Human 3.0

Piero Scaruffi

May 2023

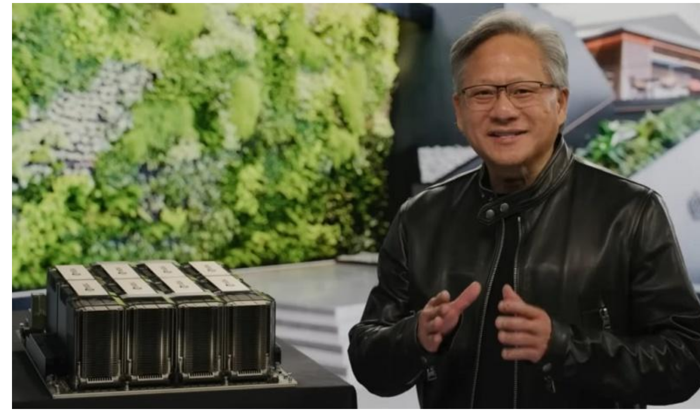
Toronto

Many of these slides are the outcome of conversations with scientists that you can view on my YouTube channel

YouTube

Piero Scaruffi
@43124121

A.I. depends on hardware

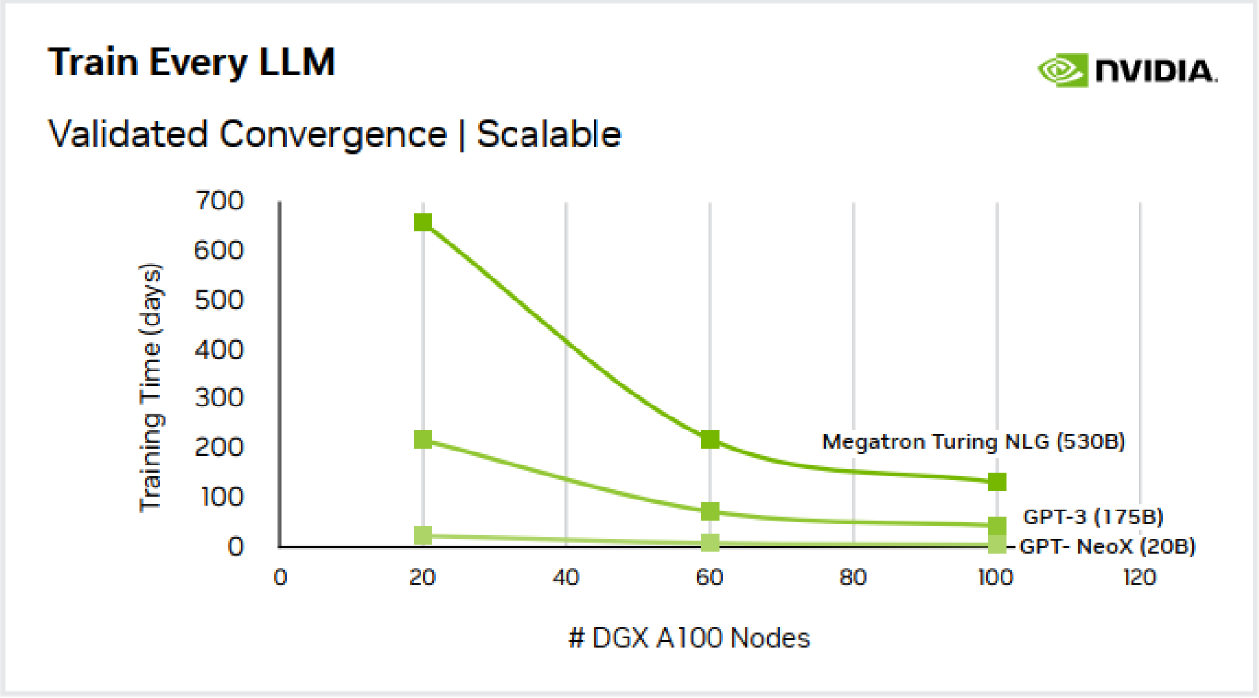


- Nvidia's supercomputers (DGX and H100) for training language models
- 2023: H100 NVL on TSMC's 4nm chips and with built-in Transformer accelerator

A.I. depends on hardware

Interesting trivia: how long does it take to train these language models?

Train Every Large Language Model with NVIDIA DGX Infrastructure and NeMo Megatron



A.I. depends on hardware

ASML

Applied Materials

Japanese tool makers

Quantum Computing

Neuromorphic Devices

Hardware 2.0

- Semiconductors (not only silicon: germanium, graphene, tin oxide, gallium nitride,...)
- Semiconductor manufacturing equipment
- Apple, Tesla, Google, and Amazon are now making their own ASIC chips

REUTERS® · December 6, 2022

TSMC triples Arizona chip plant investment, Biden hails project

Hardware 2.0

3nm: Samsung (2022), TSMC (2022), Intel (2023?)

Korea on June 30, 2022 SAMSUNG

Samsung Begins Chip Production Using 3nm Process Technology With GAA Architecture

TSMC's 3nm yields 60% - 80%
Samsung's yields 10% - 20%

December 29, 2022

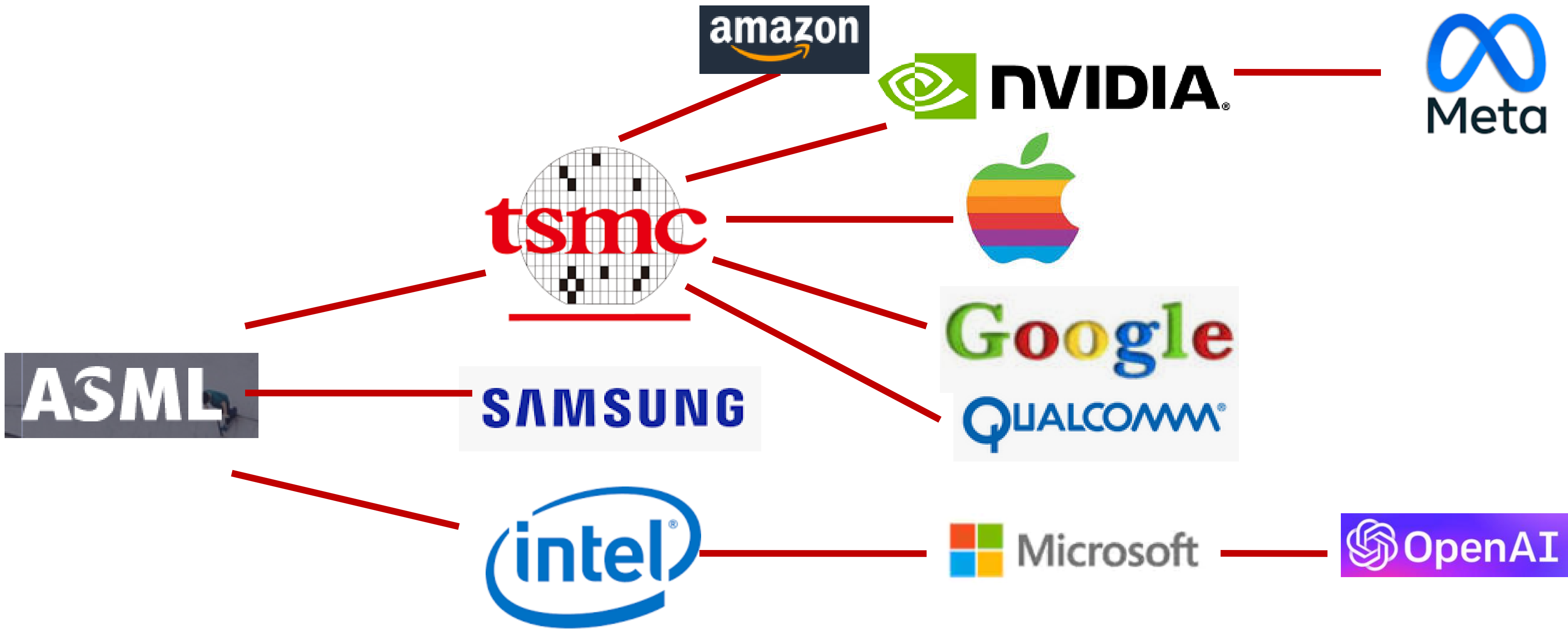
TSMC Kicks Off 3nm Production

Hardware 2.0

- Open-source Hardware (RISC-V)

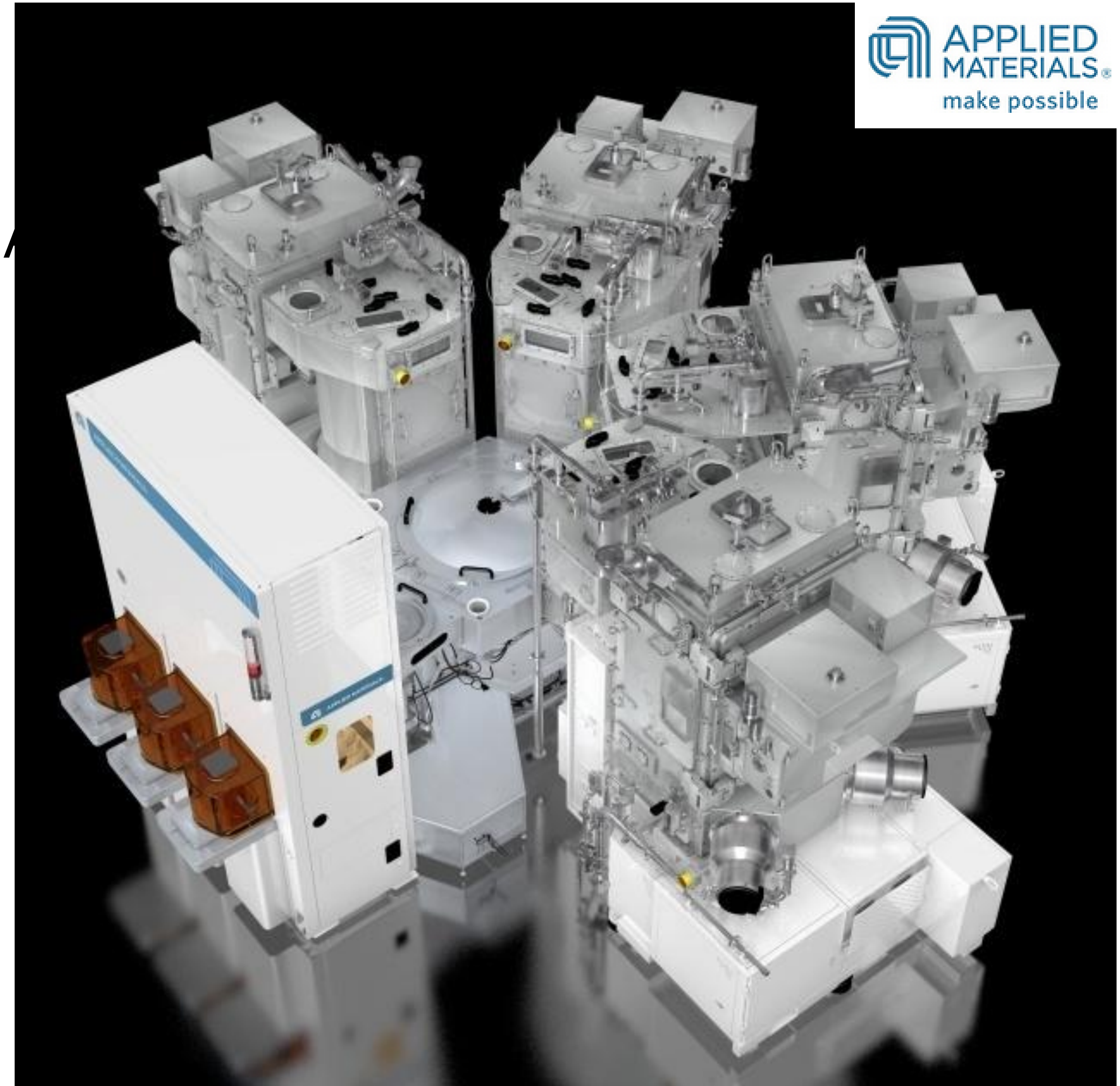
EUV Lithography

- ASML (Netherlands) has a monopoly on EUV lithography
- ASML only has five EUV customers: TSMC, Samsung, Intel, Micron, SK Hynix
- Lithography accounts for an estimated 35% of the cost of production at 3nm
- 2023: Applied Materials (Silicon Valley) introduces the etching tool Centura Sculpta (de facto a collaboration with Intel) which reduces the number of EUV lithography steps for wafer fabrication and greatly reduces the costs
- Japan still has leaders in key steps of the fabrication
  - Lasertec: mask inspection tools
  - Disco: wafer ultra-grinders,
  - JSR: highly purified chemicals



ASML's High NA second-generation EUV will allow foundries to produce chips using a process node under 3nm

The $150 Million Machine Keeping Moore's Law Alive


APPLIED
MATERIALS®
make possible

Hardware/ Japan

- Japan used to be the world’s main chip maker
- Two decades of under-investment
- Engineer shortage (mass lay-offs of engineers following the global financial crisis in 2008)
- The chip shortfall of 2021 due to covid lockdowns in China hurt Japanese auto and consumer electronics companies who had to cut production (Sony, Toyota, Nintendo…)
- Tensions between USA and China over Taiwan

Hardware/ Japan

2022: Japanese government invest in its domestic chip industry and in joint ventures with Taiwan and USA

2022: Japan and USA announce a joint research center for advanced semiconductors

2022: Government-funded construction of a chip foundry in Kumamoto (joint venture of TSMC, Sony and Denso)

2022: Government-funded joint venture Rapidus in Hokkaido (Sony, NEC, Toyota, …)

2022: Strategic partnership between IBM and Rapidus

2022: Strategic partnership between IMEC and Rapidus

Neuromorphic Devices

Von Neumann architecture and MOS transistor scaling are inadequate to meet the computational density and energy efficiency demands of deep learning systems

Solution: Neuromorphic computing using brain-like computing architectures and novel synaptic memories

Alberto Salleo created electronic devices using organic materials that can act like transistors (which amplify electrical signals) and memory cells (which store data)

Neuromorphic Materials

2020 Texas A&M scientists discover an inorganic material that exhibits an electrical switching mechanism (beta-copper vanadium bronze β'-CuxV2O5)

This material undergoes a transition similar to the transitions that neurons undergo in the brain

The scientists were actually looking for a way to optimize current energy use

And they ended up discovering a material that behaves like neurons

TEXAS A&M UNIVERSITY
Engineering

ARTICLE | VOLUME 2, ISSUE 5, P1166-1186, MAY 06, 2020

Metal-Insulator Transitions in β'-$Cu_xV_2O_5$ Mediated by Polaron Oscillation and Cation Shuttling

Abhishek Parija [9] • Joseph V. Handy [9] • Justin L. Andrews [9] • ... R. Stanley Williams • David Prendergast • Sarbajit Banerjee [10, 11] • Show all authors • Show footnotes

Open Archive • Published: February 27, 2020 • DOI: https://doi.org/10.1016/j.matt.2020.01.027 •

Neuromorphic Materials

Swiss scientists (EPF Lausanne)

discover that vanadium dioxide is capable of "remembering" (for a few hours) the entire history of previous external stimuli in a similar way to neurons in the human brain

nature electronics Published: 22 August 2022

Nature Electronics **5**, 596–603 (2022)

Electrical control of glass-like dynamics in vanadium dioxide for data storage and processing

Mohammad Samizadeh Nikoo, Reza Soleimanzadeh, Anna Krammer, Guilherme Migliato Marega, Yunkyu Park, Junwoo Son, Andreas Schueler, Andras Kis, Philip J. W. Moll & Elison Matioli

Soft robots and active materials

Learn from the natural world: Nature doesn’t use stiff materials to make intelligent beings, Nature likes flexible materials like muscles, cartilage and brains

2016: Octobot, the first-ever soft autonomous robot, at Harvard (Robert Wood and Jennifer Lewis)

2017: The Vine Robot, which moves and grows like a plant at Stanford (Allison Okamura)

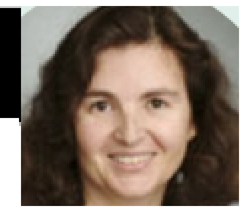
Soft robots and active materials

A new generation of surgical instruments

carbon-based titanium polymers

Daniela Rus (MIT)

Robert Shepherd (Cornell Univ)



Soft robots and active materials

Missing: a general theory of the dynamic origin of active matter locomotion

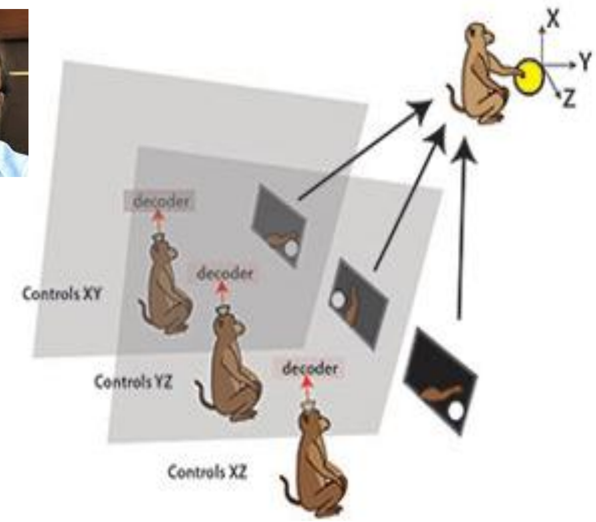
Complex locomotion is a key feature of active matter far from equilibrium

Irv Epstein (Brandeis): the active/inactive pattern of the Belousov-Zhabotinsky reaction is analogous to the exhibitory/inhibitory behavior of neurons

Brandeis UNIVERSITY

Brain-Computer Interfaces

2015: Miguel Nicolelis connects brains of monkeys so that they collaborate to perform a task



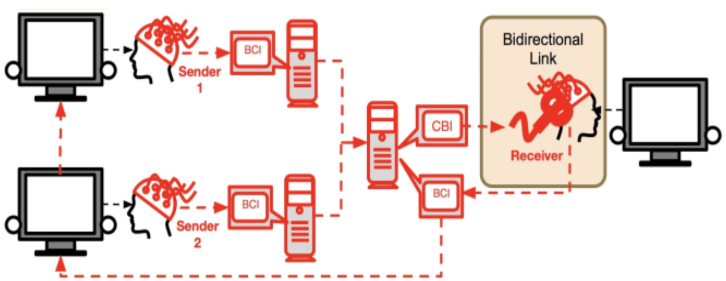
2018 BrainNet: three people play a game using only brainwaves

23 Sep 2018

BrainNet: A Multi-Person Brain-to-Brain Interface for Direct Collaboration Between Brains

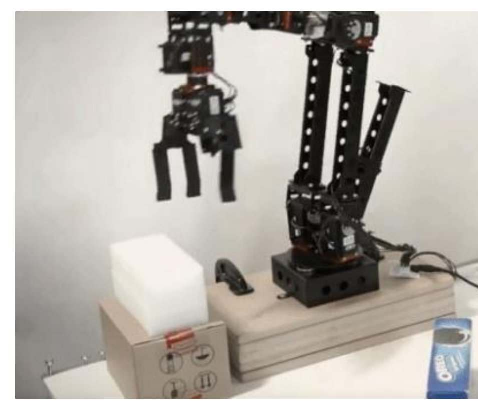
Linxing Jiang[1,*], Andrea Stocco[2,3,4,5], Darby M. Losey[6,7,8], Justin A. Abernethy[2,3], Chantel S. Prat[2,3,4,5], and Rajesh P. N. Rao[1,4,5,+]

[1]University of Washington, Paul G. Allen School of Computer Science & Engineering, Seattle, WA 98195, USA
[2]University of Washington, Department of Psychology, Seattle, WA 98195, USA
[3]University of Washington, Institute for Learning and Brain Sciences, Seattle, WA 98195, USA
[4]University of Washington, Center for Neurotechnology, Seattle, WA 98195, USA
[5]University of Washington, Institute for Neuroengineering, Seattle, WA 98195, USA
[6]Carnegie Mellon University, Program in Neural Computation, Pittsburgh, PA 15213, USA
[7]Carnegie Mellon University, Center for the Neural Basis of Cognition, Pittsburgh, PA 15213, USA
[8]Carnegie Mellon University, Machine Learning Department, Pittsburgh, PA 15213, USA



Brain-Machine Interfaces

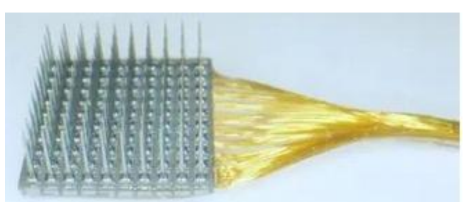
Stefan Harrer (IBM Australia, 2018): GraspNet = brainwave sensor + Deep Learning + Nvidia Jetson TX1+ robotic arm



Brain-Machine Interfaces

- Richard Normann: the Utah Electrode Array (1997) that can gather neural signals from up to 100 channels
- First experimented in humans in 2004
- Blackrock Neurotech to commercialize it (Utah, 2008, Florian Solzbacher and Marcus Gerhardt)

Blackrock Neurotech



- Neuralace (2022): 2D neural implant

Brain-Machine Interfaces

Elon Musk's Neuralink (2017)

Bryan Johnson's Kernel (2016, Los Angeles)

Thomas Oxley's Synchron (backed by Bill Gates and Jeff Bezos)

Matt Angle's Paradromics (Texas, 2015)

Neuropace

Neaurable

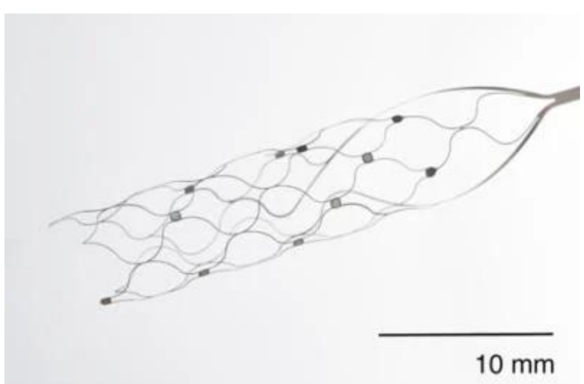
Foc.us

BrainCo

Brain-Machine Interfaces

Thomas Oxley’s Synchron (New York, 2016, backed by Bill Gates and Jeff Bezos)

- Stentrode (2022): a BCI that can access every corner of the brain using its blood vessels
- Inserted through the jugular vein to reach the motor cortex of the brain



Brain-Machine Interfaces

Neurosity (New York): The Crown (2021)

NEUROSITY

Mac Hodak’s Science.xyz: visual prosthesis for blind people Science Eye (2022)

Science

Brain-Machine Interfaces

NEURALINK

Elon Musk's Neuralink: designed a chip to be inserted into the surface of the brain, and a robot to perform the surgery

Journal of Medical Internet Research

Published on 31.10.2019 in Vol 21 , No 10 (2019) :October

Preprints (earlier versions) of this paper are available at https://preprints.jmir.org/preprint/16194, first published September 09, 2019.

An Integrated Brain-Machine Interface Platform With Thousands of Channels

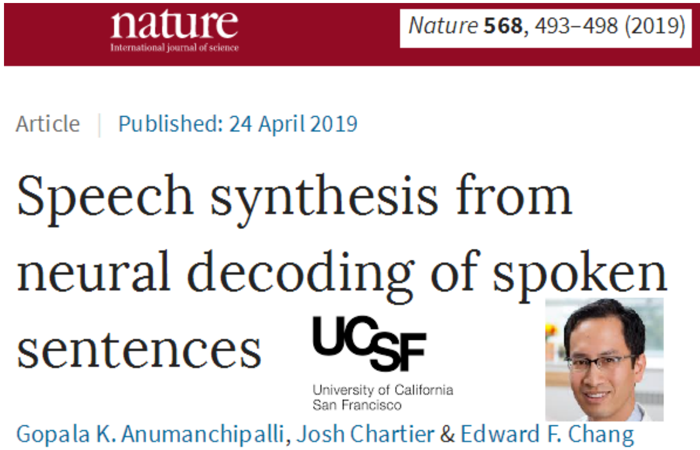
Elon Musk [1]; Neuralink [1]

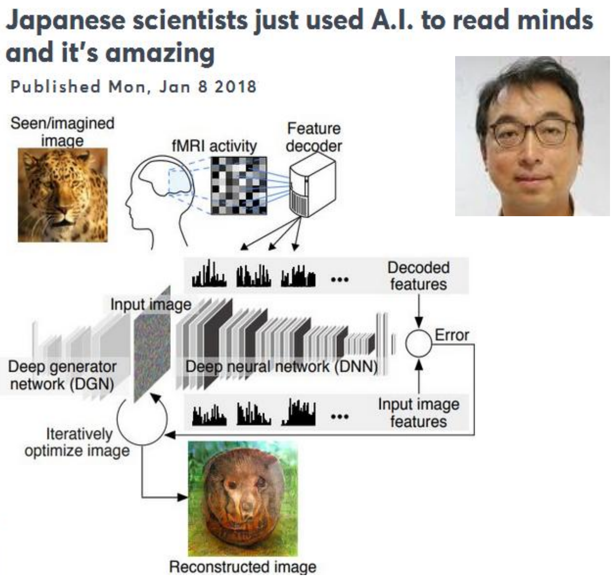
Musk's bid to start Neuralink human trials denied by FDA i

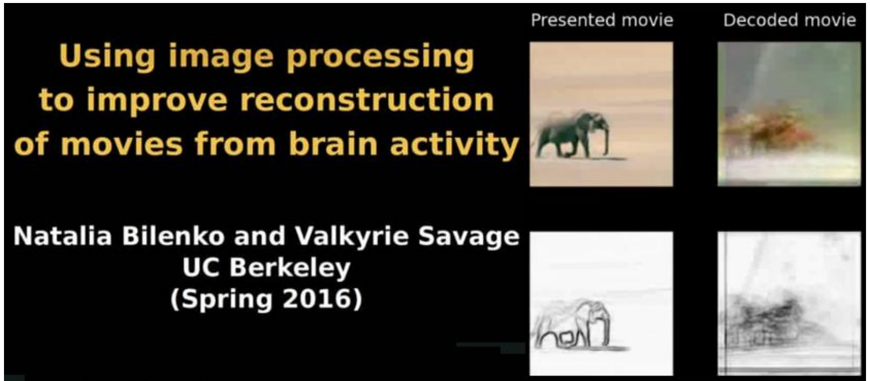
Mind Reading

Edward Chang (UC San Francisco, 2019): brain waves to speech

Jack Gallant (UC Berkeley, 2019): reconstruct dreams



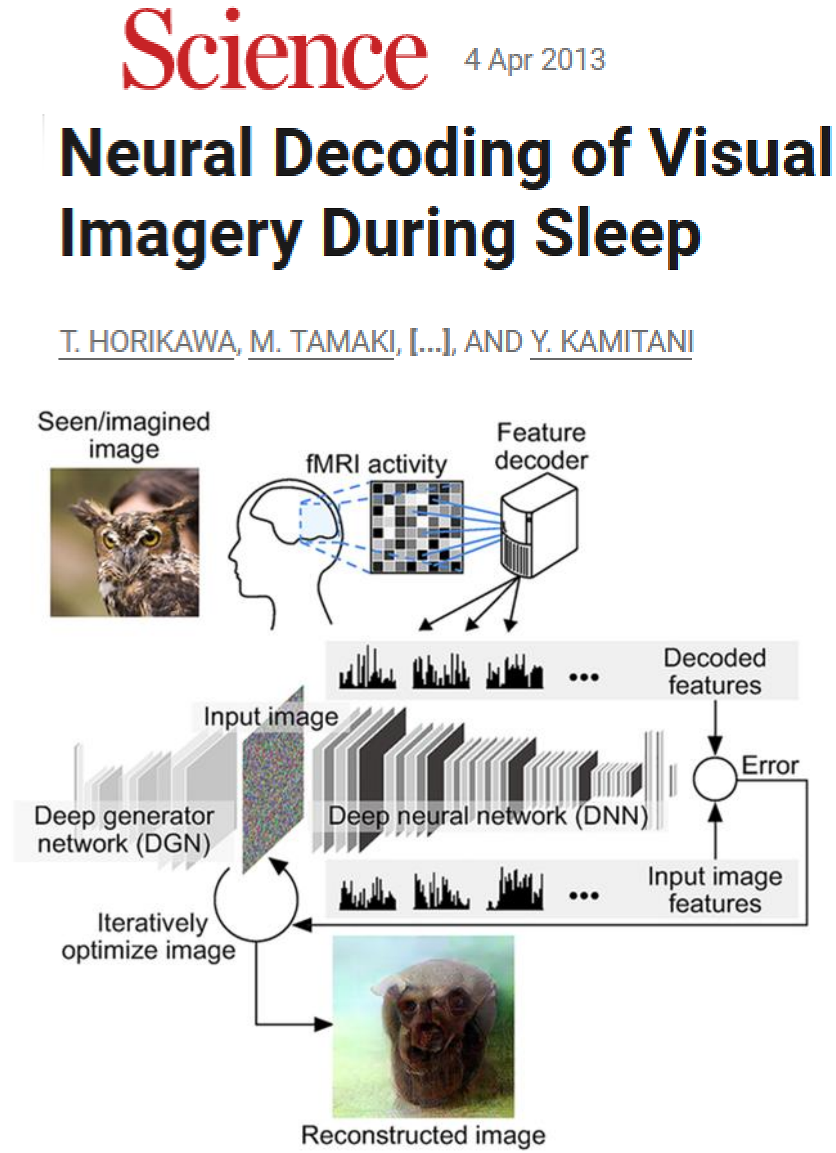




Mind Reading

Yukiyasu Kamitani (Kyoto Univ, 2012): visualize dreams

Yukiyasu Kamitani (Kyoto Univ, 2017): brain waves to images by training an A.I. to recognize visual patterns in the brain ("deep image reconstruction")

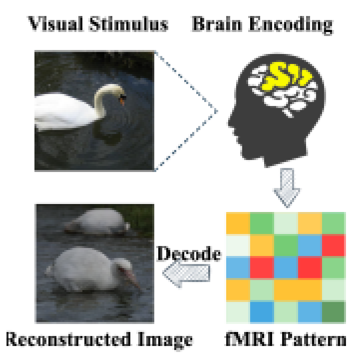


Mind Reading

Helen Zhou (National Univ Singapore, 2022): brain waves to images by training an A.I. to recognize visual patterns in the brain and generate images

Seeing Beyond the Brain: Conditional Diffusion Model with Sparse Masked Modeling for Vision Decoding

Zijiao Chen[1*] Jiaxin Qing[2*] Tiange Xiang[3] Wan Lin Yue[1] Juan Helen Zhou[1†]
[1]National University of Singapore, [2]The Chinese University of Hong Kong, [3]Stanford University



NUS
National University of Singapore

Neuroprosthesis

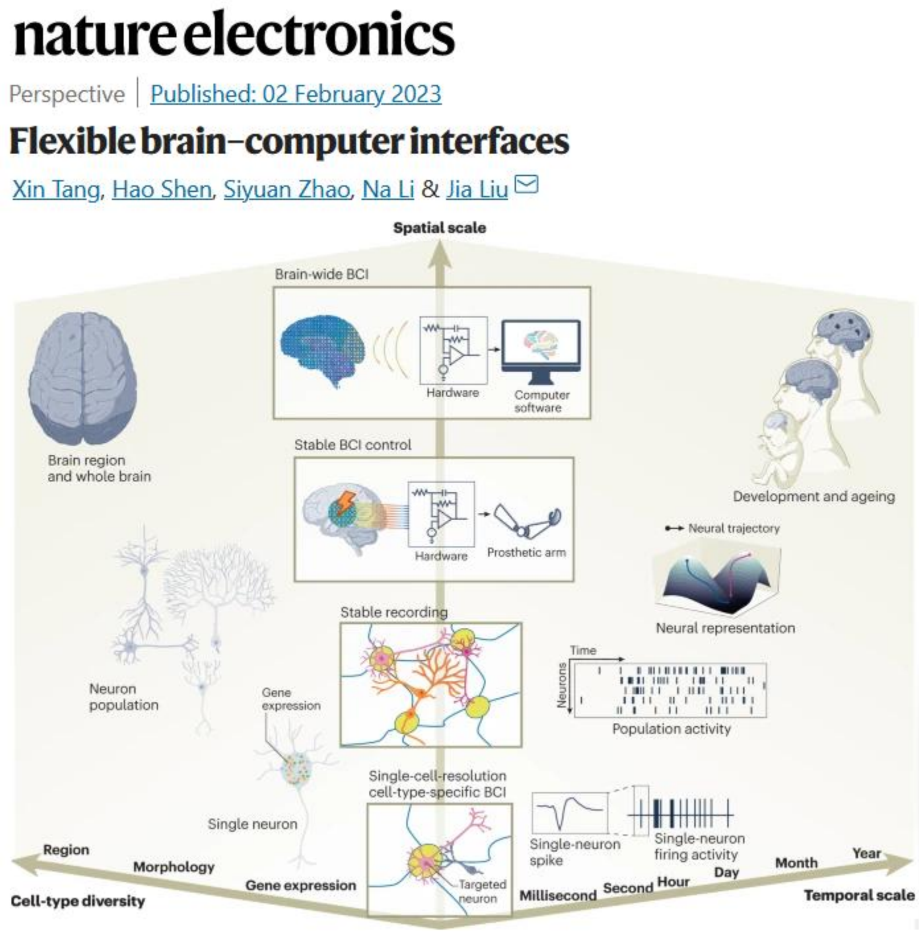
Jessie Liu (UC Berkeley), David Moses (UCSF) & Sean Metzger (UCSF) on Speech Neuroprosthesis: entire words (2021)

UCSF Media

Flexible nanoelectronics

Flexible nanoelectronics with the properties of biological tissues

Jia Liu (2023)



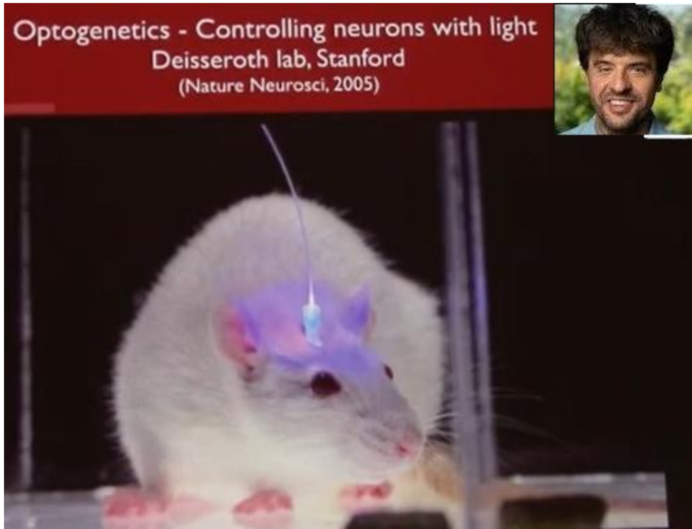
Progress in Neuroscience

Challenges:

- Temporal scale: single-neuron action potential operates at milliseconds; changes in neural population structure can take months (behavior, learning and memory) and even years (cognitive decline).
- Spatial scale: single neurons are 10–100 micrometers distributed across regions of centimetres and even meters

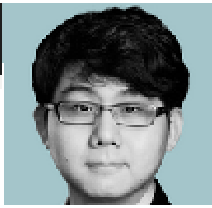
Progress in Neuroscience

- 2005: Karl Deisseroth (Stanford) uses optogenetics for monitoring and controlling neural activity
- Add extra DNA to the neuron's DNA so that the neuron makes proteins (opsins) that respond to light
- Typical opsin: channelrhodopsin-2 that only responds to blue light
- Blue light can be used to trigger neural activity



Progress in Neuroscience

- Xiao Wang (MIT): optogenetics for fine-tuning neuron excitability (2022)
- Jia Liu (Harvard): optogenetics for long-lasting changes in neuronal activity (2022)



Progress in Neuroscience

- 2020: Three labs at Stanford (Nicholas Melosh, Jun Ding and E.J. Chichilnisky) build a device that can record the activity of hundreds of neurons at the same time
- The device (made with modified silicon chips from cameras) takes a “movie” of brain activity
- And it connects directly the brain to silicon

ScienceAdvances VOL. 6, NO. 12 20 Mar 2020

Massively parallel microwire arrays integrated with CMOS chips for neural recording

ABDULMALIK OBAID, MINA-ELRAHEB HANNA, YU-WEI WU, MIHALY KOLLO, ROMEO RACZ, MATTHEW R. ANGLE, JAN MÜLLER, NORA BRACKBILL, WILLIAM WRAY, FELIX FRANKE, E. J. CHICHILNISKY, ANDREAS HIERLEMANN, JUN B. DING, ANDREAS T. SCHAEFER, AND NICHOLAS A. MELOSH

Progress in Neuroscience

- 2023: Jia Liu (Harvard) recording of neurons over the whole adult life of mice

nature
neuroscience

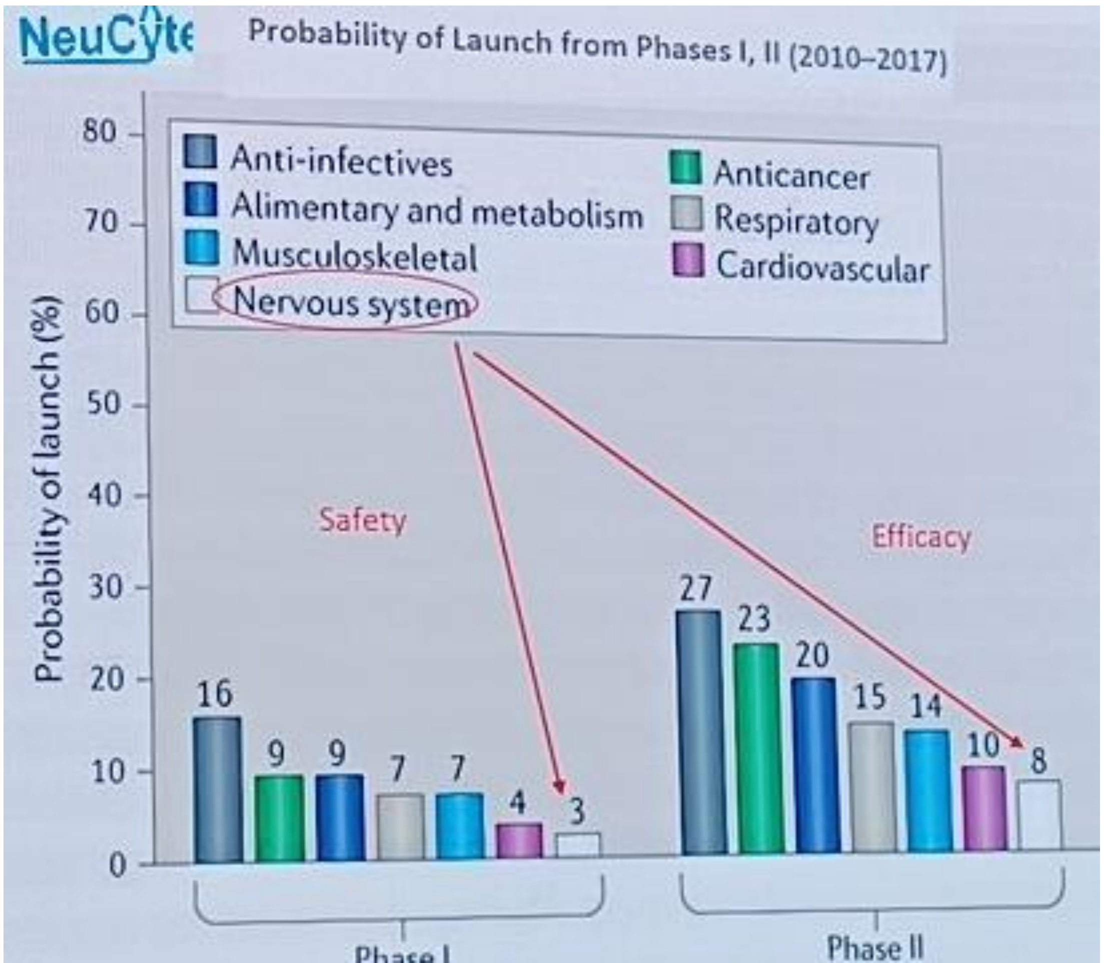
Technical Report | Published: 20 February 2023

Tracking neural activity from the same cells during the entire adult life of mice

Siyuan Zhao, Xin Tang, Weiwen Tian, Sebastian Partarrieu, Ren Liu, Hao Shen, Jaeyong Lee, Shiqi Guo, Zuwan Lin & Jia Liu

Progress in Neuroscience

- Neuro drug clinical success is among the lowest, i.e. probability of launch is very low



Progress in Neuroscience

- Platform for generating human iPSC-derived neurons (reprogramming of iPSC to produce neurons)
- Neurons for “brains-on-a-chip”
- Neucyte (San Jose, 2015)
- Creative Bioarray (New York)
- ATCC (Virginia)
- Insphero (Maine)

Brain Organoids

- Recreate the human brain in vitro ("brain-on-a-chip")
- Less need for animal models
- Three-dimensional brain organoids
- Diane Hoffman-Kim (Brown Univ, 2015)

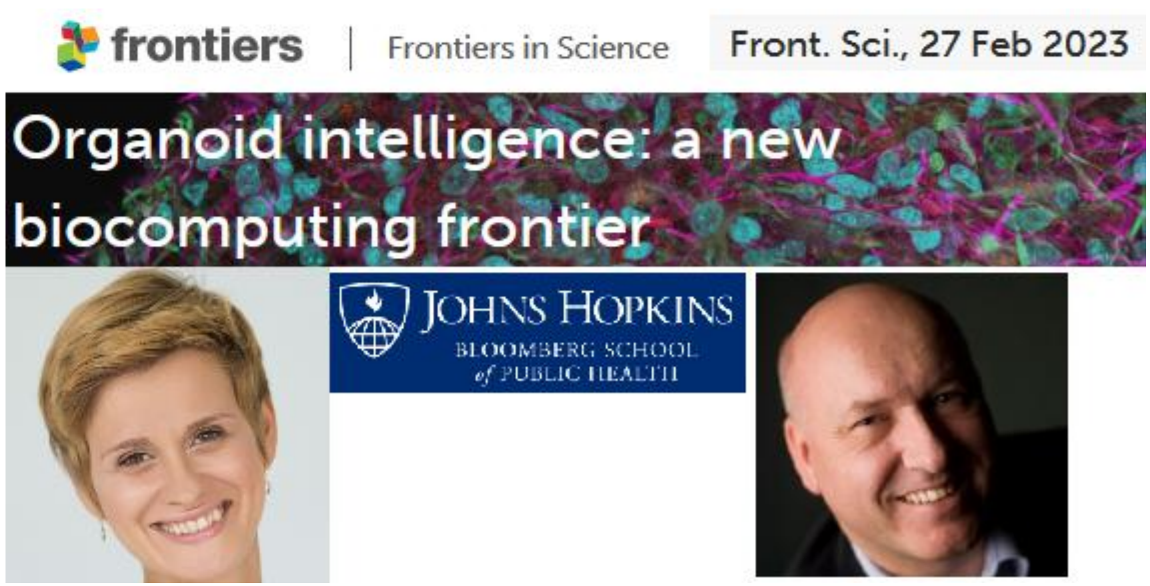
- Sergiu Paşca (Stanford, 2015)
- Alysson Muotri (UCSD)

- Pu Chen (Wuhan Univ)
- Paola Arlotta (Harvard)

Brain Organoids

If A.I. is so super-intelligent, why we still use CAPTCHA to tell humans and computers apart?

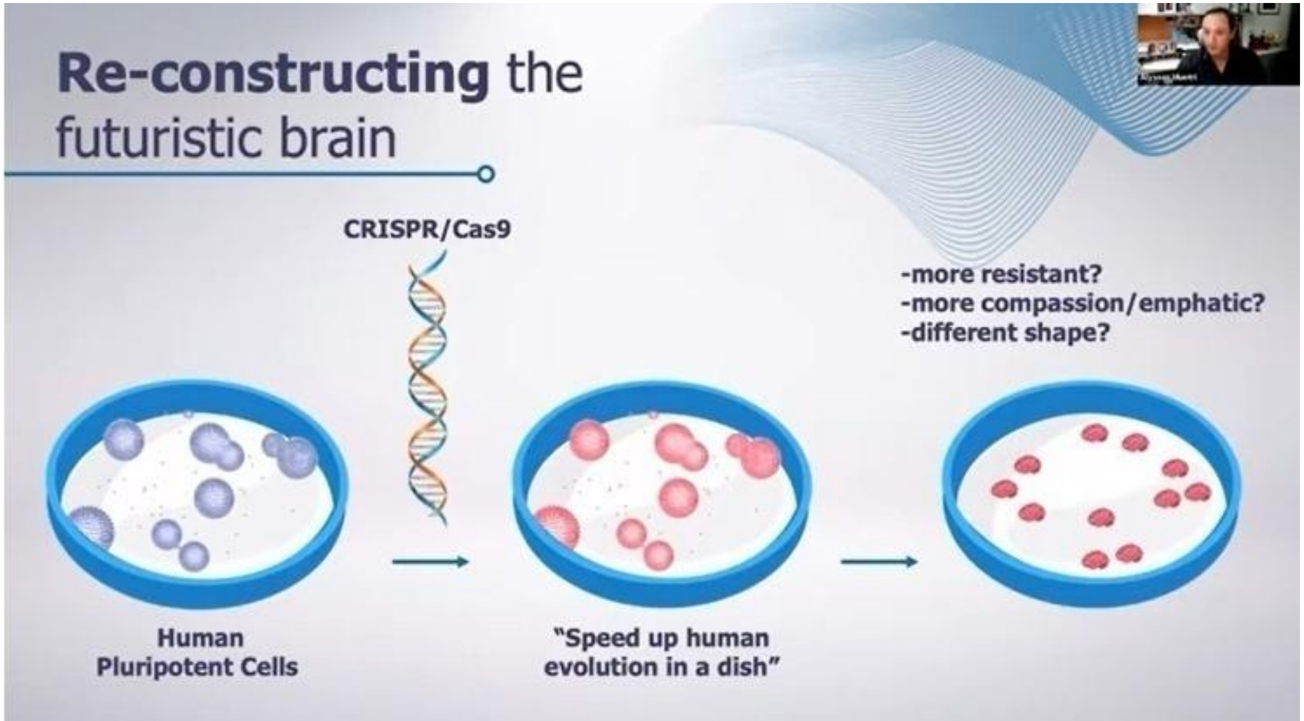
Lena Smirnova and Thomas Hartung (Johns Hopkins Univ): brain organoids (human brain cell cultures) to develop biocomputers



Brain Organoids

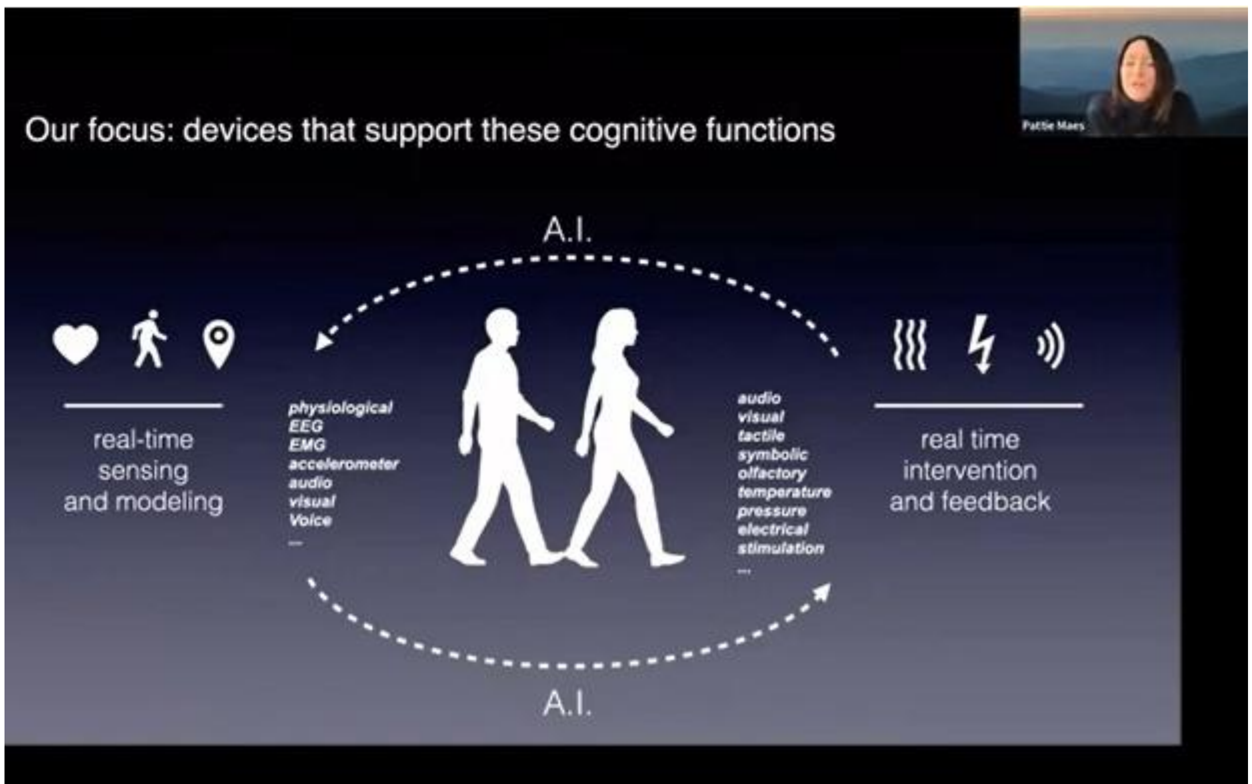
Alysson Muotri (UC San Diego):

- understanding the molecular and cellular mechanisms that cause neurological disorders
- novel therapeutic approaches



Cognitive Enhancement

Pattie Maes (MIT): using personal devices to improve attention, motivation, behavior change, memory, creativity, and emotion regulation



New Materials

Graphene

- 2004: Andre Geim and Kostya Novoselov (Manchester Univ) produce a sheet of graphene
- 2010: IBM demonstrates graphene wafers
- Graphene is the most conductive material
- 200 times stronger than steel
- Carbon is non-toxic in the body (life is made of carbon), so these carbon-based materials could be used to build vectors that travel in the bloodstream and deliver a drug to a specific site
- Microchips that used graphene could fit many more transistors than silicon
- Challenge: graphene is a gapless material (more similar to a metal than to a semiconductor)

Magic-angle Graphene

2018: Pablo Jarillo-Herrero (MIT) discovers that twisted graphene is a robust superconductor

2019: Stanford University discovers that twisted graphene can be coerced into a ferromagnetic state

2023: Pablo Jarillo-Herrero (MIT): superconductivity in magic-angle graphene that can be turned on and off

Goal: ultrafast, energy-efficient superconducting transistors

Science SCIENCE • 25 Jul 2019 • Vol 365, Issue 6453 • pp. 605-608

Emergent ferromagnetism near three-quarters filling in twisted bi-layer graphene

AARON L. SHARPE, ELI J. FOX, ARTHUR W. BARNARD, JOE FINNEY, KENJI WATANABE, TAKASHI TANIGUCHI, M. A. KASTNER, AND DAVID GOLDHABER-GORDON

nature nanotechnology

Letter | Published: 30 January 2023

Electrical switching of a bistable moiré superconductor

Dahlia R. Klein, Li-Qiao Xia, David MacNeill, Kenji Watanabe, Takashi Taniguchi & Pablo Jarillo-Herrero

Graphene

- The costs of producing graphene dropped substantially (now less than $50 per kg)
- Challenge: can’t yet produce graphene on a large scale (without losing its wonder properties)
- Ditto for carbon nanotubes (wonder material of the 1990s)
- So the real goal is: how to mass produce graphene?
  - Omar Matar & Camille Petit (Imperial College London)
  - Chris Sorensen (Kansas State Univ)
  - John Hart (MIT)
  - David Boyd (CalTech)
  - Jonathan Coleman (Trinity College, Dublin)
  - Center for Advanced 2D Materials (National Univ of Singapore)

Graphene

Graphene-based electronics

2019: Paragraf (Cambridge Univ spin-off) starts producing graphene-based electronic components

Walter de Heer (Georgia Tech)

Nai-Chang Yeh (CalTech)

Graphene

Two-dimensional Transition Metal Dichalcogenide: semiconductor with an electronic band gap, unlike graphene which is a zero-gap semicondutor

Attractive materials for optoelectronics due to the strong light-matter interaction and photon absorption

Graphene

Two-dimensional Hexagonal Boron Nitride: large band gap, no optical absorption in the visible spectrum

Ideal materials for the construction of van der Waals heterostructures, e.g. integrating 2D hBN with 2D TMDCs and graphene

Graphene/hBN heterostructures enable the creation of high-performance graphene-based electronic devices, i.e. enable the fabrication of atomically thin integrated circuits

Metamaterials

2019: Joel Therrien (Univ of Massachusetts) discovers a new carbon-based material, U-carbon

- Unlike graphene, it's magnetic
- It can be used for making biosensors or drug-delivery vectors that are controlled via magnetic devices

Discovery of U-Carbon: Metallic and Magnetic

Hong Fang[1], Michael Masaki[2], Anand B. Puthirath[3], Jaime M. Moya[4], Guanhui Gao[3], Emilia Morosan[4], Pulickel M. Ajayan[3], Joel Therrien[2]*, Puru Jena[1]*

[1] Physics Department, Virginia Commonwealth University, Richmond, VA 23284-2000, USA.

[2] Department of Electrical and Computer Engineering, University of Massachusetts, Lowell, MA, USA.

[3] Department of Materials Science and NanoEngineering, Rice University, Houston, TX, 77005, USA.

[4]Department of Physics and Astronomy, Rice University, Houston, TX 77005, USA.

*Correspondence to: Joel_Therrien@uml.edu (J.T.); pjena@vcu.edu (P.J.)

Nanomaterials

Julia Greer (Caltech) : Responsive architected materials

Foam-like solids comprised of many nanoscale building blocks

E.g. solids that deform like a fluid, brittle ceramics that deform upon compression

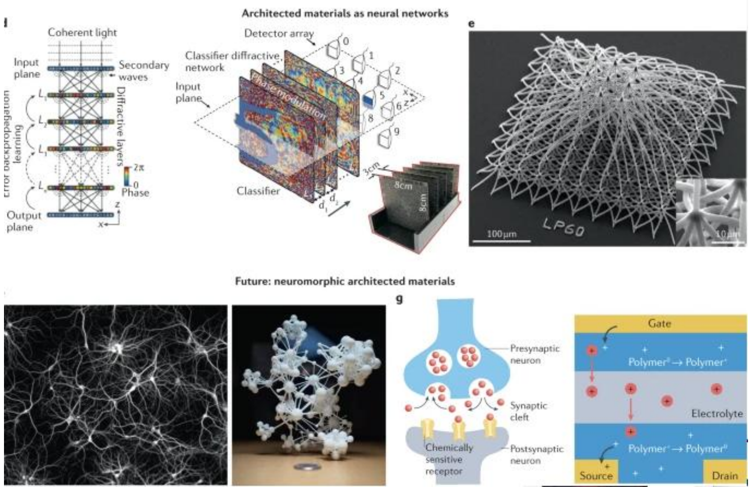
Possible application: neuromorphic computers

nature reviews materials 20 June 2022

Responsive materials architected in space and time

Xiaoxing Xia, Christopher M. Spadaccini & Julia R. Greer

Nature Reviews Materials **7**, 683–701 (2022)



Superconductivity

Superconductivity

1908: Univ of Leiden is the first place to liquify helium (the only lab to have it until 1923) - liquified helium is the best coolant

1911: Heike Kamerlingh Onnes (Univ of Leiden) discovers the first superconductor (mercury) but the temperature is just a few kelvin

1957: BCS theory (proposed by John Bardeen, Cooper, and Schrieffer): the transition to the superconducting state occurs when electrons overcome their mutual electrical repulsion to form so-called “Cooper pairs”, but no explanation what the "glue" could be

1981: Gerd Binnig and Heinrich Rohrer (IBM Zürich) invent the scanning tunneling microscope

1986: Johannes Bednorz and Karl Mueller (IBM Zürich) discover high-temperature superconductivity in La-Ba-Cu-O (lanthanum barium copper oxide, a cuprate) at 30 K (room temperature: 20 degrees = 293 K)

1987: Philip Anderson posits that superexchange accounts for high-temperature superconductivity

Superconductivity

1987: Maw-Kuen Wu (Univ of Alabama) discovers superconductivity at 93 K in Yttrium barium copper oxide Y-Ba-Cu-O (YBCO)

Main class of high-temperature superconductors: copper oxides combined with other metals, e.g. YBCO

1993: ETH Zurich discovers a new superconductor, the cuprate of mercury, barium and calcium Hg–Ba–Ca–Cu–O at around 133 K = -140 degrees (C)

2001: JC Seamus Davis (UC Berkeley) develops a quantum microscope to study superconductors

2004: Neil Ashcroft (Cornell Univ) proposes metallic hydrogen for high temperature superconductivity (high phonon frequencies and strong electron-phonon coupling)

2015: Mikhail Eremets (Max Planck Inst) discovers that hydrogen sulfide H3S is a superconductor at 203K (-70 degrees) but has to be compressed to 155 gigapascals (more than 1 million times Earth's atmospheric pressure)

High-temp Superconductivity

New age of supercondutors: under enormous pressure, hydrogen can transform into a metal (metallic hydrogen) that can superconduct at hundreds of kelvins (almost room temperature)

High-temperatures superconducting in hydrides (hydrogen-rich materials)

2017: Yanming Ma (Jilin Univ) predicts theoretically that LaH10 can be a high-temperature semiconductor

2018: Pablo Jarillo-Herrero (MIT) shows that twisted bilayer graphene is a superconductor

2019: Mikhail Eremets discovers that lanthanum hydride LaH10 is a superconductor at 250 K (again under very high pressure)

2023: Ranga Dias (Univ of Rochester) nitrogen-doped lutetium-hydride (LNH) is superconducting at room temperature (294 K = 20 degrees) at much lower pressures (1 gigapascal) – to be confirmed

High-temp Superconductivity

The origin of high-temperature superconductivity is not understood

What is the "glue" responsible for this “high-temperature” superconductivity (electrons seem to get glued together)?

High-temp Superconductivity

Latest announcements

"Superhydride" Shows Superconductivity at Record-Warm Temperature

Published May 22, 2019   https://nationalmaglab.org/

nature   Published: 22 May 2019   *Nature* **569**, 528–531

Superconductivity at 250 K in lanthanum hydride under high pressures

A. P. Drozdov, P. P. Kong, V. S. Minkov, S. P. Besedin, M. A. Kuzovnikov, S. Mozaffari, L. Balicas, F. F. Balakirev, D. E. Graf, V. B. Prakapenka, E. Greenberg, D. A. Knyazev, M. Tkacz & M. I. Eremets

?

Article | Published: 08 March 2023   *Nature* **615**, 244–250 (2023)

Evidence of near-ambient superconductivity in a N-doped lutetium hydride

Nathan Dasenbrock-Gammon, Elliot Snider, Raymond McBride, Hiranya Pasan, Dylan Durkee, Nugzari Khalvashi-Sutter, Sasanka Munasinghe, Sachith E. Dissanayake, Keith V. Lawler, Ashkan Salamat & Ranga P. Dias

UNIVERSITY of ROCHESTER

High-temp Superconductivity

HARVARD UNIVERSITY

UC San Diego

MAX PLANCK INSTITUTE FOR CHEMISTRY

UNIVERSITY of ROCHESTER

High-temp Superconductivity

2022: J. C. Ssamus Davis (now at Oxford Univ): using his quantum microscope, proves Anderson's theory that superexchange is the "glue" (to be confirmed)

Quanta magazine

High Temperature Superconductivity Understood at Last

UNIVERSITY OF OXFORD

PNAS

September 6, 2022

On the electron pairing mechanism of copper-oxide high temperature superconductivity

Shane M. O'Mahony, Wangping Ren, Weijiong Chen, +5, and J. C. Séamus Davis Authors

Quantum Computing

Quantum Computing

Why do we have deep learning (AlphaGo, ChatGPT, etc)?

Because of GPUs.

GPUs enabled A.I. scientists to train neural networks 10–20 times faster

CPU gave us symbolic AI

GPU gave us deep learning AI

QPU will give us...?

Quantum Computing

Quantum computers could solve problems that cannot be solved with today's supercomputers

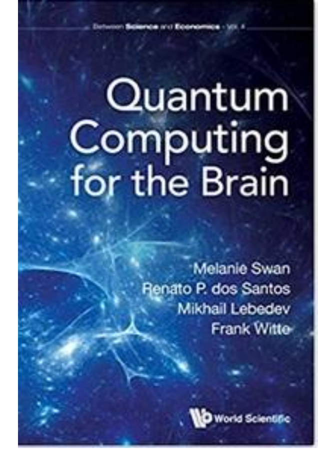
- Classical supercomputers cannot model large molecules; e.g. to create a simulation of the penicillin molecule with 41 atoms, a classical computer would need trillions of trillions of transistors (there aren't enough atoms in the universe)
- Modeling of the human brain's 86 billion neurons and 242 trillion synapses is more feasible with quantum computers
- Cracking today's cryptographic keys is impossible with today's supercomputers

Quantum Computing

Killer apps of quantum computing:

- Molecular modelling
- Whole-brain neuroscience
- Post-quantum cryptography

Quantum Computing



Whole-brain simulation

- The Blue Brain project (Henry Markram) a
simulating the entire mammalian brain, sta
mouse and progressing to the human

EPFL

Blue Brain Project

- Modeling a single neuron requires 20,000 differential equations, a brain region requires solving 100 billion equations at the same time
- Allen Institute for Brain Science aims at mapping the connectome of the mouse: a millimeter cube of mouse cortex 100,000 neurons and one billion connections
- 2023: Cambridge Univ created the detailed wiring diagram (the “connectome”) of the brain of the fruit fly larva: 3016 neurons connected by 548,000 synapses

Quantum Computing

If a country has a quantum computer right now, it is capable of reading all the encrypted top-secret documents of any other country

Quantum computers will be able to crack existing cryptography.

They will force the re-encryption of all encrypted data (the "Y2K bug" of cryptography).

Quantum Computing

1994: Peter Shor (MIT) shows that a quantum algorithm can exponentially accelerate classical computation

Shor's algorithm can factor integers in polynomial time but most run on a quantum computer

Massachusetts Institute of Technology

A computer that can run Shor's algorithm can break today's best cryptography protocols (because they rely on the assumption that factoring is impossible for large enough integers)

Quantum Computing

1996 David DiVincenzo (IBM) proposes “criteria” for a quantum computer (one is “long coherence times”)

1997 Alexei Kitaev (Landau Institute, Russia) shows that topological quantum computation is a solution to the problem of decoherence

Russian Academy of Sciences

L.D.Landau

INSTITUTE FOR

TEORETICAL

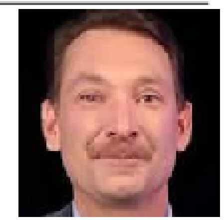
PHYSICS

Quantum Computing

1997 Isaac Chuang (IBM) and Mark Kubinec (UC Berkeley) build the first quantum computer (2-qubit)

VOLUME 80, NUMBER 15 PHYSICAL REVIEW LETTERS 13 APRIL 1998

Experimental Implementation of Fast Quantum Searching



Isaac L. Chuang,[1,*] Neil Gershenfeld,[2] and Mark Kubinec[3]
[1] *IBM Almaden Research Center K10/D1, 650 Harry Road, San Jose, California 95120*
[2] *Physics and Media Group, MIT Media Lab, Cambridge, Massachusetts 02139*
[3] *College of Chemistry, D7 Latimer Hall, University of California, Berkeley, Berkeley, California 94720-1460*
(Received 21 November 1997; revised manuscript received 29 January 1998)

2001 Isaac Chuang's 7-qubit quantum computer executes Shor's algorithm

Quantum Computing

Quantum entanglement records

2022 Gerhard Rempe's team (Max Planck Inst) entangles 14 photons together

2022 Andrew Dzurak's team (Univ of New South Wales) achieve a coherence time of two milliseconds

2023 Tracy Northup and Ben Lanyon (Univ of Innsbruck) entangle two ions over a distance of 230 meters

Quantum Computing

2017: IBM’s 50-qubit quantum computer (the quantum state is preserved for only 90 microseconds)

2018: Intel Tangle Lake (49 qubits)

2018: Google Bristlecone (72 qubits)

2018: IonQ (Maryland), the first commercial trapped-ion quantum computer

2019: IonQ first IPO of a quantum-computing startup

2019: IonQ Harmony (11 qubits) deployed on Microsoft's cloud

2019: IBM Q System One, a commercial quantum computer (20 qubits)

Quantum Computing

2019 Google Sycamore which is programmable (53 qubits)

It can perform a particular calculation in 200 seconds that would have taken a traditional supercomputer more than 10,000 years

2018 IEEE European Symposium on Security and Privacy

CRYSTALS – Kyber: a CCA-secure module-lattice-based KEM

Joppe Bos[*], Léo Ducas[†], Eike Kiltz[‡], Tancrède Lepoint[§], Vadim Lyubashevsky[¶], John M. Schanck[||], Peter Schwabe[**], Gregor Seiler[††], Damien Stehlé[‡‡],

[*]*NXP Semiconductors, Belgium. Email: joppe.bos@nxp.com*

[†]*CWI Amsterdam, The Netherlands. Email: ducas@cwi.nl*

[‡]*Ruhr-University Bochum, Germany. Email: eike.kiltz@rub.de*

[§]*SRI International, USA. Email: tancrede.lepoint@sri.com*

[¶]*IBM Research Zurich, Switzerland. Email: vad@zurich.ibm.com*

[||]*University of Waterloo, Canada. Email: jschanck@uwaterloo.ca*

[**]*Radboud University, The Netherlands. Email: peter@cryptojedi.org*

[††]*IBM Research Zurich, Switzerland. Email: grs@zurich.ibm.com*

[‡‡]*ENS de Lyon, France. Email: damien.stehle@ens-lyon.fr*

Quantum Computing

2020: IBM Falcon (27 qubits)

2021: IBM Eagle (127 qubits)

2021: USTC (China) Zuchongzhi (62 qubits)

2021: Honeywell H1 (quantum volume 512)

Honeywell Quantum and Cambridge Quantum comb
form Quantinuum

QUANTINUUM

2022: Quantinuum H1 (20 qubits)

NVIDIA QODA

2022: Nvidia QODA -- Quantum Optimized De
Architecture bridging classical and quantur

The platform for hybrid quantum-classical computing.

2022: Rigetti (2013, Berkeley) Aspen-M3 (80 qubits)

2022: IonQ Aria (23 qubits) deployed on Microsoft's cloud

2023 Quantware (2021, Netherlands) Tenor (64 qubits)

2023: IBM’s quantum processors include the 27-qubit Falcon, the 65-qubit Hummingbird, the 127-qubit and the 433-qubit Osprey

Quantum Computing

2022: Maria Spiropulu (Caltech) creates a wormhole using a Google Sycamore

Quanta magazine

Physicists Create a Holographic Wormhole Using a Quantum Computer

November 30, 2022

The team, led by Maria Spiropulu of the California Institute of Technology, implemented the novel "wormhole teleportation protocol" using Google's quantum computer, a device called Sycamore housed at Google Quantum AI in Santa Barbara, California.

Caltech

Scaling quantum computers

Qubits don’t tell the whole story

- Qubit error/yield
- Decoherence (the qubit interacts with its surroundings and loses its quantum properties)

Scaling quantum computers

The cryogenic/superconducting approach

- IBM, Google, Intel, Rigetti: qubits based on superconducting circuits or trapped ions at a temperature near absolute zero, cryogenically cooled with liquid helium

The photonic approach

- Qubits based on photons can operate at room temperature
- Qubits based on photons have longer coherence (weal interaction with the surroundings)

Scaling quantum computers

The photonic approach

- 2001 Emanuel Knill and Raymond LaFlamme (Los Alamos National Lab) and Gerald Mulburn (Univ of Queensland, Australia) show that quantum computing with linear optics (photons) is feasible
- PsiQuantum (2015, Silicon Valley), aiming for one-million qubit system
- Xanadu (2016, Toronto) introduced Borealis (216 qubits) in 2022
- USTC (China): Jiuzhang in 2020
- ORCA Computing (2019, London, Oxford spinoff)
- Quandela (2017, Paris, CNRS spinoff)
- QuiX Quantum (2019, Netherlands, Twente Univ spinoff)

Scaling quantum computers

Milestone for quantum chip fabrication: Intel demonstrates the industry's highest reported yield (95%) and uniformity to date of silicon spin qubit devices (2022)

intel. October 5, 2022

Intel Hits Key Milestone in Quantum Chip Production Research

Intel demonstrates exceptional yield of quantum dot arrays, showing promise for large-scale qubit production using transistor fabrication technology.

Scaling quantum computers

Modifying conventional silicon transistor technology to host quantum computation

Quantum computing relies on spin

Need to isolate silicon-28 atoms (that have 14 neutrons), eliminating silicon-29, to create a “semiconductor vacuum” free from both electric and magnetic disturbances

Spin qubits in silicon: one of the most promising candidates for large scale quantum computers due to

- long coherence
- high-fidelity
- compatibility with CMOS technology

Scaling quantum computers

Holes vs electrons

- Electrons are spin 1/2 particles
- Holes in semiconductors (positive charge) are spin 3/2 quasi-particles
- Creating qubits with the spin of holes
- Hole spin qubits enable up to 100 million operations per second and they have a long lifetime of up to 150 microseconds
- Artificial atoms using holes instead of electrons could allow significantly faster gate operation, while still preserving long spin lifetimes

NOMIS FOUNDATION Creating the Spark

Published: 03 June 2021

A singlet-triplet hole spin qubit in planar Ge

Daniel Jirovec, Georgios Katsaros

Nature Materials **20**, 1106–1112 (2021)

Scaling quantum computers

NCCR SPIN

University of Basel

Published: 03 March 2022

A hole spin qubit in a fin field-effect transistor above 4 kelvin

===>

nature electronics

Editorial | Published: 29 March 2022

The case for silicon again

Quantum computers based on silicon could exploit the manufacturing techniques used to create conventional computer chips – providing a potential route to scaled-up quantum processors.

Microkelvin electronics on a pulse-tube cryostat with a gate Coulomb-blockade thermometer Published 19 September 2022

ScienceDaily

Ultracold circuits

Scaling quantum computers

Why holes and not electrons and not ions?

Switching is two orders of magnitude faster with holes than with electrons and six times faster than with ions

Trapped-ion quantum computers are easier to make but much slower

APS March Meeting

March 5–10, 2023 | Las Vegas, Nevada
March 20–22, 2023 | Virtual

Semiconducting Qubits

Building small, fast and hot hole spin qubits in Si and Ge

Dominik M Zumbuhl (University of Basel)

Hole spin qubits in semiconductor quantum dots

Jiawei Wang (State Univ of NY - Buffalo)

Si/SiGe quantum devices with full 300mm process

Clement Godfrin (IMEC)

A scalable spin-shuttling architecture for Si/SiGe-based quantum computing

Alexander Willmes (RWTH Aachen University)

Si/SiGe Qubit Devices Enabled by Advanced Semiconductor Fabrication

Eric Henry (Intel)

Towards Si finFET quantum devices with reproducible behavior

Matthias Mergenthaler (IBM Research Europe - Zurich)

Quantum computation with hole spin qubits in Si and Ge quantum dots.

Stefano Bosco (University of Basel)

Integrating Si/SiGe quantum devices with on-chip classical circuitry

Michael Wolfe (University of Wisconsin - Madison)

Hole spin qubit in silicon: enhanced coherence and coherent coupling to microwave photons

Romain Maurand (CEA Grenoble)

Scaling quantum computers

Semiconductor Spin Qubits

16 Dec 2021

Guido Burkard

Department of Physics, University of Konstanz, D-78457 Konstanz, Germany

Thaddeus D. Ladd and Andrew Pan

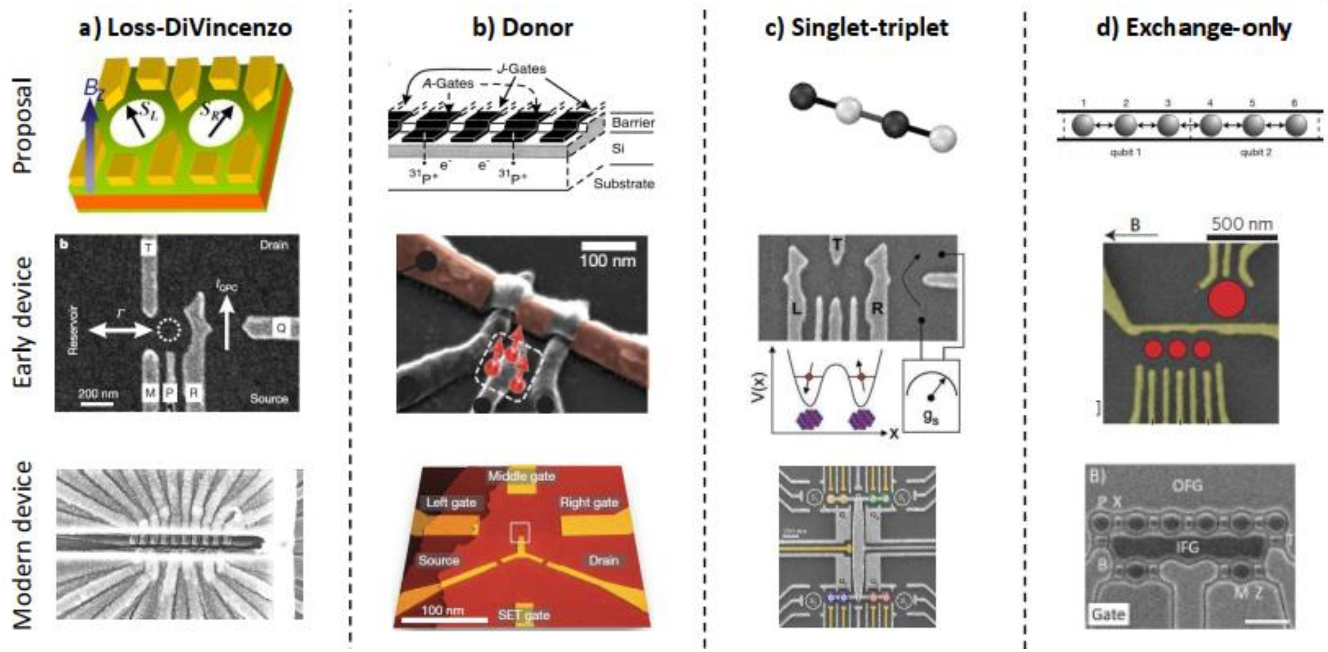
HRL Laboratories LLC, 3011 Malibu Canyon Road, Malibu, California 90265, USA

John M. Nichol

Department of Physics and Astronomy, University of Rochester, Rochester, New York 14627, USA

Jason R. Petta

Department of Physics, Princeton University, Princeton, New Jersey 08544, USA



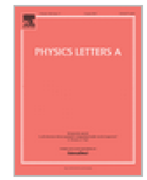
Scaling quantum computers

Silicon quantum computing

ELSEVIER

Physics Letters A

Volume 384, Issue 17, 15 June 2020, 126352



Is all-electrical silicon quantum computing feasible in the long term?

Elena Ferraro CNR-IMM

Enrico Prati CNR-IFN

- 2020: Andrew Dzurak (Univ of New South Wales, Australia) 2-qubit silicon quantum chip at 1.5K
- 2022: Michelle Simmons (Univ of New South Wales) demonstrates a quantum computer integrated circuit

UNSW SYDNEY

Scaling quantum computers

Iuliana Radu (IMEC, Belgium)

Herbert Fotso (Univ of Buffalo, USA)

Dominik Zumbühl (Univ of Basel, Switzerland)

Jim Clarke (Intel, USA)

Hendrik Bluhm (Aachen Univ, Germany)

Mark Saffman (Univ of Wisconsin, USA)

Maud Vinet (CEA, France)

Jun Zhu (Penn State, USA)

Leo Kouwenhoven (Deft Univ, Netherlands)

Jianwei Pan (USTC, China)

Andrew Dzurak (Univ of New South Wales, Australia)



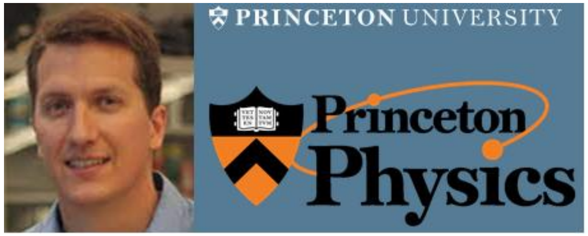








Scaling quantum computers



Jason Petta (Princeton):

- an single electron can pass its quantum information to a photon (2016)
- long-range coupling of two spins separated by 4 mm using microwave-frequency photons (2020)

Chris Monroe (Maryland):

- the first quantum logic gate (2000)
- quantum entanglement between two widely separated atoms (2008)
- IonQ is the first quantum-computing start-up to go public (2021)

Scaling quantum computers

Thaddeus Ladd (Los Angeles):

"Universal control" of silicon-based qubits (2023), i.e. the qubits can be used for any kind of quantum computational application)

Google's 53-qubit "Sycamore" (2019): first time that a quantum computer outperformed the fastest supercomputers at a task

IBM's 433-qubit "Osprey" (2022)

Scaling quantum computers

The dilemma of quantum error correction

Alexei Kitaev (1997): The topological quantum computer (but nobody has ever built one)

Google (2023): reduce errors by increasing the number of qubits

Quantum Computing in the Bay Area

PsiQuantum (2016, Palo Alto)

Rigetti Computing (2013, Berkeley)

Atom Computing (2018, Berkeley)

QC Ware (2014, Palo Alto)

Equal1 (2017, Fremont)

Bleximo (2017, Berkeley)

Hex Labs (2019, Palo Alto)

Turing (2014, Berkeley)

Post-Quantum Cryptography

NIST = National Institute of Standards and Technology

NIST already concerned about Post-quantum cryptography

NIST: PQC Project launched in 2012 for encryption methods that could resist an attack from a future quantum computer

Four winners chosen in 2022:

- CRYSTALS-Kyber for general encryption
- and three for digital signature (CRYSTALS-Dilithium, FALCON and SPHINCS+)

The NIST PQC Project

NIST July 05, 2022

NIST Announces First Four Quantum-Resistant Cryptographic Algorithms

Federal agency reveals the first group of winners from its six-year competition.

Amazon, IBM and Google are already implementing these algorithms

Post-Quantum Cryptography

2018 IEEE European Symposium on Security and Privacy

CRYSTALS – Kyber: a CCA-secure module-lattice-based KEM

Joppe Bos*, Léo Ducas†, Eike Kiltz‡, Tancrède Lepoint§, Vadim Lyubashevsky¶,
John M. Schanck‖, Peter Schwabe**, Gregor Seiler††, Damien Stehlé‡‡,
*NXP Semiconductors, Belgium. Email: joppe.bos@nxp.com
†CWI Amsterdam, The Netherlands. Email: ducas@cwi.nl
‡Ruhr-University Bochum, Germany. Email: eike.kiltz@rub.de
§SRI International, USA. Email: tancrede.lepoint@sri.com
¶IBM Research Zurich, Switzerland. Email: vad@zurich.ibm.com
‖University of Waterloo, Canada. Email: jschanck@uwaterloo.ca
**Radboud University, The Netherlands. Email: peter@cryptojedi.org
††IBM Research Zurich, Switzerland. Email: grs@zurich.ibm.com
‡‡ENS de Lyon, France. Email: damien.stehle@ens-lyon.fr

IBM

On lattices, learning with errors, random linear codes, and cryptography

TEL AVIV UNIVERSITY
Oded Regev
Tel Aviv University,

2005

NTRU: A Ring-Based Public Key Cryptosystem

Jeffrey Hoffstein, Jill Pipher, Joseph H. Silverman
BROWN

1996

Post-Quantum Cryptography

Crystals-Kyber for general encryption

- a member of the CRYSTALS (Cryptographic Suite for Algebraic Lattices) category
- based on structured lattices
- design of Kyber has its roots in the LWE-based encryption scheme of **Oded Regev** and the NTRU cryptosystem (Brown Univ, 1996)
  - Team: Joppe Bos (Belgium), Leo Ducas and Peter Schwabe (Netherlands), Eike Kiltz (Germany), T Lepoint (SRI International), **Vadim Lyubashevsky** and Gregor Seiler (IBM, Switzerland), John Schanck (Univ of Waterloo, Canada), Damien Stehle (France)

Post-Quantum Cryptography

Crystals-Dilithium, based on structured lattices

- based on the "Fiat-Shamir with Aborts" technique of Vadim Lyubashevsky (and developed by the same team as the other Crystals)

FALCON, based on structured lattices

- designed by Thomas Prest of PQShield (Oxford Univ spinoff) et al
- based on the 2007 theory of Craig Gentry (Stanford), Chris Peikert (SRI), and Vinod Vaikuntanathan (MIT)
- Vadim Lyubashevsky also contributed to Falcon

SPHINCS+, based on hash functions

- Project leader: Andreas Hülsing, Eindhoven Univ (Netherlands)

Advances in Cryptology – ASIACRYPT 2009 > Conference paper

Fiat-Shamir with Aborts: Applications to Lattice and Factoring-Based Signatures

Vadim Lyubashevsky

Department of Computer Science, Tel-Aviv University

How to Use a Short Basis:
Trapdoors for Hard Lattices and
New Cryptographic Constructions

Craig Gentry* Stanford University | Chris Peikert† SRI International | Vinod Vaikuntanathan‡ MIT

August 25, 2008

The Quantum Internet

The exploitation of entanglement to build quantum-communication networks

Quantum information is stored and delivered via photons

- Feng Pan (Stanford): invisible metamaterials that can be used to store and deliver quantum information

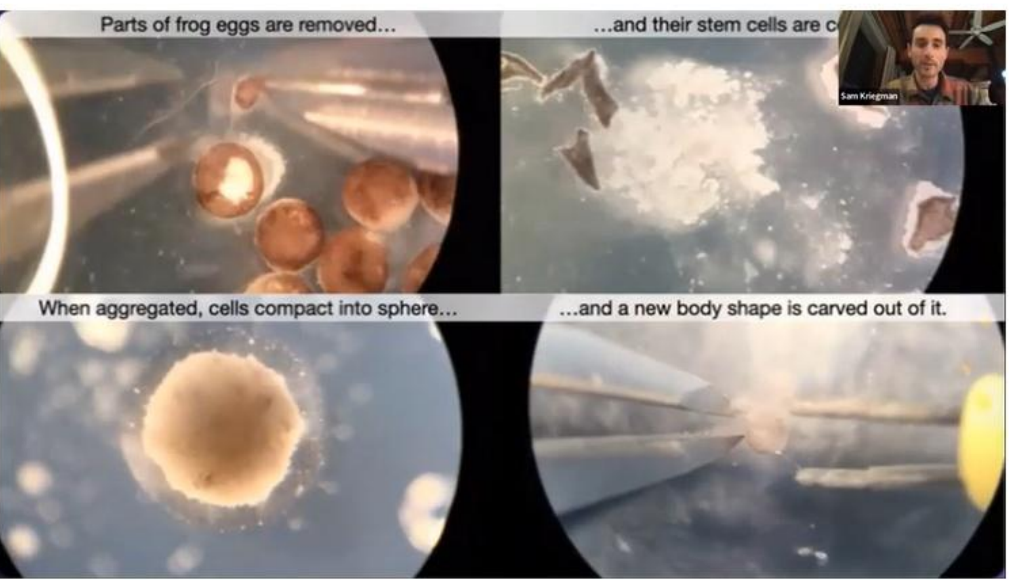
- Mete Atature (Cambridge Univ): hexagonal boron nitride, a two-dimensional material, can be used to store and deliver quantum information at room temperature

- Mikael Afzelius (Univ of Geneva, Switzerland) stores a qubit in a crystal for 20 milliseconds (2022)

New era

Computer-designed Organisms

- Sam Kriegman (Harvard Medical School)
- Josh Bongard (University of Vermont): evolutionary robotics



Immersive Tech

New era

Real-time 3D holography

- Beyond AR/VR

Tensor Holography: Towards Real-time Photorealistic 3D Holography with Deep Neural Networks

Massachusetts Institute of Technology

Nature 2021

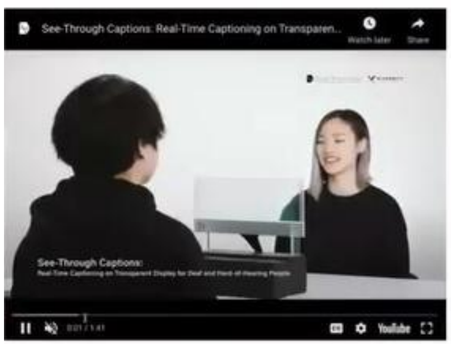
Liang Shi[1,2,✉] Beichen Li[1,2] Changil Kim[1,2] Petr Kellnhofer[1,2] Wojciech Matusik[1,2,✉]

[1]MIT CSAIL [2]MIT EECS ✉Corresponding Author

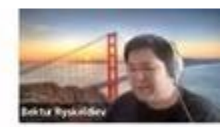
New era

Immersive Media

Bektur Ryskeldiev (Tsukuba Univ, Japan)



K. Yamamoto, et al.. "See-Through Captions: Real-Time Captioning on Transparent Display for Deaf and Hard-of-Hearing People" (2021)



Tonari - Japan-based startup that applies real-time telepresence for natural life-sized communication (2021)

Batteries

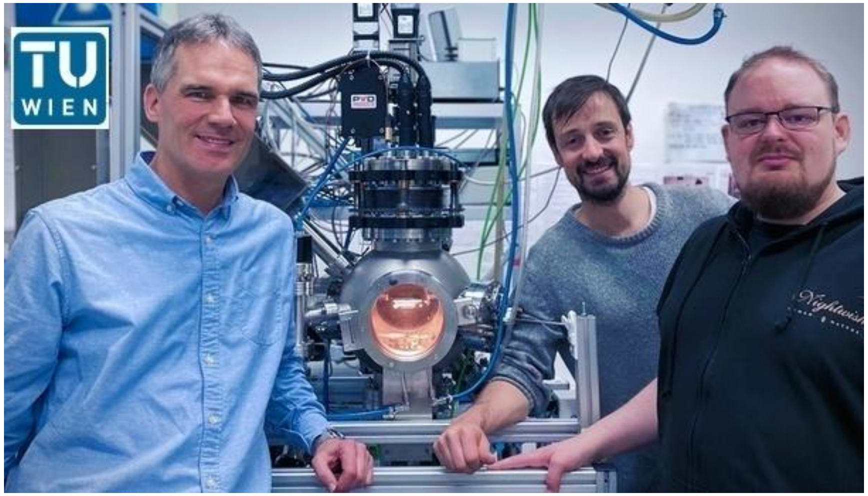
Batteries

- Lyten: lithium-sulfur battery
- QuantumScape: lithium-metal batteries
- Vienna Univ of Technology: The oxygen-ion battery (2023)

LYTEN

Three-dimensional graphene supermaterials.
Giving superpowers to products you use every day.
Creating gigaton scale impact.

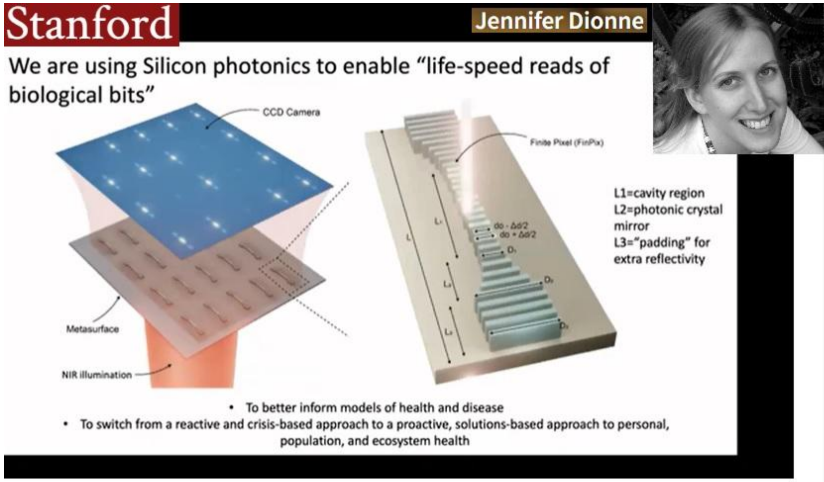
QuantumScape



Biosensors

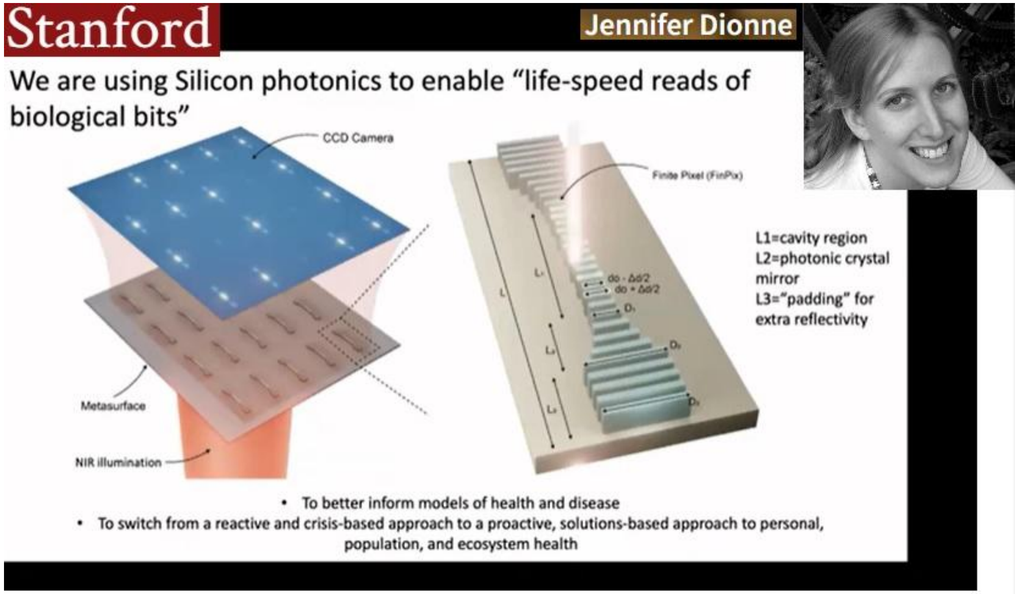
Biosensors

- Startups working on biosensors:
- Sensible Medical and EarlySense in Israel
- Profusa and Ceribell in the Bay Area
- InfoBionic and Glympse Bio in Boston
- Endotronix in Chicago
- Strella in Philadelphia
- Oxford Molecular in Britain
- Lucentix in Switzerland
- The.Wave.Talk in South Korea
- …



Biosensors

- Jennifer Dionne: speed reads of biological information
- Michael Snyder: wearables



Cell-free Systems

Most of synthetic biology relies on cell-based systems: you take a living cell and you introduce new genetic instructions in it

That's why we still don't have low-cost biosensors and the CAR-T cells that could fight cancer

BMC Biology 08 August 2019

Synthetic Biology Goes Cell-Free

Aidan Tinafar, Katariina Jaenes & Keith Pardee

BMC Biology **17**, Article number: 64 (2019) | Cite this article

25k Accesses | **54** Citations | **56** Altmetric | Metrics

Cell-free Systems

In-vitro cell-free systems present an alternative approach to synthetic biology compared with in-vivo cell systems

1961: Cell-free synthesis employed to decipher the genetic code and to establish the “central dogma” of biology (DNA-mRNA-protein)

Cell-free systems engineer an artificial cell with the desired genetic instructions

Most widely used cell-free technology: cell-free protein synthesis (CFPS), an in vitro platform for protein transcription and translation

The artificial cell is a programmable liquid that turns DNA into RNA into protein, just like a regular cell, but it is not a living cell, which also means that it is also “safer” in the human body

Cell-free Systems

A promising technology for just-in-time manufacturing of biologics that cannot be mass-produced

It could democratize access to the machinery of biology by removing the need to engineer cells genetically

Cell-free synthesis has the potential to revolutionize manufacturing like personal computers did for computing

Everything, including vaccines, could be made easier in cell-free systems

And they can be stored at room temperature

Cell-free utopia: a way to manufacture vaccines and biosensors rapidly and in large quantities

Cell-free Systems

- 2017 cell-free biomanufacturing for developing biosensors is demonstrated in Japan

Journal of Bioscience and Bioengineering
Volume 123, Issue 1, January 2017, Pages 96-100

Paper-based colorimetric biosensor for antibiotics inhibiting bacterial protein synthesis

Tran Thi My Duyen [1,2], Hideyuki Matsuura [1], Kazuki Ujiie [1], Misa Muraoka [1], Kazuo Harada [1], Kazumasa Hirata [1]

Cell-free Systems

- 2020: a joint team of Northwestern University and Shanghai Tech University use a cell-free method to make valinomycin – their cell-free approach increases production more than 5,000 times
- Platforms to rapidly produce proteins: Sutro (Bay Area), Arbor (Michigan), Michael Jewett @ Northwestern Univ

Metabolic Engineering
Volume 60, July 2020, Pages 37-44

Total *in vitro* biosynthesis of the nonribosomal macrolactone peptide valinomycin

Lei Zhuang [a] [b] [1], Shuhui Huang [a] [1], Wan-Qiu Liu [a], Ashty S. Karim [c], Michael C. Jewett [c], Jian Li [a]

Messenger RNA Technology

1990: Jon Wolff (Univ of Wisconsin) injects in vitro mRNA into mouse muscle

1990: Katalin Kariko (Univ of Pennsylvania) proposes using mRNA as an alternative to DNA for gene therapy

1995: Robert Conry (Univ of Alabama) designs the first mRNA vaccine

2005: Katalin Kariko' and Drew Weissman publish their research on how to make mRNA vaccines

2008: Ugur Sahin and Ozlem Tureci found BioNTech

2010: Derrick Rossi (Harvard) discovers a method to make mRNA-based gene therapy and founds Moderna

2017: BioNtech's mRNA cancer vaccine based on Kariko's method

2020: Moderna's and BioNtech's covid19 vaccines

BioNTech

Sahin U, Karikó K, Türeci Ö.

Messenger RNA Technology

In theory, we can make mRNA for pretty much any protein, potentially target any infectious disease, and in relatively rapid time (mRNA is easy to edit)

Potentially, mRNA vaccines can encode more one viral protein (as proven by Norbert Pa University of Pennsylvania in 2022)

Utopia: vaccine on demand (a little more reali mRNA)

Or at least a pan-coronavirus vaccine (that wo all coronaviruses and all variants)

Or at least a vaccine that can protect against multiple strains of flu (today it takes months to grow the virus to make the protein used by the flu vaccine, by which time the virus may have already mutated)

Messenger RNA Technology

mRNA can be as a custom-made “vaccine therapeutic” to treat cancer: study the cells of a specific person’s tumor and create a custom-made treatment that would help that individual’s own immune system defeat the cancer – BioNTech-Genentech test trial still underway (Cancer vaccines have been trickier to make, partly because there’s often no clear protein target)

The same technology can be used for new gene therapies to treat inherited disorders like cystic fibrosis and sickle cell anemia

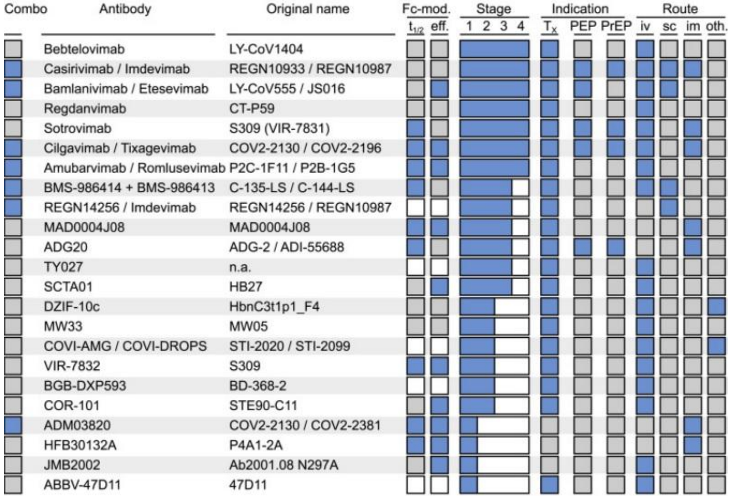
Antibodies

Another path towards a pan-coronavirus vaccine

- Transfer of antibodies has been the leading principle behind the use of convalescent plasma to treat infectious diseases
- But we still know little about antibodies
- Study the antibodies
- Chris Barnes (Stanford): classify the antibodies

Which ones would work on all coronaviruses?

Stanford University



The Rise of A.I.

Medicine

Medscape · 2d

Advanced Imaging Technology Could Help Predict Lung Cancer Progression After Surgery

Advanced imaging technology that uses artificial intelligence (AI) can potentially predict which patients with lung cancer ...

PT Pharmaceutical Technology · 8d

M2GEN partners with Zephyr AI to identify treatments for cancer patients

M2GEN has entered into a multi-year strategic collaboration with Zephyr AI for identifying treatments and cures for cancer ...

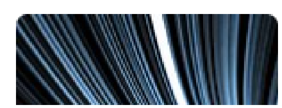
HR Becker's Hospital Review · 1d

AtlantiCare using AI to help diagnose lung cancer

AtlantiCare is using an AI-powered tool to help physicians identify and track patients at risk for lung cancer.

MM&M · 12d

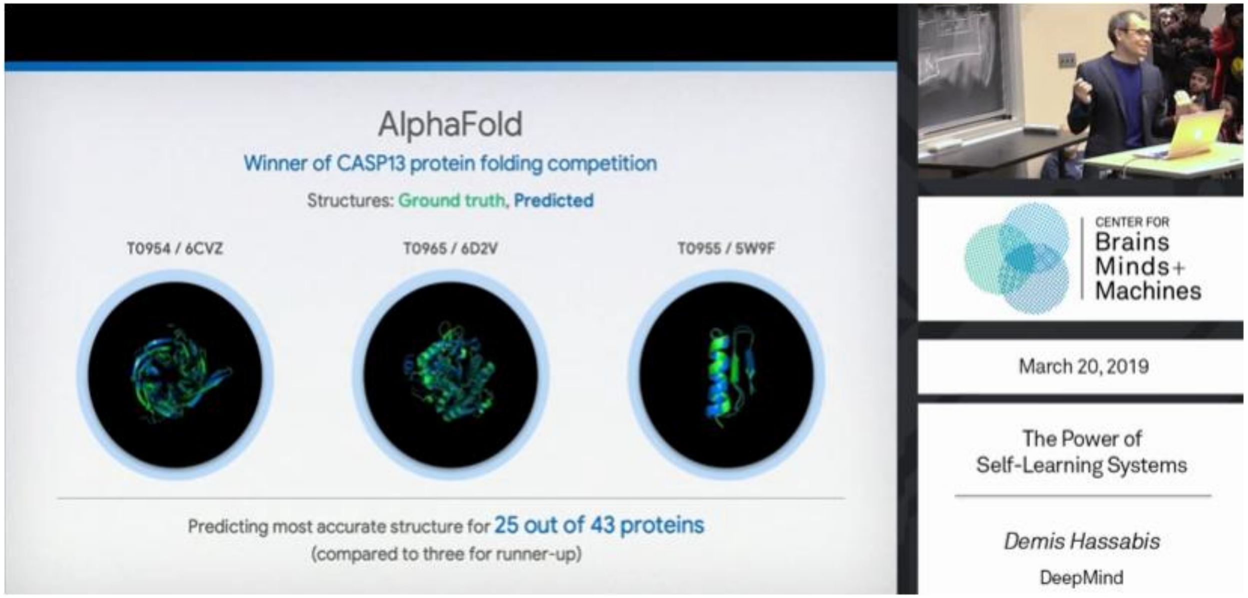
How AI can support the American Cancer Society's



The Rise of A.I.

Scientific Research

- AlphaFold (2018)



The Rise of A.I.

AI for drug discovery

- picking the right target in the body
- designing the right molecule to interact with t
- which patients are more likely to benefit from it

Exscientia (Britain)

Fenerate Buomedicines (Boston)

Absci (Vancouver)

Smart Hospitals

Precision medicine = big data + biotech + wearables + deep learning + robots

How will patients interact with the health-care system?

What kind of training will nurses and physicians require?

Precision Medicine startups

- Tempus (Chicago): the world's largest library of clinical & molecular data
- PerceivAI (Canada): intelligent patient selection
- OncXerna (Boston): AI-based RNA expression biomarker platform
- PreComb (Switzerland): in-vitro cancer drug testing
- AUM (Singapore): biomarker-based drug discovery process to create cancer therapeutics

TEMPUS AI-enabled precision medicine

Bringing the power of data and artificial intelligence to healthcare

perceivAI

Forecasting disease progression

OncXerna THERAPEUTICS

Precision for Patients

PreComb

Functional Personalized Oncology

AUM BIOSCIENCES

Precision. By Design.

A new view of life

Antony Jose (University of Maryland)

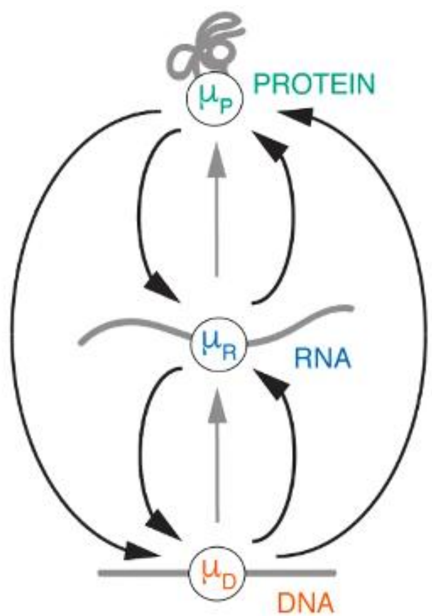
- The DNA does not contain all the information (eg DNA doesn't say where the eye will be)
- Some crucial information is somewhere else
- There is no linear DNA-RNA-Protein flow but a cycle of cycles

JOURNAL OF THE ROYAL SOCIETY INTERFACE

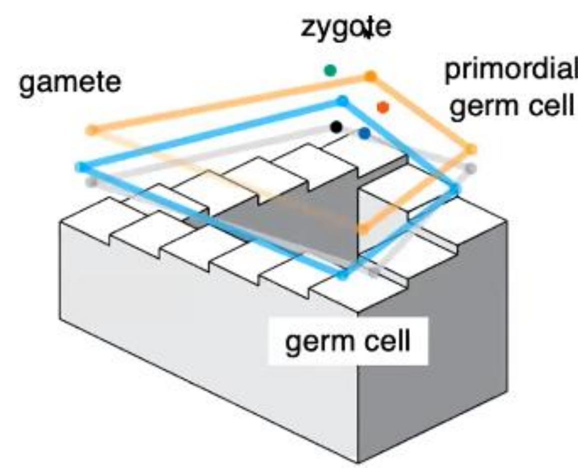
A framework for parsing heritable information

Antony M. Jose

Published: 22 April 2020 https://doi.org/10.1098/rsif.2020.0154



Decentralized Dogma



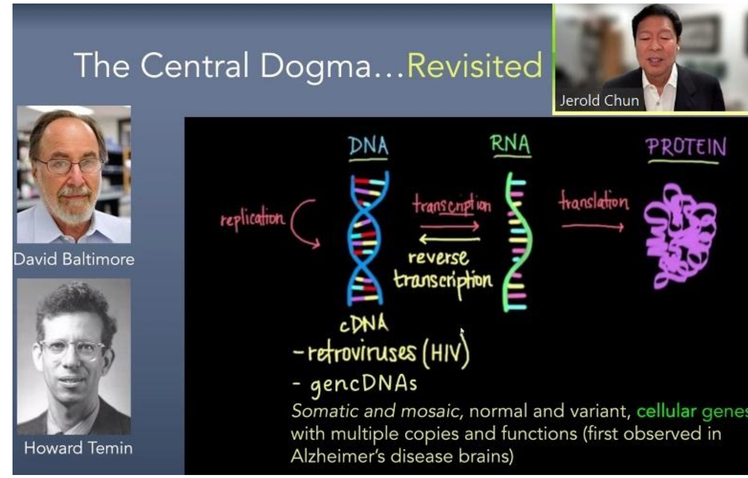
A new view of life

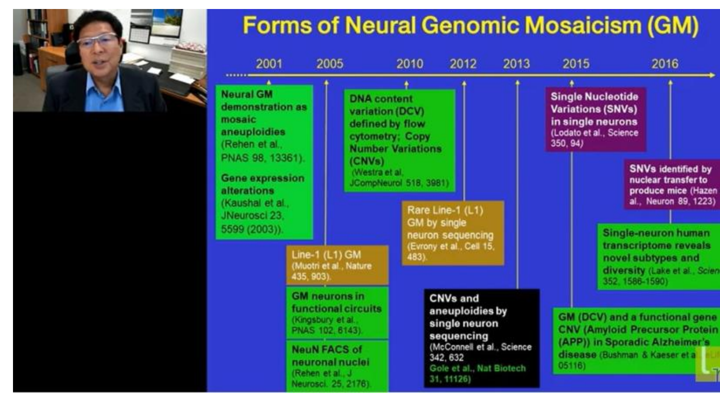
1970 David Baltimore and Howard Temin discover reverse transcriptase, an enzyme that synthesizes DNA from RNA

Genetic mosaicism is widespread

- 1976 Susumu Tonegawa discovers that cells of the immune system contain slightly different genomes that produce useful antibody diversity
- 2001: Jerold Chun shows that not all neurons are genetically alike

Every person contains a multitude of genomes





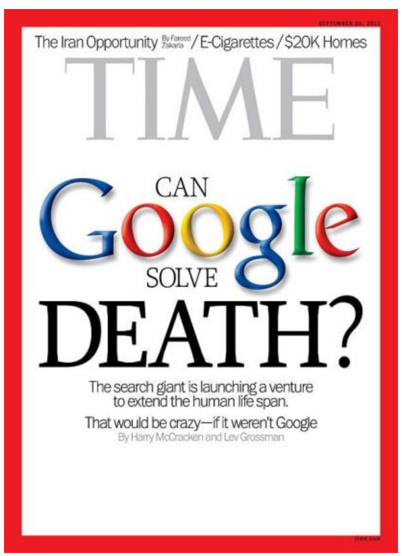
The Science of Longevity

Rapid progress in A.I. + rapid progress in Biotech = A whole new discipline and industry, the discipline of Longevity

Why is hydra immortal?
Why the turritopsis can reverse its life cycle and rejuvinate?
Why did Jeanne Calment live to 122?

The Science of Longevity

- Google’s Calico (South San Francisco, 2013)
- Craig Venter's Human Longevity (San Diego, 2013)



The Science of Longevity

AGEX THERAPEUTICS

UNITY BIOTECHNOLOGY

Insilico Medicine

Elevian

life BIOSCIENCES

BlueRock THERAPEUTICS

biosplice

ALTOS

Calico

JUVENESCENCE

LIFE EXTENSION®

The Science of a Healthier Life™

LONGEVITY VISION FUND

Science of Longevity

- 1999: Lenny Guarente and Cynthia Kenyon found Elixir
- 2004: David Sinclair founds Sirtris
- 2013: Google starts Calico, Craig Venter starts Human Longevity
- October 2020: inaugural Longevity Investors Conference

Science of Longevity

- June 2022: inaugural Gordon Research Conference in Maine
  - Steve Horvath (UCLA)
  - Cynthia Kenyon (Calico)
  - Richard Miller (Univ of Michigan)
  - Inigo Martincorena (Sanger Inst)
  - Joe Betts-LaCroix (Retro)
  - Vittorio Sebastiano (Stanford)
  - Jacob Kimmel (NewLimit)
  - Morgan Levine (Yale Univ)
  - Diljeet Gill (Altos Labs)
  - Emma Teeling (Univ College Dublin)
  - Edward Boyden (MIT)
  - Joris Deelen (Max Planck Inst)
  - Kristen Fortney (Bioage)
  - Nick Schaum (Astera Inst)

Systems Aging
Gordon Research Conference

Systemic Processes, Omics Approaches and Biomarkers in Aging

May 29 - June 3, 2022

Reprogramming Startups

- Retro Biosciences (San Francisco, 2021), funded by billionaire Sam Altman
- New Limit (South San Francisco, 2021) founded by billionaire Brian Armstrong
- Celularity (New Jersey, 2018) founded by billionaire Peter Diamandis
- Altos Labs (Redwood City, 2022), founded by billionaires Jeff Bezos and Yuri Milner
- BioSplice (San Diego - formerly Samumed), founded by billionaire Osman Kibar
- Juvenescence (Ireland), founded by billionaire Jim Mellon

MIT Technology Review March 8, 2023

BIOTECHNOLOGY

Sam Altman invested $180 million into a company trying to delay death

Can anti-aging breakthroughs add 10 healthy years to the human life span? The CEO of OpenAI is paying to find out.

Retro **Retro Biosciences** @RetroBio_

We are Retro Biosciences, a new company with the mission to add 10 years to healthy human lifespan.

Coinbase Billionaire Starts $105 Million Antiaging Company NewLimit
January 2022

NewLimit

ALTOS™

A startup backed by Jeff Bezos and Yuri Milner aims to defy aging and death through cell reprogramming.

· 01/21/22

Biosplice Therapeutics @biosplice

Biosplice is developing first-in-class, small-molecule therapeutics based on pioneering science of alternative pre-mRNA splicing.

JUVENESCENCE

FINANCIAL TIMES AUGUST 18 2019

Juvenescence raises another $100m to invest in longevity

Jim Mellon, the investor who chairs Juvenescence, has persuaded other billionaires to buy into his vision of making money by extending healthy life through science.

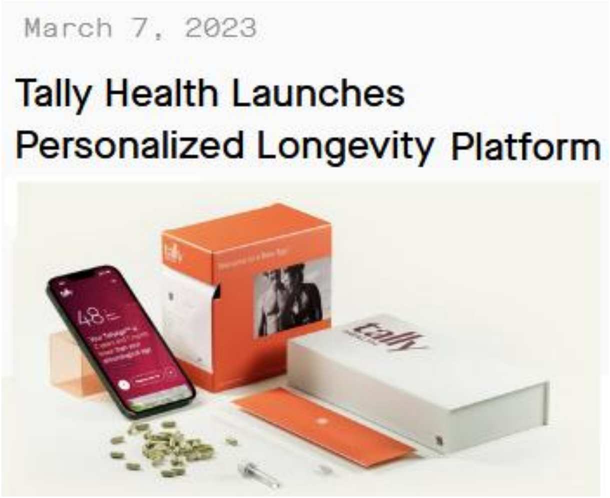
Reprogramming Startups

- Unity Biotechnology (South San Francisco, 2011)
- Insilico (New York, 2014) - Alex Zhavoronkov
- Longeveron (Miami, 2014)
- BioAge (Richmond, 2015) – Kristen Fortney (Stanford)
- CyteGen (Wisconsin, 2015)
- Elevian (Boston, 2015) - Amy Wagers (Harvard)
- Life Biosciences (Boston, 2017) - David Sinclair (Harvard)
- Shift Bioscience (Britain, 2017)
- Agex Therapeutics (Alameda, 2017) - Michael West
- Rubedo (Sunnyvale, 2018) - Marco Quarta
- Gerostate Alpha (Novato, 2018)
- Samsara Therapeutics (Germany, 2018)
- Fountain Therapeutics (South San Francisco, 2018) -Tom Rando
- Rejuveron (Switzerland, 2019)

Science of Longevity

Platforms to enhance longevity

- 318,000 health apps…
- Tally Health (Australia), founded by David Sinclair and Melanie Goldey (2023)
- Longevity AI
- etc



Science of Longevity

Aging cells

- telomere shortening
- genetic instability
- epigenetic alteration
- accumulation of misfolded proteins

Science of Longevity

Increasing consensus that biological aging can be reversed: (systemic) rejuvination

- Shinya Yamanaka reprogramming factors (2006): four transcription factors that can reprogram an adult cell into a pluripotent embryonic-like cell
- David Sinclair (Harvard): mice regain eyesight (2020), first major reprogramming success

DNA methylation clocks: powerful tools to identify potential rejuvenation therapies

Science of Longevity

Problem with reprogramming: cells lose their original identity

Diljeet Gill (Babraham Inst): “transient reprogramming” method to express Yamanaka factors for short period of time, thus achieving rejuvenation without loss of cell identity (2022)

Babraham Institute

Aging Clocks

Quantifying “aging”: the “aging clock”, an indicator of overall health, a predictor of longevity

- Biological rather than chronological age
- Many factors contribute to aging
- There is no single universal biomarker to estimate overall health status and longevity prospects
- An estimate of biological age and the pace of aging requires a combination of biomarkers: genome instability, telomere length,DNA methylation

Aging Clocks

Epigenetic clocks are based on changes over time in DNA methylation

- Gregory Hannum (UCSD): first epigenetic aging clock (2012)
- Steve Horvath (2013): DNAmAge, first widely used epigenetic clock

First generation : able to predict chronological age, but not very useful for biological age

UC San Diego

UCLA

Aging Clocks

- Epigenetic clocks: second-generation two-step clocks, designed to measure biological age
- Morgan Levine (Yale Univ) & Steve Horvath (UCLA): PhenoAge, a clock based on nine biomarkers (2018)
- Steve Horvath (UCLA): GrimAge (2018)
- Steve Horvath (UCLA): pan-mammalian clocks for 128 species (2021)
- Jonathan Mill (Univ of Exeter): first human brain-specific clock (2020)

Impact Journals: AGING Open-Access Impact Journal on Aging

2018 Apr; 10(4): 573–591

An epigenetic biomarker of aging for lifespan and healthspan

Morgan E. Levine,[1] Ake T. Lu,[1] Austin Quach,[1] Brian H. Chen,[2] Th[illegible] L. Assimes,[3] Stefania Bandinelli,[4] Lifang Hou,[5] Ar[illegible]ccarelli,[6] James D. Stewart,[7] Yun Li,[8] Er[illegible]l,[7,9] James G Wilson,[10] Alex P Reiner,[11] Abraham Aviv,[12] Kurt Lohman,[12] Yongmei Liu,[14] Luigi Ferrucci,[2,*] and Steve Horvath[1,15,*]

UCLA

DNA methylation GrimAge strongly predicts lifespan and healthspan

Ake T. Lu[1], Austin Quach[1], James G. Wilson[2], Alex P. Reiner[3], Abraham Aviv[4], Kenneth Raj[5], Lifang Hou[6], Andrea A. Baccarelli[7], Yun Li[8], James D. Stewart[9], Eric A. Whitsel[9,10], Themistocles L. Assimes[11,12], Luigi Ferrucci[13], Steve Horvath[1,14]

University of California Los Angeles August 24, 2018

Aging Clocks

Transcriptomic aging clocks, clocks that read the biological age of an organism directly from its gene expression, the transcriptome

- Marjolein Peters (Erasmus Medical Centre, 2015): first transcriptomic aging clock
- Björn Schumacher (Univ of Cologne, 2021): BiT clock

Erasmus MC

Aging Clocks

Deep age predictors use deep learning

- Alex Zhavoronkov (founder of Insilico): first DNN-based aging clock (2016)

Insilico Medicine

Aging Clocks

A clock of clocks for each cell type

Matthew Buckley & Eric Sun (Stanford, 2022): focus on the neurogenic region located in the subventricular zone (SVZ) of the adult mammalian brain which contains at least 11 different cell types correlated with tissue decay, i.e. a clock of 11 cell type-specific "aging" clocks

Cell type-specific aging clocks to quantify aging and rejuvenation in regenerative regions of the brain 2022.01.10.

Matthew T. Buckley[1,2,17], Eric Sun[1,3,17],
Tony Wyss-Coray[14,15,16], Thomas A. Rando[6,13,16], Anne Brunet[1,15,16,*]

Stanford University

Matthew Buckley

Cofounder
Retro Biosciences, USA

Aging Clocks

Commercial products

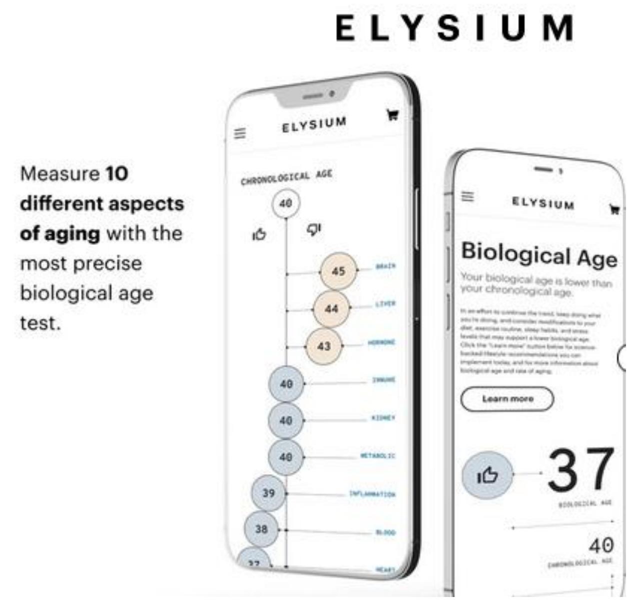
- Zymo (San Diego): myDNAge
- Elysium Health (New York): biological aging test

ZYMO RESEARCH

The Beauty of Science is to Make Things Simple®

Epigenetic Age Analysis Service

The Most Accurate Biological Age Quantification Service



Science of Longevity

- Methuselah Foundation (Virginia)
- Sheba Longevity Center (Israel, 2023)
- BioAge Labs (Bay Area)
- Craig Venter's Human Longevity (San Diego)
- Lifespan.io (New York)

HUMAN LONGEVITY

Methuselah Foundation

We incubate and sponsor mission-relevant ventures, fund research, and support projects and prizes to accelerate breakthroughs in longevity.

SHEBA LONGEVITY
Longer. Better. Life

Lifespan.io   *March 3, 2023*

This hospital intends to bring longevity medicine into clinical practice.

Science of Longevity

- Tom Rando (Stanford): heterochronic parabiosis regenerates tissue in old mice (2005)
- Tony Wyss-Coray & Saul Villeda (Stanford): blood from young organisms can rejuvenate old brains (2014)
- Therapeutic potential of young blood and oom of blood transfusion startups (Ambrosia)
- Unfortunately, no benefits from young blood
- Irina Conboy (2019):
  - Old blood drastically decreases cognitive faculties in young mice
  - Young blood has no cognitive benefits for old mice

Stanford University

Nat Med. 2014 Jun;20(6):659-63. doi: 10.1038/nm.3569. Epub 2014 May 4.

Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice

Saul A Villeda [1], Kristopher E Plambeck [2], Jinte Middeldorp [3], Joseph M Castellano [3], Kira I Mosher [4], Jian Luo [5], Lucas K Smith [6], Gregor Bieri [7], Karin Lin [8], Daniela Berdnik [5], Rafael Wabl [5], Joe Udeochu [9], Elizabeth G Wheatley [10], Bende Zou [11], Danielle A Simmons [5], Xinmin S Xie [11], Frank M Longo [5], Tony Wyss-Coray [12]

Science of Longevity

- Lee Rubin (Harvard): young blood seems to restore gene expression patterns to a more youthful state depending on cell types (2022)
- Teal Omics (Boston): proteins found in the blood provide powerful insights into the body's functional state, biological age, and risk of disease (2021)

Heterochronic parabiosis reprograms the mouse brain transcriptome by shifting aging signatures in multiple cell types

Methodios Ximerakis, Kristina M. Holton, Richard M. Giadone, Ceren Ozek, Monika Saxena, Samara Santiago, Xian Adiconis, Danielle Dionne, Lan Nguyen, Kavya M. Shah, Jill M. Goldstein, Caterina Gasperini, Scott L. Lipnick, Sean K. Simmons, Sean M. Buchanan, Amy J. Wagers, Aviv Regev, Joshua Z. Levin, Lee L. Rubin

doi: https://doi.org/10.1101/2022.01.27.477911

Science of Longevity

- Gary Steinberg (Stanford): mesenchymal stem cells or MSCs (harvested from the bone marrow of adults), when injected into the brains of stroke patients, restore motor functions (2016)
- MSCs have the potential to repair numerous kinds of tissue damages (Arnold Caplan, 1991)
- MSC treatment speeds up healing of wounds (2010)
- MSCs control tissue regeneration and therefore MSC treatment could lead to full regeneration (e.g. hair regrowth)
- More promising than MSCs: human neural stem cells NR1, derived from the embryonic stem cell line H9 (2021)

Stanford University

Science of Longevity

- APstem (Fremont, 2017): Adult Pluripotent Stem Cells (APSCs)
- Advantages: regenerate neurons, angiogenesis, immune compatibility
- APSCs from a single donor can treat more than 200,000 patients, enabling large-scale manufacture

	APSCs	Embryonic stem cells (ESCs)	Adult stem cells (HSCs, MSCs)	Induced pluripotent stem cells (iPSCs)
Able to form most/all tissues	Yes	Yes	No	Yes
Differentiation efficiency	High	Low	Medium	Low
Ability to isolate and expand	Easy	Difficult	Difficult	Medium
Immunological compatibility	High	Conditional	Low	Conditional
Tumorigenicity risk	No	Yes	No	Yes

Science of Longevity

- Shyu's research group previously demonstrated peripheral blood-derived stem-cell (PBSC) transplant efficacy in treating chronic ischemia in rats (Shyu et al., 2006)

Science of Longevity

- Saul Villeda (Stanford): exercise too restores youthful function in old cells (2022)
- Patrick Liu (Northwestern Univ): exercise fosters hippocampal neurogenesis, i.e. neurons are generated and incorporated into hippocampal circuits (2018)
- Exercise's benefits: restoration of cognitive functions, improvement of synaptic plasticity, formation of new blood vessels/ angiogenesis (important for wound healing)
- Exercise rejuvenates oligodendrocyte clocks (2022)

Stanford University

> Science. 2020 Jul 10;369(6500):167-173.

Blood factors transfer beneficial effects of exercise on neurogenesis and cognition to the aged brain

Alana M Horowitz [#, 1, 2], Xuelai Fan [#, 1], Gregor Bieri [1], Lucas K Smith [1, 2], Cesar I Sanchez-Diaz [1], Adam B Schroer [1], Geraldine Gontier [1], Kaitlin B Casaletto [3, 4], Joel H Kramer [3, 4], Katherine E Williams [5], Saul A Villeda [6, 2, 7, 8]

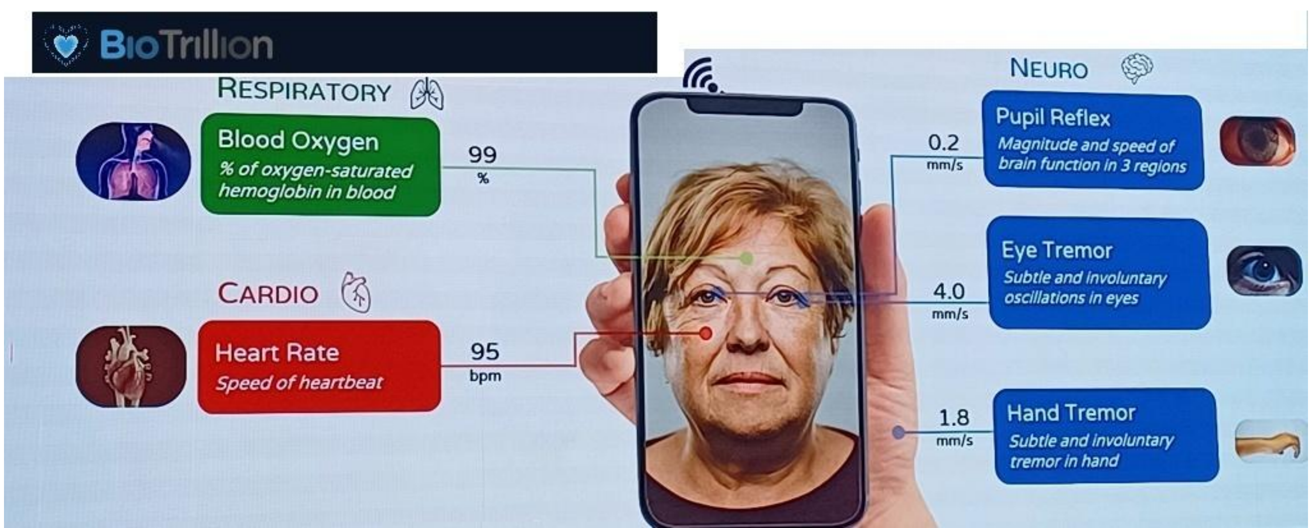
Revolution in Diagnostics

- Liquid biopsy startups:
  - Grail (Menlo Park)- Funding: $2B
  - Guardant Health (Redwood City) - $0.5B
  - Freenome (San Francisco) $1.1B
  - Scipher Medicine (Boston)
  - EverlyWell (Austin, Texas)
  - T2 Biosystems (Boston)
  - Epic Sciences (San Diego)
  - Karius (Redwood City)

Revolution in Diagnostics

The Health Selfie

- Haut AI (Estonia): PhotoAgeClock age predictor (2018)
- Eyes and face contain more embedded information about your health than any other visible area of the body
- BioTrillion (San Francisco): a ten-second selfie video can measure several biomarkers (2023)



Revolution in Medicine

Ultra-long-acting therapeutics

Lyndra (Boston) commercializing the technology developed at MIT by Robert Langer

Exavir (Nebraska)

Next-generation Sequencing

- 2004: Roche GS20, the first next-generation sequencing platform
- 2014: Illumina's HiSeq X Ten Sequencer
- 2022: Ultima Genomics' $100 whole-genome sequencing

Many rare diseases are not fully diagnosed due to the short-read methods

Third-generation sequencing:

- Pacific Bioscience (similar to Illumina but long reads)
- Oxford Nanopore (alpha-hemolysin instead of DNA polymerases): portable and long reads

Next-generation Sequencing

- Oxford Nanopore


NANOPORE

Oxford Nanopore and NVIDIA collaborate to partner the DGX AI compute system with ultra-high throughput PromethION sequencer

Tue 12th January 2021

Gene Editing

- TALEN method (2011) - Dan Voytas (Univ of Minnesota) & Adam Bogdanove (Iowa State Univ)
- CRISPR method (2012) - Jennifer Doudna (UC Berkeley) & Emmanuelle Charpentier (Umeå Univ, Sweden), Feng Zhang (Broad Inst)
- 2016: Boom of CRISPR startups

BROAD INSTITUTE

Gene Editing

- Faster better CRISPR
  - Theo Roth (UCSF, 2018)

GEN Genetic Engineering & Biotechnology News

July 12, 2018

Nonviral CRISPR Technology Developed for Faster, Cheaper T-Cell Engineering

Reprogramming human T cell function and specificity with non-viral genome targeting

Theodore L. Roth[1,2,3,4,5], Cristina Puig-Saus[6], Ruby Yu[3,4,5], Eric Shifrut[3,4,5], Julia Carnevale[7], P. Jonathan Li[3,4,5], Joseph Hiatt[1,2,3,4,5], Justin Saco[6], Paige Krystofinski[6], Han Li[8,9], Victoria Tobin[3,4,5], David N. Nguyen[3,4,5], Michael R. Lee[4], Amy L. Putnam[4], Andrea L. Ferris[10], Jeff W. Chen[11], Jean-Nicolas Schickel[11], Laurence Pellerin[12,13], David Carmody[14], Gorka Alkorta-Aranburu[15], Daniela del Gaudio[15], Hiroyuki Matsumoto[16], Montse Morell[16], Ying Mao[16], Min Cho[17], Rolen M. Quadros[18], Channabasavaiah B. Gurumurthy[18], Baz Smith[16], Michael Haugwitz[16], Stephen H. Hughes[10,11], Jonathan S. Weissman[8,9], Kathrin Schumann[3,4,5], Jonathan H. Esensten[19], Andrew P. May[17], Alan Ashworth[7], Gary M. Kupfer[20], Siri Atma W. Greeley[14], Rosa Bacchetta[12,13], Eric Meffre[11], Maria Grazia Roncarolo[12,13], Neil Romberg[21,22], Kevan C. Herold[23], Antoni Ribas[6,24,25,26], Manuel D. Leonetti[8,9,28] & Alexander Marson[3,4,5,7,17,27*]

UCSF

Beyond Gene Editing

- David Liu (Harvard, 2016): base editing (editing the single letters of DNA)
- Feng Zhang (MIT, 2017): using CRISPR to edit RNA (which carries DNA's instructions to make proteins)

Base Pairing Rules

	Replication	Transcription	Step in Translation
DNA	DNA	mRNA	tRNA
A	T	A	U
C	G	C	G
G	C	G	C
T	A	U	A

nature 19 May 2016

Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage

Alexis Komor

David R. Liu

Science 25 Oct 2017

RNA editing with CRISPR-Cas13

David B. T. Cox

Feng Zhang

Broad Institute of MIT

Gene Editing

- Shoukhrat Mitalipov repairs a genetic mutation in human embryos (2017)

Scientists edit human embryos for first time in tl
Axios - Jul 28, 2017
Shoukhrat Mitalipov of Oregon Health and Science Unive
reportedly used the gene-editing technique CRISPR to ch

Scientists edit disease-causing gene mutation in
KNWA - Aug 2, 2017
Shoukhrat Mitalipov, director of the Oregon Health & Scie
for Embryonic Cell and Gene Therapy, helped lead the ne

American scientists use CRISPR to modify huma
MIMS General News (Hong Kong) (registration) (blog) - J
Dr **Shoukhrat Mitalipov** of Oregon Health and Science Un
that edited the DNA of viable human embryos. Photo cre

Gene Therapy

2017: First gene therapy for cancer treatment approved in the USA

Regenerative Medicine

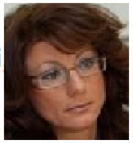
- A starfish and salamander can regenerate a limb
- Gene therapy + stem-cell research:
  - 2017: Michele DeLuca combines stem-cell techniques with gene therapy to create artificial skin to cure a skin disease

nature
International journal of science
Nature **551**, 327–332 (16 November 2017)

Regeneration of the entire human epidermis using transgenic stem cells

UNIMORE

Graziella Pellegrini



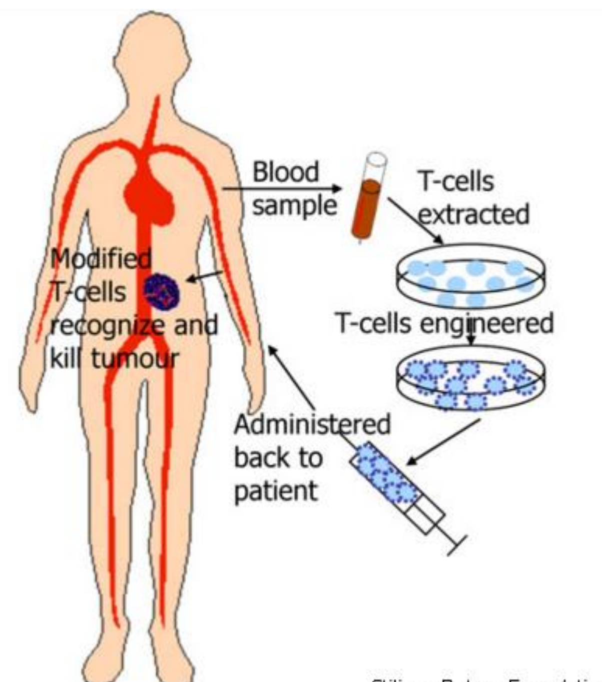
Michele De Luca

Tobias Hirsch, Tobias Rothoeft, Norbert Teig, Johann W. Bauer, Graziella Pellegrini, Laura De Rosa, Davide Scaglione, Julia Reichelt, Alfred Klausegger, Daniela Kneisz, Oriana Romano, Alessia Secone Seconetti, Roberta Contin, Elena Enzo, Irena Jurman, Sonia Carulli, Frank Jacobsen, Thomas Luecke, Marcus Lehnhardt, Meike Fischer, Maximilian Kueckelhaus, Daniela Quaglino, Michele Morgante, Silvio Bicciato, Sergio Bondanza & Michele De Luca - Show fewer authors

Nature **551**, 327–332 (16 November 2017)

Immune Therapy

- To improve the immune system
- T cells: immune cells that identify other cells infected by a virus or cancer
- CAR-T cells: genetically engineered T-cells to fight cancer
- 2017: first T-cell therapy approved by FDA (Carl June's CTL019, marketed as Kymriah by Novartis)



Stiliyan Petrov Foundation
http://www.thestiliyanpetrovfoundation.com/cart-t-cell.html

NOVARTIS AUG 30, 2017

Novartis receives first ever FDA approval for a CAR-T cell therapy, Kymriah(TM) (CTL019), for children and young adults with B-cell ALL that is refractory or has relapsed at least twice

Penn

Carl June

Immune Therapy

- CAR-T in 2017: Kite, Juno, Bluebird, Celectis

STAT

Gilead agrees to buy Kite Pharma, leaping into CAR-T cancer therapy

AUGUST 28, 2017

MarketWatch

After news of Gilead Sciences Inc.'s **GILD, +0.05%** about $11 billion acquisition of Kite Pharma Inc. **KITE, +0.03%** Juno Therapeutics Inc. **JUNO, +1.57%** shares surged 16.3%, Bluebird Bio Inc. **BLUE, +4.81%** shares surged 9.7% and Cellectis SA ADR **CLLS, +11.89%** shares surged 11.8% in extremely heavy midday trade Monday.

Juno, Bluebird and Cellectis are other biotech companies working in CAR-T.

Designer Babies

- Two ways to create human stem cells
  - Shinya Yamanaka (2006)
  - Shoukhrat Mitalipov (2013)
- Katsuhiko Hayashi & Mitinori Saitou (2015): IVG on mice - we can make eggs and sperm from skin cells

九州大学
KYUSHU UNIVERSITY

Designer Babies

- Mitinori Saitou (2018)

Science
REPORT
Science 20 Sep 2018

Generation of human oogonia from induced pluripotent stem cells in vitro

Chika Yamashiro[1,2], Kotaro Sasaki[1,2], Yukihiro Yabuta[1,2], Yoji Kojima[1,2,3,4], Tomonori Nakamura[1,2], Ikuhiro Okamoto[1,2], Shihori Yokobayashi[1,2,4], Yusuke Murase[1,2], Yukiko Ishikura[1,2], Kenjiro Shirane[5,6], Hiroyuki Sasaki[5,6], Takuya Yamamoto[3,4,7], Mitinori Saitou[1,2,3,4,*]

iCeMS
KYOTO UNIVERSITY
WPI Research Center
Institute for Integrated Cell-Material Sciences
Kyoto University
Institute for Advanced Study

Gene Editing

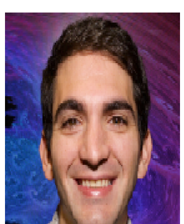
- CRISPR (2012)
- Prime Editing (October 2019)

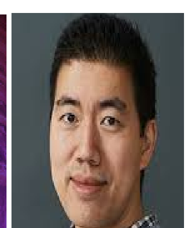
nature
International journal of science

21 OCTOBER 2019

Search-and-replace genome editing without double-strand breaks or donor DNA

Andrew V. Anzalone, Peyton B. Randolph, Jessie R. Davis, Alexander A. Sousa, Luke W. Koblan, Jonathan M. Levy, Peter J. Chen, Christopher Wilson, Gregory A. Newby, Aditya Raguram & David R. Liu





BROAD
INSTITUTE

Precision Medicine startups

- Tempus (Chicago): the world's largest library of clinical & molecular data
- PerceivAI (Canada): intelligent patient selection
- OncXerna (Boston): AI-based RNA expression biomarker platform
- PreComb (Switzerland): in-vitro cancer drug testing
- AUM (Singapore): biomarker-based drug discovery process to create cancer therapeutics

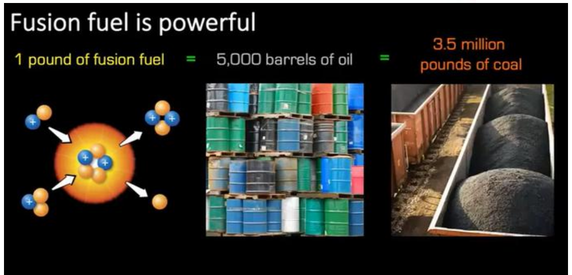
Nuclear Fusion

Nuclear Fusion

Many approaches

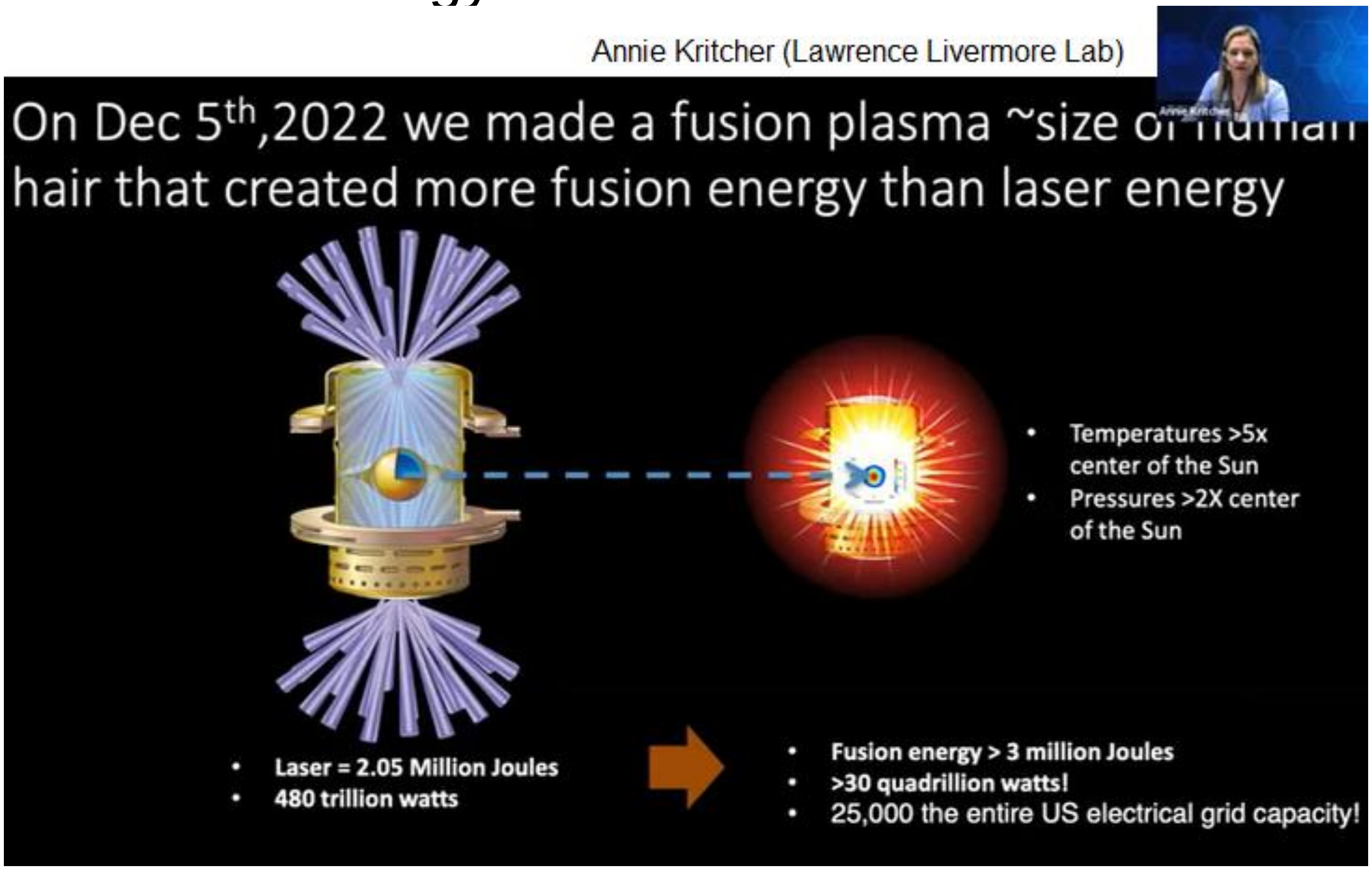
2021: Sam Altman Invests in Helion

2022: Google invests in TAE



Nuclear Fusion

2022: Lawrence Livermore Lab (National Ignition Facility) produces more energy than the lasers used



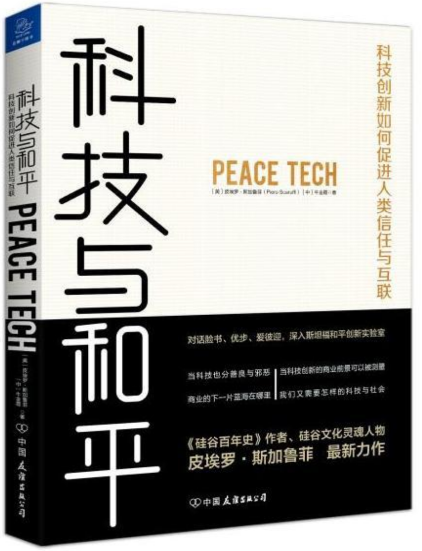
Peace Tech

Peace Tech

A new economy driven by “positive engagement”

Technologies to increase cooperation

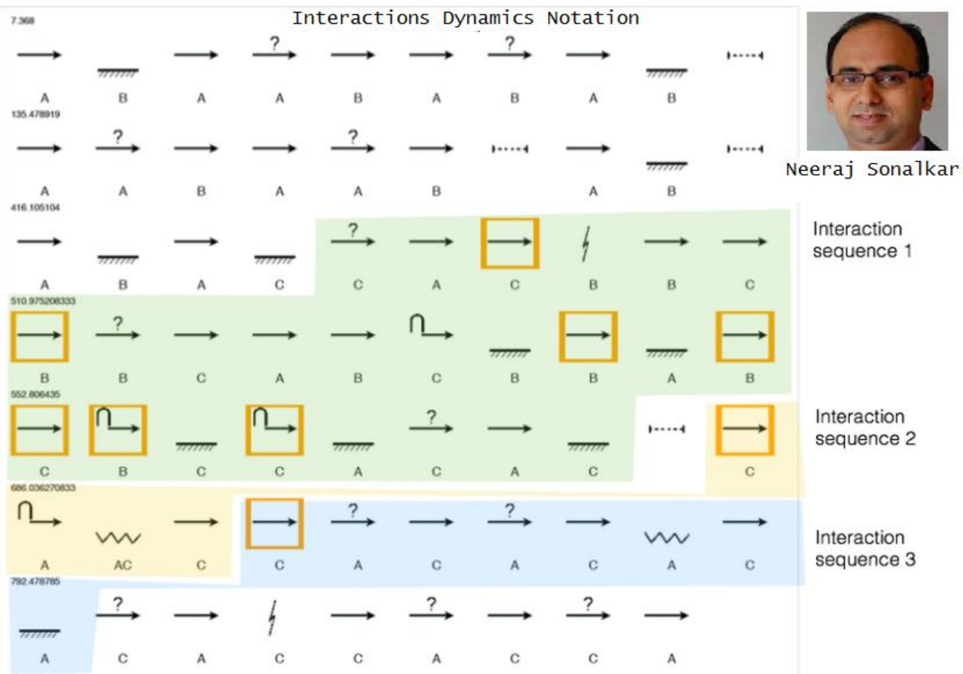
“Smart” cities become engines of creation

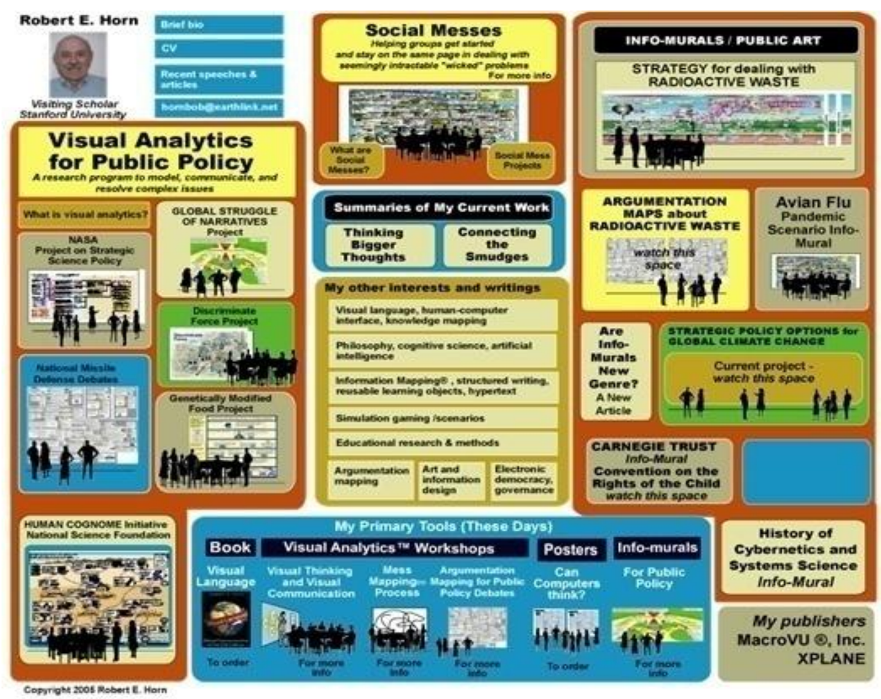


PEACE INNOVATION LAB

Stanford University

Peace Tech


Interactions Dynamics Notation
Neeraj Sonalkar
Interaction sequence 1
Interaction sequence 2
Interaction sequence 3


Robert E. Horn
Visiting Scholar Stanford University
Brief bio
CV
Recent speeches & articles
Social Messes
Helping groups get started and stay on the same page in dealing with seemingly intractable "wicked" problems
INFO-MURALS / PUBLIC ART
STRATEGY for dealing with RADIOACTIVE WASTE
Visual Analytics for Public Policy
A research program to model, communicate, and resolve complex issues
What is visual analytics?
GLOBAL STRUGGLE OF NARRATIVES Project
NASA Project on Strategic Science Policy
Discriminate Force Project
National Missile Defense Debates
Genetically Modified Food Project
Summaries of My Current Work
Thinking Bigger Thoughts
Connecting the Smudges
My other interests and writings
Visual language, human-computer interface, knowledge mapping
Philosophy, cognitive science, artificial intelligence
Simulation gaming /scenarios
Educational research & methods
Argumentation mapping
Art and information design
Electronic democracy, governance
ARGUMENTATION MAPS about RADIOACTIVE WASTE
watch this space
Avian Flu Pandemic Scenario Info-Mural
Are Info-Murals New Genre? A New Article
STRATEGIC POLICY OPTIONS for GLOBAL CLIMATE CHANGE
Current project - watch this space
CARNEGIE TRUST Info-Mural Convention on the Rights of the Child watch this space
HUMAN COGNOME Initiative National Science Foundation
My Primary Tools (These Days)
Book
Visual Analytics™ Workshops
Posters
Info-murals
Visual Language
Can Computers think?
For Public Policy
History of Cybernetics and Systems Science Info-Mural
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Peace Technology

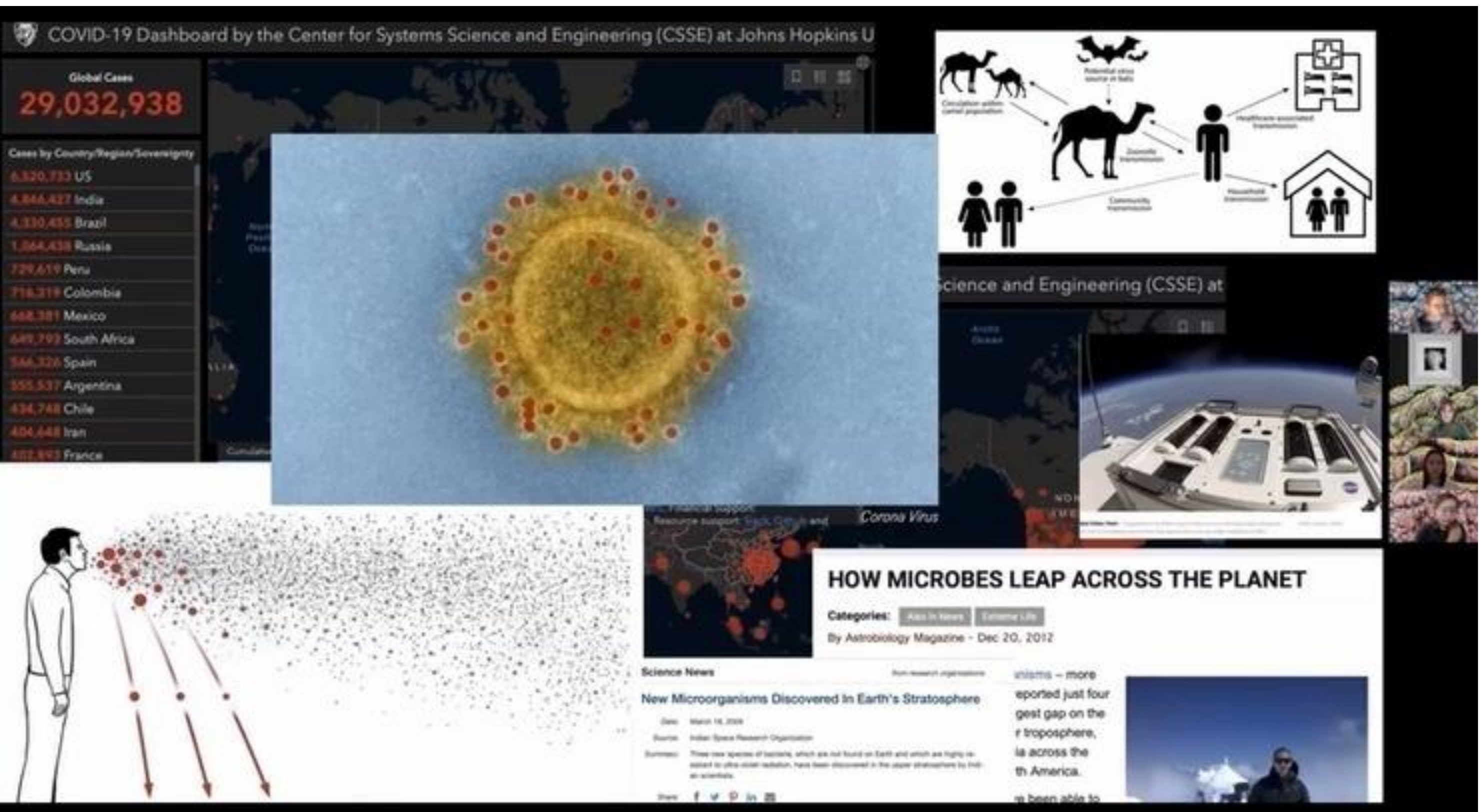
A new economy driven by “positive engagement”

Art & New Tech

You can find the videos of my conversations with these artists/inventors on YouTube

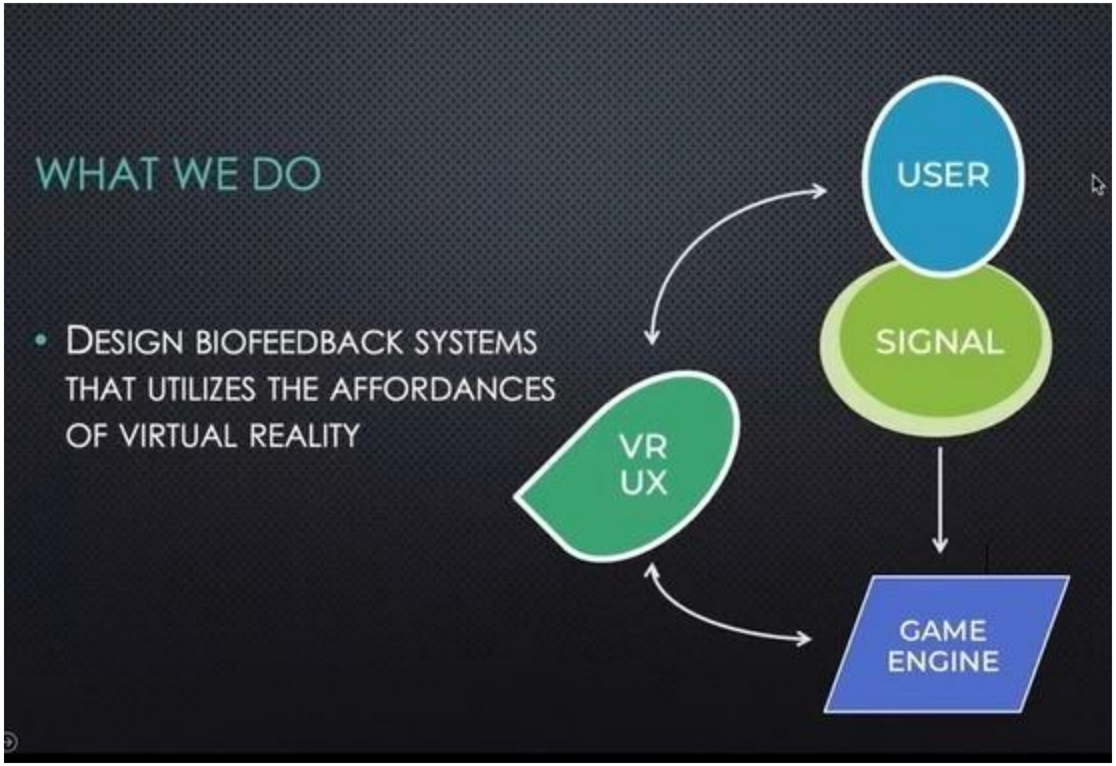
Art & New Tech

Anastasia Raina (Rhode Island School of Design) on "Microbial Cosmologies“



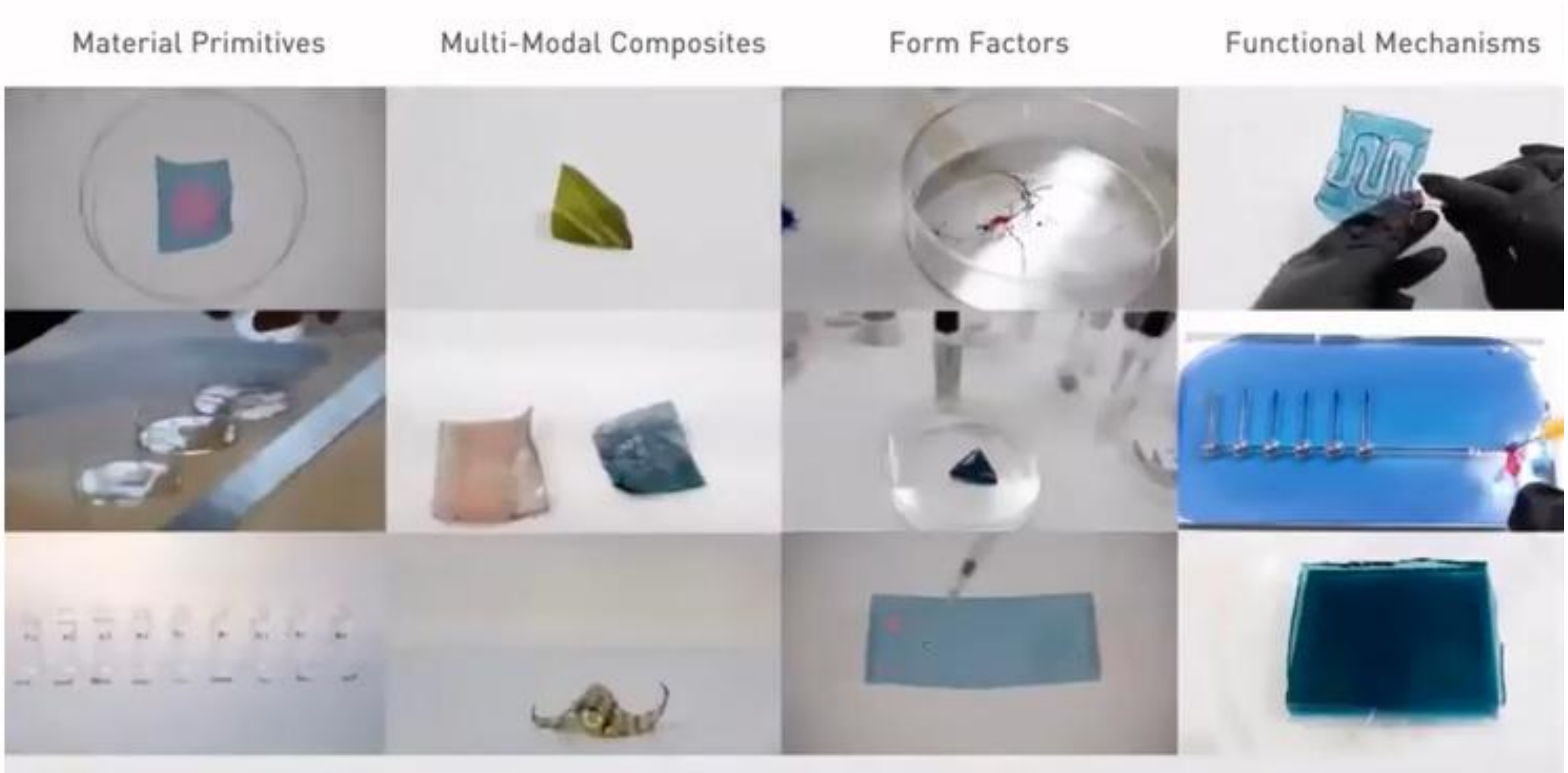
Art & New Tech

Julia Scott (Santa Clara Univ) on "Biofeedback Integration into immersive Virtual Reality Experiences"



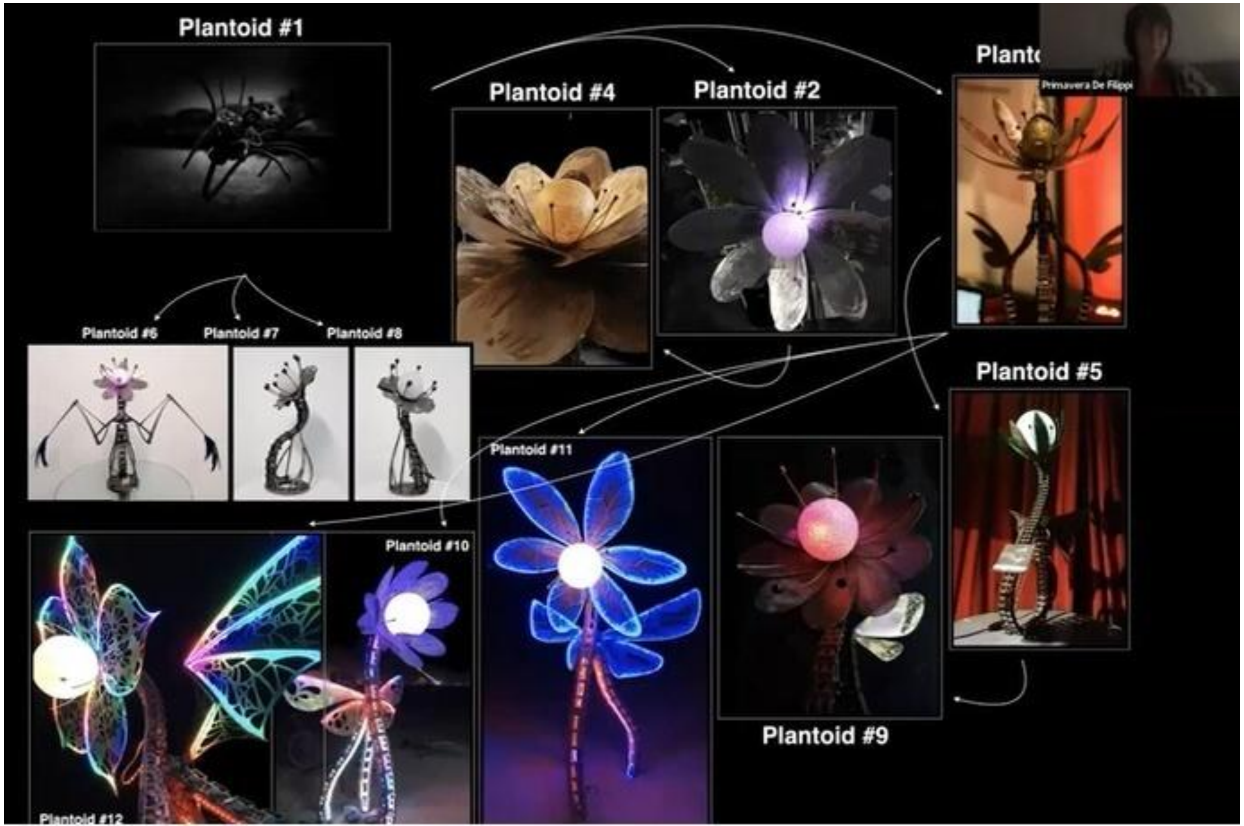
Art & New Tech

Virj Kan (Design Scientist) on "Molecular Design Interactions"



Art & New Tech

Primavera De Filippi (National Center of Scientific Research, Paris) on "Do blockchains dream of electronic flowers?"



Art & New Tech

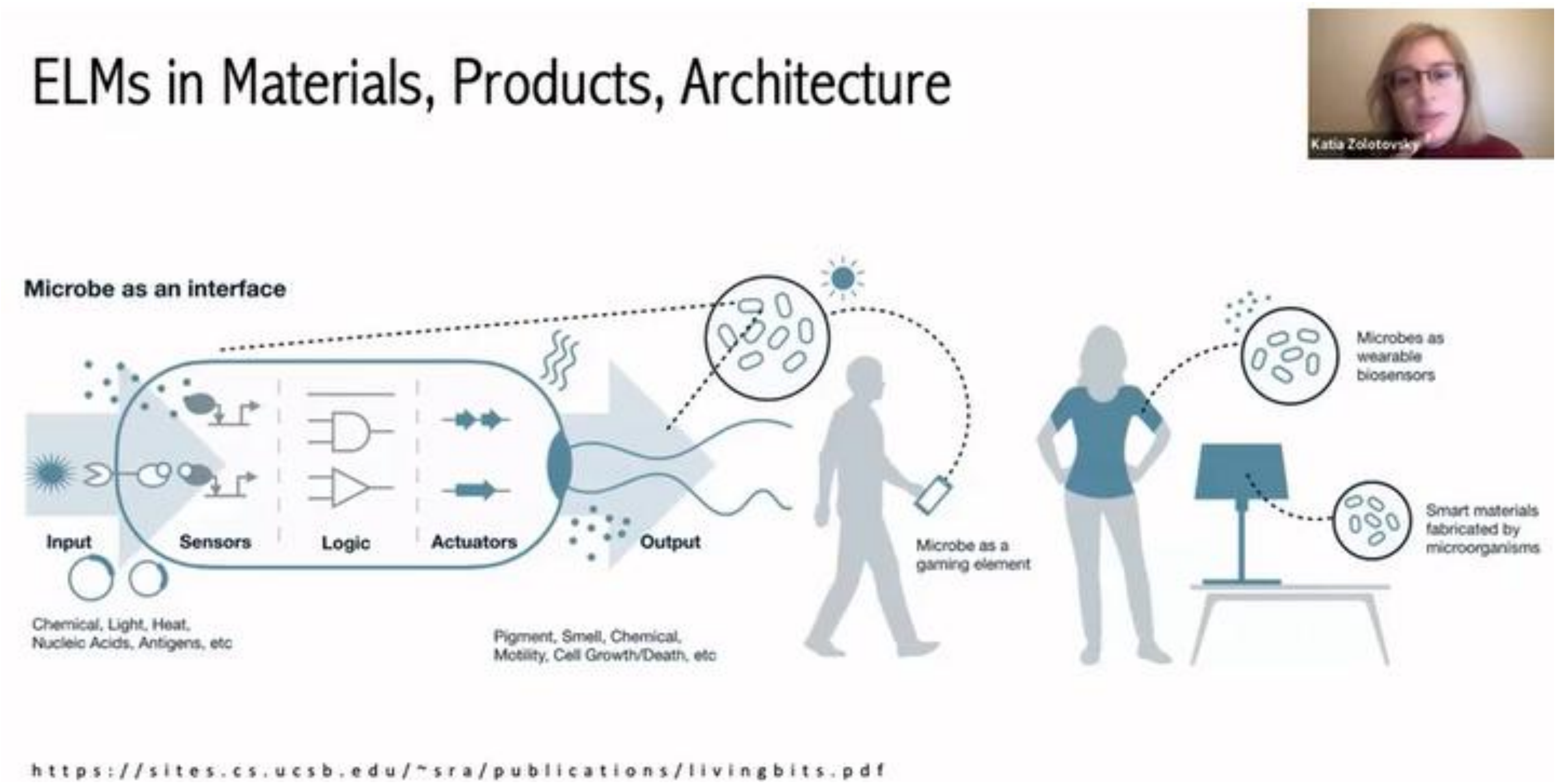
Laura Splan (Media Artist) on "Recursive Residues: Navigating Interfaces Between Virtual and Biological Worlds"

Art & New Tech

Sargeant, Betty (Media Artist) on "The Art of Collaboration: Decolonising Digital Landscapes" (video)

Art & New Tech

Zolotovsky, Katia (RISD) on "Spatial design with Engineered Living Materials"

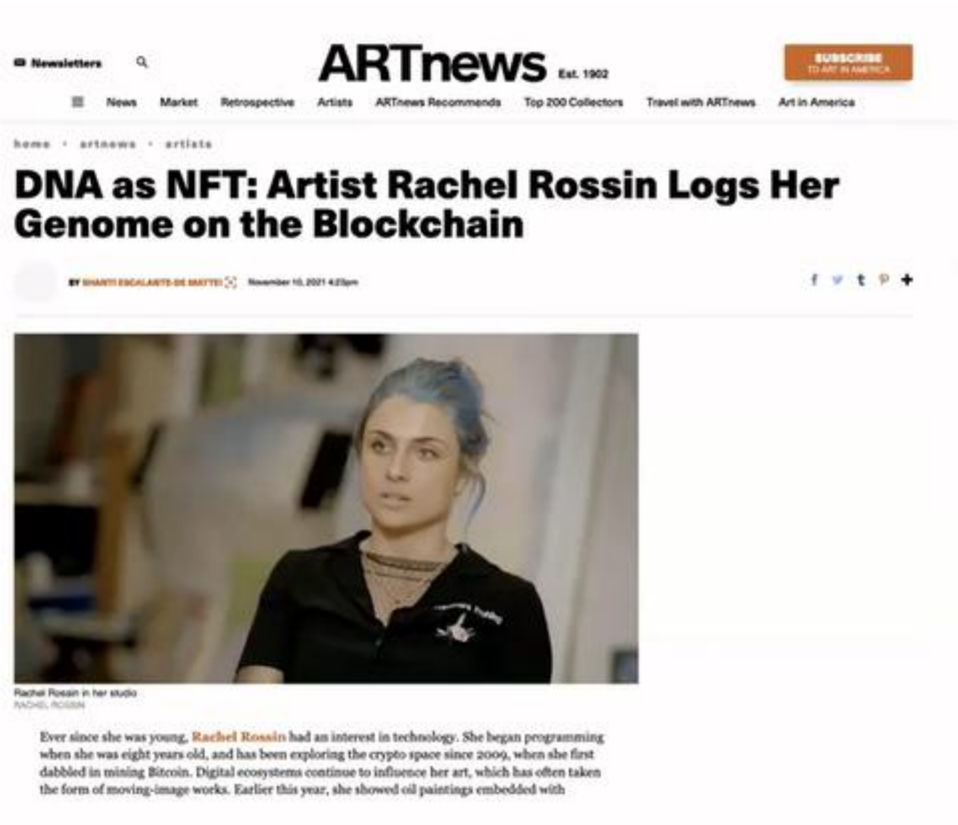


Art & New Tech

Lily Xiying Yang (Media Artist) on "Creativity and Activism in Extended Reality" (video)

Art & New Tech

Rachel Rossin (Media Artist) on "On Proxies: the vocabulary of art in the age of virtual and crypto cultures"


Newsletters

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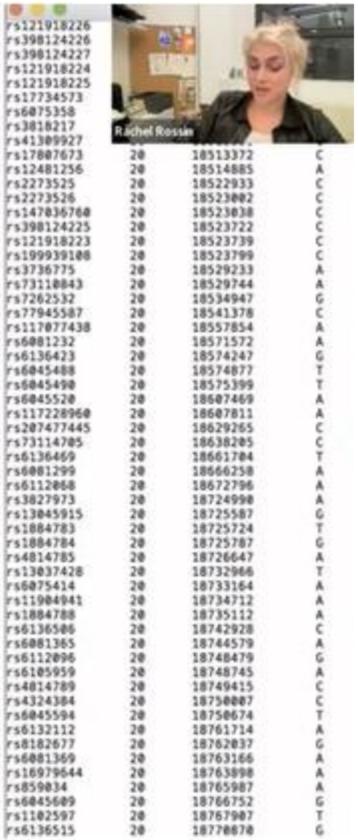
DNA as NFT: Artist Rachel Rossin Logs Her Genome on the Blockchain

November 10, 2021

Rachel Rossin in her studio
RACHEL ROSSIN

Ever since she was young, Rachel Rossin had an interest in technology. She began programming when she was eight years old, and has been exploring the crypto space since 2009, when she first dabbled in mining Bitcoin. Digital ecosystems continue to influence her art, which has often taken the form of moving-image works. Earlier this year, she showed oil paintings embedded with



Art & New Tech

Kat Mustatea (Playwright & Technologist) on "Augmented Reality and the Decaying Book"

Art & New Tech

Jessica Angel (Media Artist) on "Integrated Immersive Experiences as Doors to the Metaverse"

Art & New Tech

Sarah Friend (Cryptoartist) on "Systems as Fictions"

Art & New Tech

Amelia Winger-Bearskin (Univ. of Florida) on "Visual Storytelling with Bleeding-edge Technologies"

Art & New Tech

Alex Reben (Inventor and Artist)

Art & New Tech

Kal Spelletich (Roboticist and Artist)

china

Case study: China

US innovation didn't start with Silicon Valley

- Thomas Edison (phonegraph)
- Alexander Graham Bell (telephone)
- Henry Ford (assembly line)
- Robert Fulton (steamboat)
- Cyrus McCormick (mechanical reaper)
- Samuel Morse (telegraph)
- Jonas Salk (polio vaccine)
- Eli Whitney (cotton gin)
- Orville & Wilbur Wright (airplane)
- Philo Farnsworth (television)
- Nikola Tesla (alternating current)
- George Eastman (camera film)

US innovation is built into its social and political system

Immigrants

Case study: China (how to convince scientists and engineers NOT to immigrate to your country)

- Most social media are banned
- Even the #1 search engine is banned
- No rule of law (you can get arrested anytime)
- Censorship
- No dual citizenship (Taiwan allows it)

Result: “brain drain” of Chinese scientists, engineers, intellectuals, artists, etc to the West

The other major country that failed to attract immigrants: Japan (shortage of engineers, steady decline)

Cultural Creativity

The cultural background of the Bay Area is a mix of art, music, literature, politics, engineering and science…

A little bit like China's Song dynasty!

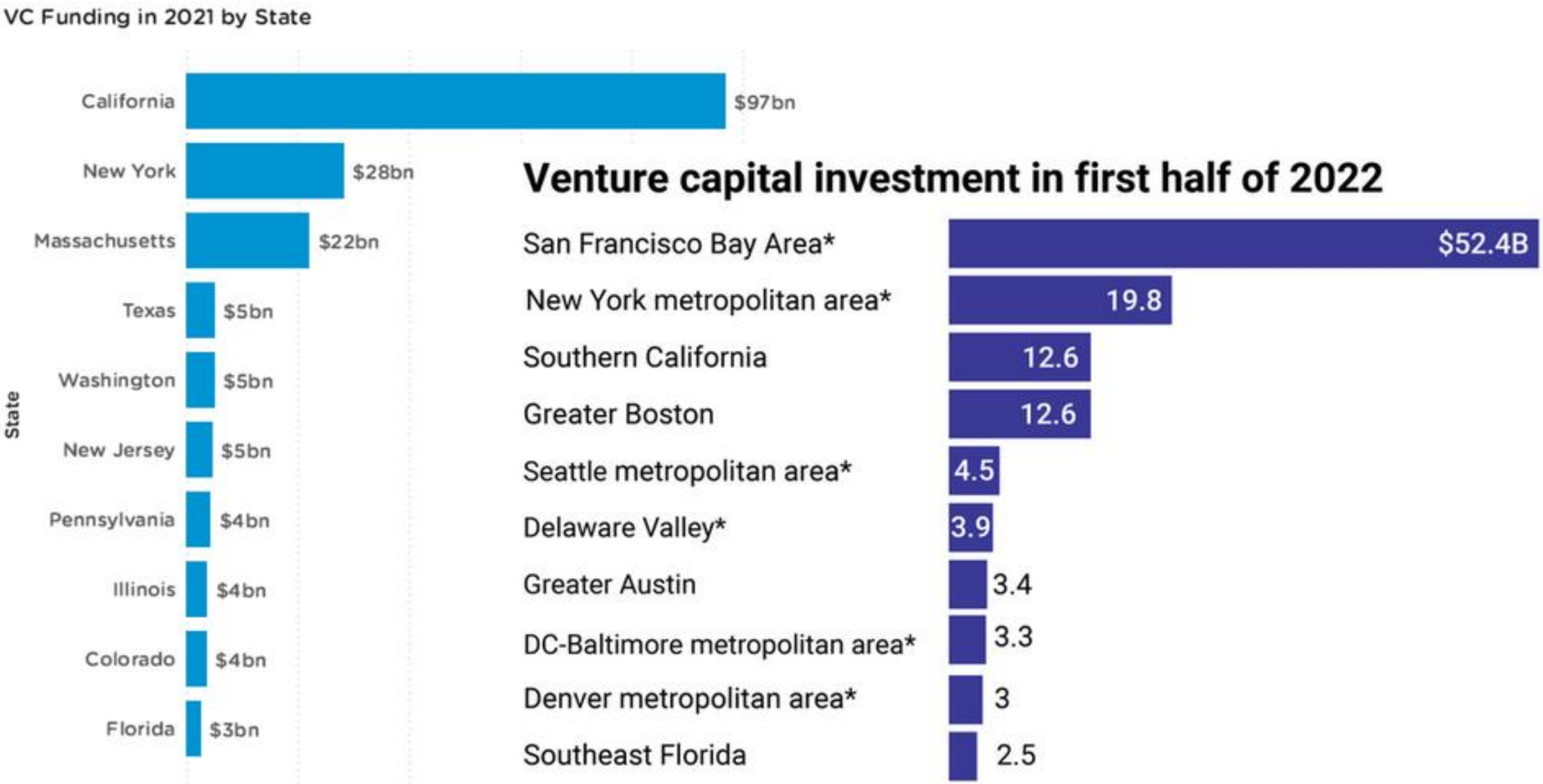
Shen Kuo

Su Song

Su Shi

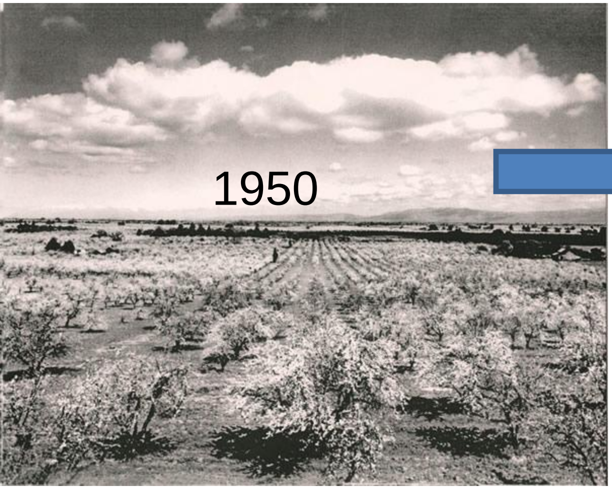
Ouyang Xiu

Silicon Valley 2022



Silicon Valley in 1950

Today

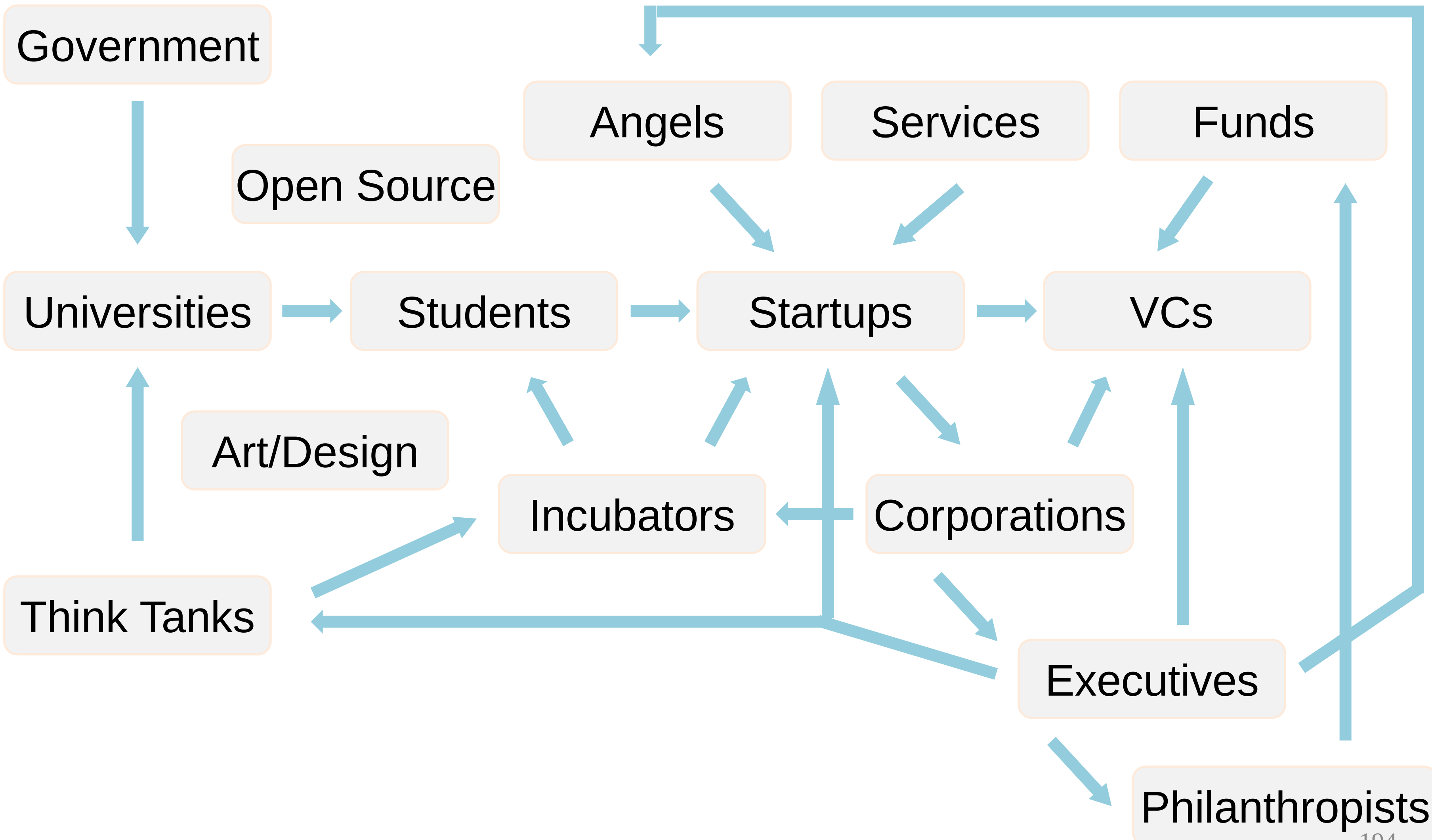

1950


AUTODESK
Berkeley
UNIVERSITY OF CALIFORNIA
zymergen
Oakland
Mt Diablo
Diablo
Tassajara
Golden
Recreation
Area
WIKIPEDIA
OpenAI
zynga
San Francisco
Alameda
airbnb
UBER
San Leandro
LinkedIn
Daly City
Hayward
Pleasanton
Genentech
Pacifica
GoPro
GILEAD
Sunol
TESLA
ROBLOX
ORACLE
Fremont
Don Edwards
San Francisco
Bay National
El Granada
23andMe
Half
Moon Bay
PayPal
zoom
Stanford
University
Palo Alto
NVIDIA
intel
Milpitas
hp
Google
vmware
Lobitos
SILICON
VALLEY
cisco
San Jose

Why Silicon Valley?

- The technology, the money and the brains were on the East Coast and in Europe
- The great universities were on the East Coast (MIT, Harvard, Moore School, Princeton, Columbia), and in Europe (Cambridge, Oxford)
- Great electronic labs: Bell Labs, RCA Labs, IBM Labs(East Coast)
- France, Britain and Germany won most of the Nobels in physics

How Silicon Valley works



Why Silicon Valley?

- What Silicon Valley does best
  - Not invented here: computer, transistor, integrated circuit, robots, Artificial Intelligence, programming languages, databases, videogames, Internet, personal computers, World-wide web, search engines, social media, smartphones, wearable computing, space exploration, electrical cars, driverless cars…

Trivia: Who invented What

Transistor: New Jersey (1947)
Programmable computer: England (1948)
Neural Network: Boston (1954)
Transistor radio: Japan (1954)
Integrated circuit: Texas (1958)
Artificial Intelligence: Boston (1956)
Robot: Detroit (1961)
Database: New York (1961)
Computer graphics: Boston (1963)
Internet: Boston (1969)
Virtual Reality: Utah (1969)
Pocket calculator: Japan (1970)
Email: Boston (1972)
Personal computer: New Mexico (1974)
DNA sequencing: England (1977)
Portable music player: Japan (1979)
CD: Japan (1982)
Camcorder: Japan (1982)

Flash memory: Japan (1984)
E-commerce: Boston (1983)
Mobile phone: Arizona (1984)
3D printing: Los Angeles (1988)
Digital camera: Japan (1988)
Search engine: Montreal (1990)
World-wide web: Switzerland (1991)
Wearable computing: Boston (1993)
Self-driving car: Germany (1994)
QR code: Japan (1994)
Gene editing: New York (1994)
Smartphone: Finland (1996)
DVD player: Japan (1996)
Hybrid car: Japan (1997)
Social media: New York (1997)
Mobile payment: Japan (2004)
Blockchain: Florida (2008)

Why Silicon Valley?

- What Silicon Valley does best
  - Invented here: disrupting products

Silicon Valley takes inventions and turns them into disruptive technologies

OpenAI

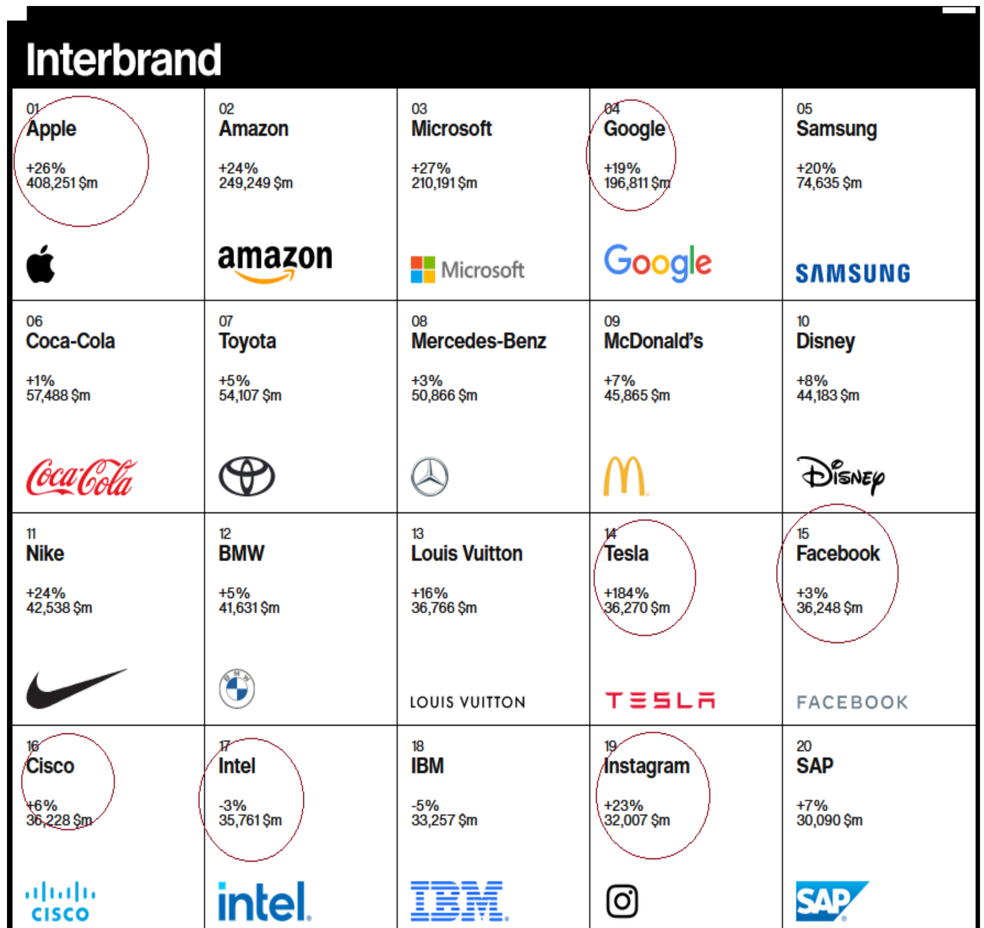
Silicon Valley is a State of Mind

The largest companies in the world by revenues (2022)

1	Walmart	WMT	$611.28 B
2	Saudi Aramco	2222.SR	$552.25 B
3	Amazon	AMZN	$513.98 B
4	Sinopec	600028.SS	$480.86 B
5	PetroChina	601857.SS	$480.69 B
6	Exxon Mobil	XOM	$398.67 B
7	Apple	AAPL	$387.53 B
8	Shell	SHEL	$381.31 B
9	CVS Health	CVS	$322.46 B
10	UnitedHealth	UNH	$322.13 B

Silicon Valley is a State of Mind

Silicon Valley specializes in “global brand value”

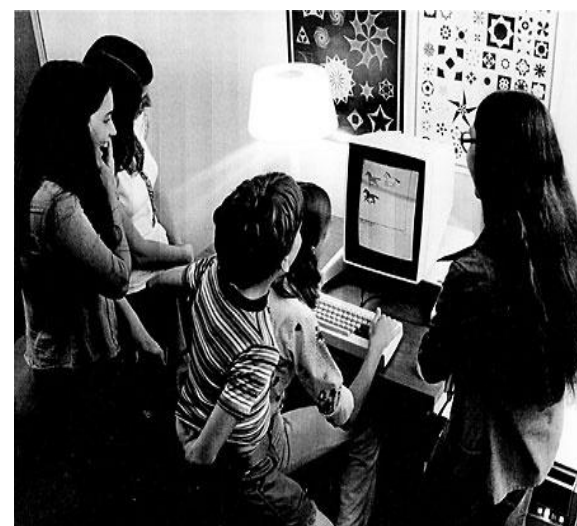


Interbrand

01 Apple +26% 408,251 $m	02 Amazon +24% 249,249 $m	03 Microsoft +27% 210,191 $m	04 Google +19% 196,811 $m	05 Samsung +20% 74,635 $m
06 Coca-Cola +1% 57,488 $m	07 Toyota +5% 54,107 $m	08 Mercedes-Benz +3% 50,866 $m	09 McDonald’s +7% 45,865 $m	10 Disney +8% 44,183 $m
11 Nike +24% 42,538 $m	12 BMW +5% 41,631 $m	13 Louis Vuitton +16% 36,766 $m	14 Tesla +184% 36,270 $m	15 Facebook +3% 36,248 $m
16 Cisco +6% 36,228 $m	17 Intel -3% 35,761 $m	18 IBM -5% 33,257 $m	19 Instagram +23% 32,007 $m	20 SAP +7% 30,090 $m

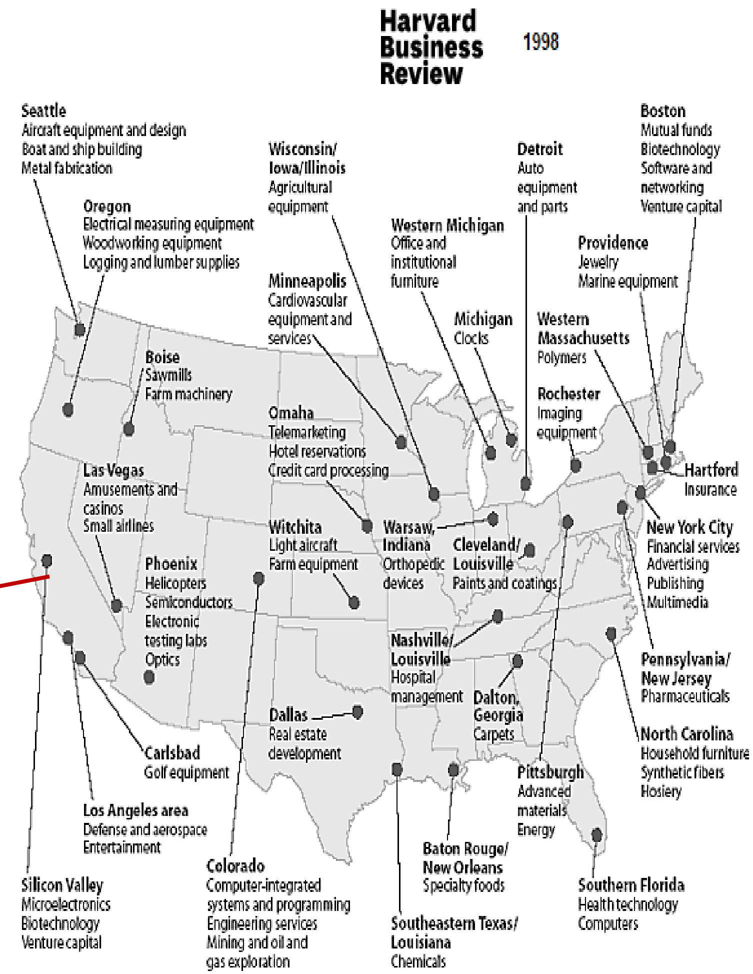
Silicon Valley is a State of Mind

- For example, Xerox PARC disrupting the computer industry with the desktop compute



A cluster of clusters

- The ability to excel in so many different technologies: no cluster!
- A cluster of clusters, a virtual cluster
- The ability to create world leaders in so many fields in such a short tin



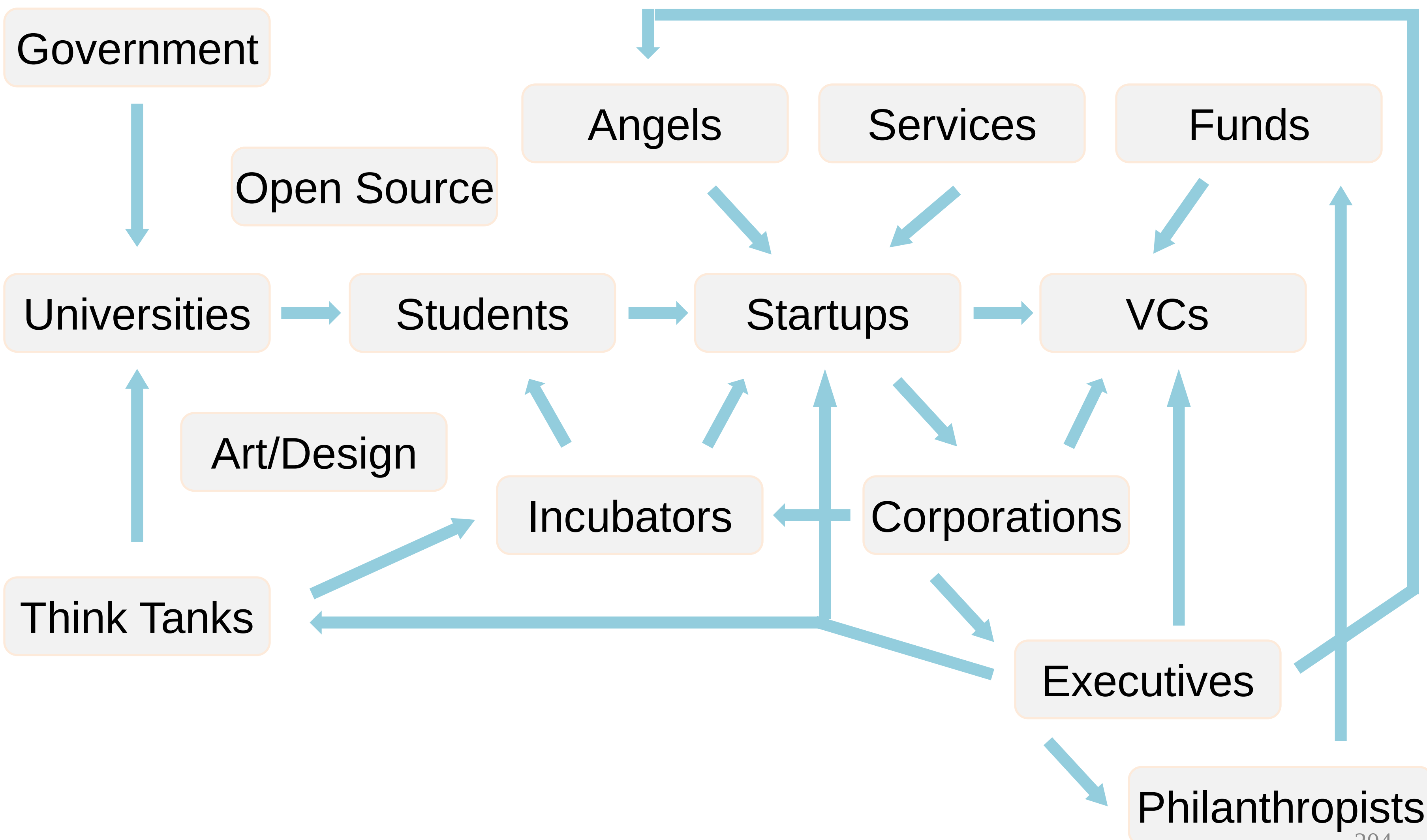
A cluster of clusters

- Is the Bay Area a “cluster”?
  - Talent mobility across borders
  - Venture capital can attract talents from anywhere
  - And talent attracts venture capital
  - The geographical location is no longer a big advantage
  - Access to capital and talent is the key to creating clusters
  - The Bay Area attracts capital and talent

A cluster of clusters

- A virtual cluster is far more complex than the traditional industrial cluster
- A virtual cluster needs an unlimited supply of new ideas, of capital and of talents in order to churn out a large number of startups in all sorts of fielc

Many places have replicated this…



… but it is not enough

What is really special?

- Small, not big
- Open source
- Immigrants
- Interdisciplinary thinking
- Moonshot projects
- Culture of failure

What is really special?

Innovation that came from big companies:

What is really special?

Innovation that came from small companies

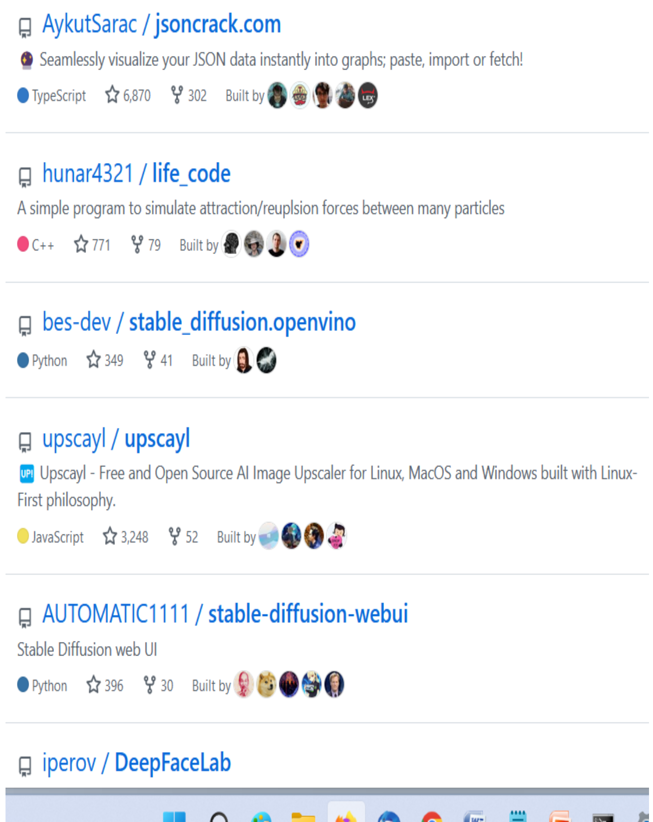
- Integrated circuit (Fairchild)
- Microprocessor (Intel)
- Unix server (SUN)
- GUI (Apple)
- SQL Database (Oracle)
- Networking switches (Cisco)
- Biotech (Genentech)
- Ecommerce (eBay)
- Search engine (Google)
- Online payment (Paypal)
- Social network (Facebook, Twitter)
- Sharing economy (Airbnb, Uber)
- Videoconferencing (Zoom)
- Generative A.I. (OpenAI)

What is really special?

Open Source

- GItHub has 101 million developers

GitHub Trending



What is really special?

Open Source gave us:

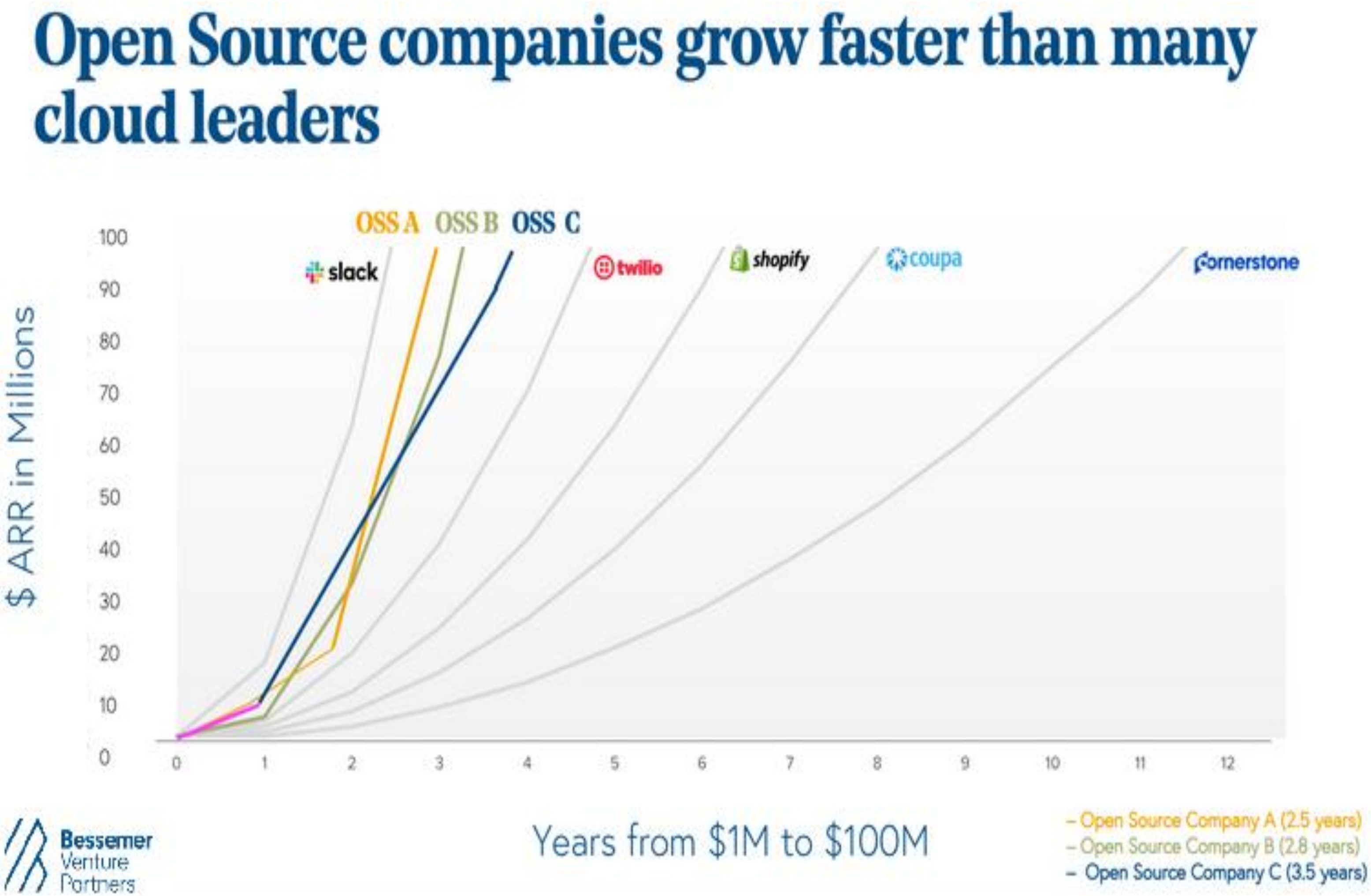
- Bitcoin/ blockchain
- Big data infrastructure (Hadoop, Spark, Cassandra…)
- Deep learning platforms (Caffe, Theano, Keras, TensorFlow)
- Android
- Firefox
- Linux
- Apache
- Java

What is really special?

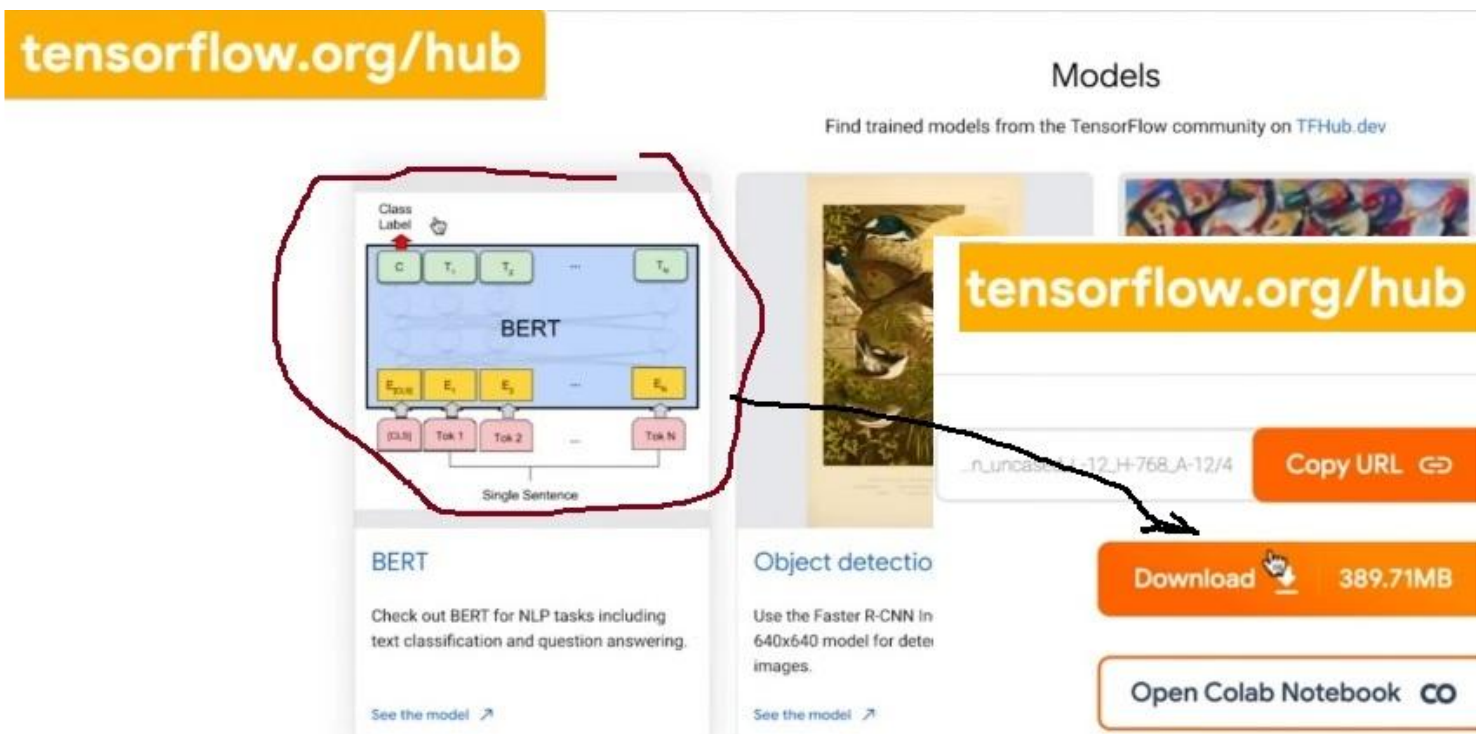
Open Source gave us:

- Astronomical progress in deep learning: A.I. would not have progressed so rapidly if Google, OpenAI, Facebook, etc and many universities had not shared knowledge in publicly available papers
- One learned from the other and together they created a whole new technology and a whole new market
- 2023: top github repos are about LLMs

What is really special?



What is really special?



What is really special?

Talents from all over the world

We find that 44.6 percent, or **223** companies, in the Fortune 500 were founded by immigrants or their children. Of those companies, 101 were founded directly by foreign-born individuals while another 122 were founded by the children of immigrants. Mar 14, 2022

https://www.shrm.org › companies-with-immigrant-roots ▾

New American Fortune 500 in 2019 - SHRM

More Than Half of America's Unicorns Have Immigrant Founders Billion-dollar startups by those born outside the U.S. have grown more than 500 percent since 2018.

https://www.inc.com

Immigrants

2022 data:

- Most billion-dollar startups in the USA (319 out of 582) were founded by immigrants.
- These startups collectively are valued $1.2 trillion, which is almost the GDP of Spain.
- 40% of semiconductor engineers in the USA are immigrants
- More than 60% of Silicon Valley engineers, computer scientists and mathematicians are born abroad, mostly from India and China

Immigrants

Tech companies founded or co-founded by immigrants

- Sergey Brin (Russia): Google
- Peter Thiel (Germany) and Max Levchin (Ukraine): PayPal
- Elon Musk (South Africa): Tesla and SpaceX
- Jen-Hsun "Jensen" Huang (Taiwan): Nvidia
- Eduardo Saverin (Brazil): Facebook
- Pierre Omidyar (France): eBay
- Jerry Yang (Taiwan): Yahoo
- Garrett Camp (Canada): Uber
- Eric Yuan (Taiwan): Zoom
- Adam Neumann (Israel): WeWork
- Mike Krieger (Brazil): Instagram
- Jan Koum (Ukraine): WhatsApp
- Andy Grove (Hungary): Intel
- Steve Chen (Taiwan) and Jawed Karim (Germany): YouTube
- Vinod Khosla (India): SUN
- Andrea Viterbi (Italy): Qualcom

Immigrants

Founded by children of immigrants:

- Steve Jobs (Syria): Apple
- Jeff Bezos (Cuba): Amazon
- Larry Ellison (Italy): Oracle
- Nathan Blecharczyk (Poland): Airbnb

Immigrants

The Internet would not exist without Paul Baran (Poland)

The microprocessor would not exist without Federico Faggin (Italy), Jean Hoerni (Swiss), Eugene Kleiner (Austria)

…

The covid vaccine would not exist without Katalin Karikó (Hungary)

Immigrants

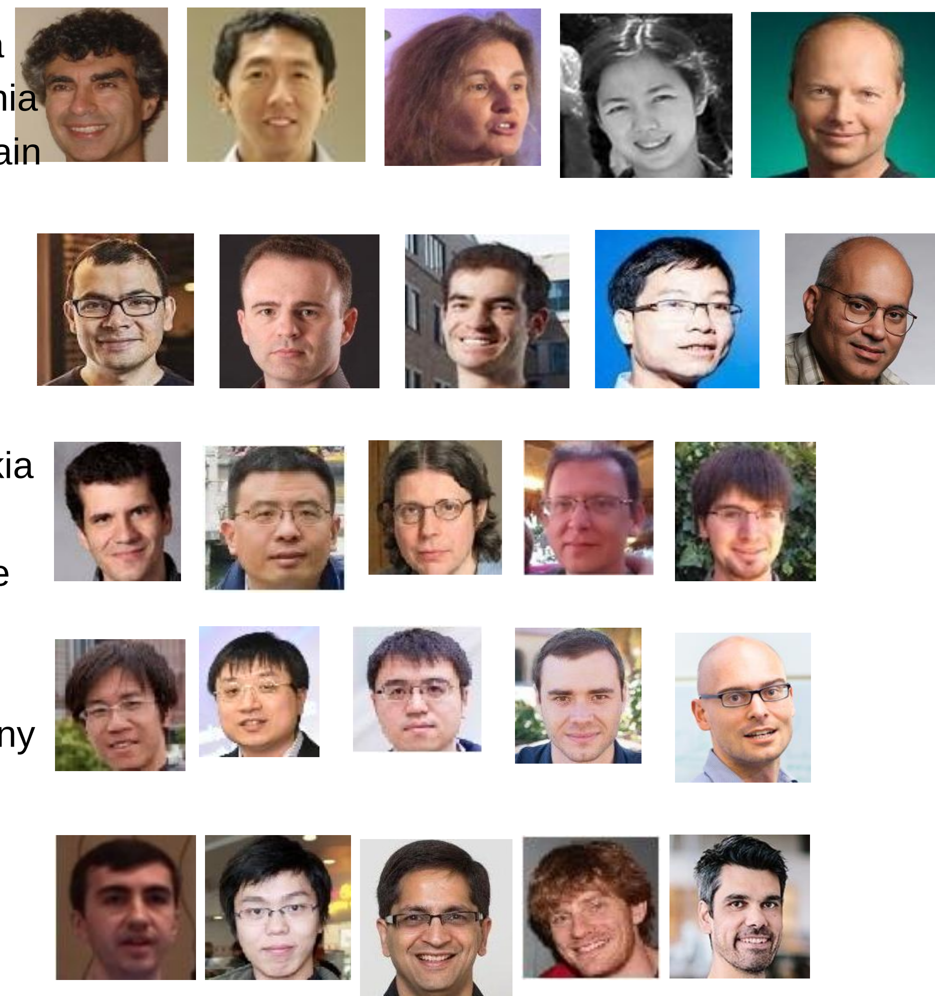
Modern A.I. would not exist without

- Feifei Li (China)
- Andrew Ng (Britain)
- Sebastian Thrun (Germany)
- …
- Geoffrey Hinton (Britain), director of Google Brain
- Andrej Karpathy (Slovakia), director of AI at Tesla
- Yann LeCun (France), director of AI at Facebook
- Pieter Abbeel (Netherland), UC Berkeley robotics
- …
- Ilya Sutskever (Canada), cofounder of OpenAI
- Mira Murati (Albanian parents), creator of ChatGPT

E.g.: the Stars of Deep Learning

Kunihiko Fukushima: Japan
Hava Siegelmann: Israel
Sepp Hochreiter: Germany
Juergen Schmidhuber: Switzerland
Yann LeCun: France
Geoffrey Hinton: Britain/ Canada
Yoshua Bengio: France/ Canada
Andrew Ng: China
Daniela Rus: Romania
Fei-fei Li: China
Sebastian Thrun: Germany
DeepMind: Britain/ New Zealand
Ilya Sutskever: Russia
Quoc Le: Vietnam
Jitendra Malik: India

Dong Yu: China
Oriol Vinyals: Spain
Ian Goodfellow: Canada
Karen Simonyan: Armenia
Andrew Zisserman: Britain
Christian Szegedy: Germany
Aja Huang: China
Kaiming He: China
Jian Sun: China
Andrej Karpathy: Slovakia
Pieter Abbeel: Belgium
Ronan Collobert: France
Yangqing Jia: China
Rajat Monga: India
Richard Socher: Germany



What is really special?

Interdisciplinary thinking

- Scientists
- Artists
- Musicians
- Politicians
- Historians
- Entrepreneurs
- Investors
- …

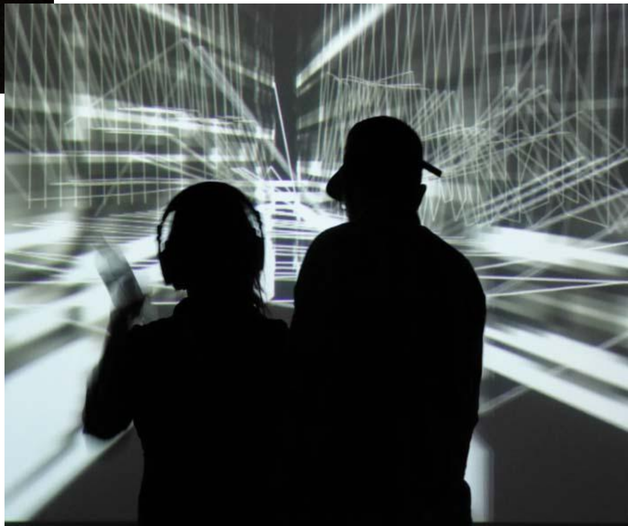
The best colleges for startup founders

1. Stanford **University**.
2. **University** of California, Berkeley.
3. Massachusetts Institute of Technology (MIT)
4. Harvard **University**. Harvard
5. **University** of Pennsylvania. .
6. Cornell **University**
7. **University** of Michigan.
8. **University** of Texas.

businessinsider.com/

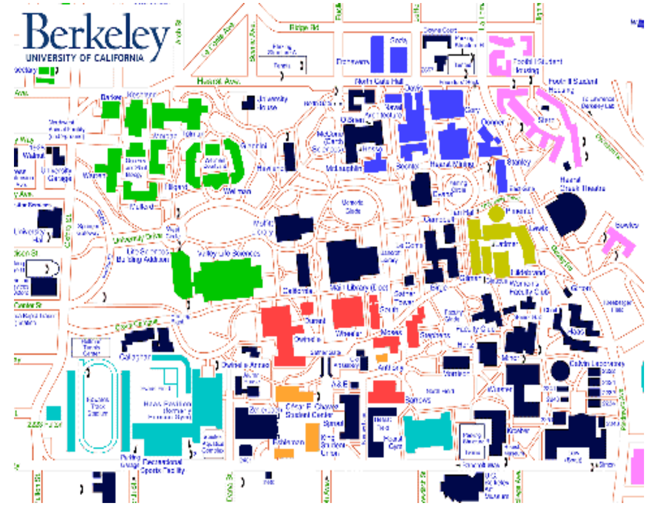
The LAST Festival
Life Art Science Technology festival

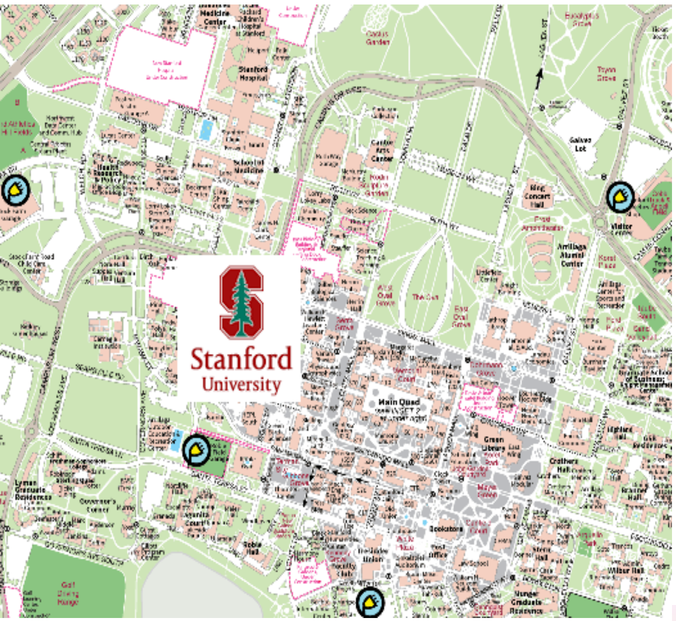
www.lastfestival.org

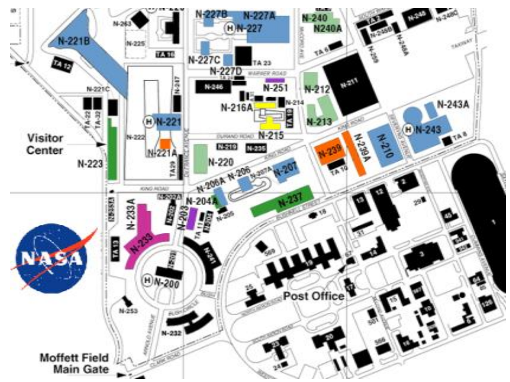


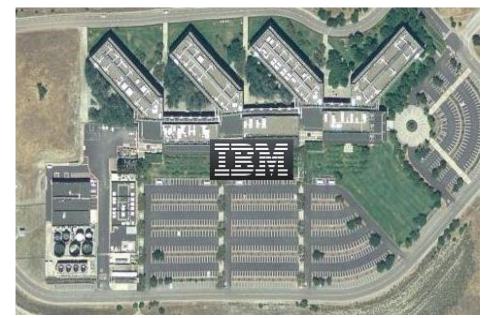
What is really special

Research





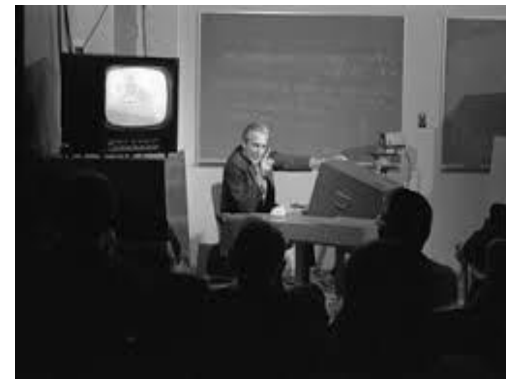




What is really special?

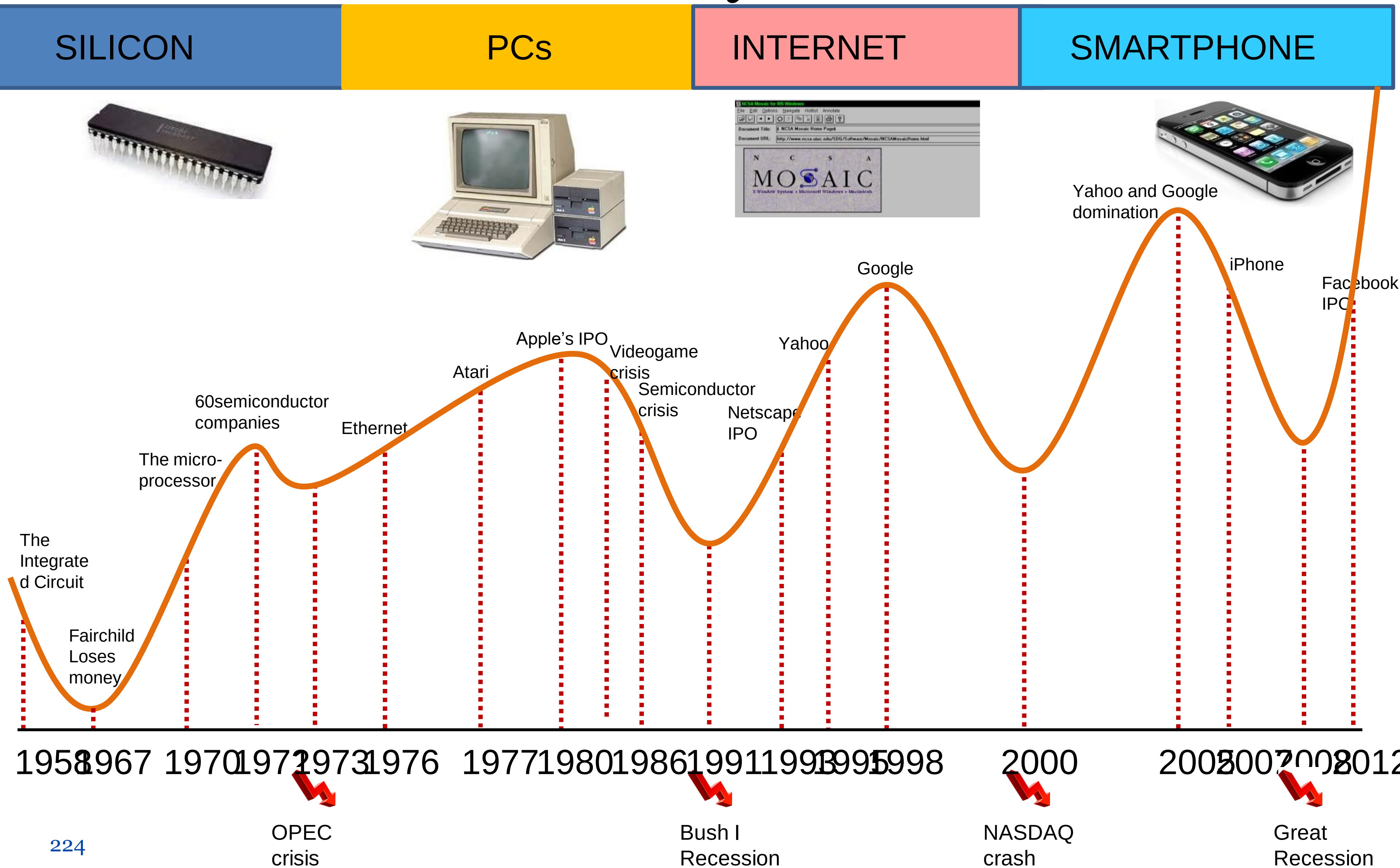
"Moonshot" projects

The PC at Xerox PARC



The Internet at SRI Intl

Silicon Valley’s Bubbles



Silicon Valleys of the World

What needs to be done to create a Silicon Valley elsewhere?

- Small, not big
- Attract international talents
- Encourage mission-impossible projects
- Establish an open-source culture
- Teach interdisciplinary thinking and foster creativity
- Bubbles and busts: culture of failure

The Secrets of Silicon Valley

- Innovation and Creativity are NOT about doing what has already been done.
- They are about doing what has NEVER been done before.
- They are about doing the impossible.
- Innovation does not happen in a vacuum.
- Invest in creativity

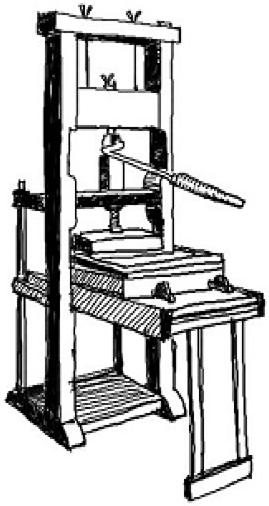
The Secrets of Silicon Valley

- Secret of Silicon Valley: a creative environment…
  - …encourages innovation
  - …attracts foreign engineers/scientists
  - …attracts foreign investment

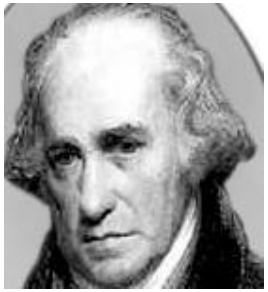
Final remarks: The Convergence

A History of Innovation
1. Mainz, Germany

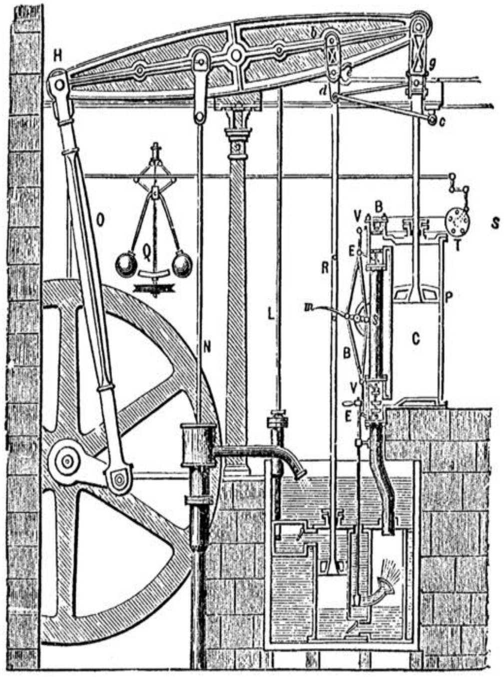
- Johannes Gutenberg's Printing Press (1456)
  - ➢ Wood block engraving +
  - ➢ Raised letters (coinage) +
  - ➢ Wine press +
  - ➢ Paper +
  - ➢ Oil-based inks +
  - ➢ Goldsmything



A History of Innovation
2. Manchester, England

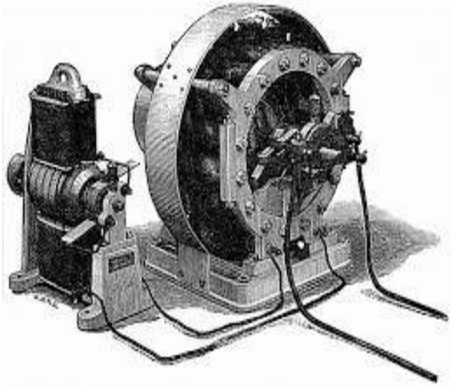


- James Watt's steam engine (1776)
  - ➢ Mill engineering +
  - ➢ Clock engineering +
  - ➢ Evangelista Torricelli's barometer +
  - ➢ Robert Boyle's vacuum pump +
  - ➢ Denis Papin's piston and cylinder +

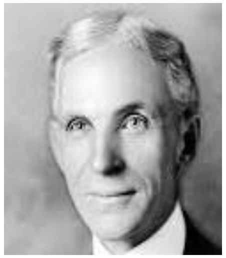


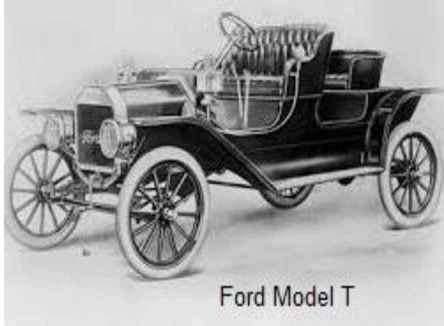
A History of Innovation
3. Hanover, Germany

- Werner Siemens' dynamo – electric motor (1866)
  - ➢ Iron technology +
  - ➢ Electromagnets (Joseph Henry) +
  - ➢ Battery (Alessandro Volta)



A History of Innovation
4. Detroit, USA





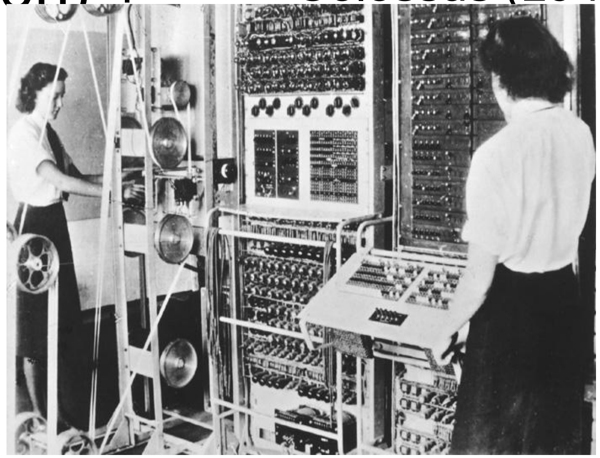
Ford Model T

- Detroit's car
  - ➢ Bicycle technology (steel tubes, differential gearing, chain drive, rubber tyres) +
  - ➢ Carriage/ wagon design +
  - ➢ Electrical machinery (Charles Kittering's electric starter) +
  - ➢ Synthetic paint (General Motors)
- and later:
  - ➢ Radio
  - ➢ A/C
  - ➢ …

A History of Innovation
5. Cambridge, Britain

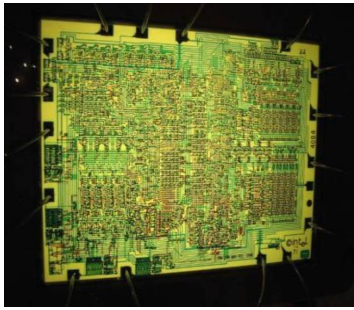
- The digital electronic programmable computer
  - Logic (Alan Turing) +
  - Information Theory (Claude Shannon) +
  - Cybernetics (Norbert Wiener) +
  - Vacuum tubes (electronics) +
  - Cathode-ray tubes +
  - Teletype printer

Colossus (1943)



A History of Innovation
6. Silicon Valley

- Silicon Valley1: The Semiconductor Disruption
  - Convergence of: Electronics (Fred Terman) + Physics (William Shockley, Robert Noyce, Jean Hoerni, Federico Faggin) + Chemistry (Gordon Moore, Andrew Grove) + Photography (planar process) + Material science (Sheldon Roberts) + Mechanical engineering (Eugene Kleiner) + Mathematics (Marcian Hoff)



A History of Innovation
7. Silicon Valley

- Silicon Valley 2: The Personal Computing Disruption
  - Convergence of: computer + CRT video + office automation + gaming + cassette tape + modem + email + …

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A History of Innovation
8. Silicon Valley

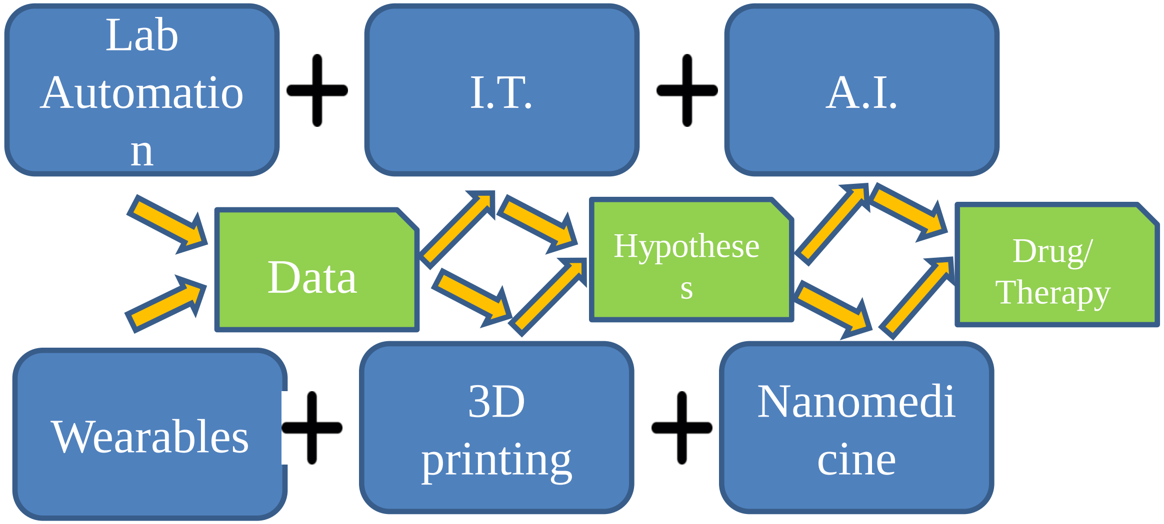
- Silicon Valley 3: The “Dotcom” Disruption
  – Convergence of: computer + fiber optics + Internet + document management + brick & mortar economy

A History of Innovation
9. Silicon Valley

- Silicon Valley 4: The Smartphone Disruption
  - Digital convergence of the **2000s**: Information Technology + Telecommunication + Mobile phone + GPS + Digital camera + Entertainment

A History of Innovation
10. Silicon Valley

- Silicon Valley 5: The Biotech Disruption
  - Convergence of: Information Technology + Lab Automation + Big Data + A.I. + Wearables + Genetics



The Future of Innovation

- The future is interdisciplinary: Sociologists + Economists + Artists/Designers + Scientists + Philosophers + Engineers +…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