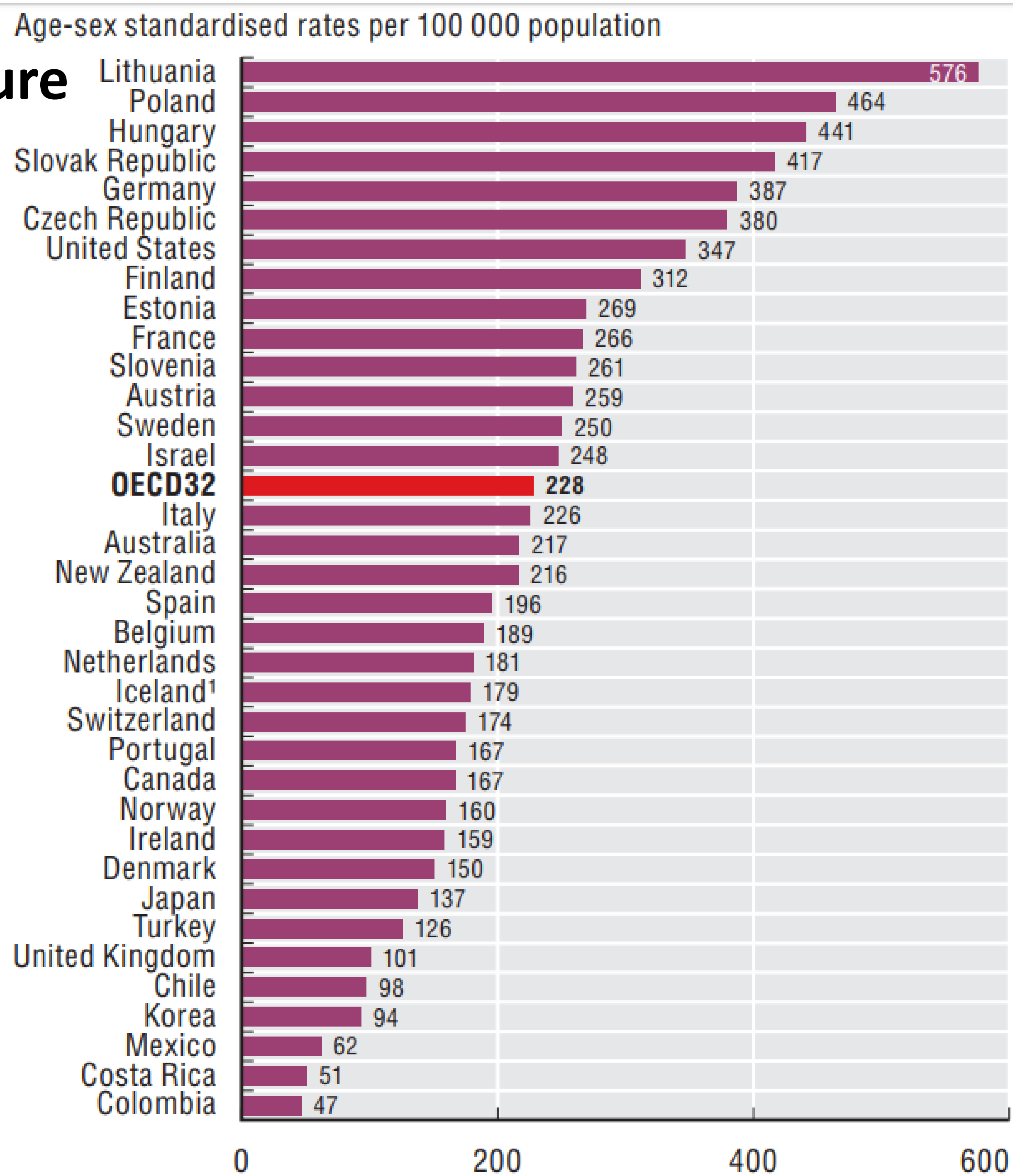


BNP pg/ml	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
	(95 percent confidence interval)				
50	97 (96–98)	62 (59–66)	71 (68–74)	96 (94–97)	79
80	93 (91–95)	74 (70–77)	77 (75–80)	92 (89–94)	83
100	90 (88–92)	76 (73–79)	79 (76–81)	89 (87–91)	83
125	87 (85–90)	79 (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.

http://www.nejm.org/doi/pdf/10.1056/NEJMoa020233

Congestive heart failure hospital admission (adults, 2015)

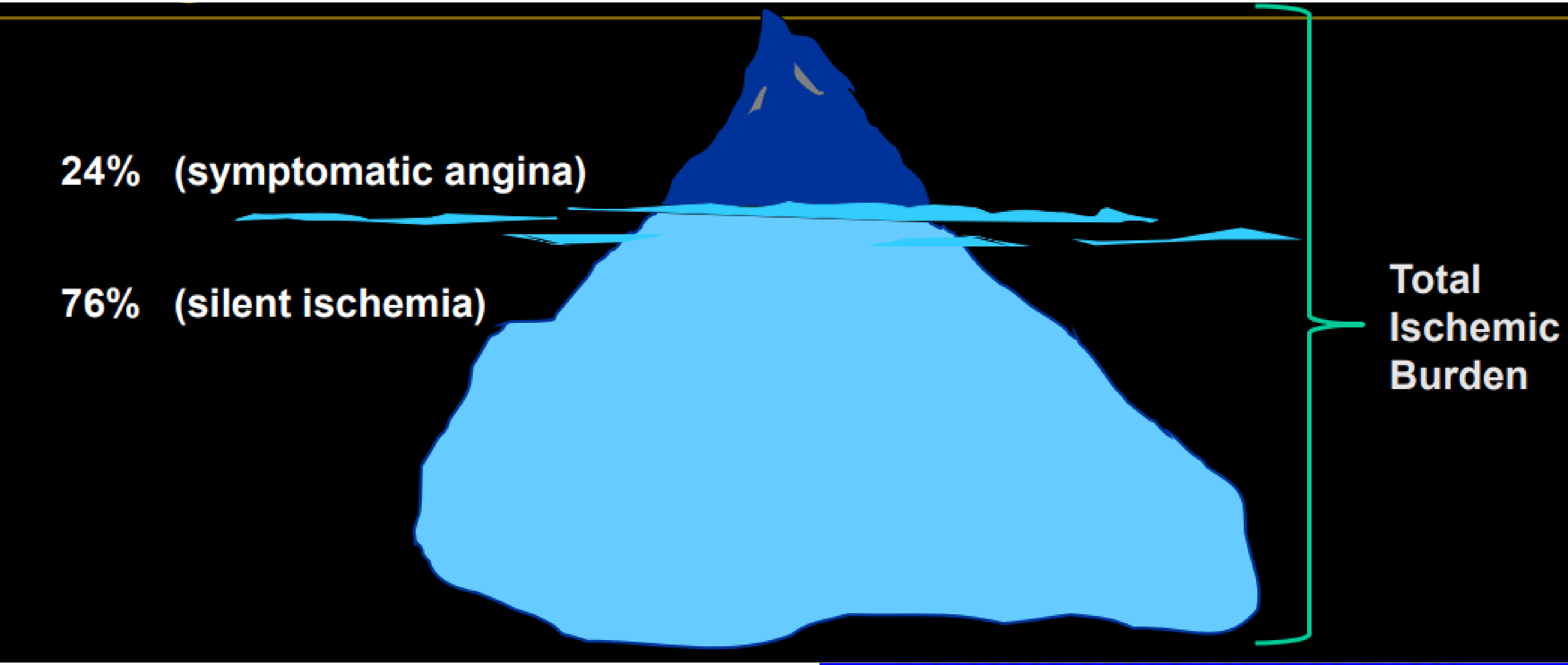


OECD Health Statistics 2017

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

Symptomatic Angina: The Tip of the Ischemic Iceberg

www.escardio.org/static_file/Escardio/education/live-events/courses/education-resource/Fri-11-SMI-Gutterman.pdf



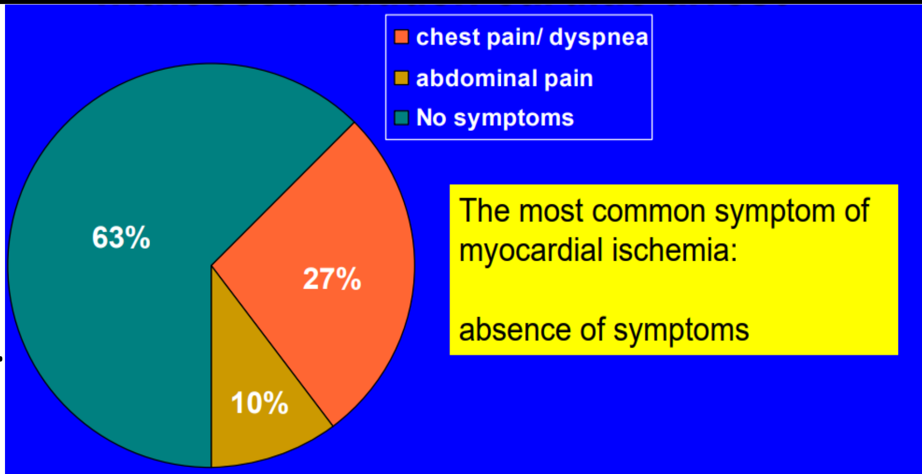
If you cannot sense, you cannot detect.

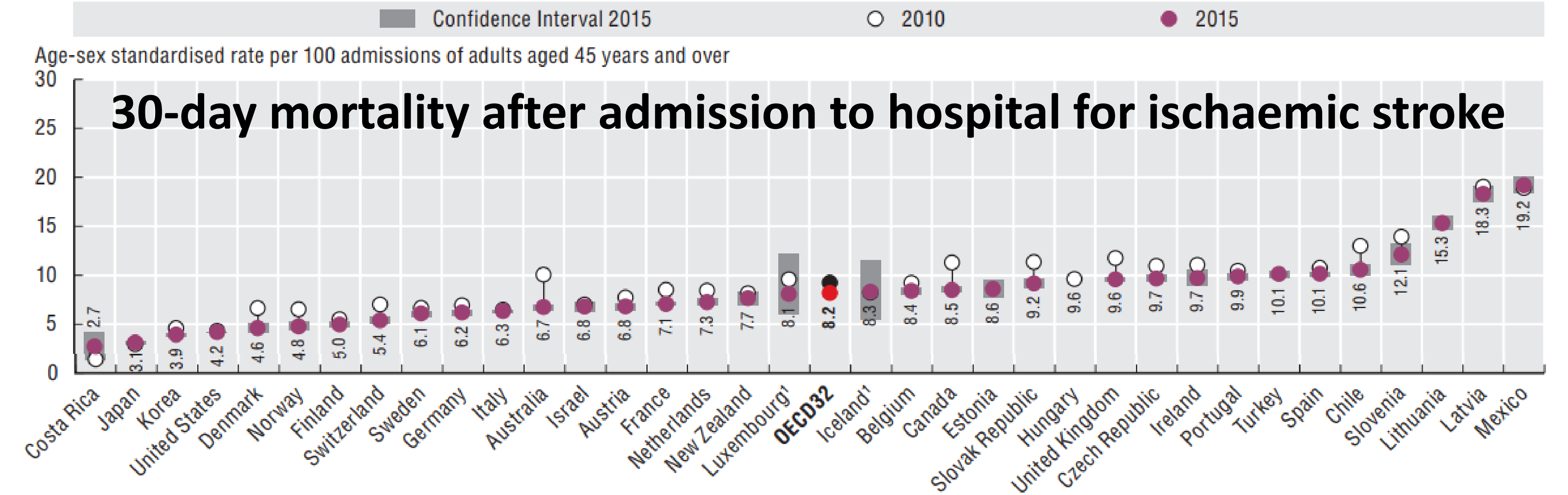
If you cannot predict, you cannot prevent.

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

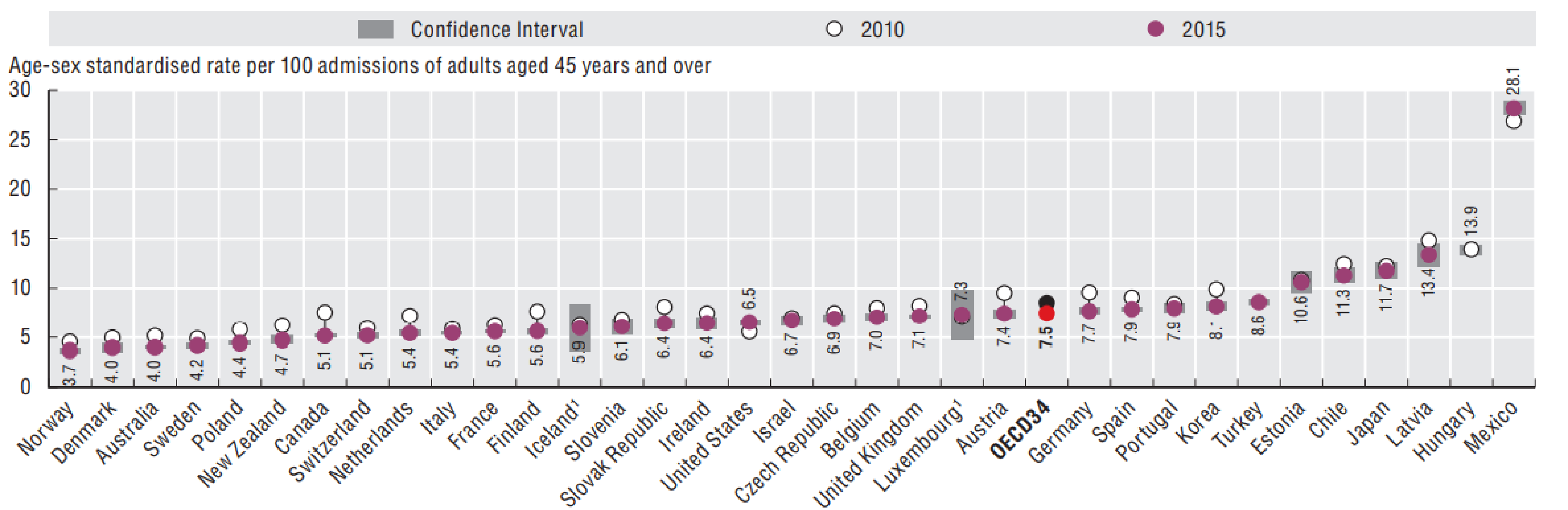




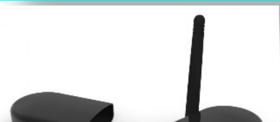
OECD Health Statistics 2017 http://dx.doi.org/10.1787/888933603602

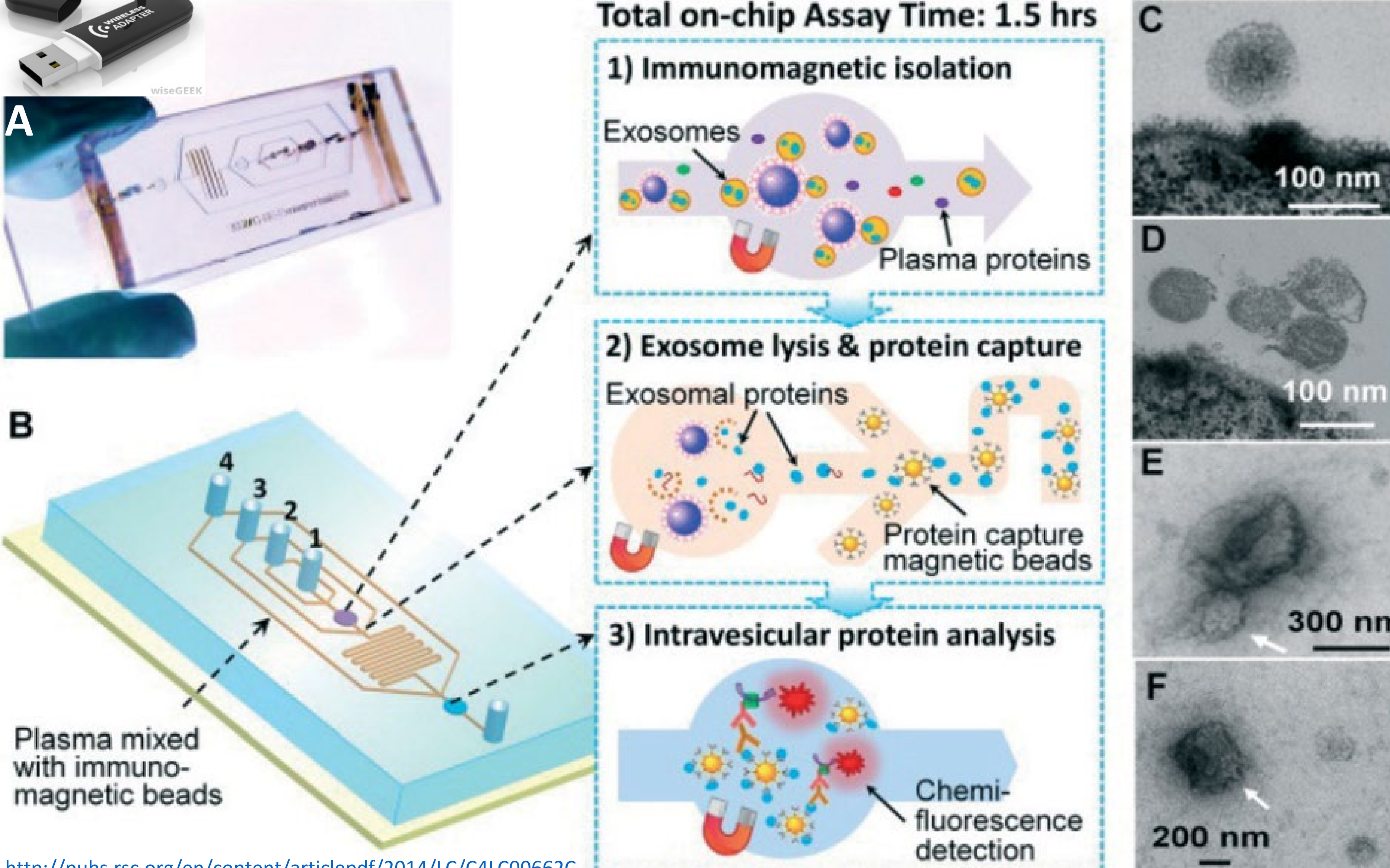
Mortality following acute myocardial infarction (AMI)

Thirty-day mortality after admission to hospital for AMI based on unlinked data, 2010 and 2015 (or nearest years)



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



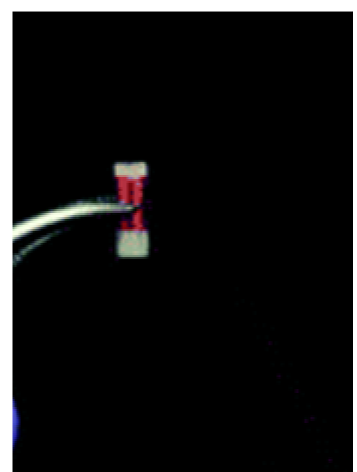


http://pubs.rsc.org/en/content/articlepdf/2014/LC/C4LC00662C

Not secure | pubs.rsc.org/en/content/articlelanding/2015/lc/c5lc00546a#!divAbstract

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



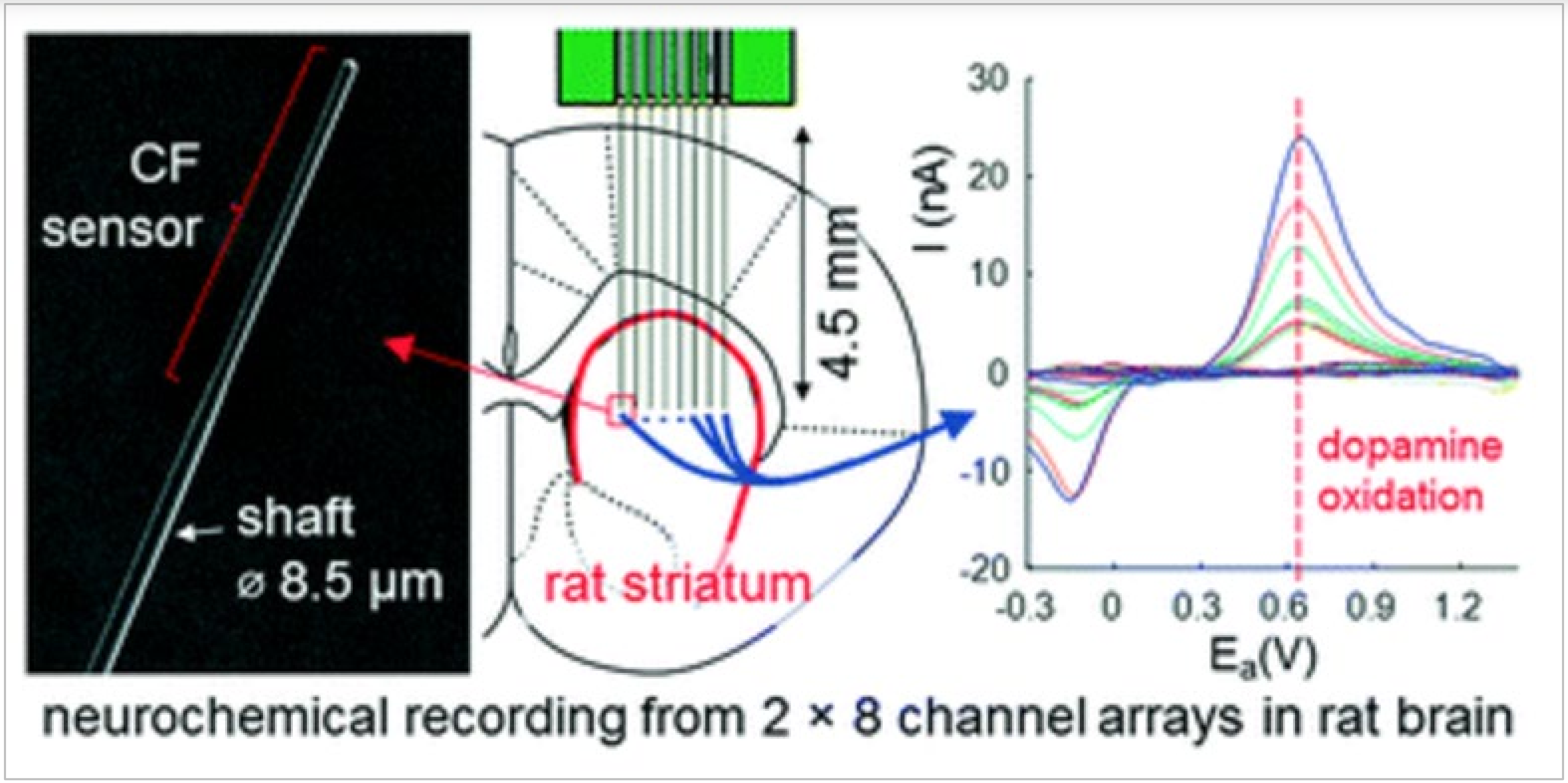
C. C. Vassiliou,[ab] V. H. Liu[ab] and M. J. Cima*[ac]

Show Affiliations

Lab Chip, 2015, **15**, 3465-3472

DOI: 10.1039/C5LC00546A

Sensor to monitor heterogeneous spatiotemporal dynamics of dopamine neurotransmission



Subcellular probes for neurochemical recording from multiple brain sites

Helen N. Schwerdt,[ab] Min Jung Kim,[b] Satoko Amemori,[b]
Daigo Homma,[b] Tomoko Yoshida,[b] Hideki Shimazu,[b]
Harshita Yerramreddy,[b] Ekin Karasan,[b] Robert Langer,[ac]
Ann M. Graybiel[b] and Michael J. Cima*[ad]

Show Affiliations

Lab Chip, 2017, Advance Article

DOI: 10.1039/C6LC01398H

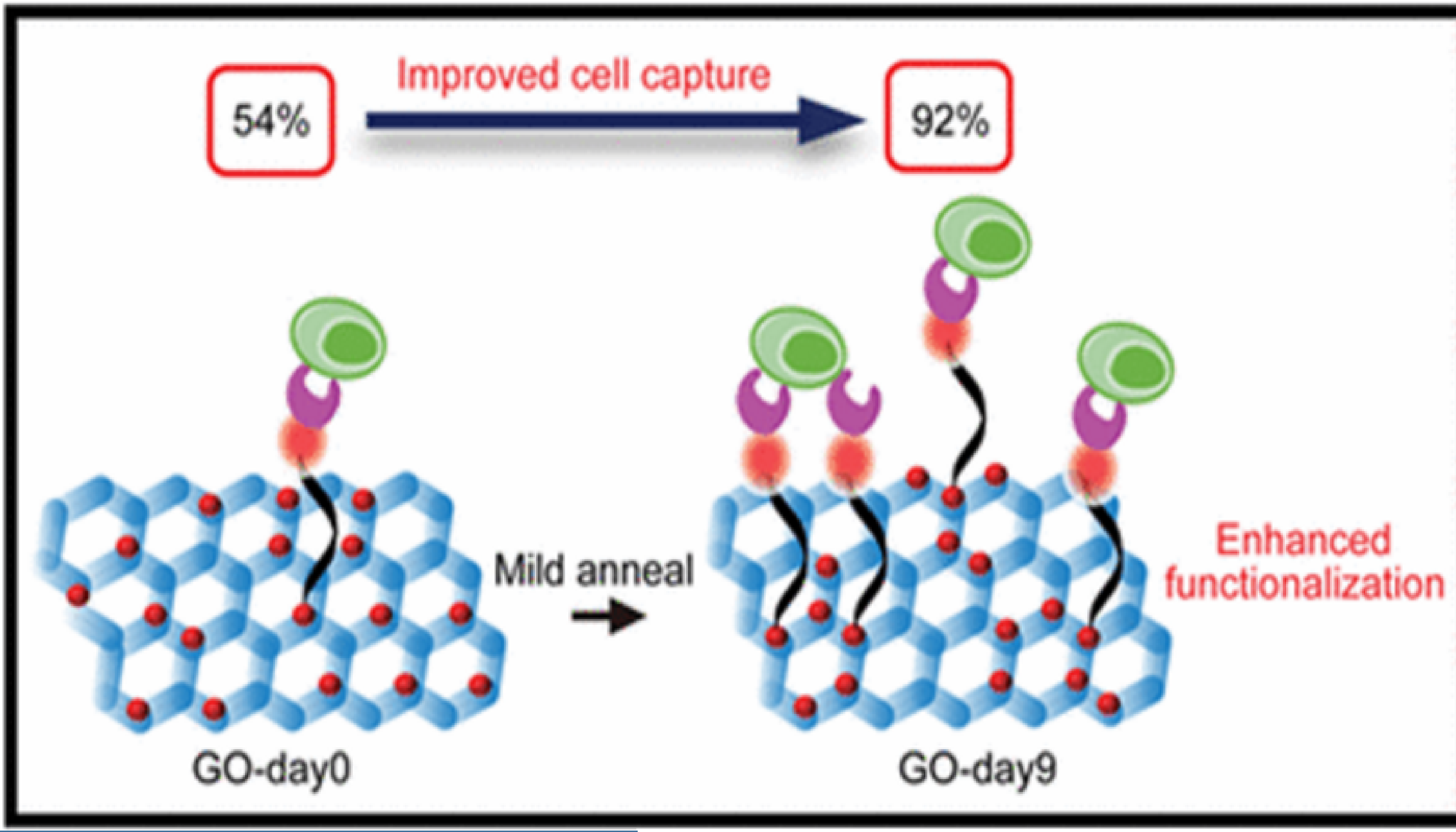
Received 11 Nov 2016, Accepted 08 Feb 2017

First published online 15 Feb 2017

http://pubs.rsc.org/en/content/articlelanding/2017/lc/c6lc01398h#!divAbstract

With the global rise in incidence of cancer & infectious diseases, there is a need for the development of techniques to diagnose, treat, and monitor these conditions. The ability to efficiently capture and isolate cells and other biomolecules from peripheral blood for downstream analyses is necessary. Graphene oxide (GO) is an attractive template nano-material for such biosensing applications.

pubs.acs.org/doi/pdfplus/10.1021/acsnano.6b06979



Favorable properties include its 2D architecture and wide range of functionalization chemistries, to tailor affinity toward aromatic functional groups. A limitation of current techniques is that as-synthesized GO nano-sheets are used directly in applications, and the benefits of their structural modification on the device performance have remained unexplored. We report a microfluidic-free, sensitive, planar device on treated GO substrates to enable quick and efficient capture of Class-II MHC-positive cells from murine blood. We achieve this by using a mild thermal annealing treatment on GO substrates, which drives a phase transformation through oxygen clustering.

Enhanced Cell Capture on Functionalized Graphene Oxide Nanosheets through Oxygen Clustering

Neelkanth M. Bardhan[†‡§¶], Priyank V. Kumar[†¶⊗], Zeyang Li[∥], Hidde L. Ploegh[∥⊥], Jeffrey C. Grossman[*†], Angela M. Belcher[*†‡§], and Guan-Yu Chen[*#∇]

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[⊥] Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States
[#] Institute of Biomedical Engineering, National Chiao Tung University, Hsinchu 30010, Taiwan
[∇] Department of Biological Science and Technology, National Chiao Tung University, Hsinchu 30010, Taiwan

ACS Nano, **2017**, *11* (2), pp 1548–1558
DOI: 10.1021/acsnano.6b06979
Publication Date (Web): January 13, 2017

*E-mail: jcg@mit.edu., *E-mail: belcher@mit.edu., *E-mail: guanyu@nctu.edu.tw.

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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Markita Patricia Landry, Linda Chio & Darwin Yang

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Markita Patricia Landry

Department of Electrical Engineering & Computer Science and Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA
Hiroki Ando, Allen Y. Chen, Jicong Cao & Timothy K. Lu

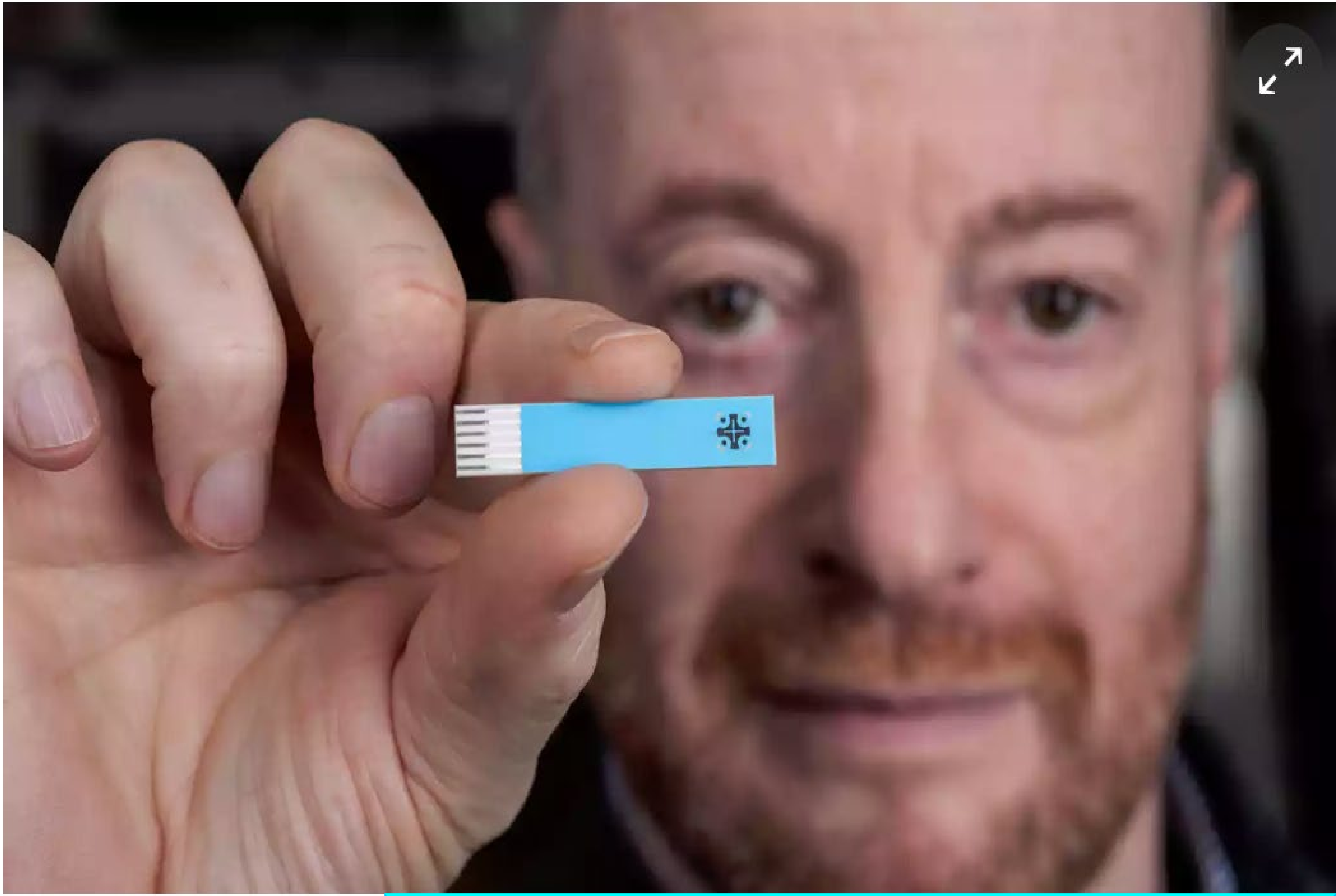
MIT Synthetic Biology Center, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA
Hiroki Ando, Allen Y. Chen, Jicong Cao & Timothy K. Lu

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.

Secure | https://www.theguardian.com/science/2017/jan/22/stroke-detector-biosensor-diagnosis-nicholas-dale--breakthrough?utm

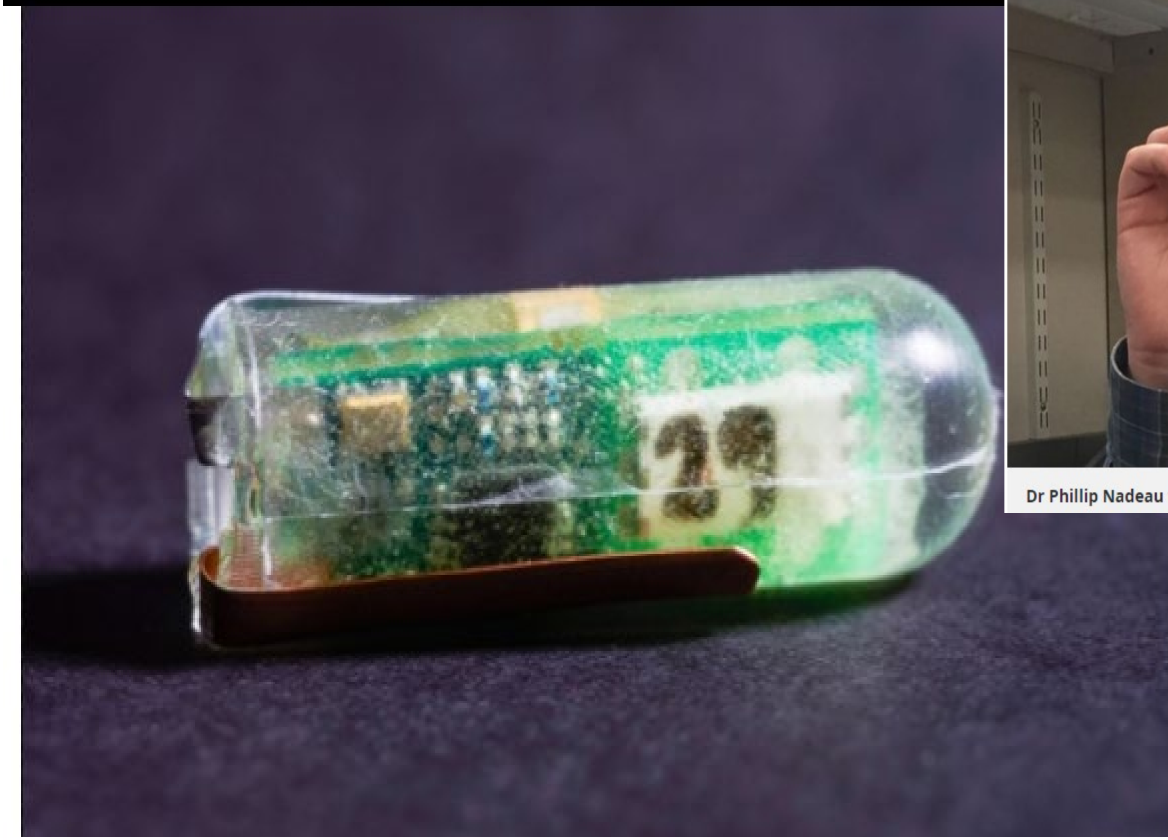


Nicholas Dale with his SMARTchip

STROKE DETECTOR – BIOSENSOR

MIT News

ON CAMPUS AND AROUND THE WORLD



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.

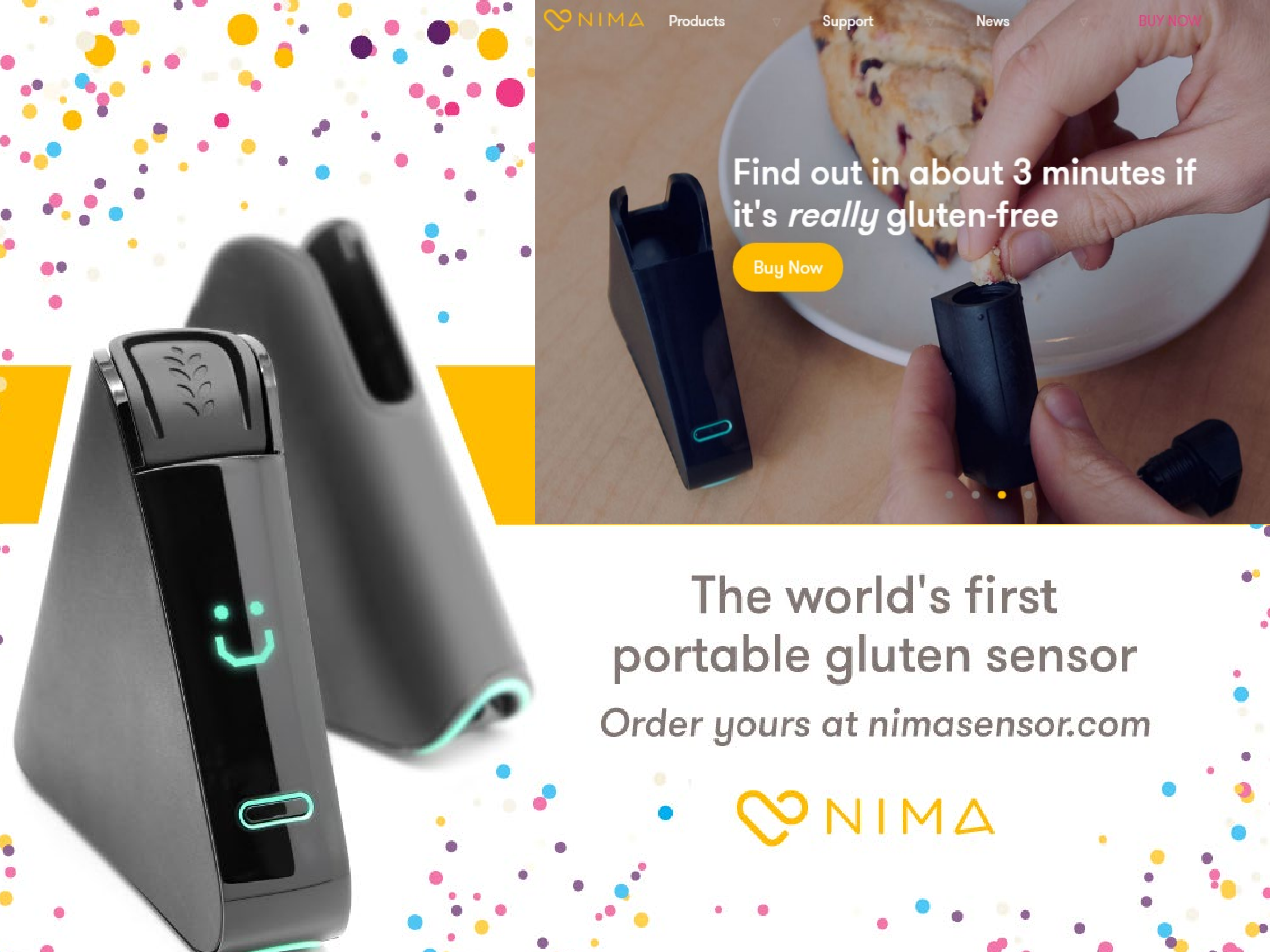
Photo: Diemut Strebe

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

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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News
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Find out in about 3 minutes if it's *really* gluten-free
Buy Now
The world's first portable gluten sensor
Order yours at nimasensor.com
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MIT News

ON CAMPUS AND AROUND THE WORLD

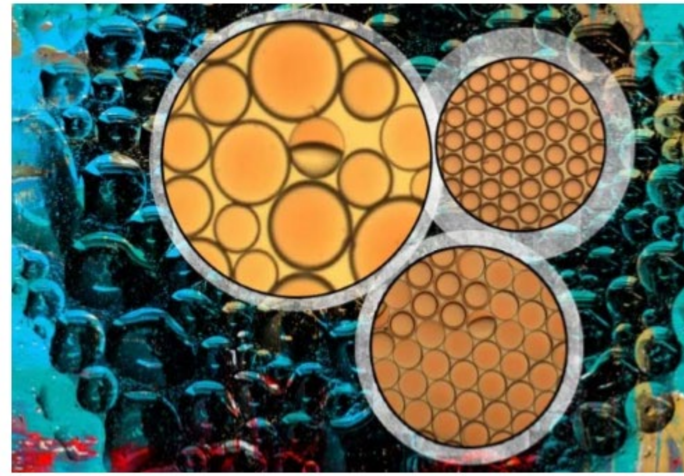
Food Testing. Blood Testing? Sputum? Mucus? Fluids?

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

Anne Trafton | MIT News
April 5, 2017

MIT News

ON CAMPUS AND AROUND THE WORLD



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,[*,‡,§] and Timothy M. Swager[*,†]

[†]Department of Chemistry and Institute for Soldier Nanotechnologies, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, United States

[‡]Department of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Am Mühlenberg 1, 14476 Potsdam, Germany

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http://pubs.acs.org/doi/abs/10.1021/acscentsci.7b00021

MIT News
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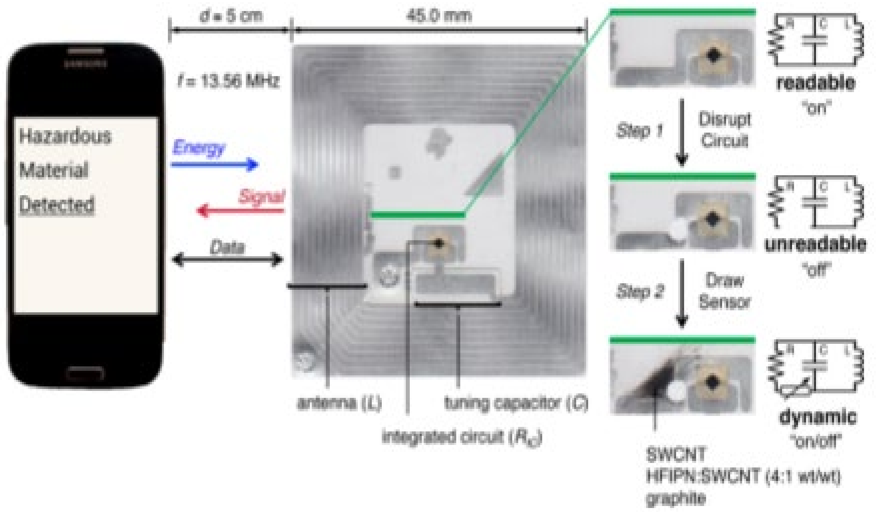
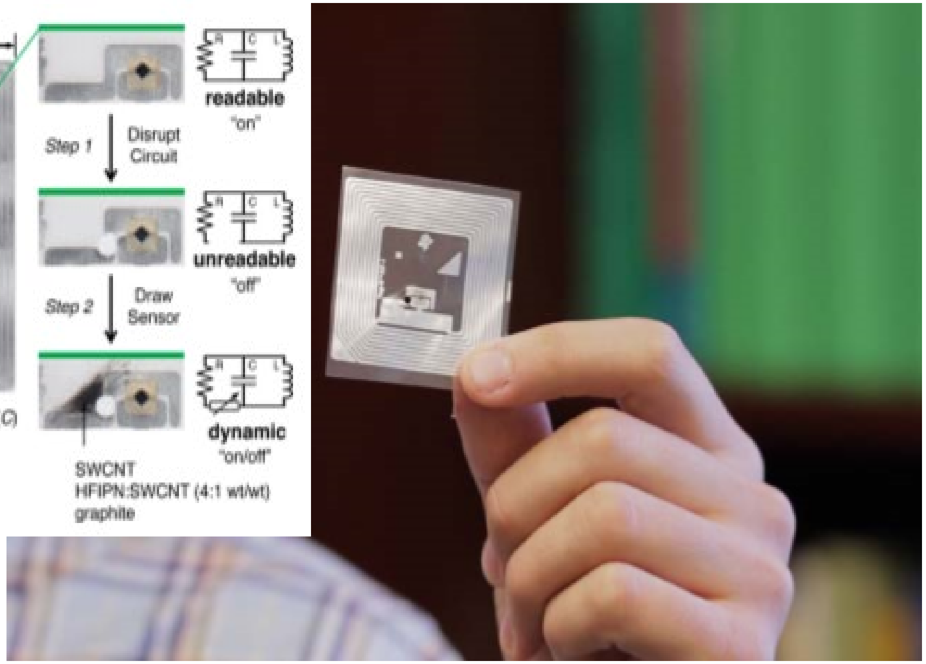




The MIT researchers' wireless chemical sensor.

Photo: Melanie Gonick

MIT News
ON CAMPUS AND AROUND THE WORLD

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. Ravnsbæk[1], and Timothy M. Swager[2]

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)

Wireless, wearable toxic-gas detector **www.pnas.org/content/111/51/18162.full.pdf**

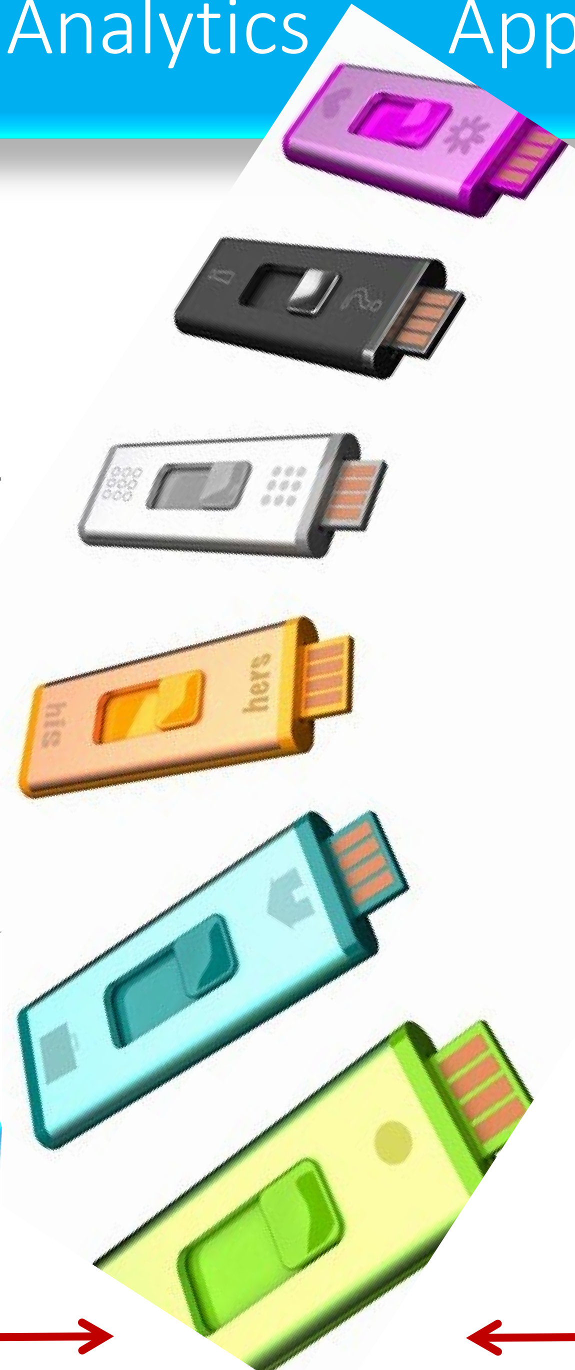
Pay 1c Per Analytics Apps, Data Distribution Service

Glucose Sensor

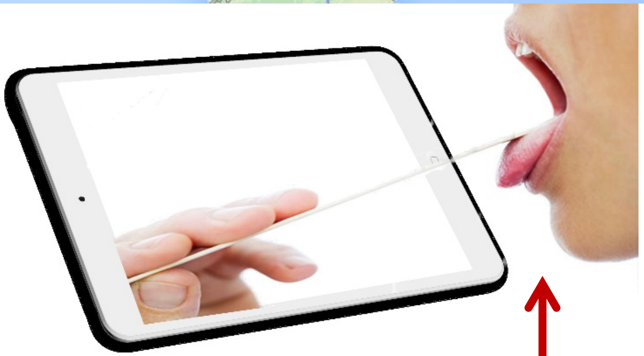
Cholesterol Sensor

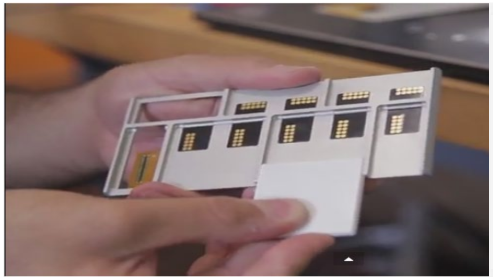
BNP Sensor

Stroke Sensor



What does the data suggest about my health?





Hot swappable, modular, smart

NK Labs
ARA Prototype

Changes to be ushered in by the connectivity potential from the IoS will shape the global economy in ways which could be limited only by our imagination

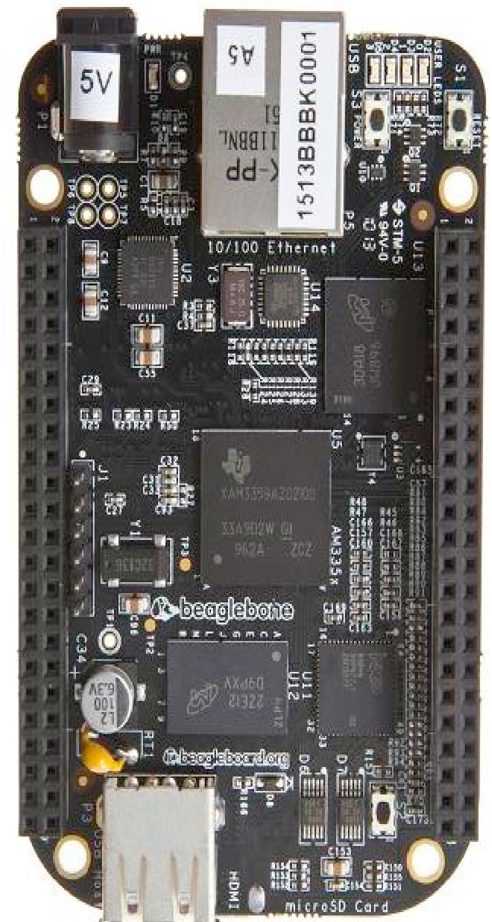
Four months ago, 16-year-old John Wall had introduced the prototype of his Atmel powered OLED smartwatch. Earlier this week, the Maker revealed that the design was on its own power and completed.

WALLTECH
@walltechOSHW

http://bit.ly/OS-ARDUINO

Drum roll please..............My BT 4.0 arduino compatible smart watch is on its own power! My prototype is complete!

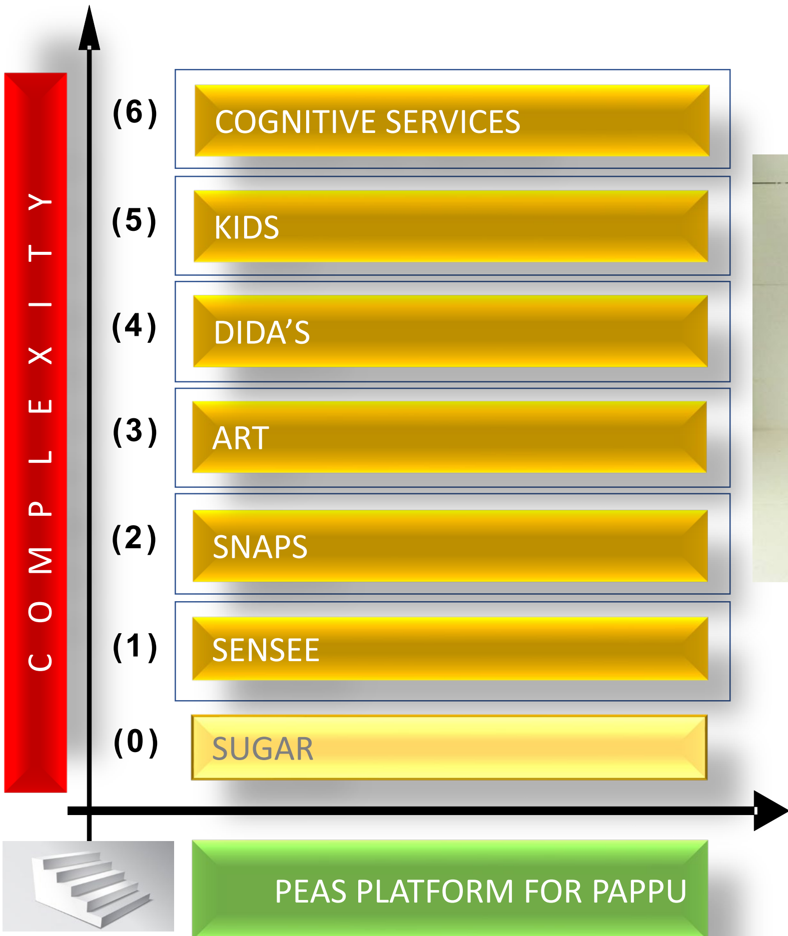
7:38 PM - 12 Oct 2014

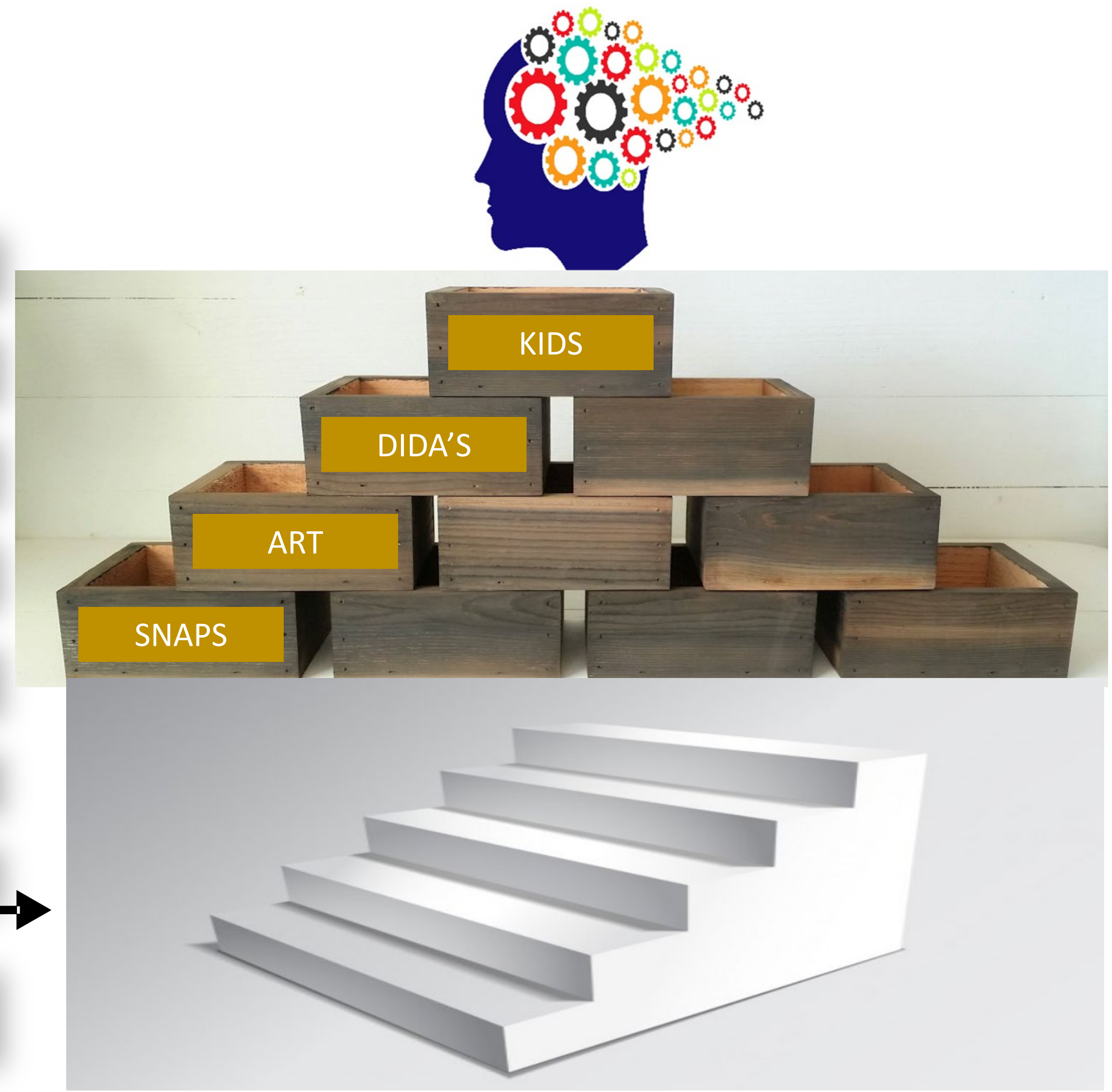


Can “Points Solutions” add up to deliver value?

WHY SYSTEMS INTEGRATION MAY BE A SUBSET OF SYNERGISTIC INTEGRATION

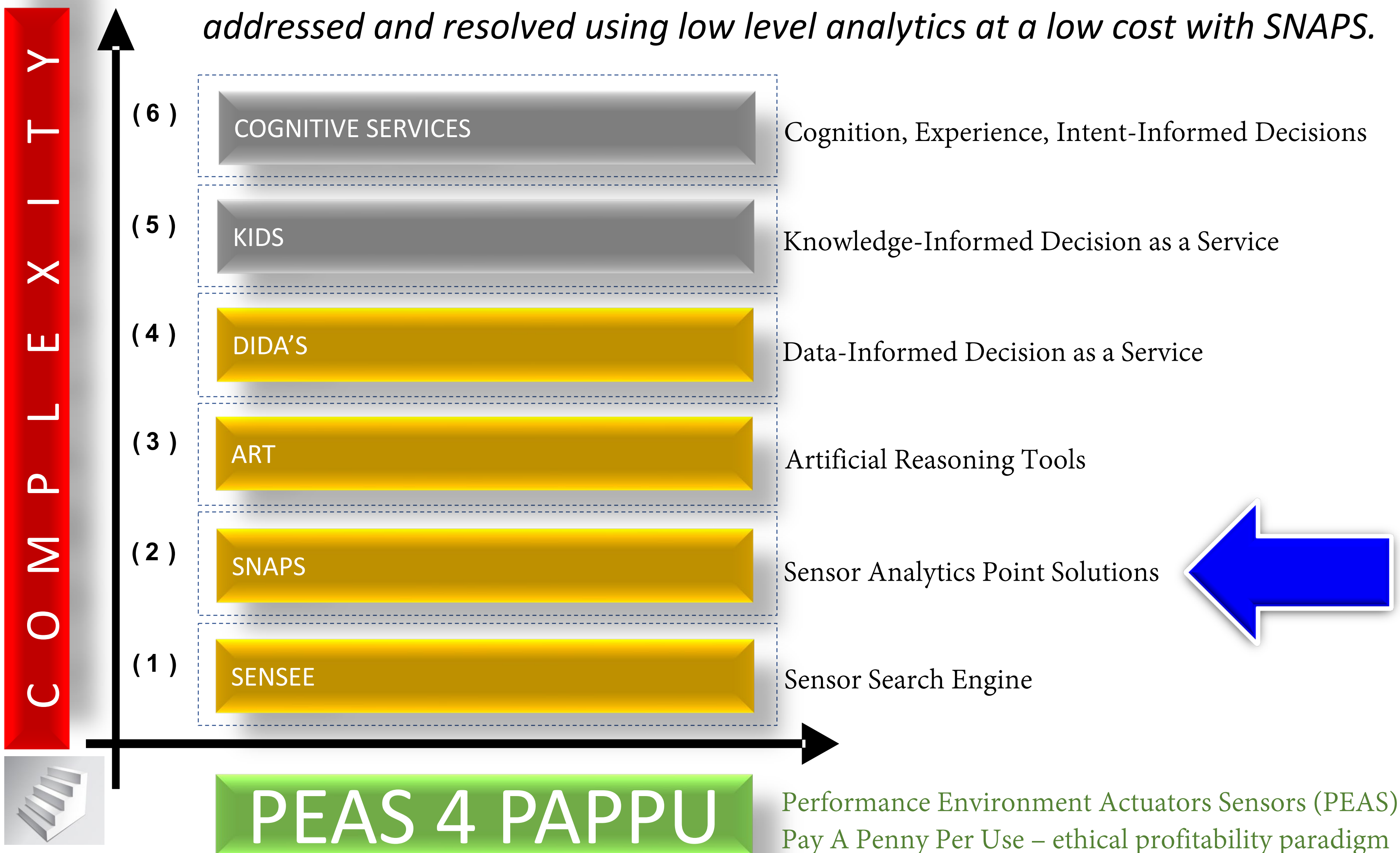
SYNERGISTIC INTEGRATION – WHEN IS IT NECESSARY ?





PEAS IN AN ALPHABET SOUP – PLATFORM ECOSYSTEM

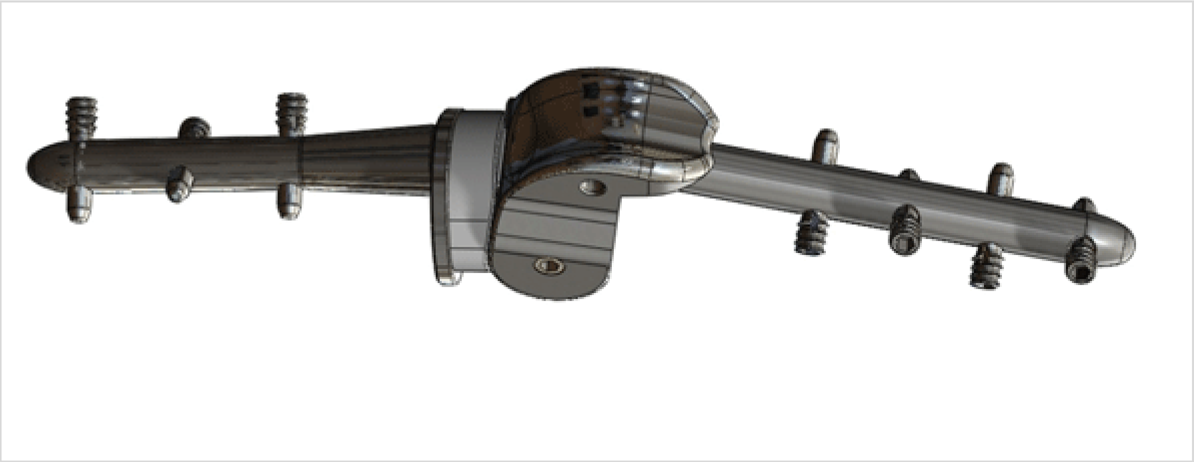
80% of the problems for 80% of the world's population may be sufficiently addressed and resolved using low level analytics at a low cost with SNAPS.



Healthy Disruption?

Printed Spare Parts ?

3-D Printing
Design of Prosthetics and Orthopedic Imaging

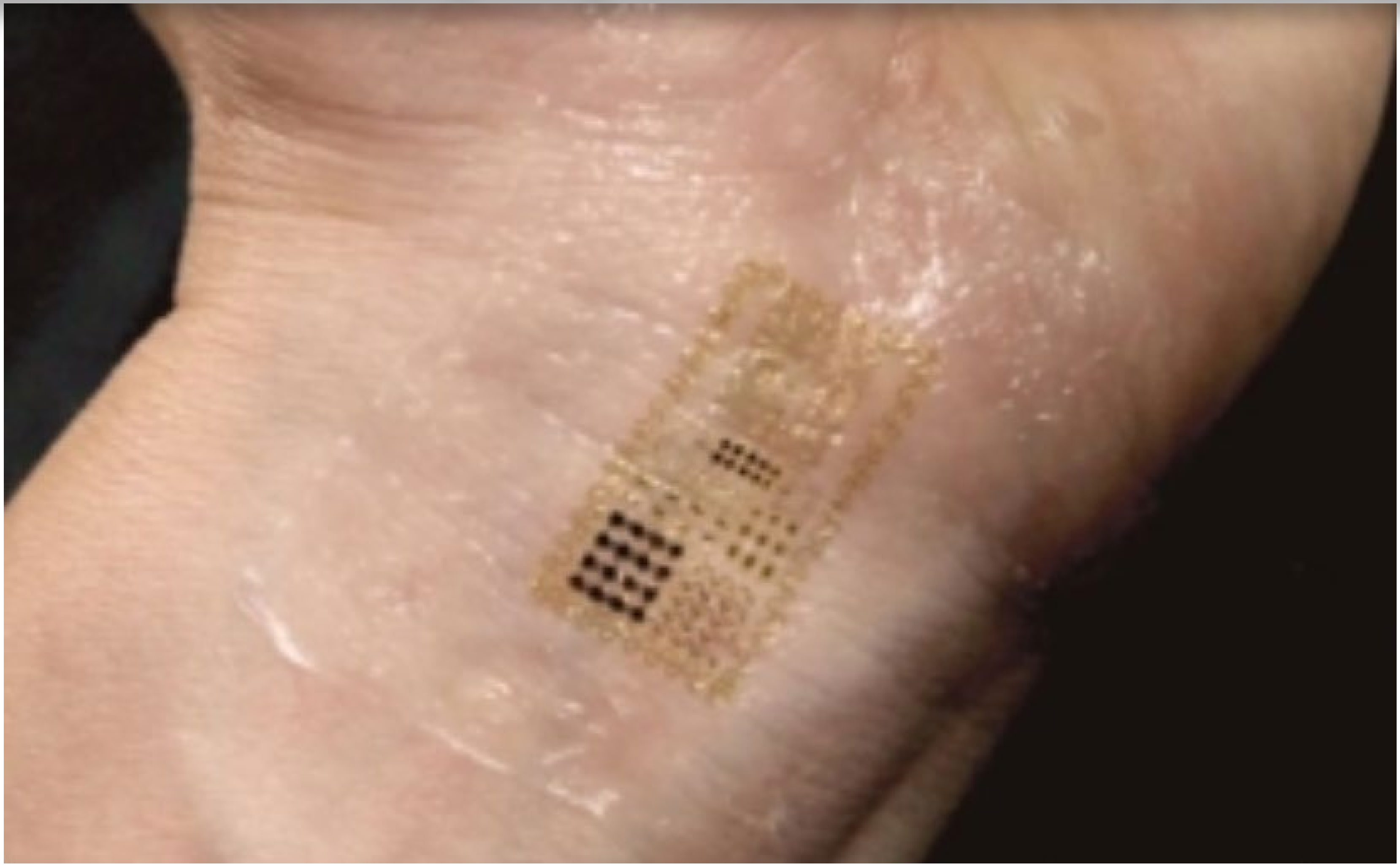


Cyrano L. Catte II (above) is the first feline to receive a total knee arthroplasty (TKA). Femoral and tibial components were created with direct metal laser sintering (EOS).

3-D Printing of Spare Parts

http://bit.ly/3D-Print-A-Tooth
http://bit.ly/3D-Print-Medical-Devices

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

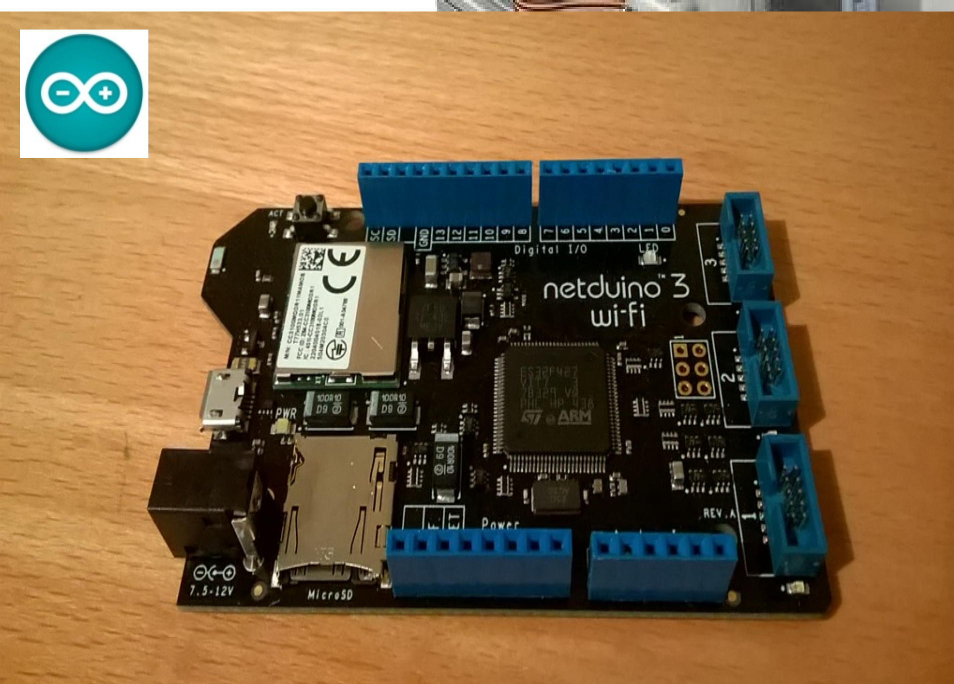


Your medicine can inform your doctor about its kinetics, bio-availability and side effects. It can alert your pharmacist about potential over-dose if multiple medications contain same or similar active ingredients. Your medicine can query and adjust dosage.

Paradigm Shift in Global Healthcare Economics
3D Printed Medical Devices + OS Hardware / Software

arduino inside

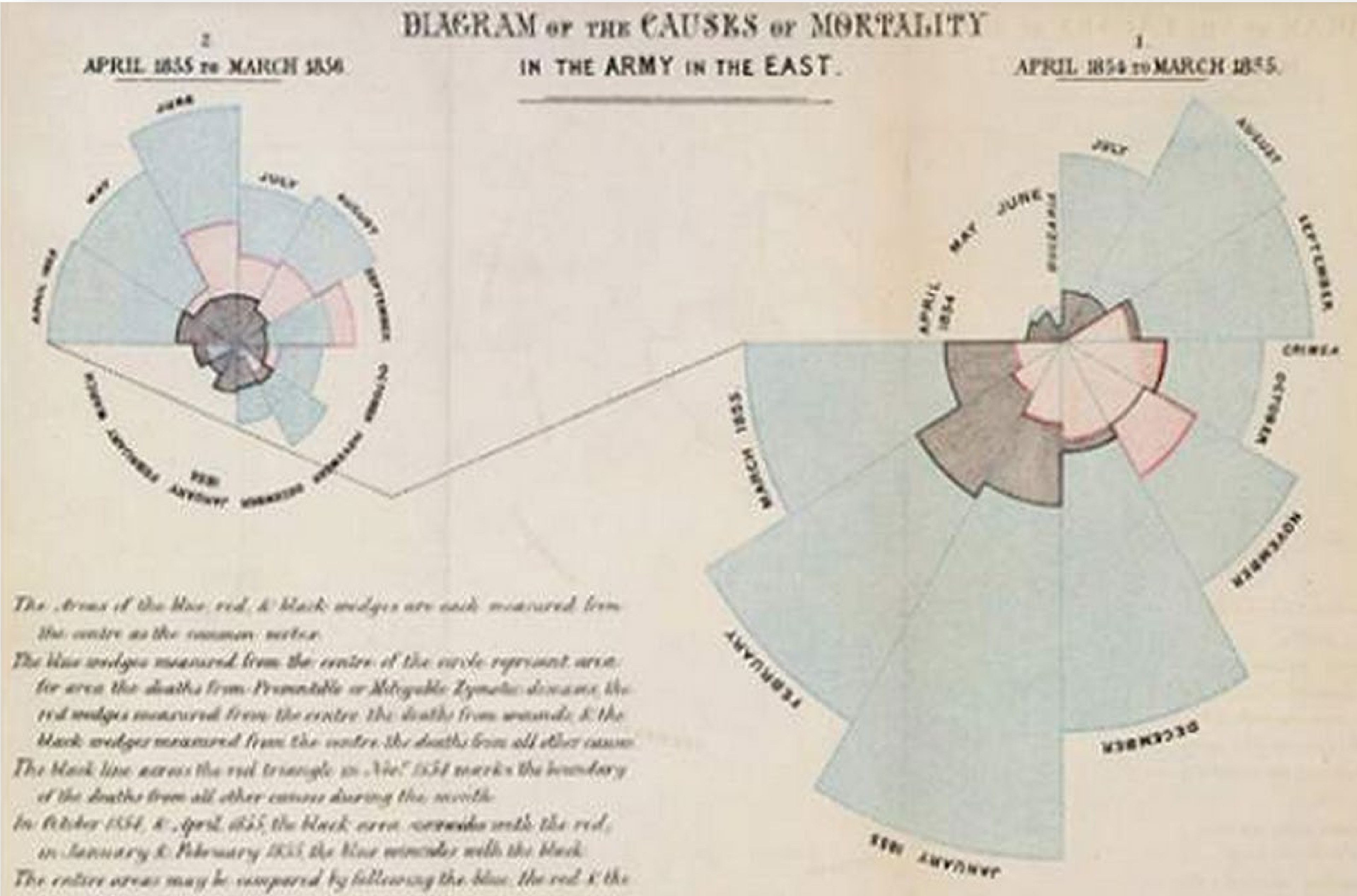
ARDUINO AT HEART



Complexity of Healthcare Data Exchange and Domain-specific Distribution of Device Data

De-Identification?

Florence Nightingale (1858) Causes of Death: Disease v Wounds - improved sanitation & nutrition of patients



http://bit.ly/VISUAL-DATA

Accuracy of prediction may improve if data is curated for context

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.

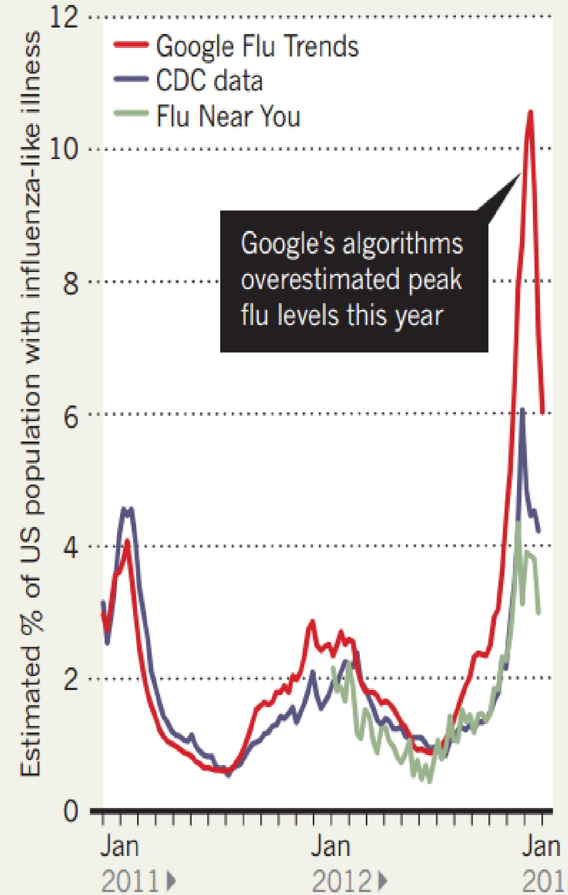
"It is hard to think today that one can provide disease surveillance without existing systems," says Alain-Jacques Valleron, an epidemiologist at the Pierre and Marie Curie University in Paris, and founder of France's Sentinelles monitoring network. "The new systems depend too much on old existing ones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

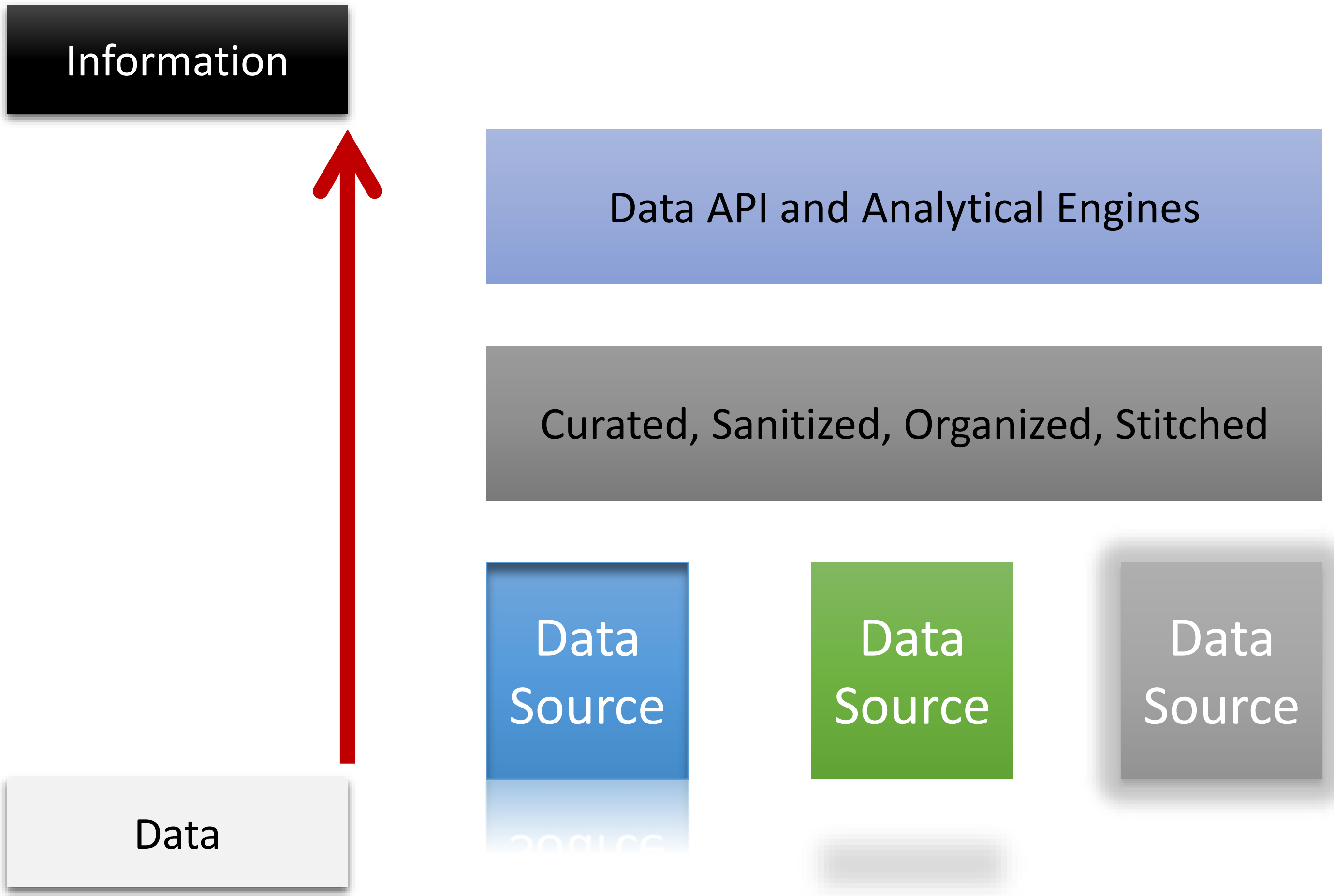
nologies could open the way to easier, faster estimates of ILI, spanning larger populations.

FEVER PEAKS

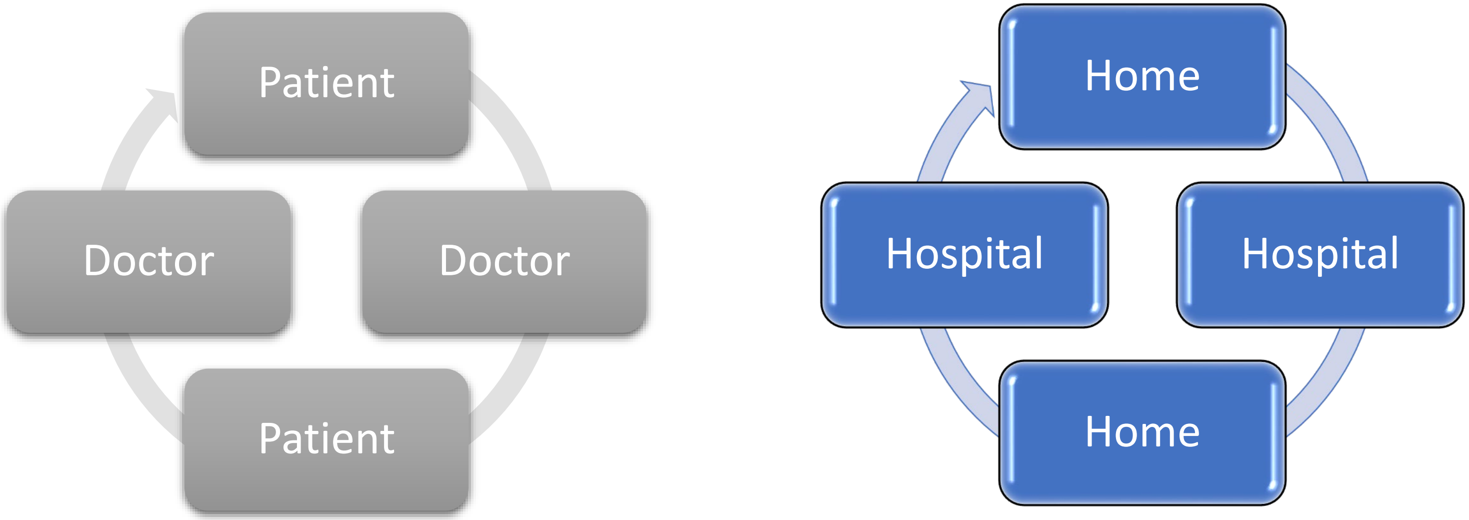
A comparison of three different methods of measuring the proportion of the US population with an influenza-like illness.



Perishability of Broad Healthcare Data → Transforming Data into Actionable Information

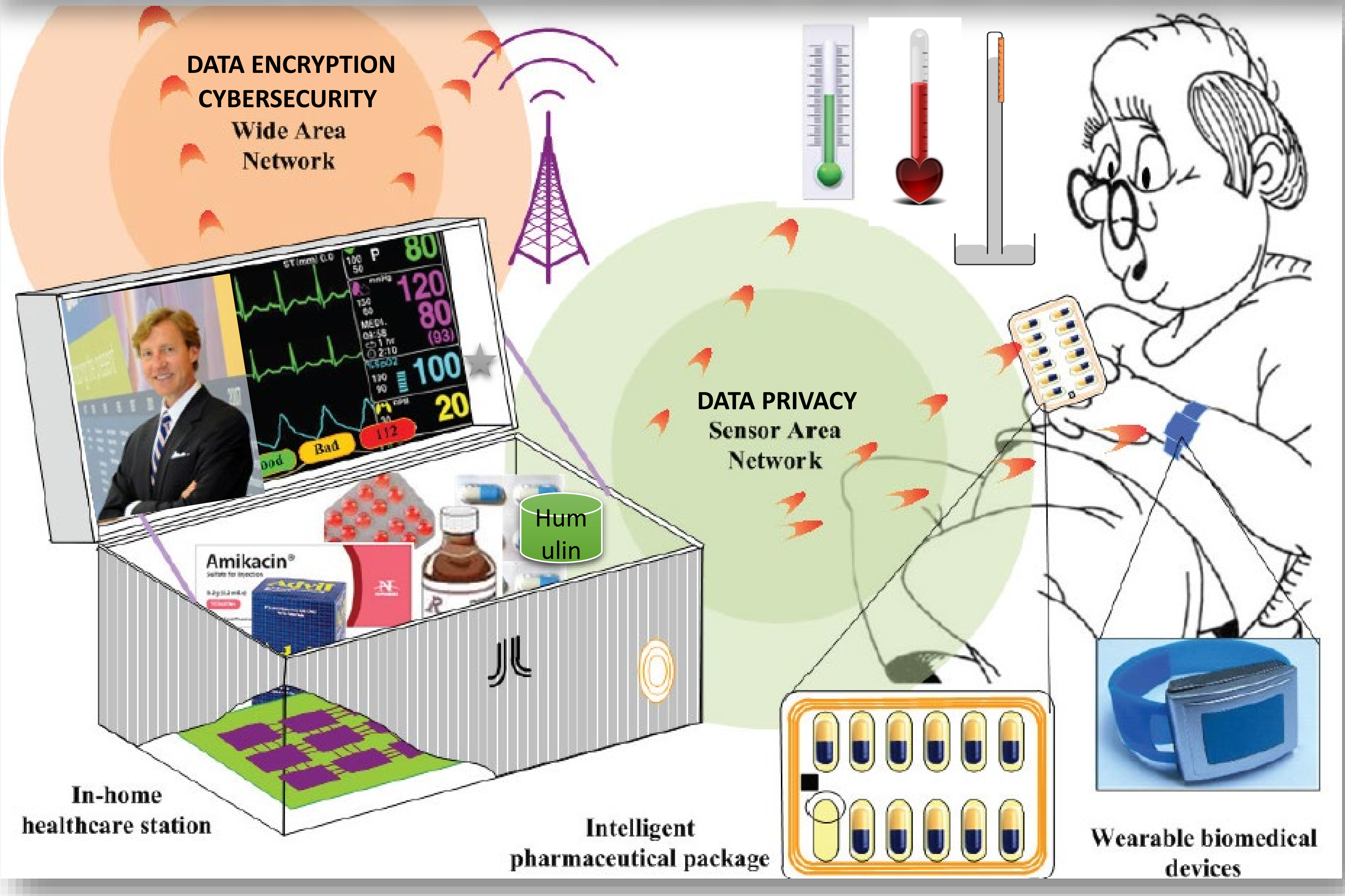


Healthcare Management - Closed Loop & Quintessentially Patient Specific



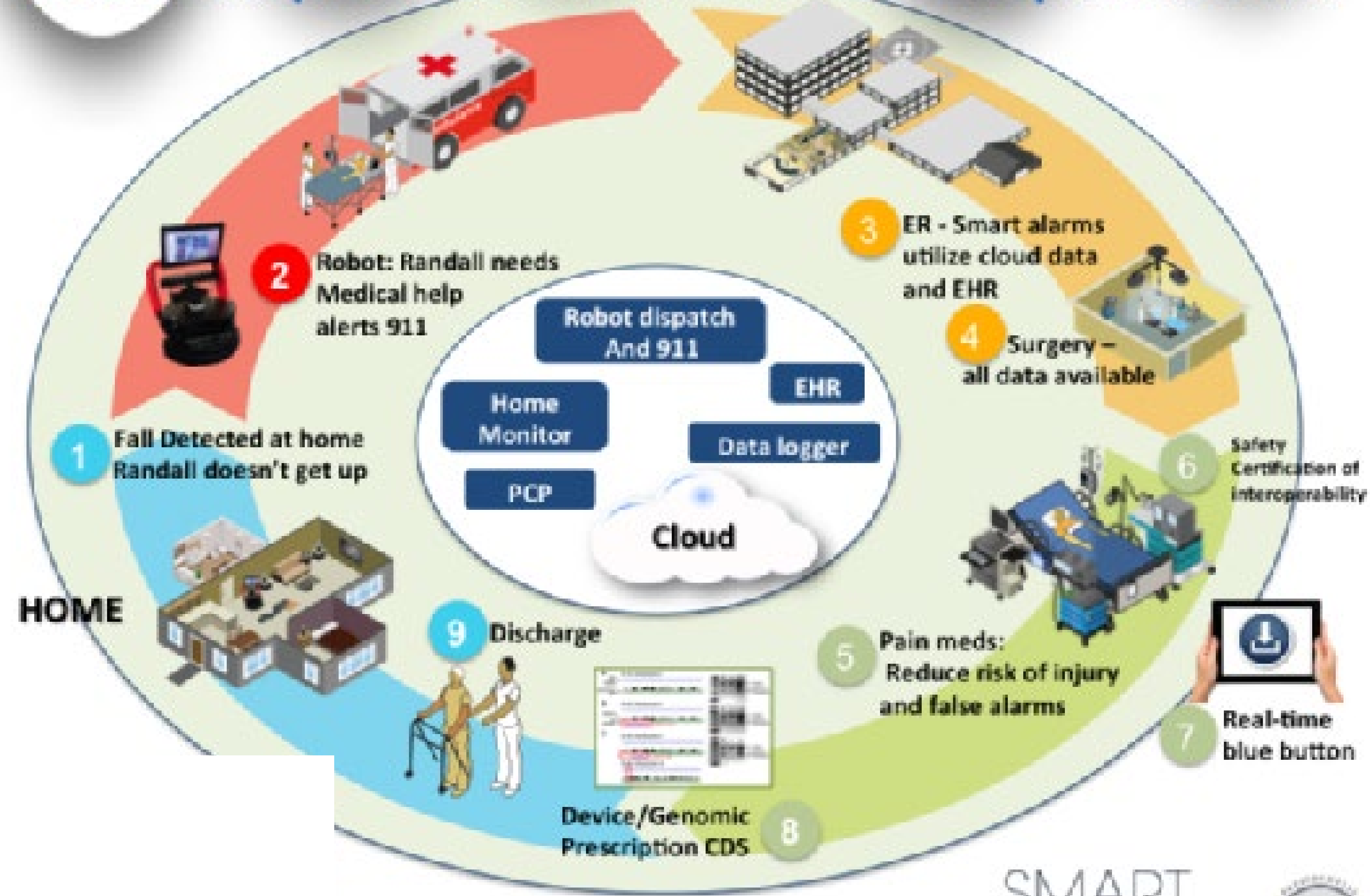
The buzz of "innovation" in healthcare often fails to differentiate between tools and services. Tools and technologies used to deliver healthcare are easy targets for innovation, modularity and scalability. This is innovation in health related tools, ***not healthcare***. Innovation in healthcare is about ***delivery*** of healthcare which is a closed loop management system uniquely focused on one patient (not scalable) and relevant tools must converge at the point of care. The infrastructure (data, transmission, security, privacy) to deliver healthcare may be scalable but innovation to enhance the quality, functionality and reliability of the infrastructure may or may not have an impact on the QoS of healthcare delivery at POC.

Harry at home with hypercholesterolemia - Larry - Do I need Lipitor today?



Dr Jameson: Thanks for avoiding KFC. Your LDL-VLDL ratio looks good. No Lipitor today.

Closed Loop HealthCare Team: Home to Hospital to Home



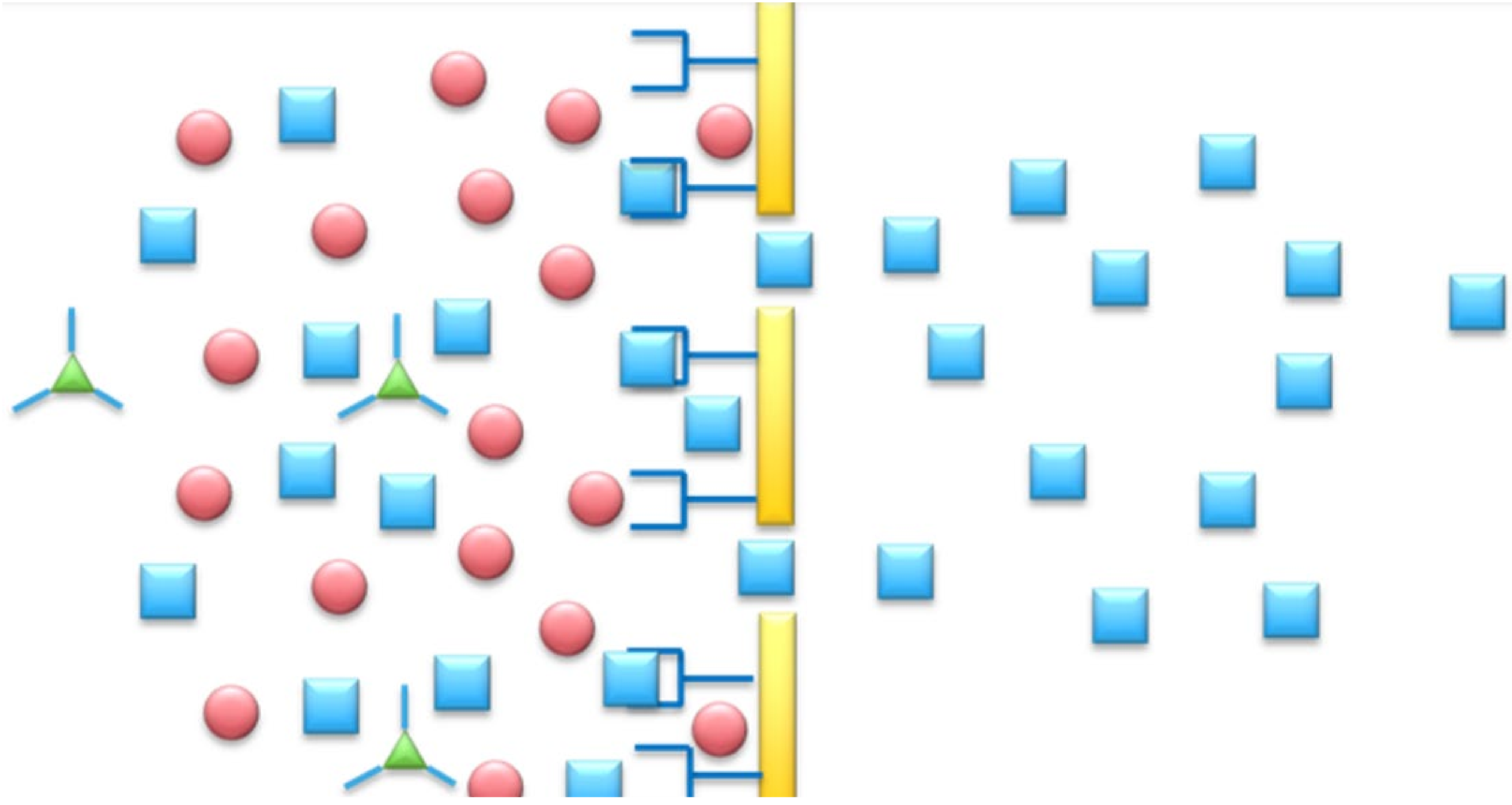
Dr Julian Goldman MD
MDPnP – MGH – HMS

Are all data created equal?

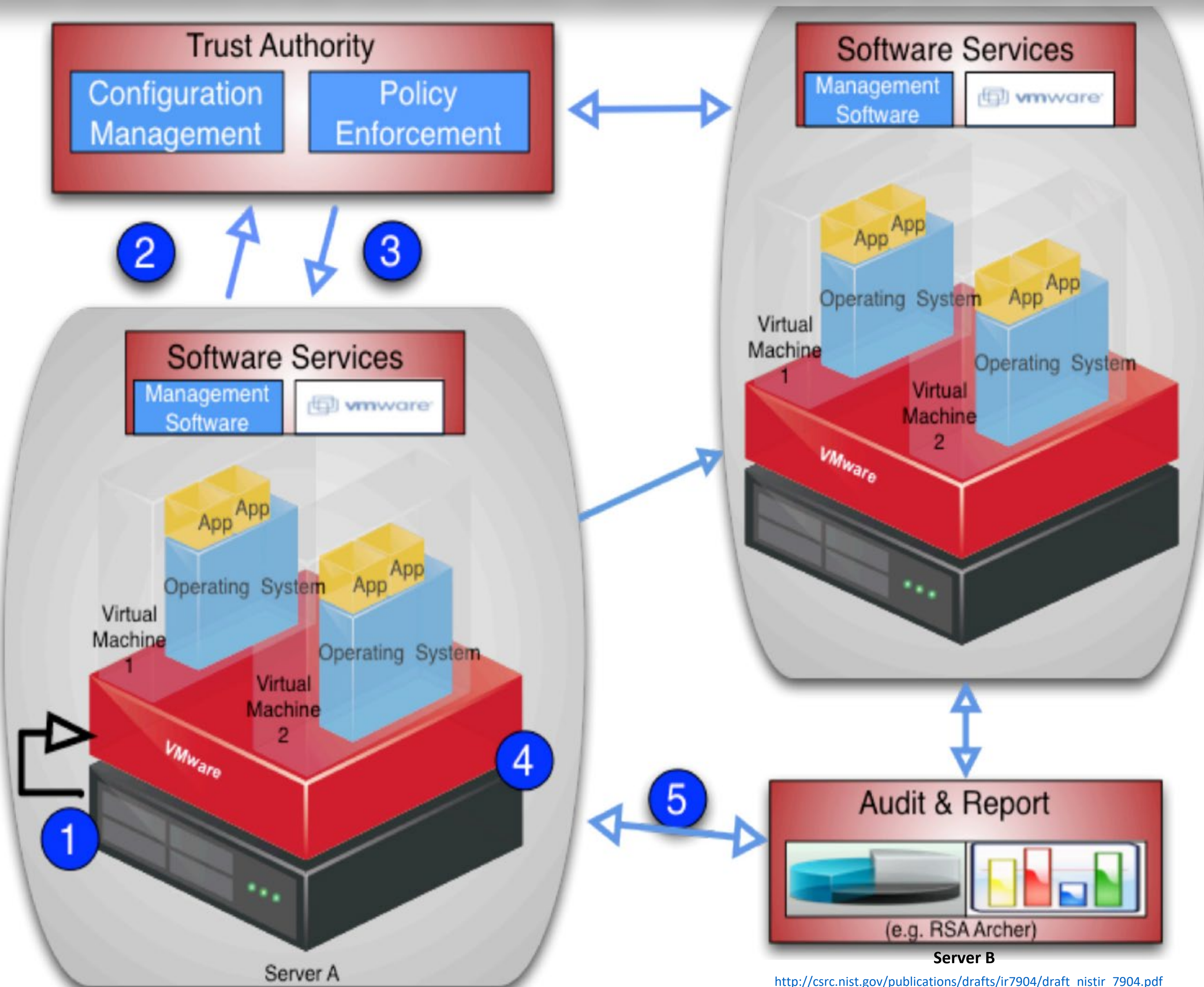
DON'T USE MY DATA

"Before I write my name on the board, I'll need to know how you're planning to use that data."

Principle of Differential Curation and De-identification of Data



Trusted GeoLocation in the Cloud (NCCOE) – Does it matter where your health data is located?

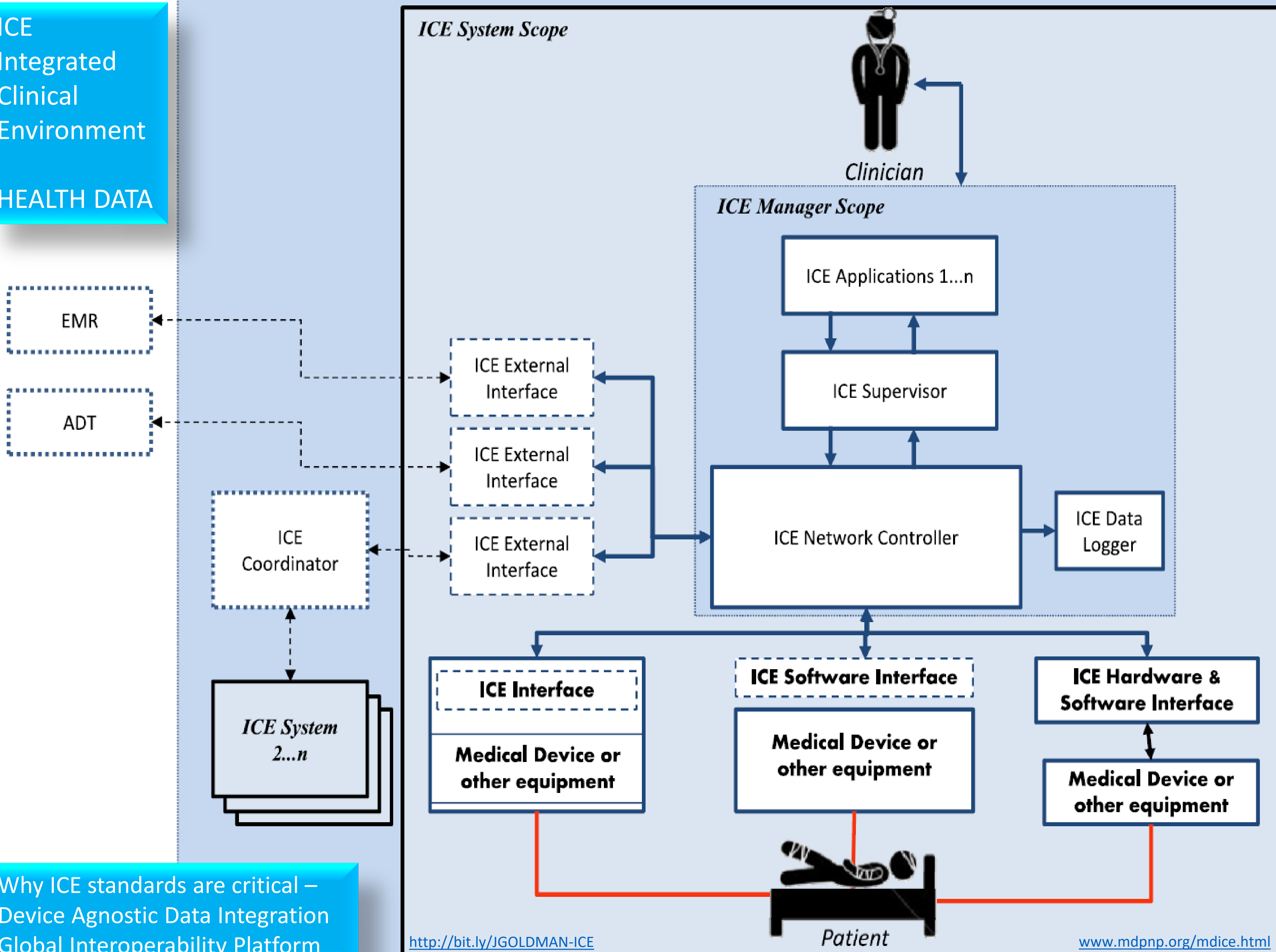


Server B

http://csrc.nist.gov/publications/drafts/ir7904/draft_nistir_7904.pdf
http://csrc.nist.gov/nccoe/health-it/index.html

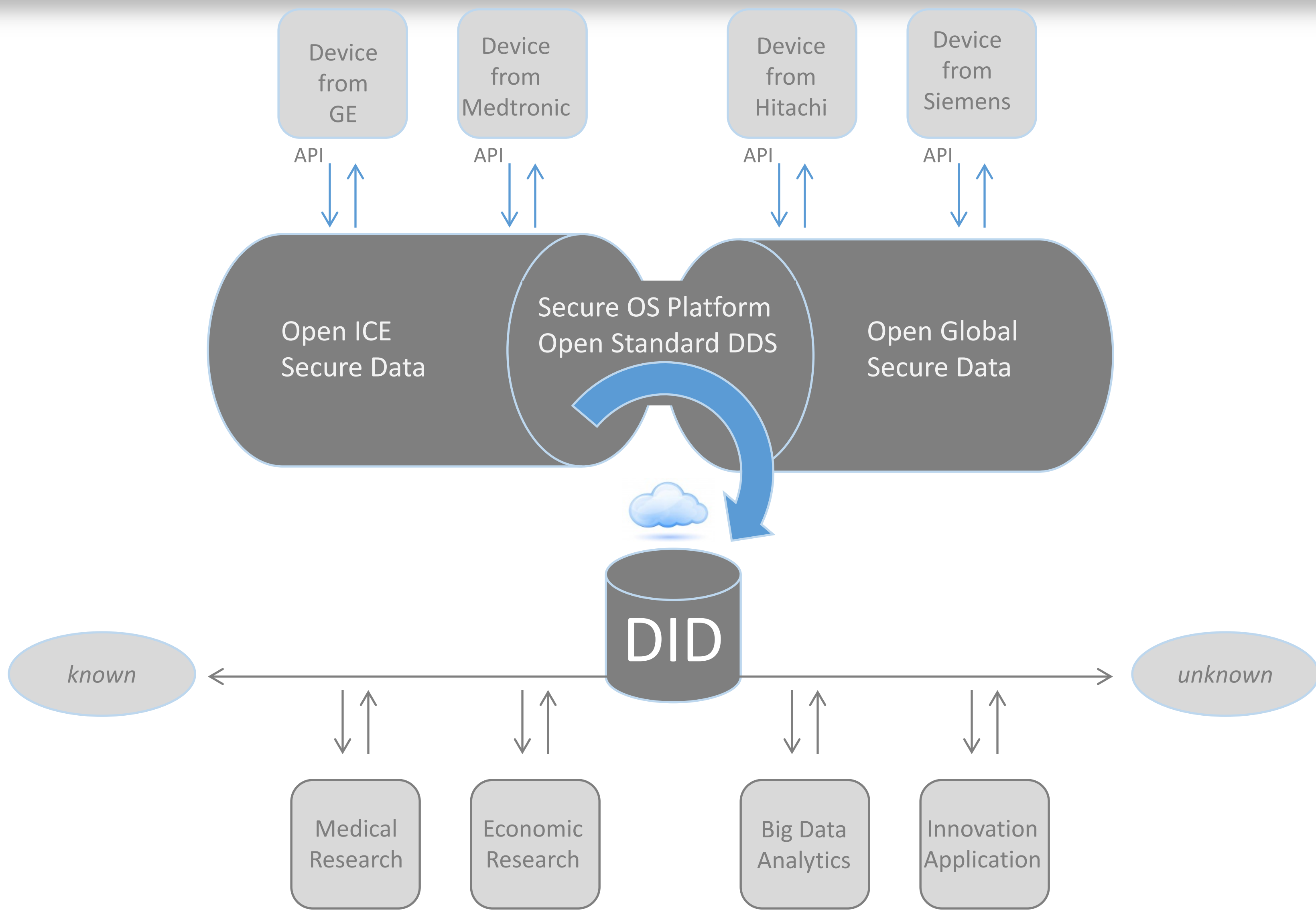
ICE
Integrated
Clinical
Environment

HEALTH DATA



Why ICE standards are critical –
Device Agnostic Data Integration
Global Interoperability Platform

De-identified Data (DID) will drive Research – Management Science – Policy – Funding



Note: In certain instances, CPS related time constraints may render traditional cloud based D2D architecture unacceptable [QoS] due to latency.

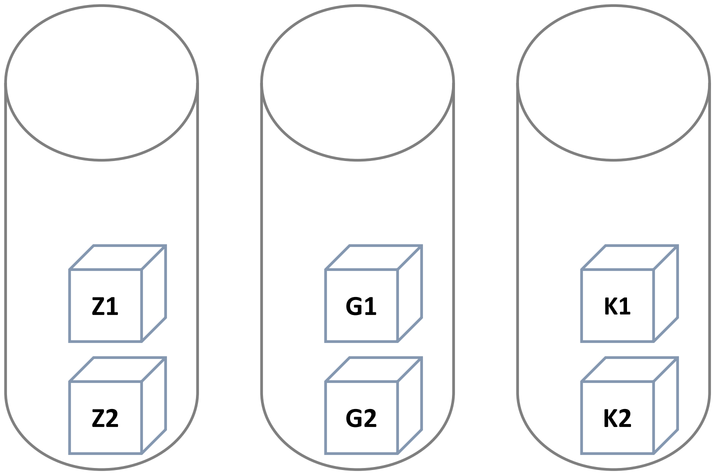
Data Dissociation using meta data to identify/label data type

Clinic VIEW

Name	SSN-UID	Street Address	Zip Code	Blood Glucose	Weight in kg
Jane Does Tag N1	123-45-6789 Tag S1	77 Mass Ave Tag A1	02139 Tag Z1	190 mg/dl Tag G1	190 Tag K1
John Does-Not Tag N2	123-45-6790 Tag S2	86 Brattle St Tag A2	02138 Tag Z2	109 mg/dl Tag G2	159 Tag K2

DID VIEW

Name	SSN-UID	Street Address	Zip Code	Blood Glucose	Weight in kg
			02139 Tag Z1	190 mg/dl Tag G1	190 Tag K1
			02138 Tag Z2	109 mg/dl Tag G2	159 Tag K2



Data Re-association using De-Identified Data (DID) Stack

Same data but ask a different

QUESTION

Same Data ← Different Questions → Extracting Information from DID

Epedimiologists

Economists

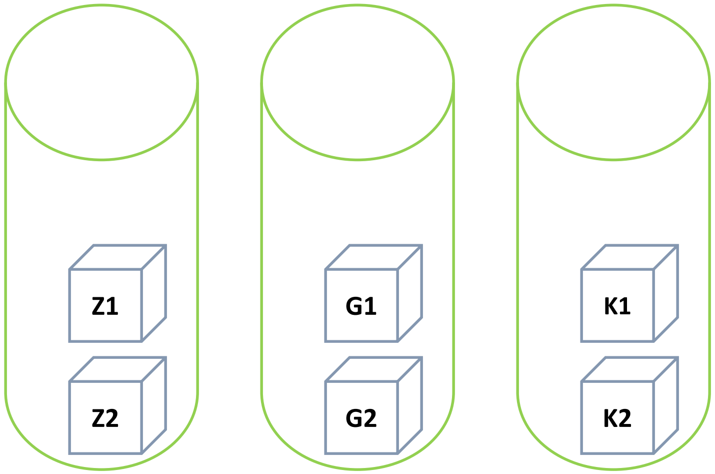
Physician

What is the distribution of potential diabetics by zip code?

Is there a relationship between per capita income and body fat?

Can we correlate high blood glucose with increased body weight?

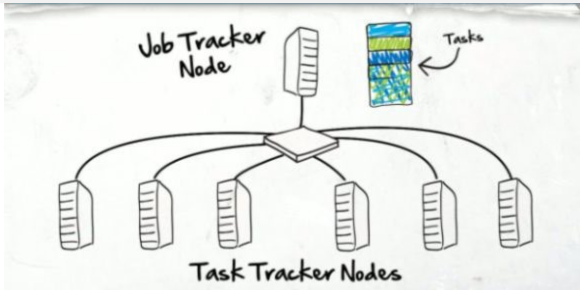
Name	SSN-UID	Street Address	Zip Code	Blood Glucose	Weight in kg
			02139 Tag Z1	190 mg/dl Tag G1	190 Tag K1
			02138 Tag Z2	109 mg/dl Tag G2	159 Tag K2

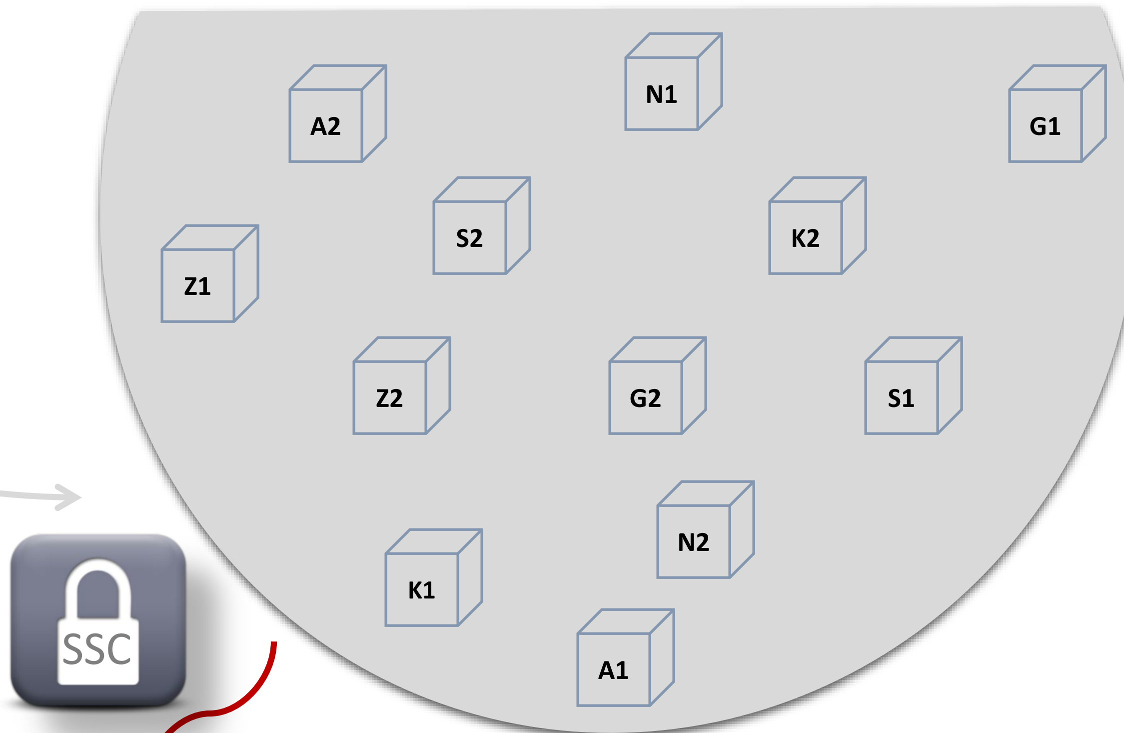


This is a suggestion by the author. Not a proven concept in practice.

Secured Data <> Re-association of De-Identified Data (DID)

Re-sequence DID → HADOOP-esque concept ?





Name	SSN-UID	Street Address	Zip Code	Blood Glucose	Weight in kg
Jane Does Tag N1	123-45-6789 Tag S1	77 Mass Ave Tag A1	02139 Tag Z1	190 mg/dl Tag G1	190 Tag K1
John Does-Not Tag N2	123-45-6790 Tag S2	86 Brattle St Tag A2	02138 Tag Z2	109 mg/dl Tag G2	159 Tag K2

This is a suggestion by the author. Not a proven concept in practice.

Re-stitch De-Identified Data - create Secure Sequencing Code (SSC)

Do we need novel approaches and innovation in curation in order to extract information from data?

- Data may be doubling approximately every 18-20 months or every 12-18 months
- Number of internet-connected devices may have exceeded 10 billion
- Payments by mobile phone alone are hurtling toward $1 trillion
- We may be generating 2.5 x 10^{18} (exabytes) of data each day
- Stored information in the world ~ 1200 exabytes
- Printed on CD-ROMs & stacked up, it will stretch to the Moon in 5 separate piles
- In 3rd century BC, Library of Alexandria represented most knowledge in the world
- Digital deluge offers each person on Earth 320 times as much information as above

Could a Neuroscientist Understand a Microprocessor?

Eric Jonas[1]*, **Konrad Paul Kording**[2,3]

1 Department of Electrical Engineering and Computer Science, University of California, Berkeley, Berkeley, California, United States of America, **2** Department of Physical Medicine and Rehabilitation, Northwestern University and Rehabilitation Institute of Chicago, Chicago, Illinois, United States of America, **3** Department of Physiology, Northwestern University, Chicago, Illinois, United States of America

* jonas@eecs.berkeley.edu

Value from data and analytics to generate information

Think and Connect like a Neuron?

http://journals.plos.org/ploscompbiol/article/file?id=10.1371/journal.pcbi.1005268&type=printable

Can detection of device data (low oxygen saturation) trigger in-network intelligence, medical alert & action?

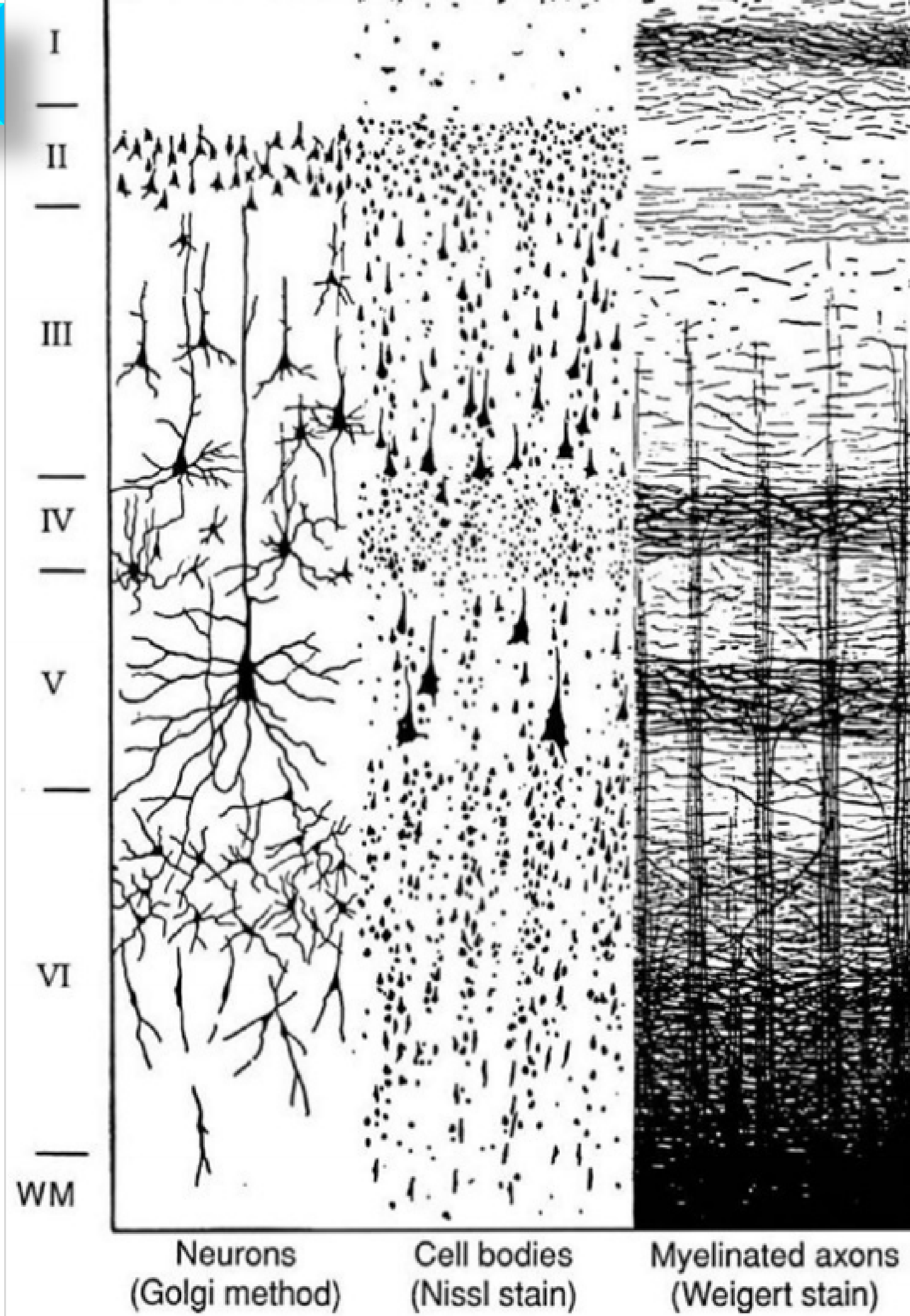
Application Aware Networking - an old concept renewed by connectivity

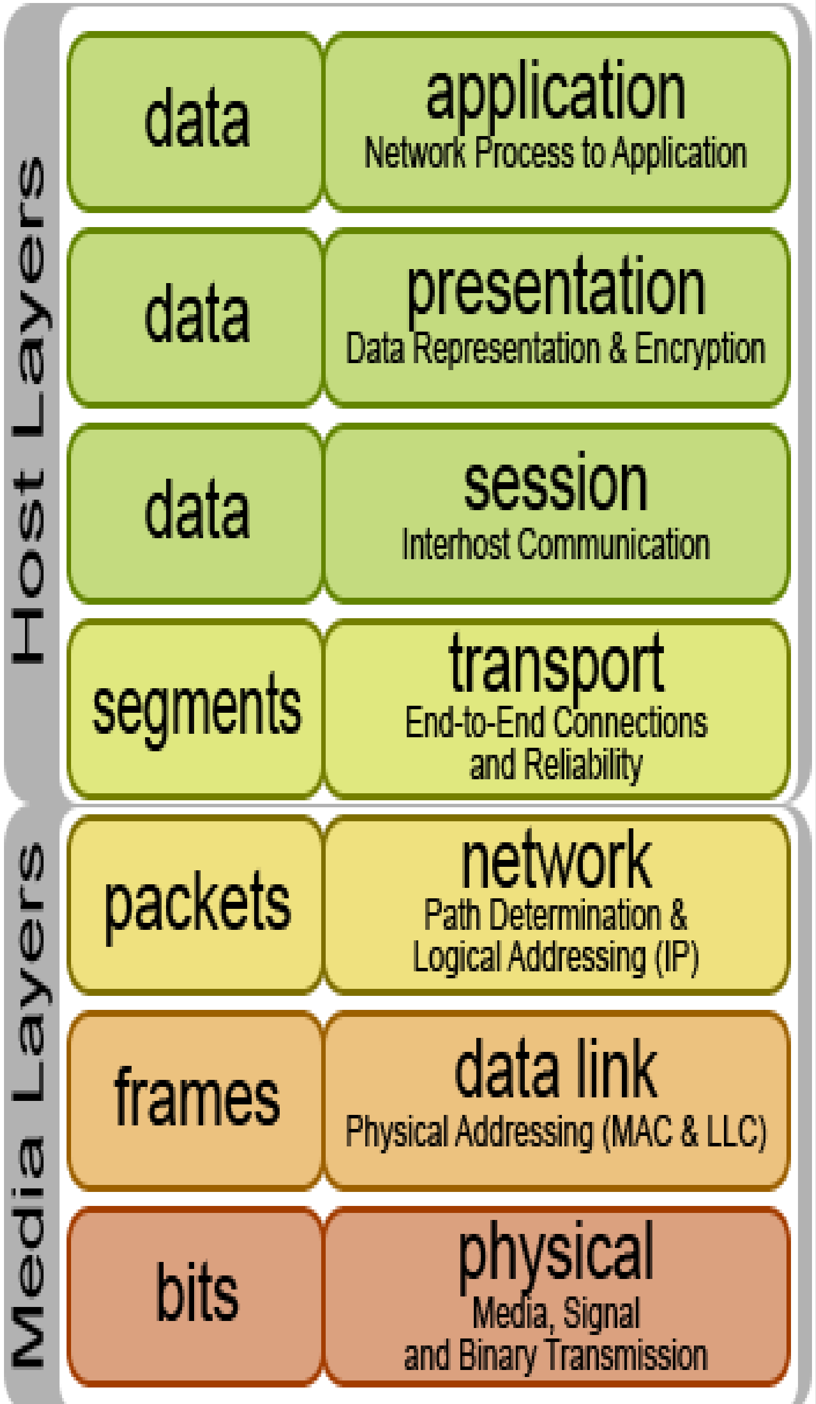
CISCO SYSTEMS

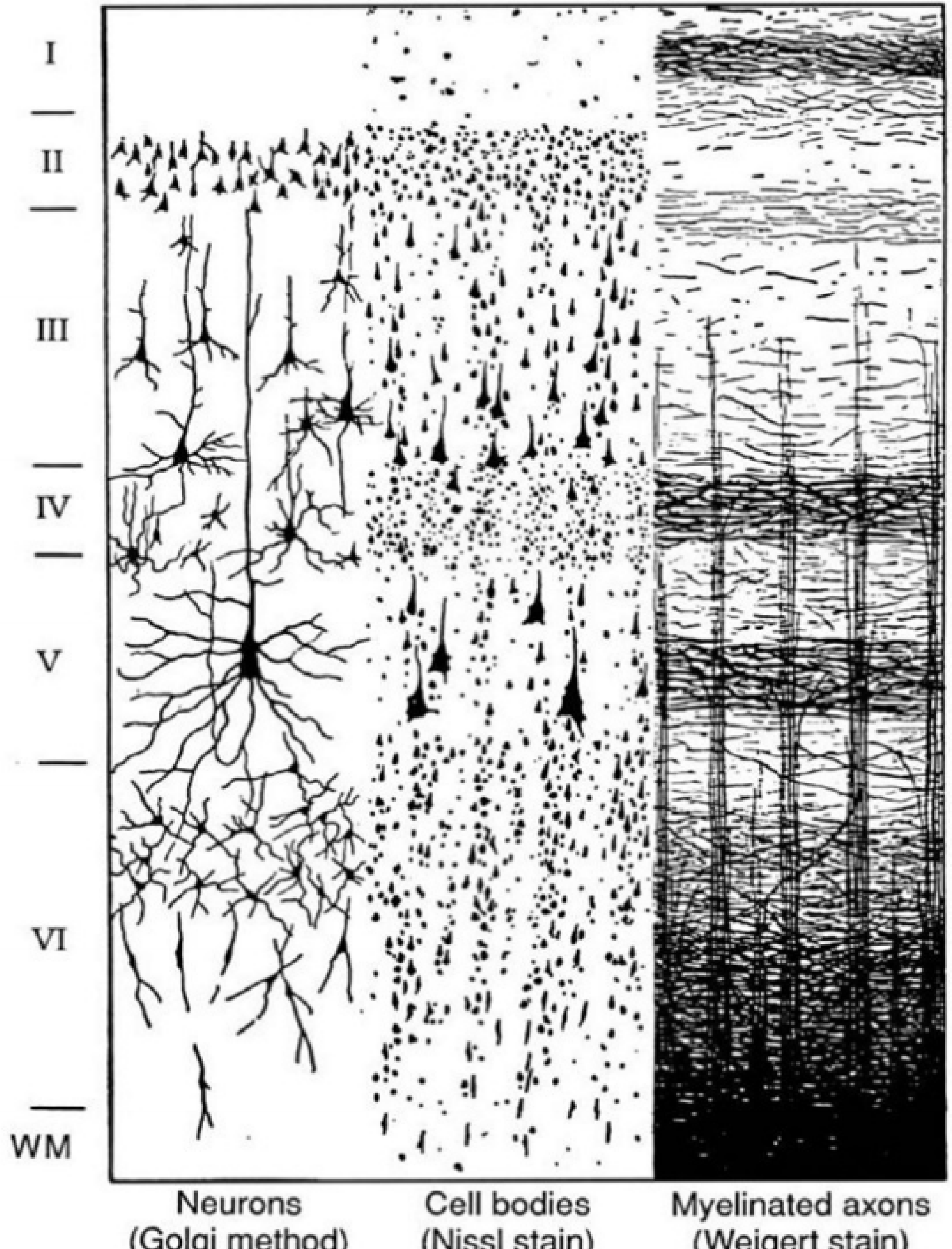
Santiago Ramón y Cajal

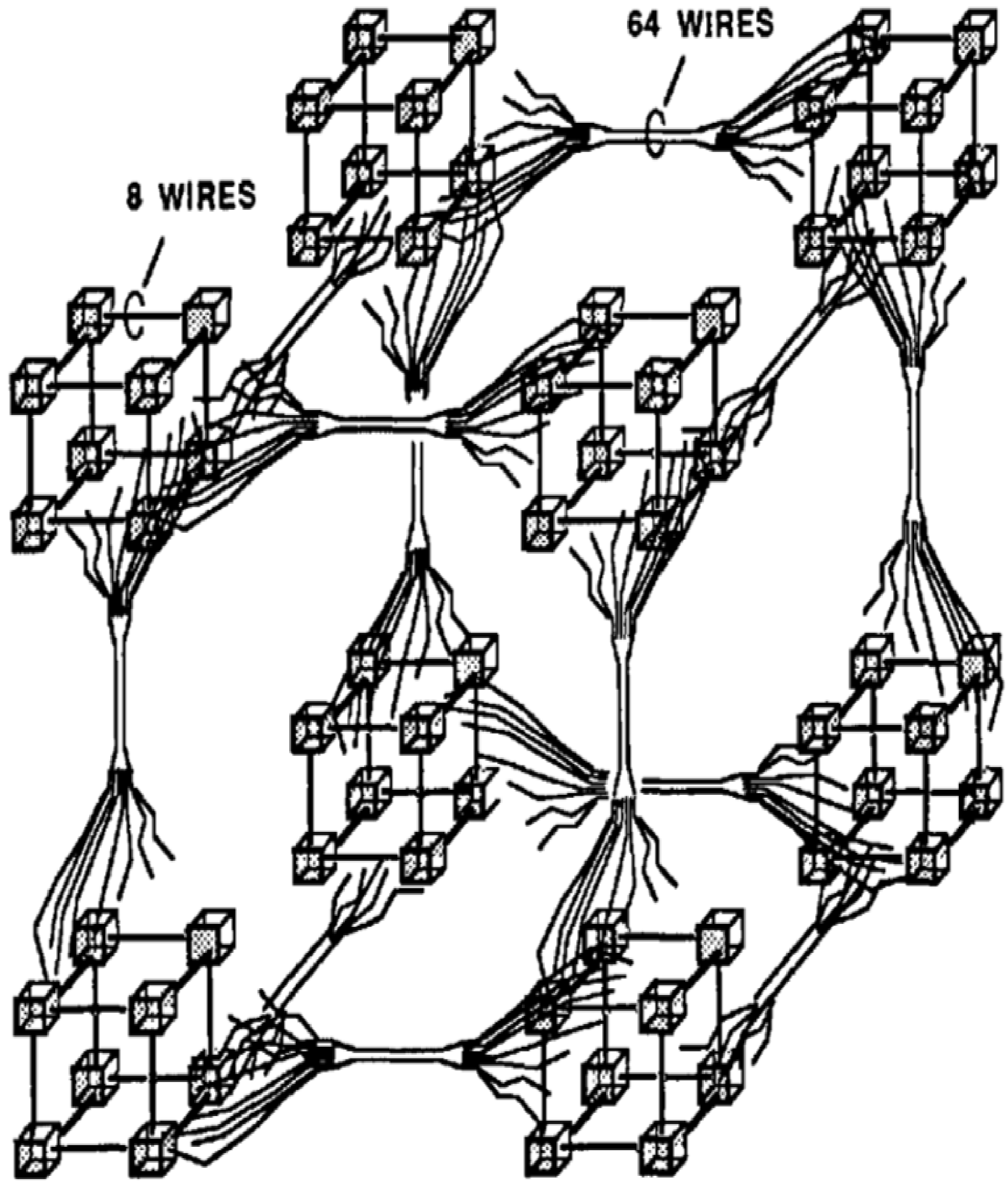
Slice of neo-cortex, as identified by Cajal. Every cubic mm contains about 100,000 neurons and 2-4 km of axons and dendrites. Layers I-VII on the right = 2mm vertical distance.

Born	1 May 1852 Petilla de Aragón, Navarre, Spain
Died	18 October 1934 (aged 82) Madrid, Spain




Host Layers
Media Layers
data
application
Network Process to Application
data
presentation
Data Representation & Encryption
data
session
Interhost Communication
segments
transport
End-to-End Connections
and Reliability
packets
network
Path Determination &
Logical Addressing (IP)
frames
data link
Physical Addressing (MAC & LLC)
bits
physical
Media, Signal
and Binary Transmission


I
II
III
IV
V
VI
WM
Neurons
(Golgi method)
Cell bodies
(Nissl stain)
Myelinated axons
(Weigert stain)



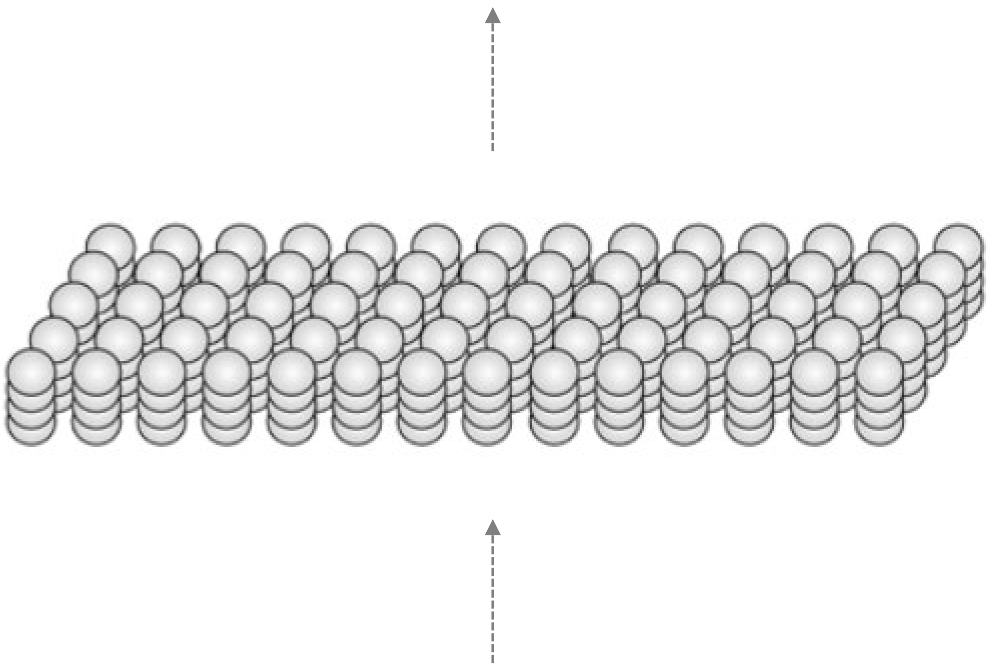
Here, 8 agents make a little cube, and 8 such cubes make a 64-agent supercube.

If we join 8 of these supercubes, we'll have 512 agents. And if we repeat this cube-on-cube pattern ten times, the resulting supercube will contain a billion agents!

But if we link each agent to 30 others instead of only 6, then each agent could communicate with a billion others in only 6 steps.

THE SOCIETY OF MIND
Marvin Minsky (1959)

Hierarchical Temporal Memory (HTM), a form of ANN, may be useful for time criticality of time series data



Section of a HTM region, equivalent to 1 layer of neurons in the neocortical region (layer 3). Each 4-cell column connects to a subset of the input and each cell connects to other cells in the region (connections are not shown). The principle of this connectivity was abstracted in Minsky's cube-on-cube.

Numenta

HTM (CLA) attributes include time and context – essential for many time sensitive healthcare applications and data analytics (context)

Hierarchical Temporal Memory (HTM) is a machine learning tool to capture the structural and algorithmic properties of the neocortex which is the seat of intelligent thought in the mammalian brain. High level vision, hearing, touch, movement, language and planning are performed by the neocortex. Given such a diverse suite of cognitive functions, the neocortex may be expected to implement an equally diverse suite of specialized neural algorithms. In reality, the neocortex displays a remarkably uniform pattern of neural circuitry. In other words, the neocortex implements a common set of algorithms to perform many different intelligence functions. It may be analogous to an abstraction which is used in a systemic context.

Programming HTM cortical learning algorithms require training through exposure to a stream of sensory data (capabilities are determined largely by exposure). HTM is a memory based ANN system. HTM networks are trained on time varying data and rely on storing a large set of patterns and sequences. A crucial distinction of HTM is embedded in the semantics of time which is an important element in applications relating to cyberphysical systems (CPS). Classic computer memory has a flat organization and does not have an inherent notion of time because the semantics of time are not available in the ISA (instruction set architecture). Therefore, in the classical programming environment, we can implement any kind of data organization and structure on top of the flat computer memory and control how and where information is stored.

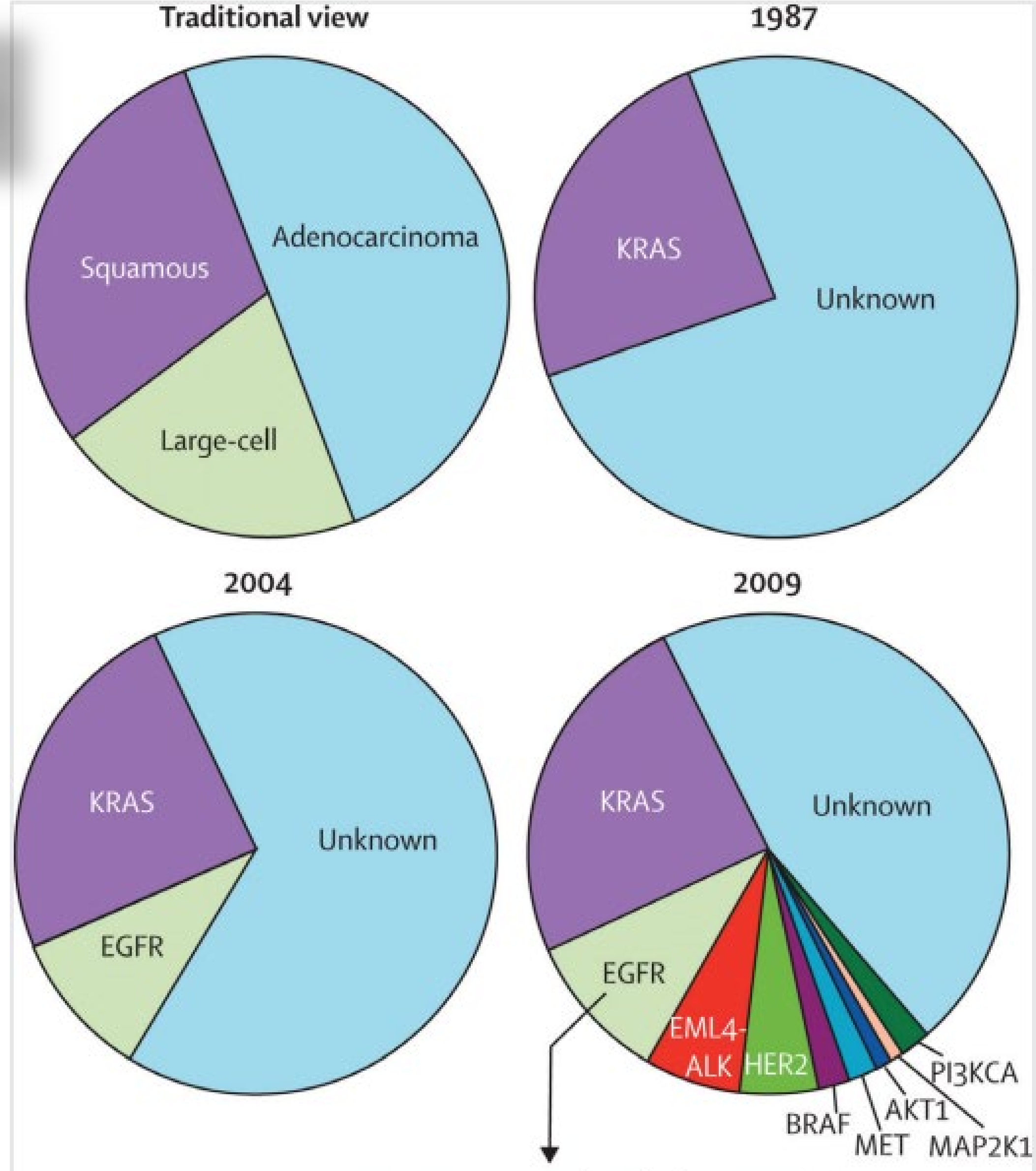
HTM memory is more restrictive. HTM memory has a hierarchical organization and is inherently time based. Information is always stored in a distributed fashion. HTM user is expected to specify the size of the hierarchy and what to train the system on but the HTM controls where and how information is stored (data, patterns, text, sequences). Hence, HTMs are learning and prediction machines that can be applied to many types of problems through the inherent abstractions in the system. Although an HTM region is equivalent to only one portion of a neocortical region (layer 3), it can perform inference and prediction on complex data streams. Hence the significance of HTMs in data analytics in multiple domains or verticals.

Although neurons in the neocortex are highly interconnected, inhibitory neurons guarantee that only a small percentage of the neurons are active at one time. Thus, information in the brain is always represented by a small percentage of active neurons within a large population of neurons. This kind of encoding is called a “sparse distributed representation” where a small percentage of neurons are active at one time. “Distributed” refers to the characteristic that the activation of many neurons are required in order to represent something. A single active neuron conveys some meaning but it must be interpreted within the context of a population of neurons to convey the full or complete meaning relevant to the context.

The Final Frontier?

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

http://bit.ly/PRECISION-MEDICINE

Imprecision Medicine

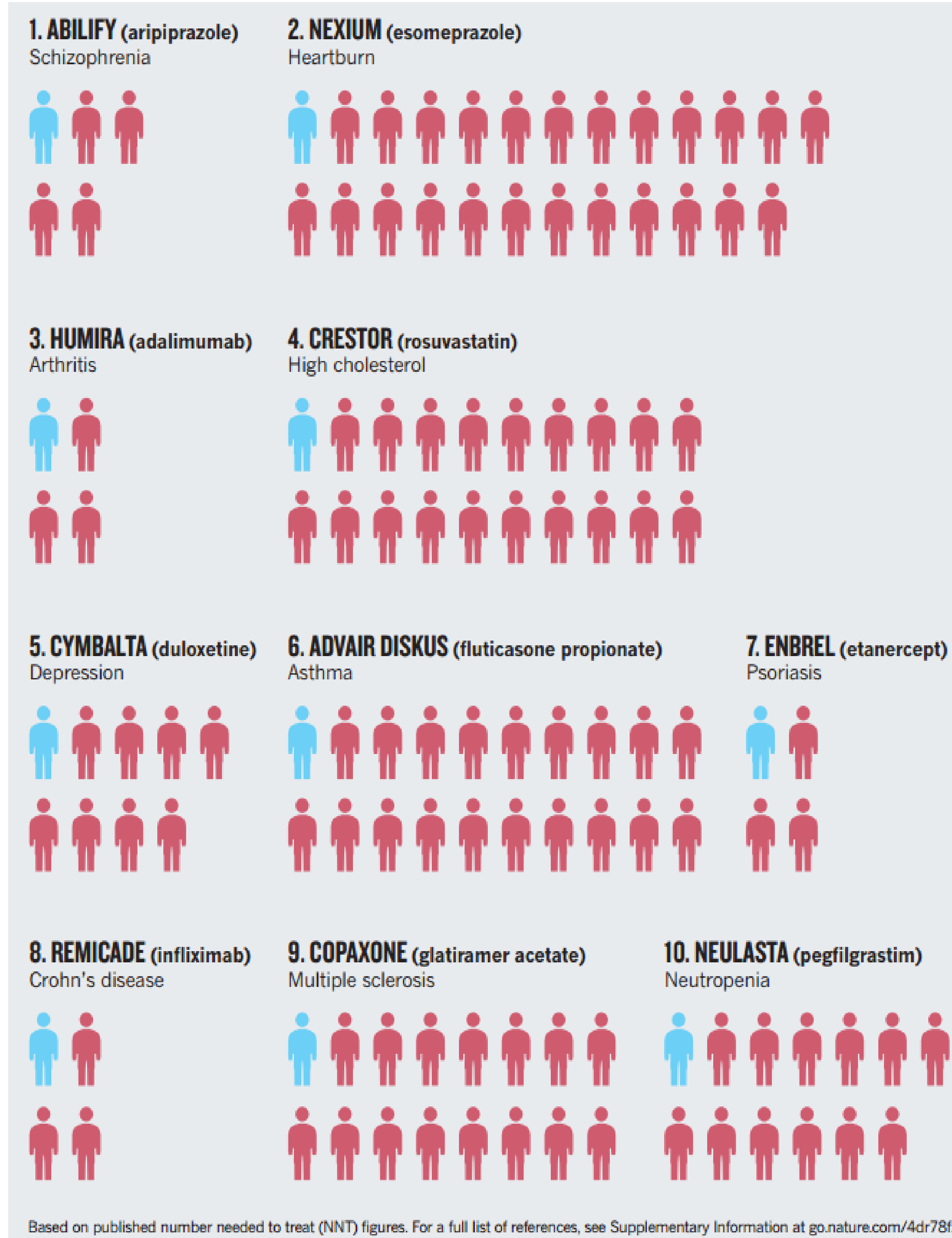
new ones and identifying appropriate disease biomarkers, such as tumour DNA circulating in the bloodstream. It will also require a cultural shift on many levels — in regulatory agencies, in pharmaceutical companies and, most of all, in the clinic.

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 responsive[3].

For instance, the drug Gleevec (imatinib) was found to double survival rates of leukaemia patients[4] 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* gene[5].

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



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.)

http://bit.ly/PRECISION-MEDICINE

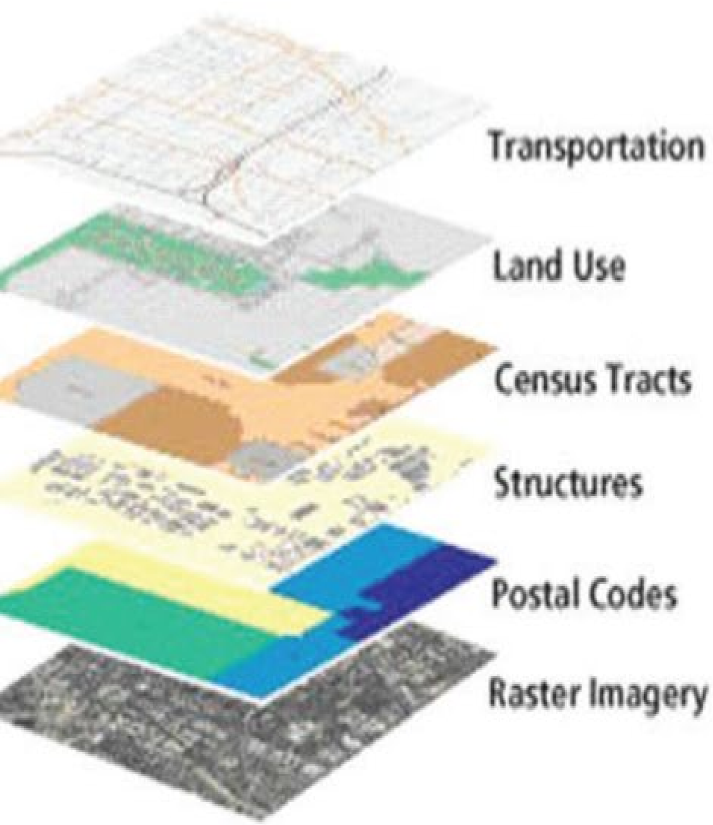
Tuesday, April 21, 2015 - 10:00am EDT

Pfizer Inc. announced today that XALKORI® (crizotinib) received Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the potential treatment of patients with ROS1-positive non-small cell lung cancer (NSCLC). Occurring in approximately one percent of NSCLC cases[1], ROS1-positive NSCLC represents a particular molecular subgroup of NSCLC.[2] XALKORI currently is approved in the U.S. for the treatment of patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

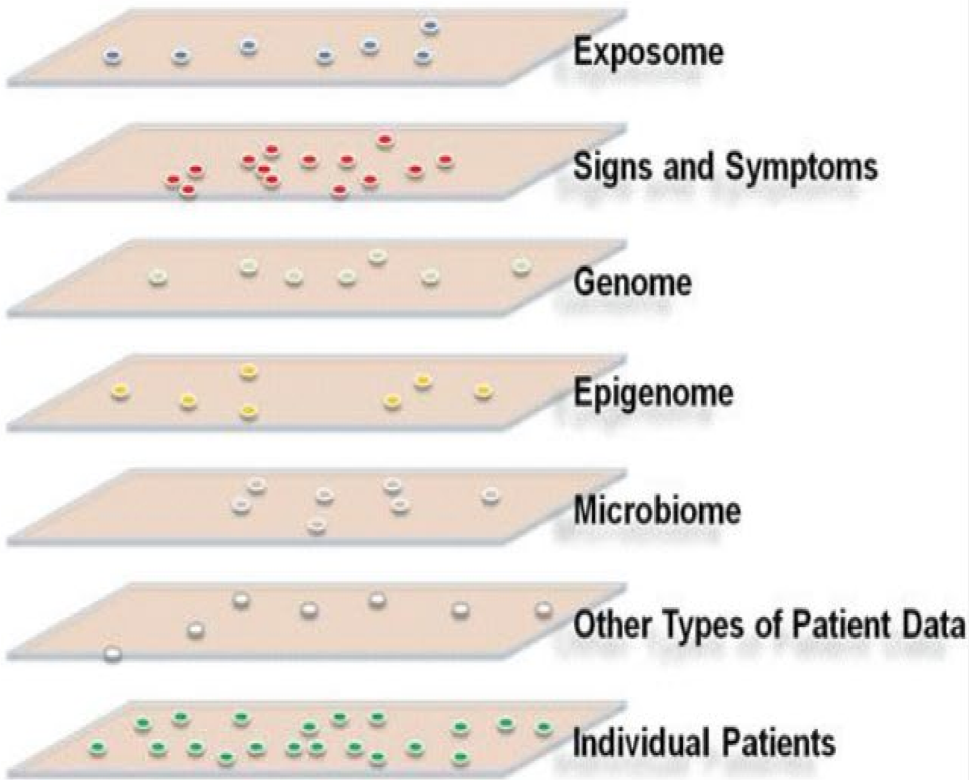
https://clinicaltrials.gov/ct2/show/NCT01154140

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



Data, Devices and Connected Information (IoT)
▪Factors Influencing Future Precision Medicine▪

Bio-medical Knowledge Network

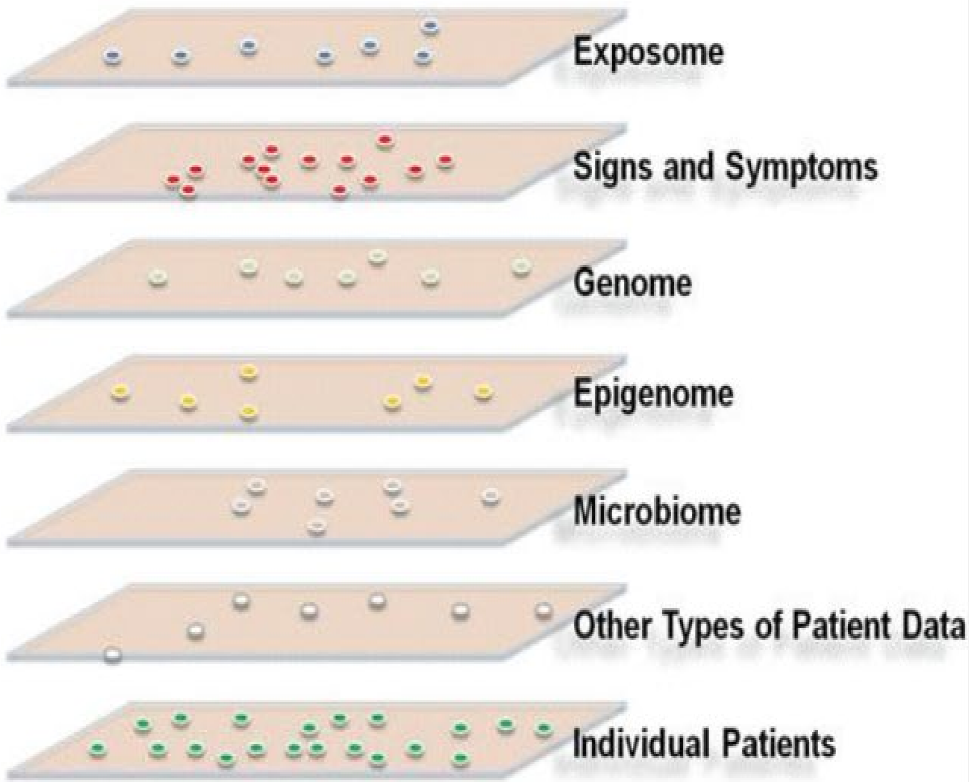
Information Commons
Organized Around Individual Patients

External Exposure: Where are you? GPS

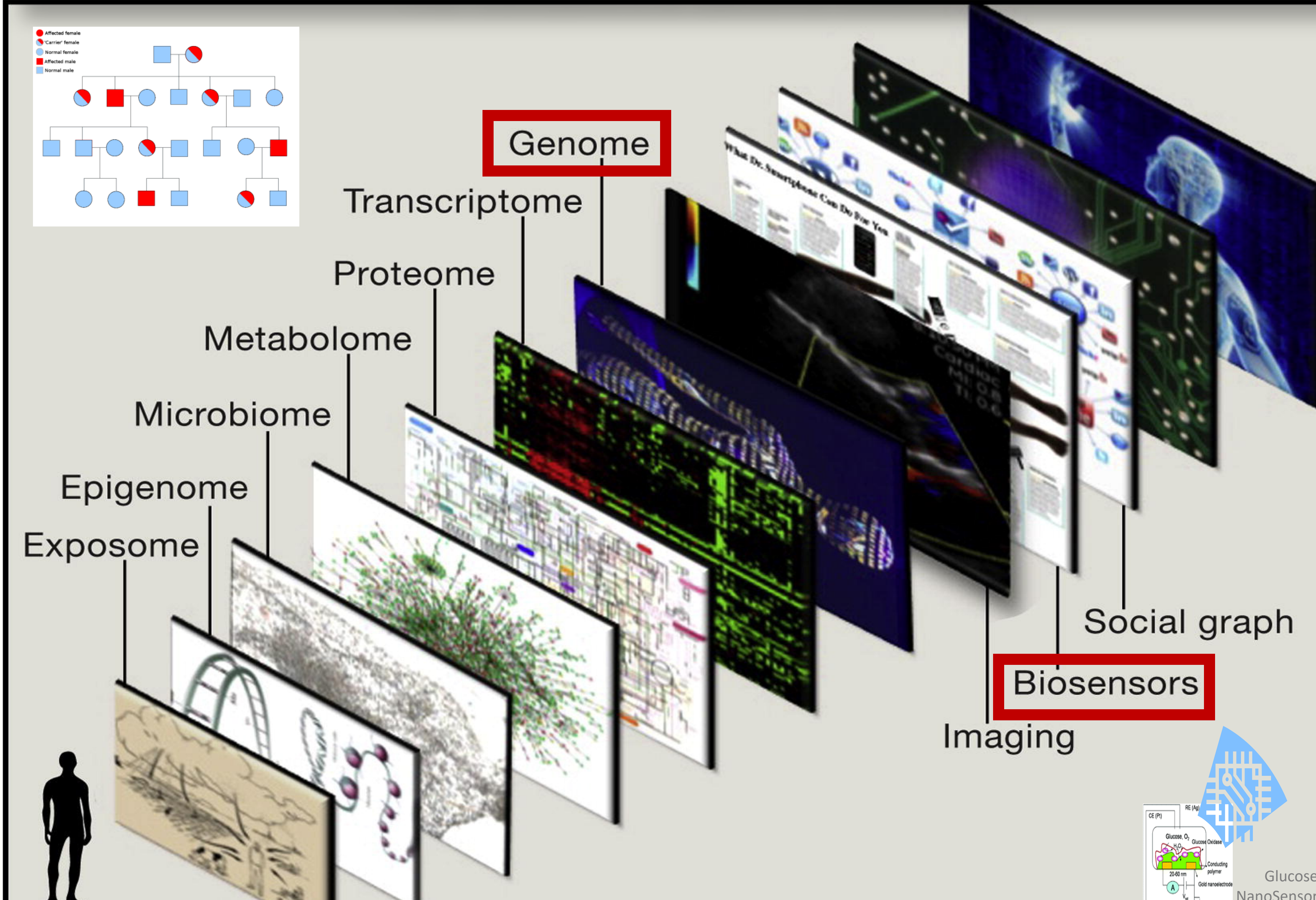
Constant wearables: temp, bp, rr, hr, oximetry

Food, hours of sleep, frequency of urination

Blood glucose, cholesterol, urea, hemoglobin



The Foundations of Genomic Medicine



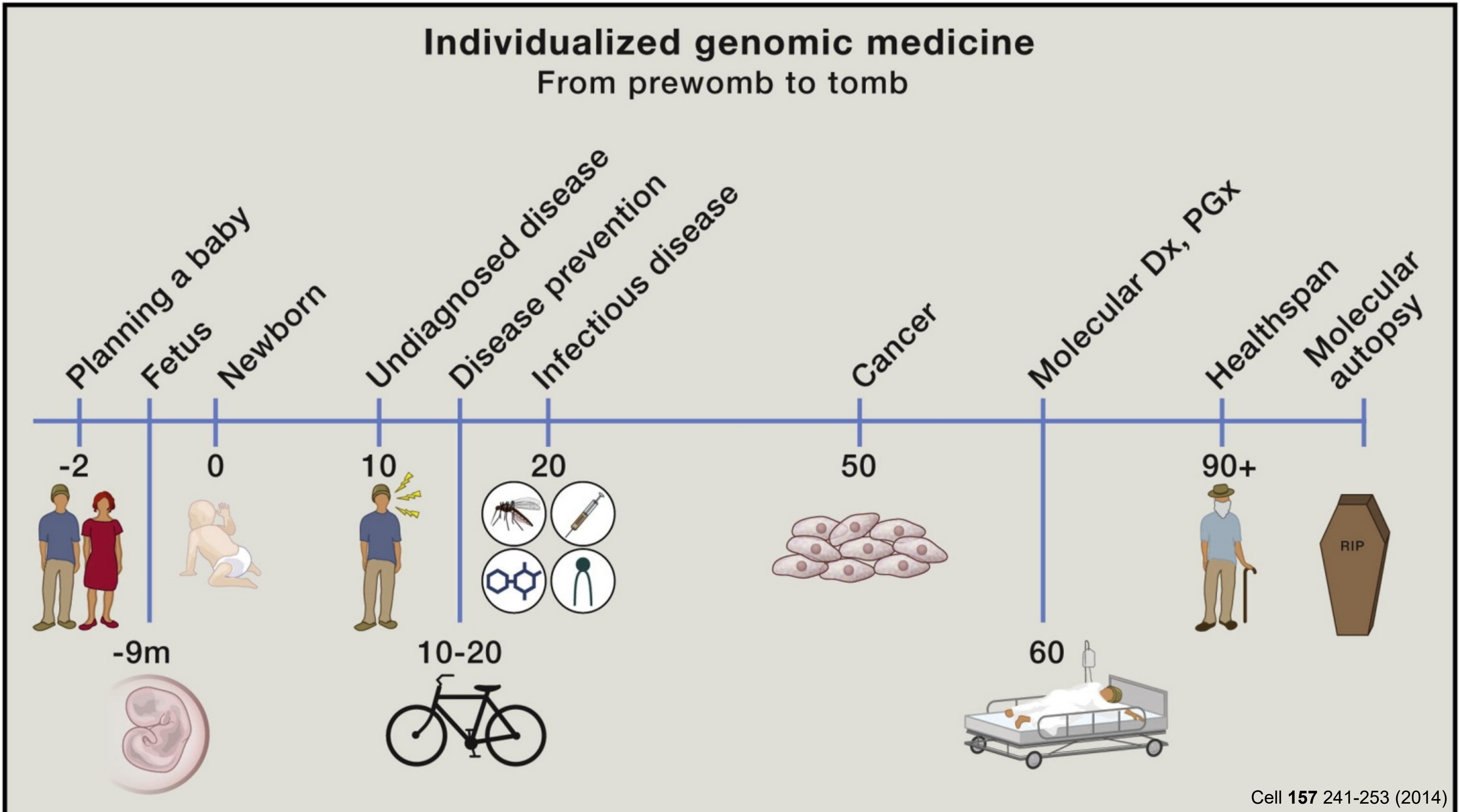
Cell **157** 241-253 (2014)

Mendelian Inheritance in Man: A Catalog of Human Genes and Genetic Disorders by Victor A. McKusick

Human Genomics in an Age of Precision Medicine

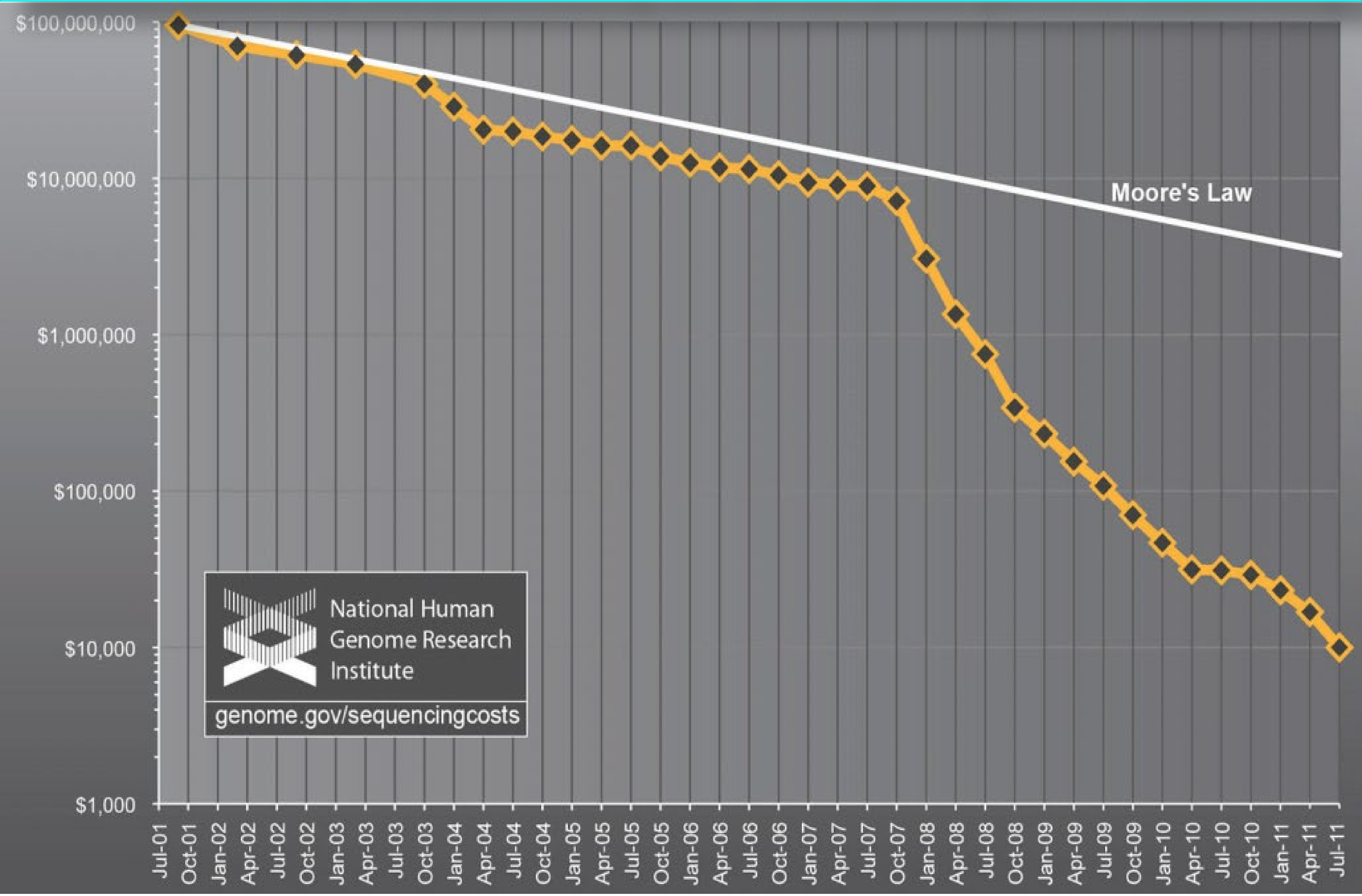
Designer Drugs Delivered by Drones in the Wireless Hospital

Irrational exuberance ?



Cell **157** 241-253 (2014)

What may make precision medicine feasible – the rapid advances in automation and the plummeting cost of complete genome sequencing



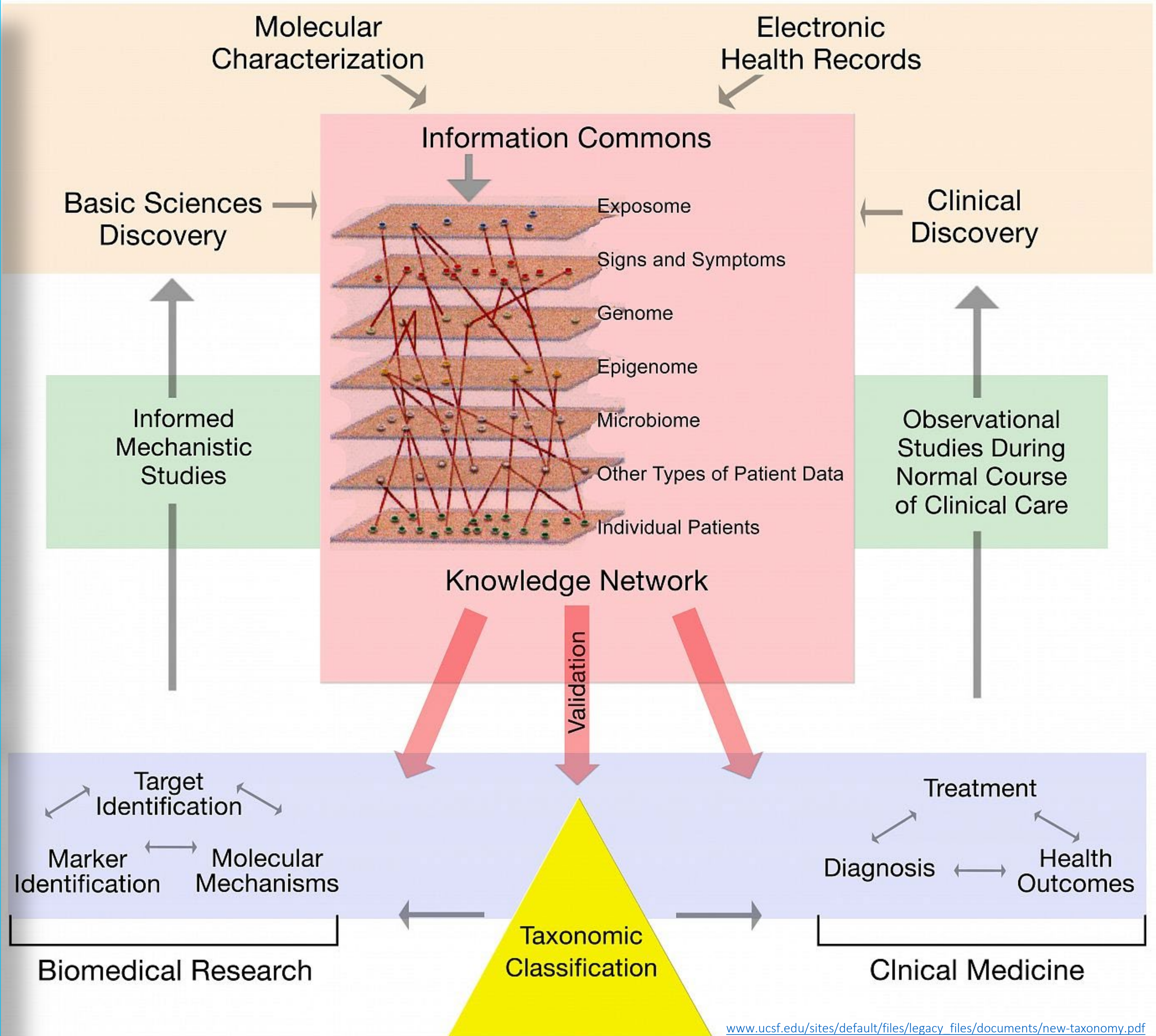
MinION USB stick gene sequencer finally comes to market

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

What is the challenge of precision medicine?

Integration

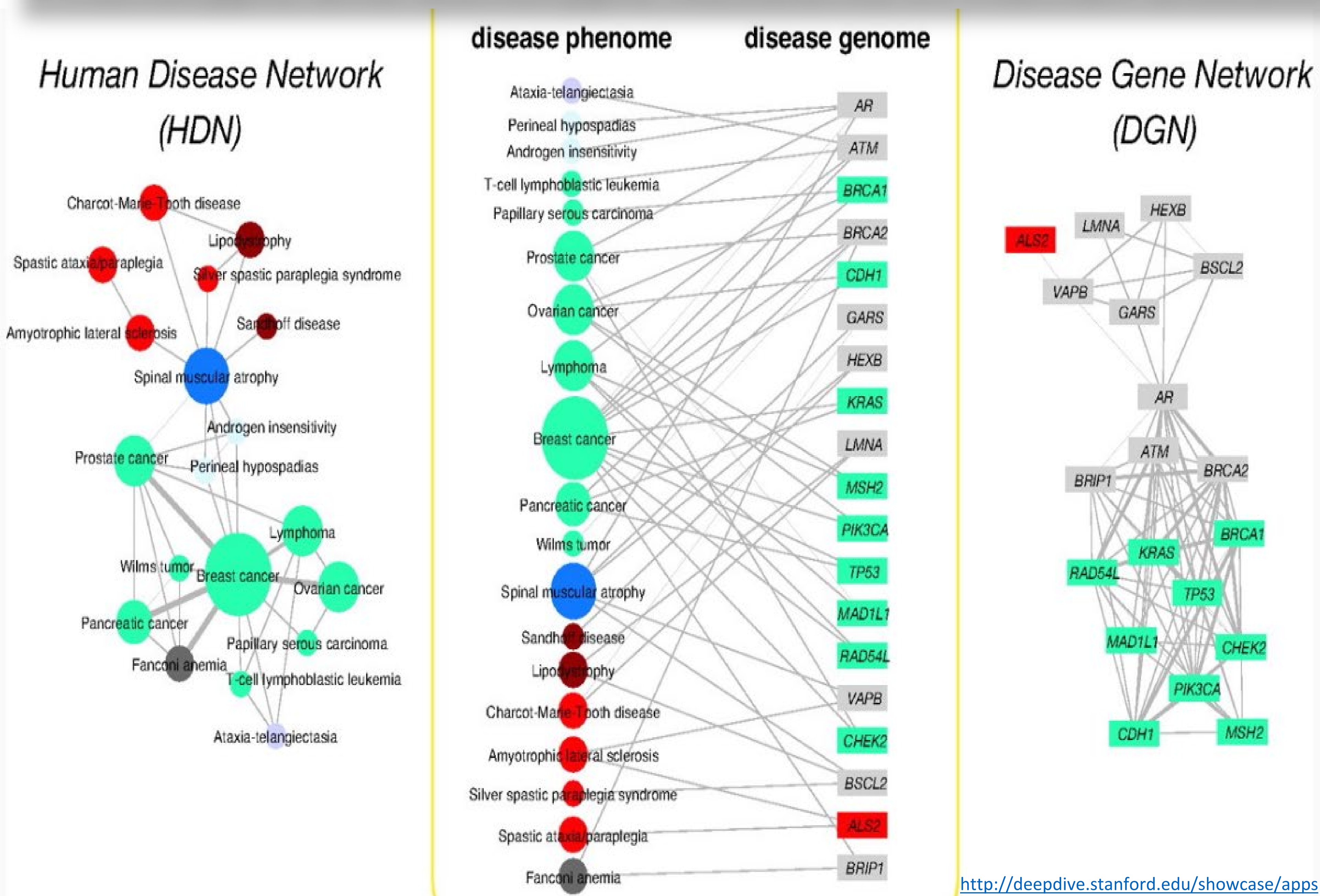
How do we integrate data and information from these systems with diverse open source healthcare platforms?



www.ucsf.edu/sites/default/files/legacy_files/documents/new-taxonomy.pdf

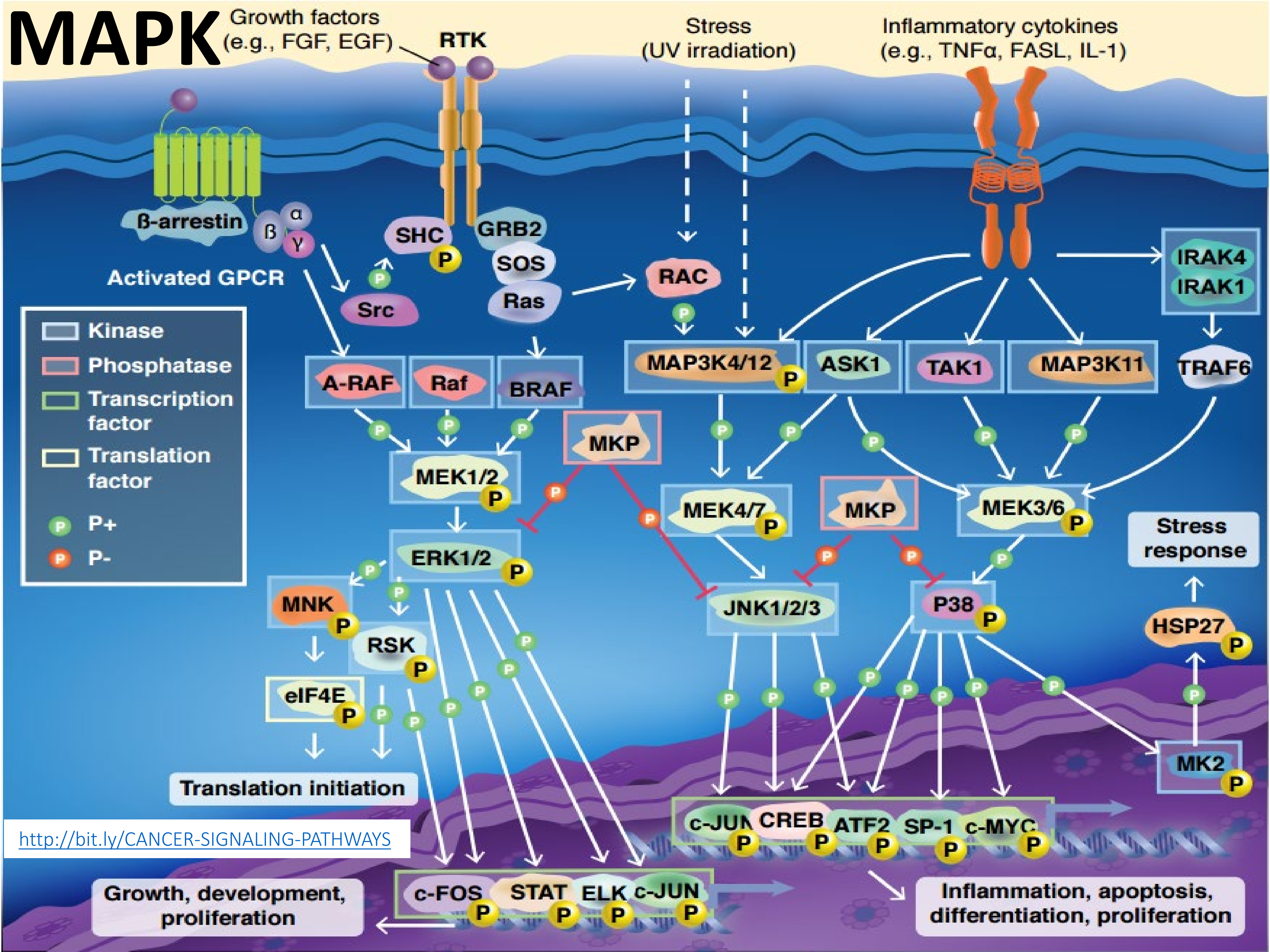
How close are we to the “knowledge network” of biological/disease networks?

Phenotypic and Genotypic Networks in Human Disease



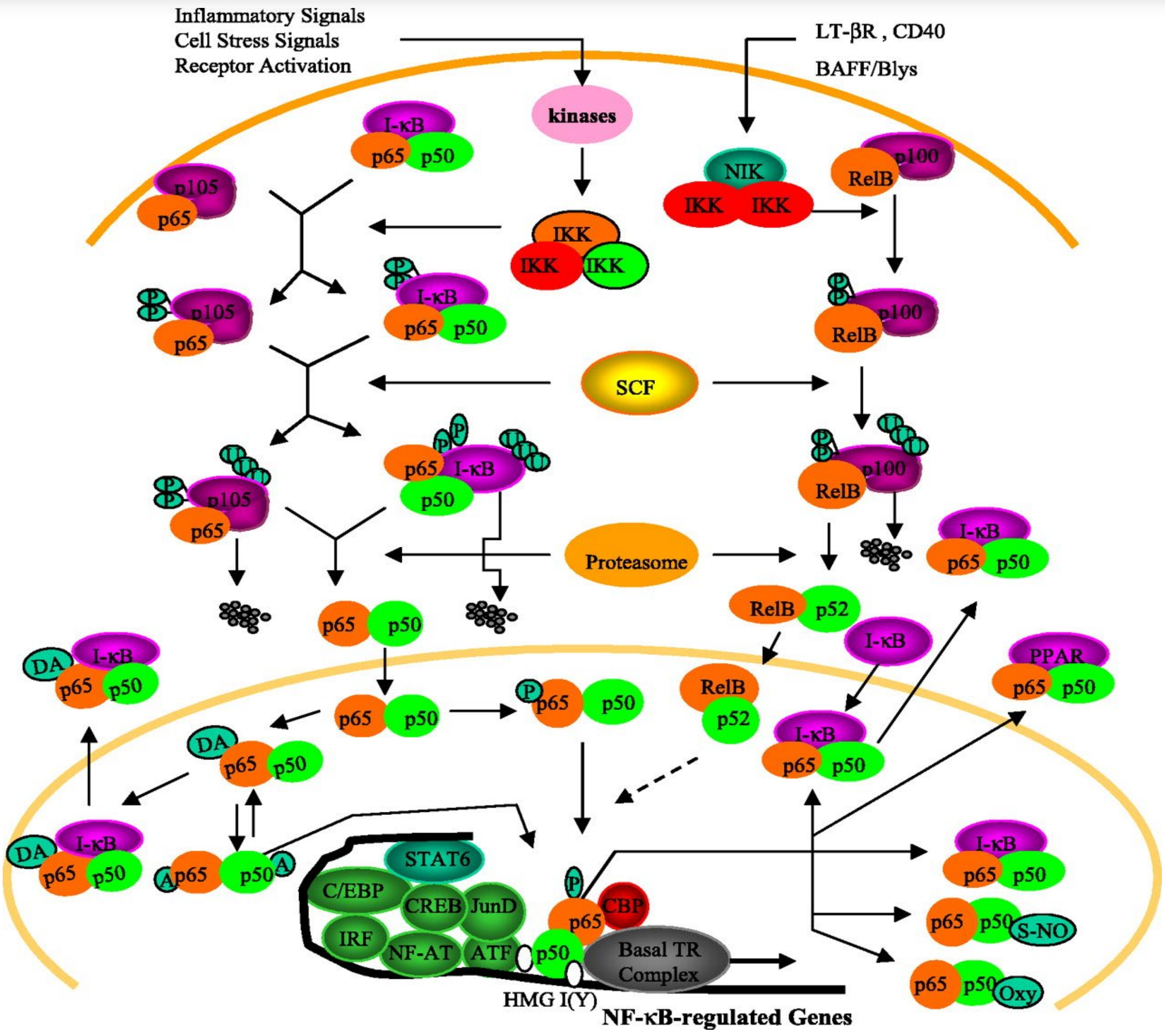
http://deepdive.stanford.edu/showcase/apps

MAPK



http://bit.ly/CANCER-SIGNALING-PATHWAYS

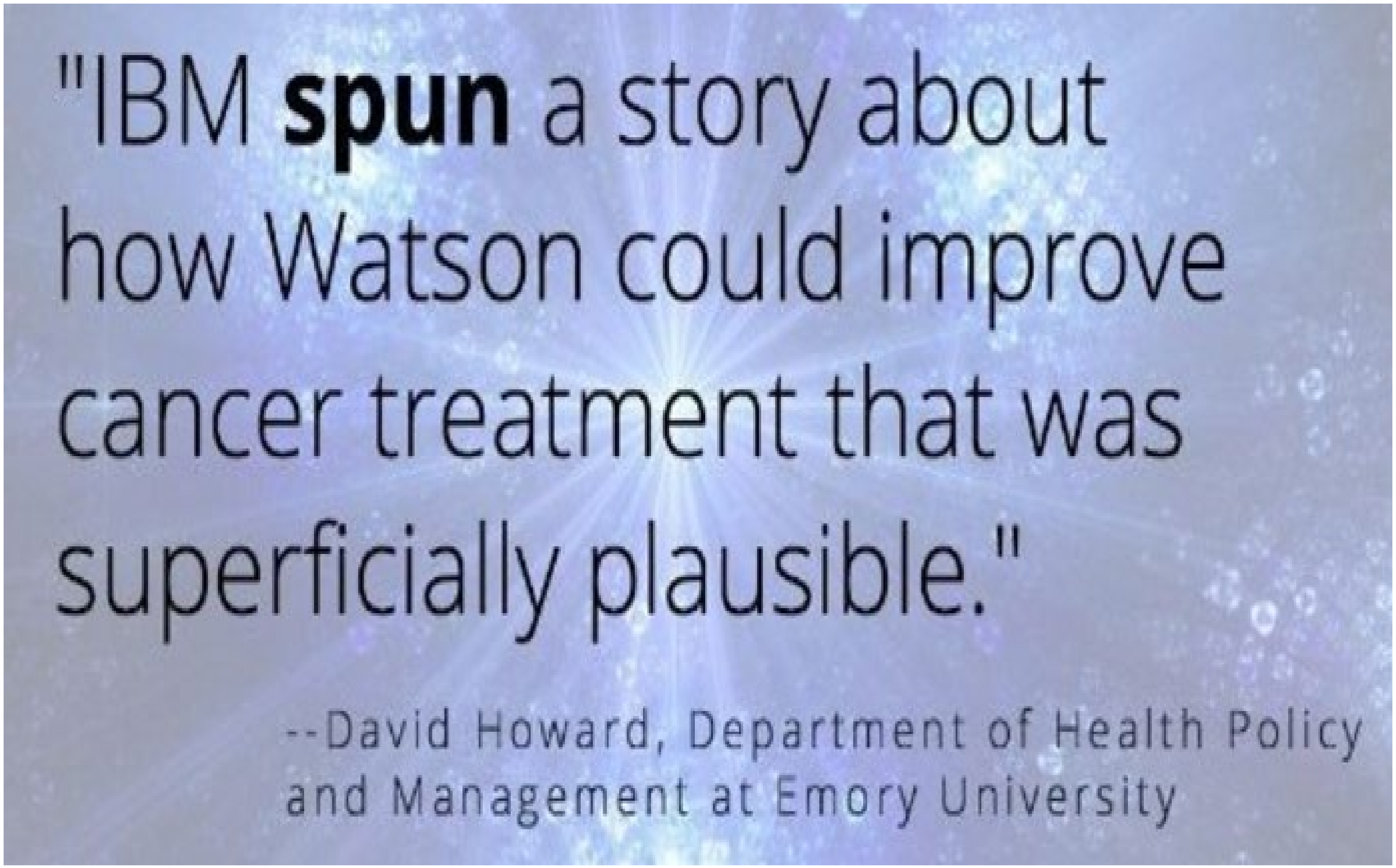
NF-κB activation cascade in the canonical pathways



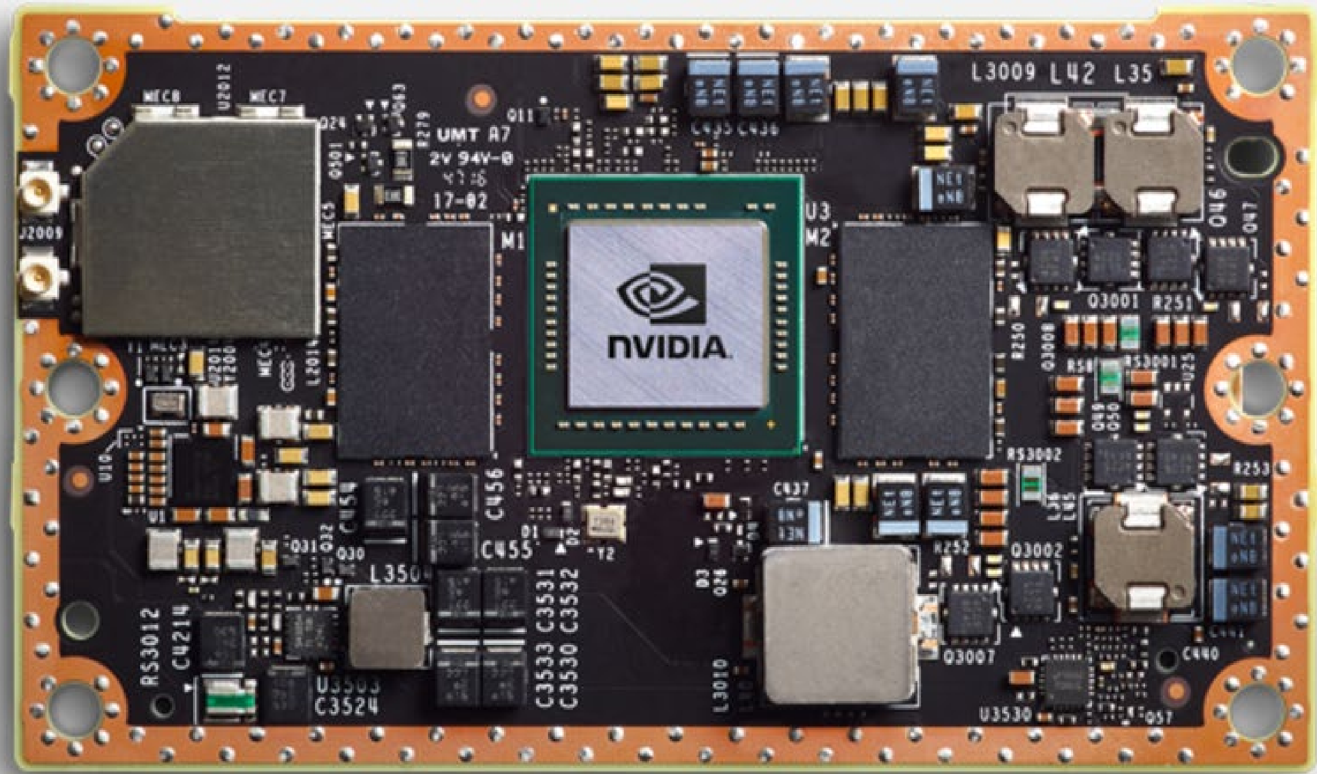
Shu Fang Liu and Asrar B. Malik (2006) Am J Physiol Lung Cell Mol Physiol 290 L622-L645

Digital Health Market

Healthcare Analytics - Crucial for the future but can we avoid the promotion of rubbish?

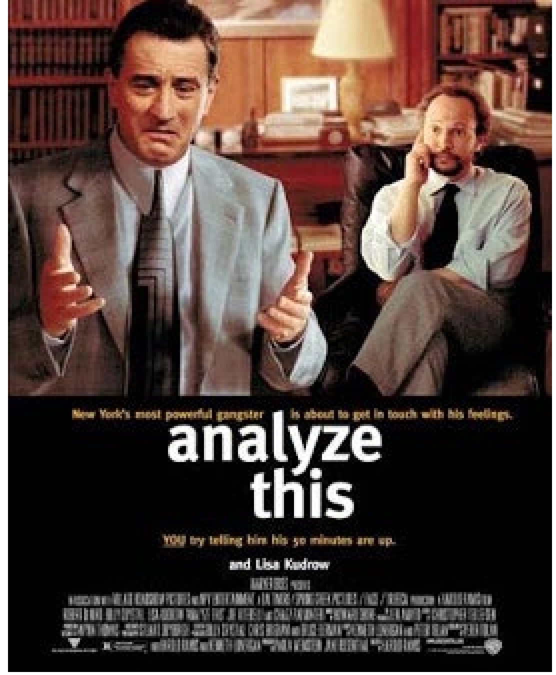


www.healthnewsreview.org/2017/02/md-anderson-cancer-centers-ibm-watson-project-fails-journalism-related



Healthcare Edge Analytics at Point of Care – grand vision but where are the systems?

Jetson TX2 is the fastest, most power-efficient embedded AI computing device. The latest addition to the industry-leading Jetson embedded platform, this 7.5-watt supercomputer on a module brings true AI computing at the edge. It's built around an NVIDIA Pascal™-family GPU and loaded with 8 GB of memory and 59.7 GB/s of memory bandwidth. It features a variety of standard hardware interfaces



PAY-PER-ANALYTICS

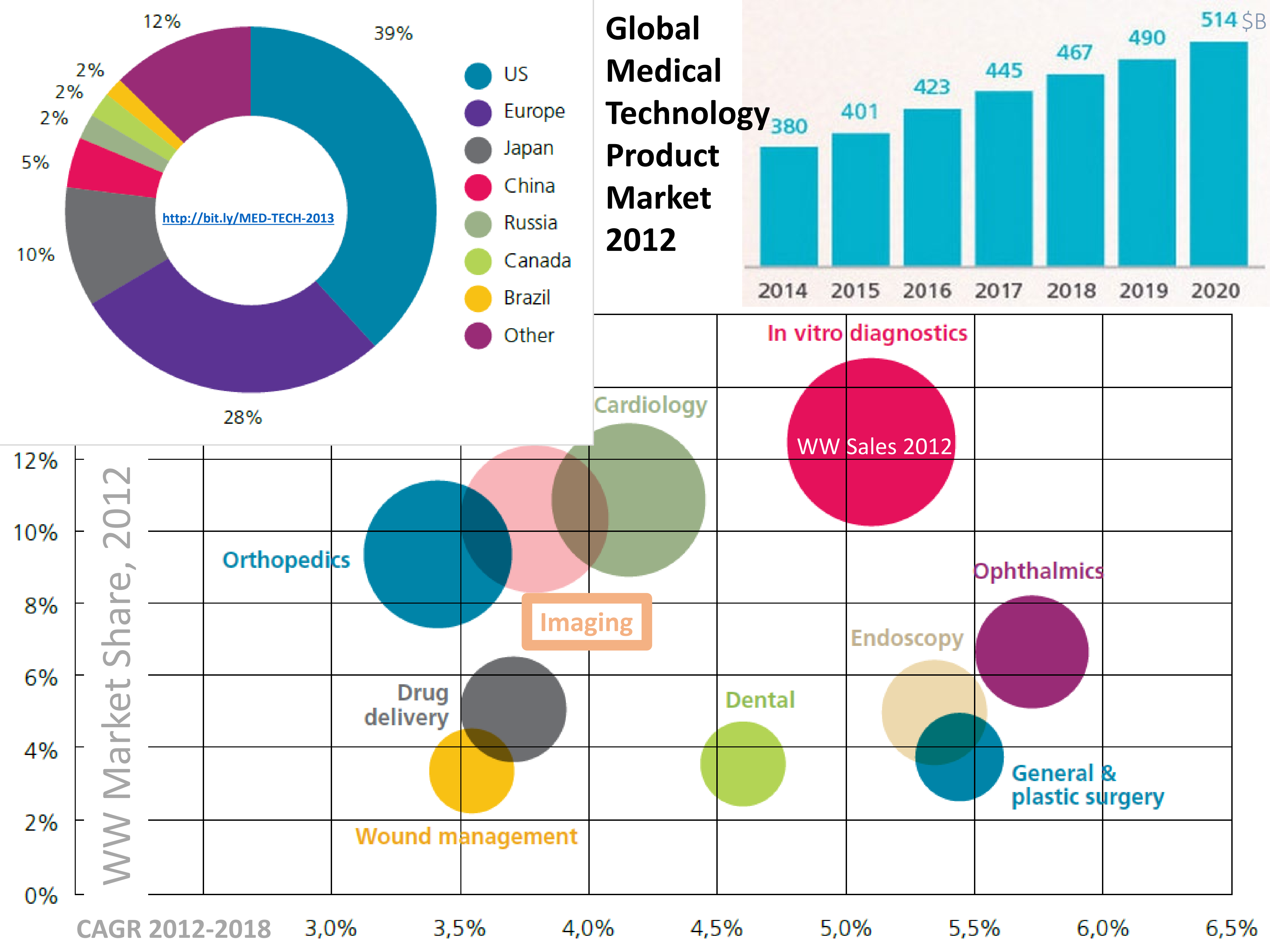
Samsung, UCSF Partner to Accelerate New Innovations in Preventive Health Technology

Pair Will Work to Validate Promising New Sensors and Analytics for Next-Generation Digital Health Solutions

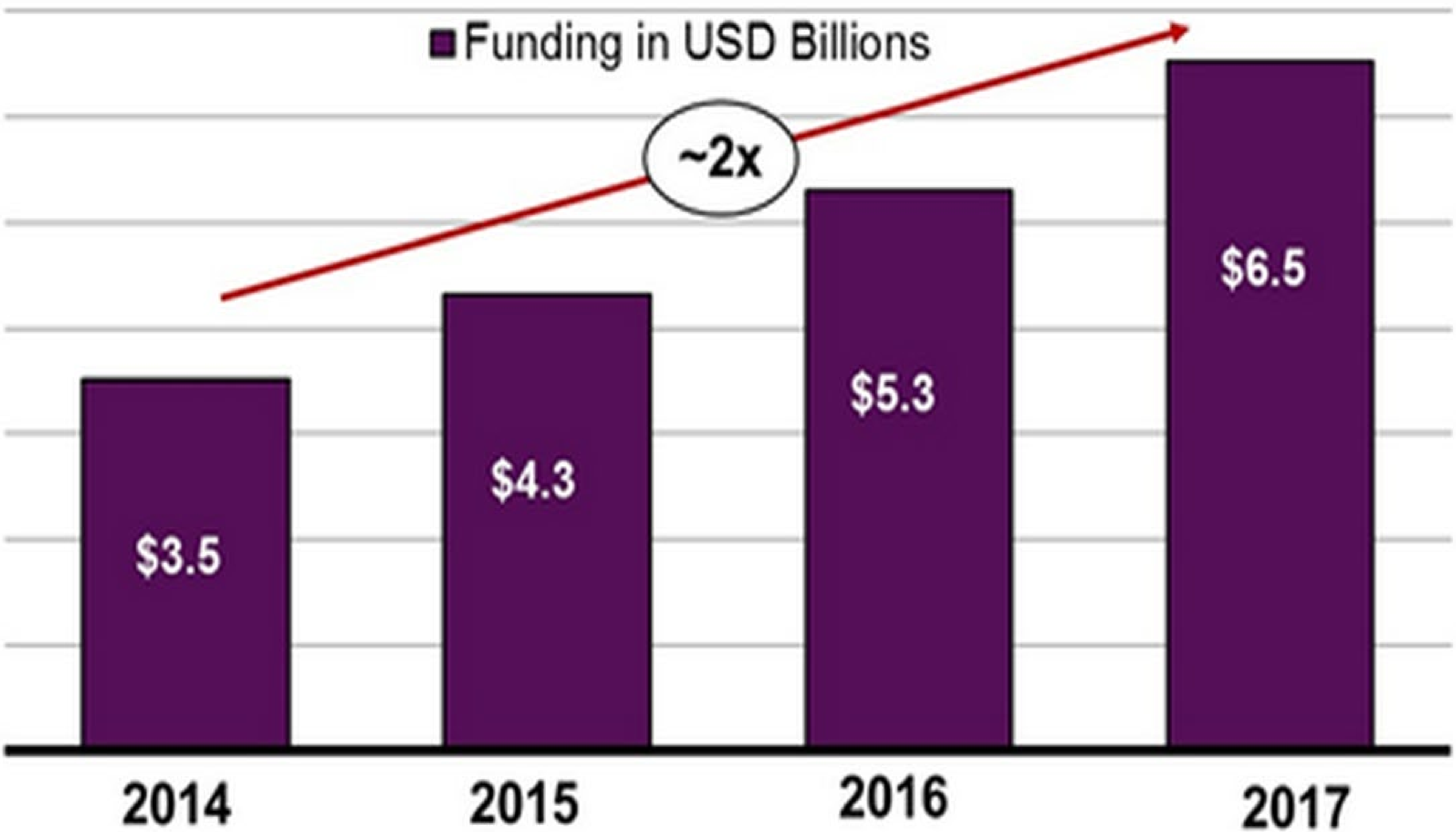
02/21/2014

Global Top 40 Medical Device Manufacturers

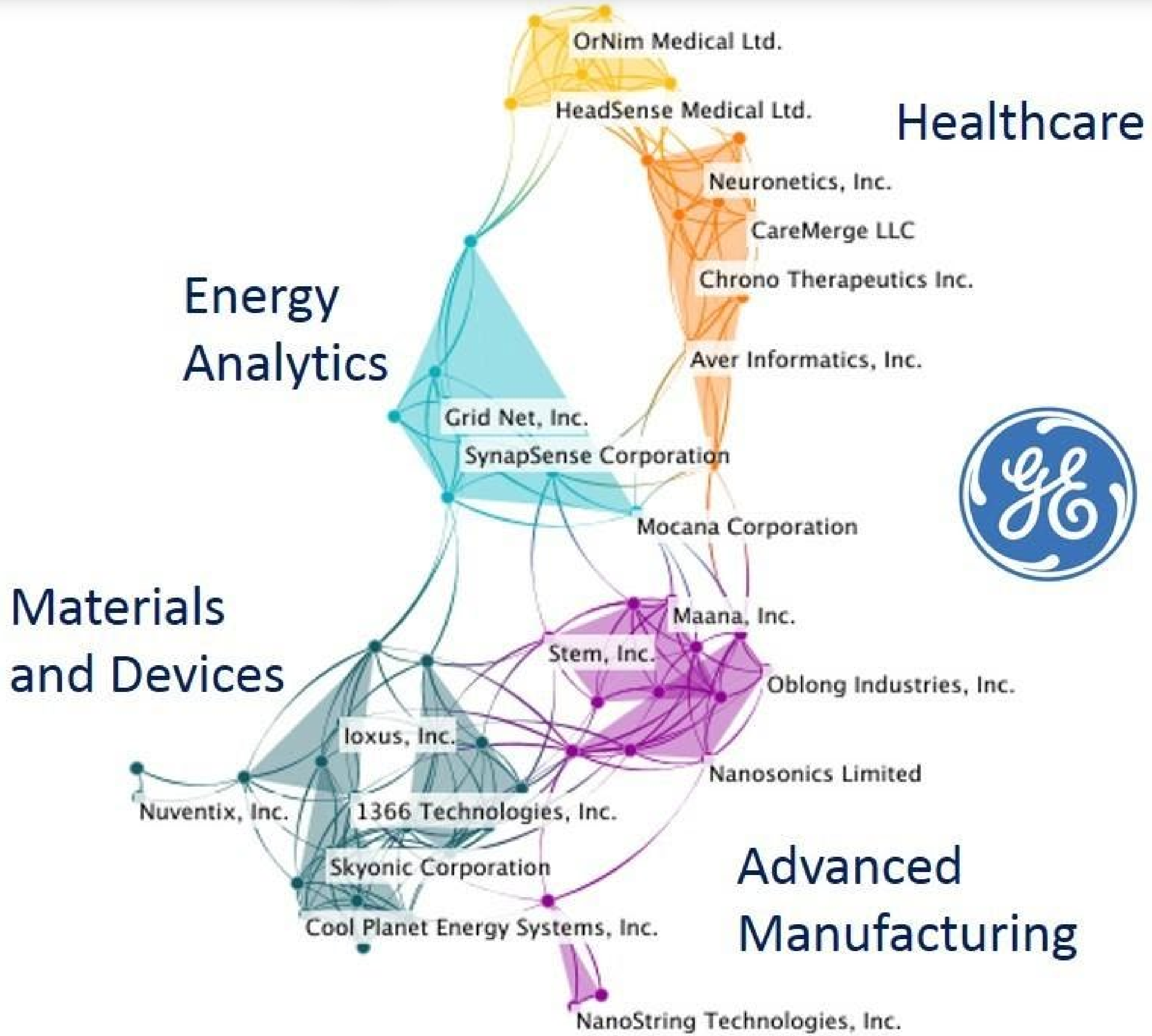
2014			Revenue	MKT CAP
1	Johnson & Johnson	NYSE: JNJ	$28.7 billion	$294.2 billion
2	General Electric Co.	NYSE:GE	$18.1 billion	$243.6 billion
3	Medtronic Inc.	NYSE:MDT	$17.1 billion	$61.2 billion
4	Siemens AG	DB:SIE	$17.0 billion	$92.2 billion
5	Baxter International Inc.	NYSE:BAX	$16.4 billion	$38.7 billion
6	Fresenius Medical Care AG & Co. KGAA	DB:FME	$15.2 billion	$21.1 billion
7	Koninklijke Philips NV	ENXTAM:PHIA	$11.8 billion	$26.1 billion
8	Cardinal Health Inc.	NYSE:CAH	$11.0 billion	$25.1 billion
9	Novartis AG[1]	SWX:NOVN	$10.7 billion	$227.5 billion
10	Covidien plc	NYSE:COV	$10.4 billion	$40.1 billion
11	Stryker Corp.	NYSE:SYK	$9.3 billion	$30.8 billion
12	Becton, Dickinson and Co.	NYSE:BDX	$8.3 billion	$21.8 billion
13	Boston Scientific Corp.	NYSE:BSX	$7.2 billion	$15.6 billion
14	Essilor International SA	ENXTPA:EI	$7.2 billion	$22.9 billion
15	Allergan Inc.	NYSE:AGN	$6.7 billion	$53.4 billion
16	St. Jude Medical Inc.	NYSE:STJ	$5.6 billion	$17.2 billion
17	3M Co.	NYSE:MMM	$5.5 billion	$84.0 billion
18	Abbott Laboratories[2]	NYSE:ABT	$5.5 billion	$61.9 billion
19	Zimmer Holdings Inc.	NYSE:ZMH	$4.7 billion	$17.0 billion
20	Terumo Corp.	TSE:4543	$4.7 billion	$9.0 billion
21	Smith & Nephew plc	LSE: SN	$4.4 billion	$14.9 billion
22	Toshiba Corp.	TSE:6502	$3.9 billion	$17.6 billion
23	CareFusion Corp.	NYSE:CFN	$3.8 billion	$9.2 billion
24	Getinge AB	OM:GETI B	$3.8 billion	$6.0 billion
25	Olympus Corp.	TSE:7733 OTC: OCPNY	$3.7 billion	$11.7 billion
26	Bayer AG[3]	DB:BAYN	$3.2 billion	$115.0 billion
27	CR Bard Inc.	NYSE:BCR	$3.1 billion	$10.6 billion
28	Varian Medical Systems Inc.	NYSE:VAR	$3.0 billion	$8.3 billion
29	DENTSPLY International Inc.	NasdaqGS:XRAY	$3.0 billion	$6.4 billion
30	Ship Healthcare Holdings Inc.	TSE:3360	$2.5 billion	$1.3 billion
31	Paul Hartmann AG	DB:PHH2	$2.5 billion	$1.4 billion
32	Hologic Inc.	NasdaqGS:HOLX	$2.5 billion	$6.6 billion
33	Nipro Corp.[4]	TSE:8086	$2.3 billion	$1.4 billion
34	Coloplast A/S	CPSE:COLO B	$2.2 billion	$17.9 billion
35	Sonova Holdings	SWX:SOON	$2.2 billion	$10.4 billion
36	Danaher Corp.[5]	NYSE:DHR	$2.1 billion	$38.6 billion
37	Edwards Lifesciences	NYSE:EW	$2.1 billion	$11.0 billion
38	Intuitive Surgical Inc.	NasdaqGS:ISRG	$2.1 billion	$16.6 billion
39	MIRACA Holdings Inc.	TSE:4544	$2.0 billion	$2.4 billion
40	Dragerwerk AG & Co. KGa[6]	DB:DRW3	$2.0 billion	$1.4 billion


Global Medical Technology Product Market 2012
12%
39%
2%
2%
2%
5%
10%
28%
http://bit.ly/MED-TECH-2013
US
Europe
Japan
China
Russia
Canada
Brazil
Other
380
401
423
445
467
490
514 $B
2014
2015
2016
2017
2018
2019
2020
In vitro diagnostics
WW Sales 2012
Cardiology
Orthopedics
Imaging
Ophthalmics
Endoscopy
Drug delivery
Dental
General & plastic surgery
Wound management
WW Market Share, 2012
12%
10%
8%
6%
4%
2%
0%
CAGR 2012-2018
3,0%
3,5%
4,0%
4,5%
5,0%
5,5%
6,0%
6,5%

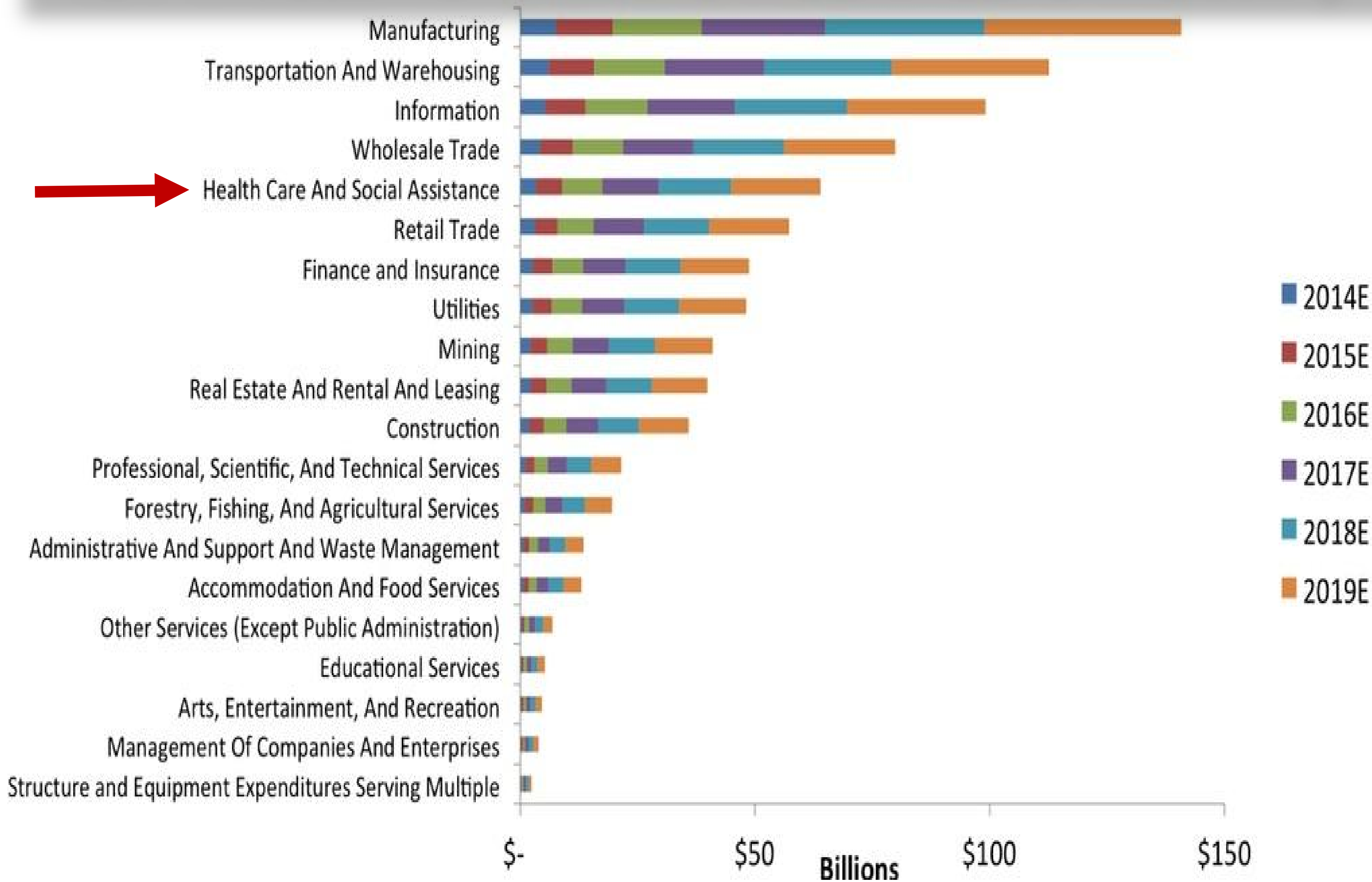
US Funding for Digital Health



GE Investing in Healthcare Startups

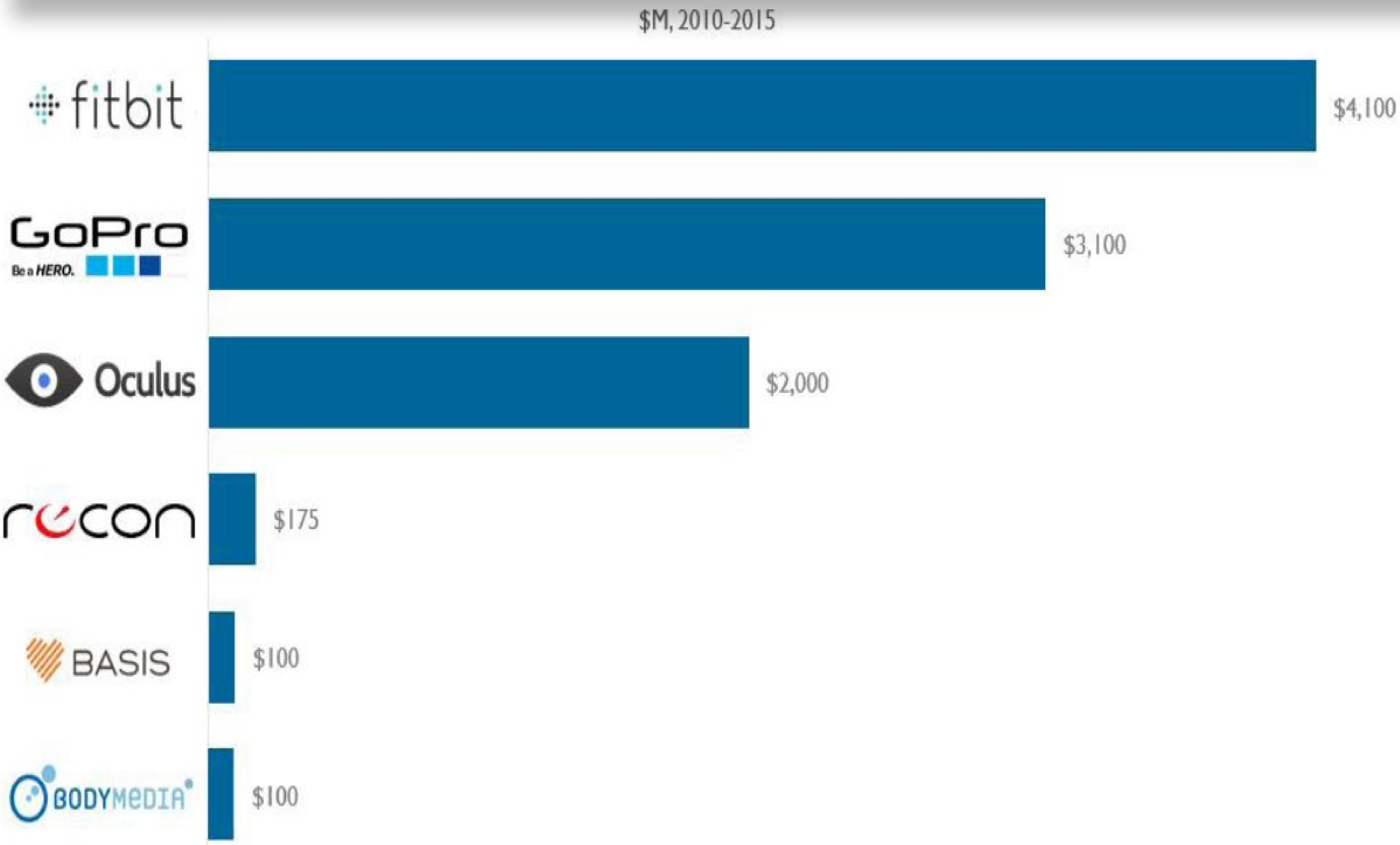


IoT Investment in the Healthcare Industry



Source: BI

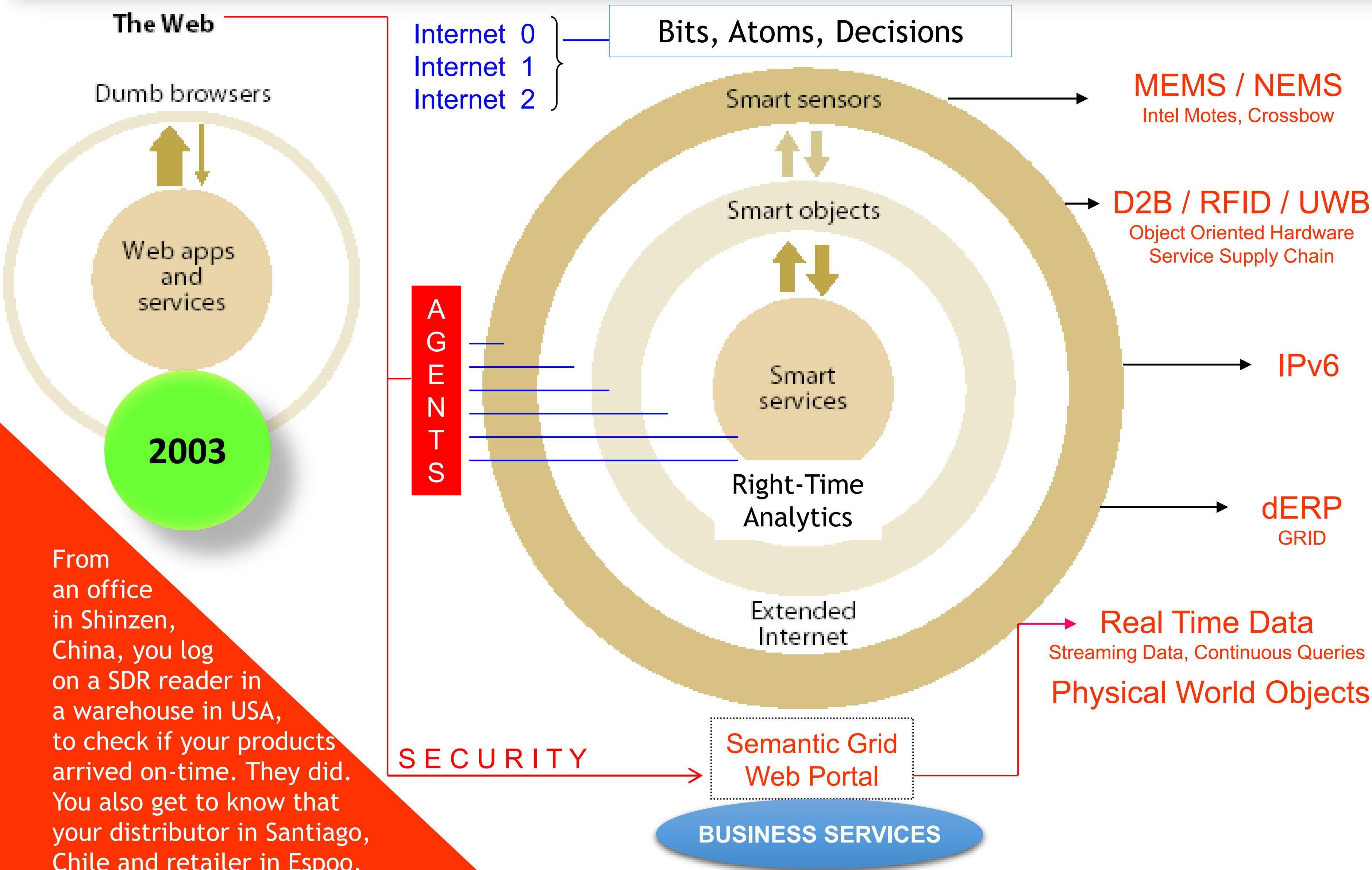
Wearable Tech Exits (valuation at time of exit)



Healthcare Platforms?

Systems of Digital Twins for Health and Wellness

Integrating Ubiquitous Analytics in Real-Time with Data, Information, Application



From an office in Shinzen, China, you log on a SDR reader in a warehouse in USA, to check if your products arrived on-time. They did. You also get to know that your distributor in Santiago, Chile and retailer in Espoo, Finland also checked the delivery status, moments before you logged on.

SDR Data Interrogators as Ubiquitous Internet Appliances in IoT (2003)

Healthcare Data Integration and Interoperability Platform is a Quintessential Global Infrastructure

Infrastructural technologies, in contrast, offer far more value when shared than when used in isolation. Imagine yourself in the early nineteenth century, and suppose that one manufacturing company held the rights to all the technology required to create a railroad. If it wanted to, that company could just build proprietary lines between its suppliers, its factories, and its distributors and run its own locomotives and railcars on the tracks. And it might well operate more efficiently as a result. But, for the broader economy, the value produced by such an arrangement would be trivial compared with the value that would be produced by building an open rail network connecting many companies and many buyers. The characteristics and economics of infrastructural technologies, whether railroads or telegraph lines or power generators, make it inevitable that they will be broadly shared—that they will become part of the general business infrastructure.

Nicholas Carr in Harvard Business Review, 2003 ● https://hbr.org/2003/05/it-doesnt-matter

Investment to Create and Deploy Integrated Healthcare Platforms

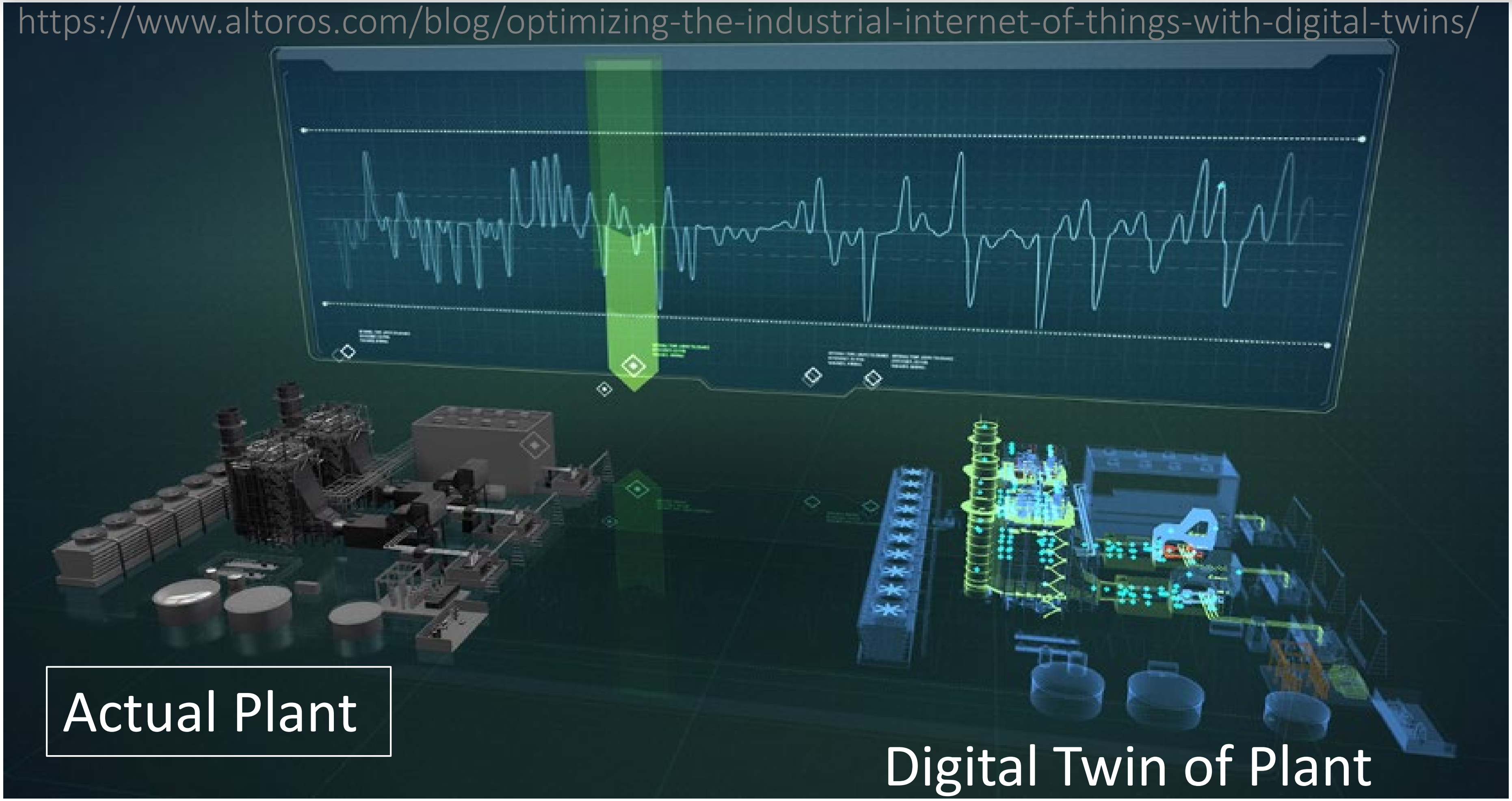
The trap that executives often fall into, however, is assuming that opportunities for advantage will be available indefinitely. In actuality, the window for gaining advantage from infrastructural technology is open only briefly. When the technology's commercial potential begins to be broadly appreciated, huge amounts of cash are inevitably invested in it, and its build out proceeds with extreme speed. Railroad tracks, telegraph wires, power lines—all were laid or strung in a frenzy of activity. In the 30 years between 1846 and 1876, reports Eric Hobsbawm in *The Age of Capital*, the world's rail trackage increased from 17,424 km to 309,641 km. During this same period, total steamship tonnage also exploded, from 139,973 to 3,293,072 tons. The telegraph system spread even more swiftly. In Continental Europe, there were just 2,000 miles of telegraph wires in 1849; 20 years later, there were 110,000 miles. The pattern continued with electrical power. The number of central stations operated by utilities grew from 468 in 1889 to 4,364 in 1917, and the average capacity of each increased tenfold.

Nicholas Carr in Harvard Business Review, 2003 ● https://hbr.org/2003/05/it-doesnt-matter

Platform Synthesis?

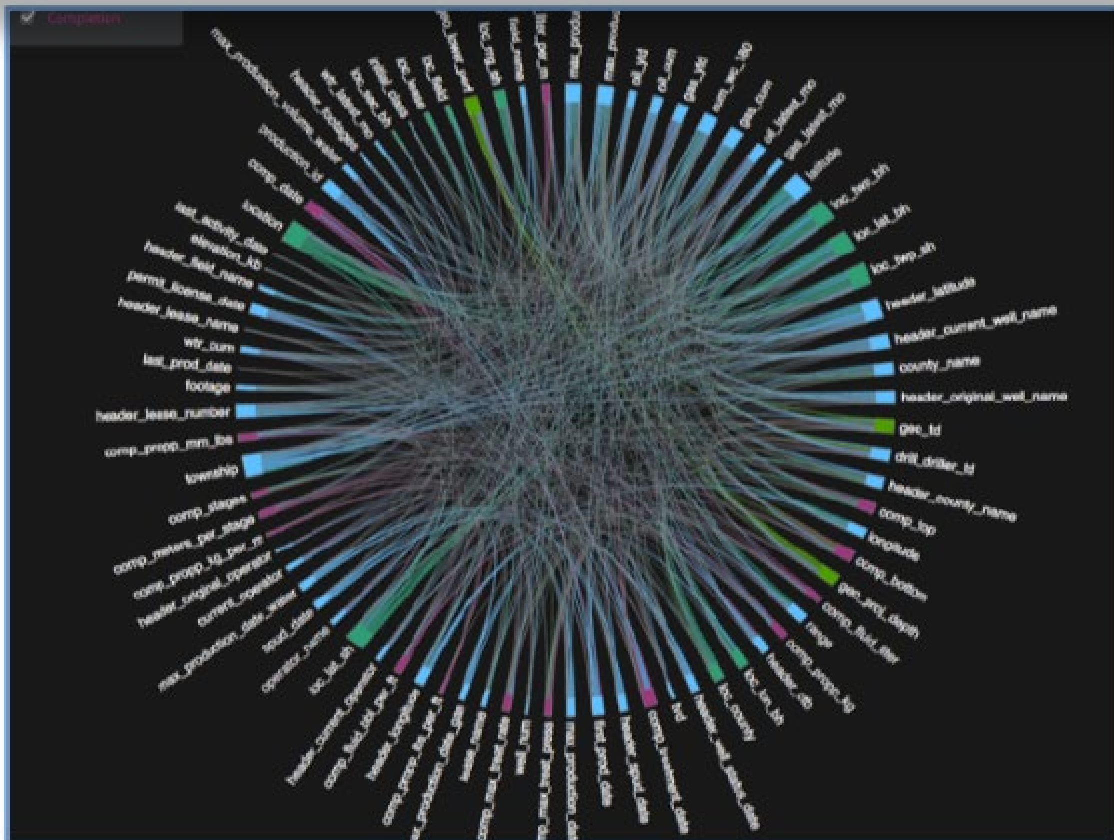
Integrated health data – simulate equivalent of industrial digital twins

The concept of “digital twins” is one of a “soft companion” to a real-world entity, eg, industrial plant (entire system), jet engine sensor (sub-system), gear box (parts), maintenance (process), car tire (product) or a city (system of systems). An individual and her health profile may generate a “digital twin” with her data feed from metabolomics, vital signs and other medical devices. Hence the need for platforms, data synthesis, analytics and real-time risk prediction, alerts or treatment.



Explore – Industrial “Digital Twins” here https://dspace.mit.edu/handle/1721.1/104429

Medical Digital Twins of individuals or patients may use machine learning and AI tools (eg CNN) to analyze and correlate data – for example – what is the physiological status or risk to the individual if the respiratory rate is low, end tidal carbon dioxide is low but blood pressure is in normal range.



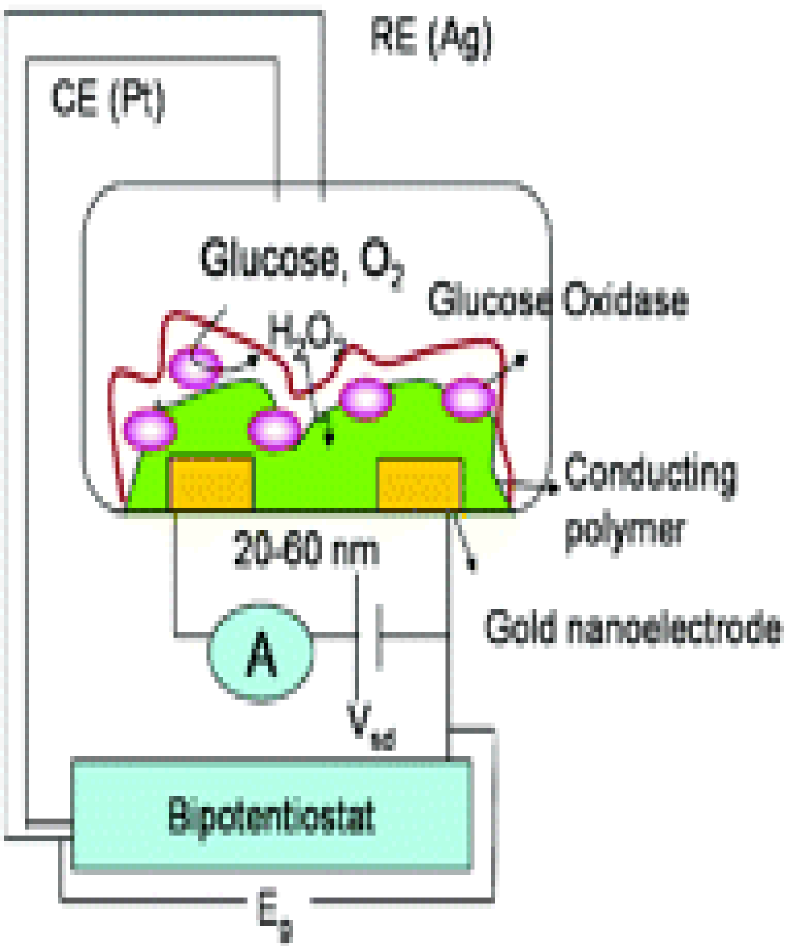
Navigate network of autocorrelations and build optimized ensembles of machine learning models

www.altoros.com/blog/industrial-internet-is-powering-more-efficient-well-drilling-for-oil-and-gas/

Pursuit of Ideas

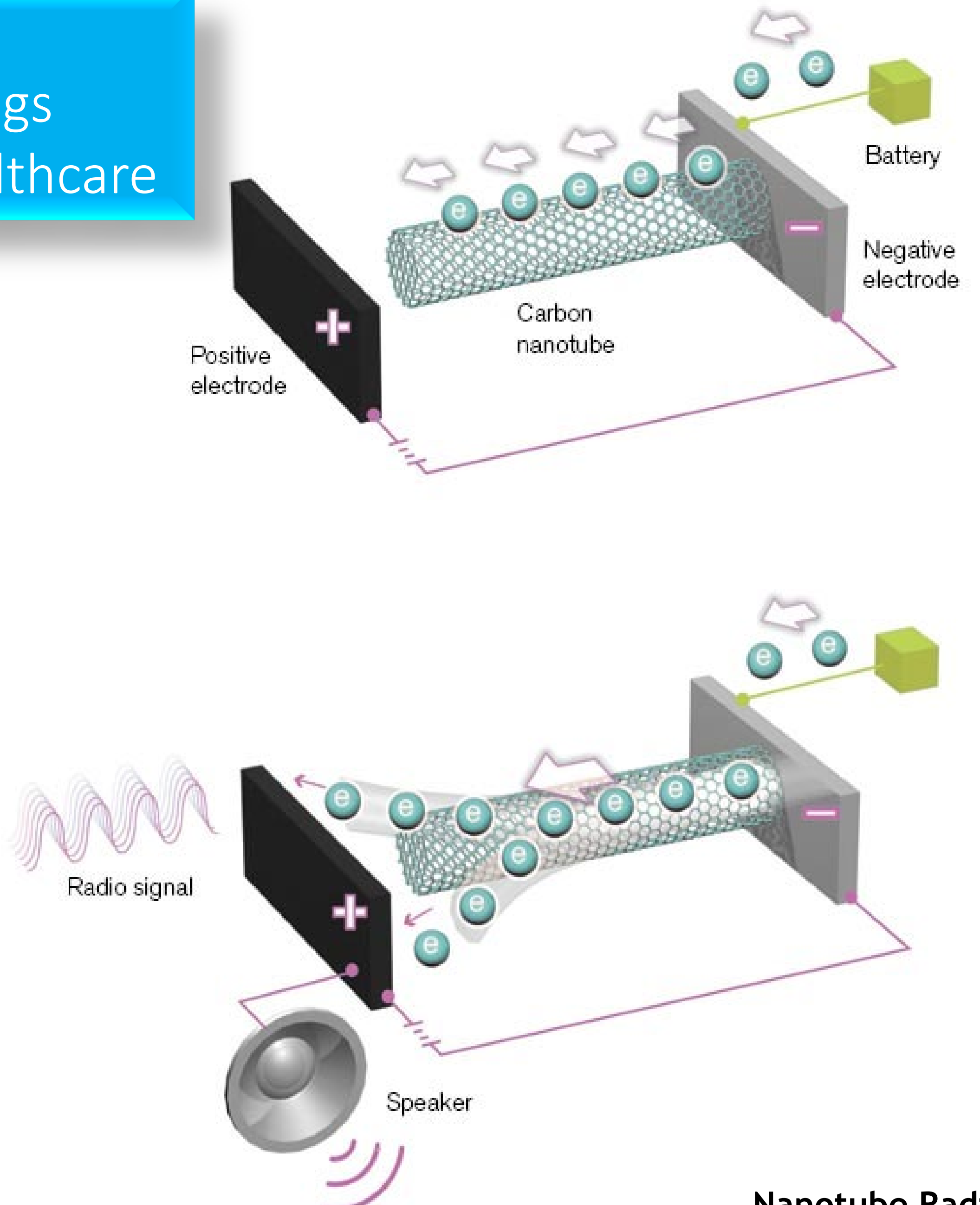
Let us re-visit nanotube radios

The Industrial Internet
The Industrial Internet of Things
The Industrial Internet of Healthcare



Blood Glucose Nano-sensor

NanoLetters (2004) 4 1785-1788



Nanotube Radio

NanoLetters (2007) 7 3508-3511

What about biological radios inside our body?

http://bit.ly/Terahertz-Imaging

Proteins are Radios

We can detect, diagnose and correct RF radiation.

Can we?

Some of the material presented in the next section were sourced from Dr Ogan Gurel http://bit.ly/OGAN-GUREL-BIO

Protein Electrodynamics

The Nobel Prize in Chemistry 2013

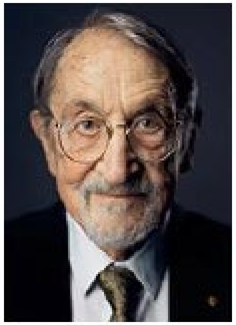


Photo: A. Mahmoud
Martin Karplus
Prize share: 1/3

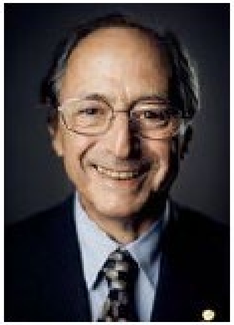


Photo: A. Mahmoud
Michael Levitt
Prize share: 1/3

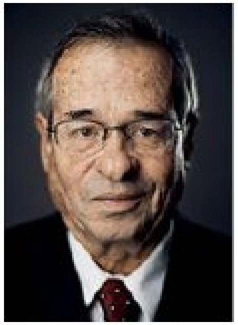


Photo: A. Mahmoud
Arieh Warshel
Prize share: 1/3

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"*.

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.

Seminal contribution to the field of protein electrodynamics by Martin Karplus, Harvard University

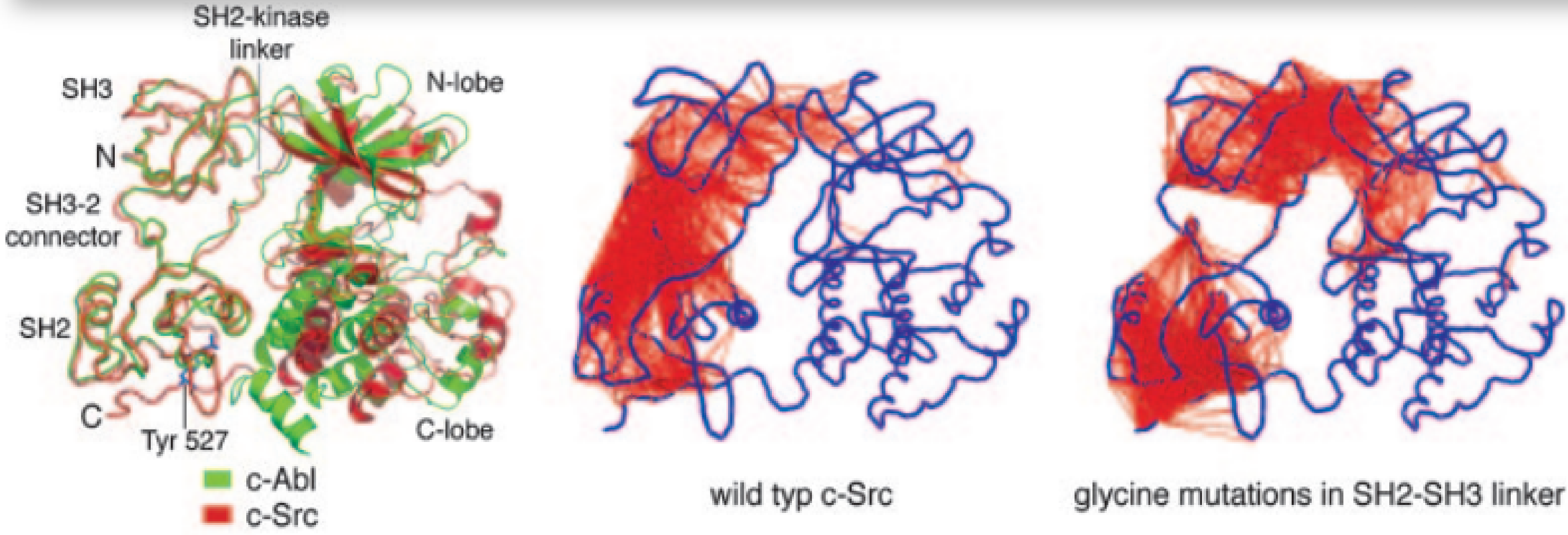
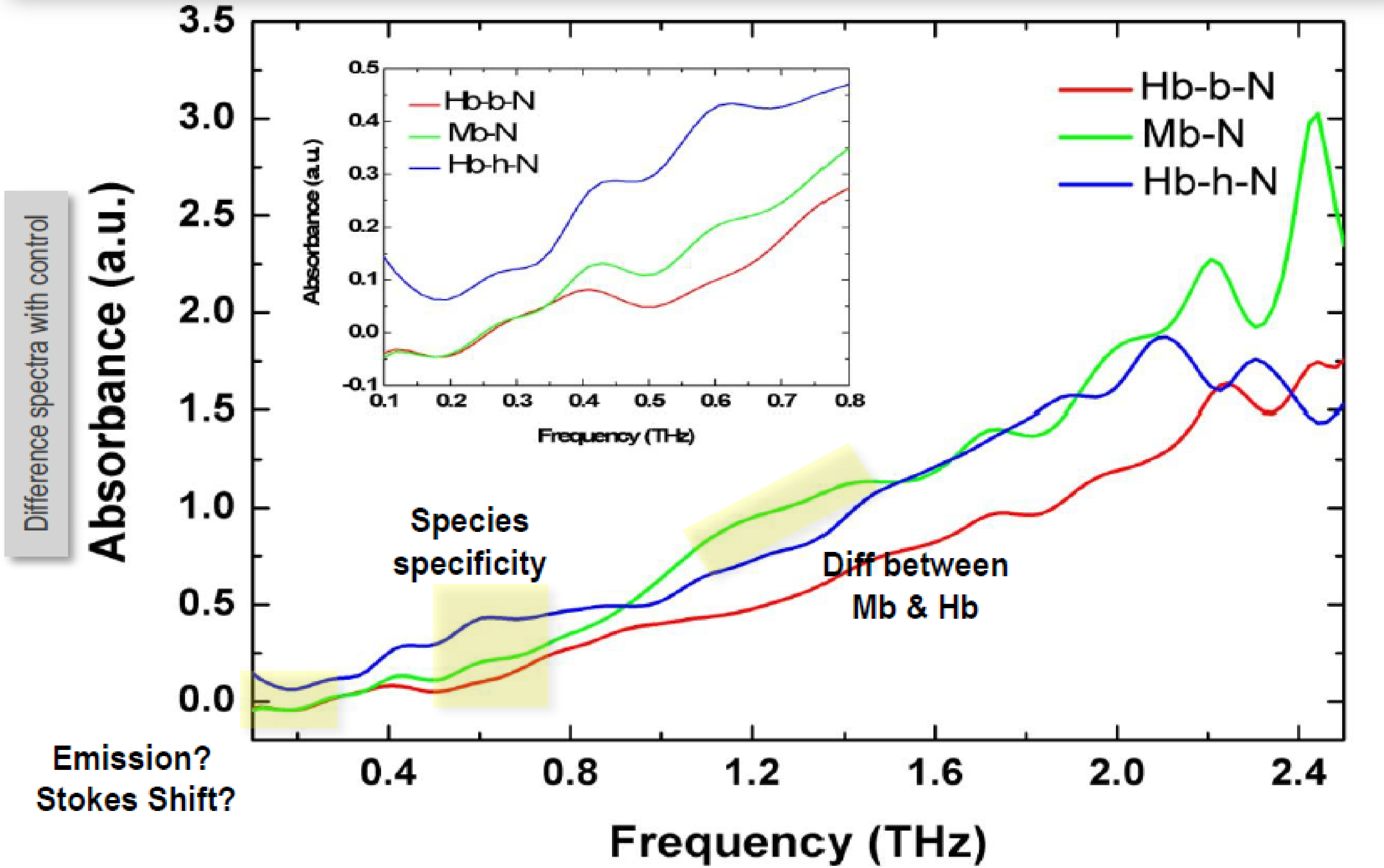


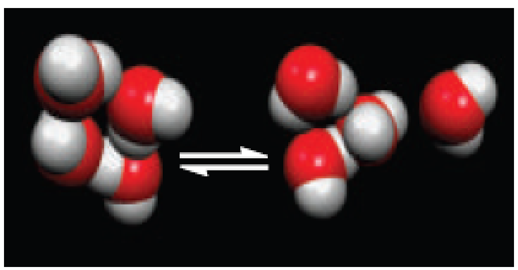
Fig. 5. Structure and dynamics of the Src and Abl kinases. (*Left*) The structures of c-Abl (green) and c-Src (red) are shown superimposed on their SH2 and SH3 domains (69, 70, 75). Note the dissimilarity in the conformation of the kinase domains. (*Center* and *Right*) The results of unbiased molecular 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 Range

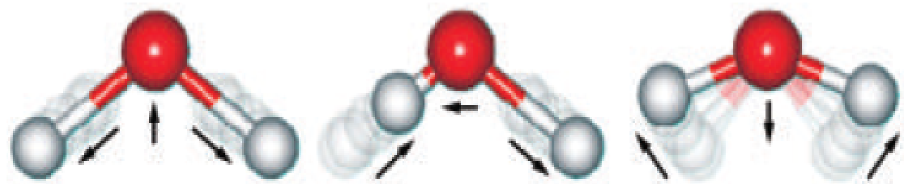


Terahertz 101

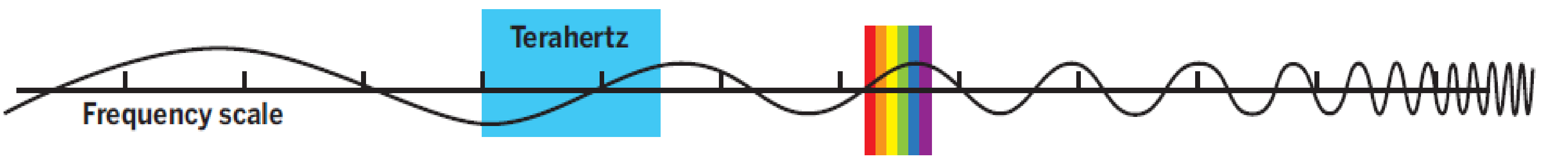
Light with submillimeter wavelengths and a frequency range of roughly 0.1 to 10 THz, or 3 to 300 cm^{-1}, is known as terahertz radiation. It can penetrate plastics, paper, and textiles, but it is absorbed strongly by water, making it a sensitive probe of biological tissue. Unlike the relatively high-frequency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



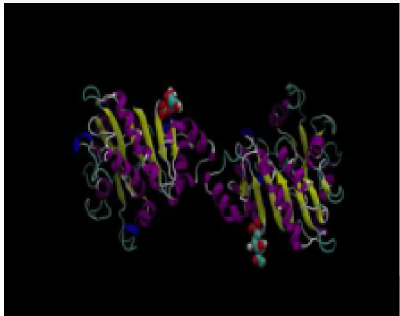
MATTHIAS HEYDEN/ RUHR UNIVERSITY BOCHUM



MARTIN CHAPLIN/ LONDON SOUTH BANK U.



Axioms of Protein Electrodynamics

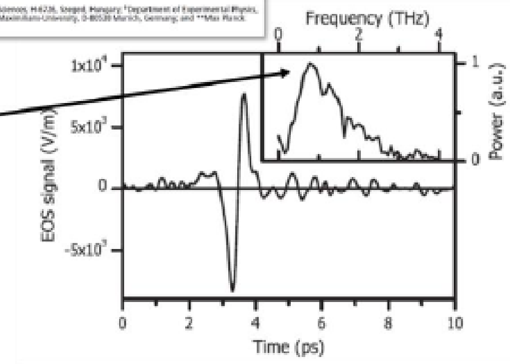


1. Proteins Vibrate

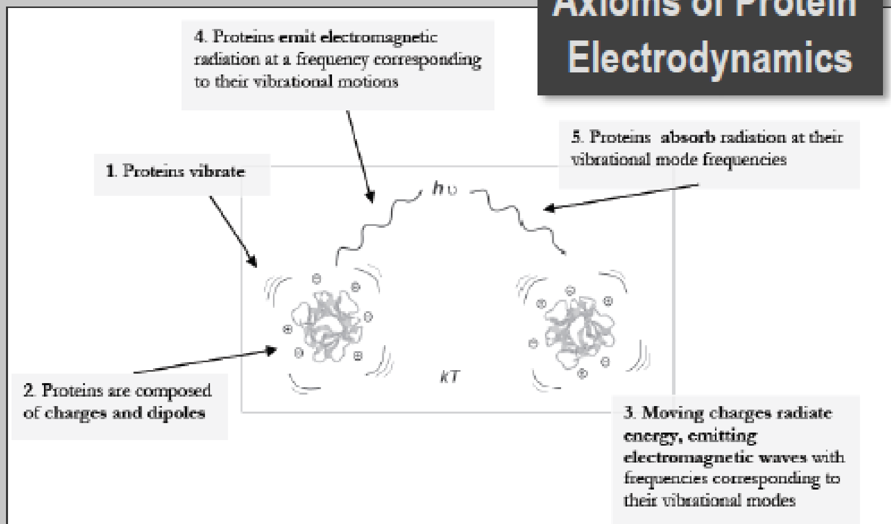
PNAS

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

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



4. Proteins emit THz radiation



2. Proteins Are Charged

The Poisson-Boltzmann Equation

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

$$\nabla \cdot [\varepsilon(\mathbf{r})\nabla \cdot \phi(\mathbf{r})] - \varepsilon(\mathbf{r})\kappa(\mathbf{r})^2 \sinh[\phi(\mathbf{r})] + 4\pi\rho^f(\mathbf{r})/kT = 0 \quad (1)$$

where $\phi(\mathbf{r})$ 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^f is the fixed charge density (in proton charge units). The term $\kappa^2 = 1/\lambda^2 = 8\pi q^2 I/\varepsilon kT$, where λ is the Debye length and I is the ionic strength of the bulk solution. The variables ϕ, ε, κ, and ρ are all functions of the position vector $\mathbf{r}$.

Science

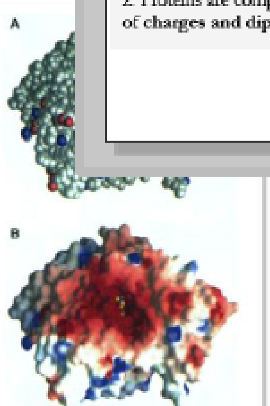


Fig. 1. Surface representations of acetylcholine esterase.

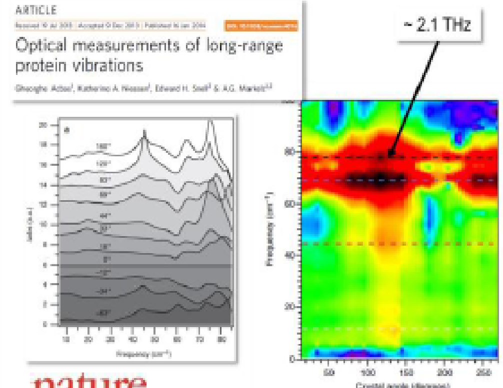
3. Maxwell's Equations

$$\nabla \cdot \mathbf{E} = 0 \qquad \nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t},$$

$$\nabla \cdot \mathbf{B} = 0 \qquad \nabla \times \mathbf{B} = \frac{1}{c^2}\frac{\partial \mathbf{E}}{\partial t}.$$

ARTICLE

Optical measurements of long-range protein vibrations



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.

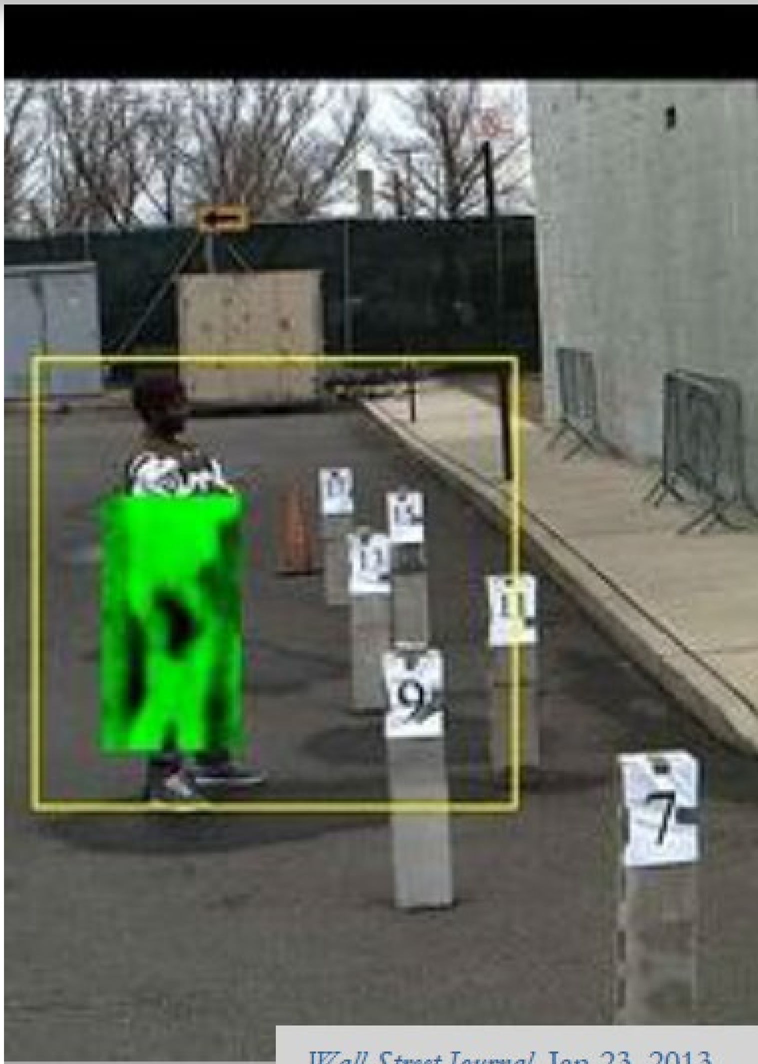
The so-called T-Ray machine detects terahertz radiation, a high-frequency electromagnetic natural energy that is emitted by people and can penetrate many materials, including clothing.

Enlarge Image

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.



Wall Street Journal, Jan 23, 2013

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 reconfigure protein structure to activate "normal" function or detect/deactivate harmful proteins?

Do different proteins vibrate at **different frequencies?** Yes

Protein motion **anharmonicity:** how significant? May depend

Can we identify different proteins based on their spectrum? Yes, but not easy (now)

Can one influence protein function by modulating their vibrations? Unknown

How far might protein electrodynamic wave fields be expected to propagate? ? 1 – 2 mm

Could proteins communicate "over a distance"? Unknown

Could protein electrodynamics mediate specific attractive forces between proteins? Unknown

Diagnosis | **Treatment**

Key technical challenges in TeraHertz Medicine

Concept of protein vibration as a signature is clouded by water

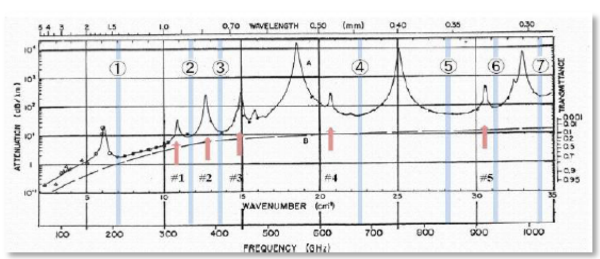
The “noise” from RF vibration of water molecules may significantly distort the TeraHertz profile.

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
[These suggestions are due to SD]

- **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)

http://bit.ly/OGAN-GUREL-BIO

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

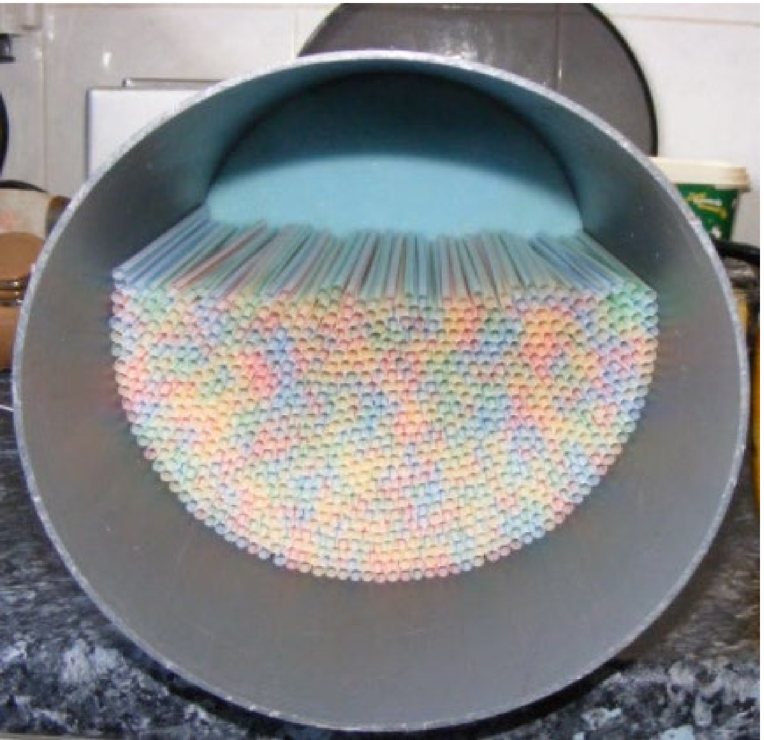
The data (TeraHertz profile) is a mix of RF due to water and protein (which needs to be separated).

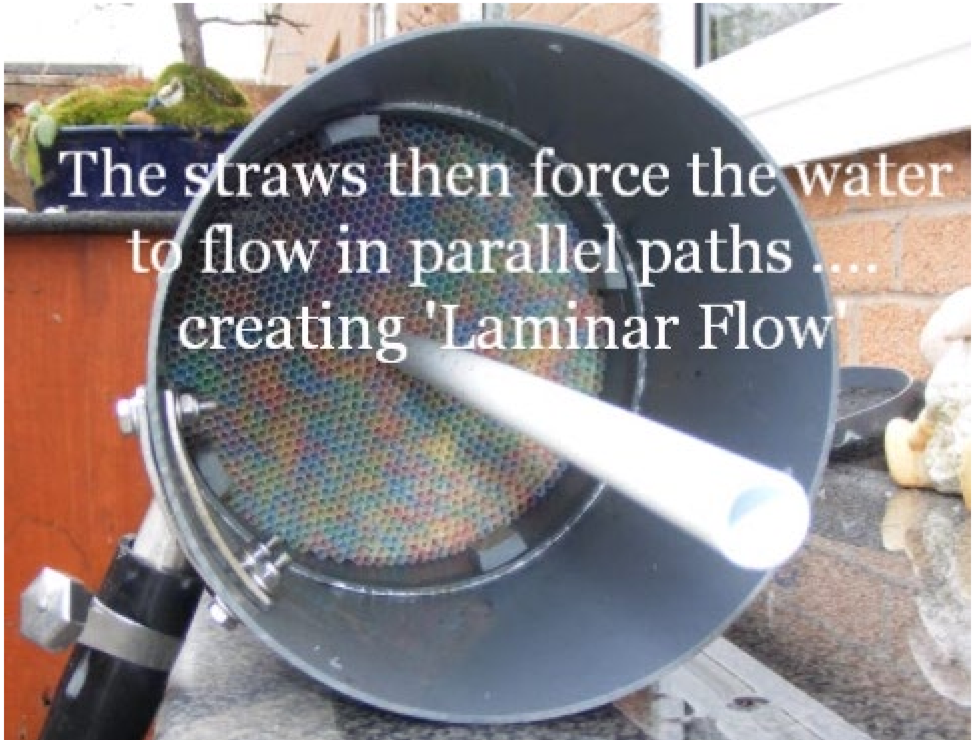
Is this a data curation problem? Are we observing related signal/noise issues in big data analytics?

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

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

[These suggestions are due to SD]





What if I want only one take-away from MIoT?

http://bit.ly/IOT-MIT explore HEALTHCARE

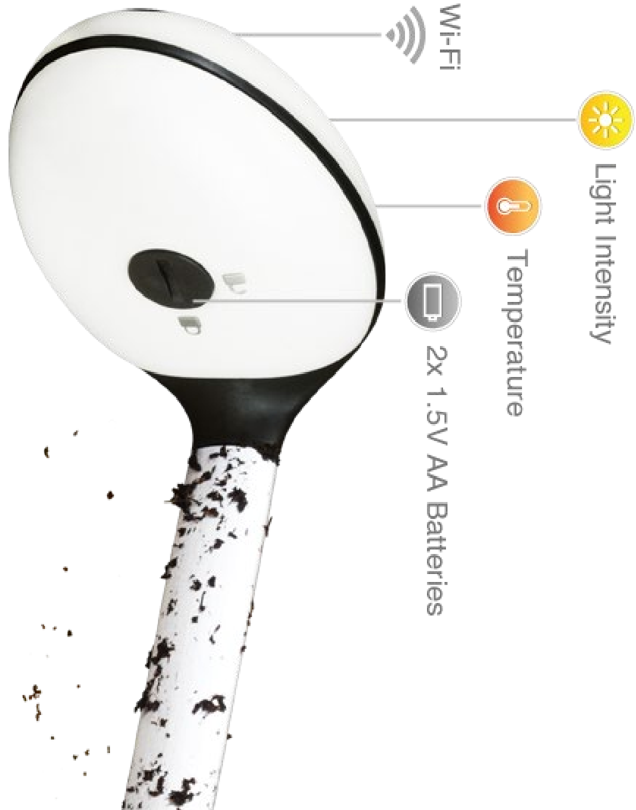
Reality Check ☑ Arsenic in Water (Bangladesh)

Internet of Systems

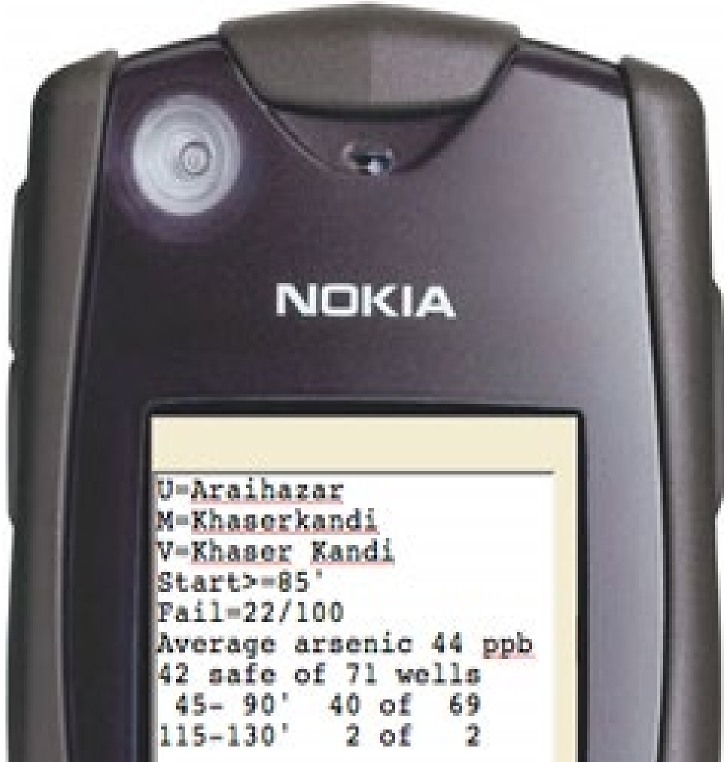
MIoT

Health IoT – Impact of Clean Water

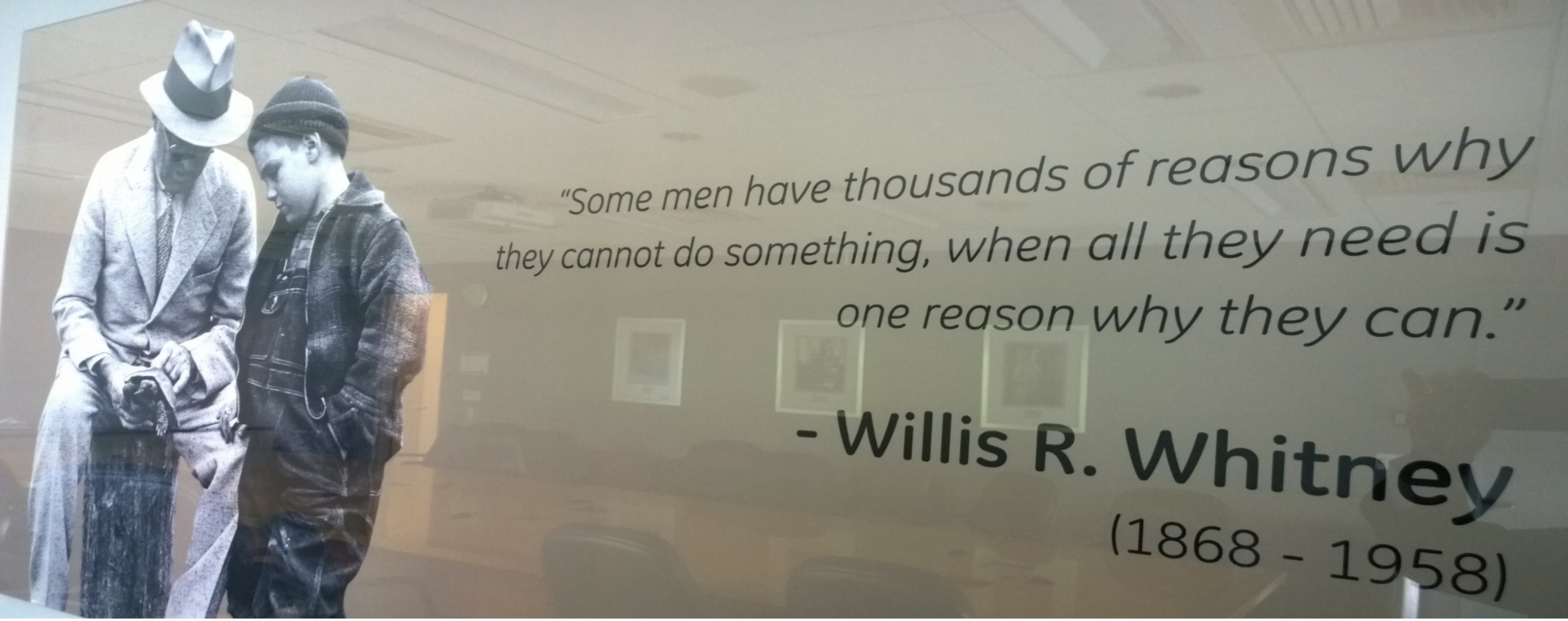
http://bit.ly/ROHIT-KARNIK_MIT



Nokia 'sensor as a service' can improve lives ☑ IoT Tool - Arsenic in water



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



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- Dr Prashant Jain – DOTRI (Los Alamos National Lab) http://bit.ly/EMG-BioFeedback
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- Dr Gin Jose – University of Leeds http://bit.ly/BLOOD-FREE-BLOOD-GLUCOSE
- Dr Ram Dantu – University of North Texas http://www.cse.unt.edu/~rdantu/
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- Security → http://bit.ly/SECURITY-HIT-NIST

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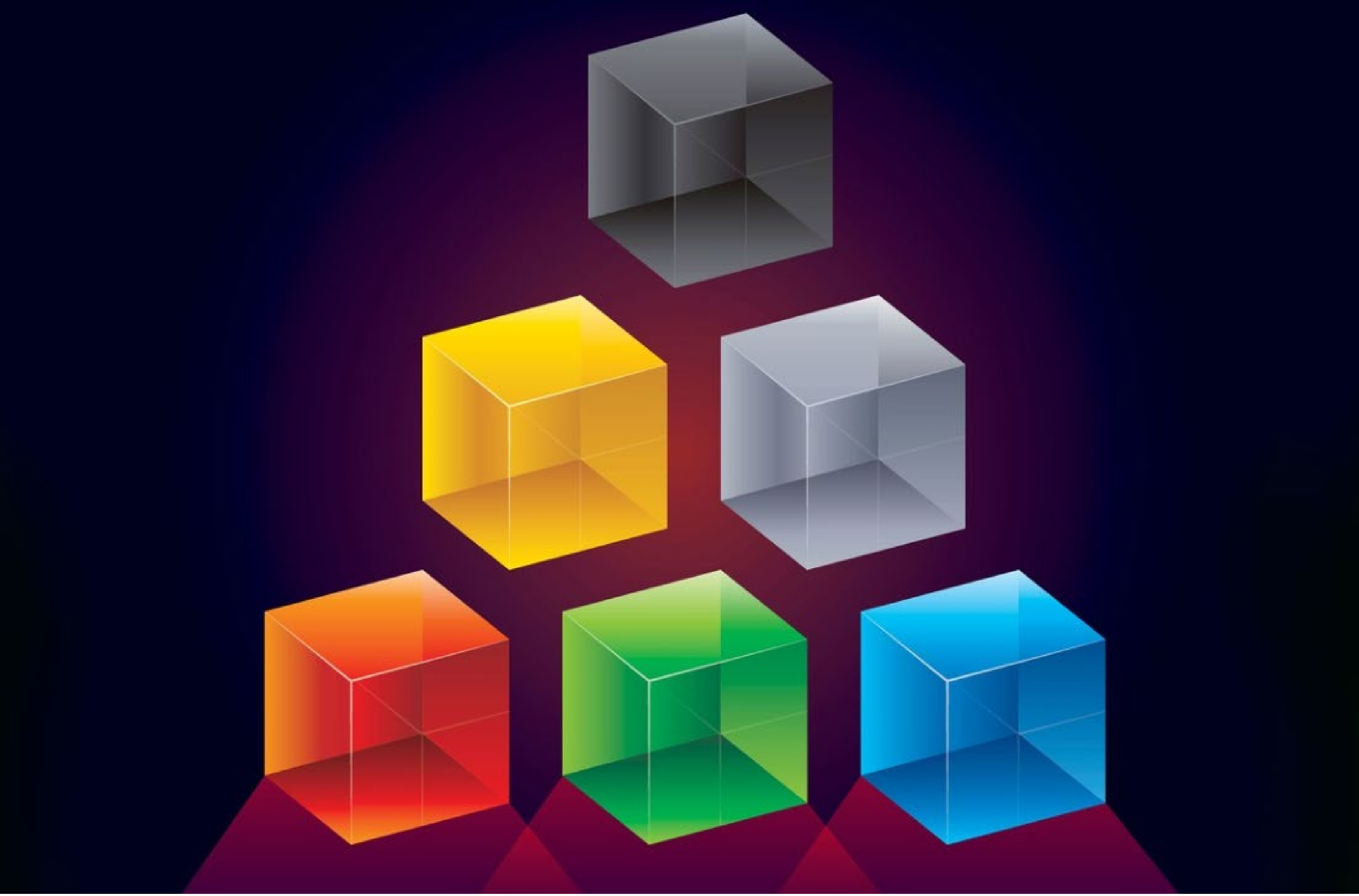
2001 ● MIT Forum for Supply Chain Innovation

2003 ● MIT Data Center ● Semantics

2009 ● MIT Energy Initiative

2013 ● Industrial Internet

2018 ● Nano-Sensors



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