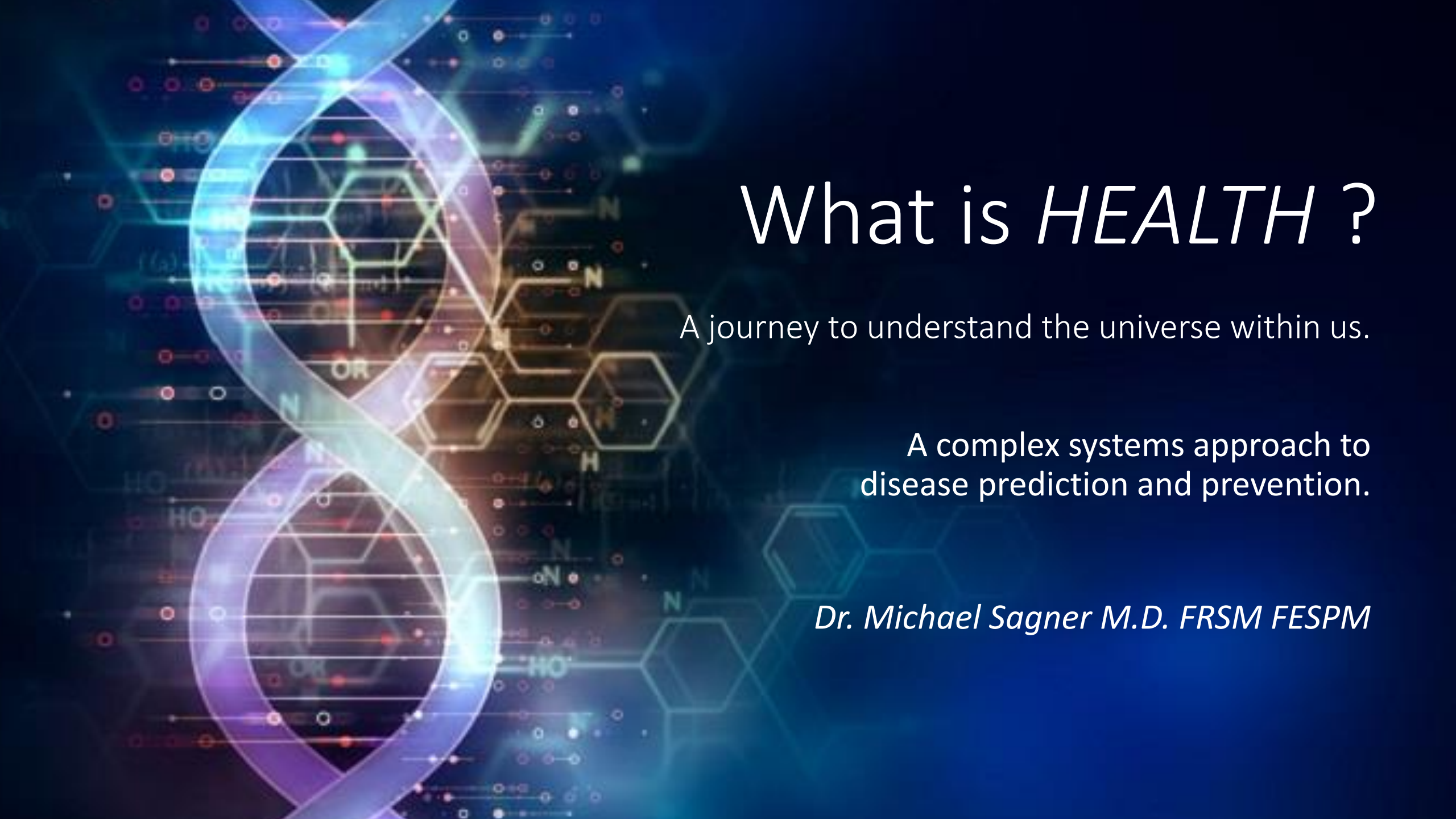


What is *HEALTH* ?

A journey to understand the universe within us.

A complex systems approach to disease prediction and prevention.

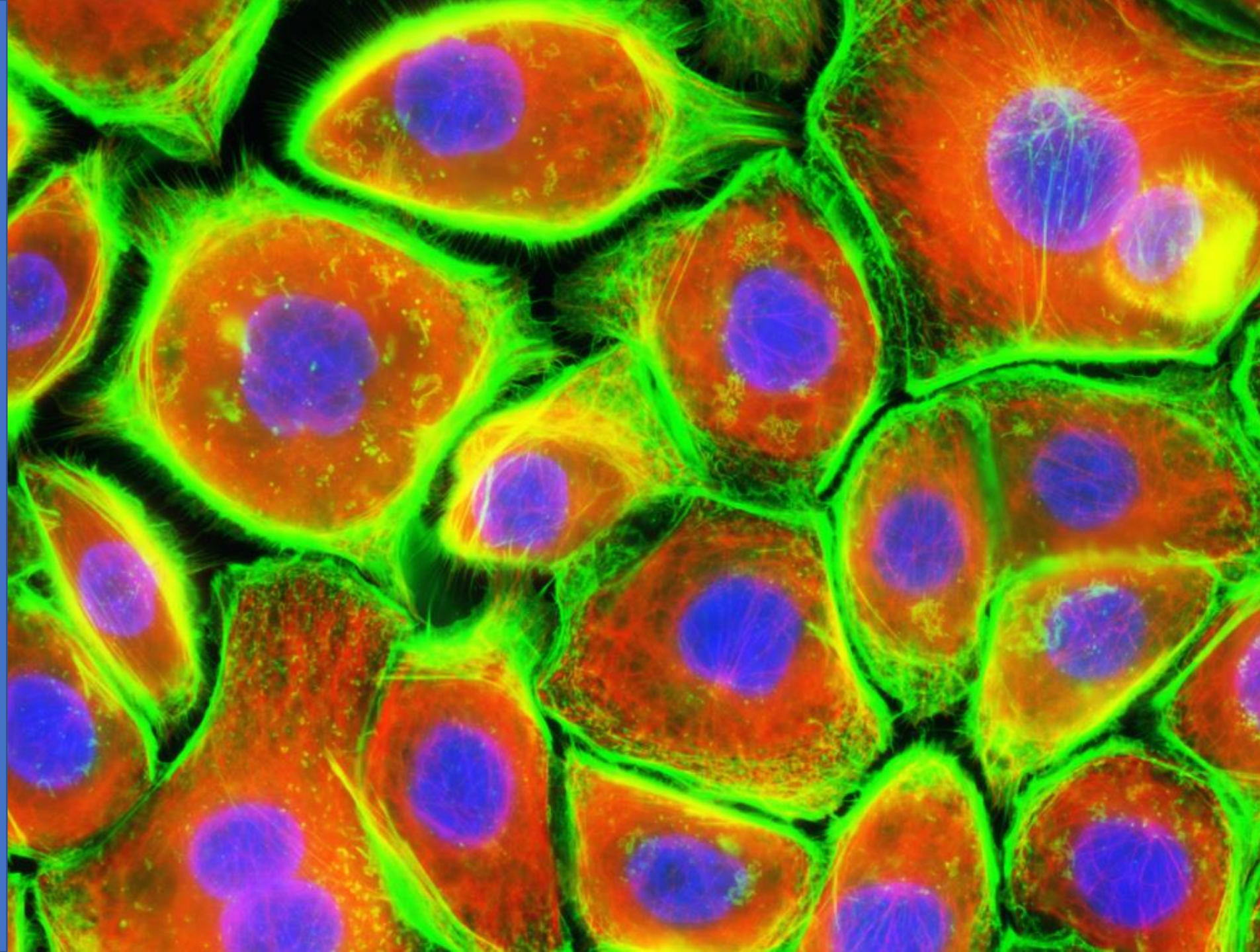
Dr. Michael Sagner M.D. FRSM FESPM

Why…

Exploring Universes

Exploring Universes

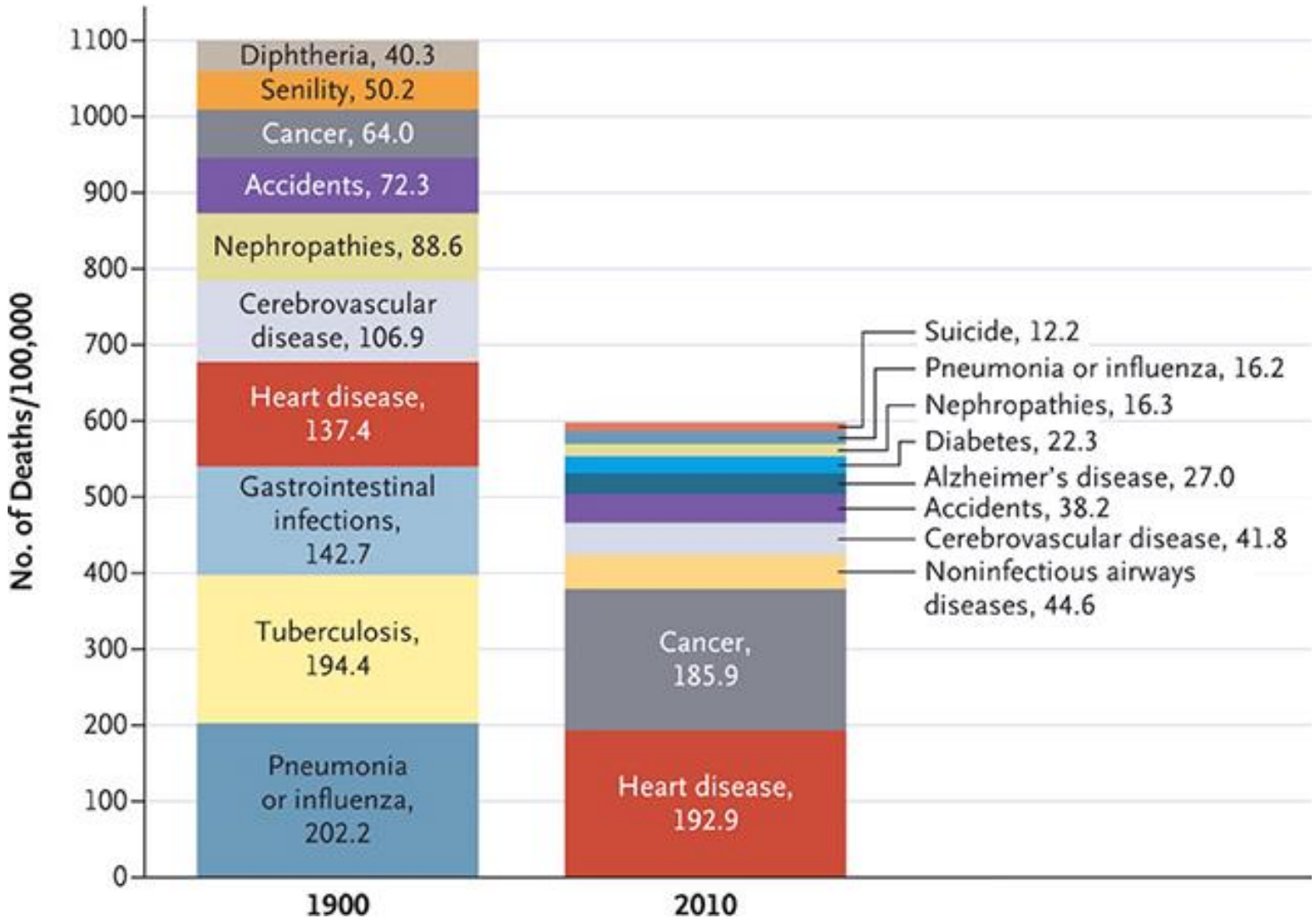
Exploring Universes



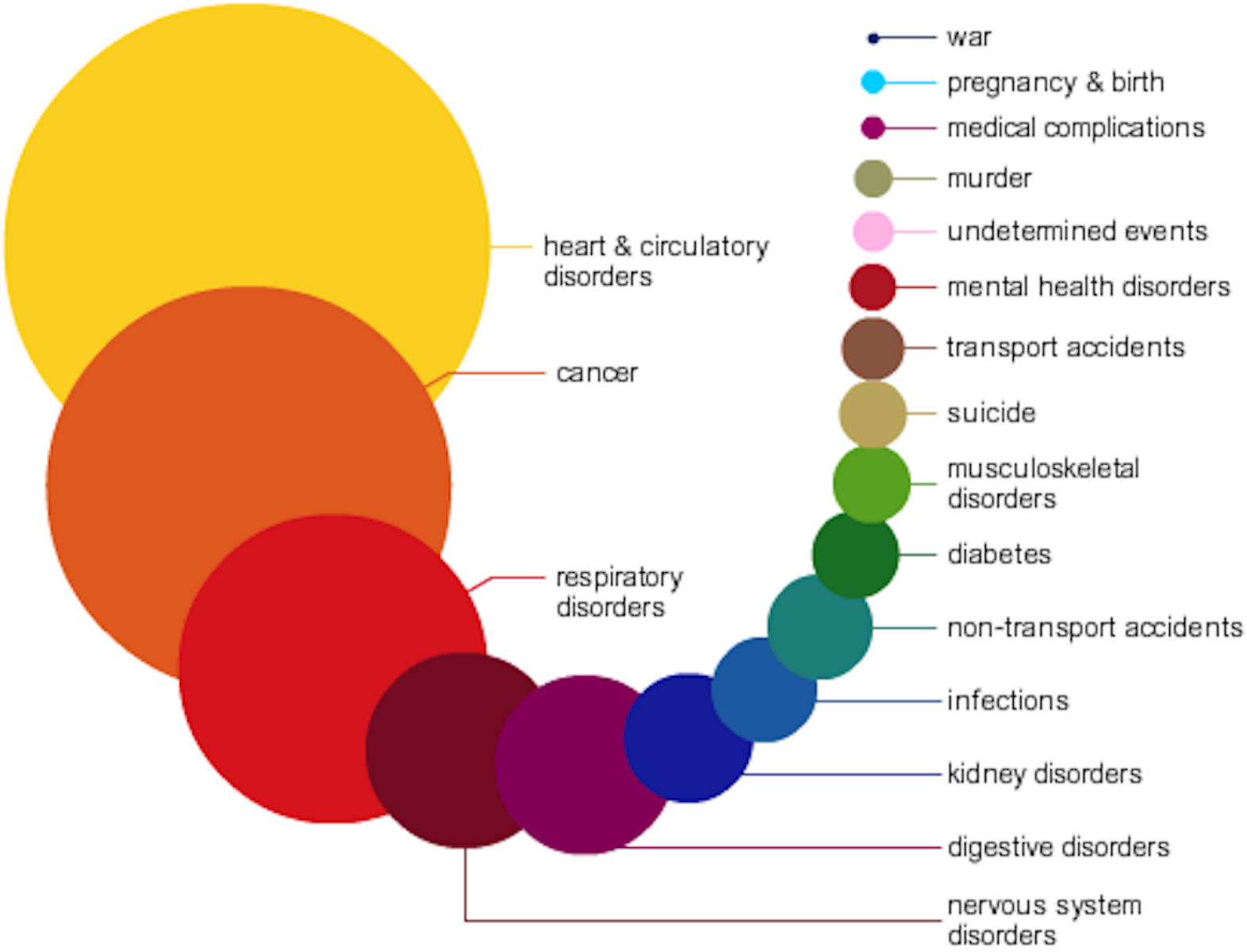
A few Definitions…

- **Chronic Diseases**
  A chronic disease is one lasting 3 months or more, by the definition of the U.S. National Center for Health Statistics. Chronic diseases generally cannot be prevented by vaccines or cured by medication, nor do they just disappear.
- **Non-communicable diseases**
  Noncommunicable diseases (NCDs), also known as chronic diseases, are not passed from person to person. They are of long duration and generally slow progression. The four main types are:
  cardiovascular diseases (like heart attacks and stroke), cancers, chronic respiratory diseases and diabetes. (WHO)

The leading causes of death today

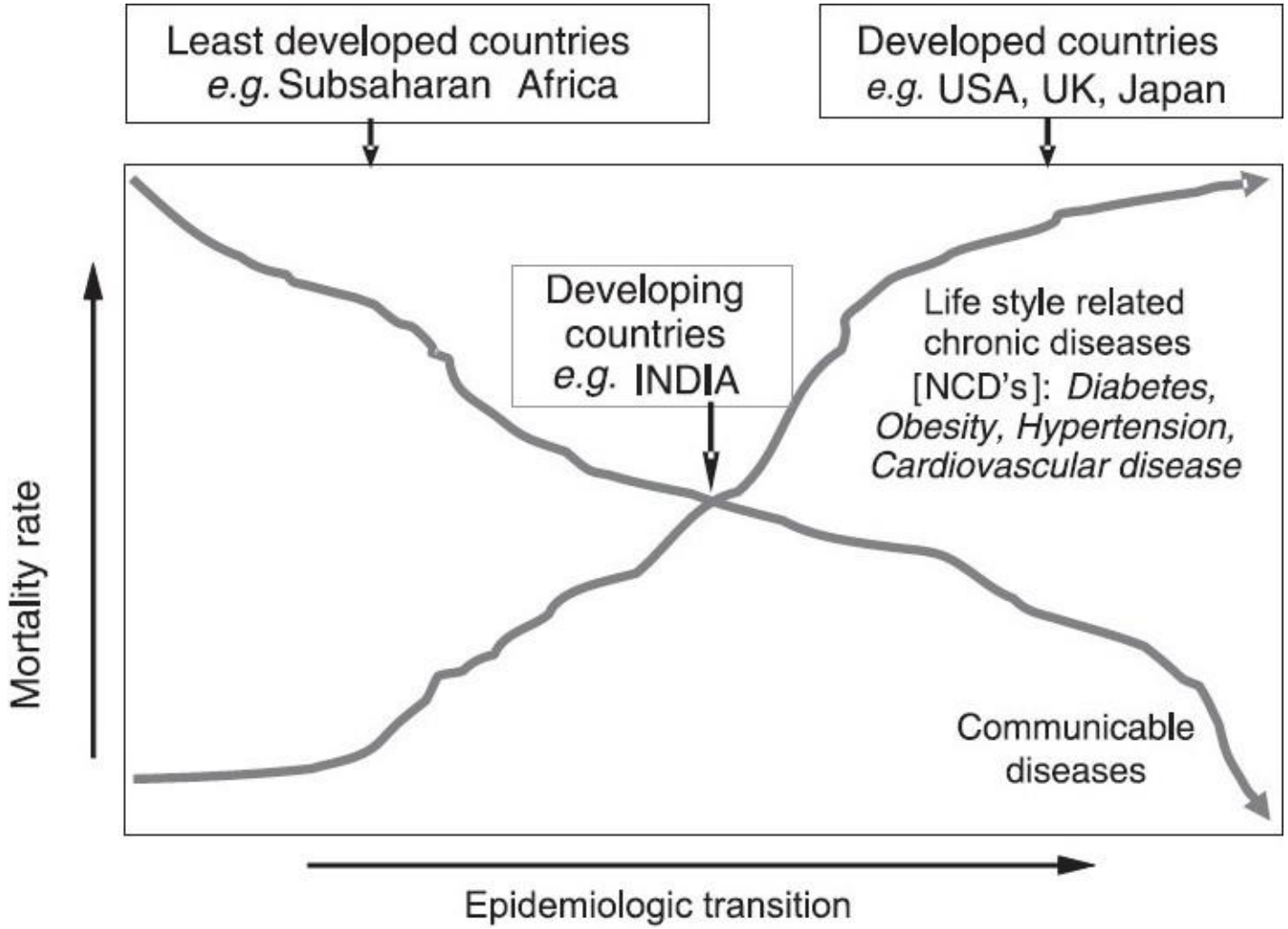


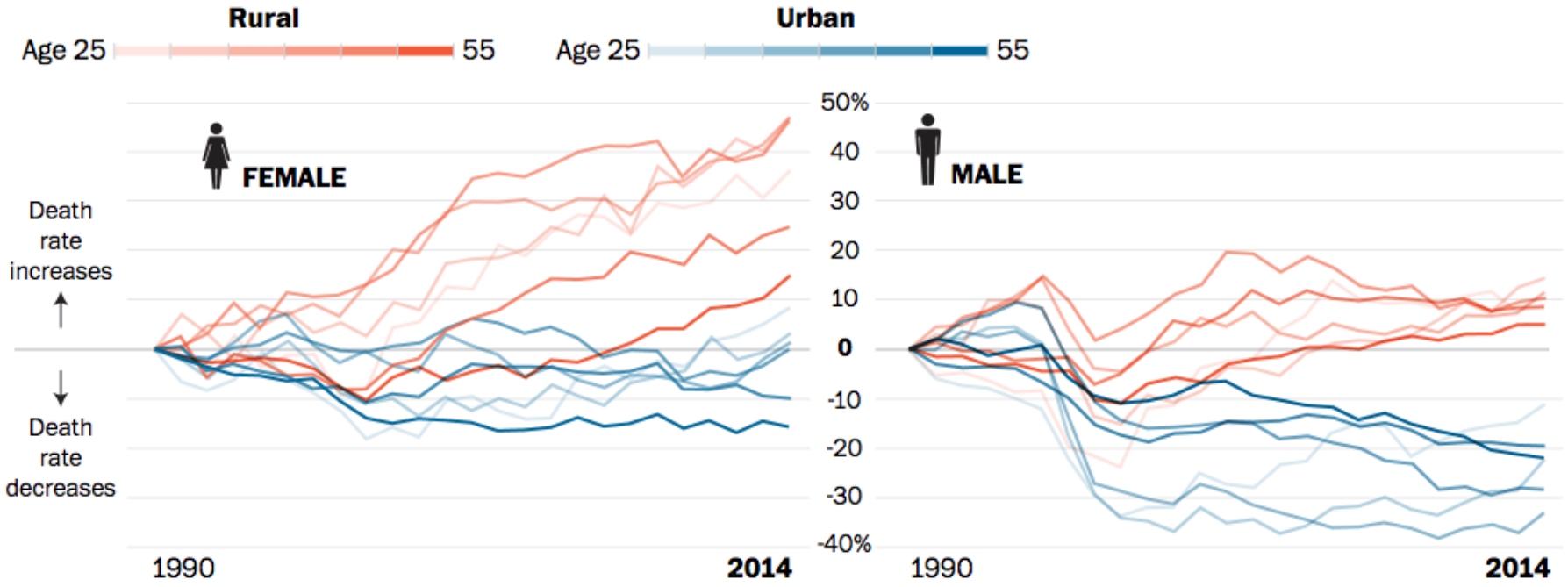
Lancet Global Burden of Disease - The Lancet



Leading Causes of Death in Perspective

The Epidemiological Transition



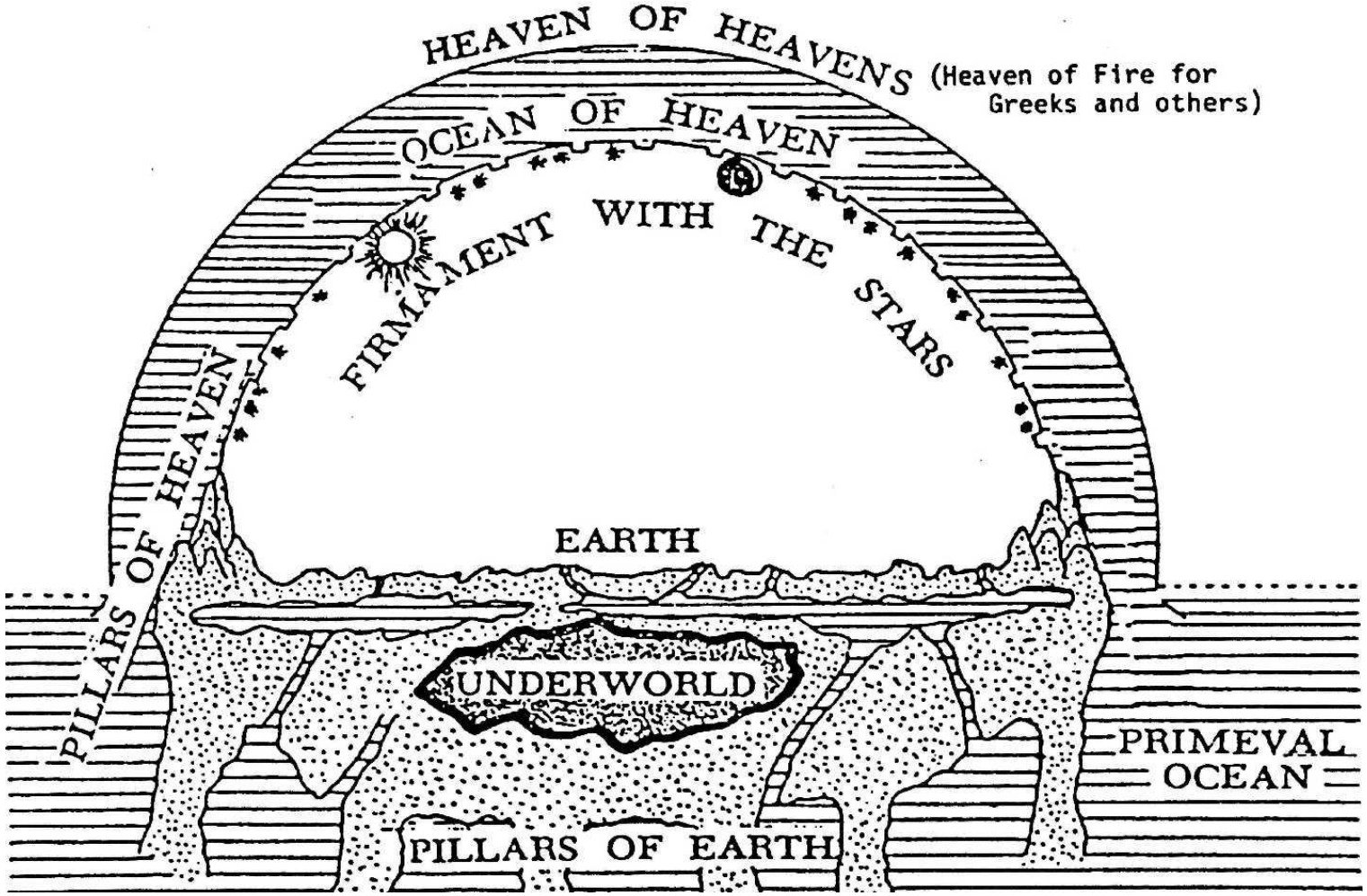


Source: Washington Post analysis of Centers for Disease Control and Prevention mortality data

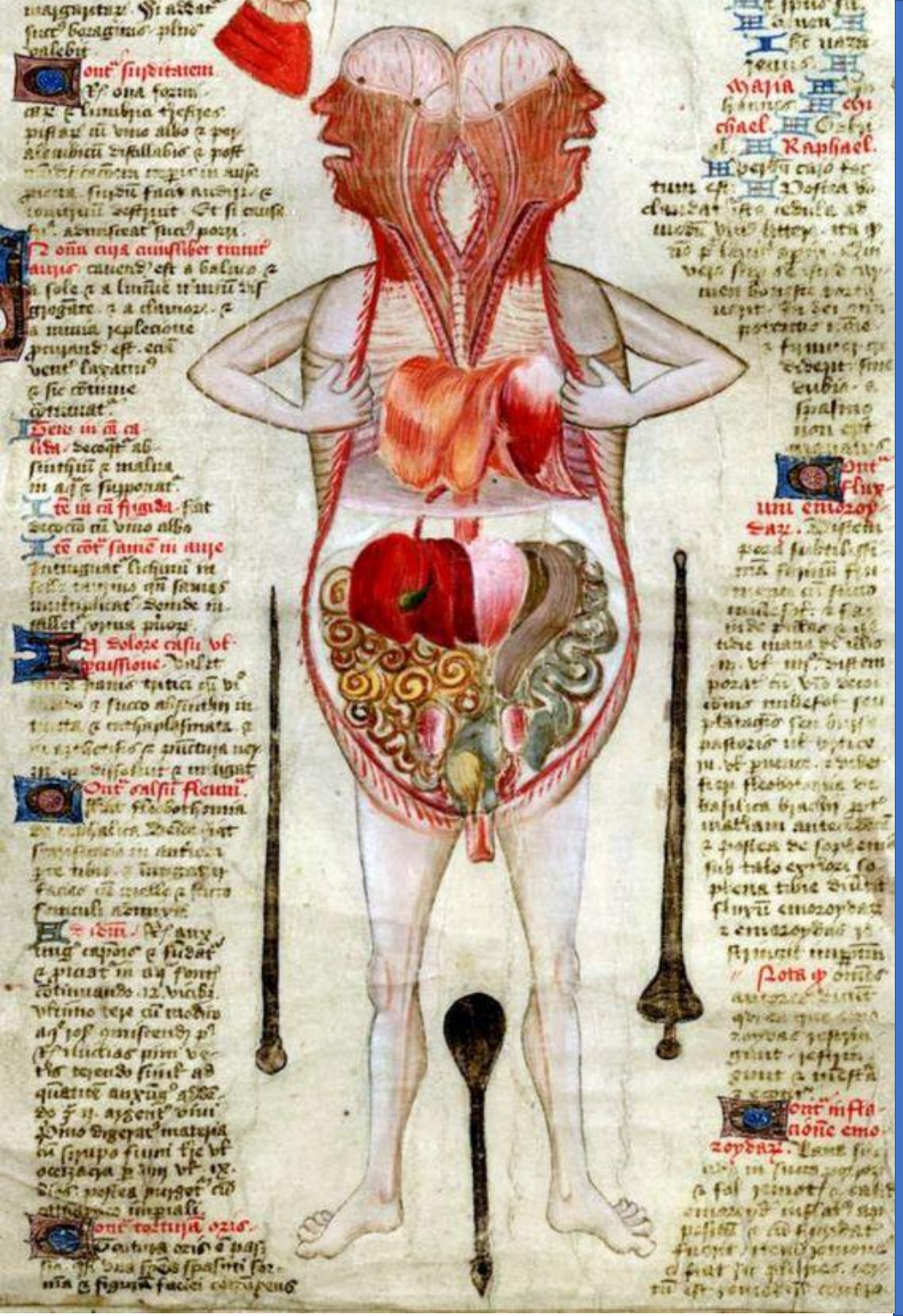
In 2015, for the first time in nearly 25 years, life expectancy decreased in the United States

Life Expectancy is Decreasing in certain Places

How we used to see the world…

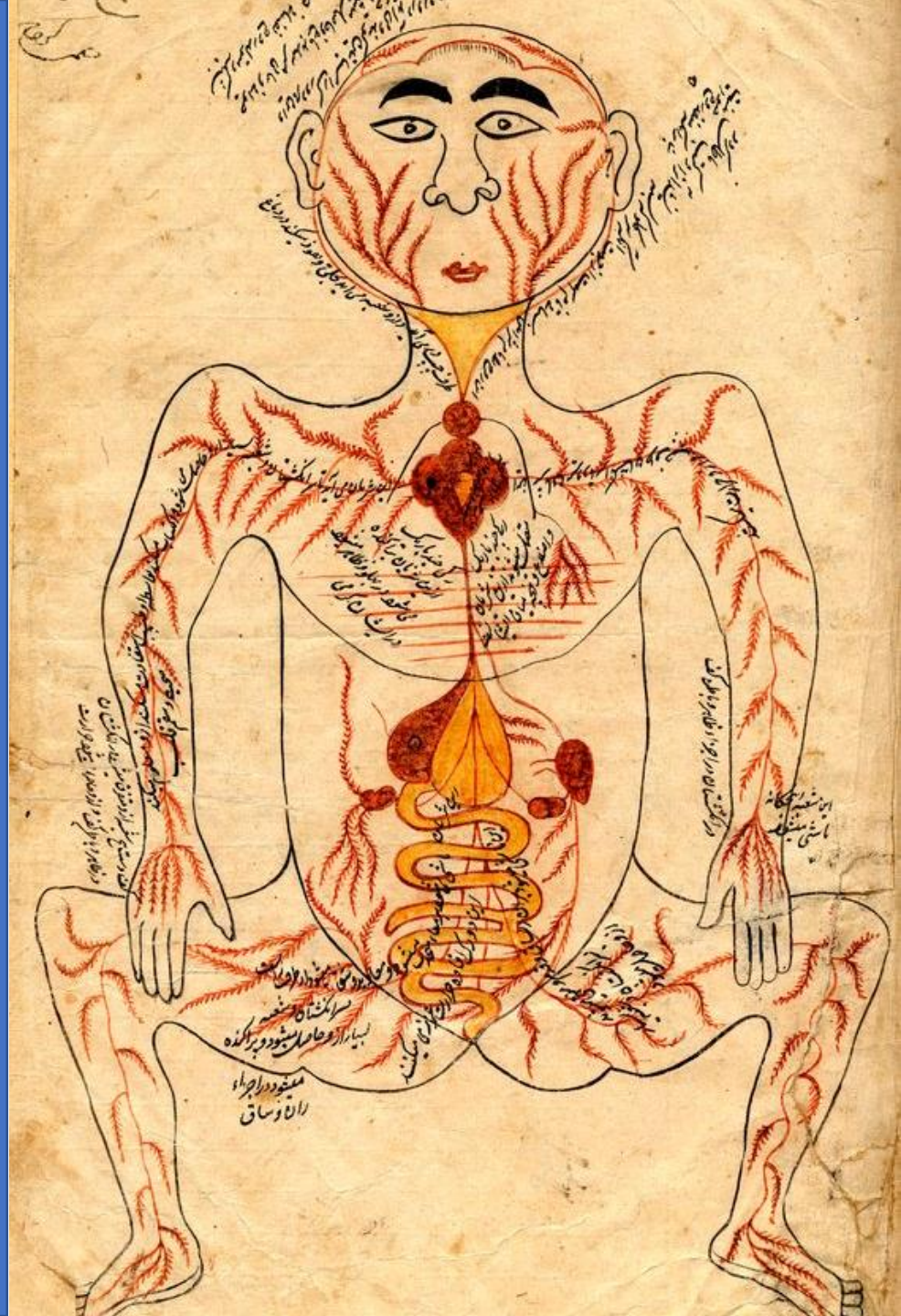


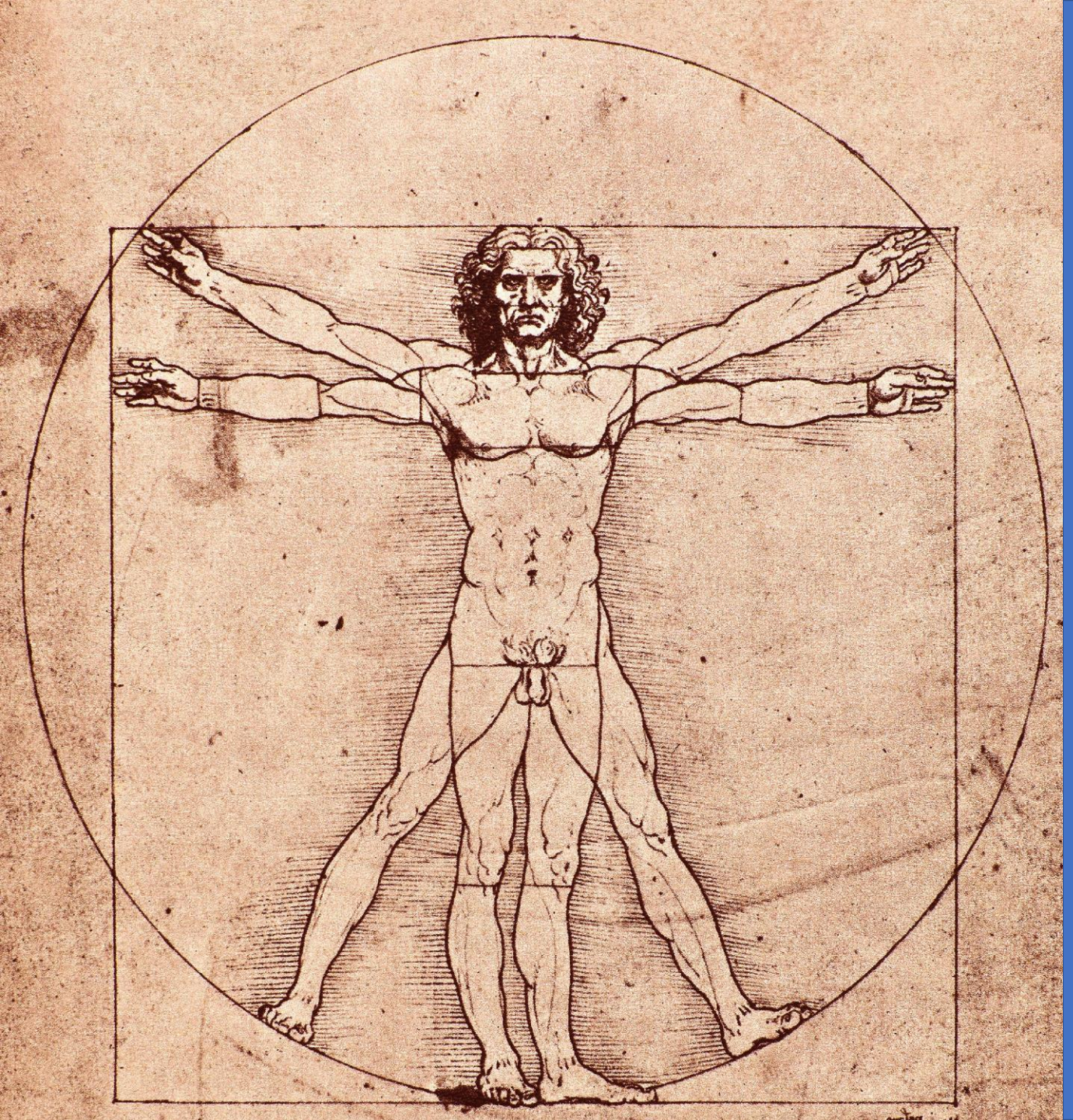
A COMMON COSMOLOGY OF THE ANCIENT WORLD



How we used to see the human body…

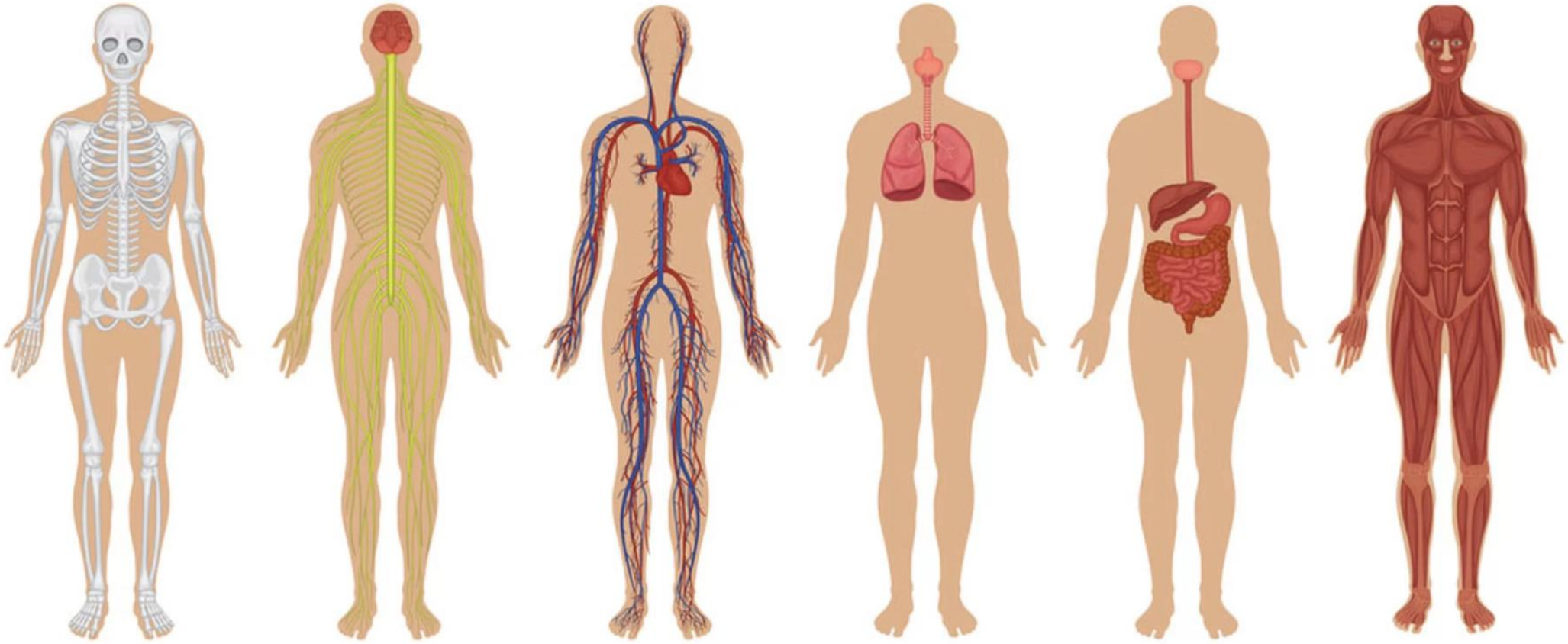
How we used to see the human body…





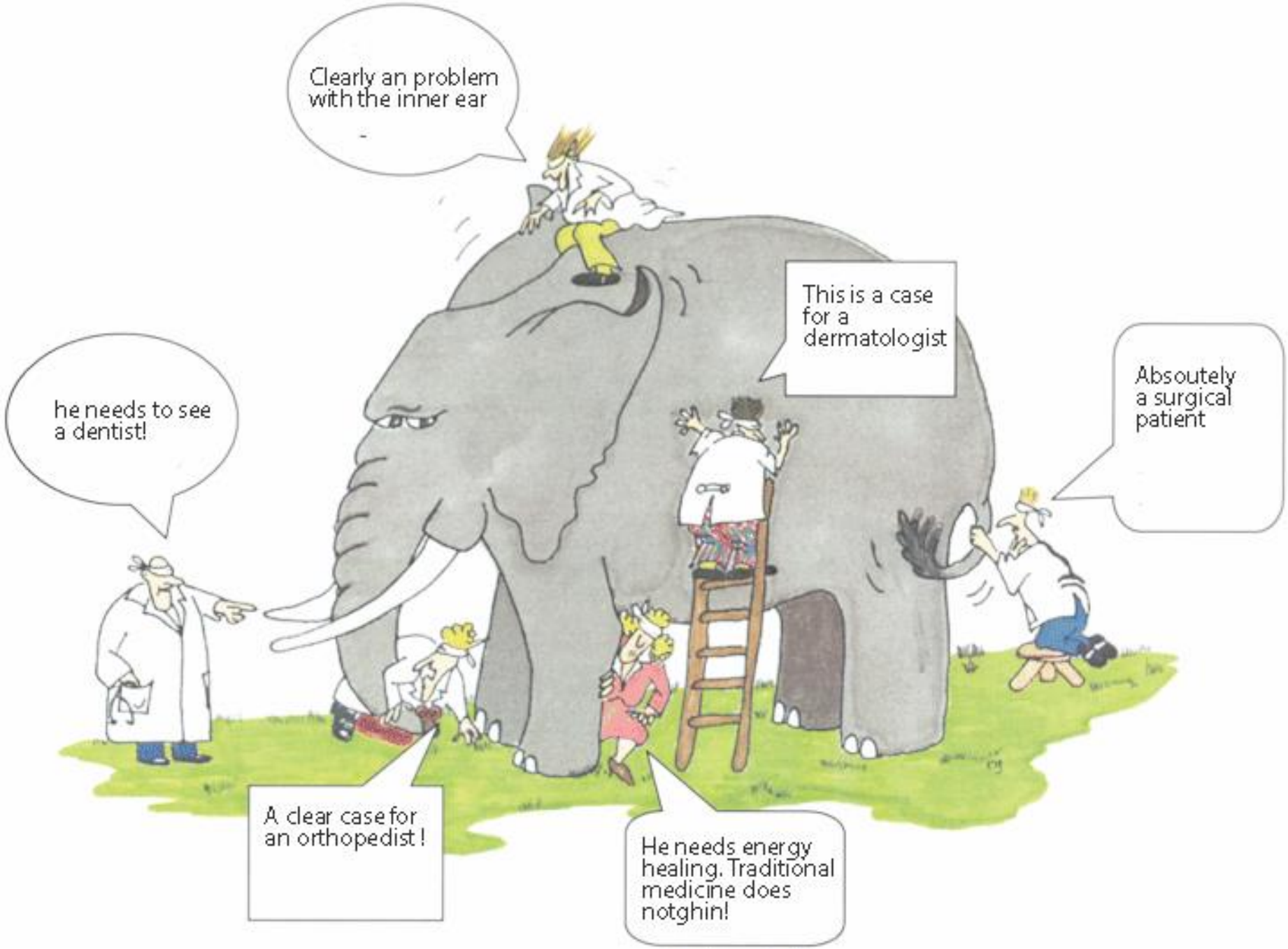
A bit later…

How medical doctors see the human body today…



A Complex Systems View of the Human Body

Result..


Clearly an problem with the inner ear
he needs to see a dentist!
This is a case for a dermatologist
Absoutely a surgical patient
A clear case for an orthopedist !
He needs energy healing. Traditional medicine does notghin!

- Medical doctors are good at tinkering
- Focus: to treat an existing disease
- Using interventions they do not understand on a system they do not understand

"The problems we have cannot be solved at the same level of thinking with which we created them"

-Albert Einstein

What is a healthy human body?

The World Health Organization (WHO) defined health as

"a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity."

Would an engineer be OK with a similar definition to define the status of a complex system, say an airplane?

What is a healthy human body?

- A visit to the doctor…

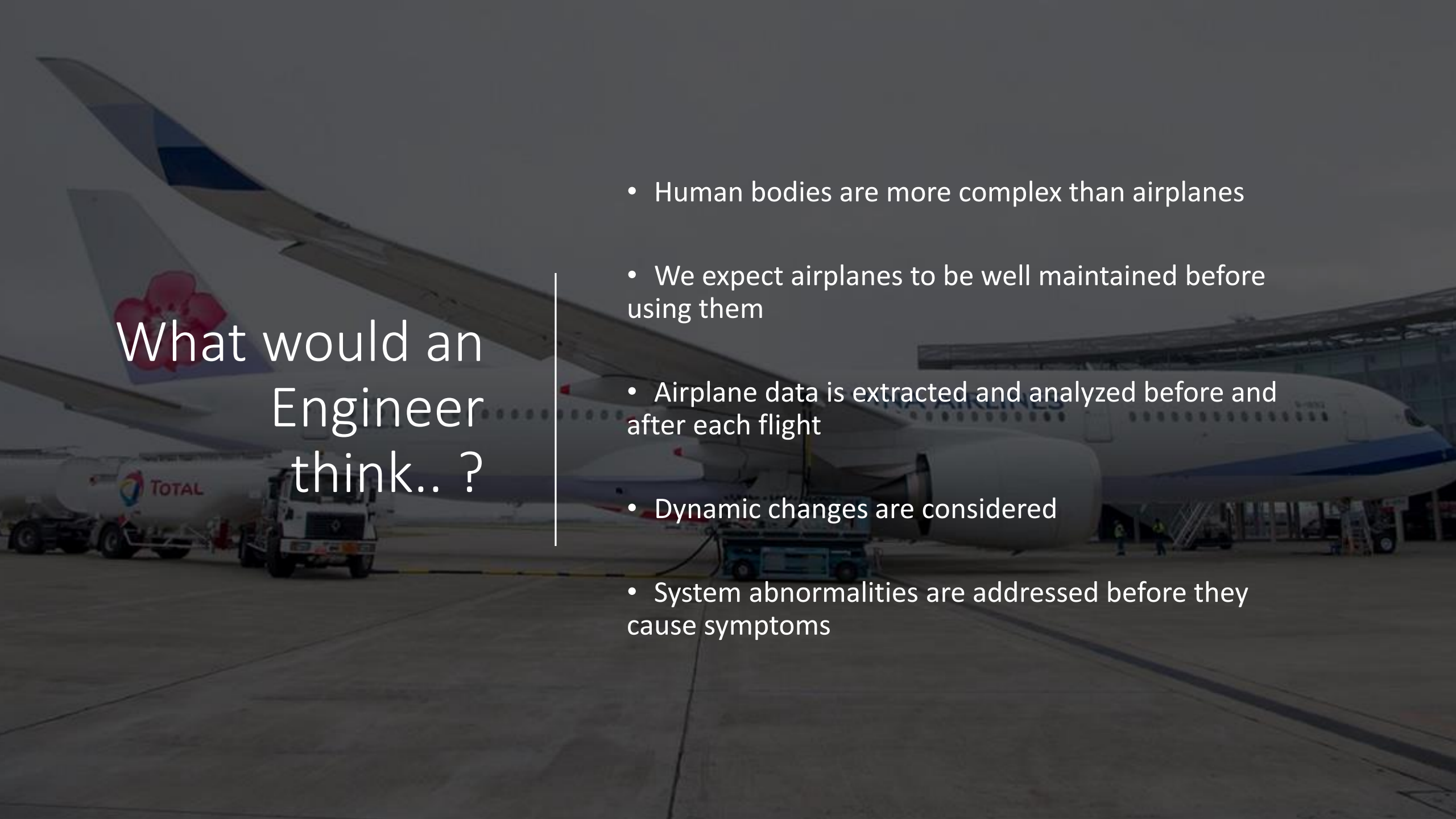
    - Interview
    - Auscultation (Stethoscope)
    - Visual examination of skin, larynx
    - Physical tests of joints, muscles
    - Blood test (10-15 markers such as cholesterol, glucose…)

to determine whether a patient is healthy…

How many solid data points were collected ?

What are First Things your Doctor Measures on an Exam?

Vital Signs	
	"Normal" values:
Height / Weight:	BMI : 18.5 – 25 kg/m^2
Pulse:	60 –100 beats/min
Blood pressure:	<120/80 mmHg
Respiratory rate:	12 – 18 per min
Temperature:	97.8 – 99.1°F



What would an Engineer think.. ?

- Human bodies are more complex than airplanes
- We expect airplanes to be well maintained before using them
- Airplane data is extracted and analyzed before and after each flight
- Dynamic changes are considered
- System abnormalities are addressed before they cause symptoms

‘Modern’ Medicine

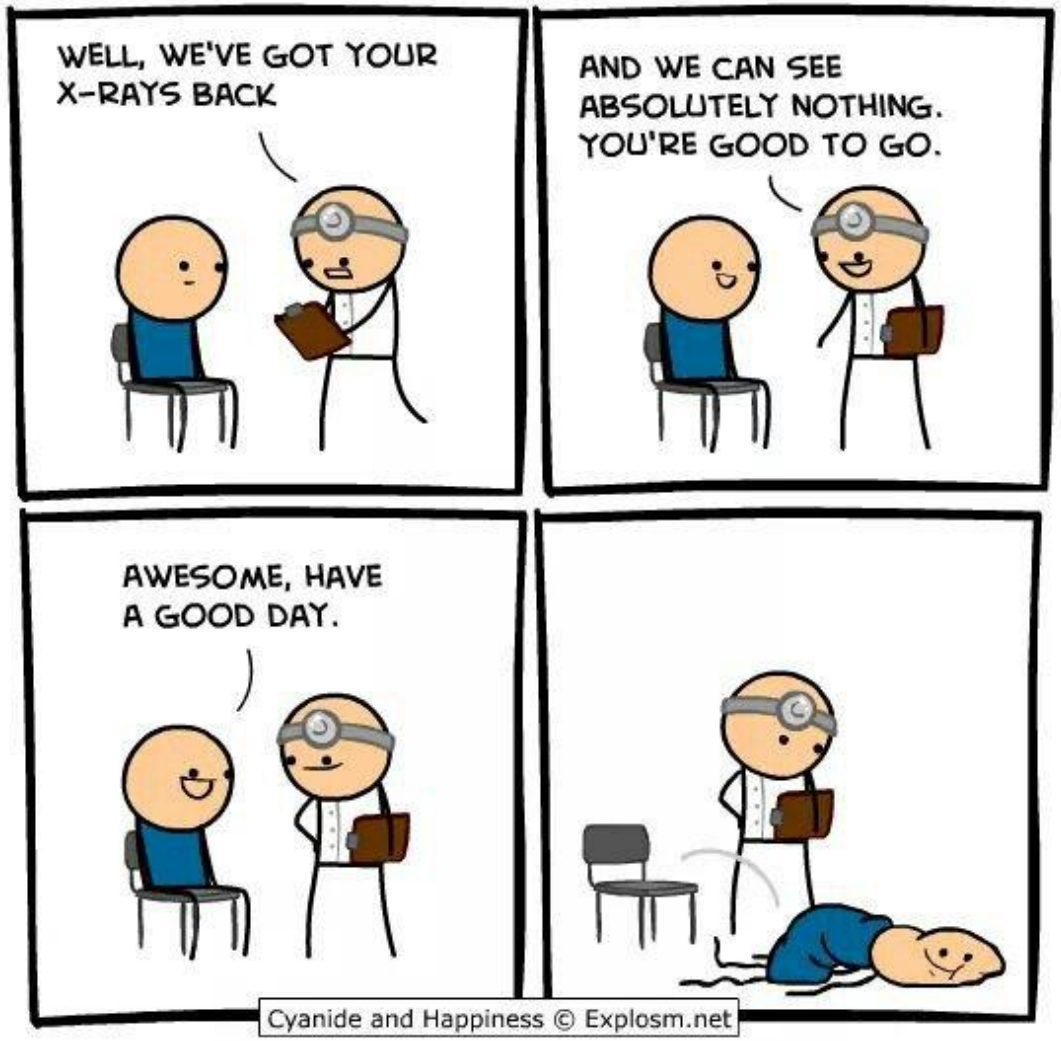
- Todays ’health care’ system is not designed to keep patients / people healthy
- Characteristics of the current “disease care system” :
  - Waiting for symptoms to occur to start interventions
  - Patients are not participating in treatment decisions
  - Doctors do not get reimbursed to prevent diseases
  - Non-linearity and complex systems are not considered
  - In clinical practice sub-specialities compete with each other

Let me tell you a medical secret

- Current practice pays almost no attention to physiological dynamics (e.g. time series)

- It is mainly about single values or means (+/- SD)

Limits of todays medical approach



How medicine determines Health

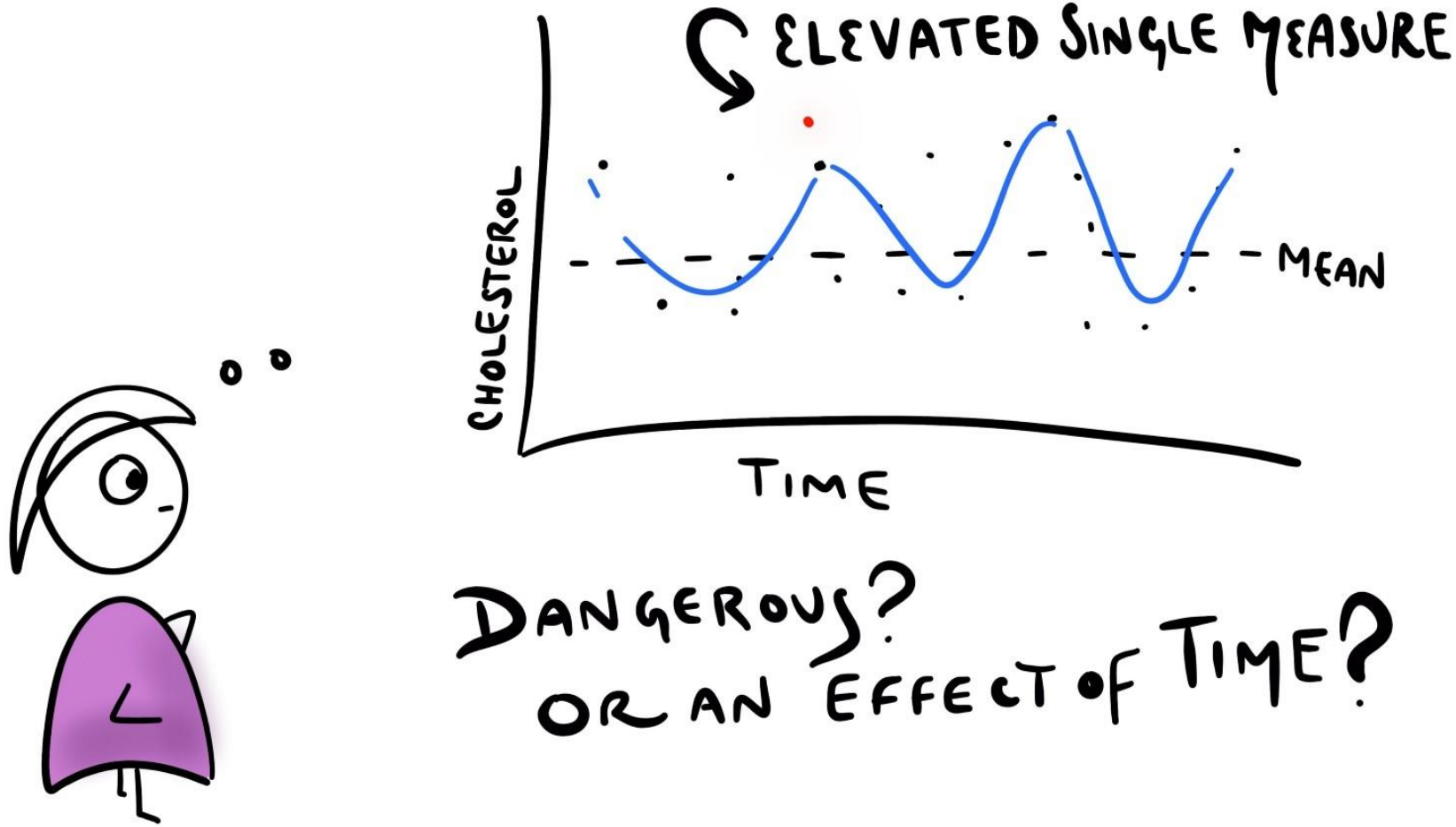
- Cholesterol

  LDL cholesterol below 100 mg/dL
  Total cholesterol less than 200 mg/dL

- Blood Pressure

  People with readings of 130 as the top number or 80 as the bottom one now are considered to have high blood pressure, according to the guideline released Monday by the American Heart Association.

  High blood pressure used to be defined as 140/90


ELEVATED SINGLE MEASURE
CHOLESTEROL
MEAN
TIME
DANGEROUS?
OR AN EFFECT OF TIME?

A next step, the Allostatic Load

Table 1
Criterion cut-points for individual biological components of allostatic load index in the MacArthur Study of Successful Aging, 1988

Biological parameters	Criterion cut-point	Mean (SD)
High diastolic BP (mmHg)	83.30	76.70 (10.49)
High systolic BP (mmHg)	148.00	137.76 (19.21)
High glycosylated hemoglobin (Hb_{A1c}) (%)	7.10	6.81 (1.88)
Low HDL cholesterol (mg/dl)	37.00	47.89 (15.20)
High total/HDL cholesterol ratio	5.92	5.03 (1.80)
High waist–hip ratio	0.94	0.88 (0.08)
High urinary cortisol (CORT) (μg/g creatinine)	25.69	21.70 (16.60)
High urinary norepinephrine (NE) (μg/g creatinine)	48.00	40.44 (21.89)
High urinary epinephrine (EPI) (μg/g creatinine)	4.99	4.00 (2.30)
Low albumin (mg/dl)	3.90	4.11 (0.29)
High IL-6 (pg/ml)	4.64	4.56 (5.53)
High C-reactive protein (CRP) (μg/ml)	3.19	3.23 (5.32)
Low best peak (l/min)	300.00	383.14 (117.68)
Low DHEA-S (mg/dl)	35.00	69.27 (48.74)
High fibrinogen (mg/dl)	336.00	91.97 (85.89)
Low creatinine clearance (ml/min)	44.64	62.79 (27.97)

Source: Seeman, TE et al. 2004. Cumulative biological risk and socio-economic differences in mortality: MacArthur Studies of Successful Aging. *Soc Sci Med*, 1985-1997

The human body creates enormous amounts of information / data

- 37 trillion cells
- 7 octillion atoms
- 42 billion blood vessels
- 22 internal organs
- 3 to 5 lbs is made up of bacteria, the Microbiome
- One gram of DNA can store 700 terabytes of data

  Dense (you can store one bit per base, and a base is only a few atoms large);
  Volumetric (beaker) rather than planar (hard disk);

  Stable;

What is Health ?

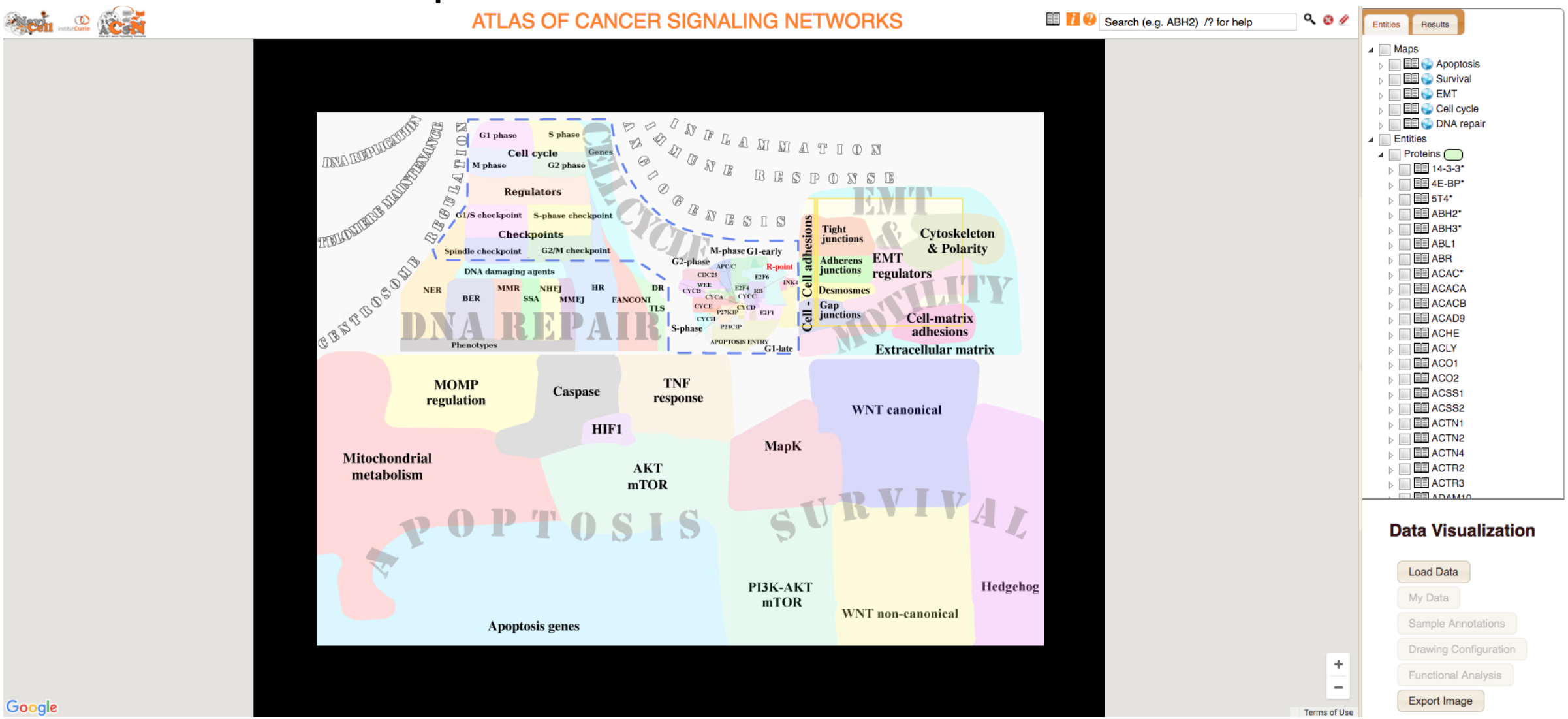
e.g. the ’normal’ functioning of the human body.

Q: how to define ’normal’

What is ”health” for any individual ?

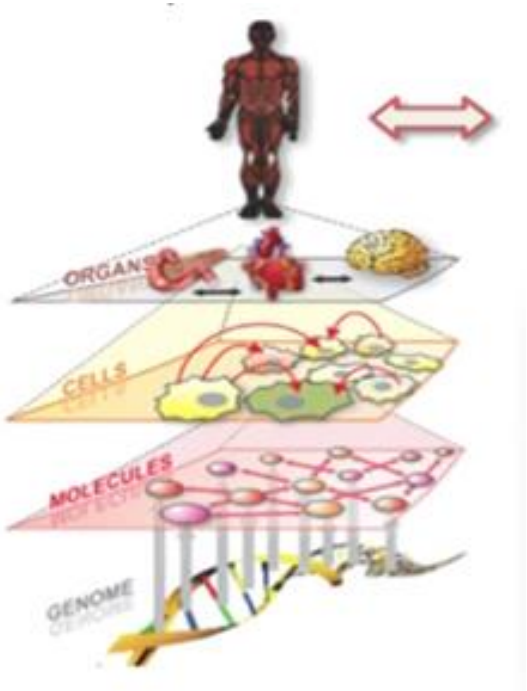
- Physiological functioning of organ systems
- The subjective feeling of health, wellness
- The ability to adapt (to extremes)
- Ability to perform physically and mentally
- The ability to ’pro-create’ ?

Disease Maps

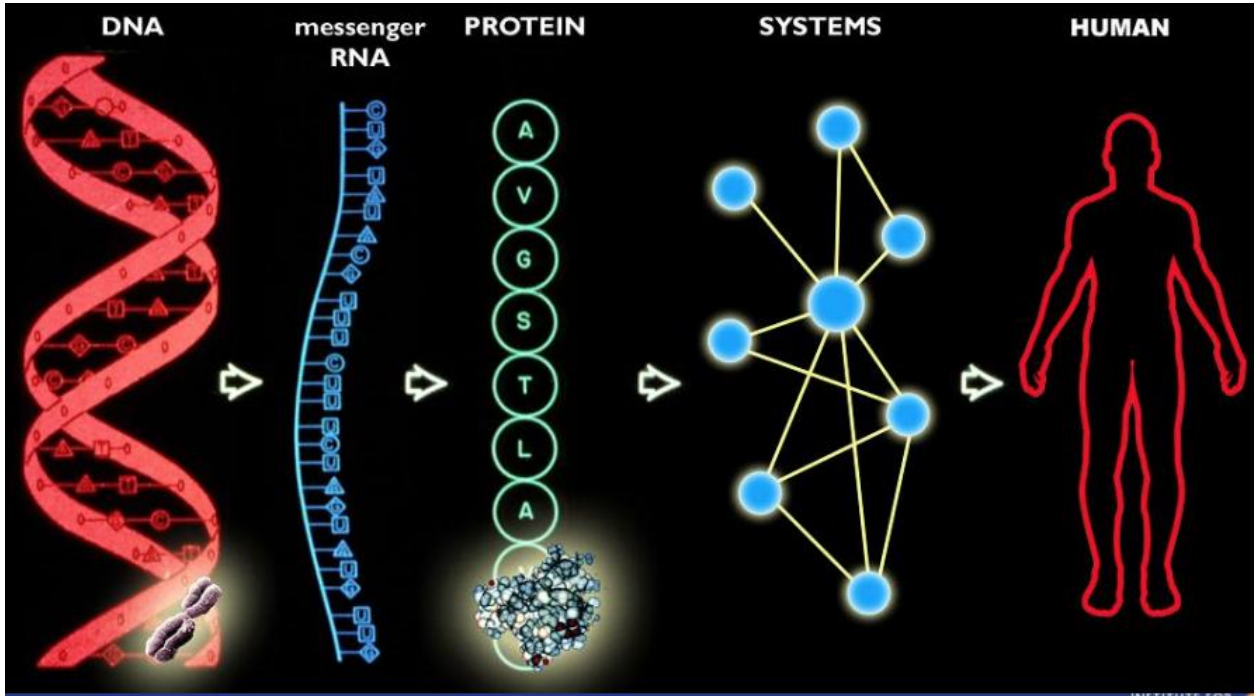


http://disease-maps.org/

Sytems Medicine



- Biological Networks carry information and mediate development, physiology and aging.
- Biological networks operate at different spatial levels
- Disease-pertubated networks mediate disease
- Integration of patient data will reveal biological networks that specify health and are altered in disease
- Understanding differences in normal and disease-perturbed networks will provide fundamental insights into disease mechanisms



- The digital information of the genome
- The environmental information that impinges upon and modifies the digital information

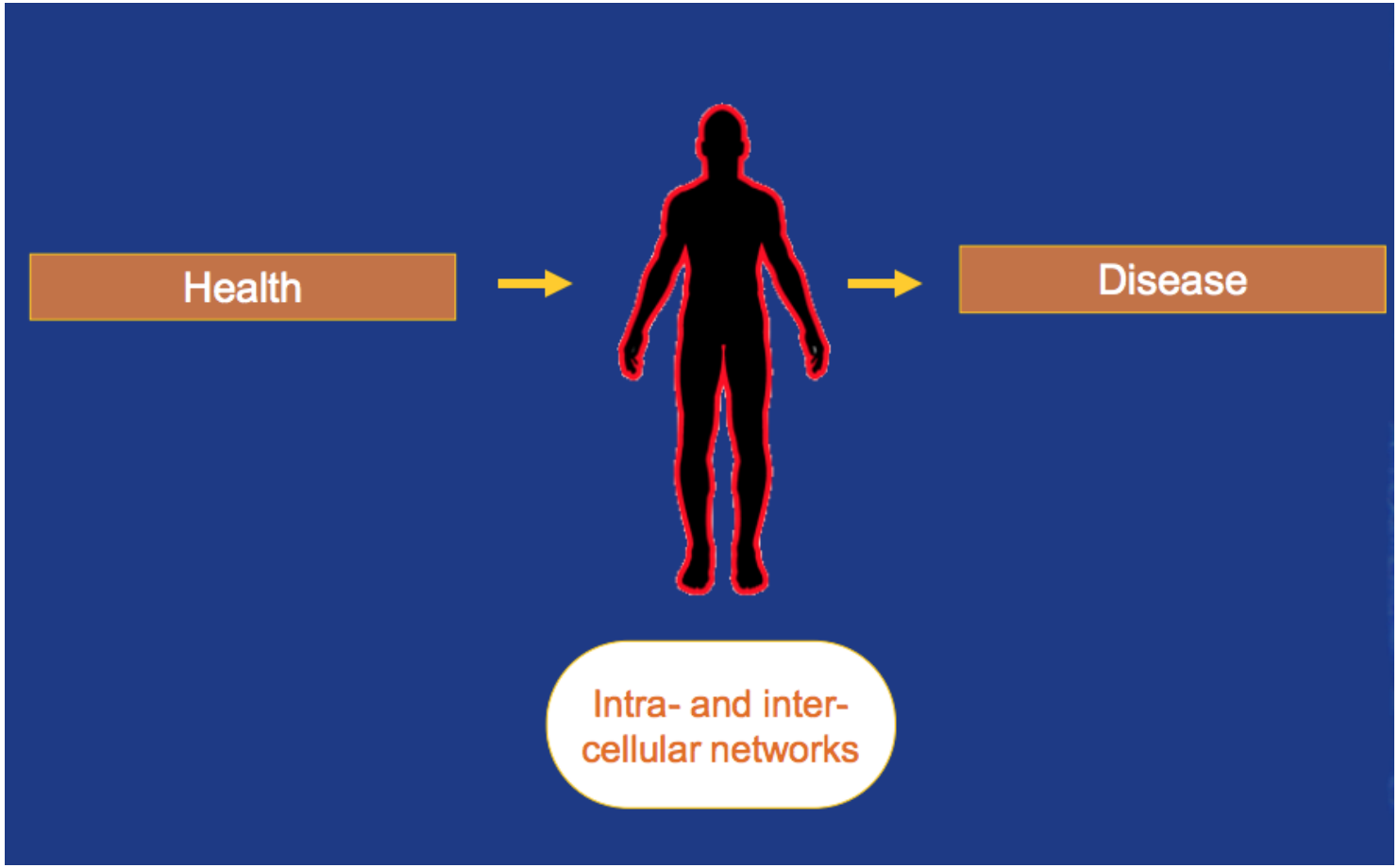
There are Two Types of Biological Information

The Future: **P4 Medicine**

- **Preventive - Predictive – Personalized - Participatory**

- Digitalization of Biology and Medicine Will Transform Medicine
- Analysis of single molecules, single cells and single individuals
- Will lead to dramatically lower health care costs

Wellness-Health – Disease Transitions



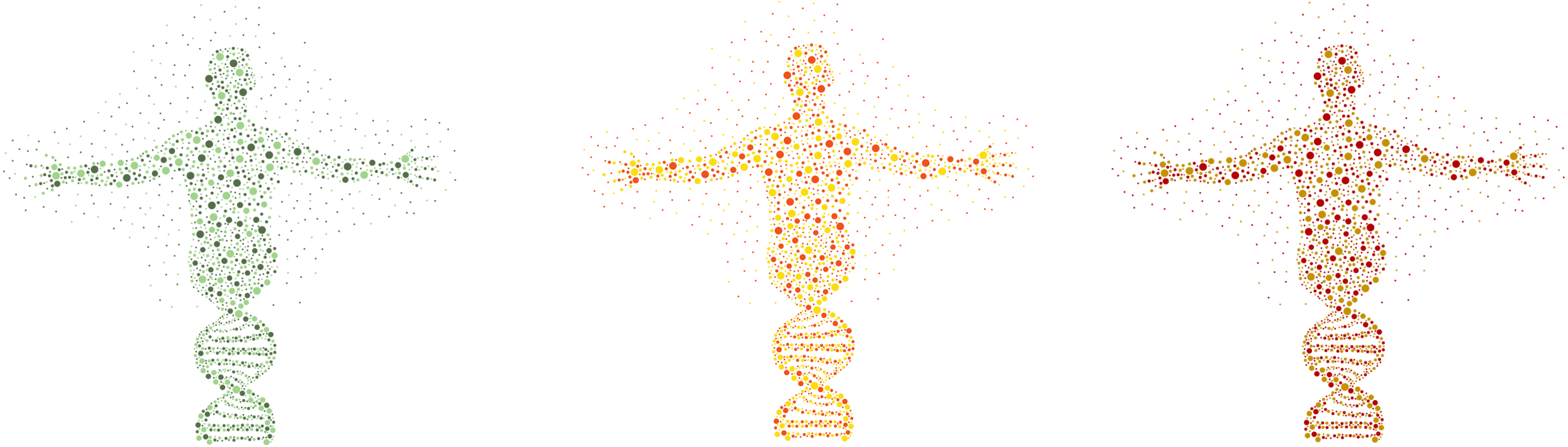
Wellness-Health – Disease Transitions and Network Perturbations

Stress Hits

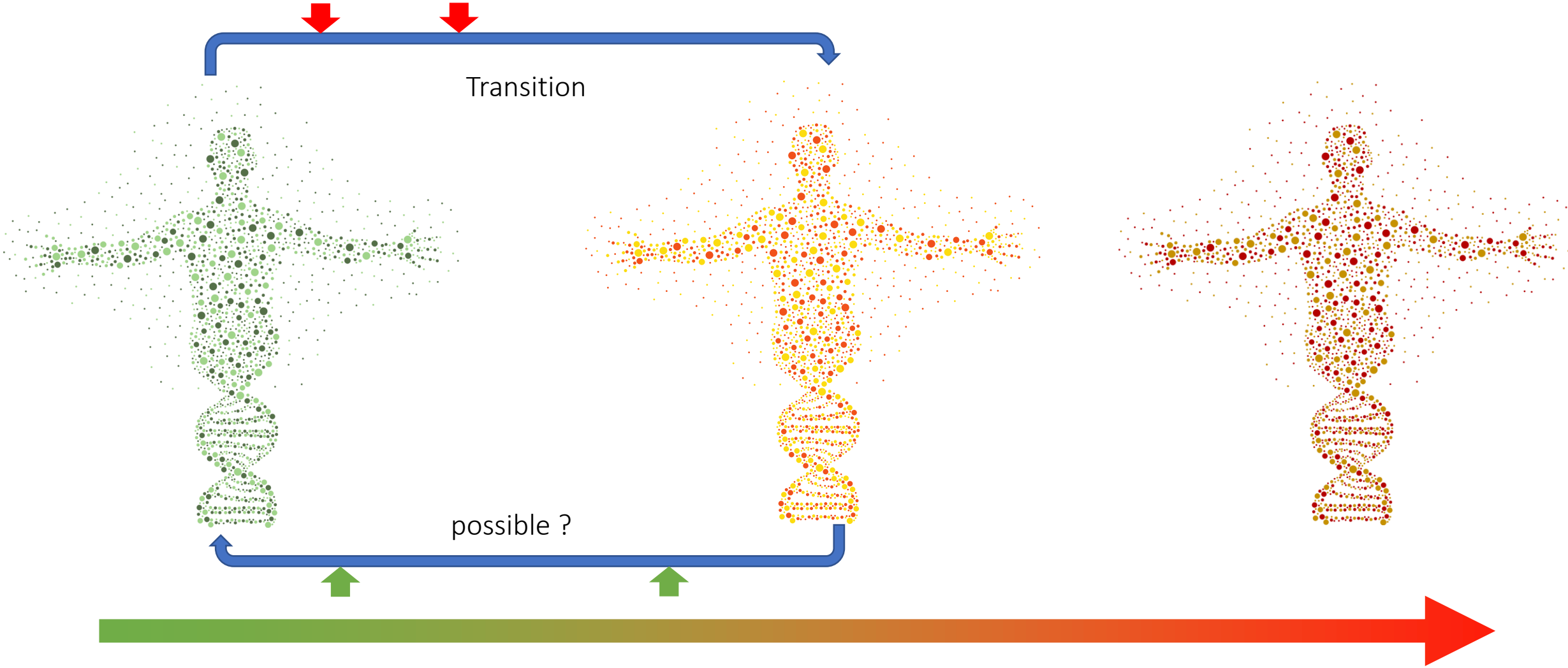
Lifestyle
Smoking, Diet, Physical Inactivity, Physiological Stress

Environment

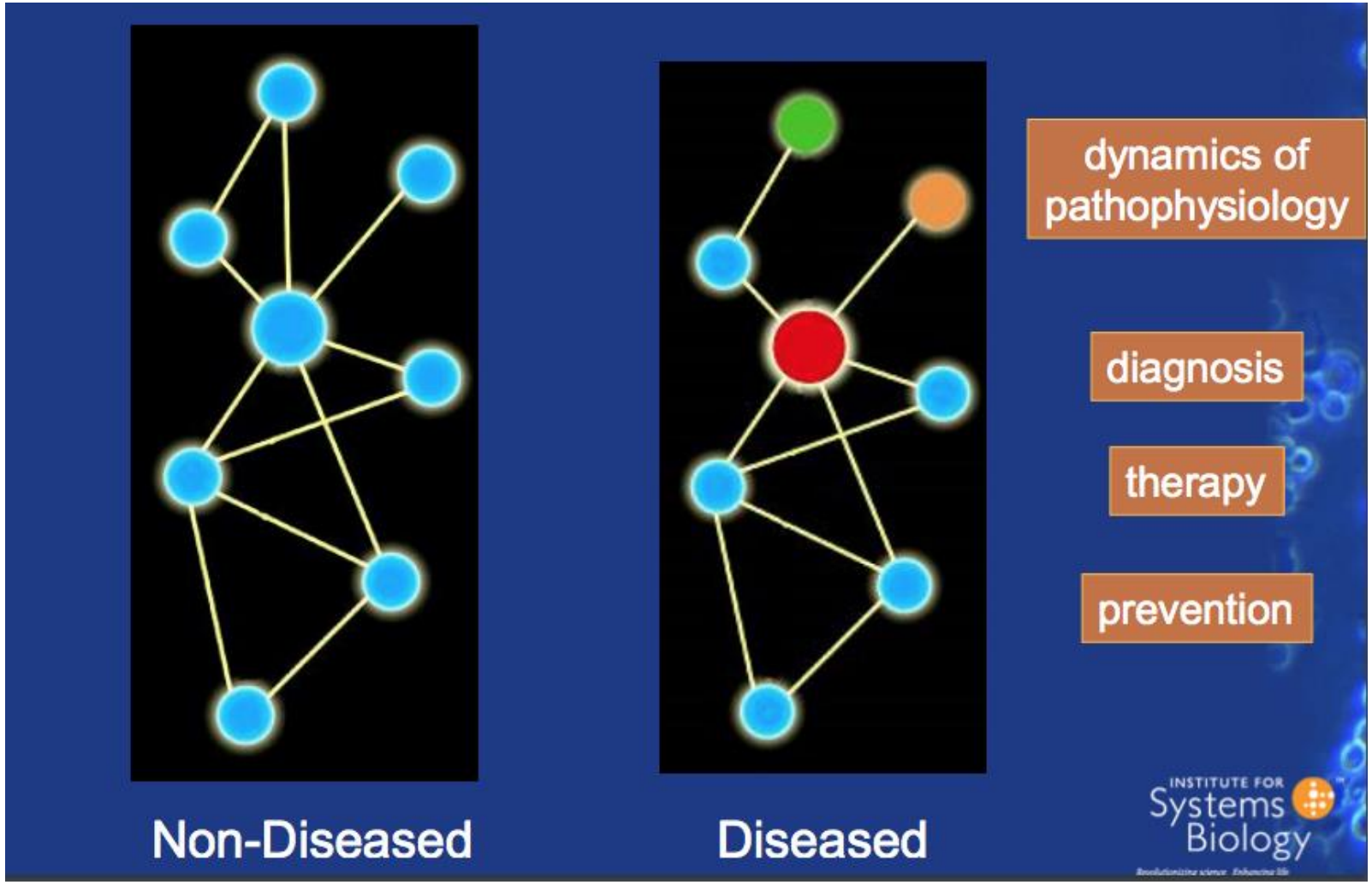
Aging



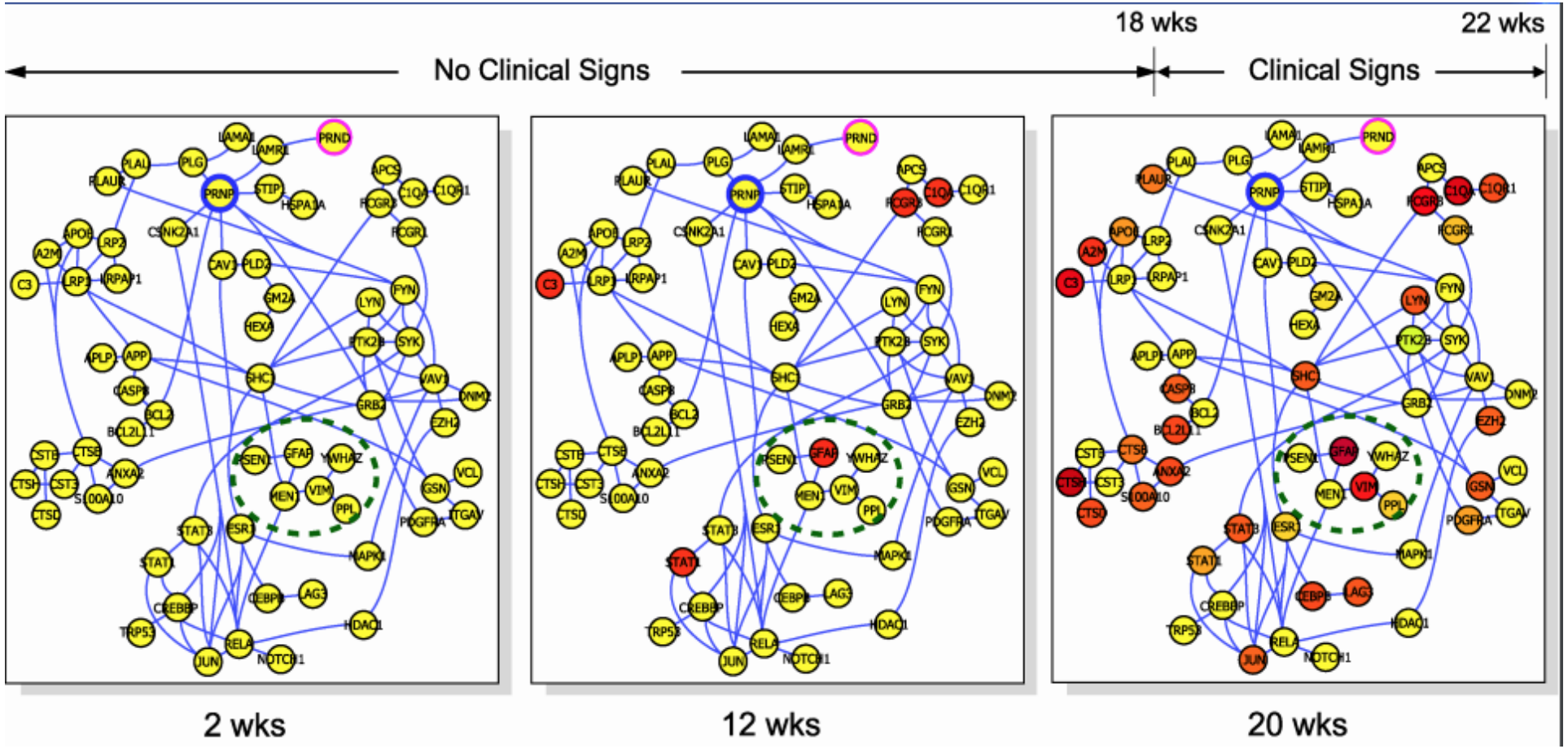
The Health Continuum



A Systems View of Disease Postulates that Disease Arises from DiseasePerturbed Networks

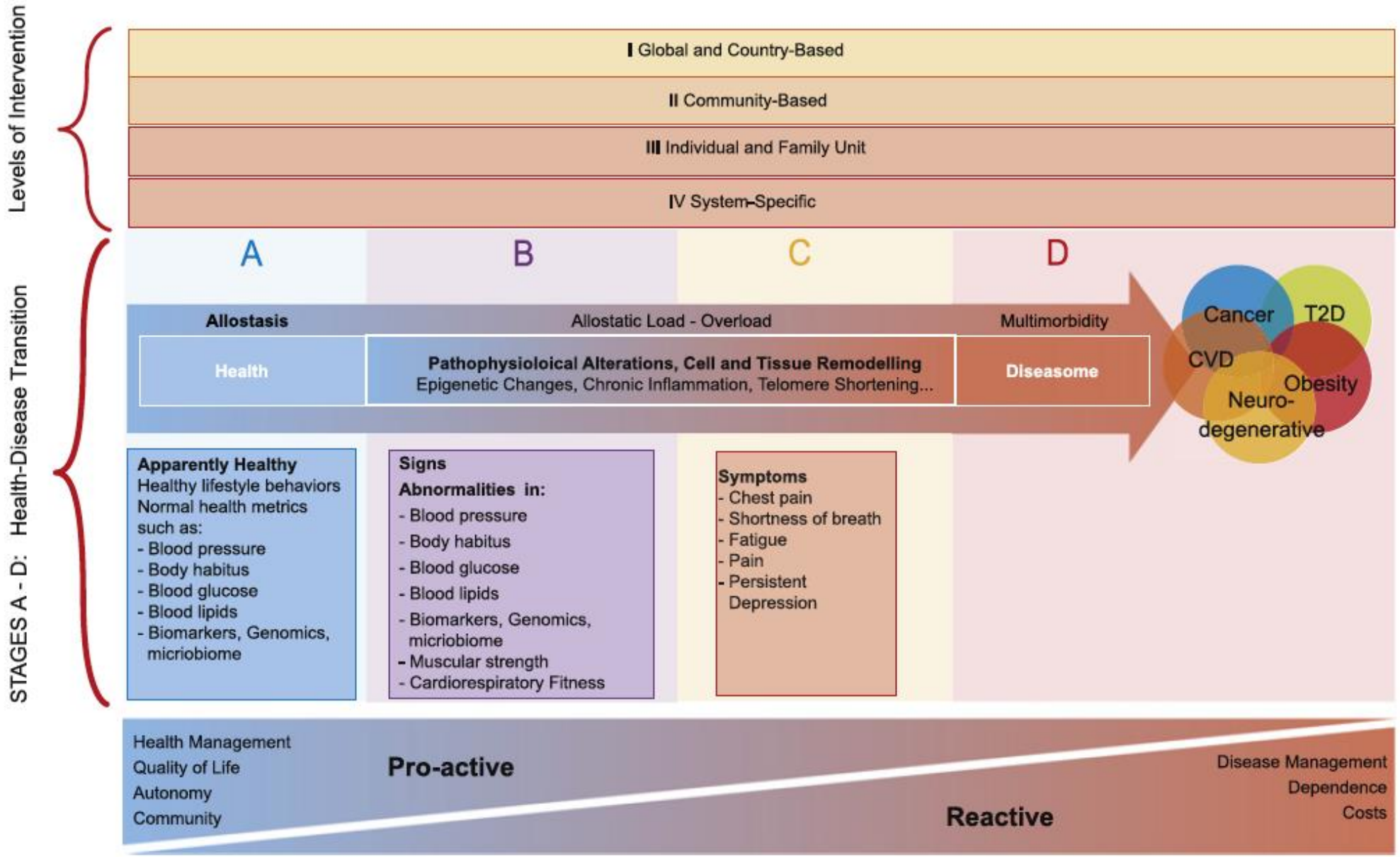


Dynamics of a Neurodegenerative Disease-Perturbed Network in Mice

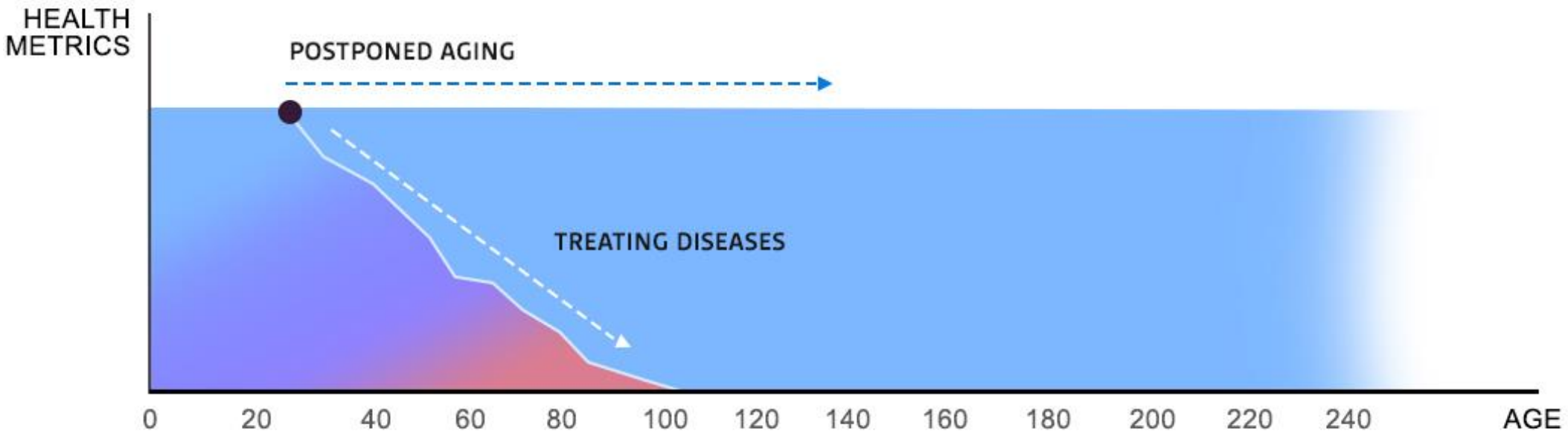


Sagner M., Auffray C. et al. 2016

The Health Continuum

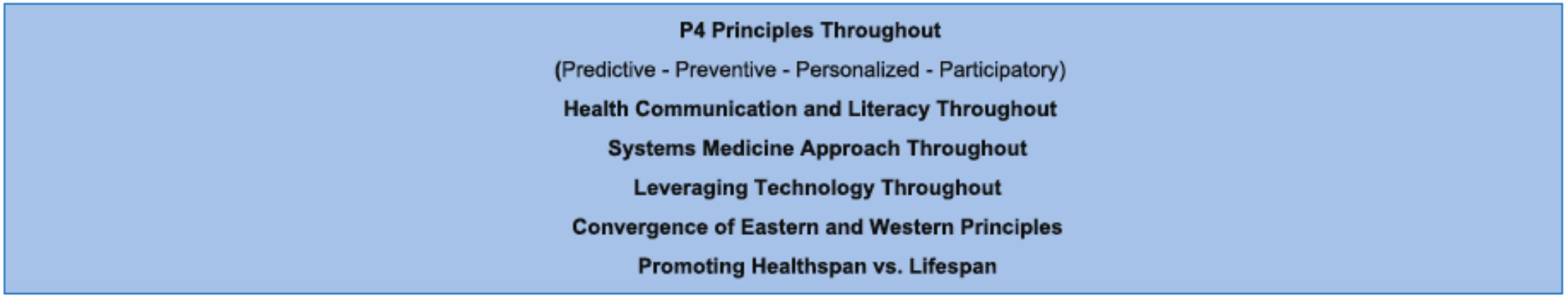


Extending the arc of life



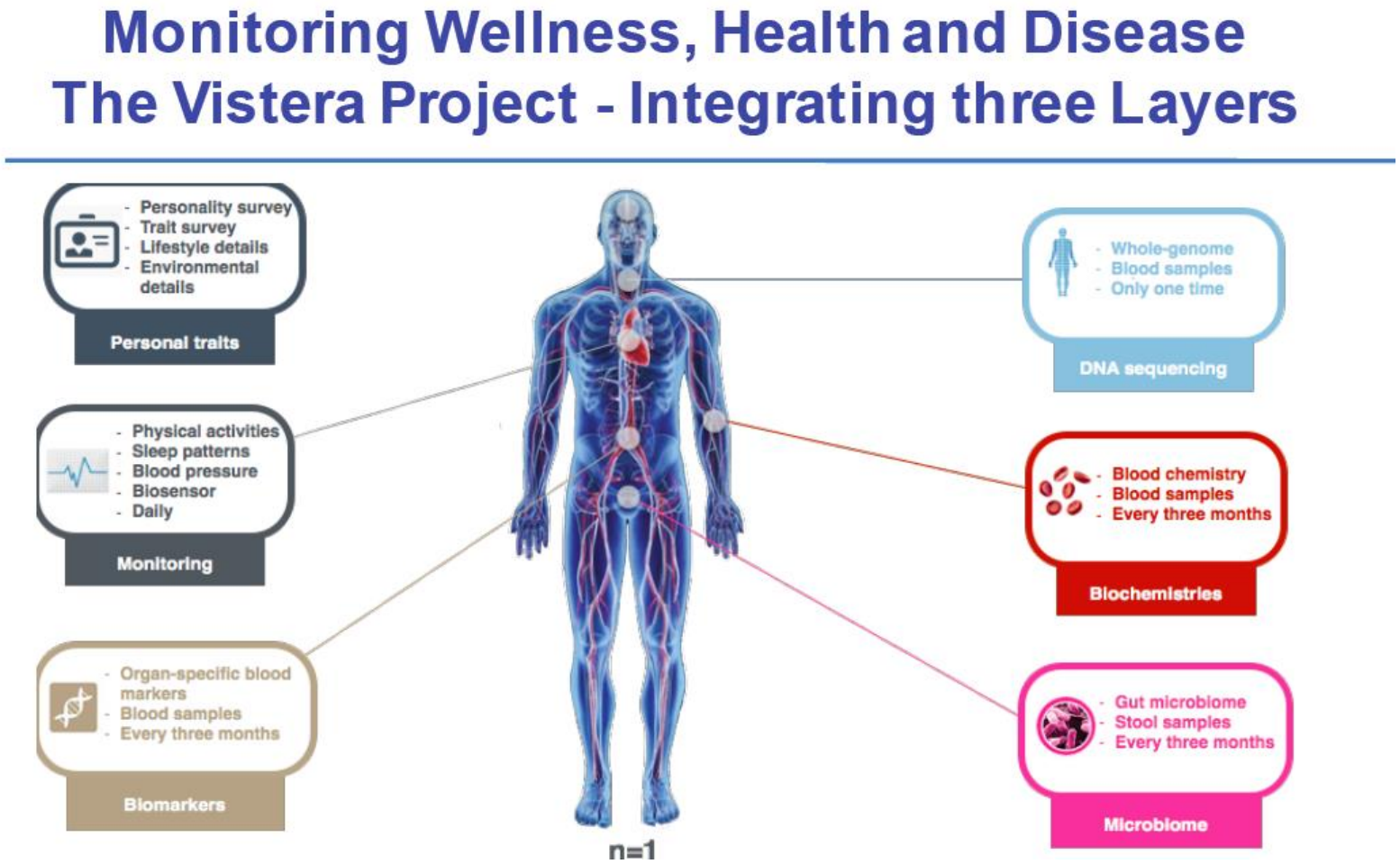
Yaneer Bar-Yam

Systems Medicine (P4 Medicine) Principles



Sagner M., Auffray C. et al. 2016

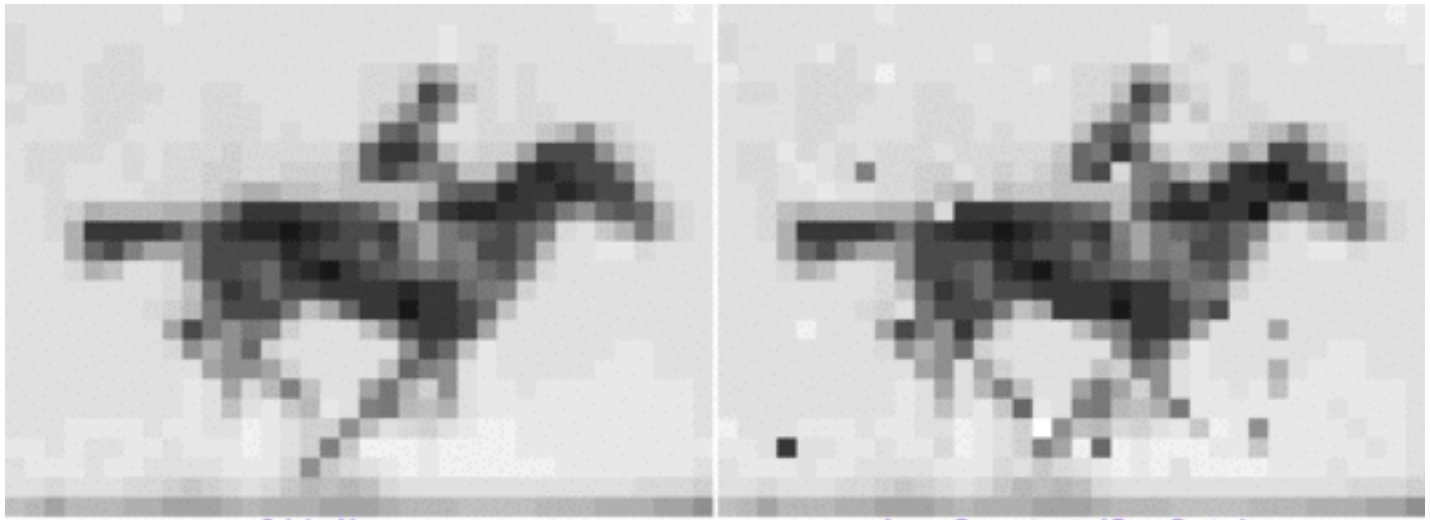
Data Collection



Auffray, C. www.visteraproject.fr

We already can turn living cells into digital data warehouses

- Using Crispr system to insert bits of DNA encoded with photos and a GIF of a galloping horse into live bacteria

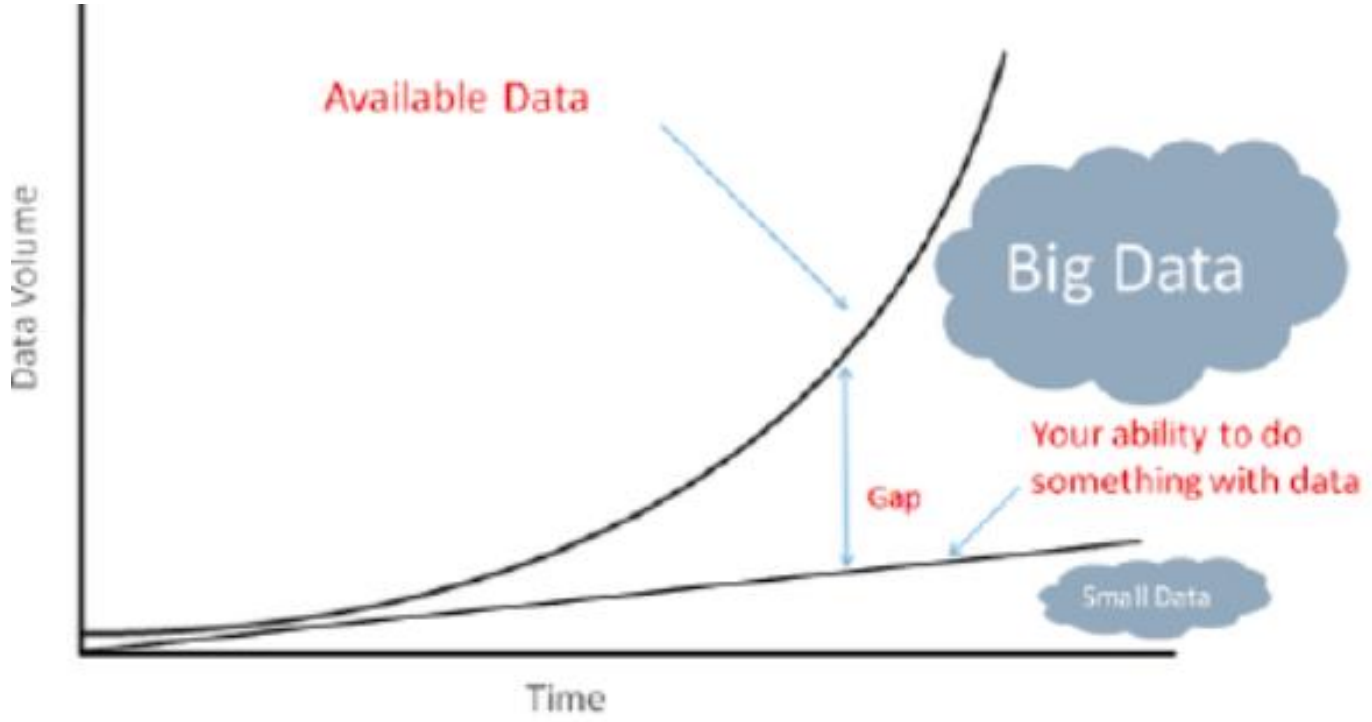


CRISPR–Cas encoding of a digital movie into the genomes of a population of living bacteria. Seth L. Shipman et al. Nature 2017

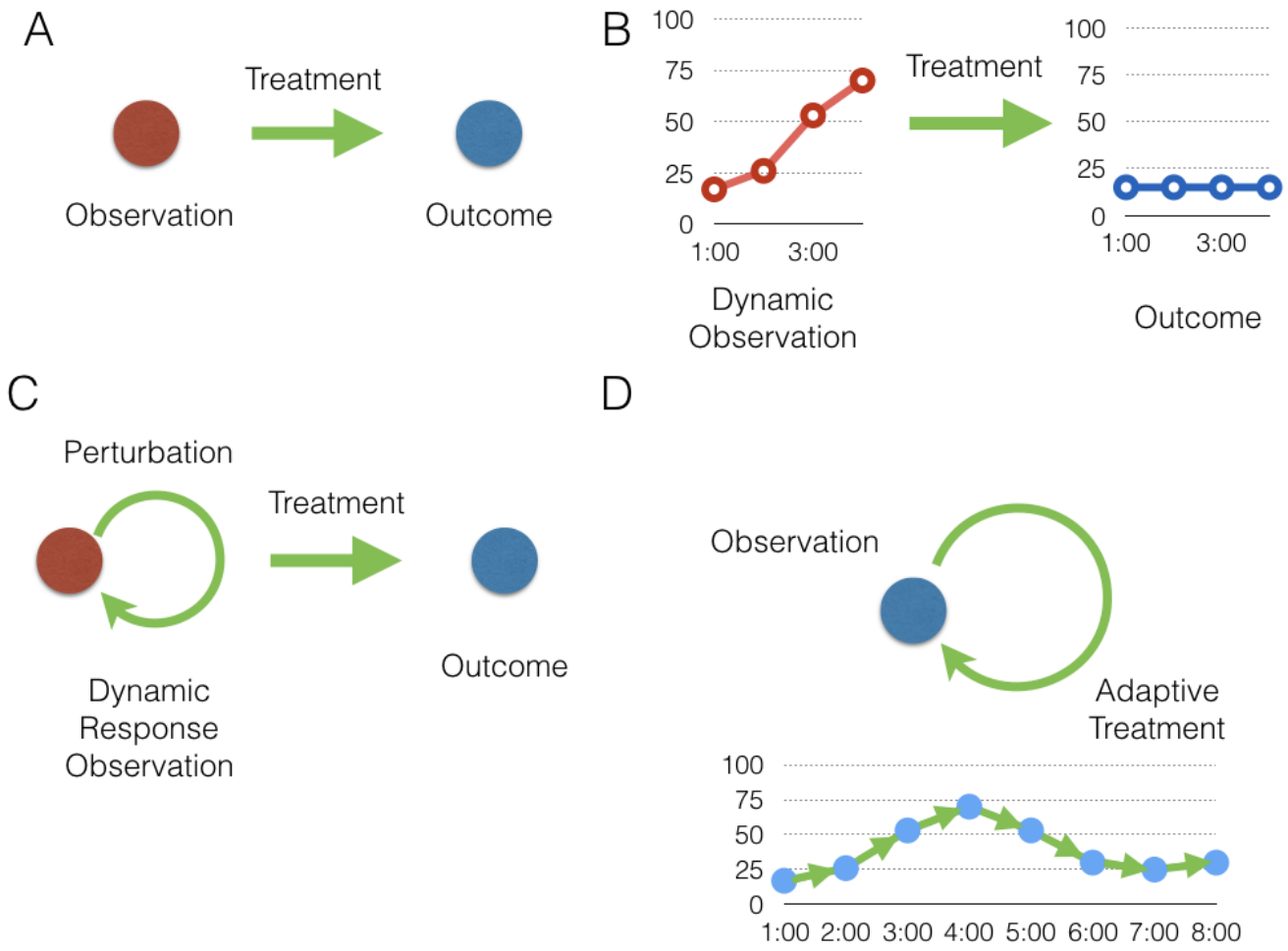
Modern diagnostics can capture a glimpse. Which already overwhelms doctors

There were roughly 800 million multi-slice exams performed in the United States in 2015 alone. Those studies generated approximately 60 billion medical images. At those volumes, each of the roughly 31,000 radiologists in the U.S. would have to view an image every two seconds of every working day for an entire year in order to extract potentially life-saving information from a handful of images hidden in a sea of data.

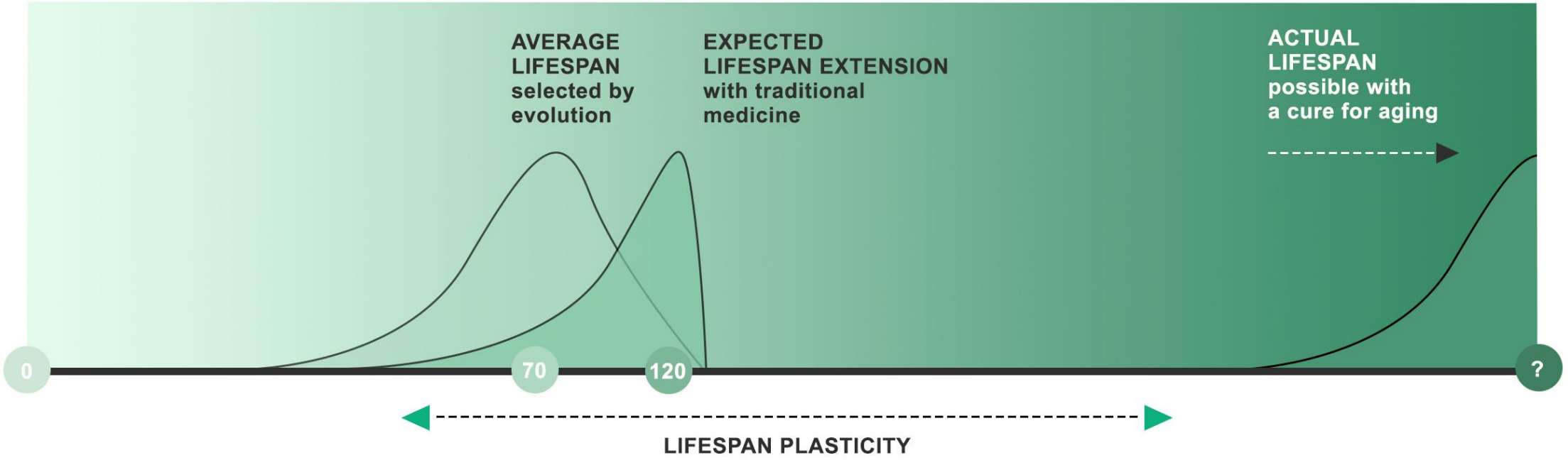
The human body creates enormous amounts of data.



Dynamic P4 Medicine



Yaneer Bar-Yam



The traditional theory that evolution selects for the longest possible life leads biologists to think that lifespans are inherently limited to the ones we have today. In this view, aging cannot be stopped and lives can be extended only to about 120 years.

The new understanding that evolution selects for shorter lifespans implies that aging is a mechanism for limiting lifespans which can be changed. Aging as we experience it is unnecessary, and can be postponed until the actual intrinsic lifespan limit is reached.

Yaneer Bar-Yam

Inventing the Future

- Data collection of human body functions
- Data analysis and mining
- Using AI and advanced computing to define ’normal’ states
- Identifying wellness-health-disease transition stages
- Identifying potential interventions to prevent and reverse system perturbations

- Academics and industry
- Strategic partnerships for hard scientific problems industrial, academic, government, international

INTERNATIONAL SOCIETY FOR

P4 MEDICINE