

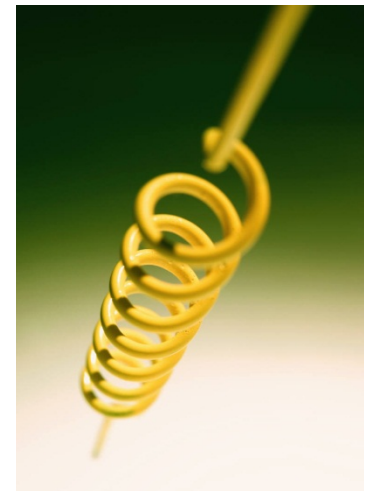
# Dynamic biomarkers to capture the complexity of health



# Healthy nutrition .....

Maintains or improves *normal physiological functioning*

Reduces or modifies *risks*\* for the development of a disease...



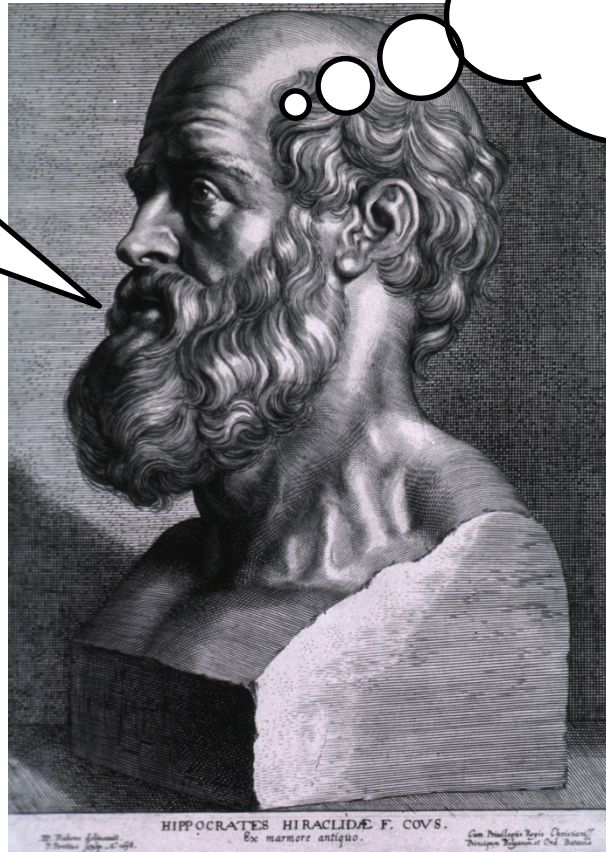
\* EFSA: risk *factor* in the development of a disease

# Main points

- To measure (improvement of -) *normal* physiological functioning ('health')....
  - *Biomarkers for disease* have very limited use
  - So do *RCTs*
  - Individual *homeostasis* and *phenotypic flexibility* are key
- Food is **NOT** 'thy medicine'
- Taking single nutrients usually don't make us more healthy
- Experimental and nutritional physiology will rapidly (have to) move out of the lab

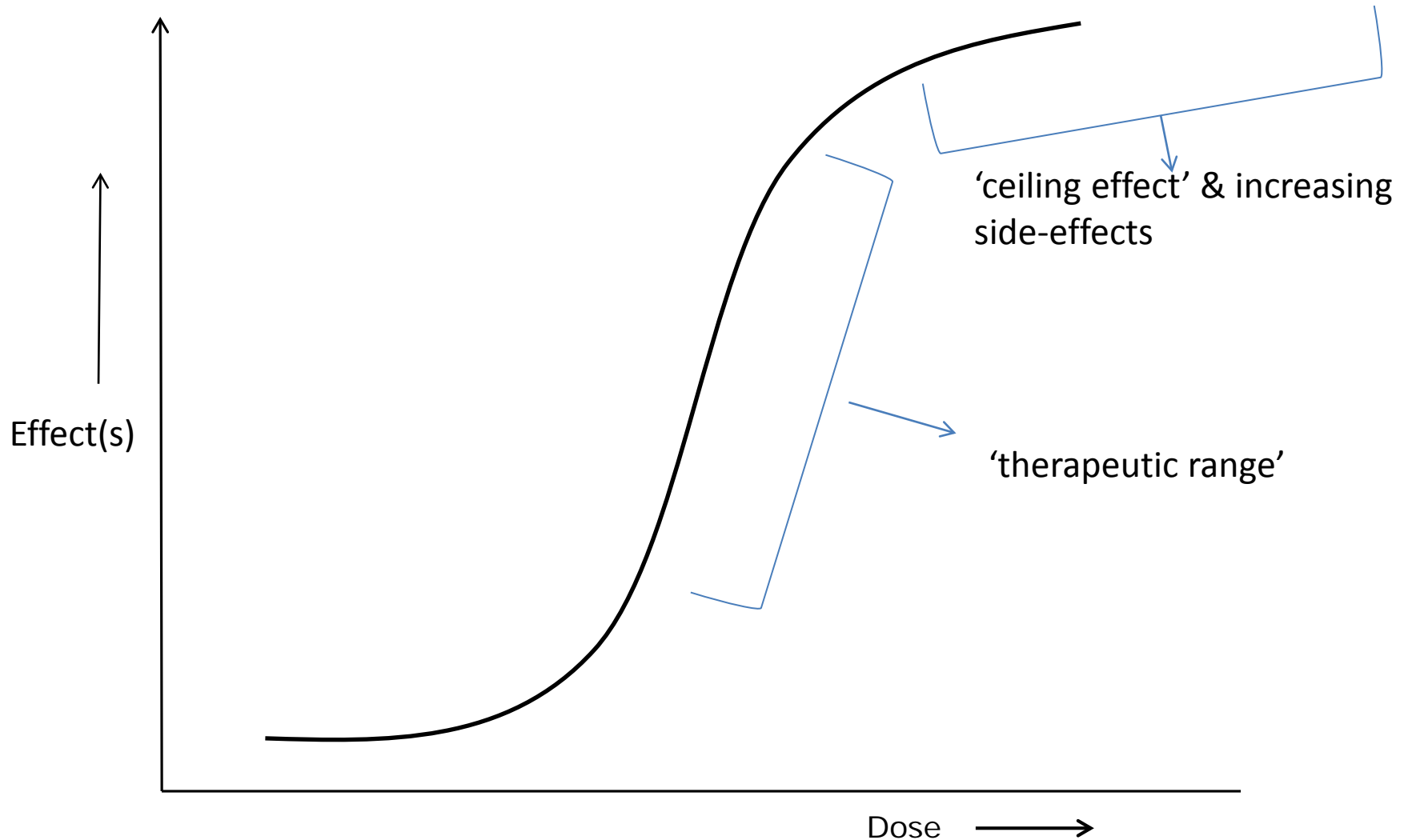
# Food is not pharma ....

*"let food be  
thy medicine  
and medicine  
be thy  
food"*

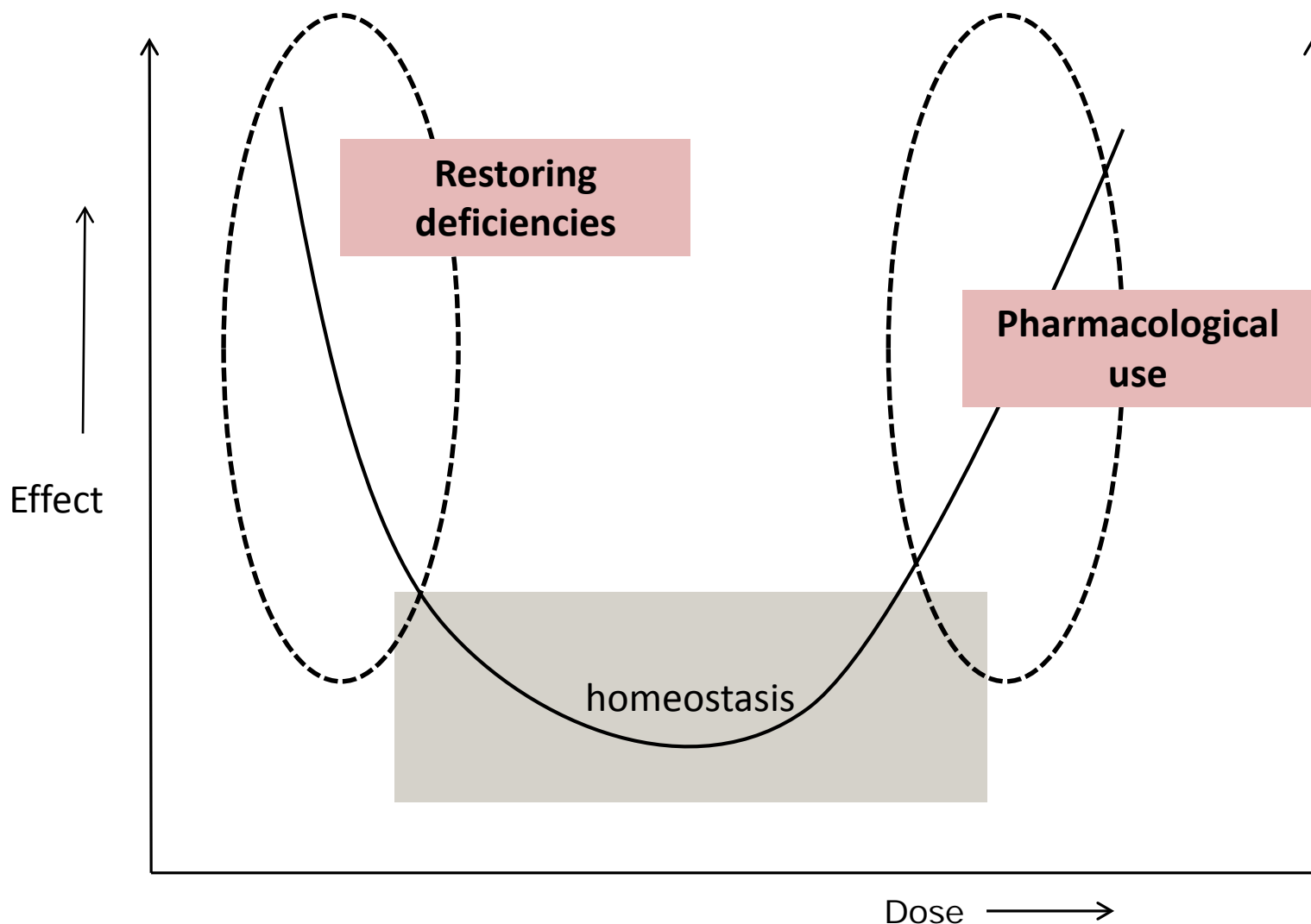


*Did I ever say  
that? Sorry, but I  
really can't recall\*  
Actually I don't  
even agree !*

# Dose-effect relationship – Drug



# Dose-effect relationship – Nutrient





## Glycan Biosynthesis and Metabolism

Glycosphingolipid biosynthesis - globo and isoglobo series

O-glycan biosynthesis

Glycosaminoglycan biosynthesis - heparan sulfate / heparin

Glycosphingolipid biosynthesis - lacto and neolacto series

N-Glycan biosynthesis

[B] Glycosyltransferases

Is this the right switch to press ?

Various types of N-glycan biosynthesis

GPI - biosynthesis

Starch metabolism

Galactose metabolism

[B] Proteoglycans

Glycosphingolipid biosynthesis - ganglio series

Glycosaminoglycan biosynthesis - keratan sulfate

Glycosaminoglycan degradation

alpha-Linolenic acid metabolism

Linoleic acid metabolism

Arachidonic acid metabolism

Biosynthesis of unsaturated fatty acids

Retinol metabolism

[B] Lipids

[B] Lipids biosynthesis proteins

Lipid Metabolism

Or should I have this one?

Glycerolipid metabolism

Ether lipid metabolism

Sphingolipid metabolism

Fructose metabolism

Inositol phosphate metabolism

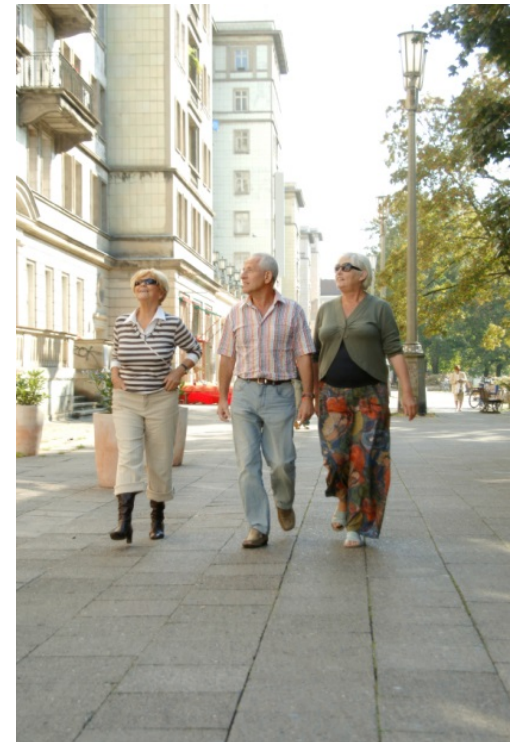
Carotenoid biosynthesis

Fatty acid biosynthesis

Fatty acid degradation

# Health – what is it ?

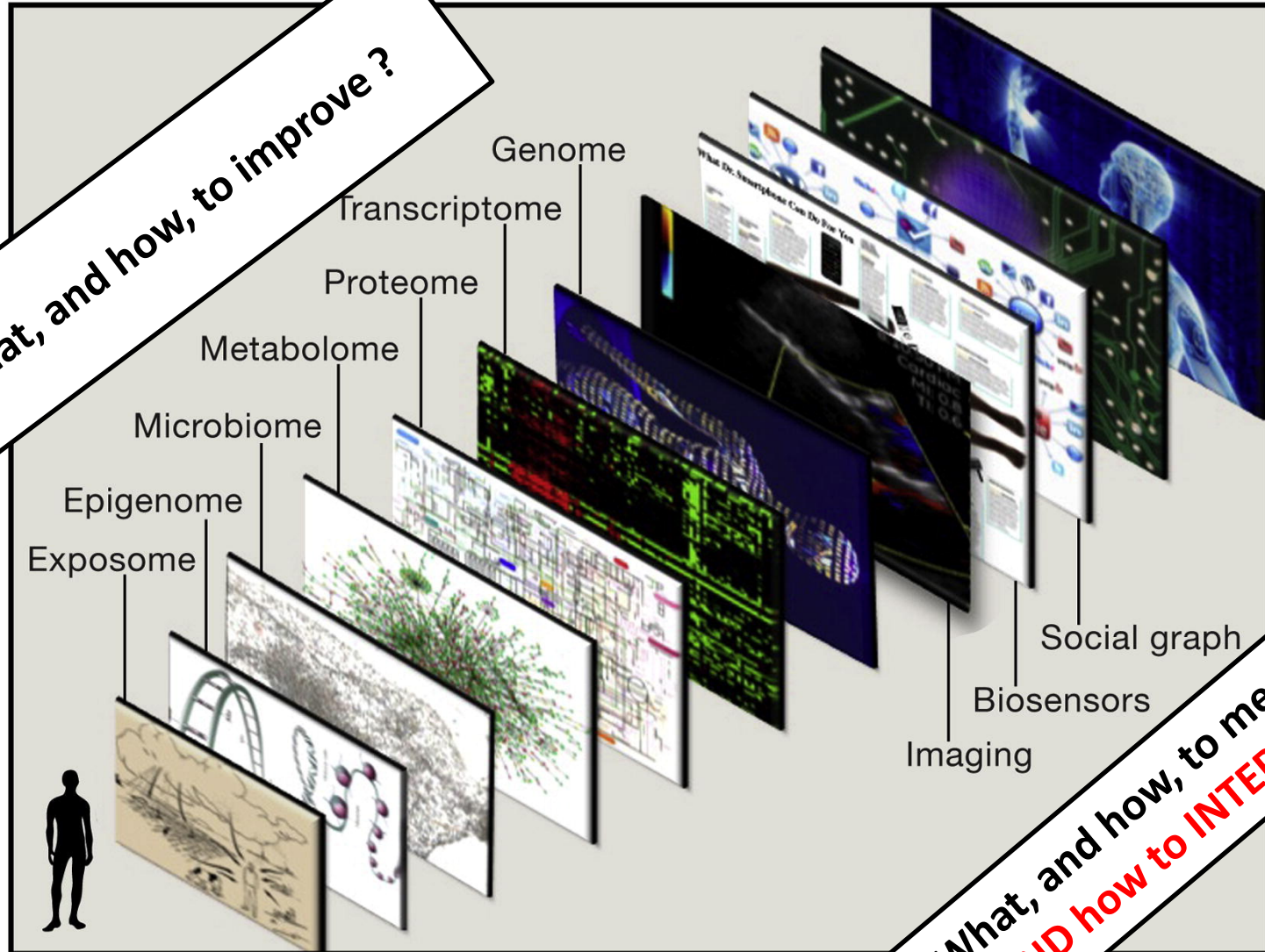
- Multi-dimensional
- Not strictly defined or limited
- Individually determined; perceived personally
- Dynamic and time-dependent





# Are we getting closer to measuring health?

What, and how, to improve?



What, and how, to measure?  
**AND how to INTERPRET ?**

# THE HUMAN

Bacteria, fungi, and viruses outnumber human cells in the body by a factor of 10 to one. The microbes synthesize key nutrients, fend off pathogens and impact everything from weight gain to perhaps even brain development. The Human Microbiome Project is doing a census of the microbes and sequencing the genomes of many. The total body count is not in but it's believed over 1,000 different species live in and on the body.

## 25 SPECIES

in the **stomach** include:

- *Helicobacter pylori*
- *Streptococcus thermophilus*

## 500-1,000 SPECIES

in the **intestines** include:

- *Lactobacillus casei*
- *Lactobacillus reuteri*
- *Lactobacillus gasseri*
- *Escherichia coli*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Lactobacillus rhamnosus*
- *Clostridium difficile*

# MICROBIOME

## 600+ SPECIES

in the **mouth, pharynx and respiratory system** include:

- *Streptococcus viridans*
- *Neisseria sicca*
- *Candida albicans*
- *Streptococcus salivarius*

## 1,000 SPECIES

in the **skin** include:

- *Pityrosporum ovale*
- *Staphylococcus epidermidis*
- *Corynebacterium jeikeium*
- *Trichosporon*
- *Staphylococcus haemolyticus*

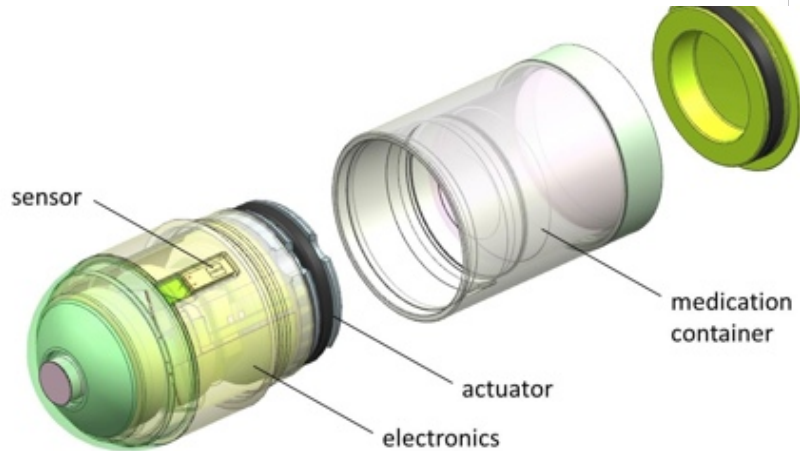
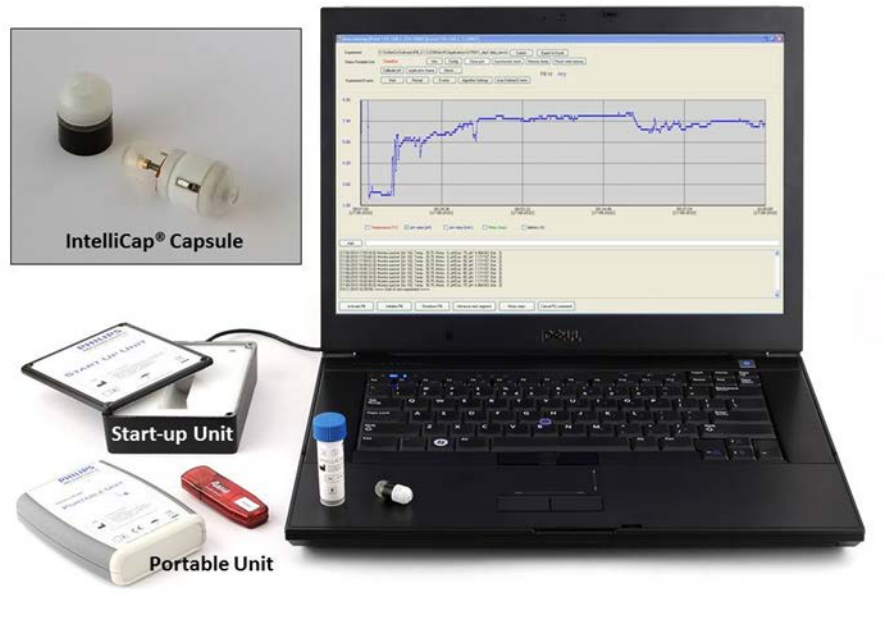
## 60 SPECIES

in the **urogenital tract** include:

- *Ureaplasma parvum*
- *Corynebacterium aurimucosum*



# IntelliCap System



**WAGENINGENUR**  
For quality of life

# Data collection: a lot is possible



Measuring effects in muscle  
after one-leg exercise;  
Sander Kersten et al., 2013

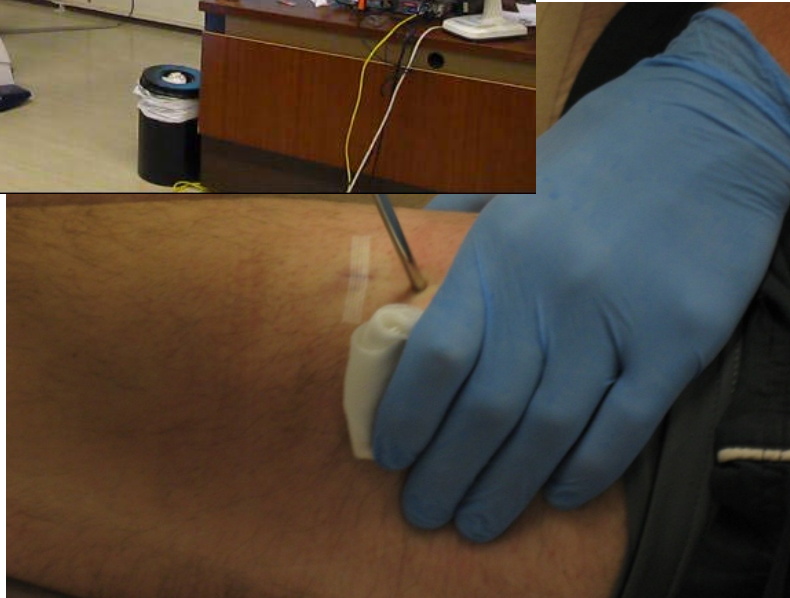
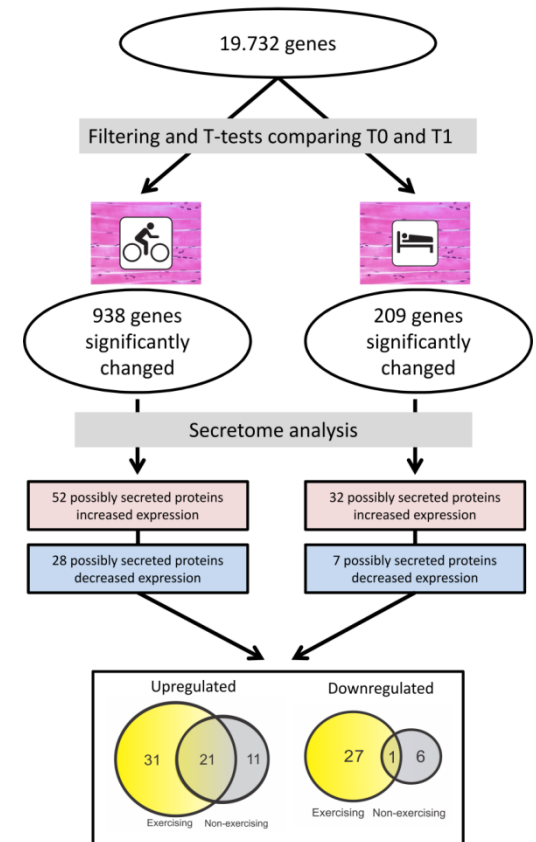
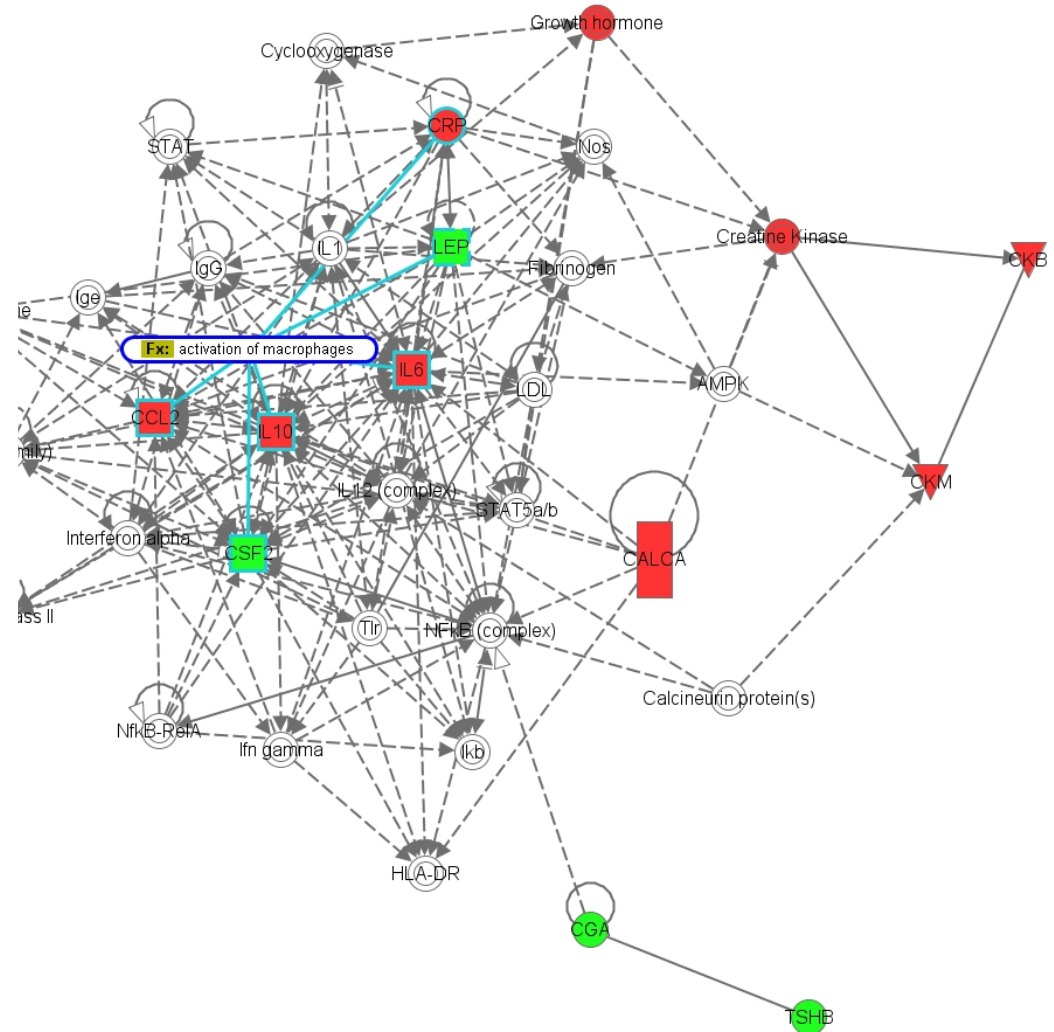
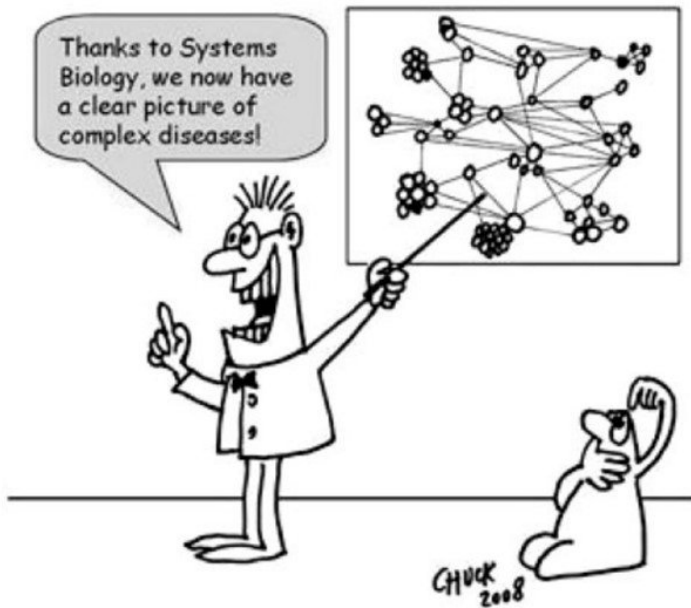


Figure 1

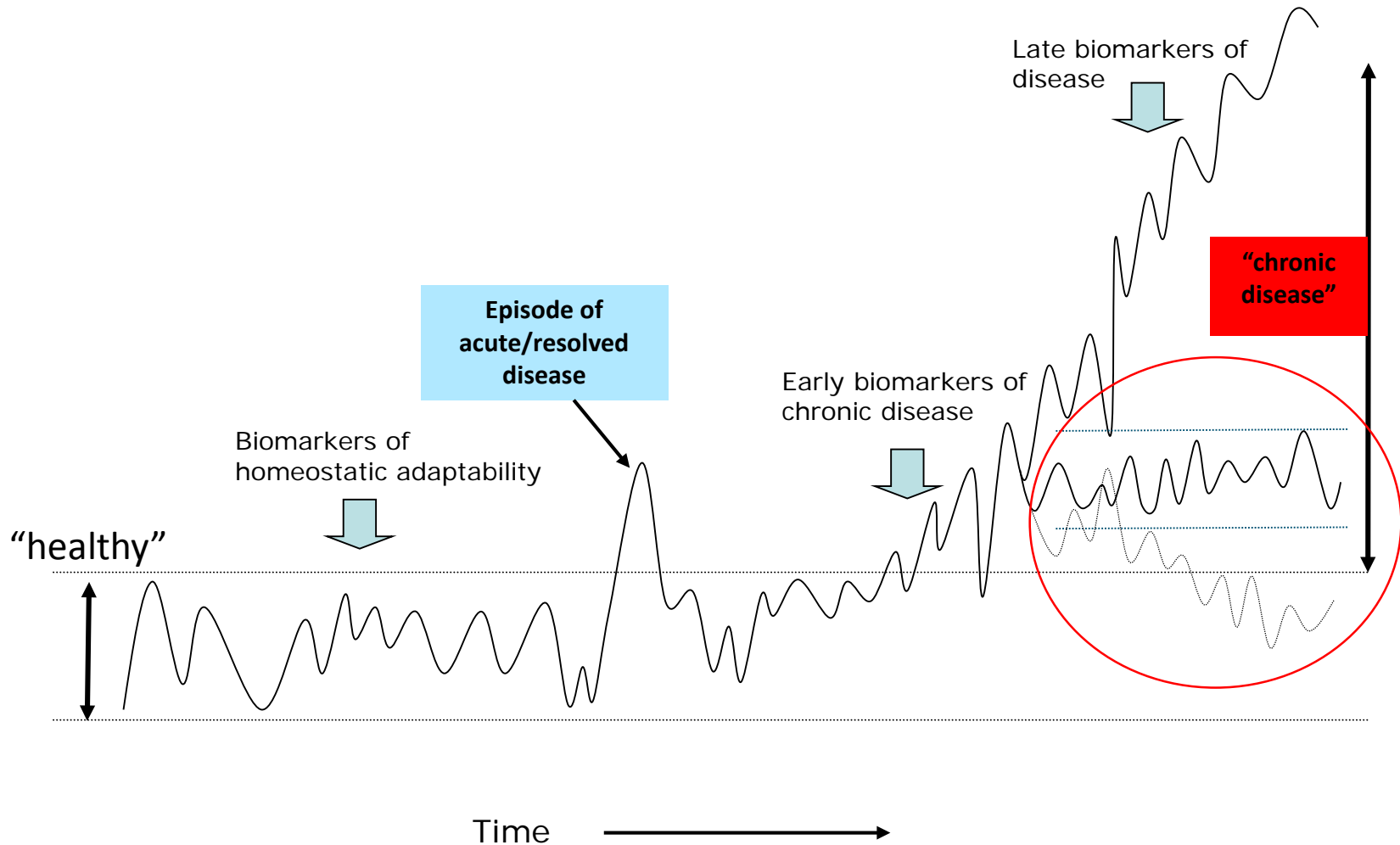


But interpretation hasn't become easier

Network 1 : Exercise\_overlap\_col\_pla - 2009-10-22 03:12 PM : overlap\_col\_pla.xls : Exercise\_overlap\_col\_pla - 2009-10-22 03:12 PM

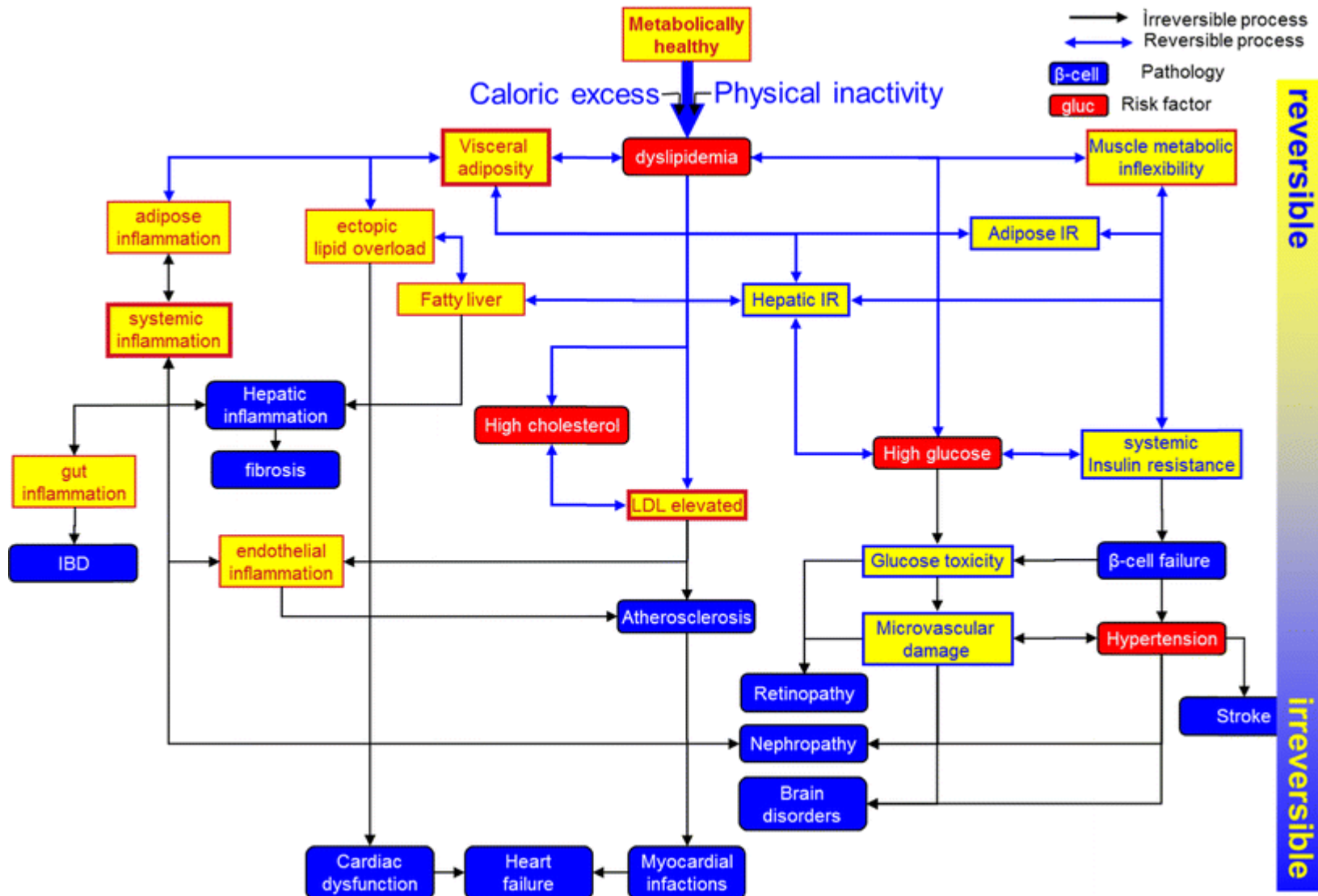


# Processes and biomarkers from health to disease





# Losing flexibility → disease



~~Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO 1948)~~

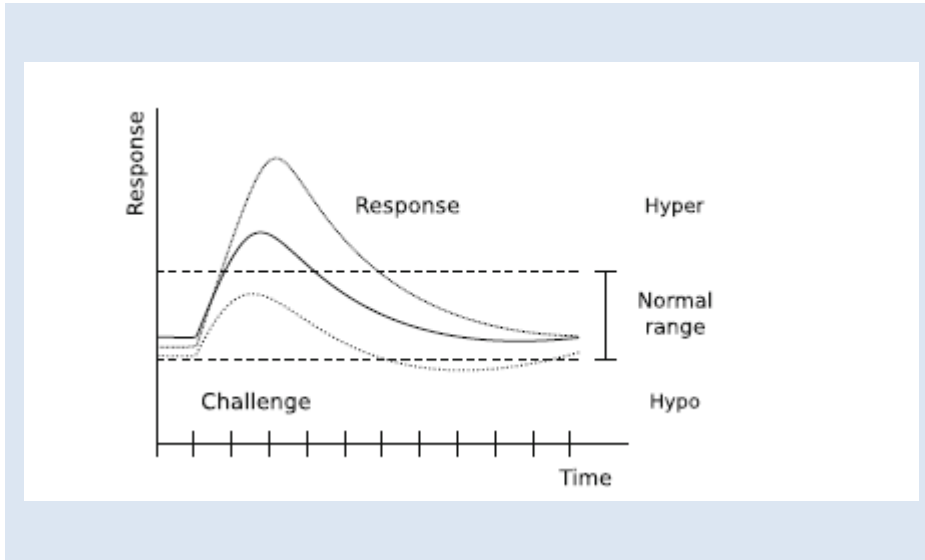


## The ability to adapt

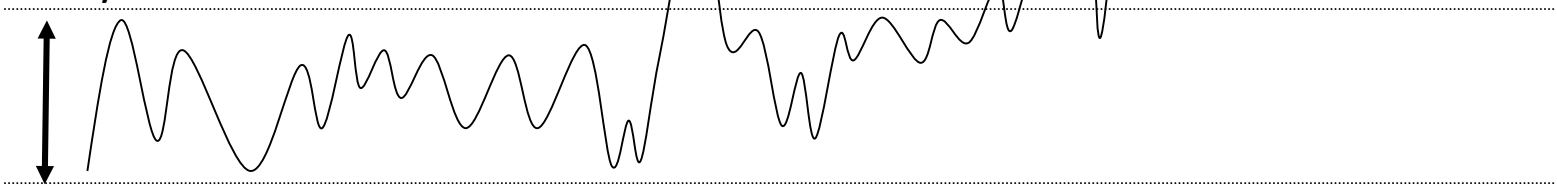


The ability to adapt and self-manage in the face of social, physical and emotional challenges' (Lancet 2009; Huber et al. 2011).

# Challenge test to analyze phenotypic flexibility

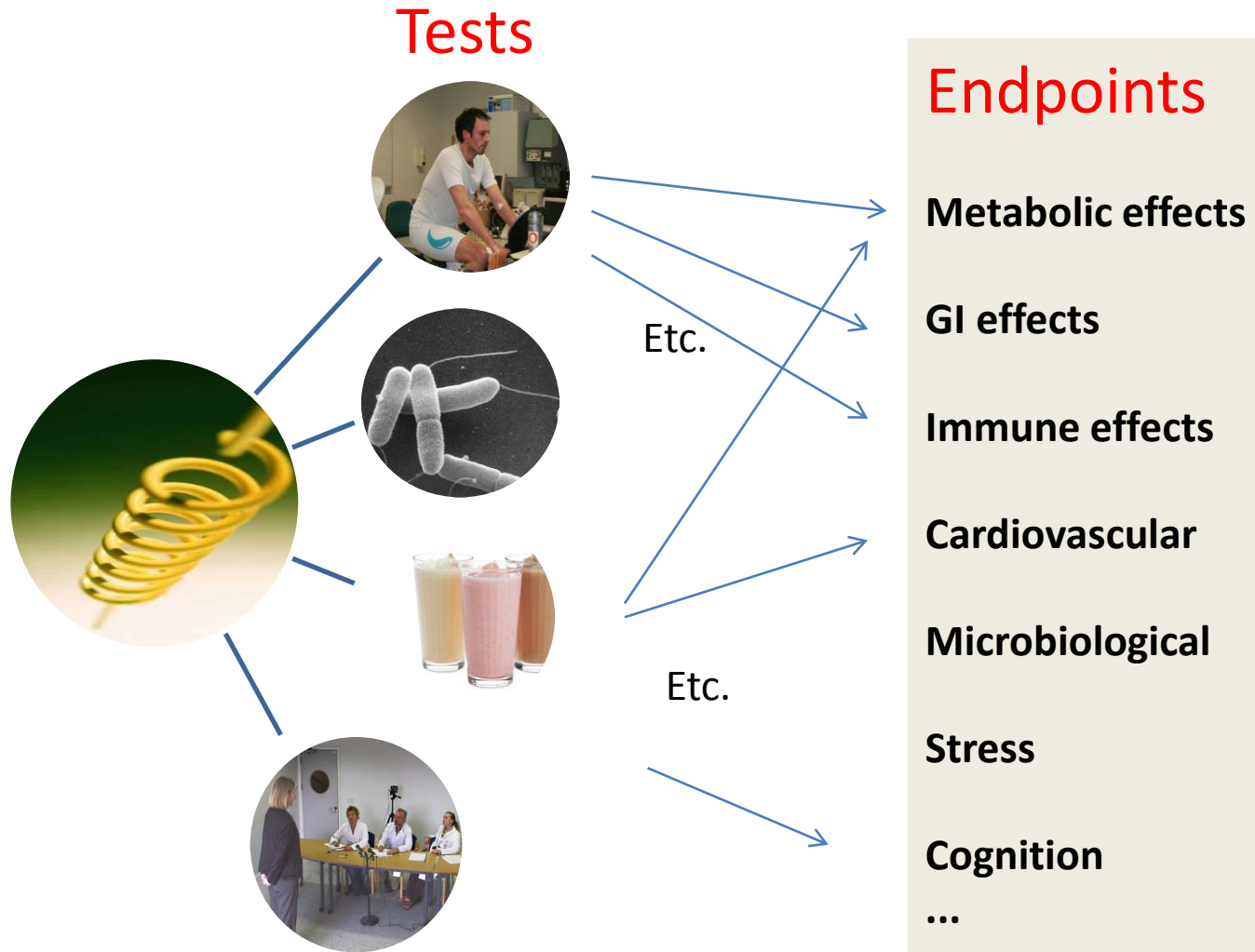


“healthy”

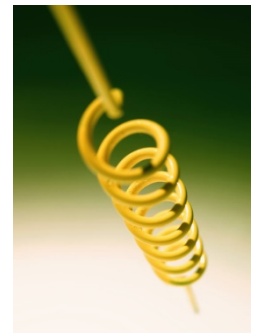
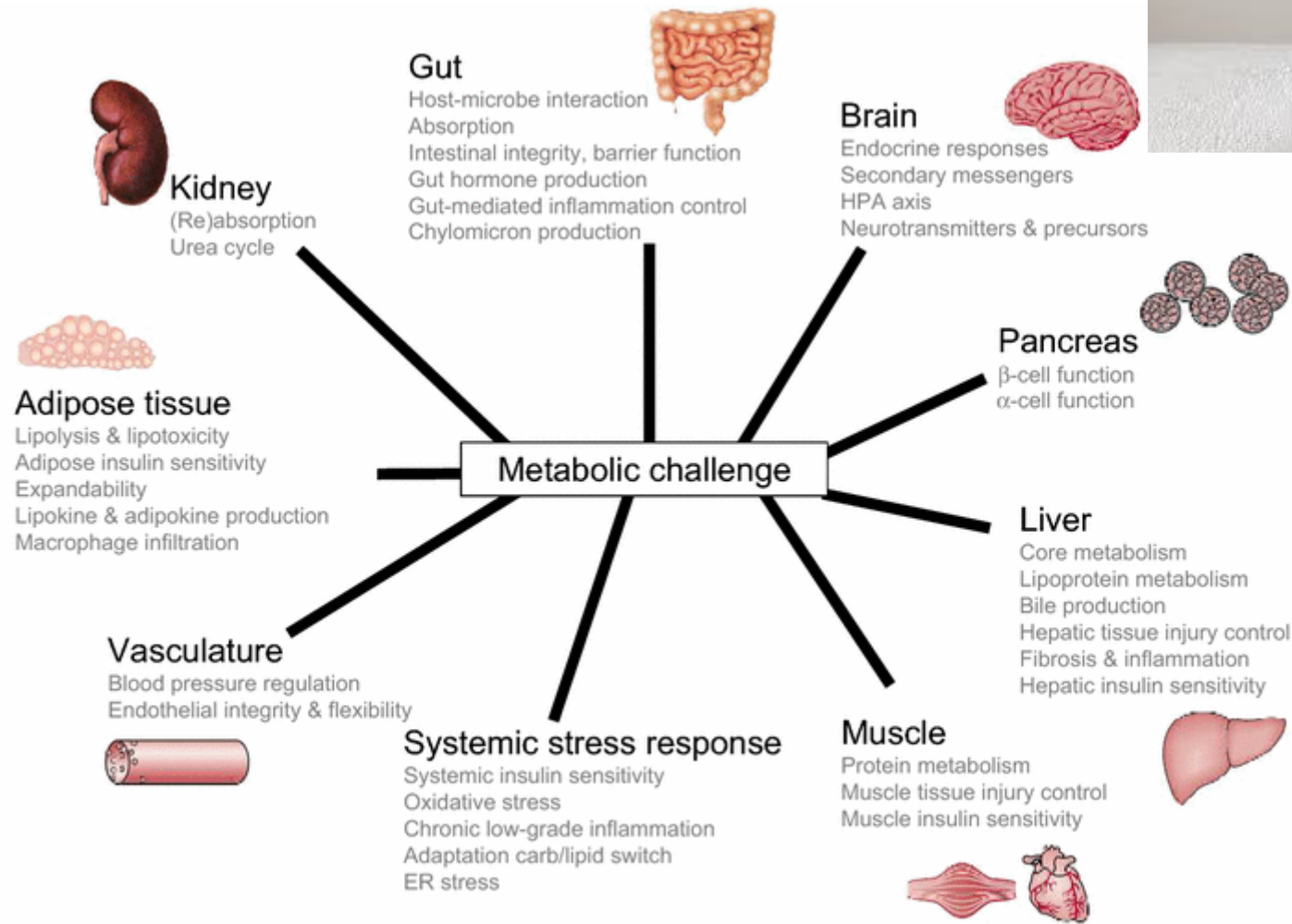


Time →

# How to measure Phenotypic flexibility?



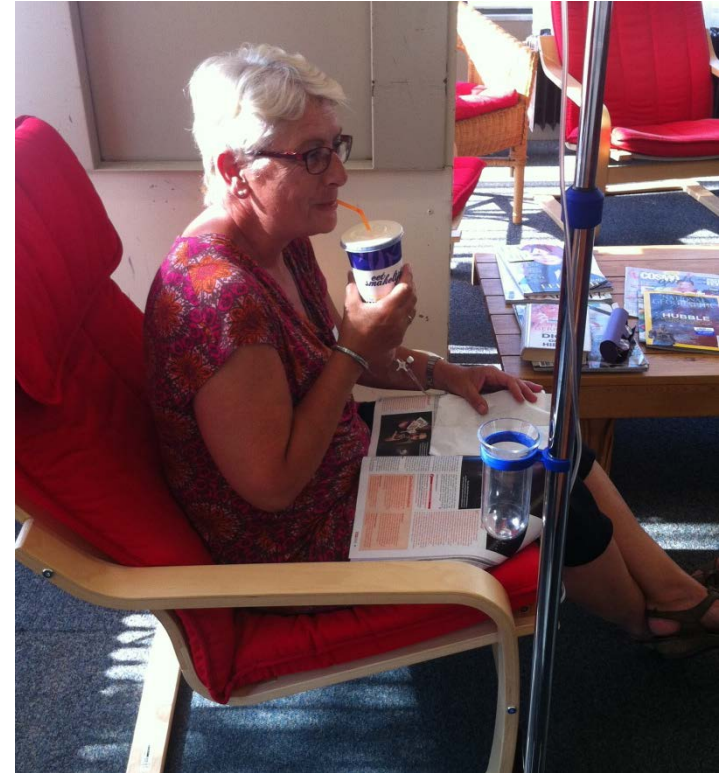
# Metabolic stress test



Stroeve et al., genes and Nutrition, 2015

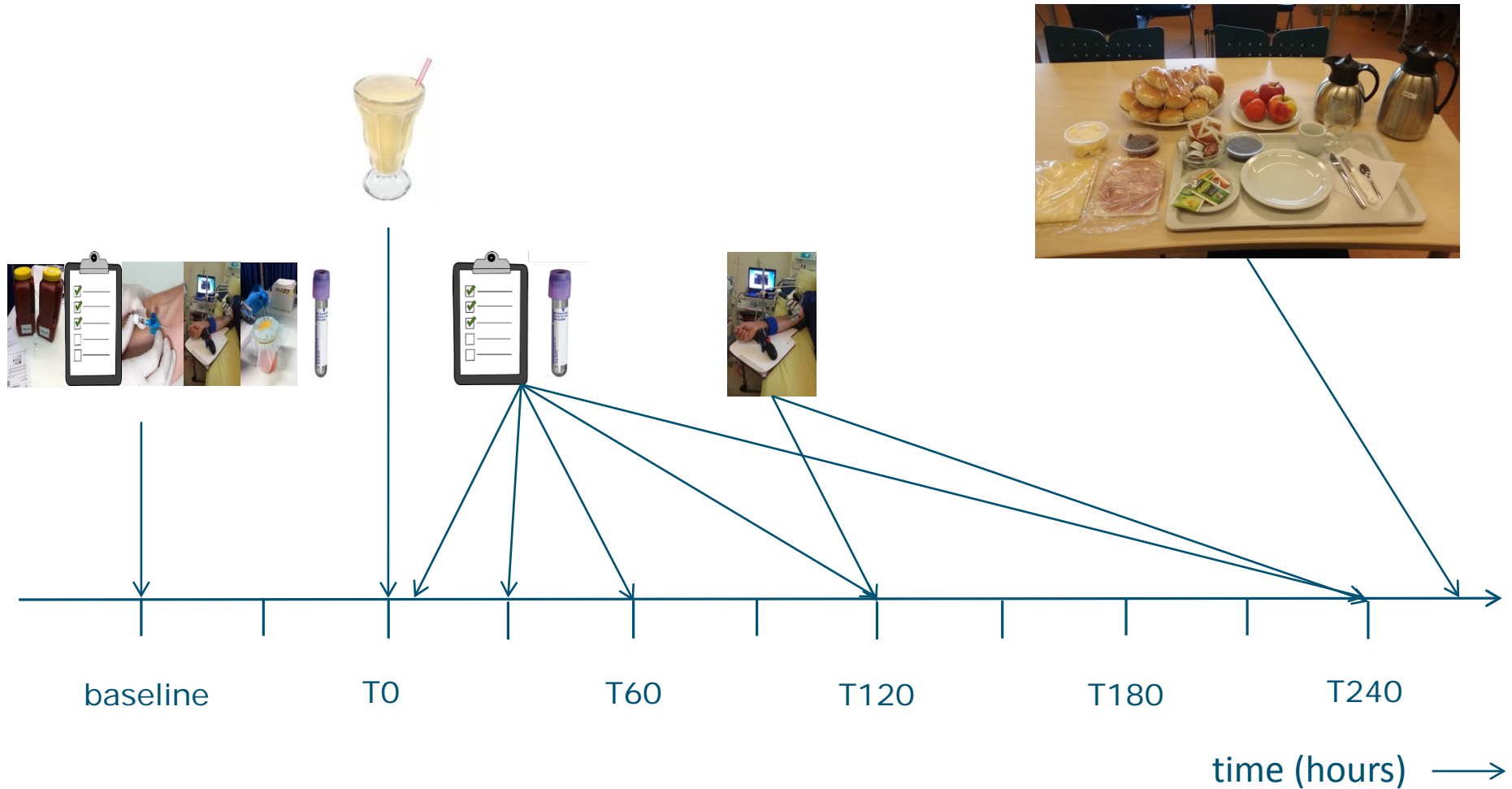
# Mixed meal challenge

	Amount	kcal
<b>Protein</b> Protifar®	<b>17.6g</b>	<b>72</b>
<b>Carbohydrates</b> Dextrose	<b>76.3g</b>	<b>310</b>
<b>Fat</b> Palm olein	<b>60g</b>	<b>531</b>
Water Vanilla flavour		-
<b>Total</b>		<b>912</b>

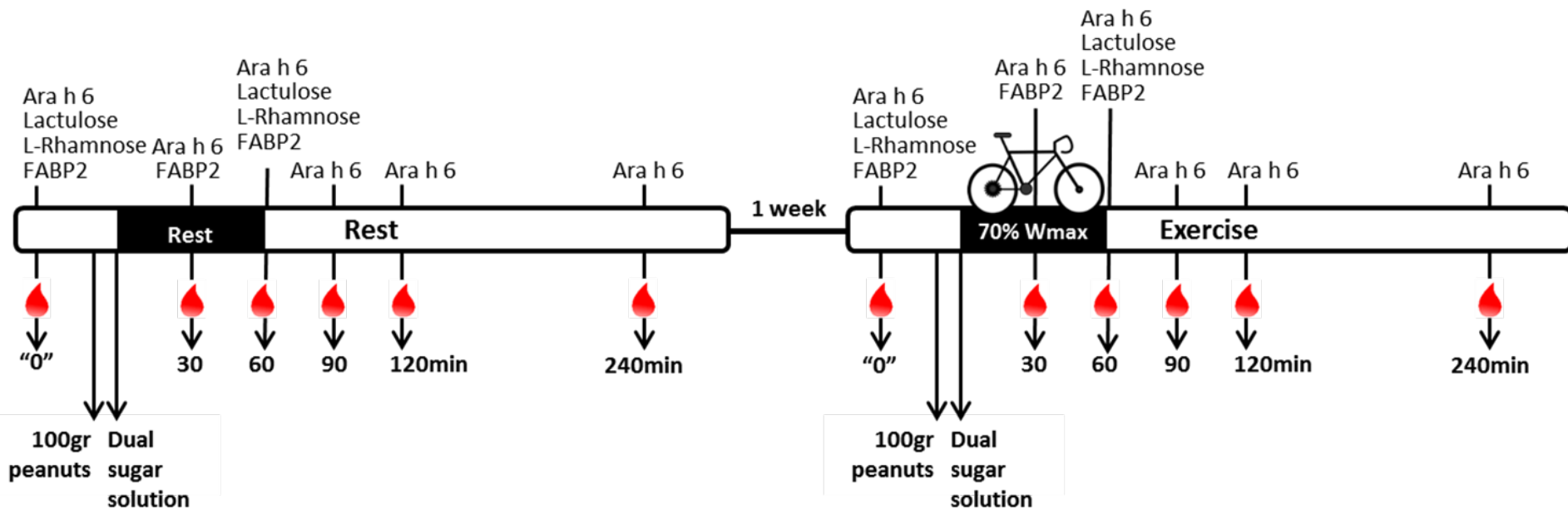




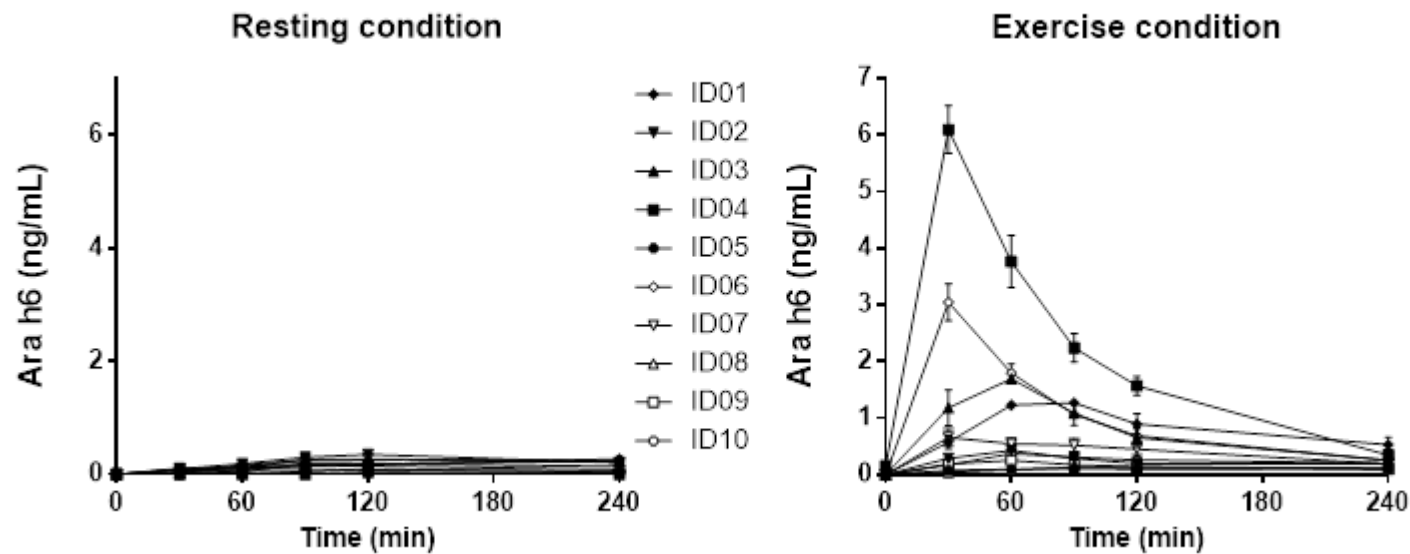
# Challenge test study day example



# Physical challenge test



# GI permeability: effect of physical stress on absorption of the peanut allergen Ara h 6 in healthy individuals



# Important scientific and economic challenges remaining

- Not (yet?) possible to grasp ‘full picture’
- Interindividual differences are large
- Tests are very standardised and, therefore within-subject variation is smaller than in reality
- Between labs, standardisation and data exchange is limited
- Studies become complex and expensive

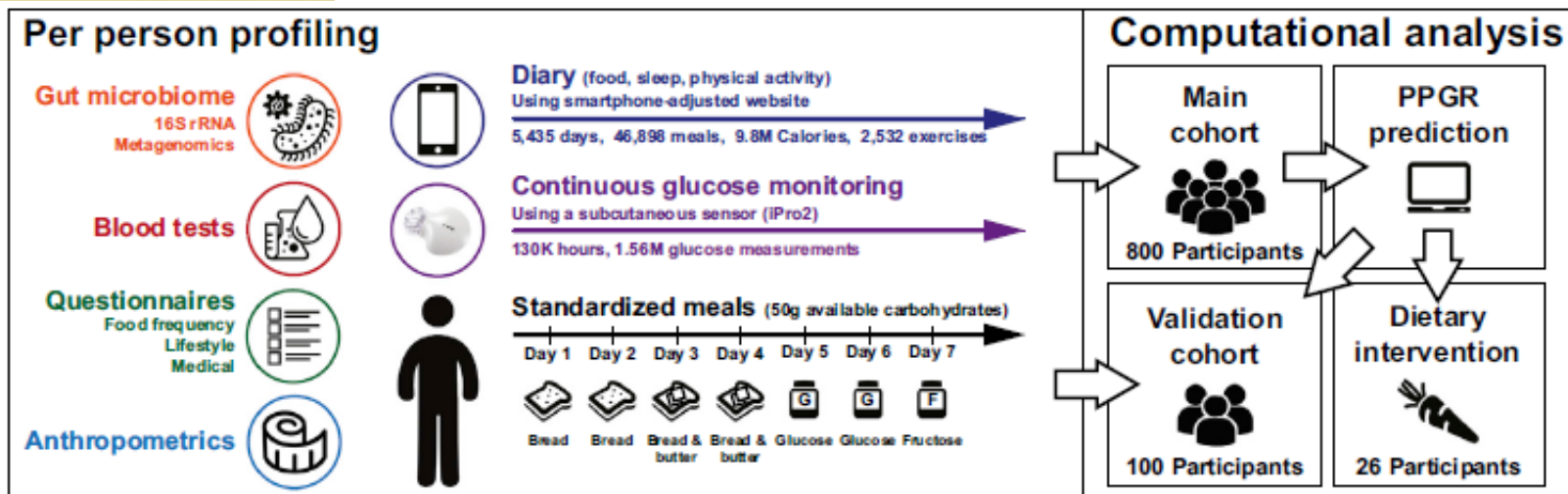
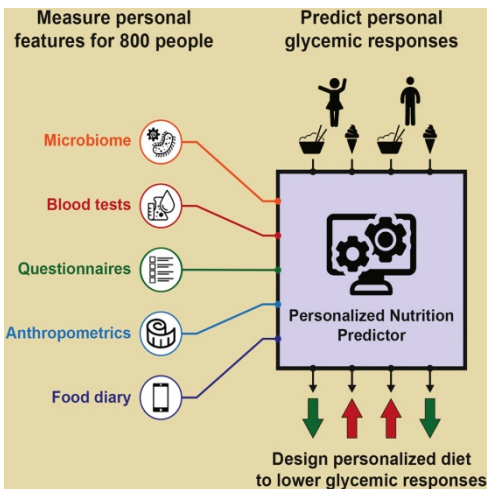
# Personalized Nutrition by Prediction of Glycemic Responses

Cell

## Article

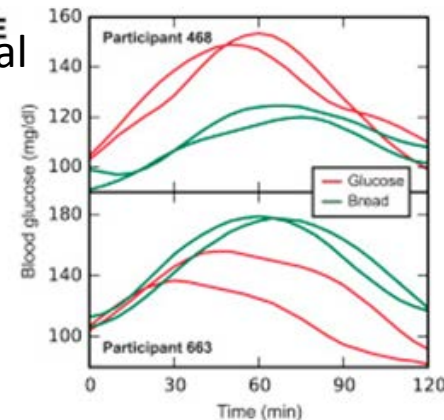
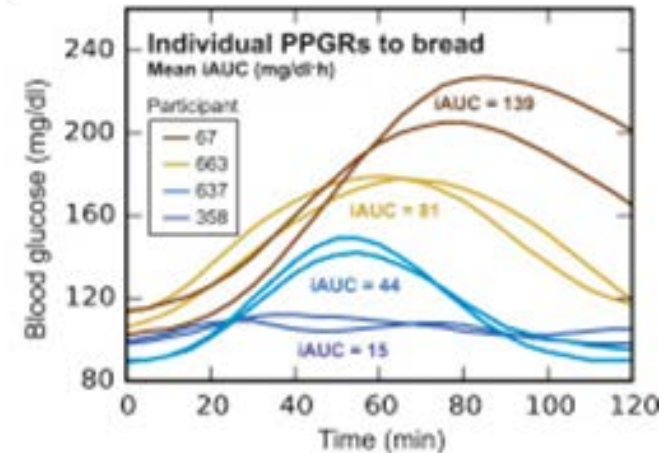
### Personalized Nutrition by Prediction of Glycemic Responses

David Zeevi,<sup>1,2,8</sup> Tal Korem,<sup>1,2,8</sup> Niv Zmora,<sup>3,4,5,8</sup> David Israeli,<sup>6,8</sup> Daphna Rothschild,<sup>1,2</sup> Adina Weinberger,<sup>1,2</sup> Orly Ben-Yacov,<sup>1,2</sup> Dar Lador,<sup>1,2</sup> Tali Avnit-Sagi,<sup>1,2</sup> Maya Lotan-Pompan,<sup>1,2</sup> Jotham Suez,<sup>3</sup> Jemal Ali Mahdi,<sup>3</sup> Elad Matot,<sup>1,2</sup> Gal Malka,<sup>1,2</sup> Noa Kosower,<sup>1,2</sup> Michal Rein,<sup>1,2</sup> Gili Zilberman-Schapira,<sup>3</sup> Lenka Dohnalová,<sup>3</sup> Meirav Pevsner-Fischer,<sup>3</sup> Rony Bikovsky,<sup>1,2</sup> Zamir Halpern,<sup>5,7</sup> Eran Elinav,<sup>3,8,\*</sup> and Eran Segal<sup>1,2,8,\*</sup>



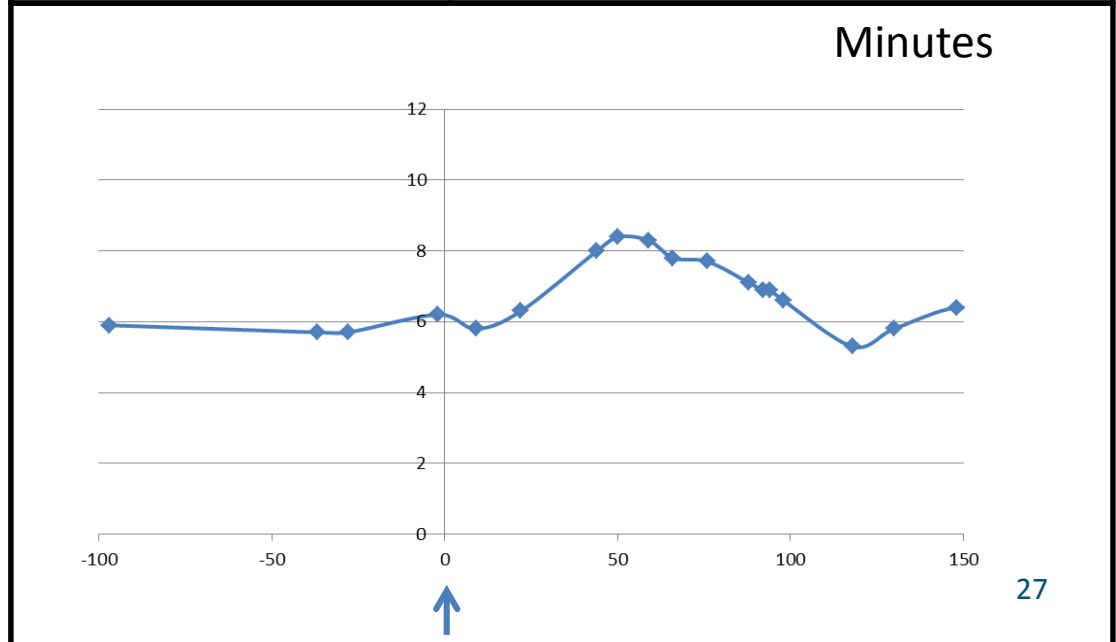
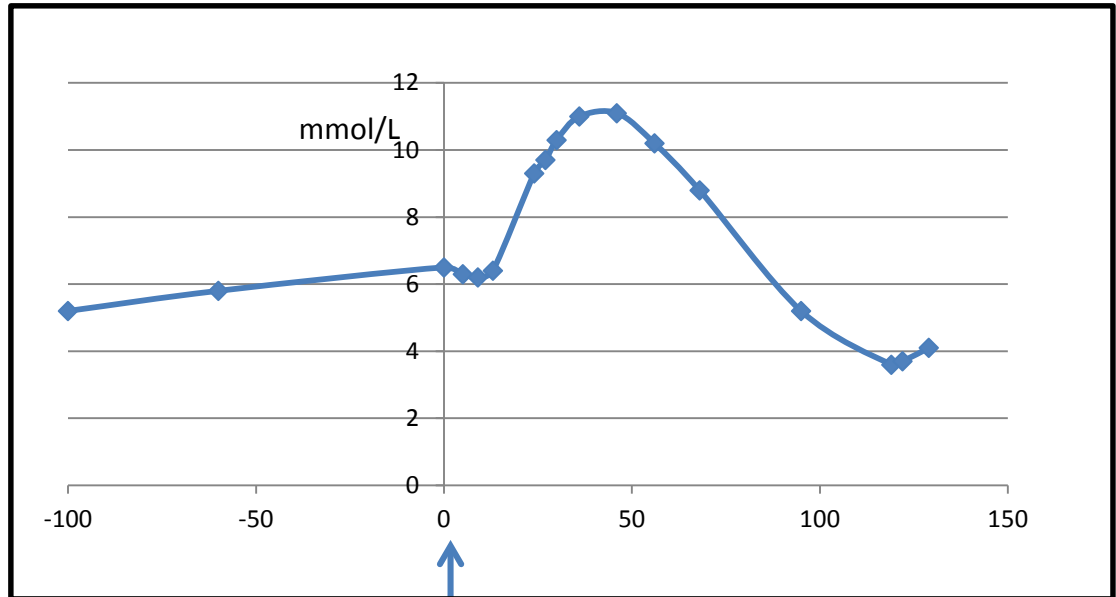
# Large inter- and intra-individual responses to foods & nutrients found

- High interpersonal variability in post-meal glucose observed in an 800-person cohort
- •Using personal and microbiome features enables accurate glucose response prediction
- •Prediction is accurate and superior to common practice in an independent cohort
- •Short-term personalized dietary interventions successfully lower post-meal glucose

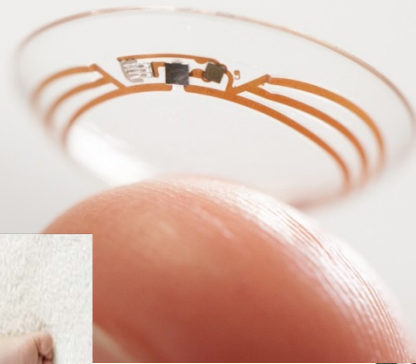




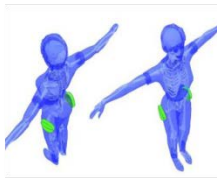
# My own n=1 experiment




# Study the dynamics and differences under real life conditions



More Diversified Market Than Investors Realize



# And BIG data management....



why vit

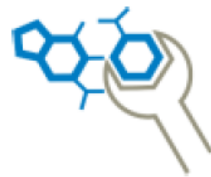
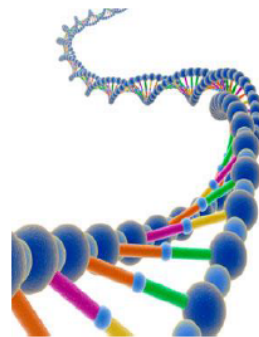
As broad  
as your  
imaginati

Build wireless health innovation  
wearable biosensor. We're revo  
the way healthcare is delivered

Join Us

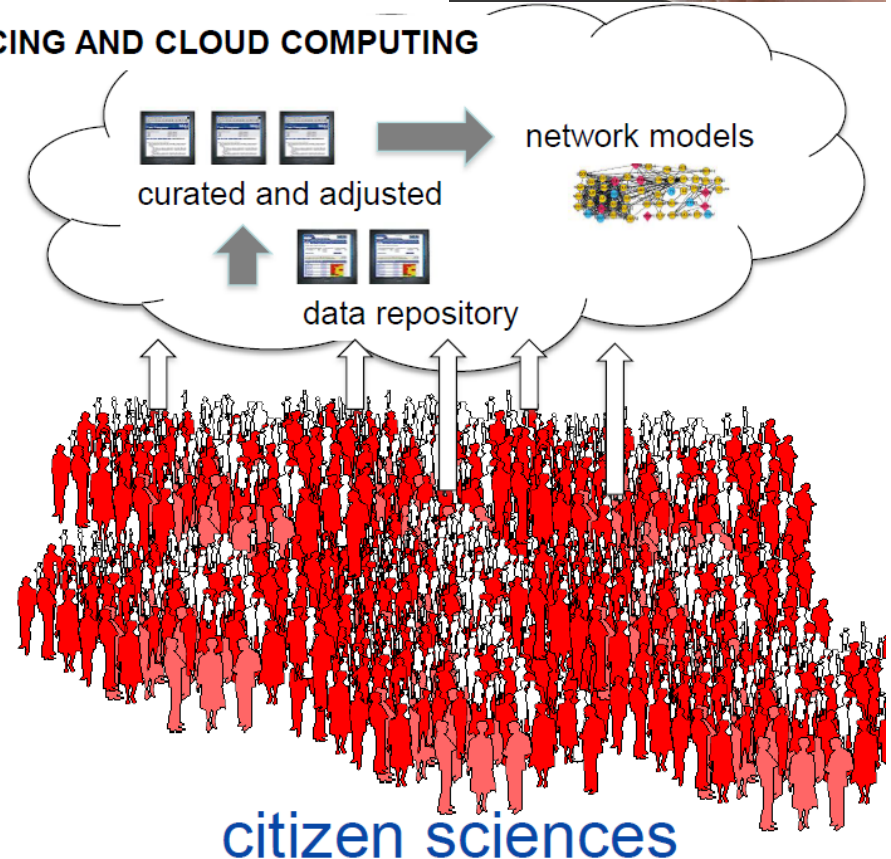


## CROWD SOURCING AND CLOUD COMPUTING



DIYgenomics

DIYgenomics  
... crowd-sourced clinical trials  
and personal genome apps



# Some take home messages

- The dynamics of physiology is crucial to understand how nutrition works
- Supplements: correct the deficiencies while maintaining homeostasis
- Food is no pharma; RCTs have not much future in nutrition research





# Some take home messages (2)

- The future of nutrition studies lies largely outside our labs
- More integration between physiology, epidemiology, geo-informatics, microbiology, consumer science lies ahead
- For this we need more knowledge on BIG data management

