



**Presented at:**



**IEEE-CNSV**

Consultants' Network of Silicon Valley

**Aging and AI**

**IEEE CNSV – January 11, 2022**

**Ronjon Nag, PhD, SMIEEE**

President R42 Ventures and Institute

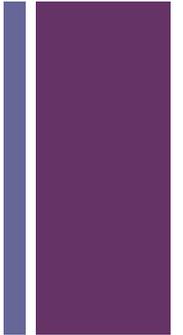
Fellow, Stanford Center for the Study of  
Language and Information

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# Topics

- Who is R42
- Who is Ronjon Nag
- What is Artificial Intelligence ?
- AI and aging
- Can AI make you live longer with better, smart diets?
- Protein folding impacts on aging
- Can AI help you exercise better?
- Can AI detect cancerous cells and destroy them?
- Can you upload your brain in a machine and live forever?
- Can AI assist us as we get older?



# + Who is R42 ?



## ■ R42 Group

- Invent, Invest, Inform
- Palo Alto, California and London, UK

## ■ R42 Ventures: Investments in over 50 Deep Science & Technology Companies

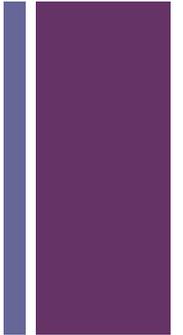
- Biotech
- Artificial Intelligence
- Tough Tech

## ■ R42 Institute: Education in AI and Deep Science at various venues & online

- Universities
- AI & Design Thinking workshops for Corporations
- AI Fellows Program for University Students (FREE)
  - Learn AI and undergo an AI project (FREE)



# R42 Remote Opportunities



- R42 Fellows
  - AI course
  - Work on cutting edge AI projects
  - Free
- R42 Mentors
  - Opportunities to mentor bright students
- R42 Co-founder projects to create companies
  - Propose an idea
  - R42 will co-found it with you
  - R42 will attach Fellow and Mentor resources to the best ideas
- Go to [r42group.com](http://r42group.com) for details

# + Stanford Continuing Studies Course

The screenshot shows the Stanford Continuing Studies website interface. At the top, there is a navigation bar with the Stanford logo, a search bar, and a 'WINTER QUARTER' banner indicating that late-start classes are still available. Below the navigation bar is a red menu with options: COURSES, EVENTS, WRITING CERTIFICATE, REGISTRATION, POLICIES & INFO, and MASTER'S PROGRAM. A 'Quick Links' button is also present. The main content area features a 'COURSES' section with a sidebar for filtering by format, category, course code, day, and department. The main content displays details for 'SCI 52 – Introduction to Artificial Intelligence and Beyond', including its quarter, format, duration, dates, time, refund deadline, tuition, instructor, and status. A 'Please Note' section provides additional information about the course's meeting time, and a 'DOWNLOAD THE SYLLABUS' link is provided at the bottom. An 'Add to cart' button is located in the bottom right corner of the course details.

**Stanford** Continuing Studies  **WINTER QUARTER**  
Winter Quarter Underway  
Late-Start Classes  
Still Available

COURSES EVENTS WRITING CERTIFICATE REGISTRATION POLICIES & INFO MASTER'S PROGRAM Quick Links

## COURSES

[ALL COURSES](#)

**Courses by Format**

- Live Online
- Flex Online

**Courses by Category**

- Liberal Arts & Sciences
- Creative Writing
- Professional & Personal Development

**Courses by Course Code**

**Courses by Day**

**Courses by Department**

[◀ Back to Professional & Personal Development](#)

### SCI 52 – Introduction to Artificial Intelligence and Beyond

<b>Quarter:</b> Winter	<b>Day(s):</b> Saturdays
<b>Course Format:</b> Live Online ( <a href="#">About Formats</a> )	<b>Duration:</b> 7 weeks
<b>Date(s):</b> Jan 22–Mar 12	<b>Time:</b> 8:30 - 10:30 am (PT)
<b>Refund Deadline:</b> Jan 24	<b>Unit:</b> 1
<b>Tuition:</b> \$430	<b>Instructor(s):</b> Ronjon Nag
<b>Class Recording Available:</b> Yes	<b>Status:</b> Open

**Please Note:** This course has a different meeting time than what appears in the print catalogue. The course will meet from 8:30 am - 10:30 am each week. Note: There will be no class on February 19.

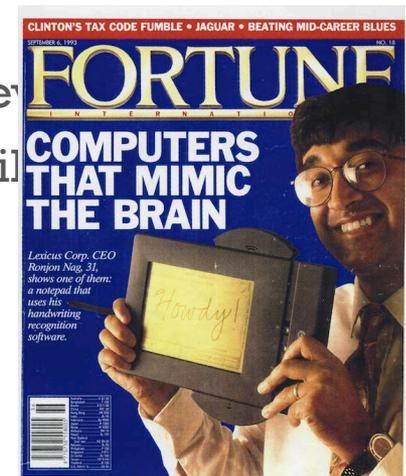
[DOWNLOAD THE SYLLABUS](#) » (subject to change)

[Add to cart](#)

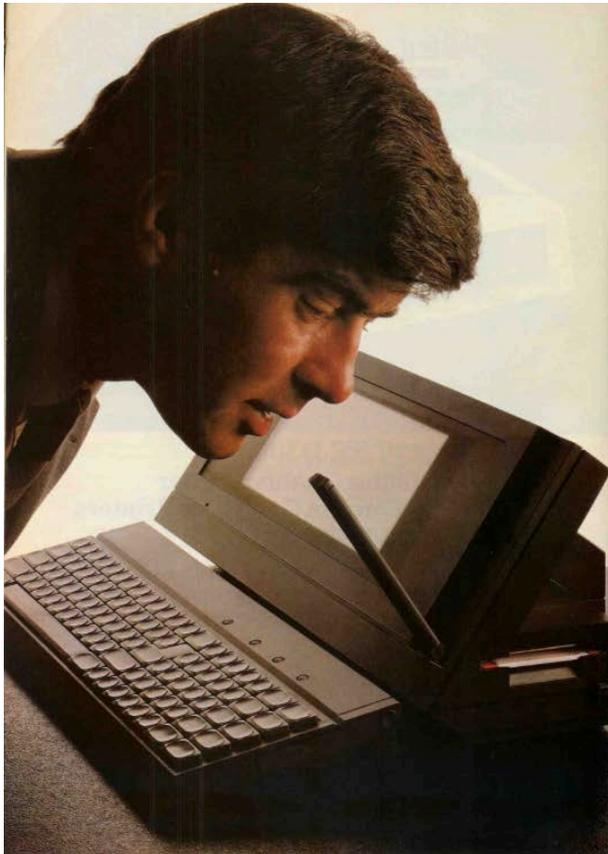
# Who is Ronjon Nag

- AI & Data Scientist, Multiple Entrepreneur, CEng, FIET, SMIEEE
- Founded, Advised and sold companies to Motorola, BlackBerry and Apple
- Teach Longevity Science, Healthcare Venture Capital, Stanford Genetics Department
- Interdisciplinary Fellow, Stanford Distinguished Careers Institute
- Involved in numerous AI-healthcare companies through R42
  - CRISPR-HR : a new non-toxic gene editing technology
  - Healx: AI for drug discovery
  - GTCardio: Early COVID-19 Detection through Telehealth De
  - Oxford Drug Design: Machine Learning to develop new anti
  - BioampDX: Antibiotic resistance Detection
  - Sqzbiotech: Drug Delivery Platform
  - Cura Therapeutics: Cancer therapeutic
  - Melio Technologies: multi-pathogen detection
  - PantherTX: Pancreatic Cancer treatment

ronjon@r42group.com



# + Speech recognition in a product : 1984



**Our rivals  
are speechless.**

Hello.  
I'm an Apricot Portable. The computer you can talk to.

I'm a very good listener. I can understand over four thousand words. And I'll learn to recognise any accent from Glasgow to Grosvenor Square.

I can respond to commands in foreign languages and even a personal code if it's hush hush.

Rather surprisingly for my size, I can easily run a medium sized business on my own.

My maximum memory is 1 MByte and I can store up to 720K on a 3 1/2" disk.

I tip the scales at just under 13lbs. (Most of my rivals weigh in at two stones.)

So packed away in my slim, charcoal grey carrying case I'll slip practically unnoticed onto the 6.30 with you.

One of the reasons I'm so trim is my full sized flat screen. It's a bit like looking at a big digital watch.

My cordless keyboard and mouse work by infra red signals, the way you probably operate your TV set at home.

What's a mouse?

It's a piece of gadgetry that lets you use the computer by simply pointing the mouse at the machine and moving around the ball control with your thumb.

Or you can use the desk to roll the ball if it's more comfortable for you.

Want to know more?

With every machine you get a free tutorial disk that demonstrates all my features.

It shows how words and pictures are cleverly mixed on screen and explains everything you haven't gathered already.

You will also get a powerful bundle of free software which, among other things, gives you a word processor, spreadsheet and diary.

Then when you've mastered those, you can choose from two thousand packages specially developed for Apricot, which will include Lotus 1-2-3.

That'll make me do almost anything except sugar your tea.

Give them time. They're working on it.

Please send me details of the Apricot Portable to: ACT (UK) Ltd, FREEPOST, Halesowen, West Midlands B63 1BR.  
Or Freefone Apricot via Operator.

Name \_\_\_\_\_  
Position \_\_\_\_\_  
Company \_\_\_\_\_  
Address \_\_\_\_\_  
Tel \_\_\_\_\_

**THE ANSWER IS AN  
Apricot Portable**

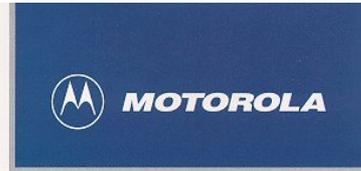
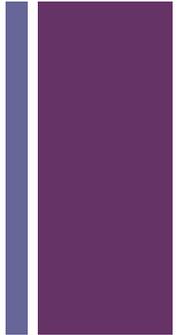
APRICOT PORTABLE FROM £187 PLUS VAT NOT INCLUDING MOUSE

• Circle No. 140

Apricot Computers: first computer with speech recognition: 1984  
4096 words, maximum 64 words at any one time



# Lexicus: 1<sup>st</sup> cursive handwriting recognition system: 1991



Now you can write — in your own natural handwriting — directly into Windows™ 3.1 applications, with Lexicus Longhand™ Professional.

Lexicus Longhand Professional brings cursive handwriting to your Windows for Pen Computing applications. Lexicus Longhand Professional uses its 25,000 word dictionary to accurately recognize words, numbers and commonly used punctuation symbols in most cursive handwriting styles. Also, a customizable user dictionary adds recognition for any special words, acronyms or proper names.

### New Features Include:

**Easier Correction in Windows Applications:** Alternate word choices for easy correction are now available in your favorite pen-enabled Windows applications, including Microsoft® Word™ and Microsoft PowerPoint™. Tap on any word, and the top alternate word choices appear, use your pen to select one quickly and easily.

**Artificial Intelligence:** Not only is Lexicus Longhand Professional ready to use right out of the box — no training required — but new technology allows your accuracy to improve as you use the product.

**Macro Expansions:** Easy "short-cut" feature allows you to link acronyms of your choice to long phrases. For example, you can write "janed" and the program will type in janedoc\_EIM32419,5372@xyz.corp.com.

**Save Your Ink:** Now you can edit as you go, or save your hand written text for later editing. Save as many files as you want during the day, then revise and edit your text at a more convenient time.

**Improved Accuracy**  
Lexicus Longhand Professional includes new "artificial intelligence" so recognition accuracy now improves with use.

**Enhanced Ink Control**  
Manipulate your ink by using the Split or Join feature to ensure accurate translation of your handwriting.

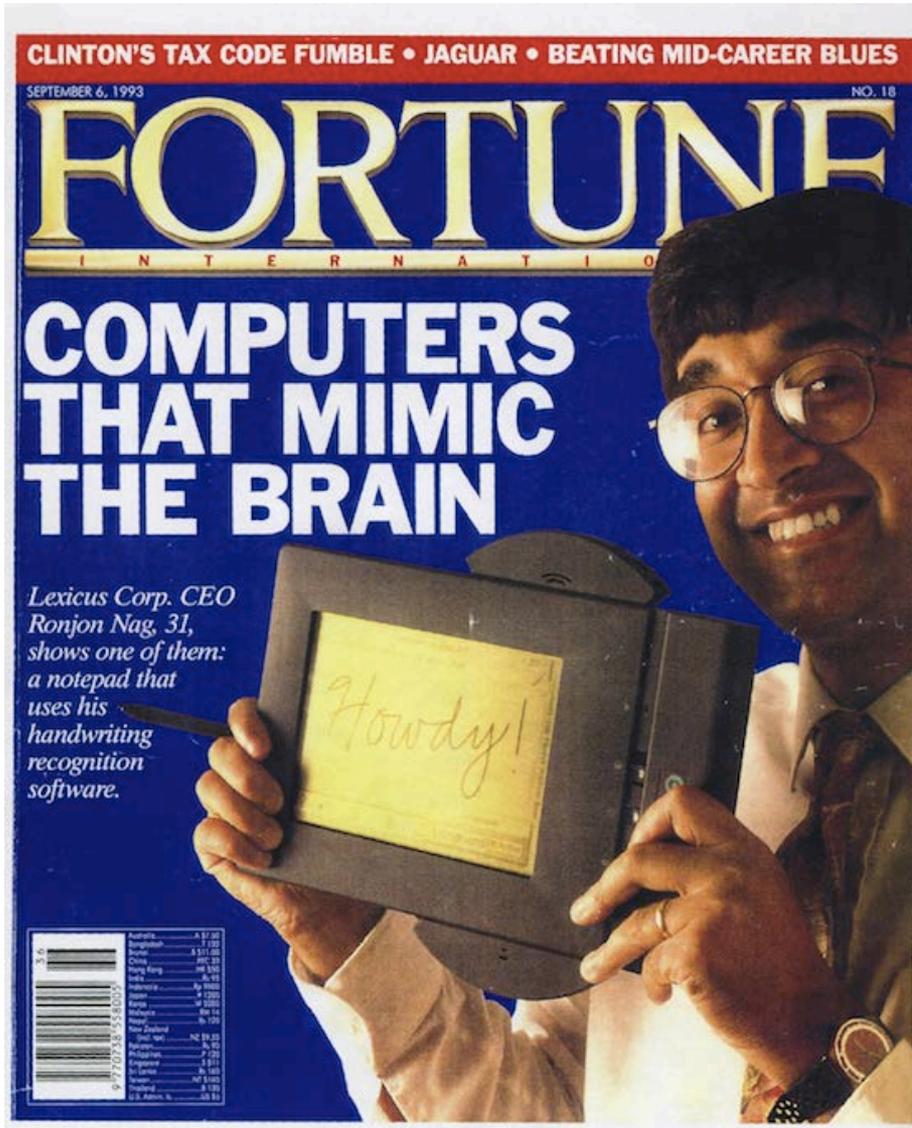


**Cursive Recognition**  
Lexicus Longhand Professional turns handwritten input into ASCII text within your favorite Windows applications.

**Quick Editing**  
The alternates menu allows for quick editing. It offers a selection of alternative dictionary and non-dictionary translations, as well as space to edit, if necessary.



# + Mobile device



1993: EO Personal Communicator  
Mobile Data

Pen based operating system  
by GO

Contacts, wireless fax,  
notetaker

Cursive handwriting  
recognition by Lexicus

# + Vocal IQ acquired by Apple

## Apple acquires deep learning startup VocalIQ to make Siri smarter

MARK SULLIVAN OCTOBER 2, 2015 11:22 AM

TAGS: ACQUISITIONS, APPLE, DEEP LEARNING, SPEECH RECOGNITION

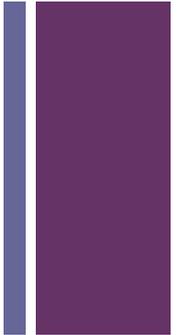


Image Credit: Lester Balajadia / Shutterstock.com

Apple has bought a U.K.-based artificial intelligence startup called VocalIQ, whose

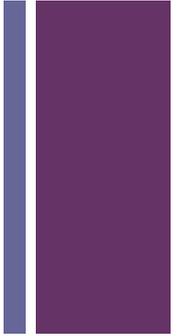


# + What is intelligence



- Self Awareness
- Emotional Knowledge
- Planning
- Creativity
- Language Understanding

# + What is artificial intelligence



# + AI in Daily Life

Siri/Alexa/Google Now

iRobot cleaners

Robot Grass Cutters

Fingerprint recognizers

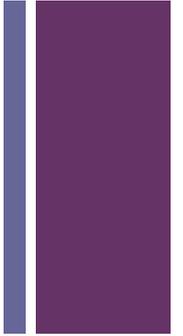
Collision avoidance systems

Loan Scoring

Stock market predictor

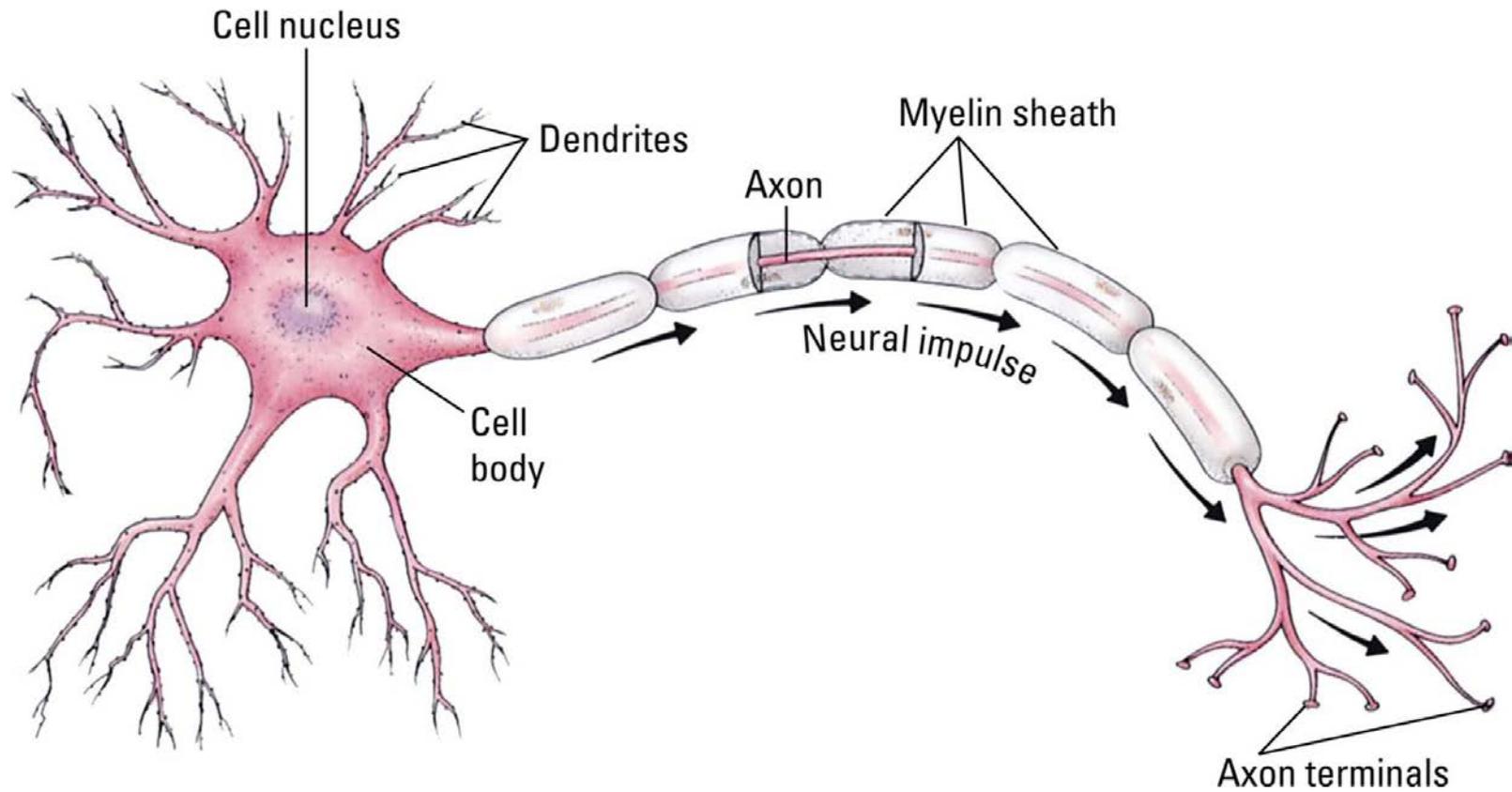
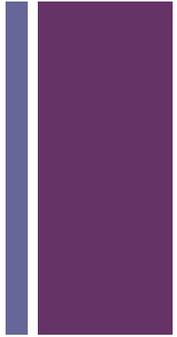


# + Neural Networks and Deep Learning

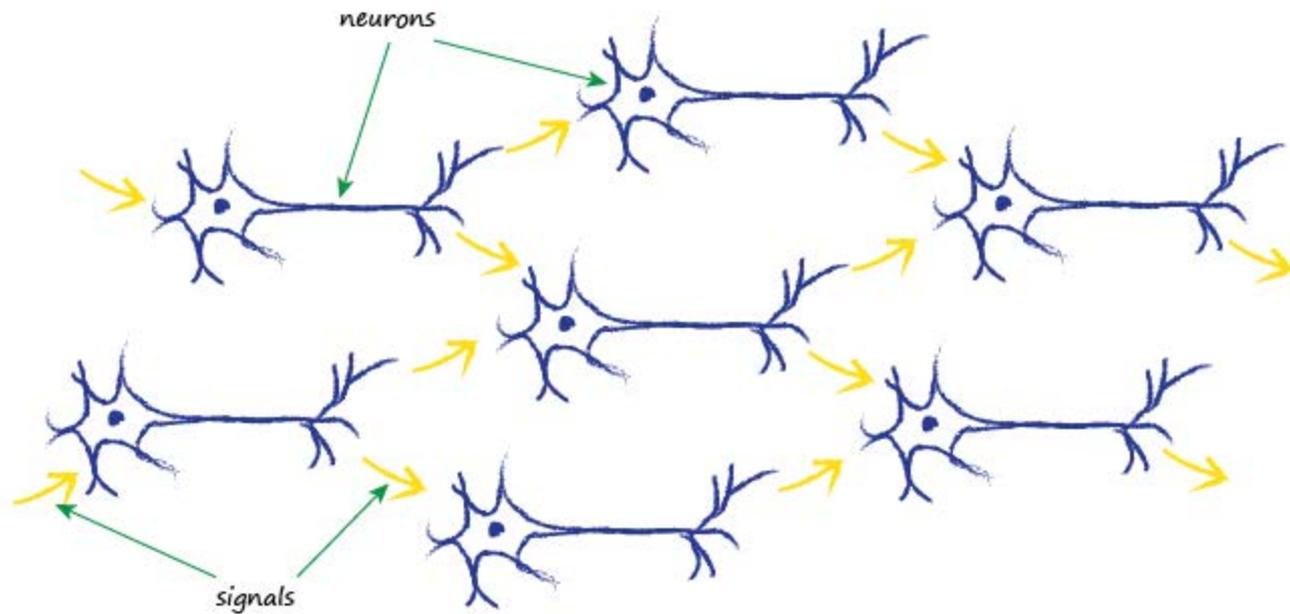




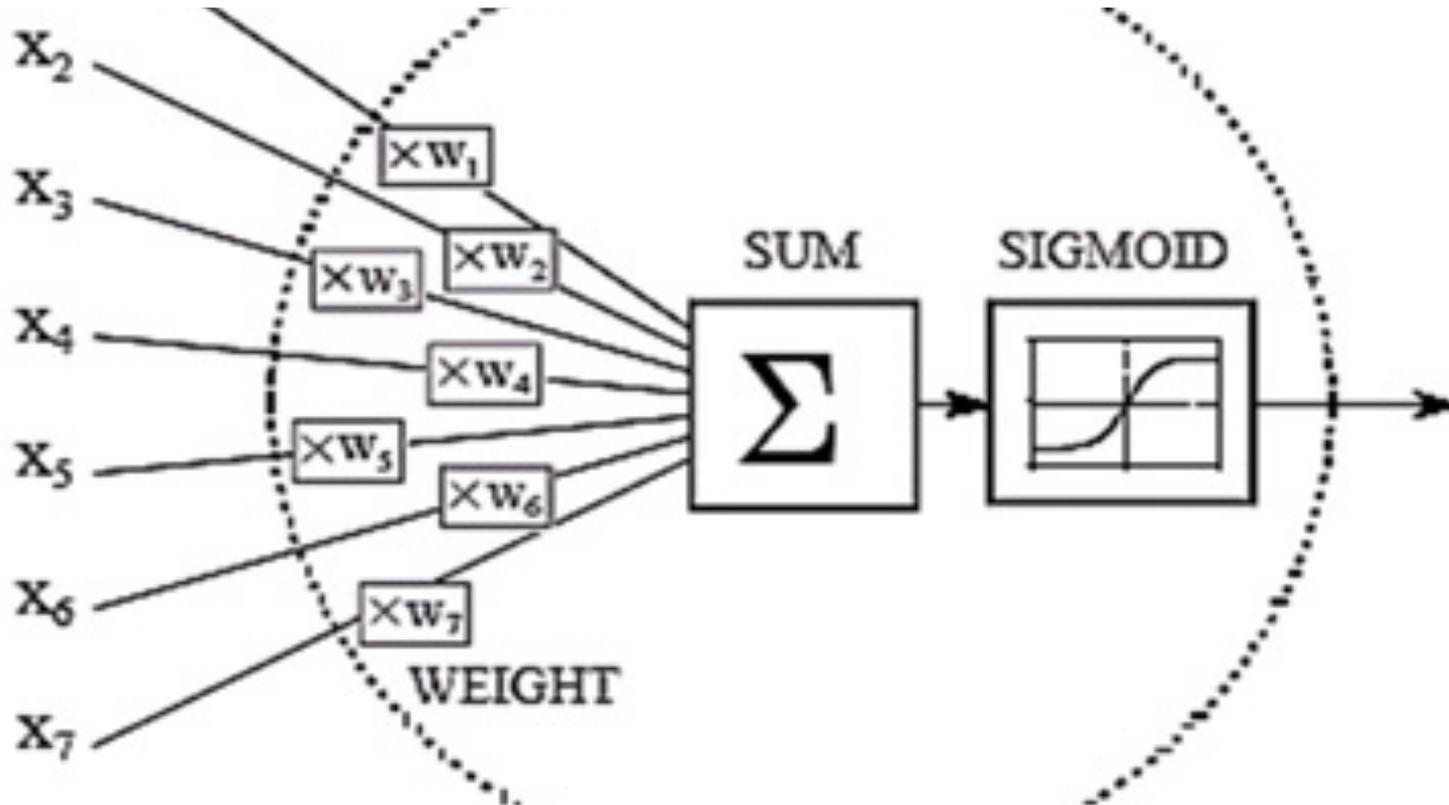
# Neural networks: First the real neuron structure



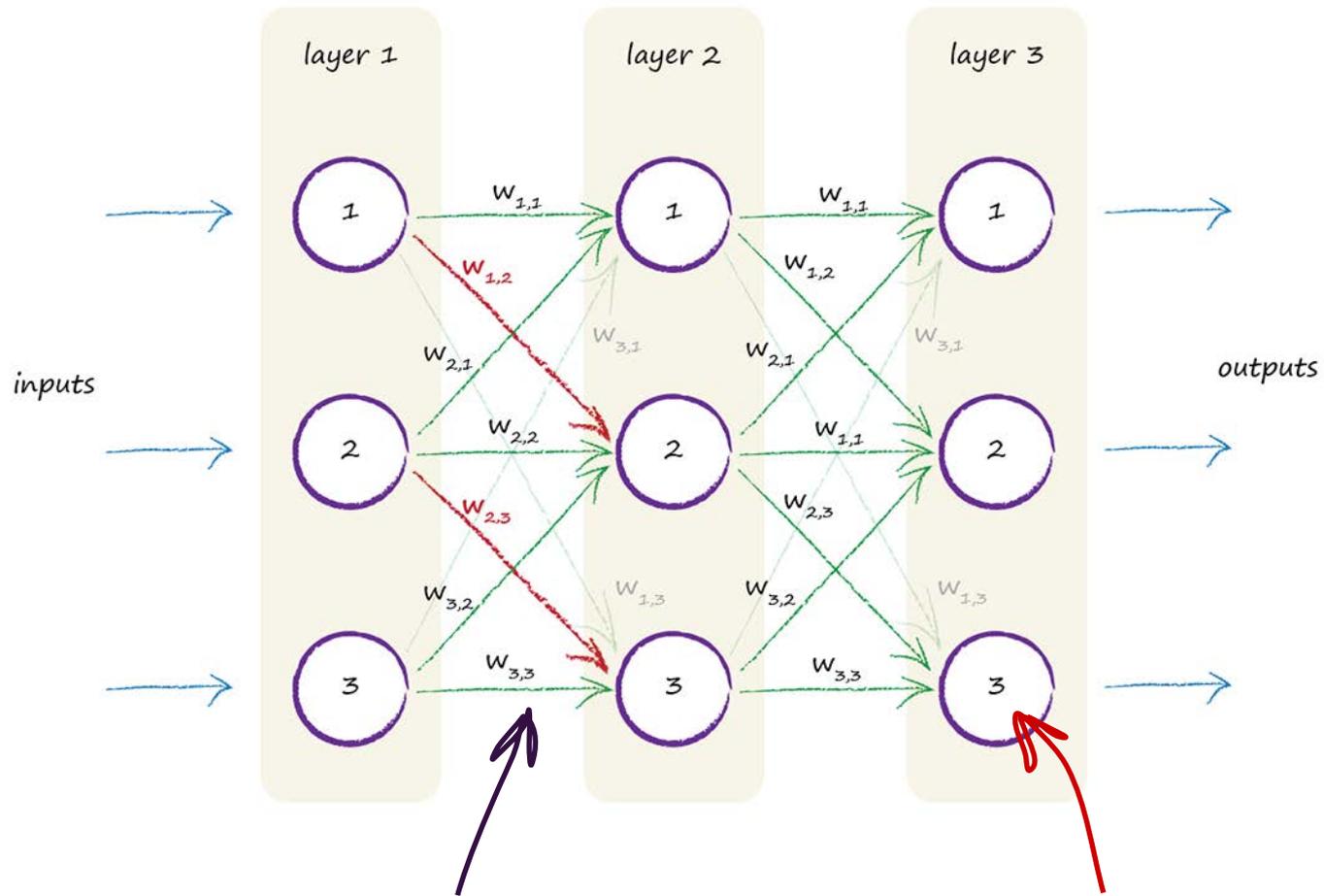
# Brains in Nature



# + Computational Neuron model



# Where Does The Learning Happen?

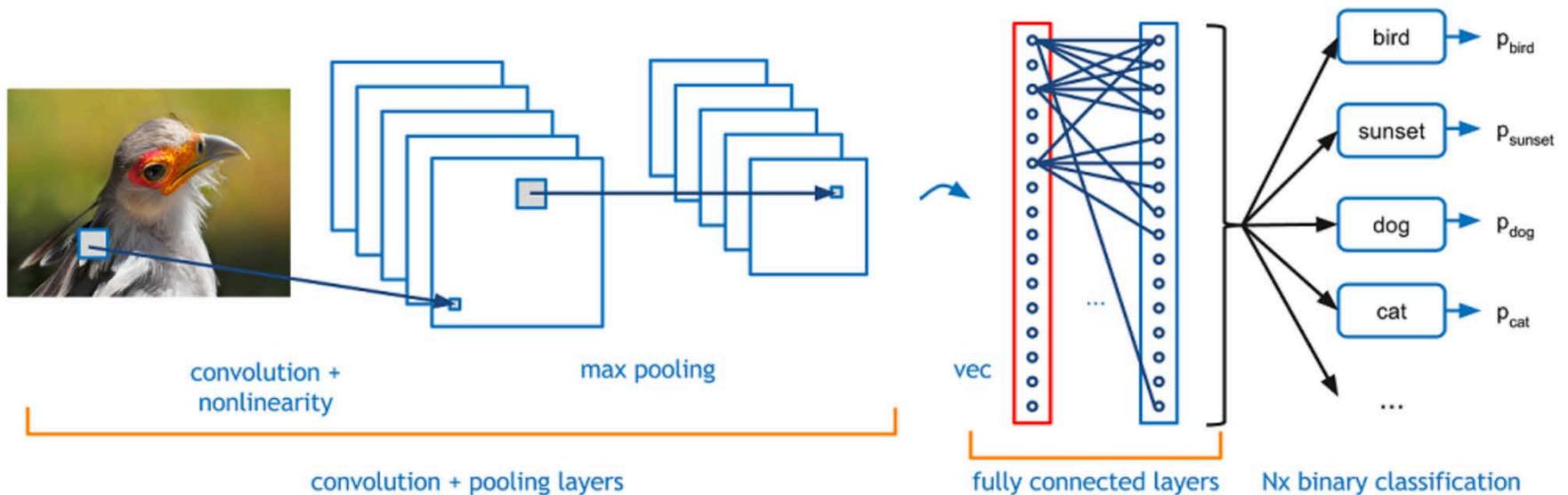


link weight?

sigmoid function slope?

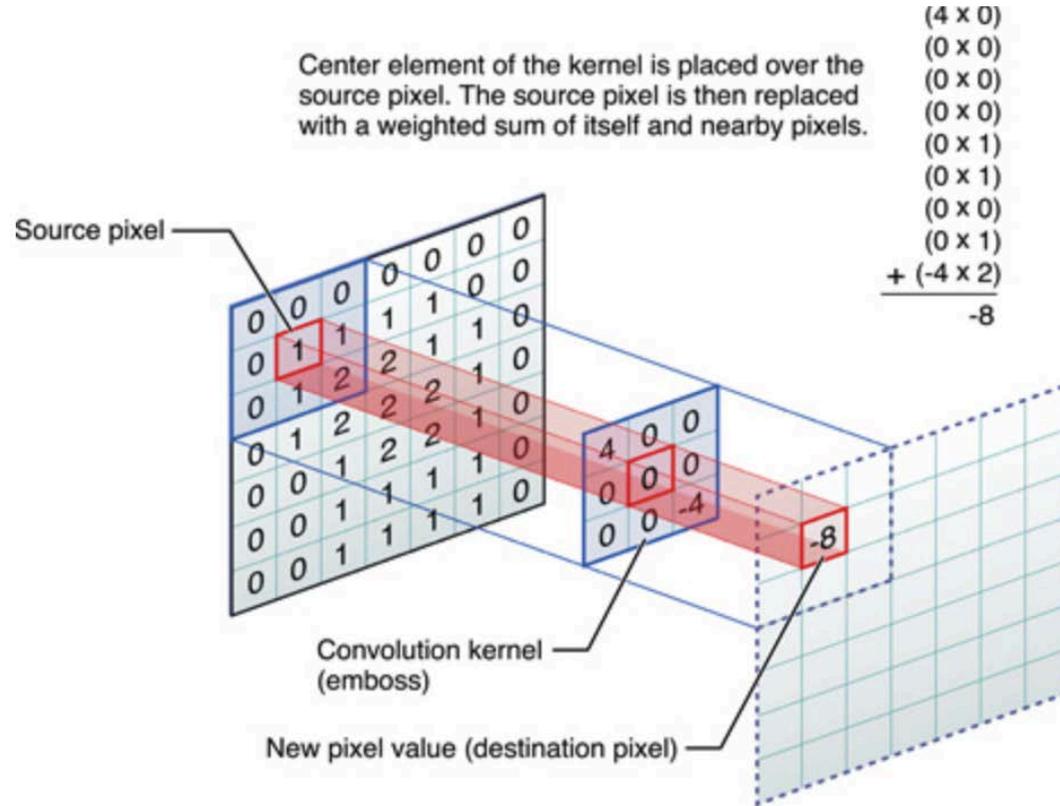
# + Convolutional Neural Networks

## A Beginner's Guide To Understanding Convolutional Neural Networks

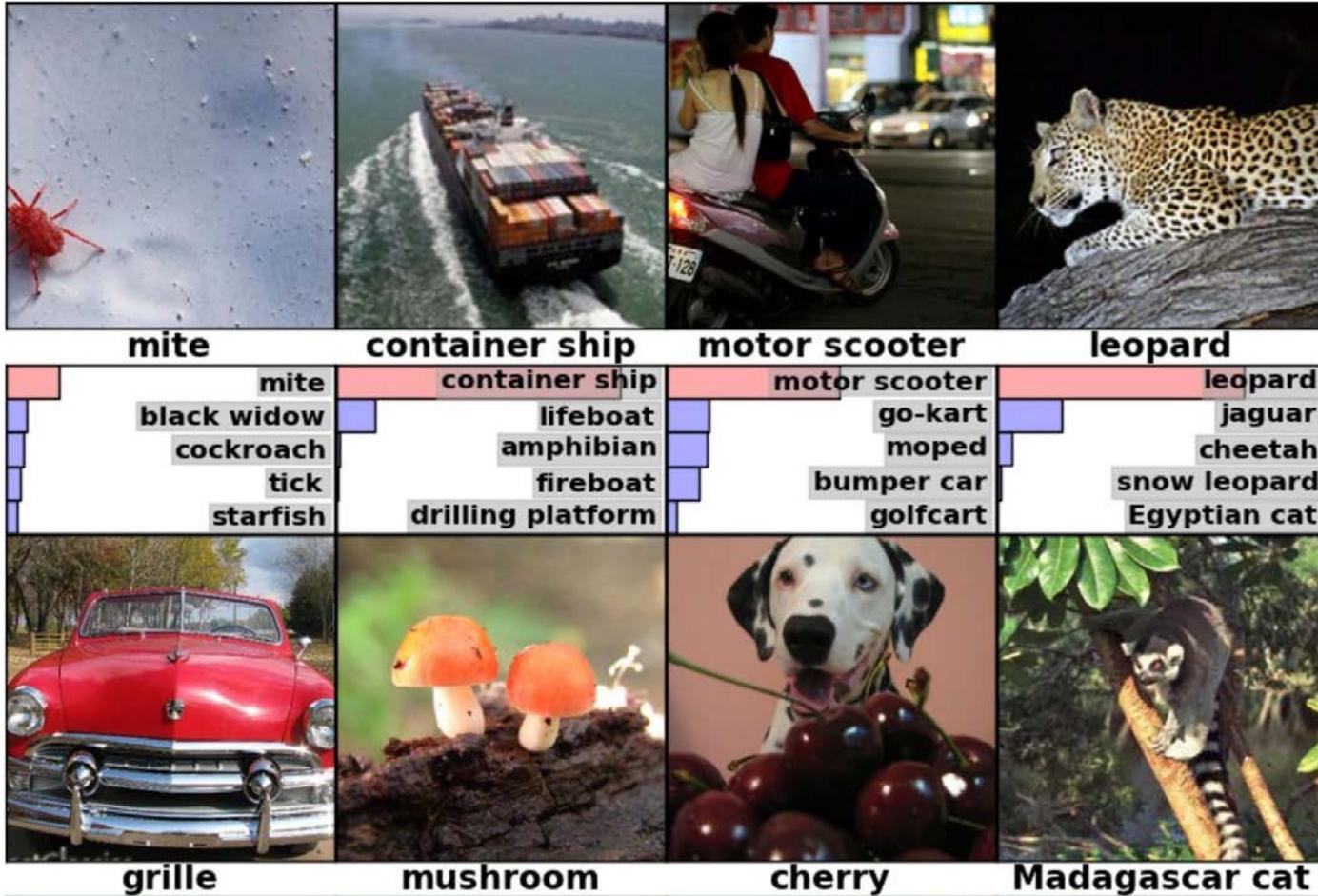


Source: <https://adeshpande3.github.io/adeshpande3.github.io/A-Beginner%27s-Guide-To-Understanding-Convolutional-Neural-Networks/>

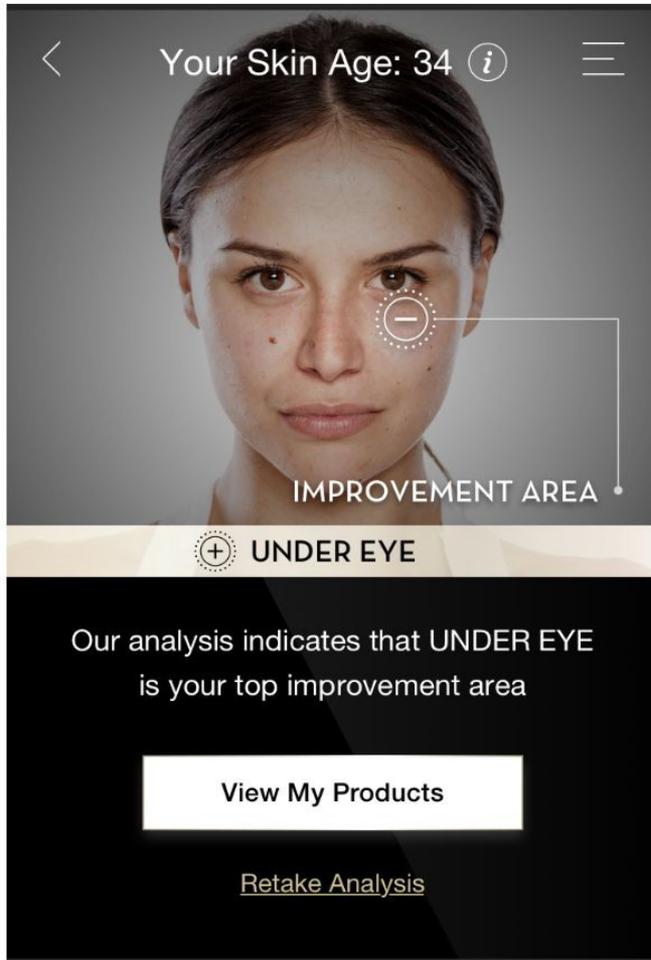
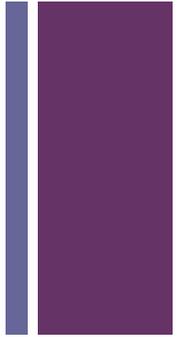
# Example of convolution calculations



# + Example results



# + Olay Neural Network Skin Advisor Age Predictor

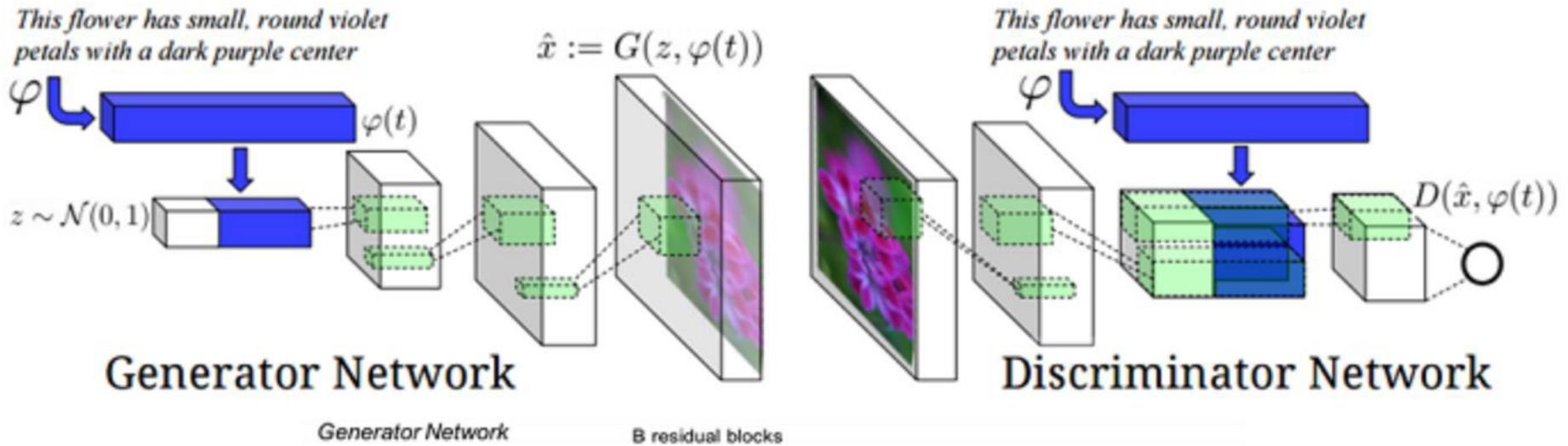


Deep learning neural network system  
Trained on 50,000 selfies of P&G employees  
Take a picture of your face with a phone  
App then scans face and provides skin age  
Then provides list of Olay products to help

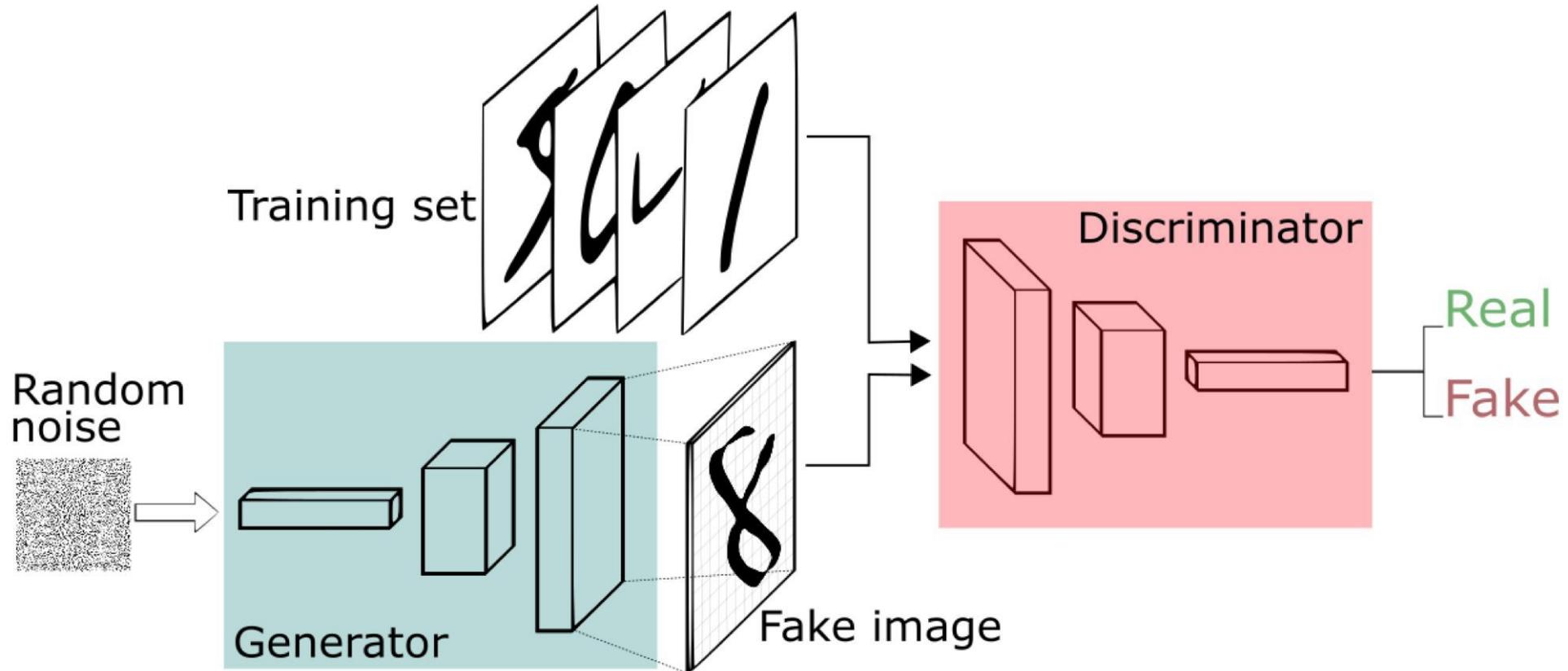
<https://www.olay.com/skinadvisor>

# + Generative Adversarial Networks (GANs)

- One network produces answers (generative)
- Another network distinguishes between the real and the generated answers (adversarial)
- Train these networks competitively, so that after some time, neither network can make further progress against the other



# + GAN architecture



# AI can make paintings



**Bloomberg  
Businessweek**  
Mag. 7. 2018

THE SOONER  
THAN YOU  
THINK ISSUE



*A.I. Painted This*

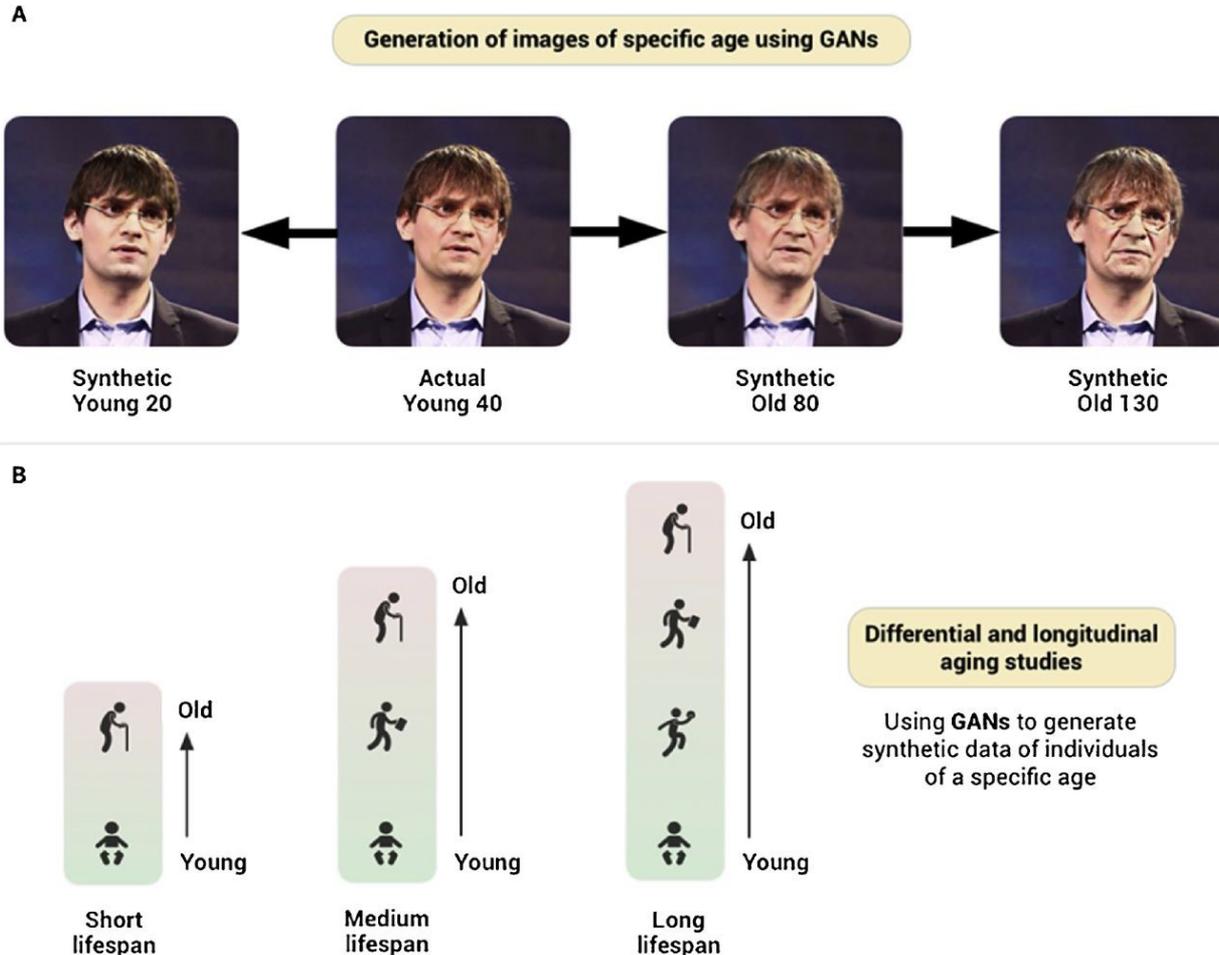
*It's also driving cars, making money, exploring oceans...and freaking people out*

Source: Robbie Barrat

# Age prediction using GANs

A. Zhavoronkov et al.

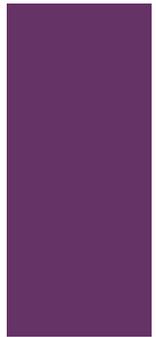
Ageing Research Reviews 49 (2019) 49–66



**Fig. 7.** GANs are well known for their abilities to generate models from data. These features have been largely used for image generation. Combining this ability with the capabilities of GAN to handle large sets of data to capture complex features across individuals at different age, one can build GAN-based architecture to generate synthetic health data and pictures of individuals at any age using the health data at a known given age.



# Superbio.ai: Using cloud computing to build AI systems for biology using drag and drop UX

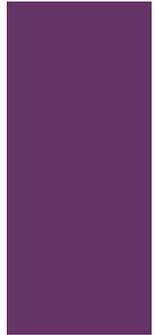


The screenshot shows the Superbio.ai dashboard with a dark blue sidebar on the left containing navigation icons. The main content area is titled "Dashboard" and includes a user profile for "Ronjon Nag" with a "Feedback" button. Below the header is a "QUICK ACCESS" section with three columns:

- Create a dataset:** Includes a description, a code icon, and a list of recently created datasets: "Cervical cancer risk" (1/10/2022, 7:37:33 PM) and "dementia\_dataset" (1/10/2022, 7:28:04 PM). A "New dataset →" button is at the bottom.
- Build a workflow:** Includes a description, a workflow icon, and a list of recently created workflows: "Predict dementia" (1/10/2022, 7:34:14 PM). A "New workflow →" button is at the bottom.
- Browse the app store:** Includes a description and a "Created Recently" section with a "New app →" button at the bottom.



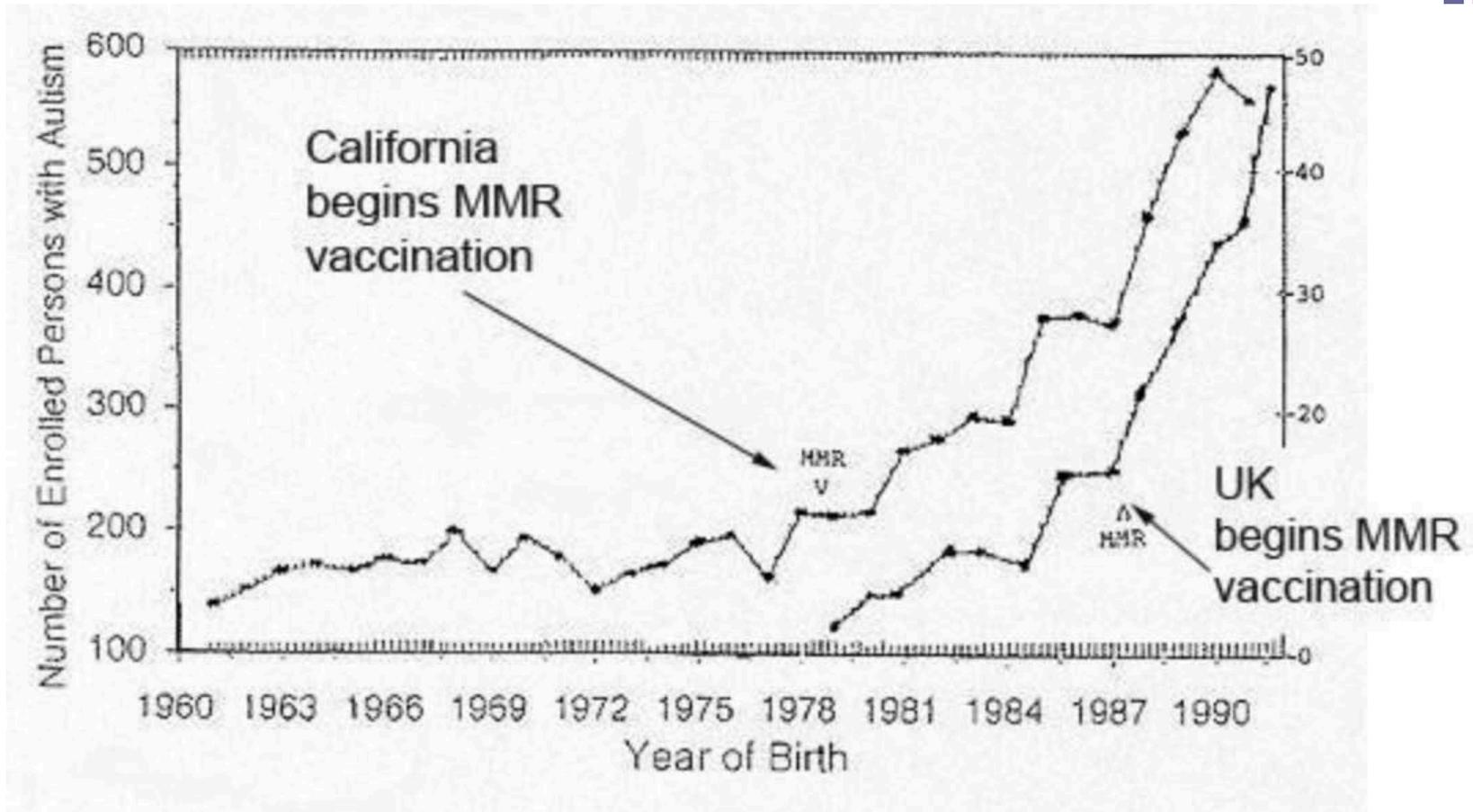
# Superbio project: make AI easier to use



The screenshot displays the Superbio web application interface. At the top, there is a navigation bar with the Superbio logo, a search bar containing the text "Upload a dataset or pick an existing one to analyze", and user information including "Feedback" and "Ronjon Na". Below the navigation bar, there are tabs for "My Data" and "Open Data". A sidebar on the left contains navigation options: "Dashboard", "Datasets", and "Workflows". The main content area features a search bar and a grid of ten data analysis tool cards. Each card includes a title, a brief description, and a "View Details" link.

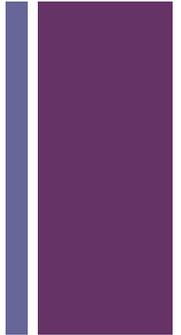
Tool Title	Description
Alternative isoform regulation in human tissue transcriptomes	Through alternative processing of pre-messenger RNAs, individual mammalian...
Analysis and design of RNA sequencing experiments for identifying isoform regulation	Through alternative splicing, most human genes express multiple isoforms that o...
Biodiversity in National Parks	Context The National Park Service publishes a database of animal and plant s...
Bioprocess performance prediction	Context Biotechnological solutions have a wide range of important applicatio...
Cardiotocography	Context Biomedical -Signal Classification for Cardiotocography Data Set Content...
Genetic cancer risk factors	Genetic Cancer Risk Factors for Blotchy. This set is Obtained from UCI Repo...
Diabetes in Indian Women	Context This dataset is originally from the National Institute of Diabetes ...
Evaluating gene expression in mouse striatum	C57BL/6J (B6) and DBA/2J (d2) are two of the most commonly used inbred mouse st...
Evaluation of statistical methods for normalization and differential expression in mRNA-Seq experiments	Background: High-throughput sequencing technologies, such as the Illumina Genom...
Hepatitis C Virus	Data Set Information: The target attribute for classification is Category (bla...

# + Neural networks model correlations not causations





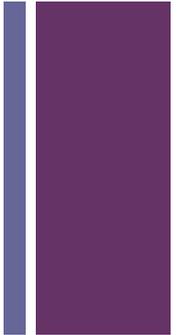
# Bradford Hill Criteria for Causation



- **Strength** ( effect size): A small association does not mean that there is not a causal effect, though the larger the association, the more likely it is causal.
- **Consistency** ( reproducibility): Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.
- **Specificity**: Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.
- **Temporality**: The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).



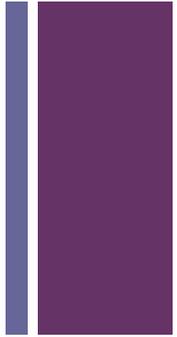
# Bradford Hill criteria (cont.)



- **Biological gradient:** Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.
- **Plausibility:** A plausible mechanism between cause and effect is helpful - though can be limited by the current state of knowledge
- **Coherence:** Coherence between epidemiological and laboratory findings increases the likelihood of an effect. However, Hill noted that "... lack of such [laboratory] evidence cannot nullify the epidemiological effect on associations".
- **Experiment:** "Occasionally it is possible to appeal to experimental evidence".
- **Analogy:** The effect of similar factors may be considered.

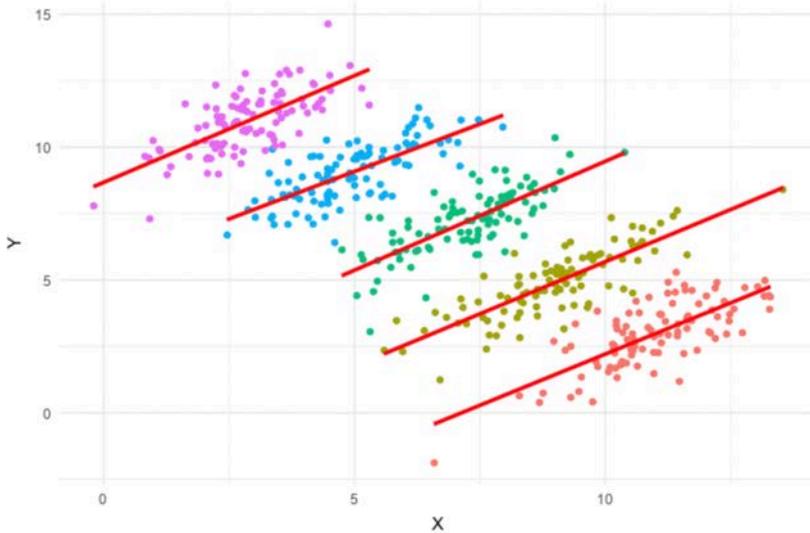


# Simpson's paradox shows the same data can have different conclusions

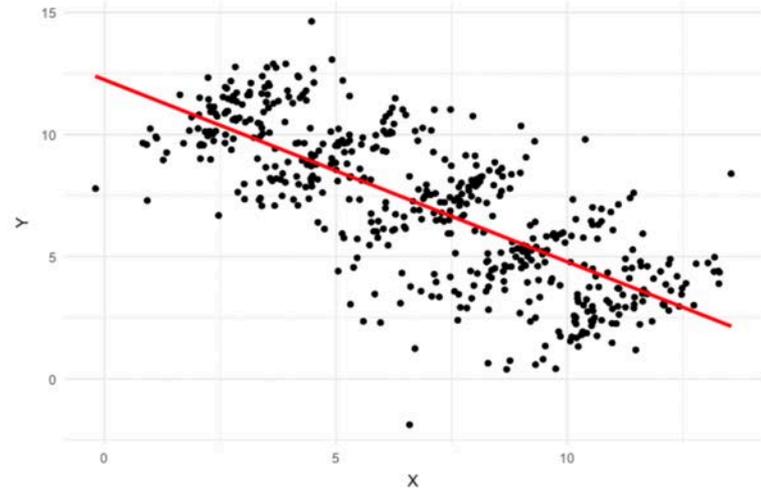


Trend appears in several different groups of data but disappears or reverses when these groups are combined

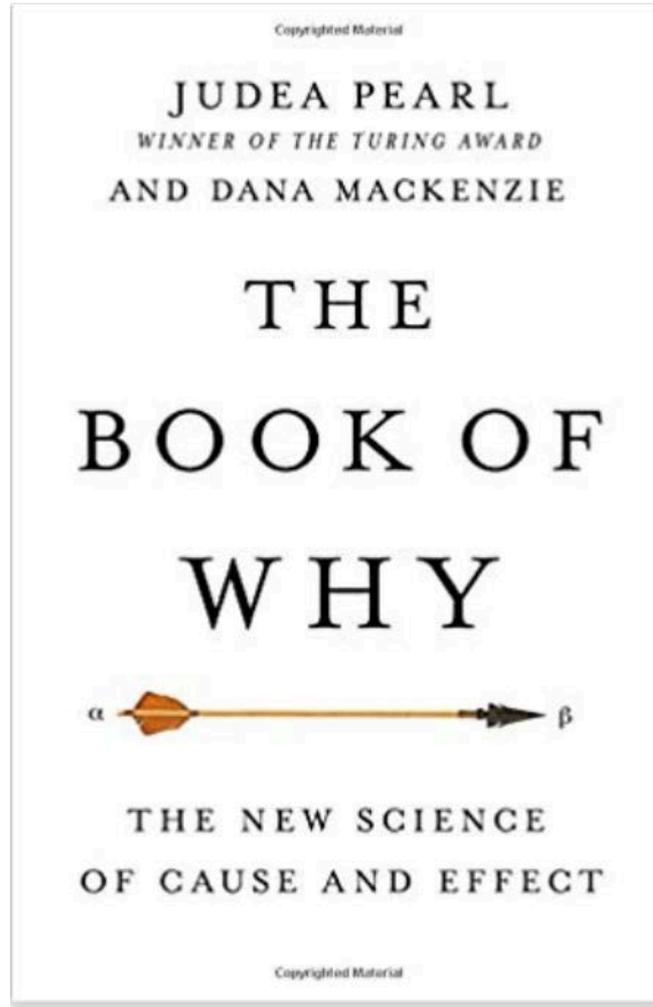
Korrelation: 0.74, 0.82, 0.75, 0.72, 0.69



Korrelation: -0.74



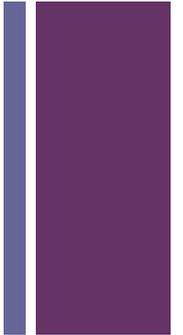
# + Causal Inference



# AI and Aging



# What is age and aging in place

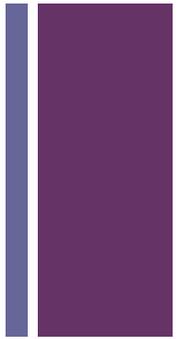


- Chronological Age – can't modify
  - Number of years since birth
- Biological Age – is it possible to modify ?
  - Dunedin Study: 1000 tracked from birth since 1970 in New Zealand: 18 Biological measures: eg. blood sugar, cholesterol, balance, heart measures, gum recession
  - Human performance: VO2 max, max heart rate, running speed
  - Cell age: telomere length, DNA mutations
- Aging in place: maintaining same biological age by adopting lifestyle measures
- Biology and Lifestyle affect aging but in what proportion ? 50-50; 30-70; 80-20 ? Can you do anything about it ?

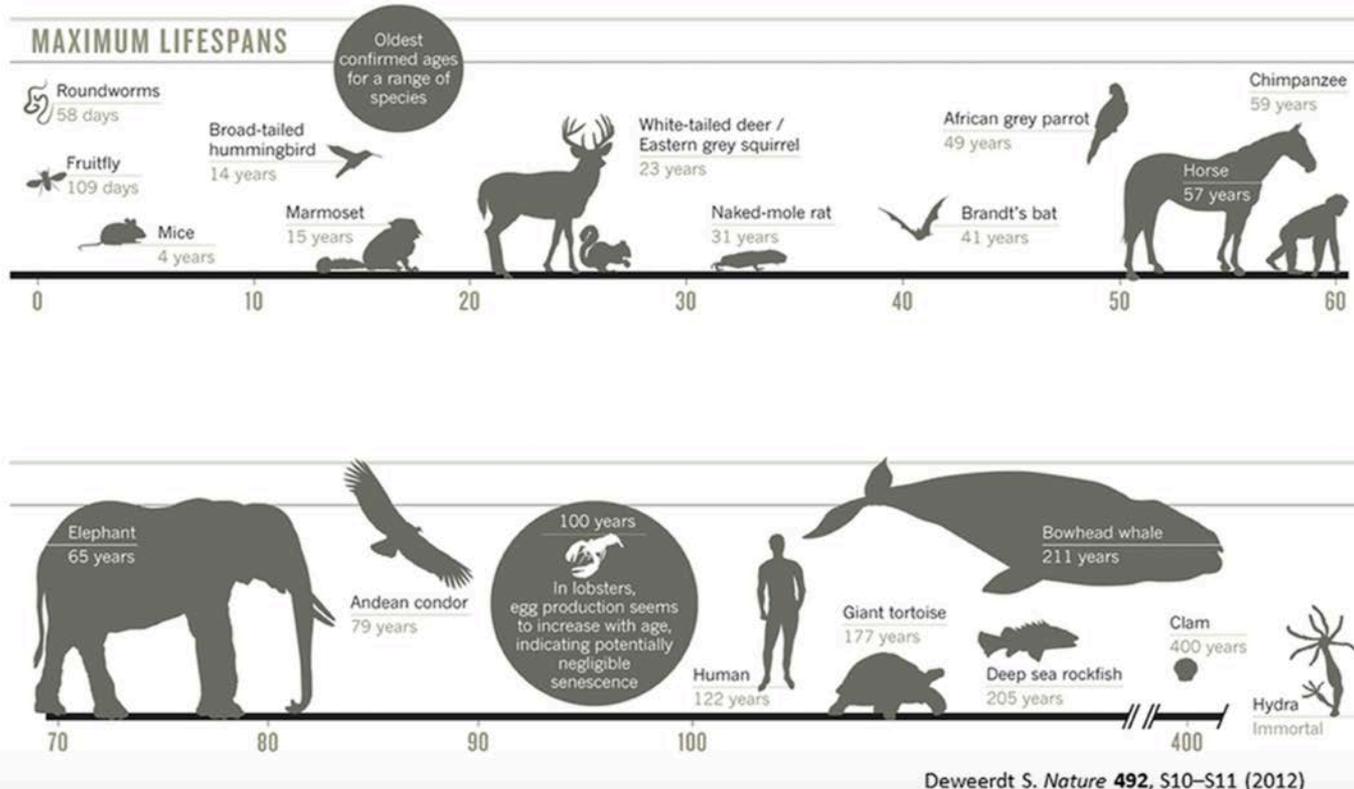
# + Long lived animals

- Clams last 500 years
- Humans have 30,000 times more cells than a mouse
  - Therefore each cell needs to be 30k better than a mouse in cancer protection
- Now a whale has a 1000 times more cells than us
  - So they need even better cancer protection
- For elephants we have some hints
  - In elephant has a gene that is protective vs humans
- Naked mole rats are of interest in aging
  - Live for 30 years, and also resistant to cancer
  - compared with mice who live 3 years and usually die of cancer

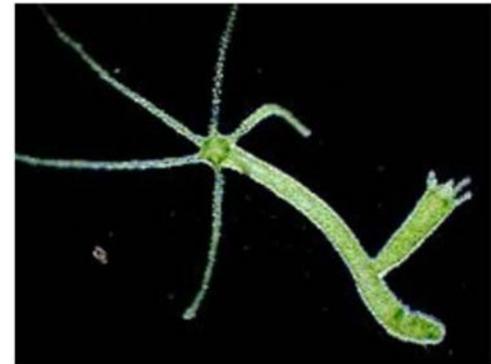
+ In general larger animals live longer, but not always



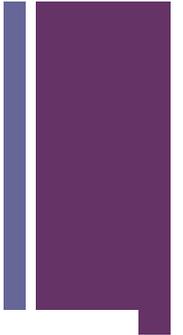
## How does nature extend lifespan ?



## Immortal Hydra



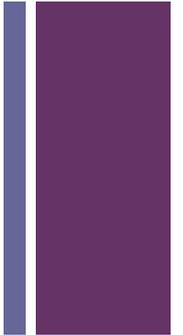
# + Primate lifespans



Species	Maximum reported life span (years)
White-tufted-ear Marmoset	23
South American Squirrel Monkey	30
Rhesus Monkey	40
Brown Capuchin	46
Chimpanzee	59
Human	122

*Source: Animal Ageing and Longevity Database <http://genomics.senescence.info/species>.*

# + The strange case of the naked mole rat

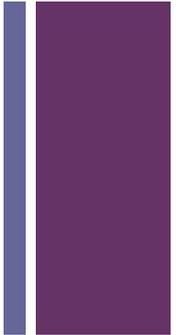


- These rodents also called 'sand puppies'
- They can live for > 35 years
- They are very resistant to environmental stresses
- Live underground like bees with a single queen
- Naked mole rats do not undergo senescence
- Clues for longevity
  - Rat splicing factors do not decline with time
  - Create Hyaluronic acid with higher molecular weight than versions humans create
    - Seems to protect against cancer





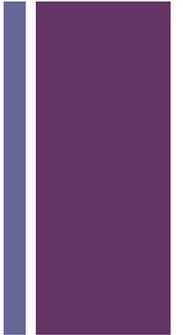
# More animals: bats



- Bats: exceptionally long lived, if corrected for body size
  - Bat will live for 30 or 40 years, even in the wild
  - Bats can hibernate for 6 or 8 months, then wake up and fly away
  - Muscles don't degenerate after this time unlike humans
  - High frequency hearing, use echo to locate prey, critical to survival
  - Humans, high frequency starts to deteriorate around age 15



# Since the bronze age we've been living longer and longer



- Early iron and bronze age – 18
- 2000 years ago 22
- 1838-1854: 41
- Before 1789 36
- 1902: 47
- 1946: 67
- 2018: 79

# Life expectancy – rich people (usually) live longer



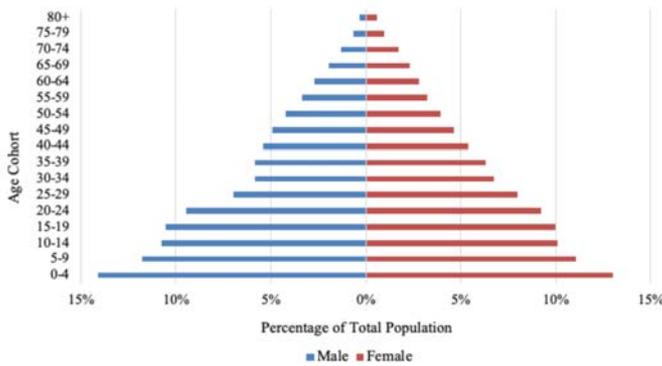
Source: [https://www.gapminder.org/tools/#\\$state\\$time\\$value=2018;;&chart-type=bubbles](https://www.gapminder.org/tools/#$state$time$value=2018;;&chart-type=bubbles)

# In the future population will be more evenly distributed by age

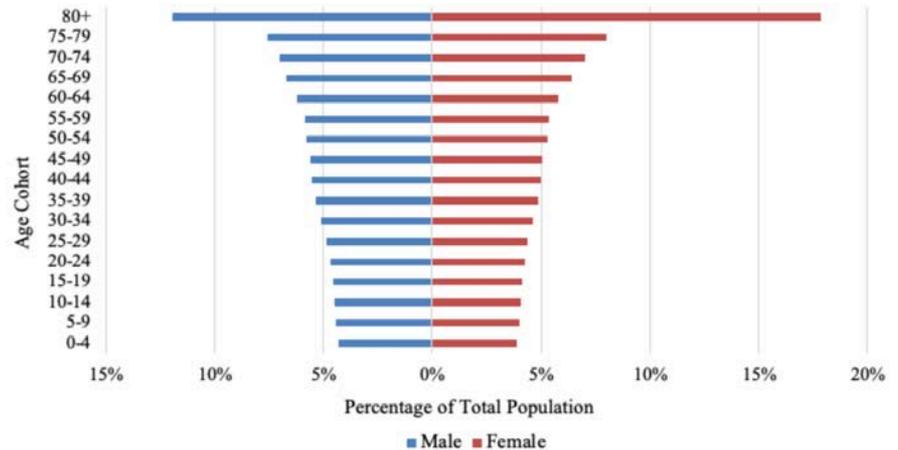
## Population distribution in Japan

Figure 1 Population of Japan by age and sex

a) 1950



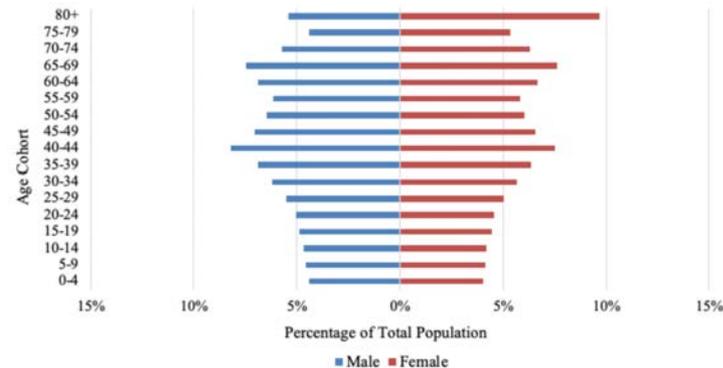
c) 2050 (projected)



Source: United Nations, [World Population Prospects 2017](#).

Note: Medium variant 2050 estimates.

b) 2015

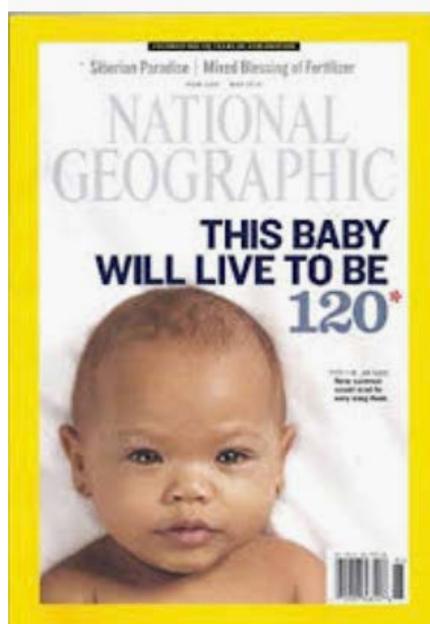


# Longevity has increased due to technology and added 30+ years in 20<sup>th</sup> century

- Agricultural systems to provide steady food supply
  - We make more food with 98% less effort
  - And it costs less: 10% of income versus 90% in 1780
  - Pasteurised milk
- Electricity: led to refrigeration
- Developed world famine has decreased profoundly
- 1900: average number of children born to american women: 4, now 2.1; 25% of babies born died before age 5
- As a result distribution age now redistributed
- Now education prevalent: all children can read and write
  - Education a better predictor of life expectancy
- Garbage collection, sewage systems; prior to this, disease rampant

# + Many babies who will live 120 years have already been born

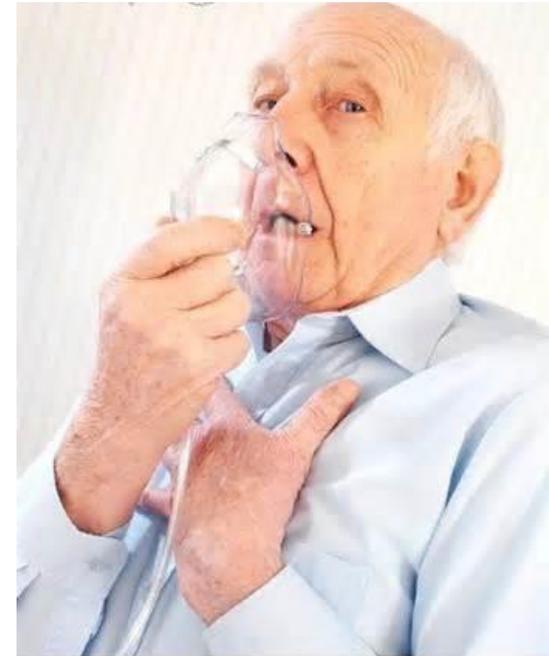
- Demographic Shifts
- What we are learning about aging
- This baby will live to 120 – Time magazine



+ So how do we solve problems that cause us to age

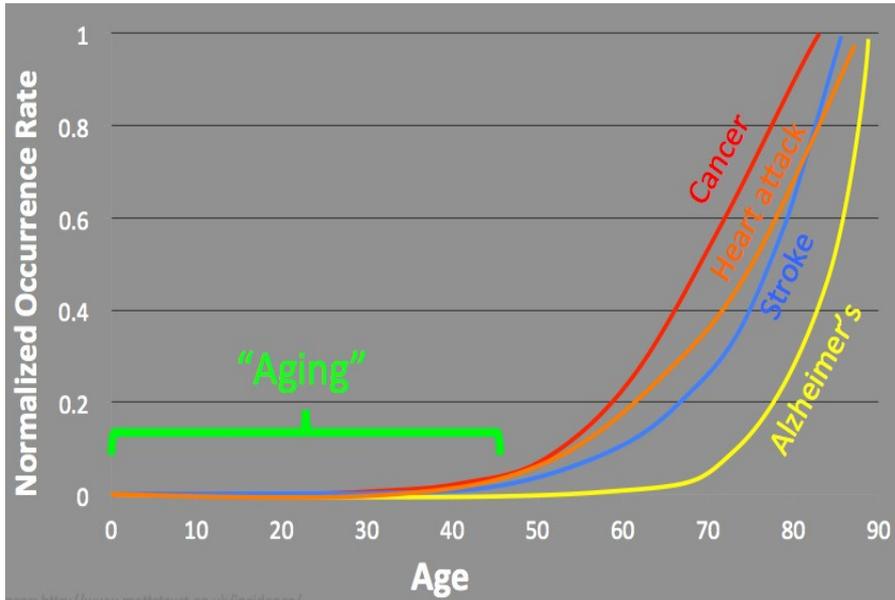
- Increasing age is associated with most of the common, chronic diseases in humans:

- Dementia
- Cardiovascular disease
- Osteoarthritis
- Diabetes
- Cancer
- **Covid-19**



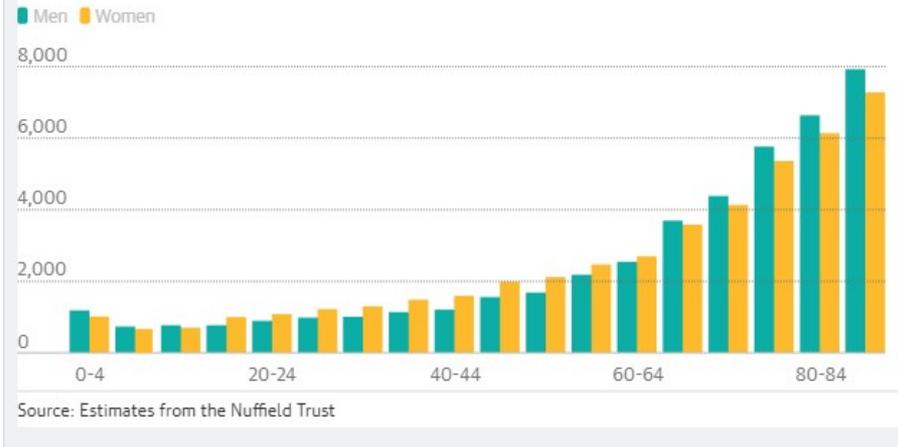
m526285 [RM] © www.visualphotos.com

# + Aging diseases are expensive



<http://healthextension.co/wp-content/uploads/2013/06/aging-graph.png>

Average health spending per person in the UK in 2013/14 was highest for people aged 85 and over. **£7,274 for women, and £7,917 for men**



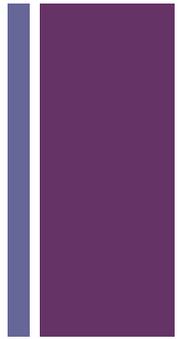
Nuffield Trust 2016

- As of April 2018, 41% of adult hospital admissions were people over 65.
- 10% of people over 65 are classified as frail.
- >10M people living with arthritis.
- 1 in 6 people over 80 have dementia *'Later Life in the United Kingdom' – Age UK, April 2018*

**Estimates from the USA suggest that if we could cure all the diseases of ageing tomorrow, we could save ~4 trillion dollars by 2060! \*AFAR foundation**



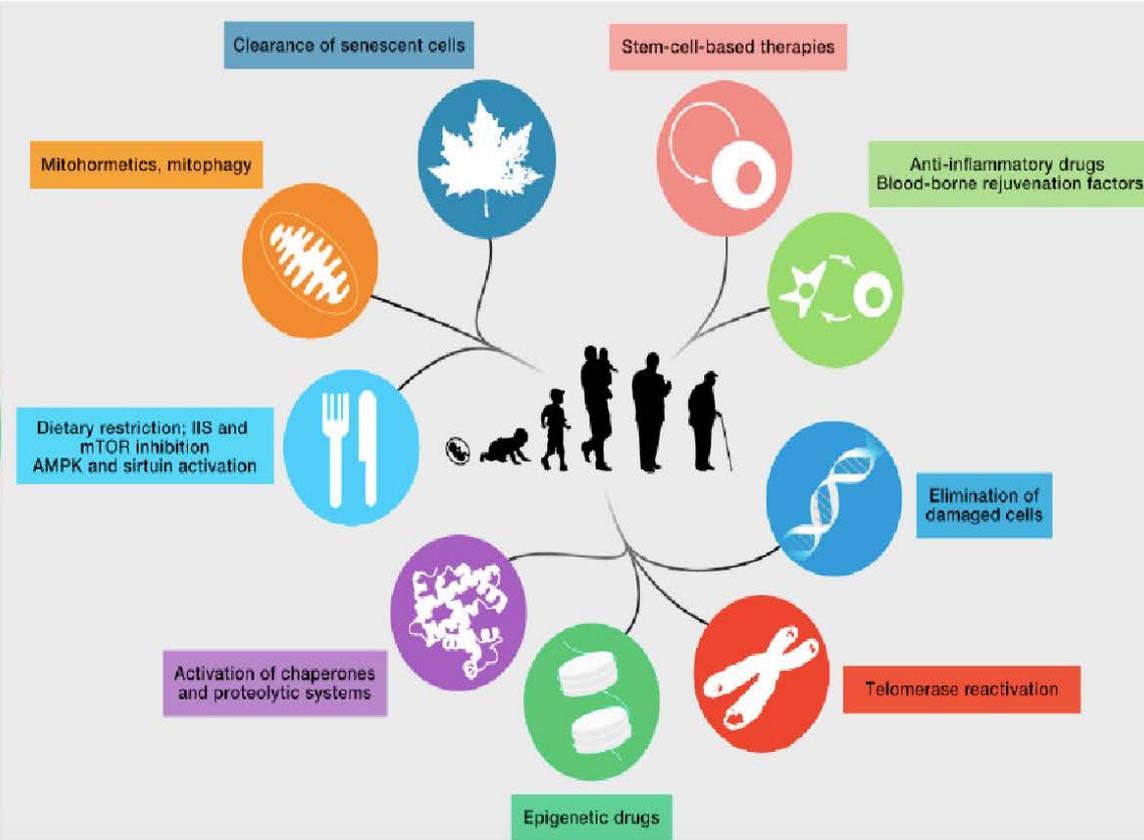
# Basic mechanisms fail that result in aging of cells, organs and people



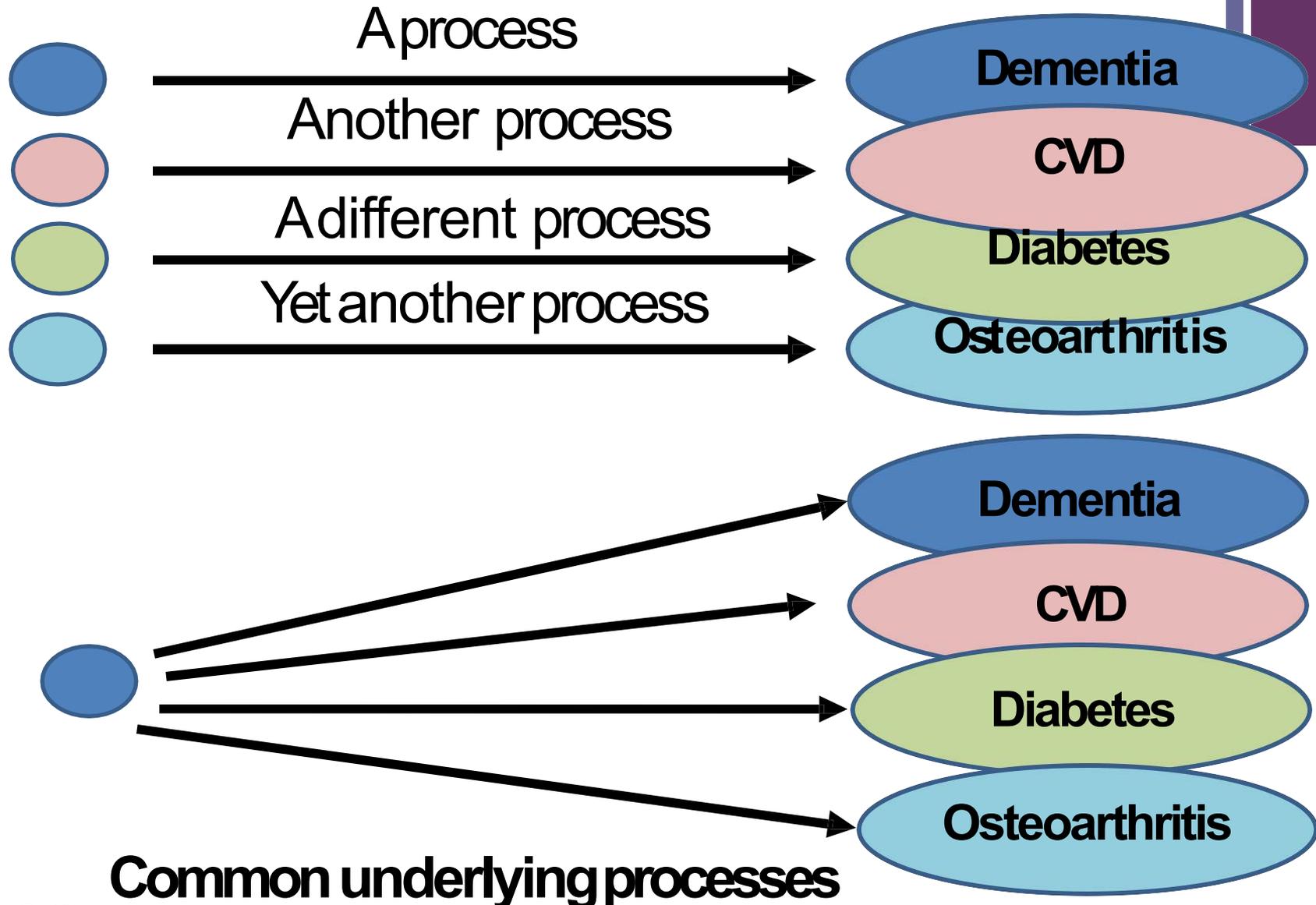
## Hallmarks of Aging



## Intervention Mechanisms



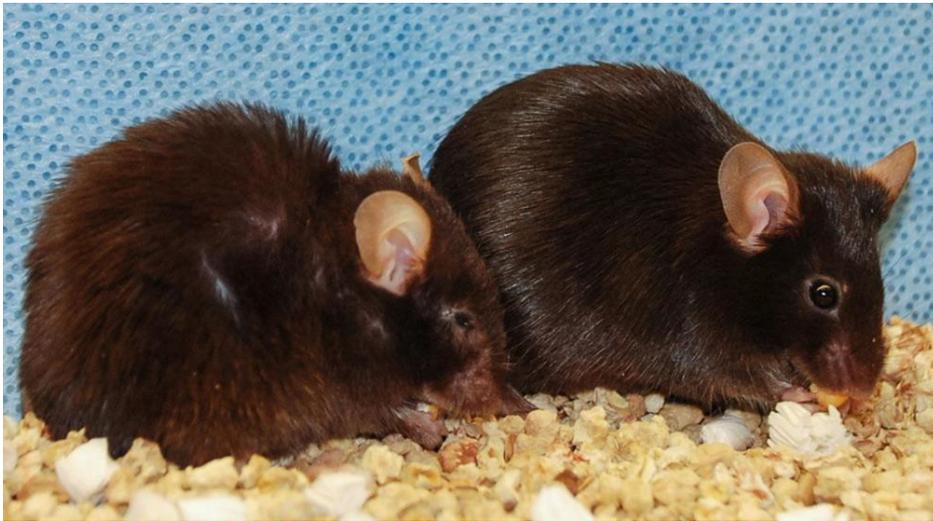
# + Can we find a root cause of aging ?



# + If we can remove senescent cells we can make mice younger



Remove old cells



## Clearance of p16<sup>Ink4a</sup>-positive senescent cells delays ageing-associated disorders

Darren J. Baker<sup>1,2,3</sup>, Tobias Wijshake<sup>1,4</sup>, Tamar Tchkonja<sup>3</sup>, Nathan K. LeBrasseur<sup>3,5</sup>, Bennett G. Childs<sup>1</sup>, Bart van de Sluis<sup>4</sup>, James L. Kirkland<sup>3</sup> & Jan M. van Deursen<sup>1,2,3</sup>



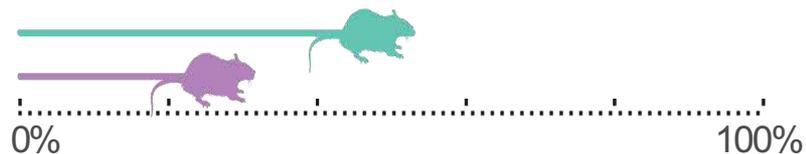
 **Old mouse with senescent cells removed**  
 **Old mouse**

Distance travelled at time of exhaustion



+175%

Running time to exhaustion



+100%

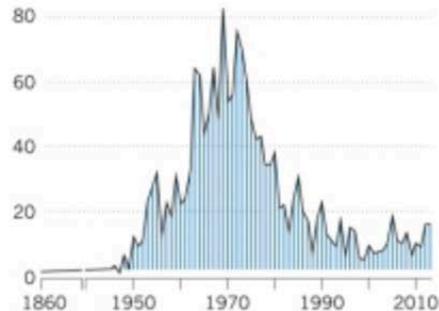
# + Parabiosis has recently taken more interest...

## Share and share alike

Parabiotic experiments, in which two animals share a common bloodstream, were first attempted in the 1860s. By connecting animals with different qualities or conditions, scientists can investigate how blood factors, such as cells, proteins or hormones, influence health. In recent years, a few researchers have looked at heterochronic (old and young) mouse pairs to understand how young blood helps to repair many tissues.

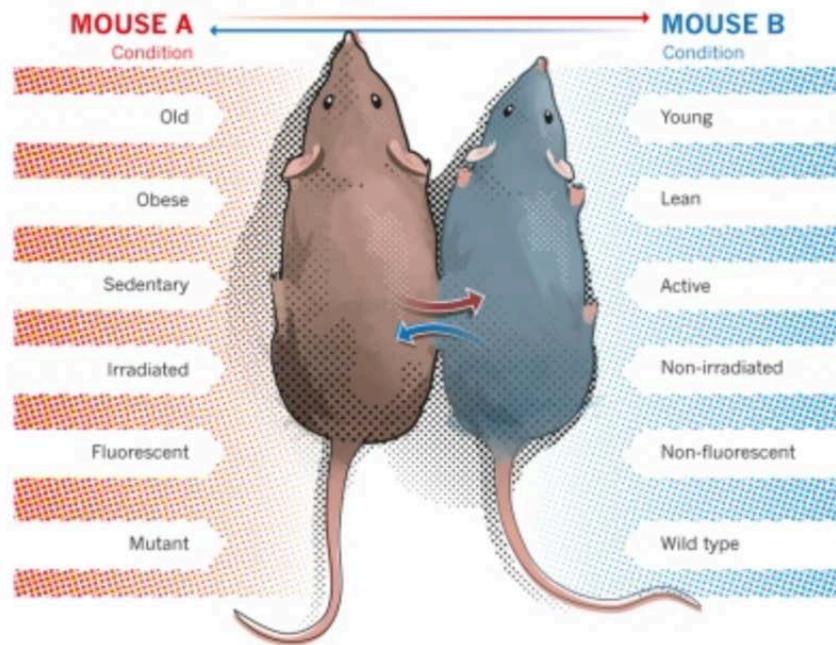
### Publications on parabiosis

Parabiosis gained popularity during the 1960s and 1970s, but eventually fell out of wide practice.



### A simple surgery

A veterinary surgeon will anaesthetize the animals, peel away a thin layer of skin along their sides and stitch or staple the exposed surfaces together. Wound-healing processes join the bloodstreams through a capillary network, and in one to two weeks, the animals are pumping each other's blood.



# + Maybe there is something in young blood that is rejuvenating

## Young blood versus old blood

Factors in "young blood" activate stem cells and rejuvenate organs and cells in old mice. Factors in "old blood" appear to inhibit regenerative capacity in young mice.

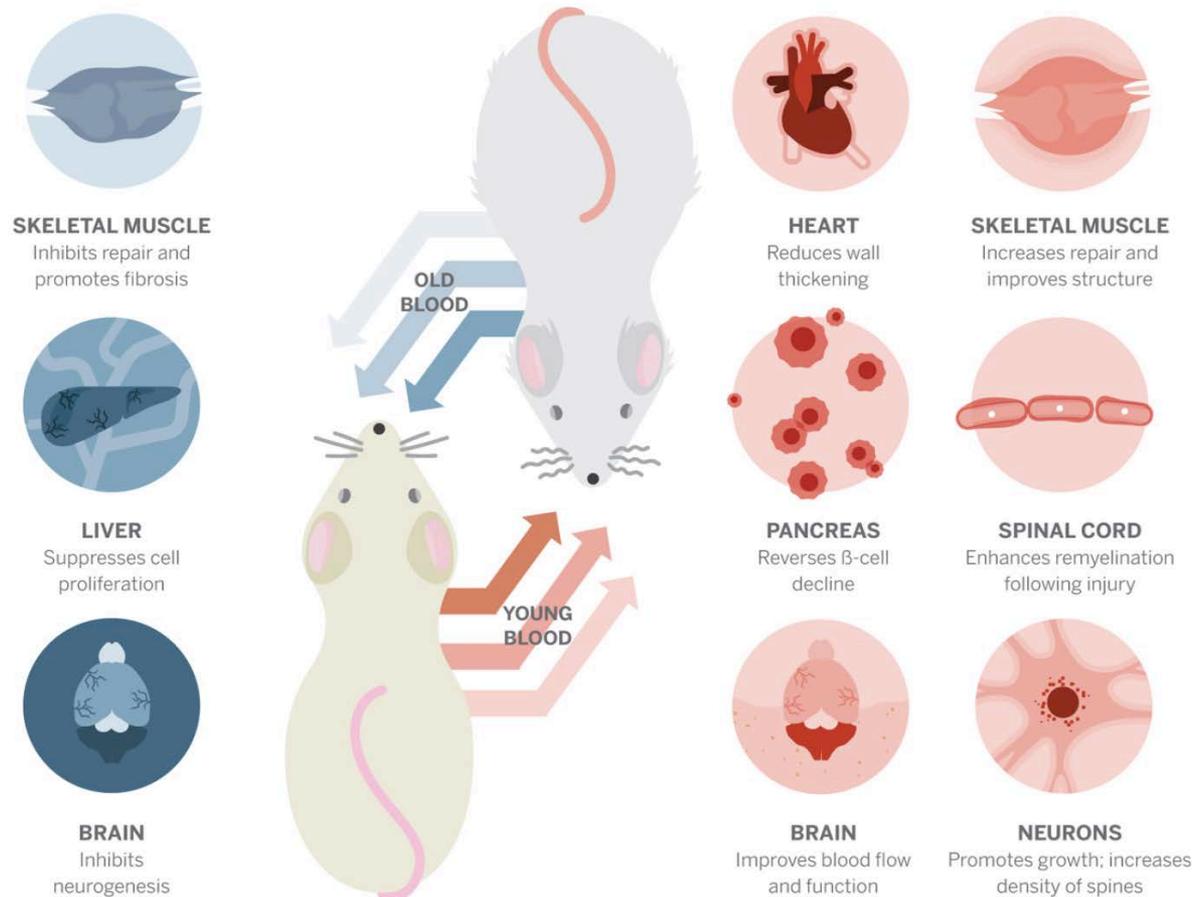
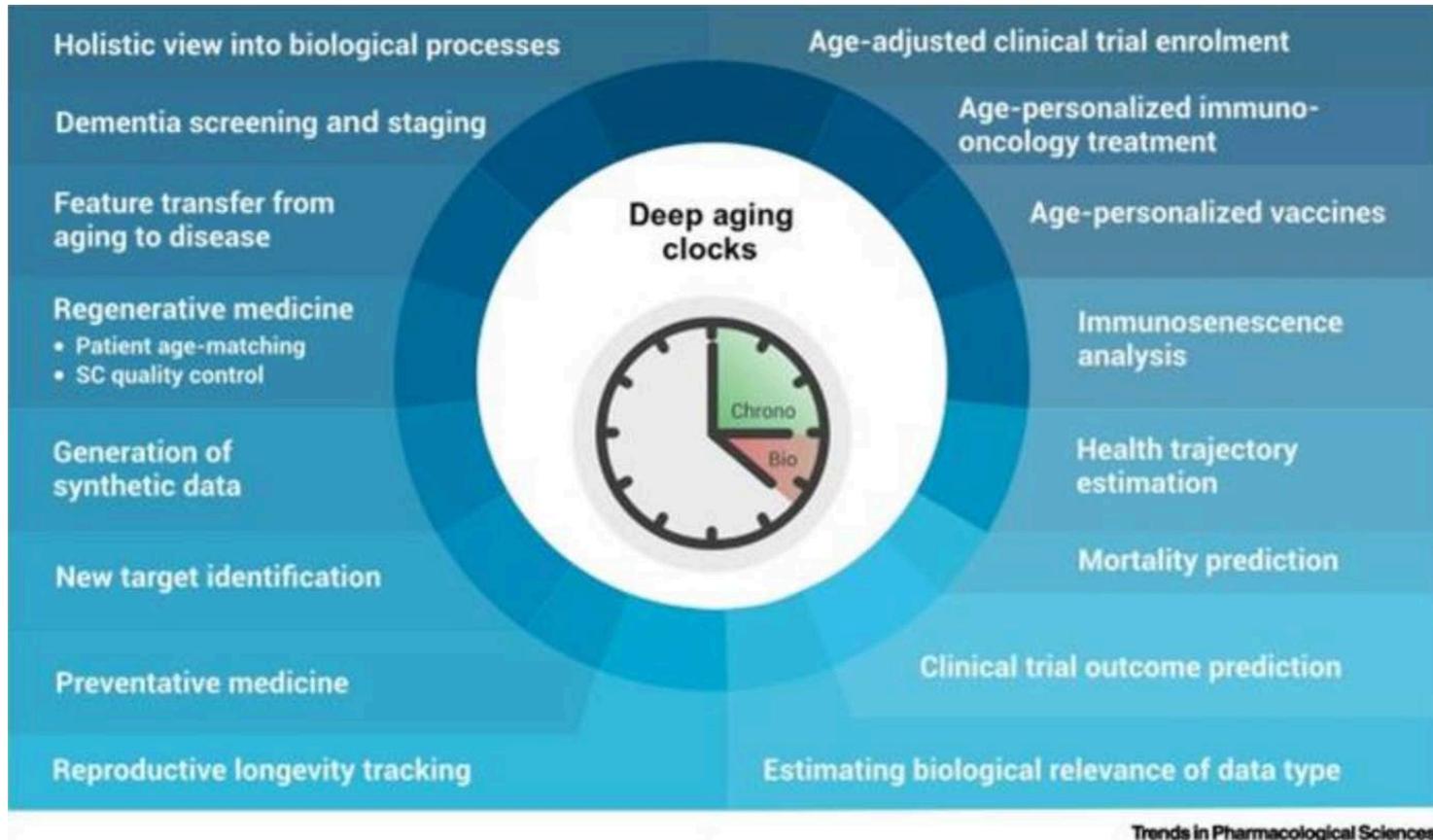


ILLUSTRATION: G. GRULLÓN/SCIENCE

Source: *Science* 12 Sep 2014:  
Vol. 345, Issue 6202, pp. 1234-1237  
DOI: 10.1126/science.345.6202.1234

# + Many applications of AI to Aging



Source: Zhavoronkov and Polina Momoshina

[https://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147\(19\)30114-2](https://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147(19)30114-2)

# + Aging biomarkers

- Biomarkers predict functional capacity at some later age better than will chronological age.
  - Gives “biological age”
  - Different to chronological age
- Problem: Difficult to do longitudinal studies because humans live a long time
  - Difficult to verify with maximal age
  - Need to do assays of biomarkers during life and measure relation of functional capacity to those biomarkers
    - Framingham Study
- Biomarkers should ideally assay the biological process of aging and not a predisposition to disease, should cause a minimal amount of trauma
- Be reproducibly measurable during a short interval compared to the human lifespan

# + Biomarkers

Biomarkers	High risk cutpoints	Source
Biomarkers of cardiovascular system		
Systolic blood pressure	≥140 mm Hg (N)	[159]
	≥148 mm Hg (M)	[160]
Diastolic blood pressure	≥90 mm Hg (N)	[159]
	≥83 mm Hg (M)	[160]
Pulse pressure	≥88 mm Hg (N)	NHANES III 1999–2002 fourth quartile <sup>a</sup>
Resting pulse rate	≥90 bpm (N)	[150]
Homocysteine	≥15 μmol/liter (N)	[161, 162]
	≥13.38 μmol/liter (M)	[163]
Biomarkers of metabolic processes		
Serum total cholesterol	≥240 mg/dl (N)	[164]
Serum HDL cholesterol	≥40 mg/dl (N)	[164]
	≥37 mg/dl (M)	[160]
Total/HDL cholesterol	≥5.92 (M)	[160]
Serum LDL cholesterol	≥160 mg/dl (N)	[164]
Serum triglycerides	≥200 mg/dl (N)	[164]
Fasting blood glucose	≥126 mg/dl (N)	[164]
Glycosylated hemoglobin	≥6.4% (N)	[164]
	≥7% (M)	[160]
Body mass index	≥30 kg/m <sup>2</sup> (N)	[166]

[Open in a separate window](#)

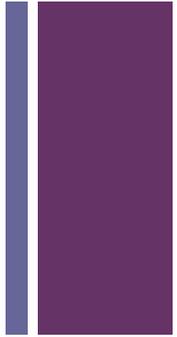
(N) NHANES; (M) MacArthur.

HDL = high-density lipoprotein; LDL = low-density lipoprotein; IL-6 = interleukin-6; DHEA-S = dehydroepiandrosterone sulfate.

<sup>a</sup>Individual data from NHANES III (1988–1994), using the highest quartile as at risk.

Source: Crimmins et al: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5938178/>

# + Aging.AI



Deep Learning Neural network trained on blood profiles  
81% accuracy



## Deep Biomarkers Of Human Aging

How old by basic blood test

### Aging.AI <sup>1.0</sup>

- 41 input parameters
- $r = 0.91$
- $Rsq = 0.82$
- $MAE = 5.5$  years

Test your samples

### Aging.AI <sup>2.0</sup>

- 33 input parameters
- $r = 0.79$
- $Rsq = 0.63$
- $MAE = 6.2$  years

Test your samples

This is a deep-learned predictor of your age made with a deep neural network trained on hundreds of thousands anonymized human blood tests. Enter your data below and Aging.ai will guess your age and gender

5 most important markers: albumin, glucose, alkaline phosphatase, urea and erythrocytes

# + Enter blood information

MCHC	<input type="text" value="32.6"/>	31.5 - 35.7 g/dL
MCV	<input type="text" value="85"/>	79 - 97 fL
Platelets	<input type="text" value="193"/>	150-379 $10^3$ /uL
Erythrocytes (RBC)	<input type="text" value="4.78"/>	3.77 - 5.28 $10^6$ /uL
Leukocytes (WBC)	<input type="text" value="4.9"/>	3.4-10.8 $10^3$ /uL
AST	<input type="text" value="25"/>	< 40 U/l
Basophils	<input type="text" value="0.9"/>	< 1.0 %
Eosinophils	<input type="text" value="0.9"/>	< 5.0 %
Lymphocytes	<input type="text" value="39.4"/>	20 - 40 %
Monocytes	<input type="text" value="6.8"/>	3 - 9 %
Neutrophils	<input type="text" value="52.1"/>	45 - 70 %

Submit

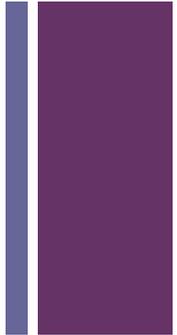
# + Medical databases – MD.AI

The screenshot shows the MD.AI Public Projects interface. The browser address bar displays <https://public.md.ai/hub/projects/public>. The page title is 'Public Projects' with a search bar. The left sidebar contains navigation options: Search, Starred, History, PROJECTS (Public Projects, My Projects, New Project), MODELS (Public Models, My Models, Deploy Model), and TOP TAGS (CT). The main content area shows a project titled 'The Cancer Genome Atlas - Ovarian Cancer' (PUBLIC). Below the title is a table with the following data:

DATASET ID	DATASET NAME	DATASET TYPE	SOURCE	# EXAMS	# SERIES	# IMAGES	SIZE
d_DNVjNB	Dataset	DICOM	Upload	321	843	53,572	28.26 GB

Below the table are 'SERIES THUMBNAILS' showing five medical scan images. To the right of the thumbnails is a '+ 838 more' link and a 'SHOW MORE' button. On the right side of the project page, there are 'Users' (three profile icons) and 'Labels' (Chest, Abdomen, Pelvis, Shape, Box). A 'LAUNCH' button is located at the bottom right of the project card. The top right of the page has 'Order By' set to 'last updated' and 'Descending' selected.

# + Longevity supercentennarian database



**IDL Project**  
Database  
Publications  
Acknowledgements  
Contact

**Copyright & Legal**  
Privacy Policy

**International Database on Longevity** Ronjon Nag | Logout | Change your password

## Database

### MetaData - United States

**Name of the list**  
List of individuals dead at age 110 and over according to the SSA (Social Security Administration) (age validated)

**Vital status**  
dead

**Number of observations**  
341

**Definition of the list according to IDL public variables**  
Age: 110+  
Sex: women and men  
Country of birth: no restriction  
Date of birth: 1867 to 1889  
Country of death: United States  
Date of death: 1980 to 2003  
Validation level: A  
Source: Social Security Administration (USA)

**Source of the data**  
Social Security Administration records for persons enrolled in Part B of the Medicare program on their 110<sup>th</sup> birthday and beyond. According to estimates from the U.S. Bureau of the Census, more than 96 percent of the population ages 70 and over participate in the Medicare program.

# + Betula database

## Betula - Aging, memory and dementia

**RESEARCH PROJECT** The Betula Project is a longitudinal study on aging, memory and dementia and has been going on for a period of over 25 years.

The main objectives of the project is to study how memory functions change during adult life and old age, to identify risk factors for dementia and to identify early preclinical signs of dementia.

### Project overview

**Project period**

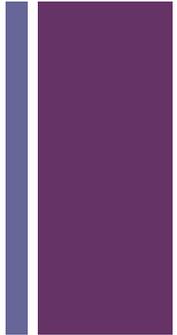
#### On this page

[Project overview](#)

[Head of project](#)

[Project description](#)

# + GenAge

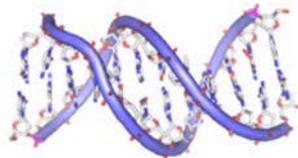


HAGR  ■ Genomics ■ Drugs ■ Animal Longevity ■ Ageing Changes ■ Ageing Information

Quick Search

## GenAge: The Ageing Gene Database

at the [Human Ageing Genomic Resources](#)



GenAge: The Ageing Gene Database

- Human
- Human Microarray
- Models
- Statistics
- Release notes
- Help
- Downloads

### GenAge Database of Ageing-Related Genes

Welcome to GenAge, the benchmark database of genes related to ageing. GenAge is divided into genes related to longevity and/or ageing in [model organisms](#) (yeast, worms, flies, mice, etc.) and ageing-related [human genes](#). The section on [human ageing-related genes](#) includes the few genes directly [related to ageing in humans](#) plus the best candidate genes obtained from [model organisms](#). [Human genes](#) are thus considerably better annotated and include more information. GenAge is manually curated by experts to ensure high-quality content.

Search human genes

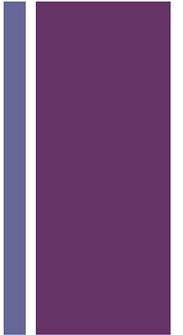
Search model organism genes



Search Human Genes

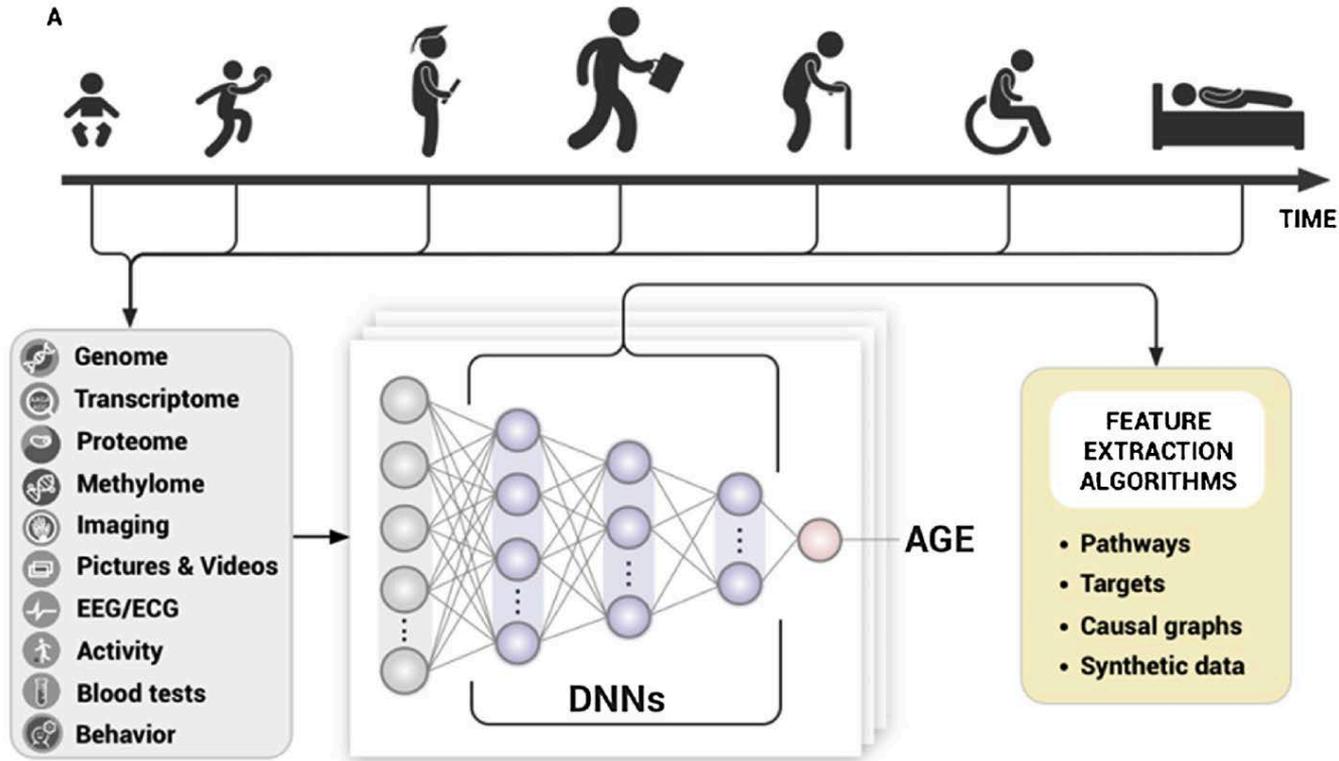


# + Age prediction



A. Zhavoronkov et al.

Ageing Research Reviews 49 (2019) 49–66



# + Cell and tissue aging

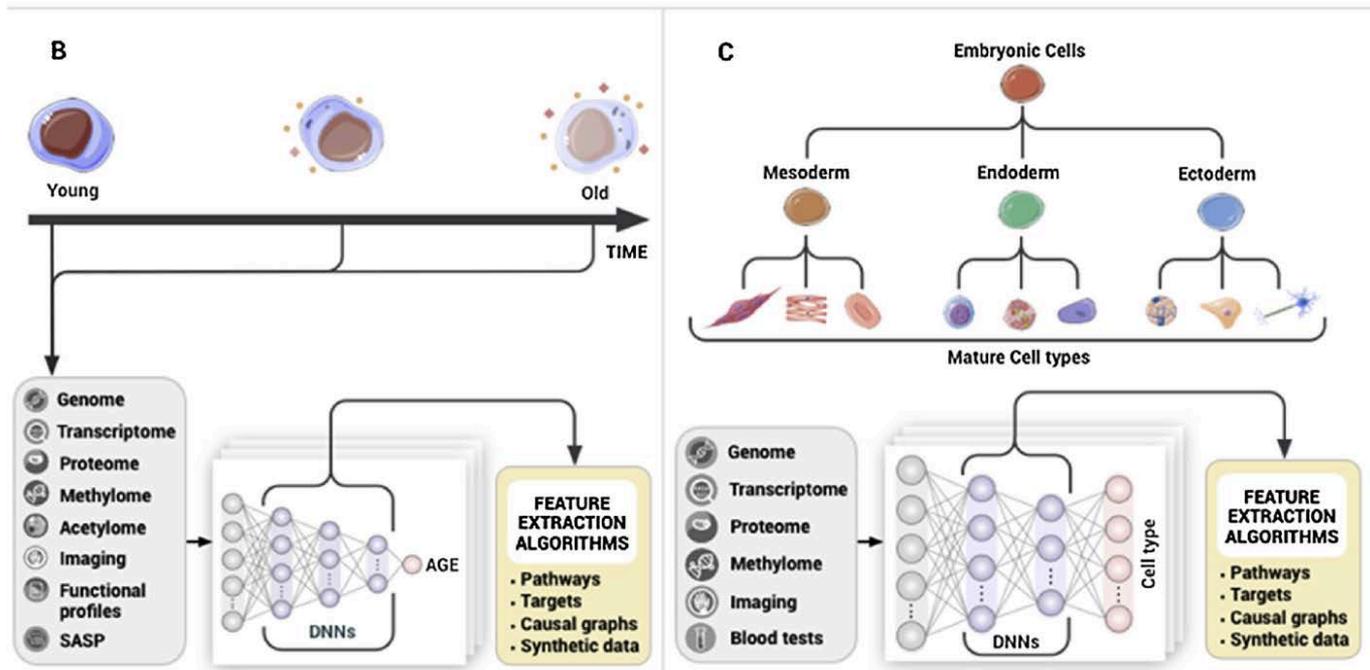
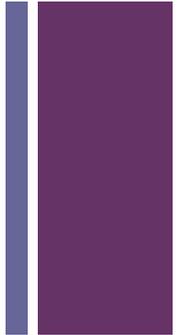
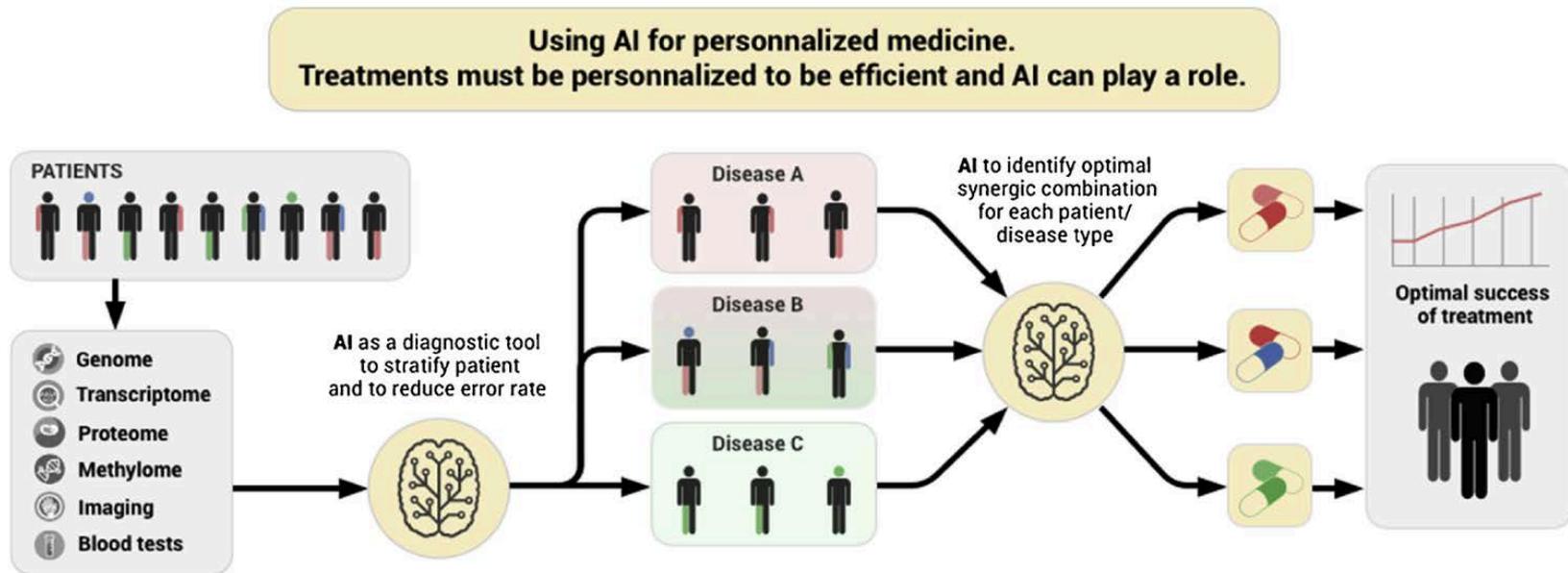


Fig. 1. Applications of artificial intelligence to aging research for biomarker development and target identification. 1 A. Machine-learned predictors of biological age at the organismal level and population level. 1B. Machine-learned age predictors at the cell and tissue-level. 1C. Machine-learned predictors of cell type and differentiation state.

# + Personalized treatments

A. Zhavoronkov et al.

Ageing Research Reviews 49 (2019) 49–66



**Fig. 5.** AI can be used in different ways for designing personalized treatments. AI platforms can be used as a diagnostic tool to reduce error rate. It is also useful to stratify patients according to their specific health condition. By combining more accurate diagnostics and a better knowledge of the health conditions of the patients, AI platforms can be applied to design more effective treatments.



## Market Overview for Technology for Aging in Place

Updated March 5, 2019!

## Related News Articles

### [Comcast Wants to Monitor Your Health](#)

05/25/2019

Device monitoring a number of basic health metrics by way of ambient sensors.

### [Empowering Our Aging Population with Voice Assistant Enabled Hearing Aids](#)

05/24/2019

Nearly every hearing aid is Bluetooth compatible with an iPhone, Android phone or both.

### [Alexa Program at UK Care Home Shows the Power of Voice-First](#)

05/16/2019

"Alexa is an absolute lifeline. I'd be bored stiff without her."

### [How design fails the elderly -- and everyone else](#)

05/10/2019

Bad design reflects poorly on company (see [article about](#)

## [Home](#)

### Voice First/AI/Voice Assistants

Title:

#### Voice First/AI/Voice Assistants

## Empowering Our Aging Population with Voice Assistant Enabled Hearing Aids

Sat, 05/25/2019 - 09:18 - Laurie Orlov

Nearly every hearing aid is Bluetooth compatible with an iPhone, Android phone or both.

**category tags:** [hearing loss](#), [Voice First/AI/Voice Assistants](#)

[Empowering Our Aging Population with Voice Assistant Enabled Hearing Aids](#)

05/24/2019

» [Read more](#)

## Alexa Program at UK Care Home Shows the Power of Voice-First

Thu, 05/16/2019 - 11:00 - Laurie Orlov

"Alexa is an absolute lifeline. I'd be bored stiff without her."

**category tags:** [mHealth-Digital Health-Telehealth-Voice Health](#), [Voice First/AI/Voice Assistants](#)

[Alexa Program at UK Care Home Shows the Power of Voice-First](#)

05/16/2019

» [Read more](#)

## Amazon Wants You to Use Alexa to Track Health Care

Sat, 04/20/2019 - 09:00 - Laurie Orlov

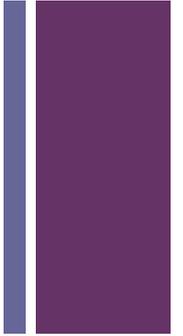
Pilots are underway, giving device a potential daily role with patients.

**category tags:** [Voice First/AI/Voice Assistants](#), [mHealth-Digital Health-Telehealth-Voice Health](#)

[Amazon Wants You to Use Alexa to Track Health Care](#)

04/08/2019

# + Can AI help you exercise better?



# + Can AI help you exercise better?

## ■ *AI can make you faster*

- [Sensoria](#) has a wearable that connects to your shoes and Instead of only having data on distance and pace tells how *well* you did on your run advises on form.

## ■ *AI is helping your yoga flow*

- Nadi X guides on better alignment during your yoga practice? Sensors on clothing seems to be a trend that we might be seeing more of in the coming years.

## ■ *AI can help you get stronger*

- [Fitbod](#) and [Fitnessai.com](#) learns from the data you input into it during and after your workouts to help guide you on suggestions for rep count and weights the next time you hit the gym.

## ■ *AI can monitor you through your sweat*

- [Iamsweati.com](#) is developing patches to monitor glucose, hydration, and lactate through sweat



# Tools and Apps

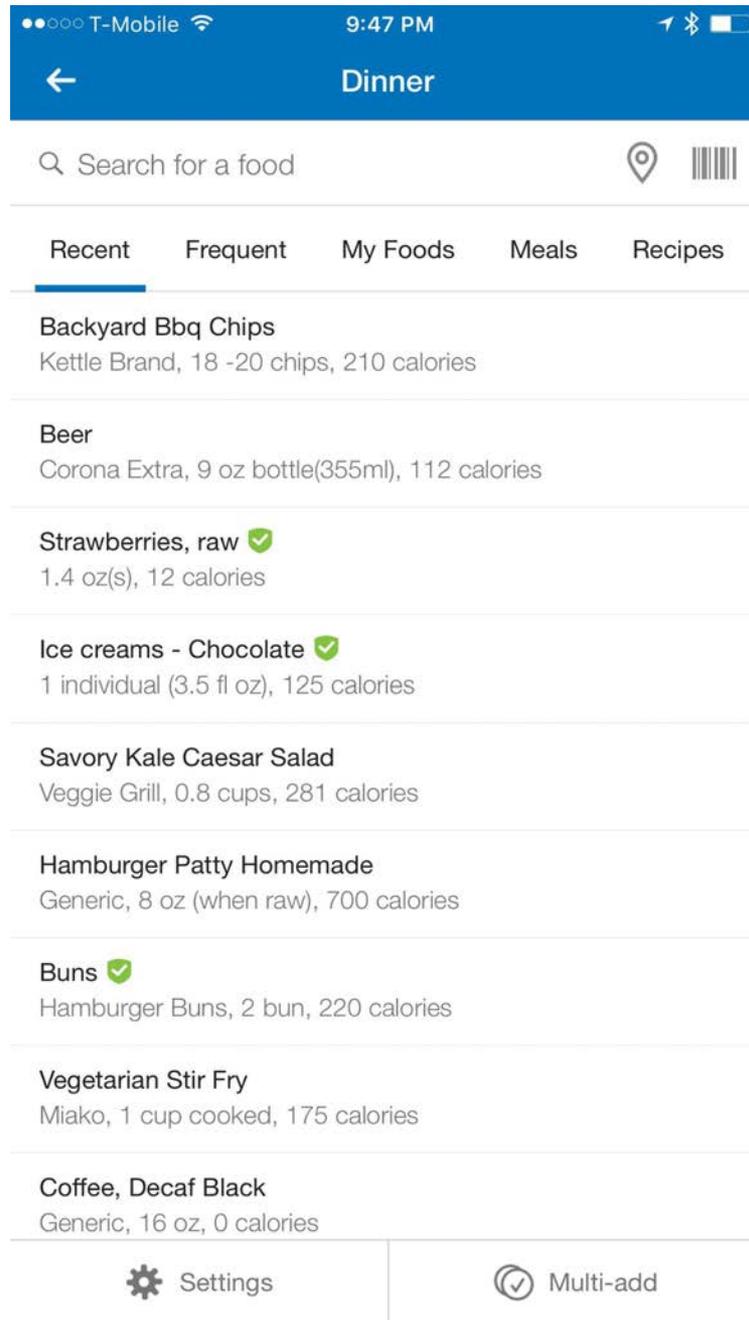
- Diet tracker: MyFitnessPal, healthwatch 360
- Internet weighing scale: Withings, Fitbit
- Aggregator apps: Apple iHealth, Google Health
- Blood Pressure cuffs: Withings
- Fat measurement devices: OMRON, Skulpt, Withings, DXA
- PWM measurement: Withings
- Step trackers: Fitbit, Garmin
- Heart rate monitors:
  - Exercise: Apple, Garmin, with heart rate strap, or now more commonly on watch

# + Internet weighing scale

- Measures weight, fat%, bone density, BMI
- Measures Pulse Wave Velocity (stiffness of artery)
- Connects to phone and stores measurements in the cloud



# MyFitnessPal



The screenshot shows the MyFitnessPal app interface. At the top, the status bar displays 'T-Mobile' and '9:47 PM'. Below that, a blue header bar contains a back arrow and the word 'Dinner'. A search bar with the placeholder text 'Search for a food' is positioned below the header. To the right of the search bar are icons for location and barcode scanning. Below the search bar is a horizontal menu with five tabs: 'Recent', 'Frequent', 'My Foods', 'Meals', and 'Recipes'. The 'Recent' tab is currently selected. The main content area lists several food items, each with a title and a description including quantity and calories. The items are: 'Backyard Bbq Chips' (Kettle Brand, 18 -20 chips, 210 calories), 'Beer' (Corona Extra, 9 oz bottle(355ml), 112 calories), 'Strawberries, raw' (1.4 oz(s), 12 calories), 'Ice creams - Chocolate' (1 individual (3.5 fl oz), 125 calories), 'Savory Kale Caesar Salad' (Veggie Grill, 0.8 cups, 281 calories), 'Hamburger Patty Homemade' (Generic, 8 oz (when raw), 700 calories), 'Buns' (Hamburger Buns, 2 bun, 220 calories), 'Vegetarian Stir Fry' (Miako, 1 cup cooked, 175 calories), and 'Coffee, Decaf Black' (Generic, 16 oz, 0 calories). At the bottom of the screen, there are two buttons: 'Settings' with a gear icon and 'Multi-add' with a checkmark icon.

T-Mobile 9:47 PM

← Dinner

Search for a food

Recent Frequent My Foods Meals Recipes

**Backyard Bbq Chips**  
Kettle Brand, 18 -20 chips, 210 calories

**Beer**  
Corona Extra, 9 oz bottle(355ml), 112 calories

**Strawberries, raw** ✓  
1.4 oz(s), 12 calories

**Ice creams - Chocolate** ✓  
1 individual (3.5 fl oz), 125 calories

**Savory Kale Caesar Salad**  
Veggie Grill, 0.8 cups, 281 calories

**Hamburger Patty Homemade**  
Generic, 8 oz (when raw), 700 calories

**Buns** ✓  
Hamburger Buns, 2 bun, 220 calories

**Vegetarian Stir Fry**  
Miako, 1 cup cooked, 175 calories

**Coffee, Decaf Black**  
Generic, 16 oz, 0 calories

Settings Multi-add



### See How Fit You Are

Discover your Cardio Fitness Level & Score

[Learn More](#)

#### This Week

► Today 57 resting bpm



Sun 54 resting bpm



#### Last Week

Fri



#### Did you know...

Light sleep doesn't mean weak sleep! Your body actually performs a number of important functions during this sleep stage. The name simply refers to how conscious you are.

♥ Like ✕ Dislike

#### This Week 7 hr 11 min avg

Today 12:05 AM – 8:02 AM 6 hr 55 min ★

Sun 12:44 AM – 8:54 AM 7 hr 27 min >

#### Last Week 6 hr 38 min avg

Sat 1:17 AM – 8:59 AM 7 hr 6 min >

Fri 12:09 AM – 7:57 AM 6 hr 50 min >

Thu 11:59 PM – 7:32 AM

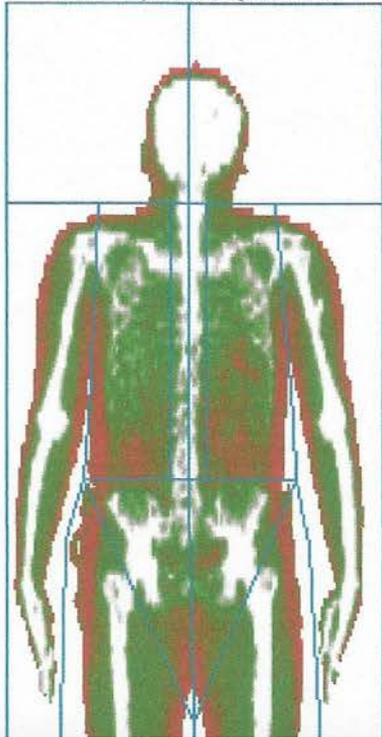


# + DEXA Body Scan

- Low radiation scan of bone and fat density

Measured Date	Total Body Fat %	Total Mass (lbs)	Fat Tissue (lbs)	Lean Tissue (lbs)	Bone Mineral Content (BMC)
03/02/2016	26.3%	161.6	42.5	112.6	6.5

Total Body Tissue Quantitation



## Body Fat Percentile Chart

This table provides target body fat percentages based on empirical DEXA scan results. It is meant to provide general guidance for individuals, and to help set goals.

### WOMEN

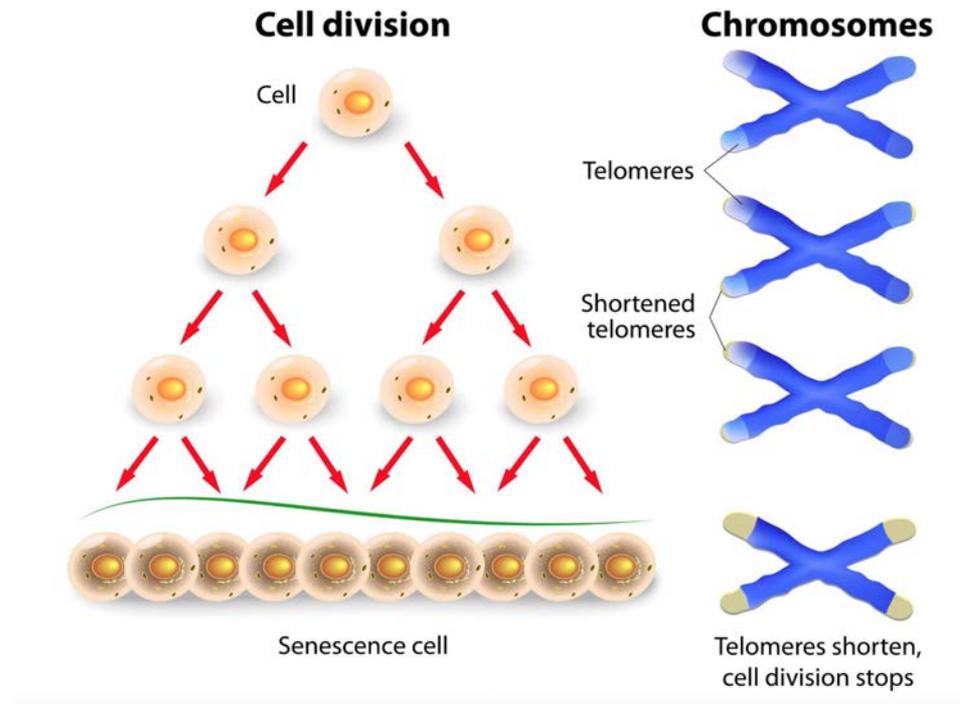
Age	0 - 20 <sup>th</sup> Percentile	20 <sup>th</sup> - 40 <sup>th</sup> Percentile	40 <sup>th</sup> - 60 <sup>th</sup> Percentile	60 <sup>th</sup> - 80 <sup>th</sup> Percentile	80 <sup>th</sup> - 99 <sup>th</sup> Percentile
20-29	< 24%	24% - 28%	28% - 32%	32% - 37%	> 37%
30-39	< 25%	25% - 29%	29% - 33%	33% - 38%	> 38%
40-49	< 26%	26% - 31%	31% - 35%	35% - 39%	> 39%
50-59	< 27%	27% - 32%	32% - 37%	37% - 42%	> 42%
>60	< 30%	30% - 33%	33% - 38%	38% - 42%	> 42%

### MEN

20-29	< 16%	16% - 20%	20% - 24%	24% - 27%	> 27%
30-39	< 18%	18% - 22%	22% - 26%	26% - 30%	> 30%
40-49	< 20%	20% - 24%	24% - 27%	27% - 31%	> 31%
50-59	< 21%	21% - 25%	25% - 29%	29% - 33%	> 33%
>60	< 21%	21% - 25%	25% - 30%	30% - 33%	> 33%

# + Telomeres

**Telomeres** are the caps at the end of each strand of DNA that protect our chromosomes, like the plastic tips at the end of shoelaces. Without the coating, shoelaces become frayed until **they** can no longer do their job, just as without **telomeres**, DNA strands become damaged and our cells can't do their job



\$89 test: [Teloyears.com](http://Teloyears.com)

# + Measure brain size over time

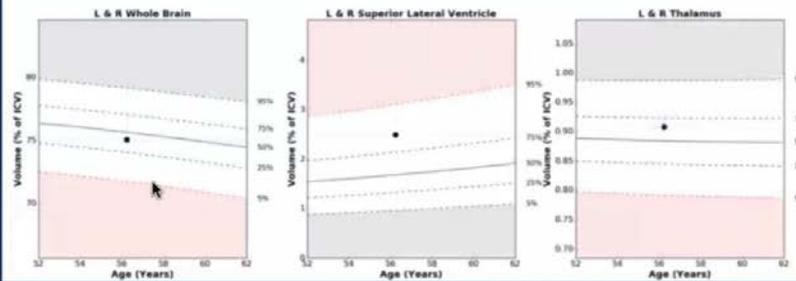


Nervous

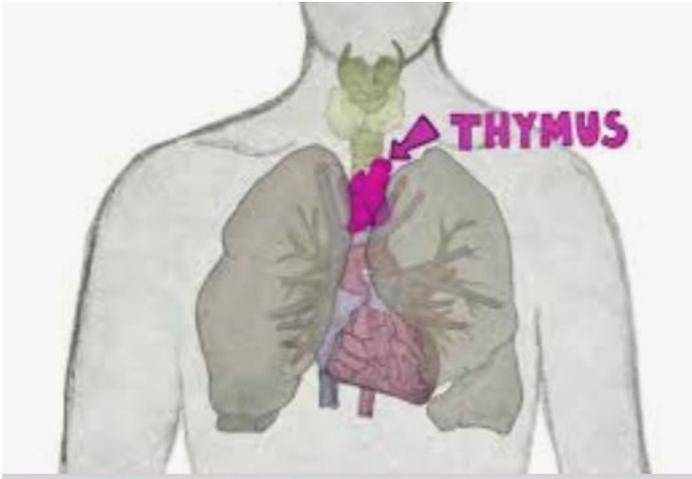
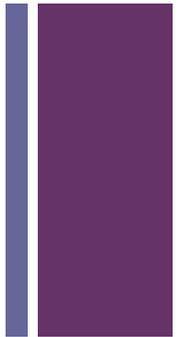


Brain Structure	Volume (cm <sup>3</sup> )	% of ICV (5%-95% Normative Percentile)	Normative Percentile
Whole Brain	1191.09	75.10 ( 71.76 - 79.19 )	40
Superior Lateral Ventricles	39.57	2.49 ( 0.96 - 3.11 )	86
Thalamus	14.41	0.91 ( 0.79 - 0.99 )	66

AGE-MATCHED REFERENCE CHARTS



+ Thymus creates the immune system but is tiny in old age – try to regrow

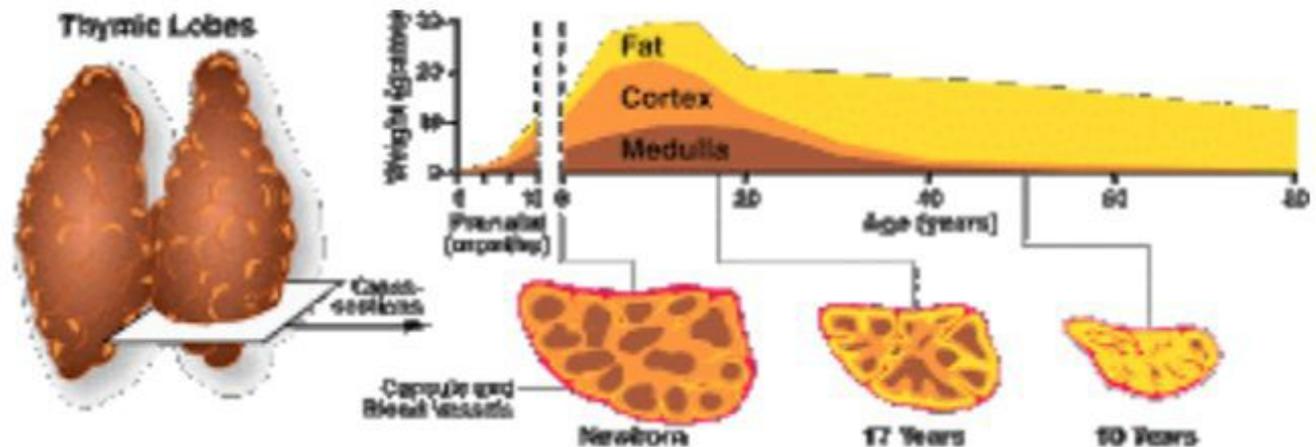


Builds immune system from birth

Starts to get smaller in late teens

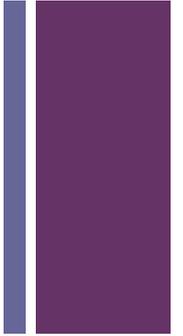
Very small in late decades

## THE THYMUS AND IMMUNE FUNCTION:



Changes in Thymus with age.

+ Can AI make you live longer with smart diets ?



+

# Examine Glucose Dysregulation Using Continuous Glucose Monitoring



DexCom CGM

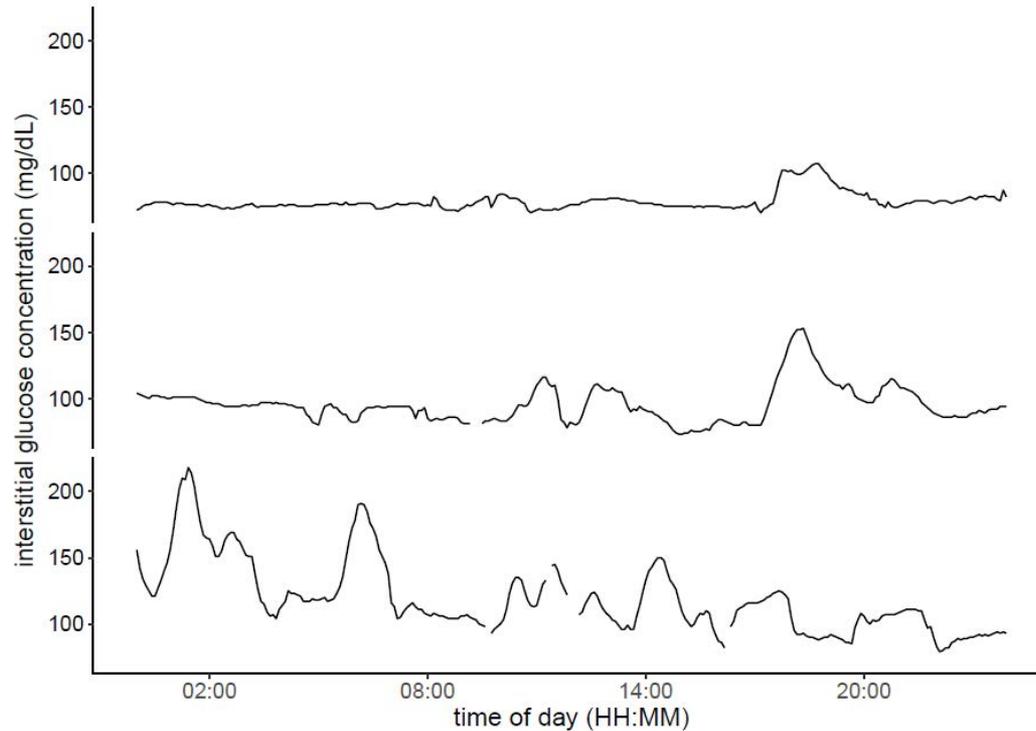
Hall, Perelman, Brecchi et al., 2018 PloS Biology

# Interindividual variation of CGM profiles: can we classify people into "gluotypes"?

2-4 weeks



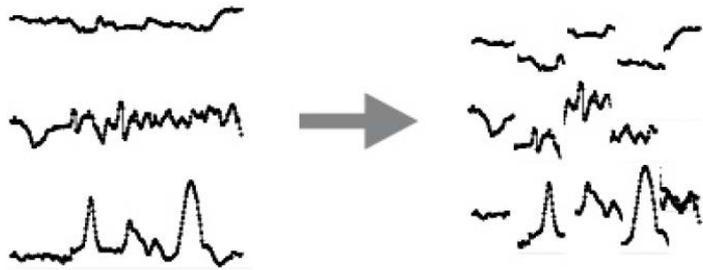
Dexcom G4



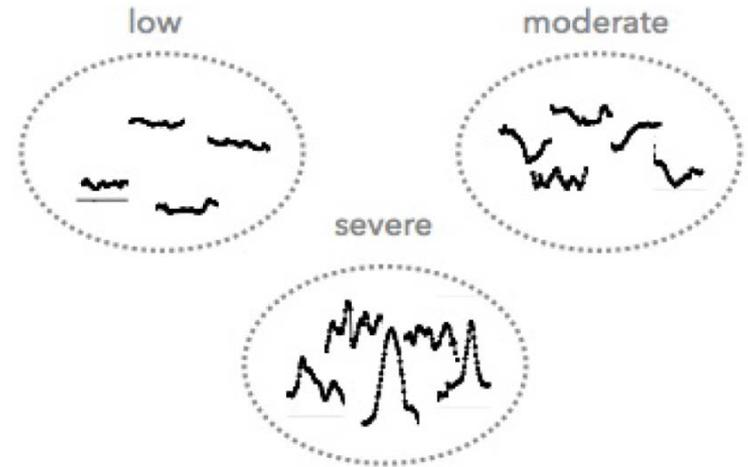
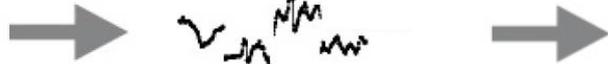
24 hours



# Classification of CGM profiles based on variability, unsupervised learning



Segment CGM profiles into overlapping 2.5 hour **windows**

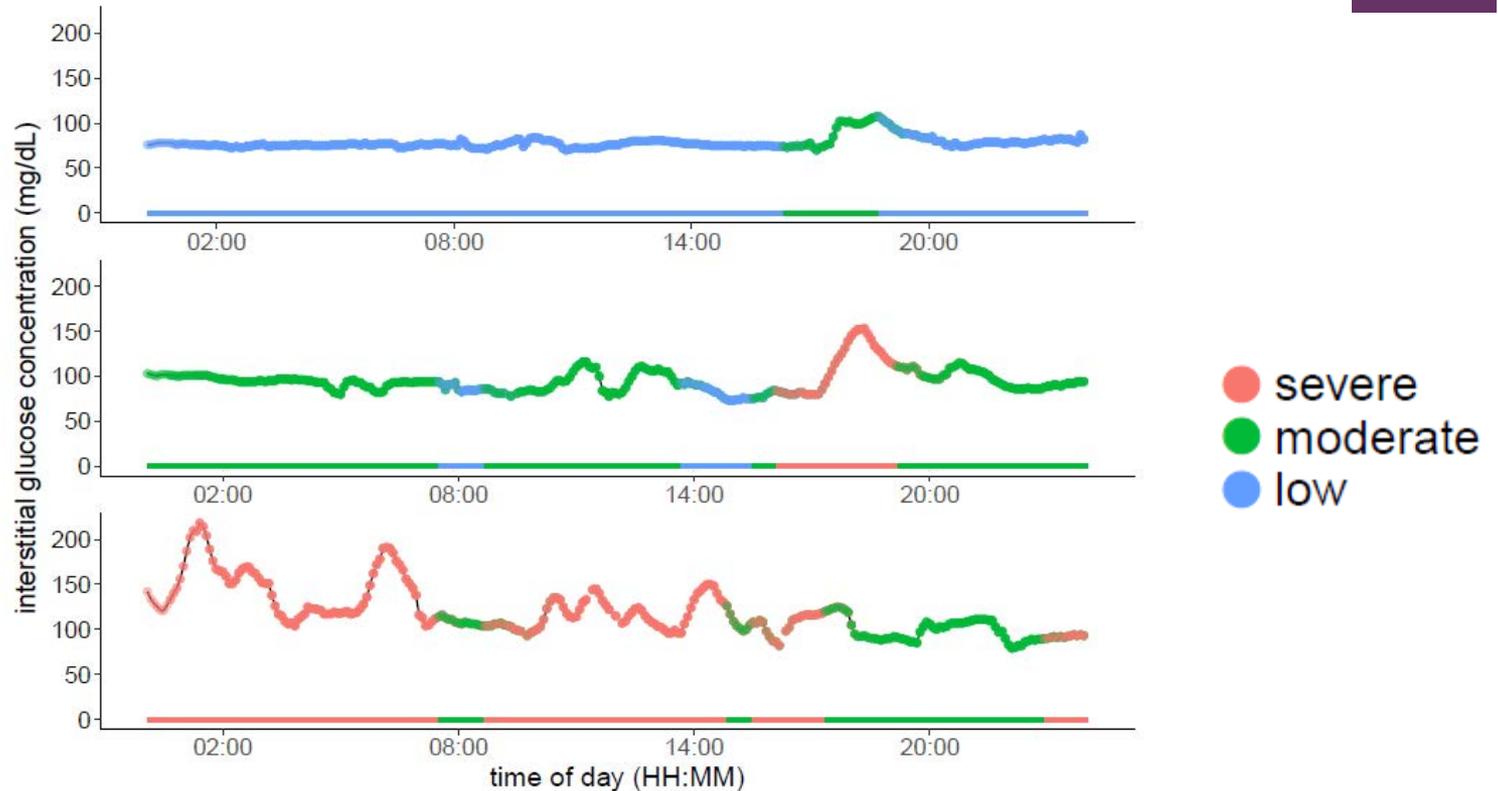


Clustering windows based on shape (variability)

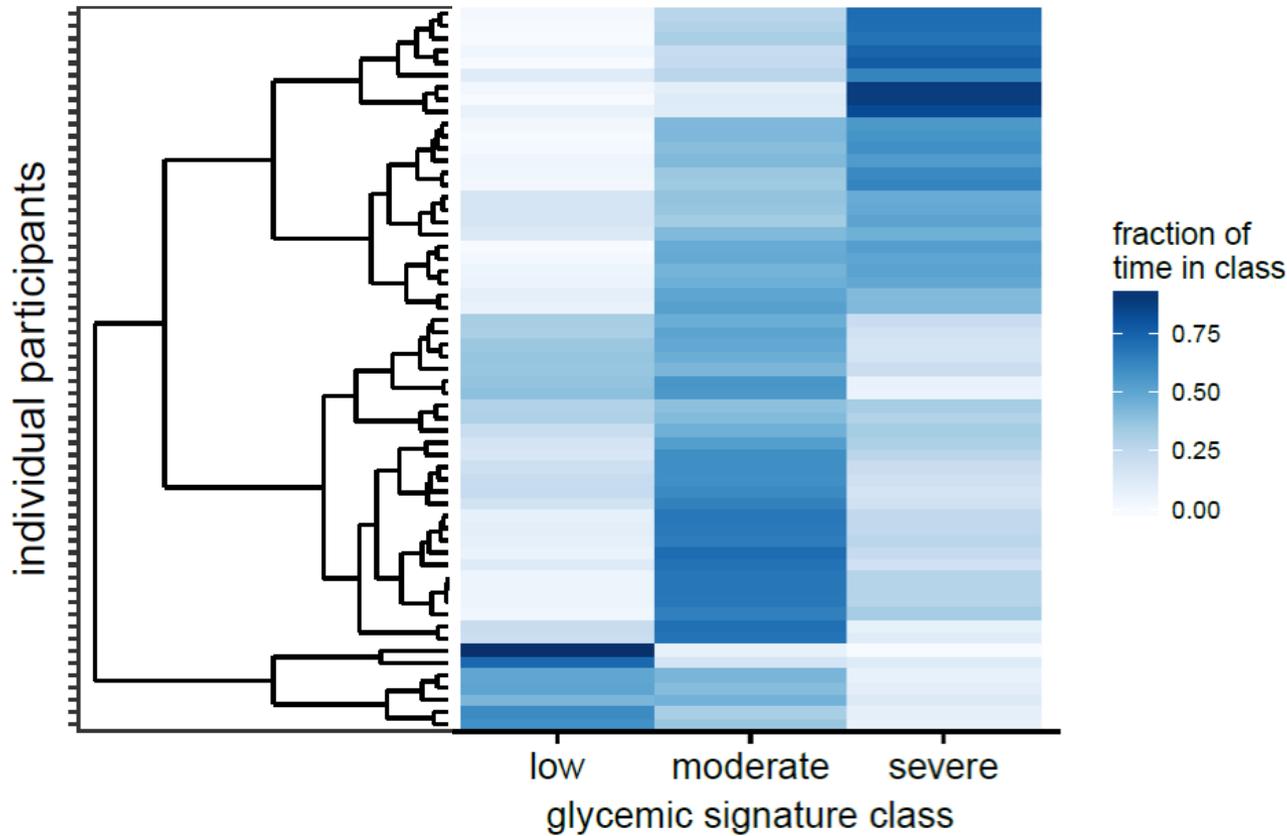
Spectral clustering on time warping distance



# Continuous Glucose Monitoring profiles classified by degree of variability

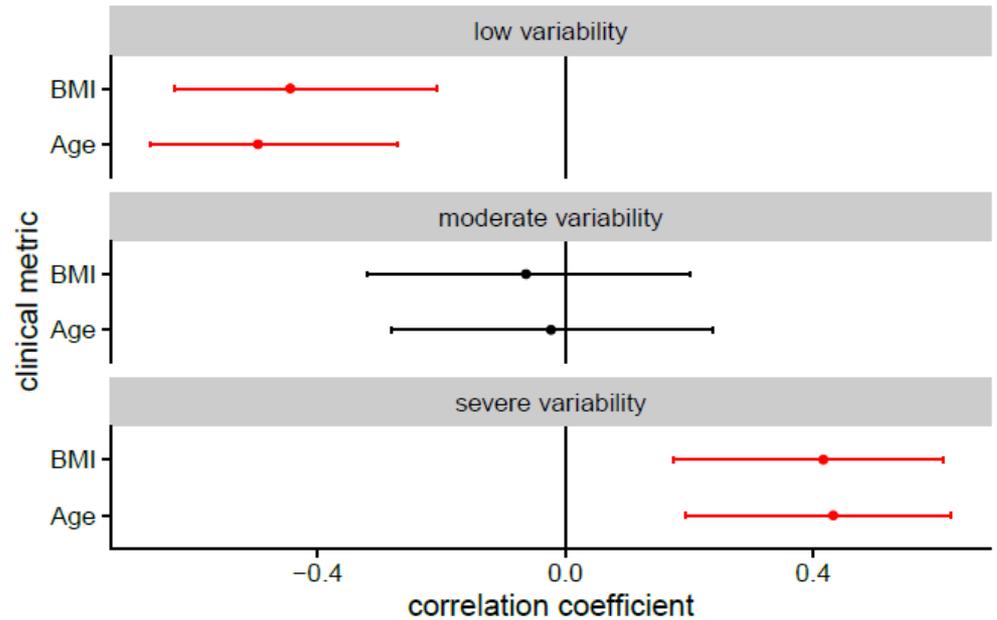
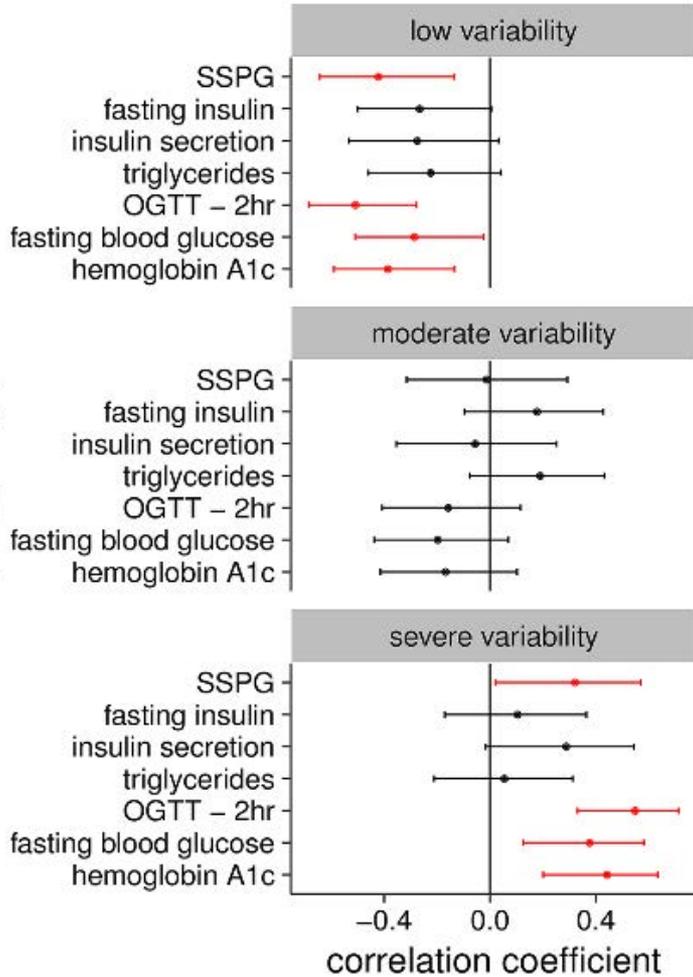
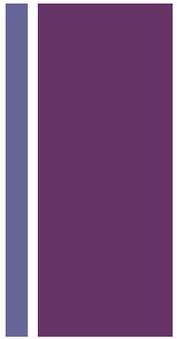


# + Different people have different frequency of variability windows

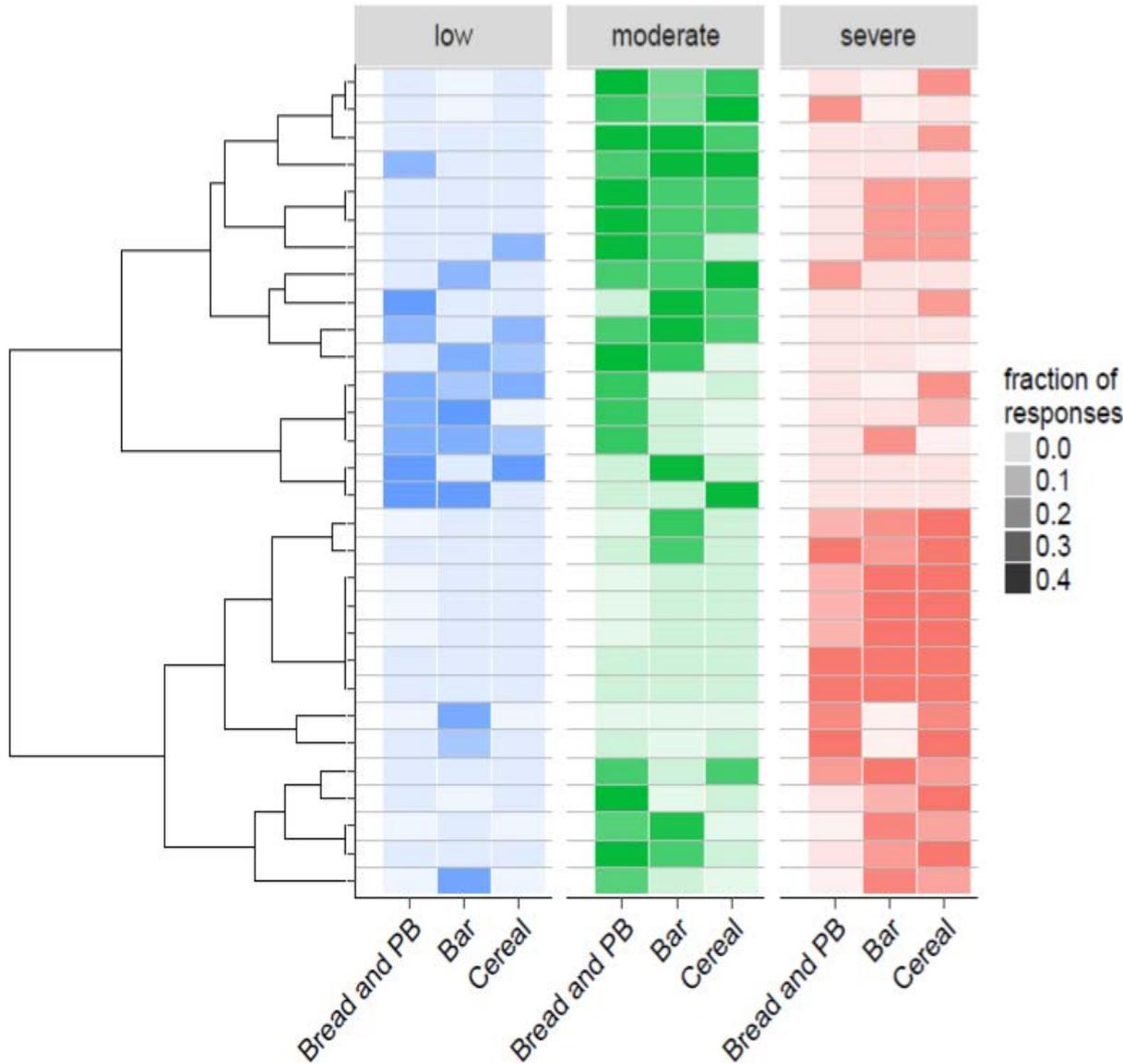


Frequency of variability windows define "glucotypes"

# + Glucose variability from CGM correlated with several clinical parameters



# + The same meal triggers different glycemic responses in different people



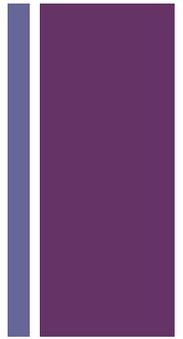
Bread +  
Peanut  
Butter



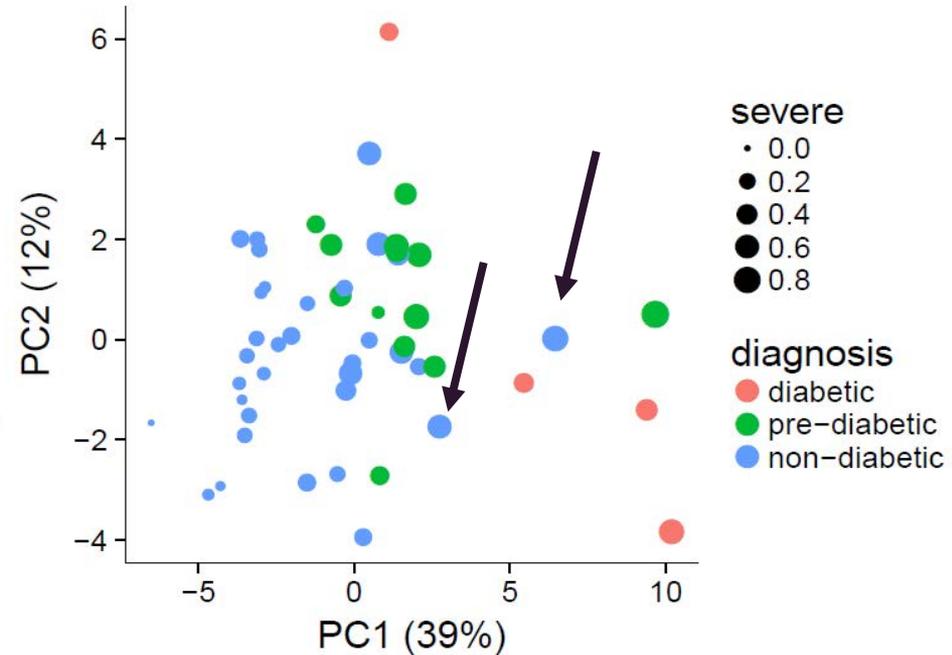
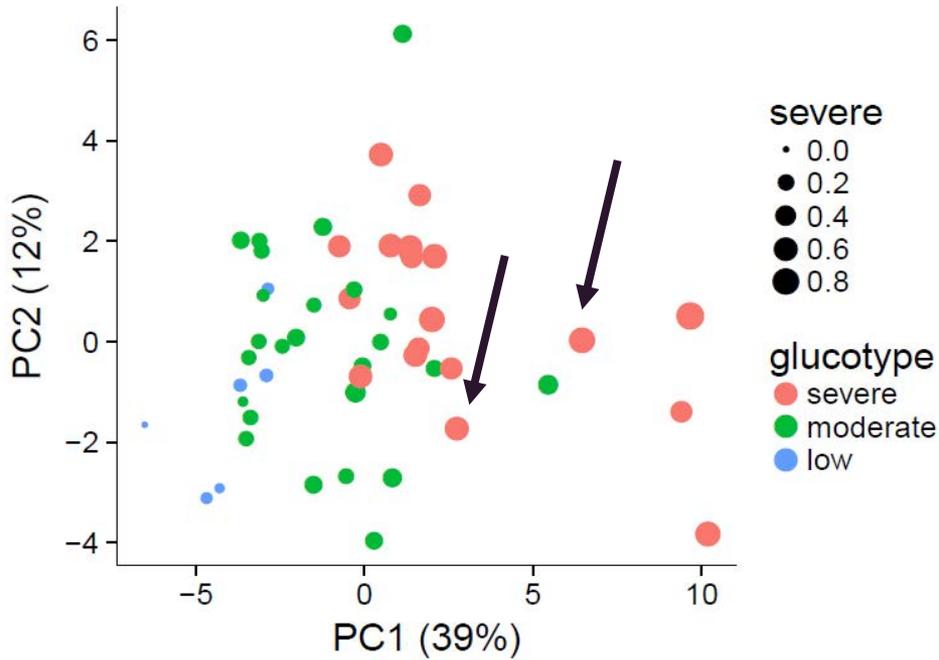
Protein  
Bar



Cornflake  
s  
+ Milk



# + Glucotype classification may help find diabetes risk

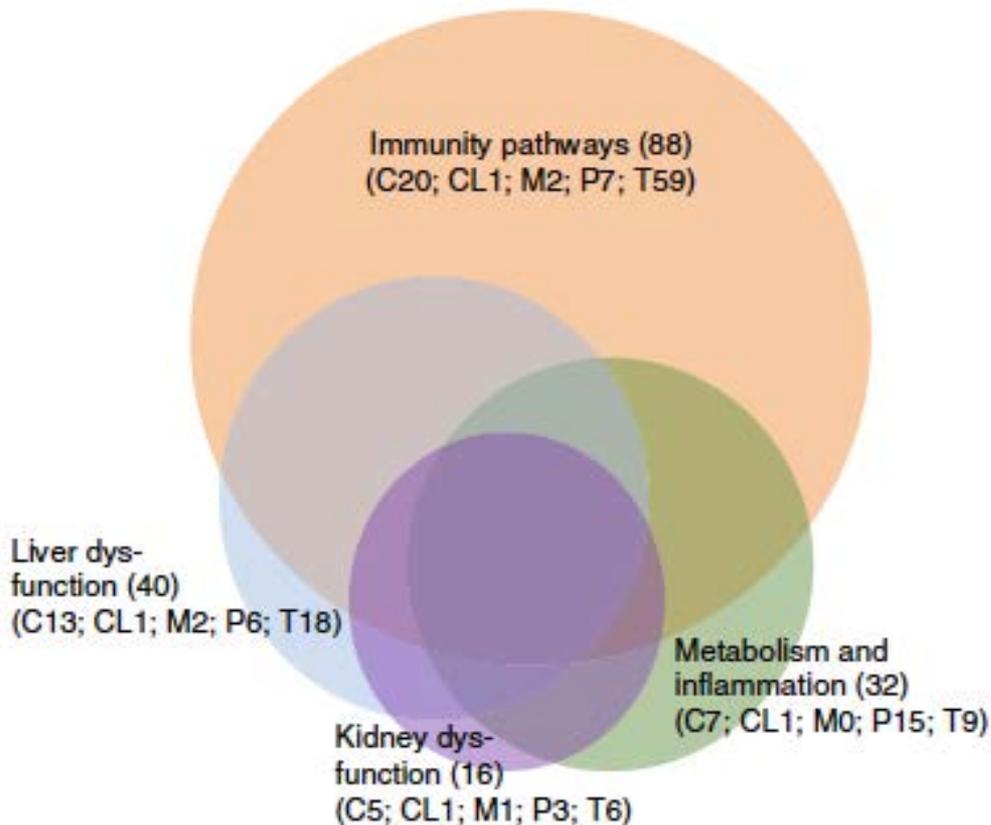


Clustering based on clinical and glucose data

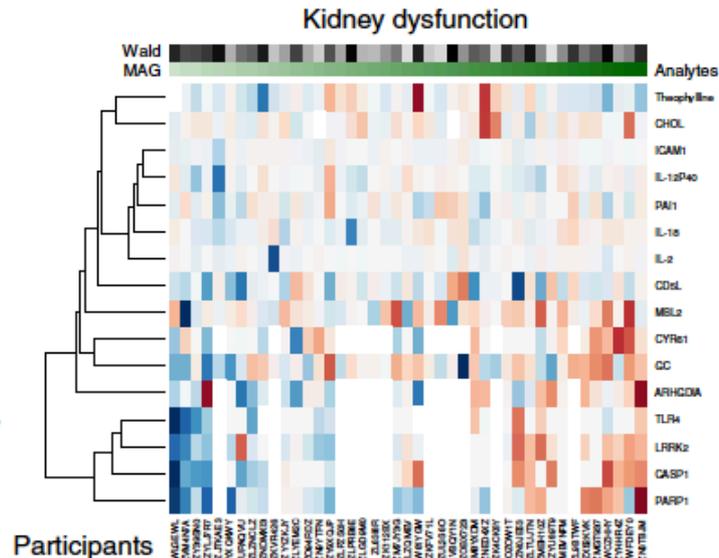
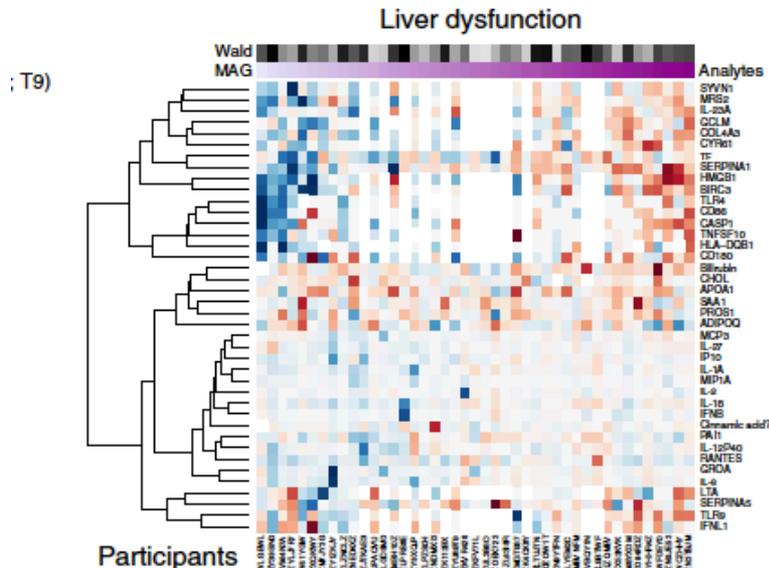
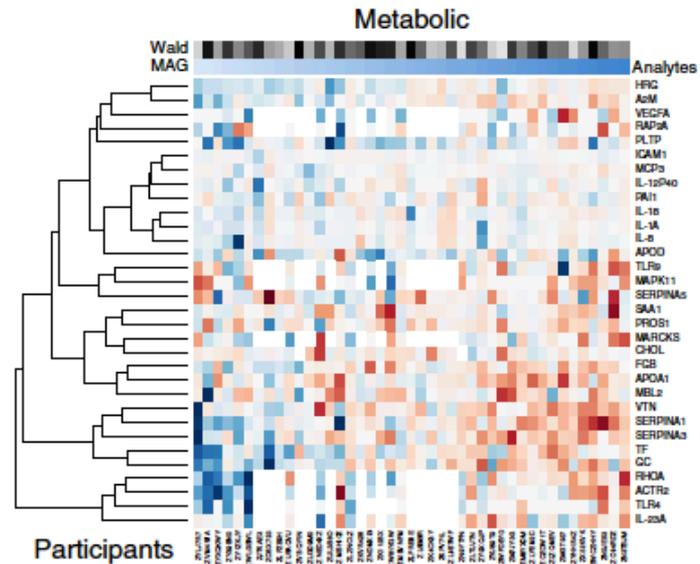
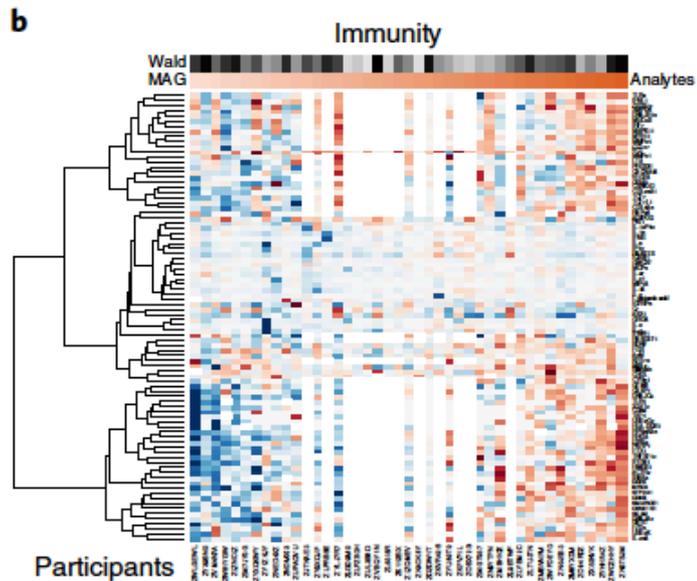
# + Ageotype

- Stanford study sorted 106 (age 29-75) people into aging categories, or "ageotypes," based on biological samples collected over the course of two years.
- The samples included blood, inflammatory substances, microbes, genetic material, proteins and by-products of metabolic processes.
- By tracking how the samples changed over time, identified about 600 so-called markers of aging — values that predict the functional capacity of a tissue and essentially estimate its "biological age."
- Identified four distinct ageotypes:
  - Immune
  - Kidney
  - Liver
  - metabolic

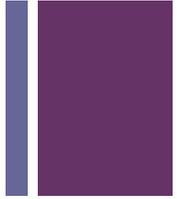
# + Many people are compromised through multiple ageotypes



# + Finding the analytes that map



# + Different people have different ageotypes



Immunity pathways (93)

## Four General Classes of Aging Molecules

Liver dysfunction (42)

Metabolism and inflammation (34)

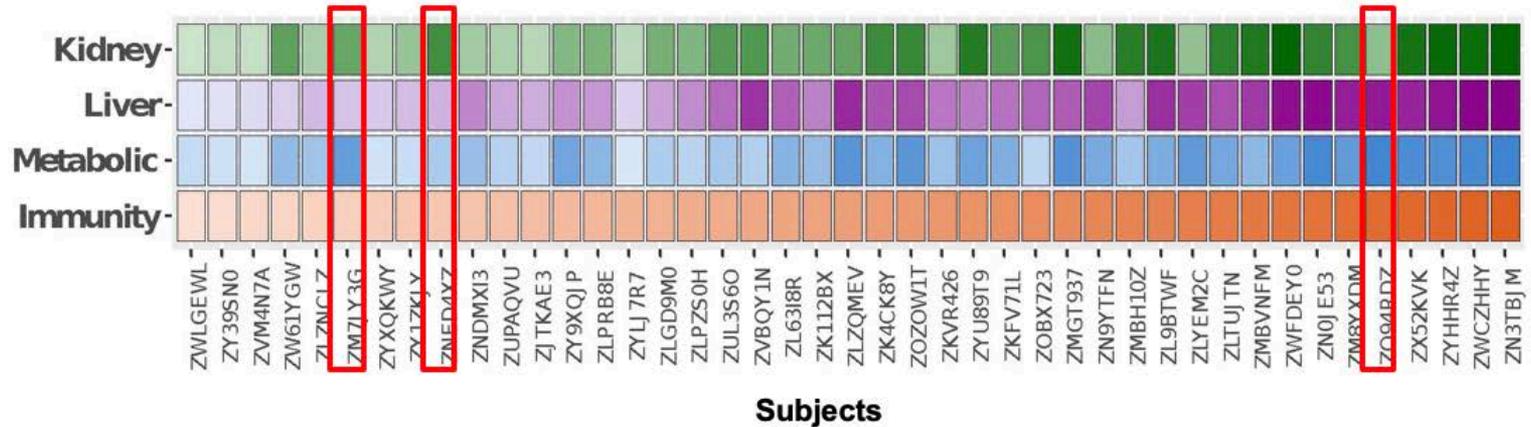
Kidney dysfunction (17)

Immunity

Liver

Metabolism and Inflammation

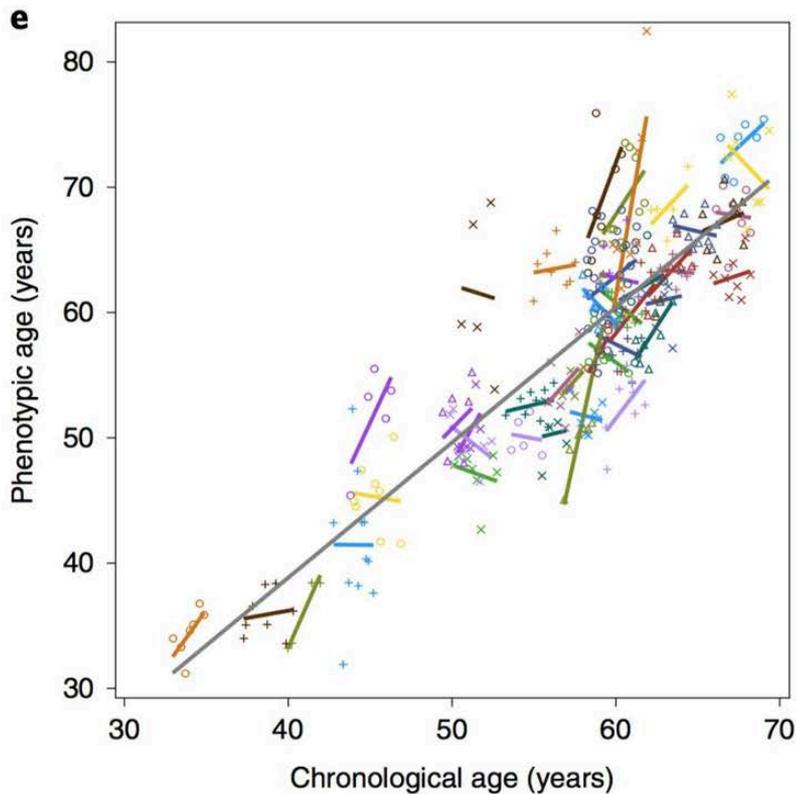
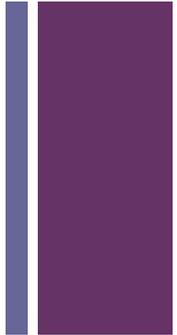
Kidney dysfunction



Source: Ahadi & Zhou et al, *Personal aging markers and Ageotypes revealed by deep longitudinal profiling*, Nature Medicine, Vol 26,



# Over 3 years, track biomarkers against phenotypic age measure



A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: A cohort study

Zuyun Liu, Pei-Lun Kuo, Steve Horvath, Eileen Crimmins, Luigi Ferrucci, Morgan Levine

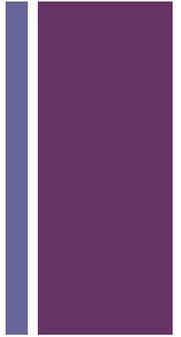
Published: December 31, 2018 • <https://doi.org/10.1371/journal.pmed.1002718>

*Phenotypic age:*

Chronological age and nine biomarkers, including albumin, creatinine, glucose, log (C-reactive protein), lymphocyte percent, mean cell volume, RDW, ALKP and white blood cell count

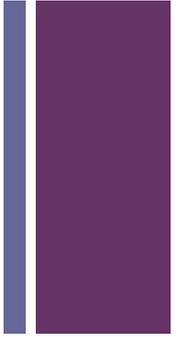
Ahadi, Zhou et al. Nat. Medicine 2020

# + Recommendation: collect a baseline and track over time



	Multi-variate evidence	Rate of change evidence
Early Stage Leukemia		
Low Grade Brain Lesion		
Aortic Aneurysm		
Fatty Liver & Diabetes		
Cardiovascular Disease & Pre-Diabetes		
Early stage pancreatic cancer		
Early stage prostate cancer		
Early stage ovarian cancer		

# + Protein folding impacts on aging





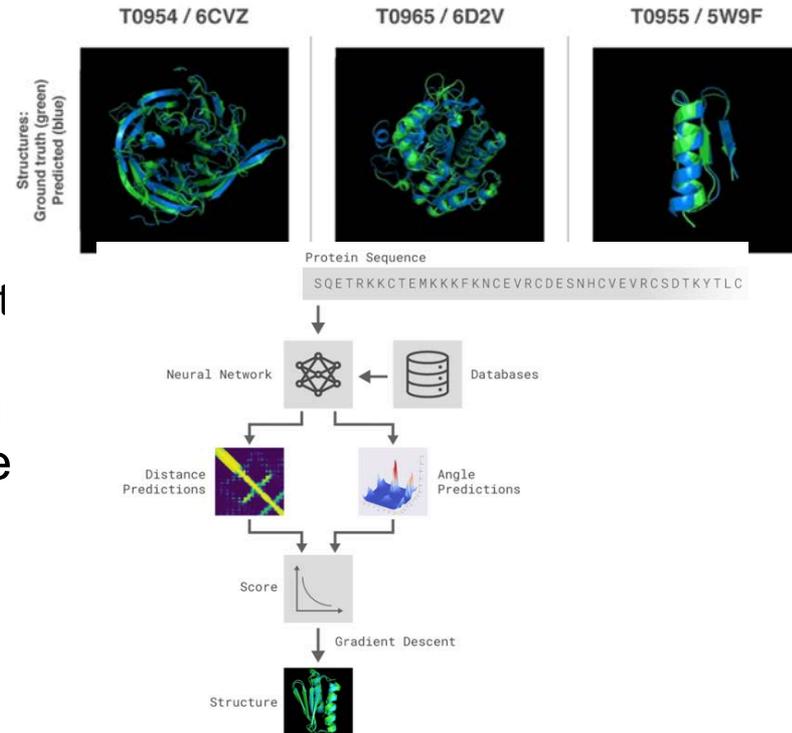
# + Why is protein folding important

- The ability to predict a protein's shape is fundamental to understanding its role within the body
- Diagnosing and treating diseases believed to be caused by misfolded proteins
- More knowledge about the shapes of proteins and how they operate through simulations and models
- Opens up new drug discovery methodologies while also reducing the costs associated with experimentation.



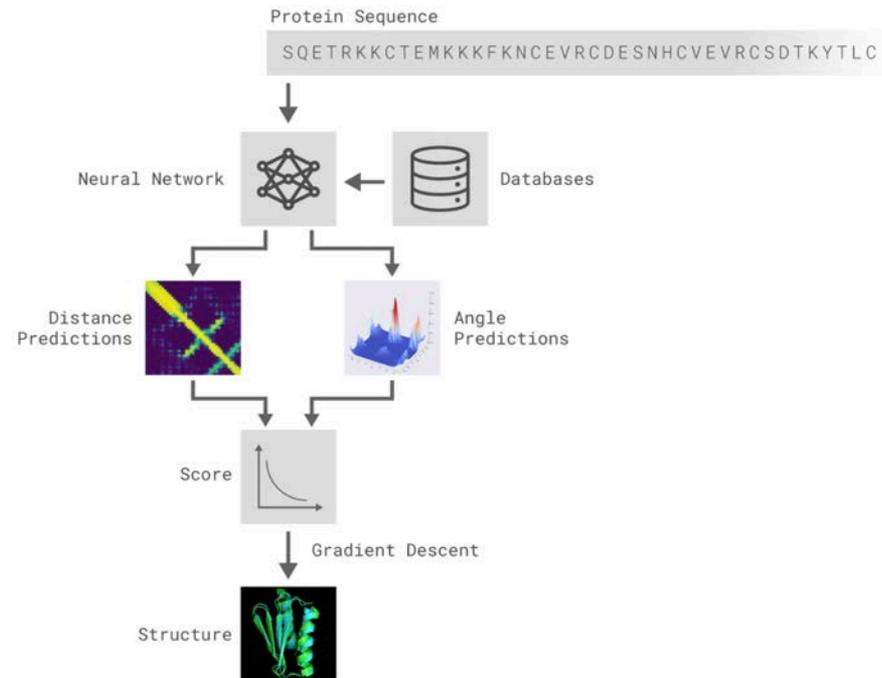
# + Neural network solution: AlphaFold

- Genomic databases available
- Predict
  - the distances between pairs of amino acids
  - the angles between chemical bonds that connect those amino acids.
- These probabilities were then combined into a score that estimates how accurate a proposed protein structure is.
- Trained a separate neural network that uses all distances in aggregate to estimate how close the proposed structure is to the right answer.



# + Generating protein fragments

- Search the protein landscape to find structures that matched predictions.
- First method built on techniques commonly used in structural biology, and repeatedly replaced pieces of a protein structure with new protein fragments.
- Then train a generative neural network to invent new fragments, which were used to continually improve the score of the proposed protein structure.



<https://deepmind.com/blog/alphafold/>

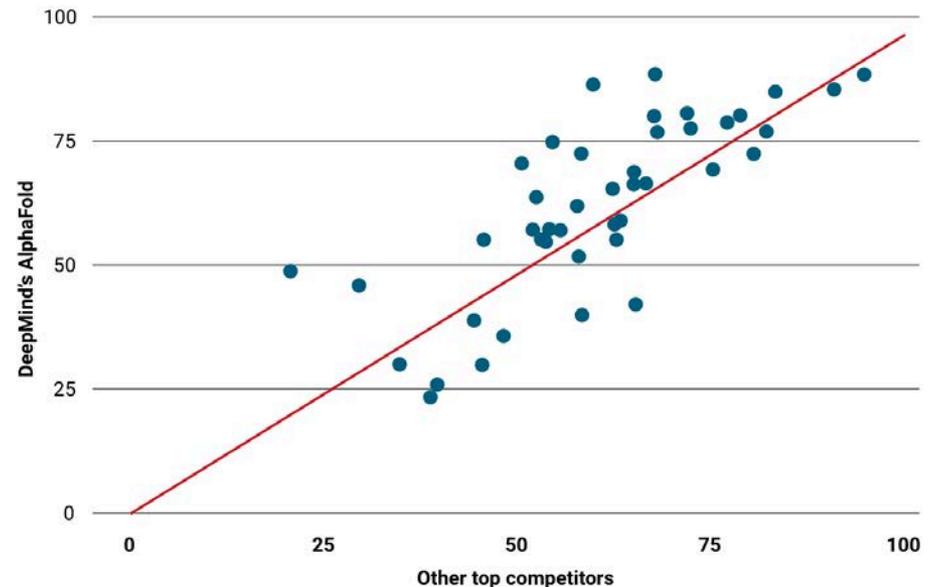


# + Protein Folding Competition

- 13th Critical Assessment of Structure Prediction (CASP), a biannual competition aimed at predicting the 3D structure of proteins.
- AlphaFold was most accurate in 25 of the 43 tests
- Next best entrant was most accurate 3 of the 43 tests

## Ready, set, fold!

Points above the red line show protein-folding predictions where AlphaFold won. It lost those below the line. Those on the line were essentially a tie.



# + Supplements being explored based on the protein misfolding theory of aging

Kikis EA, Gidalevitz T, Morimoto RI 2010. [Protein homeostasis in models of aging](#) and age-related conformational disease. *Adv Exp Med Biol* 694: 138–159. PMID: 20886762

SENS Research Foundation 2019. *The Root Causes of Aging*.

<https://www.fightaging.org/archives/2019/06/exosomes-in-harmful-senescent-cell-signaling/>

**Concept: with age, our bodies synthesize proteins too rapidly (or, amino acid supply is deficient).**

- Insufficient time to find the proper amino acids during translation
- Insufficient time during synthesis for them to fold into the proper shape
- Misfolded proteins are degraded by proteasomes. But as we age, they accumulate more quickly, clump together, and form globs too large for the proteasomes to degrade.
- This leads to
  - mitochondria unable to produce energy
  - senescent cells that persist and produce harmful signals
  - plaque consisting of dysfunctional proteins.
    - plaque consisting of macrophages bloated from consuming oxidized low-density lipoproteins (ox-LDL) contributes to heart disease.
    - in the brain, both forms of plaque contribute to memory loss, Alzheimer's, Parkinson's, and other dementias [NIH 2019].

# Based on the protein misfolding theory of ageing

## Quercetin and EGCG (green tea)

-EGCG inhibits MAPK and NF-κB activation, attenuates IL-1, IL-6, IL-8, COX-2 and PGE2 production. Also induces BDNF, NGF secretion, and inhibits cas3 and ROS level.

- Quercetin inhibits COX-2, 5-LOX enzymes and GSK-3β in PI3K pathway, and inhibits NF-κB activation, and captures free radicals

- Some recommend eating blueberries followed by a cup of green tea. Together they **may reduce protein misfolding**, one of the main causes of aging and mental deterioration. Quercetin delays the degradation of EGCG giving 6-fold higher levels.

*P Wang, D Heber, SM Henning. 2012. Quercetin increased the antiproliferative activity of green tea polyphenol (-)-epigallocatechin gallate in prostate cancer cells. Nutr Cancer 64:580-7. doi:10.1080/01635581.2012.*

## Amino acids tyrosine and cysteine

**Deficiency contributes to protein misfolding** during transcription.

- Many diets are deficient in these 2 amino acids. (Note low levels in vegan diet, with higher levels of stroke – though a lower heart attack rate!)
- In regions of the world with greatest longevity, people have higher levels of these 2 amino acids in their diets

*Fra et al. Cysteines as Redox Molecular Switches and Targets of Disease. Front. Mol. Neurosci. 10:167. doi: 10.3389/fnmol.2017.00167*

*Moosmann et al. Mitochondrially encoded cysteine predicts animal lifespan. Aging Cell 2008, 7, 32–46 Doi: 10.1111/j.1474-9726.2007.00349.x*

# +Also based on the protein misfolding theory of ageing

Caloric restriction (CR) substantially lengthens the lives of animals, and reduces the rate of age-associated diseases.

CR maintains all essential nutrients in the diet but reduces caloric intake substantially.

12-16 hours of fasting per day (TRE) on a regular basis has been shown to improve health in humans.

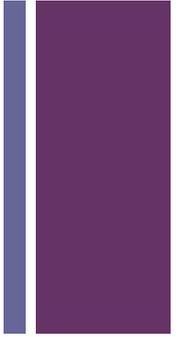
A biochemical mechanism for this has been identified, involving inhibition of translation, so that proteins are properly synthesized from mRNA.

This suggests that a process which can reduce protein misfolding may slow decline from ageing.

*Hahm J et al 2019. Diet restriction-induced healthy aging is mediated through the immune signaling component ZIP-2 in Caenorhabditis elegans. Intl Fed Assoc Anatomists. 19th Congress.*

<https://doi.org/10.1111/acef.12982>

+ Can AI detect cancerous cells and destroy them?



# AI is revolutionising imaging in medicine



HOME / CIVIC / HEALTH NEWS

## AI Beats Doctors at Cancer Diagnosis

The machine was able to more accurately diagnose malignant melanoma and benign nevi.

By Alexa Lardieri, Staff Writer May 28, 2018, at 7:00 p.m.



## Dermatologist-level classification of skin cancer

PODCAST | ARTIFICIAL INTELLIGENCE | APRIL 01, 2019

## Is Artificial Intelligence The Doom of Radiology?



Stanford ML Group


<b>Input</b> Chest X-Ray Image
<b>CheXNet</b> 121-layer CNN
<b>Output</b> Pneumonia Positive (85%)

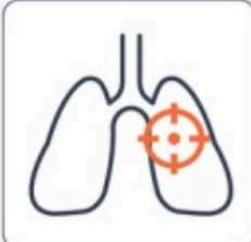

Our model, CheXNet, is a 121-layer convolutional neural network that inputs a chest X-ray image and outputs the probability of pneumonia along with a heatmap localizing the areas of the image most indicative of pneumonia.

We train CheXNet on the recently released ChestX-ray14 dataset, which contains 112,120 frontal-view chest X-ray images individually labeled with up to 14 different thoracic diseases, including pneumonia. We use dense connections and batch normalization to make the optimization of such a deep network tractable.

# + Detection, characterization and monitoring

## DETECTION

- Highlighting suspicious regions in images
- Detecting indeterminate nodules
- Addressing high false-positive rates and overdiagnosis

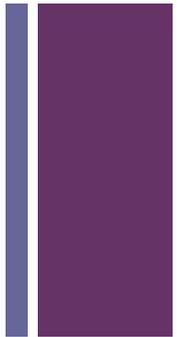
	<b>Lung</b> Early detection of lung cancer is associated with improved outcomes		<b>CNS</b> Detection tools for the incidental finding of asymptomatic brain abnormalities
	<b>Breast</b> More robust screening mammography interpretation and analysis		<b>Prostate</b> “Clinically significant” prostate lesion detection allows for targeted biopsy sampling

Source: Bi et al...Artificial intelligence in cancer imaging: Clinical challenges and applications,

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6403009/>

ronjon@r42group.com

# + What kind of cancer is it ?

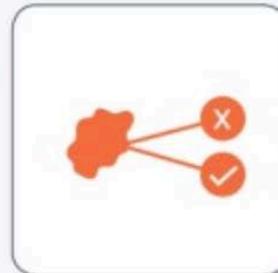


## CHARACTERIZATION

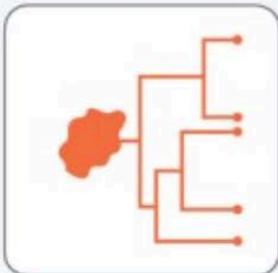
- Providing robust tumor descriptors to capture intra-tumor heterogeneity and variability



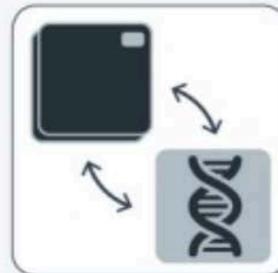
**Segmentation**  
Defining the extent of an abnormality in terms of 2D or full 3D assessments



**Diagnosis**  
Classifying abnormalities as benign or malignant



**Staging**  
Categorizing tumors into predefined groups based on expected course & treatment strategies



**Imaging Genomics**  
Associating imaging features with genomic data for comprehensive tumor characterization

# + Monitoring with time...

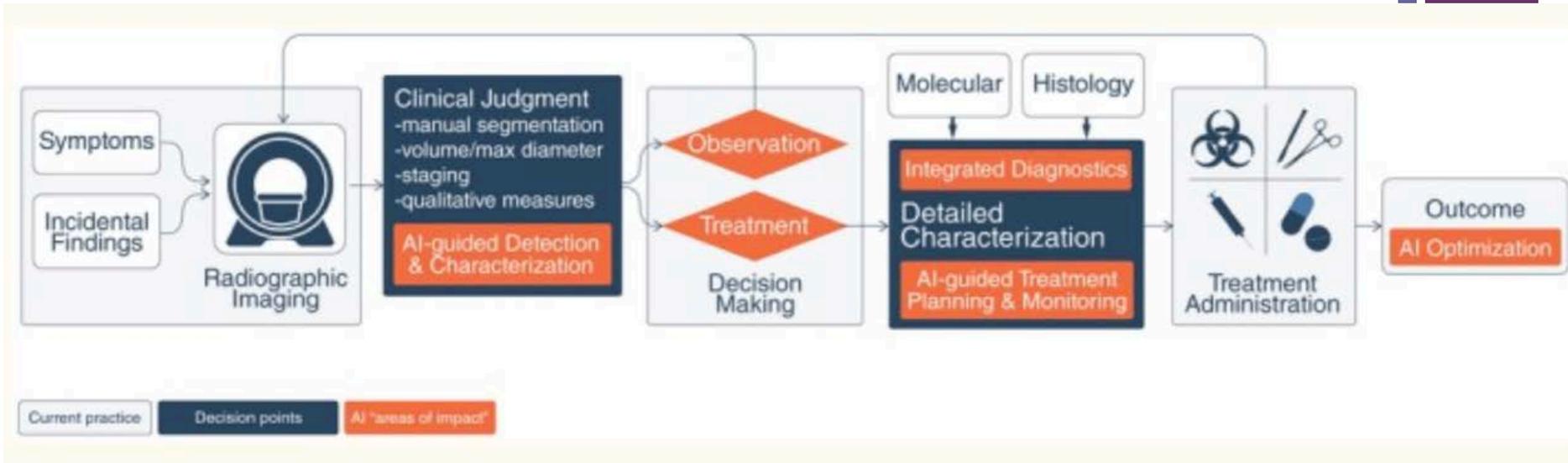
## MONITORING

- Capturing a large number of discriminative features that go beyond those measured by traditional evaluation criteria



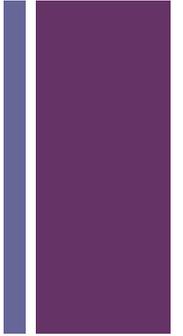
**Change Analysis**  
Temporal monitoring of tumor changes either in natural history or in response to treatment

# + Use AI to augment the sequential cancer monitoring workflow



+

Can you upload your brain in a machine and live forever?



# Can we upload a brain into a machine

- The idea of consciousness being transferred into computers is typically portrayed in one of two ways:
  - In sci-fi movies, conscious identity is "extracted" (somehow) from the brain and "injected" into a computer that has a capacity for conscious emulation.
  - In philosophical thought experiments and in the singularity community it is imagined that eventually brain scanning will be so detailed that the entire brain down to every neuron, synapse, and receptor can be scanned and simulated brute-force in a giant computer.
  - Even if we could do it, transferring a human consciousness into that "body" will produce something not-human and maybe more like a recording or parody of a conscious being than a "person."
  - Consciousness may be so complex that it can't run on a computational system that isn't a unique replica of the mind in which it emerged.



# Can you replace a brain ?

- Accepted that a person with a transplanted heart is still the same person.
- Since 1997 (when Deep Brain Stimulation received FDA approval for treatment of essential tremor) accepted that a person, part of whose "natural" brain was replaced by a machine, is still the same person. In 2002, such treatment also received FDA approval as treatment for Parkinson's.
- Now, it a HUGE leap to claim that the replacement of a tiny brain section with a machine is in any way a "proof" that consciousness can be transferred.
- However, it is also possible that, over the next 50-100 years, we will invent new machines, as part of neurosurgery that are able to replace more and more parts of the brain.

# + Thought experiment

- A person is diagnosed with Parkinson's receives a DBS implant and replaces a part of his brain that has failed, with a machine. This makes him, say, 99.9% "original brain", but 0.1% computer-based.
- Later he is diagnosed with something else, perhaps a degeneration of part of the optical cortex. By 2025, this can be replaced by another machine. He is now 99% original brain, and 1% machine...
- Over the following century, increasing developments in partial-brain devices occur, no one replacing more than 1% of the brain at a time. In each case, he receives an operation that makes him less and less "original brain" and more and more "silicon."
- Finally, he ends up over 50% silicon. Yet we still accept that he is the same person, and a "continuous consciousness."
- ... 90%, 99%, 99.9%, 100% silicon. What then?

# + Guidelines to Solutions

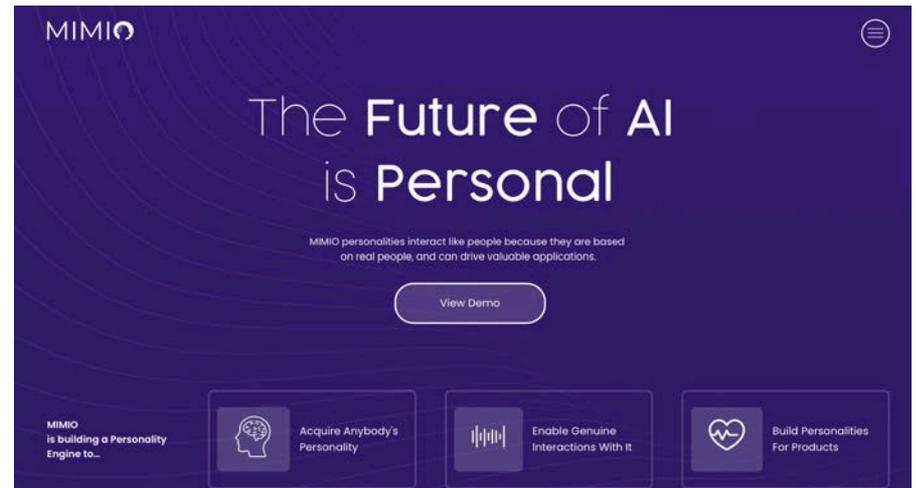
- What are the necessary and sufficient for a person at one time to being the same person, at a later time ?
- **Biological Continuity.** Your biological organ brain is transplanted to a new body. The brain defines you. So, you are still the same you.
  - Same DNA subject to mutations
  - Every cell replaced over time
- - **Psychological Continuity. (John Locke)** But, if we view the brain as just a biological organ, did the transplanted brain preserve all your "*software*" (memories, experiences, beliefs), i.e. your "*mind*"? Would we achieve the same "*you*" then, without brain transplant, if we could replicate your "*software*", onto another person's brain, or an artificial brain?

# + Molecular replacement

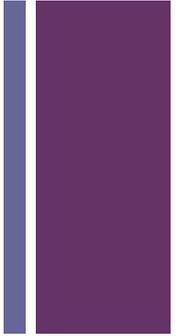
- "After about fifty population doublings (Avogadro's number), most molecules present in the founding cell(s) have been eliminated, repaired or re-synthesized. The element of "sameness" is then gone. Cells present later in a lineage consist of molecules/atoms (including DNA which also turns over) that were not present in the founding cell(s). Immortality of identical molecules in biology is non-existent.
- ...Leonard Hayflick (Hayflick's number – stated that cells will divide 40-60 times before they die)
- (Avogadro's number = the number of molecules contained in one mole of any substance or  $6.02 \times 10^{23}$ . One mole of carbon = 12.01 grams and one mole of glucose, (180.16 grams) both contain  $6.02 \times 10^{23}$  molecules.  $10^{23}$  is roughly equivalent to  $2^{50}$ )

# + Use avatar and voice creation to create a model of yourself

## Mimio.ai case study



+ Can AI assist us as we get older?



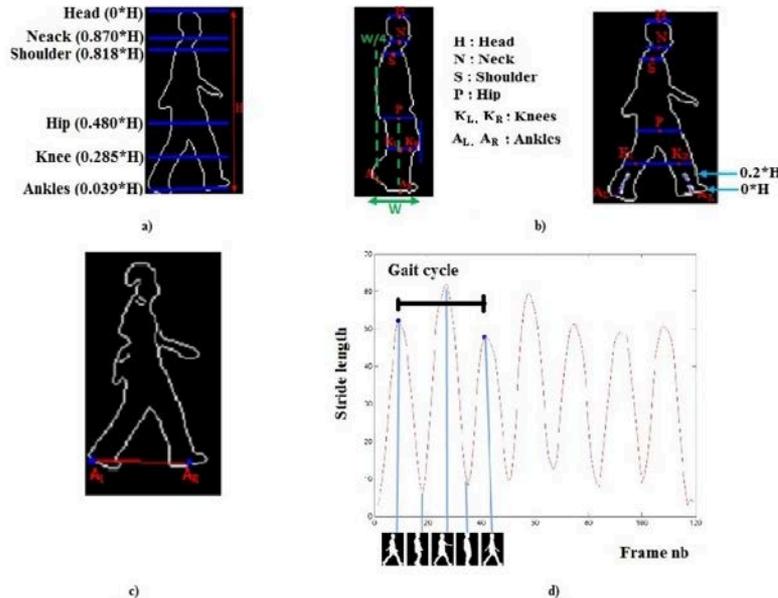
# + AI for Aging in Place

- At home health monitoring
  - Carepredict
  - Biotricity
- Smart Device Assisted Living
  - Wearables; inconsistencies in biometric data
  - Wander detection
- Fall detection
  - Livio integrated fall detection in hearing aids
  - Fall detection integrated hip airbags
- Virtual Companions
  - Paro

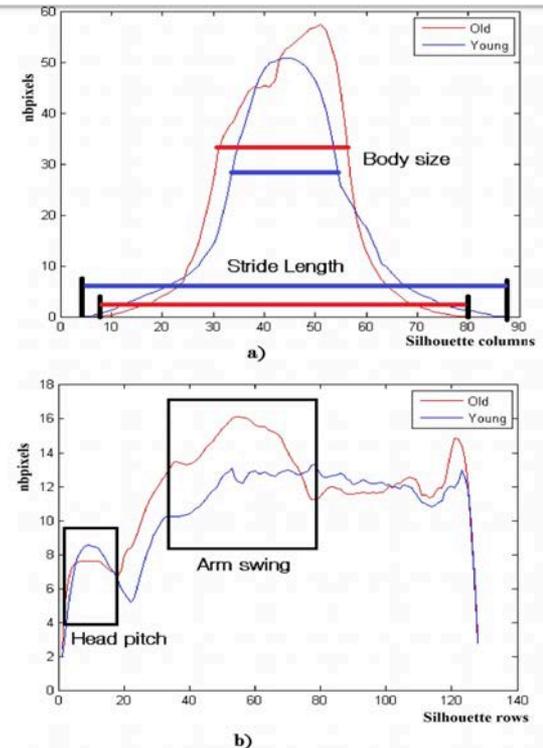
# + Gait Analysis

- Use parameters affirmed by medical and biomechanical studies
  - arm swing
  - head pitch
  - stride width
  - body size

(Figure 1. d).



**Fig. 1. Gait cycle detection process**  
 a Vertical body points' positions [42]  
 b Horizontal body points' position: Simple and double support cases [40]  
 c Stride detection  
 d Stride variation and gait cycle detection



**Fig. 5. Old/Young silhouette projections**  
 1 Old/Young silhouette longitudinal projection (SLP)  
 2 Old/Young silhouette transverse projection (STP)

# + Body Area Network Concept

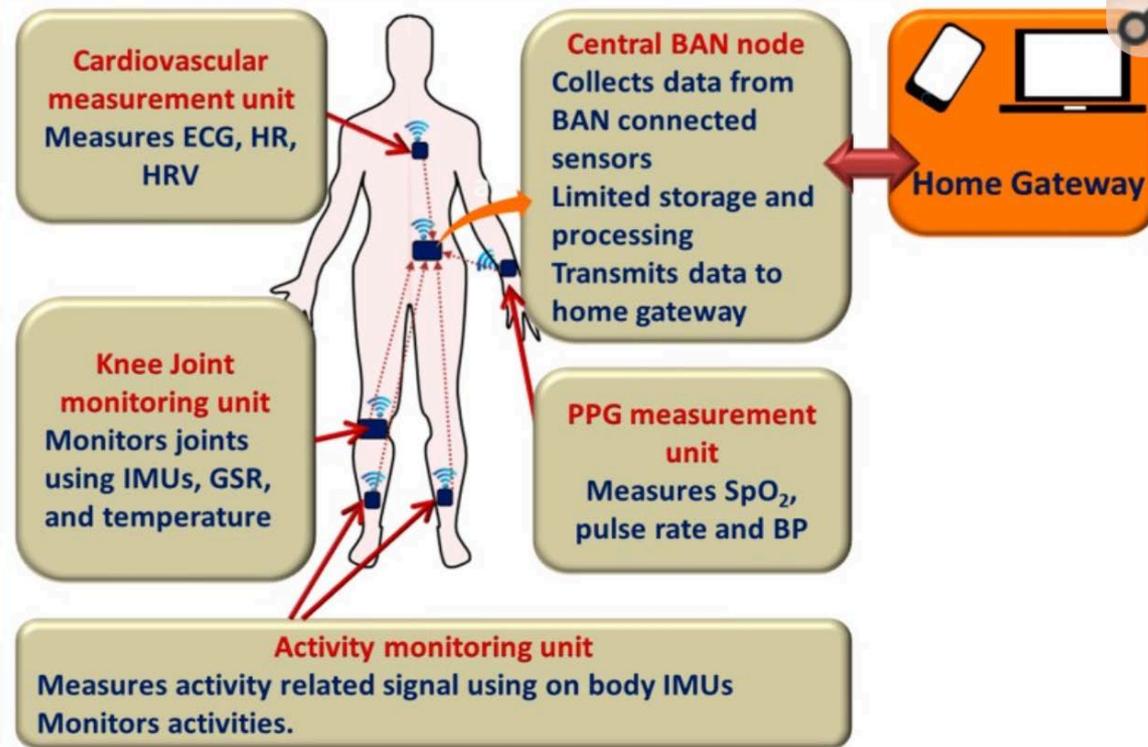


Figure 1

Wireless Body Area Network (WBAN) for wearable medical sensors.

# + Connect to smart health ecosystem

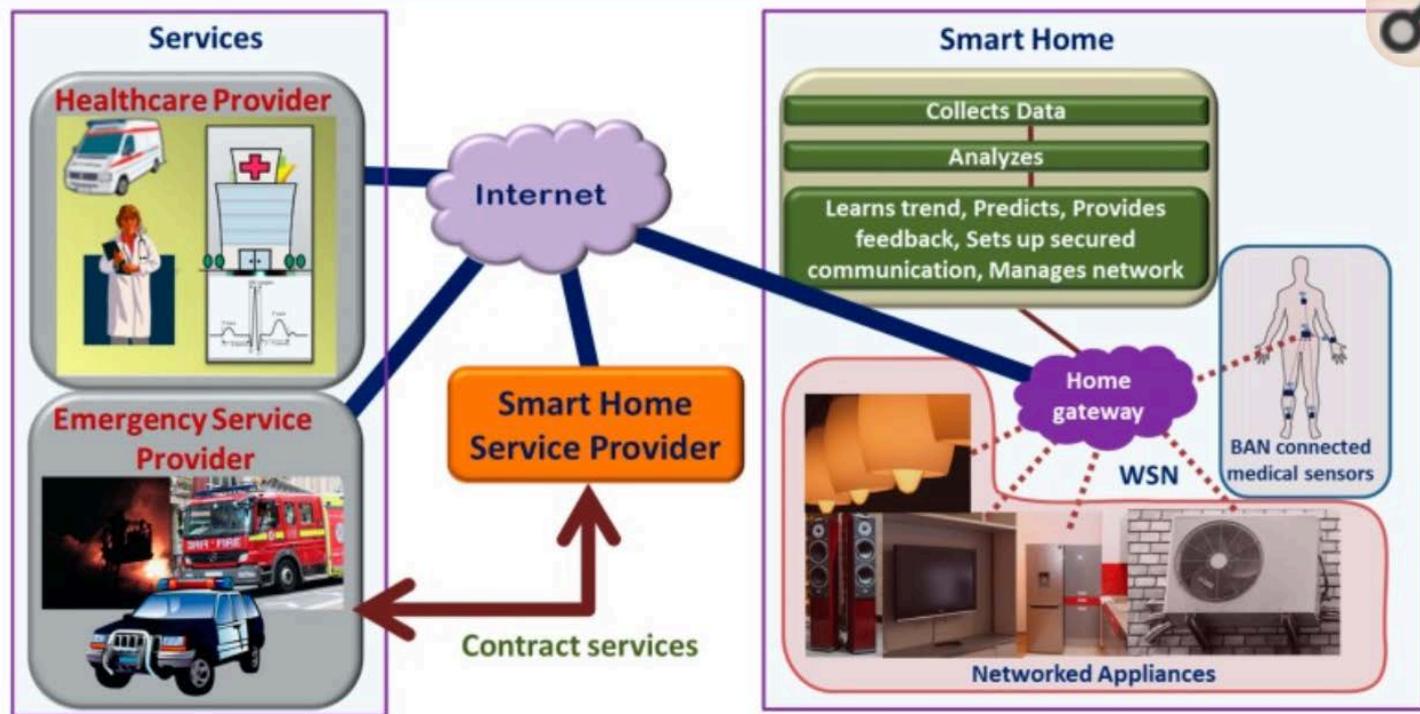
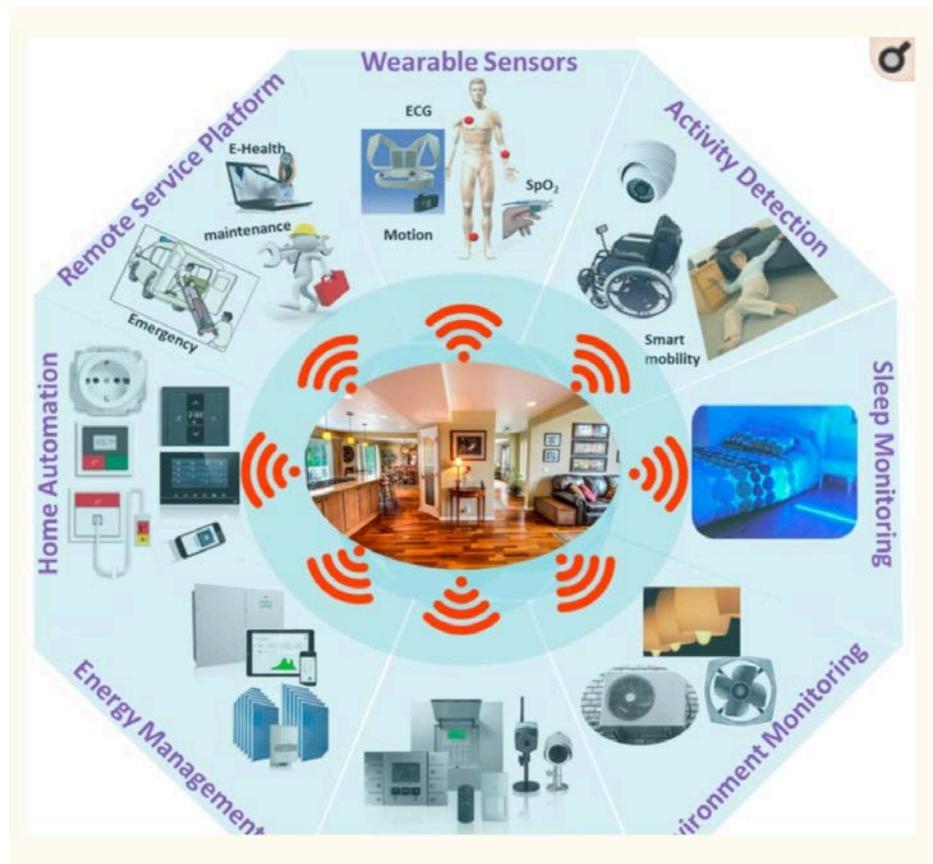


Figure 6

Schematic diagram of a smart home showing the network among different stakeholders.

# + Enhanced home gateway to monitor health

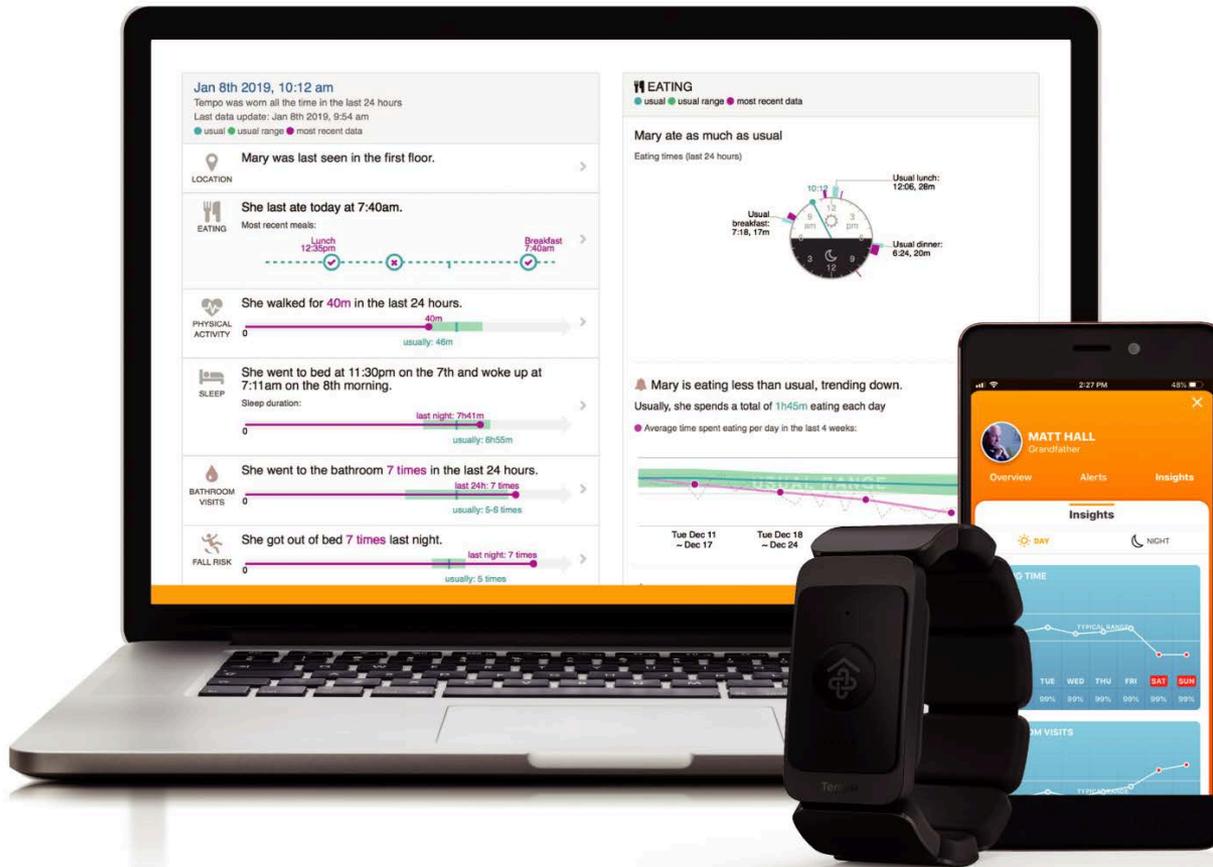


# + Monitor people with wearables and sensors (Carepredict case study)



Innovation Solutions Learn More Company

SCHEDULE



# + AI can be used for fall detection

## ■ Smart device assisted fall detection

- Emergency situations such as a [simple slip and fall](#) can trigger a series of medical conditions in geriatric patients.
- [Xsens](#), [Kardian](#) and [Qventus](#) have built AI-powered fall detectors.
- Starkey has integrated AI-powered fall detectors within its hearing aid [Livio AI](#).
- Audio-based technology is more convenient and is cheaper than video technology.
- However audio-based technology is hard to set up compared to video and wearable-based technologies.
- Video-based technology is accurate and easy to set up. At the moment, video-based technology is the most expensive and it is also prone to occlusion.
- However as homes become smarter and prices for cameras continue to drop, it is expected that this technology will be the best of the three due to its versatility.

# + Predicting falls...

## The Facts on Falling

Falls are a major public health problem both in the U.S. and worldwide. They can cause injuries, sometimes serious, and can negatively impact quality of life for the person who falls and their loved ones.



**Every 11 seconds,** an older adult is seen in an emergency department for a **fall-related injury.**<sup>1</sup>



**One in four** older adults falls each year, but **less than 50%** tell their doctor.<sup>2</sup>



**Falls are the second leading cause** of accidental or unintentional injury deaths worldwide.<sup>3</sup>



Falls lead to **20-30% of mild to severe injuries** and are the underlying cause of **10-15% of all emergency department visits.**<sup>4</sup>



**Falls** are the leading cause of **hip fractures.**<sup>2</sup>



An older adult falls **every second of every day.**<sup>2</sup>



People with **mild hearing loss** are three times more likely to have a **history of falling.**<sup>5</sup>

<sup>1</sup>National Council on Aging. <sup>2</sup>Centers for Disease Control and Prevention. <sup>3</sup>World Health Organization <sup>4</sup>National Aging Research Institute for the Commonwealth Department of Health and Aged Care. <sup>5</sup>Johns Hopkins Medicine.

© Starkey Hearing Technologies. All Rights Reserved.

# + Hip air bags



## HIP'SAFE AT A GLANCE

The airbag is designed to protect seniors from hip fractures. The device is **COMFORTABLE**, **EASY-TO-USE** and **REUSABLE**.

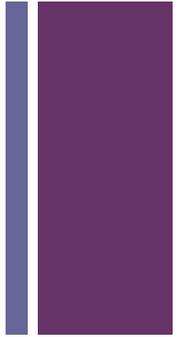
In case of fall both airbags will deploy automatically above the hips before ground impact to protect the hips.



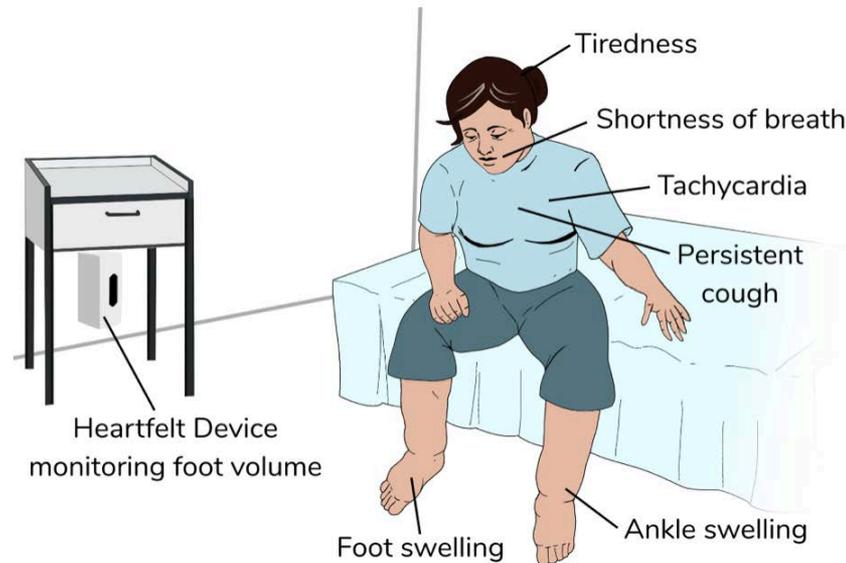
**INFLATION  
TIME  
0,08 sec**  
→



# + Detecting heart failure from leg oedema



**Heartfelt Technologies Example:** Walk past sensor to detect foot swelling  
Foot swelling is early indicator of heart failure



# + Remote monitoring for Eldercare

Zemlee Case study... Place sensors around house, on bed – use non-wearable technologies

## Tracking



Respiratory rate



Heart rate



Sleep patterns



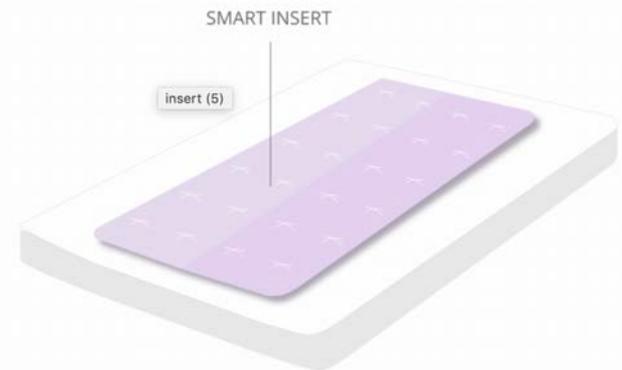
Isolation monitoring



Movement detection



Medication tracking



Zemlee can also be used for doctor enabled remote patient monitoring.

# +Virtual companions appearing for the elderly

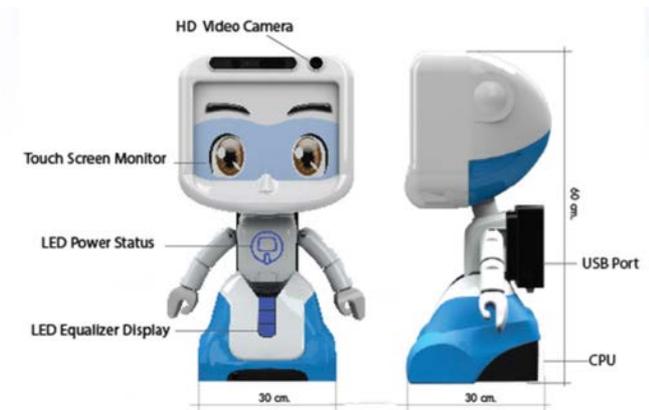
- The lack of skilled caregivers who can help elderly patients who live alone and require daily assistance, has given rise to need for robotic helpers.



ElliQ – robot helper for elderly

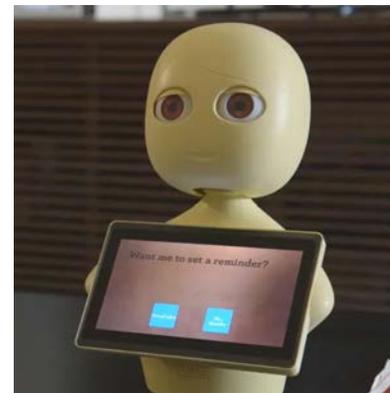


Paro – fluffy companion



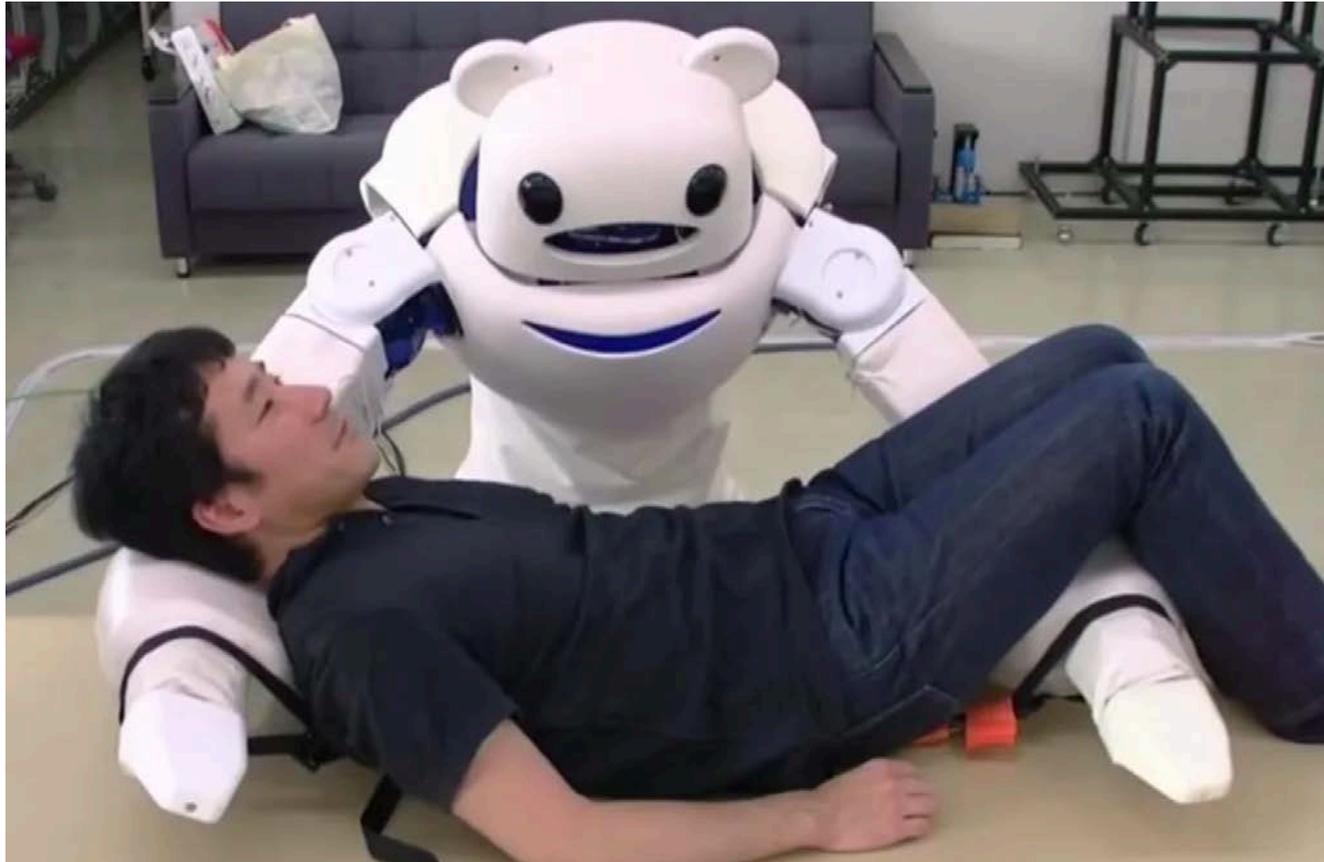
Dinsow from Thailand helps  
Alzheimer's patients

ronjon@r42group.com



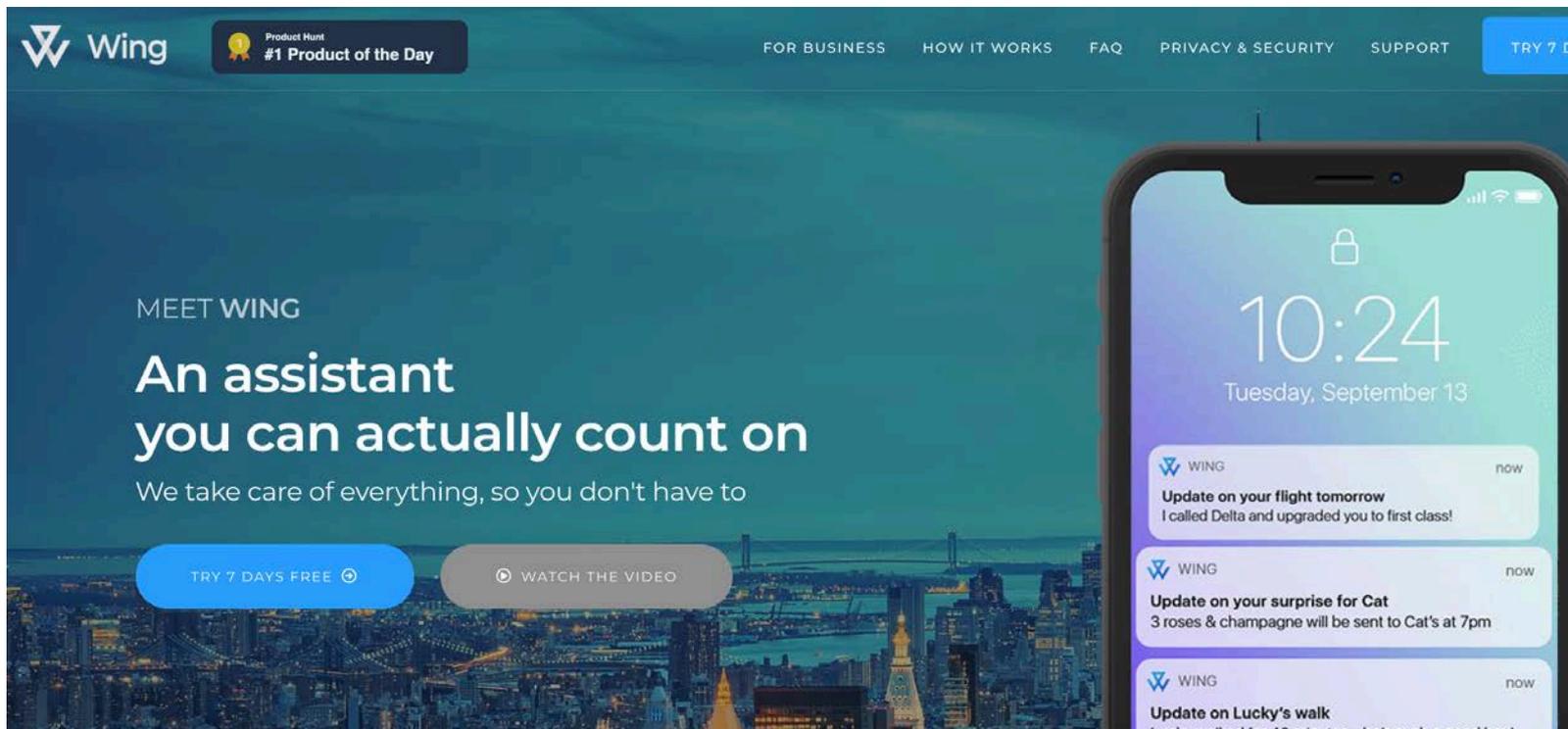
Mabu by Catalia health,  
helps patients take  
prescriptions on time

# + Robobear – caring for Japan's elderly



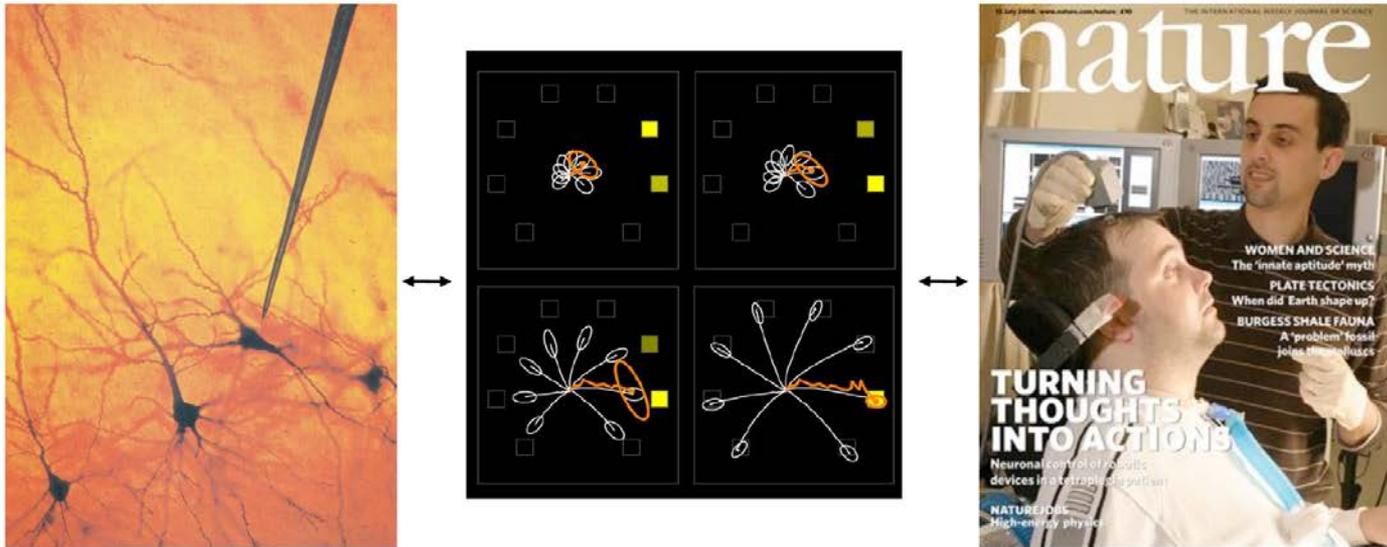
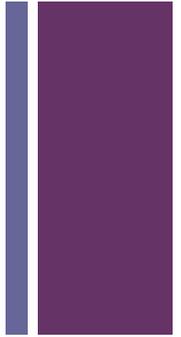
# + Virtual assistants – AI – human hybrids

Wing.AI hybrid human – computer concierge



The image shows a screenshot of the Wing.AI website. The background is a night cityscape. At the top left is the Wing logo and a 'Product Hunt #1 Product of the Day' badge. The top right has navigation links: 'FOR BUSINESS', 'HOW IT WORKS', 'FAQ', 'PRIVACY & SECURITY', 'SUPPORT', and a 'TRY 7 D' button. The main text reads 'MEET WING' followed by 'An assistant you can actually count on' and 'We take care of everything, so you don't have to'. Below this are two buttons: 'TRY 7 DAYS FREE' and 'WATCH THE VIDEO'. On the right, a smartphone displays a lock screen with the time '10:24' and date 'Tuesday, September 13'. Three notification cards from WING are visible: 'Update on your flight tomorrow' (flight upgrade), 'Update on your surprise for Cat' (roses and champagne), and 'Update on Lucky's walk'.

# + Brain machine mapping



# + Shenoy Lab: Neural Prostheses

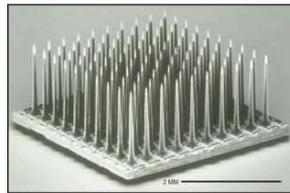
## Designing High-Performance Neural Prostheses Neural Prosthetic Systems Laboratory (Shenoy Group), Stanford University

**Problem:** Millions of people are unable to move due to neurological injury and disease.

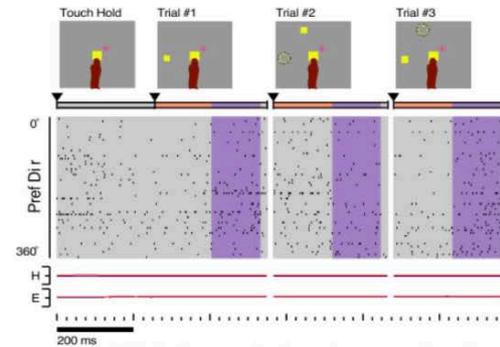
**Solution:** Bypass injury by using neural signals (from the brain) to control prosthetic devices.



b) Integrated electronics & telemetry



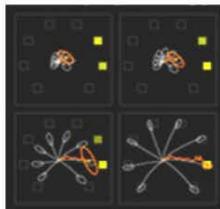
a) Silicon BioMEMS electrode arrays



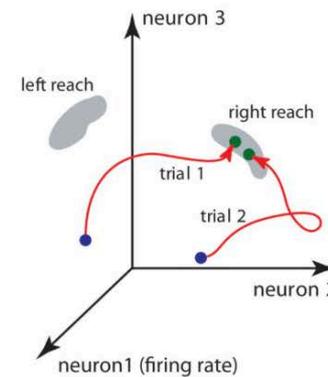
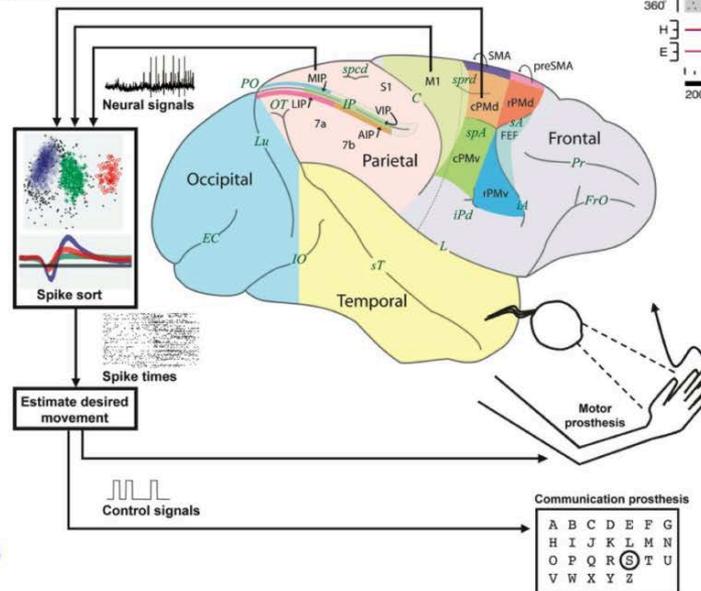
e) Real-time prosthetic system experiments



c) Mobile recording systems



d) Real-time decode algorithms



f) Basic systems neuroscience

# + Typing shakespeare with brain interface

PUBLIC RELEASE: 12-SEP-2016

## Brain-sensing technology developed by Stanford scientists allows typing at 12 words per minute

*Technology for reading signals directly from the brain developed by Stanford Bio-X scientists could provide a way for people with movement disabilities to communicate*

STANFORD UNIVERSITY



PRINT E-MAIL

[https://www.eurekalert.org/pub\\_releases/2016-09/su-btd090816.php](https://www.eurekalert.org/pub_releases/2016-09/su-btd090816.php)



VIDEO: A TEAM LED BY ELECTRICAL ENGINEER KRISHNA SHENOY DEVELOPED TECHNOLOGY THAT DETECTS BRAIN SIGNALS TO MOVE A CURSOR. ANIMALS TRAINED TO COPY TEXT USING THE TECHNOLOGY WERE ABLE TO TYPE... [view more >](#)

# + Recommendations

- Building codes: allow for smart sensors
- Classify aging as a disease so root causes can be financed and researched
- Enable more longitudinal studies so correlation and causation can be teased out
- Enable preventative fall technologies to be reimbursed by health systems
- Enable more preventative health care systems to be reimbursed
  - Measure baseline for each person
  - Allow smart sensors to be reimbursed