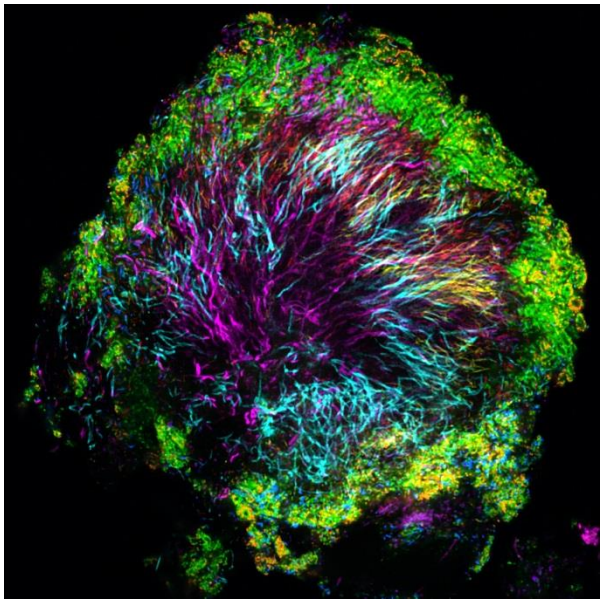
Computational Methods in Metagenomics and Microbiome Research

0368-3116-01

Prof. Elhanan Borenstein
School of Computer Science
Semester B, 2019

TEL AVIV UNIVERSITY אוניברסיטת תל אביב

Let me know who you are ….

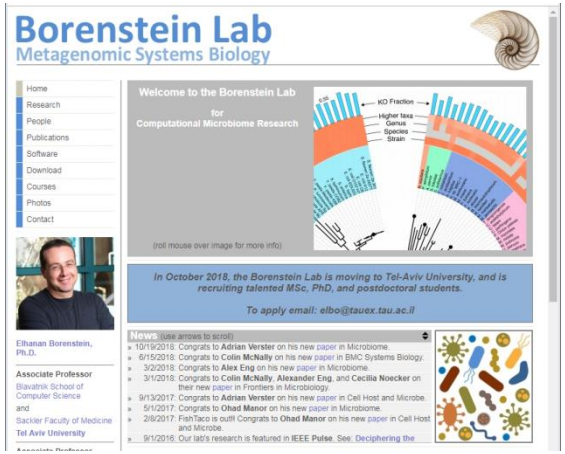


1. Name
2. Degree (undergraduate, MSc)
3. Background (CS/Biology)
4. Registered / not registered
5. Why are you here? Have you ever heard about the microbiome? Metagenomics?
6. Place your bet:
   What is the total number of bacteria in/on the human body?

Welch et al., 2017

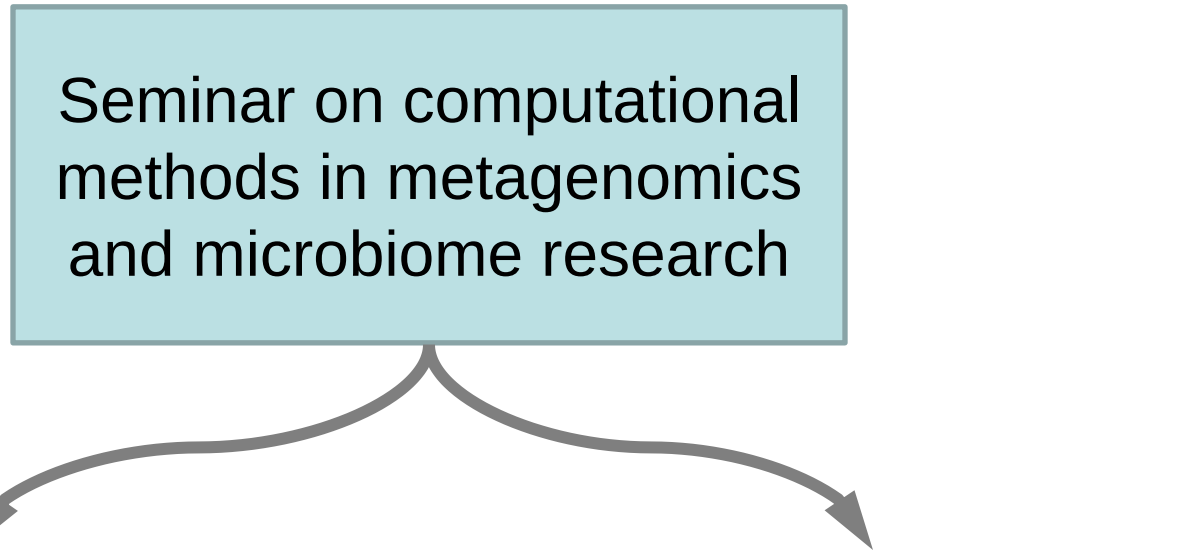
Who am I?

- Faculty at Computer Science & Medicine, TAU
- Until 2018: Faculty at Genome Sciences & CS, UW
- Training: CS; Physics; Hi-tech; Computational/ mathematical Biology; Complexity
- Interests: Metagenomics; Human Microbiome; Complex networks; Computational systems biology



http://www.borensteinlab.com/

The Seminar's 'Mission Statement'



Domain Knowledge

Learn key algorithms/methods developed for processing and analyzing metagenomic data and for accurately mapping the composition of the human microbiome and its role in human health.

Science Communication

Practice and master the art of scientific presentation, including slide preparation, presentation skills, talk delivery, and scientific discussion

Outline

About the Seminar

Tips for Giving a Good Talk

A *Very* Brief Background about Microbes, Microbiomes, and Metagenomics

Q&A

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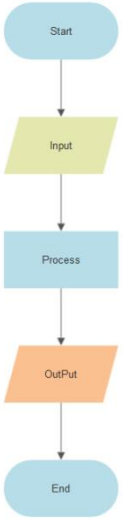
Seminar Format

- Student presentations!!
  - 1-2 students per paper

    (when 2 students present the same paper, both should understand everything and the presentation should be split evenly and logically)
  - Talk: Hebrew or English
  - Slides: English
  - Paper selection: “First come first served”, or “Random Rank Preference Selection”
- Feedback
- Discussion

In Your Presentation:

- Emphasize the main task the paper aims to address
- Cover the required comp/bio background
  - Don’t lose your audience
- Focus more on methods than on results
  - You will sometimes need to dig deep for the methods (methods sections, supplementary materials, previous papers)
  - Don’t leave ‘black-boxes’
  - The paper may contain more than you can cover; choose what to include (and what to drop) **wisely**
- In the end, summarize
  - Main results, importance, weaknesses, future work
- Add something original
  - Thoughts, ideas, concerns



Feedback and Discussion

- Feedback about presentation:
  - Everyone (we are all expert listeners)
  - Likes and dislikes
  - What was clear, what wasn't
  - **Be genuine but kind and constructive**
- Discussion about the paper
  - Speaker should prepare 2 or 3 discussion points
  - Aim to discuss what's NOT in the paper (hidden rationales, future directions, applications, concerns, …)

Class Structure

- When presenting one paper per class:
  - 1:10 Start talk
  - 2:00-2:10 Break
  - 2:30 End talk
  - 2:30-3:00 Feedback/Discussion
- When presenting two papers per class:
  - 1:10 Start talk 1
  - 1:50 End talk 1
  - 1:50-2:00 Feedback/Discussion
  - 2:00-2:10 Break
  - 2:10 Start talk 2
  - 2:50 End talk 2
  - 2:50-3:00 Feedback/Discussion

קביעת הציון הסופי

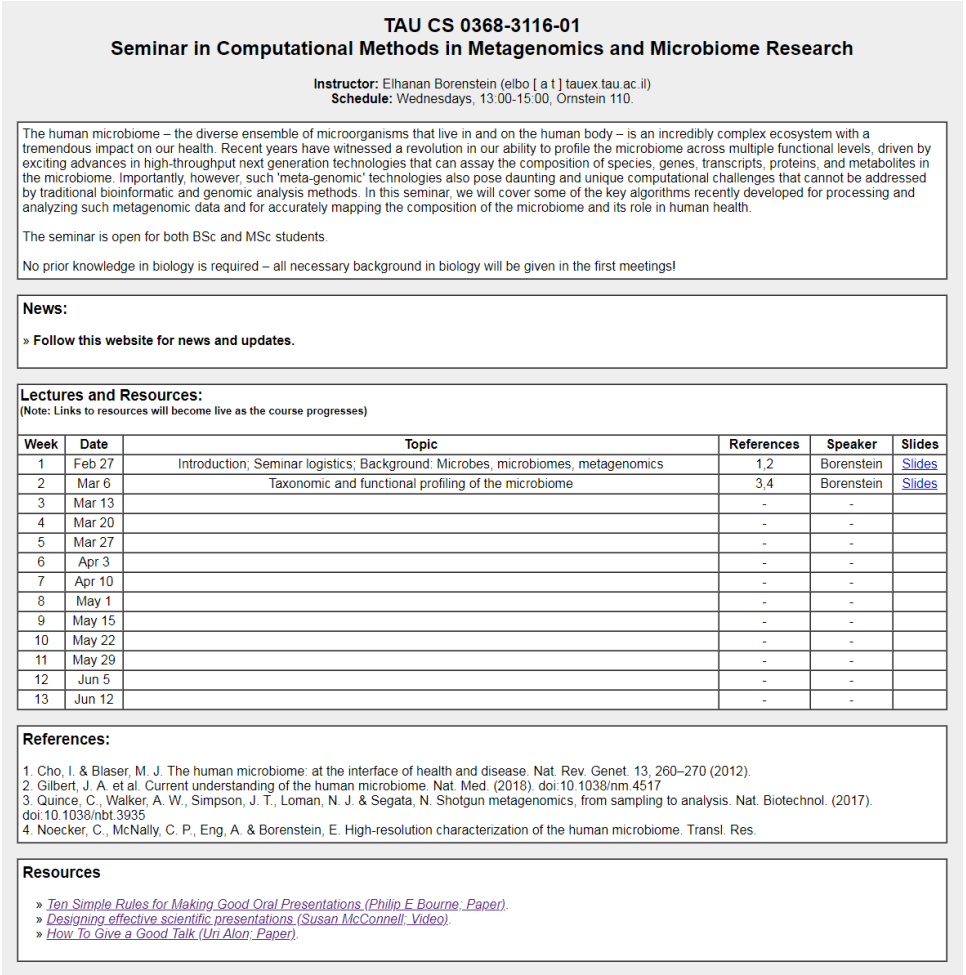
- הבנת החומר: 40%
- הצגת החומר: 40%
- השתתפות פעילה בסמינר: 20%
- בונוס מקוריות: עד 10%
- בונוס משכימי קום: עד 5%
- חריגה מהזמן: עד 10% -

- **קיימת חובת נוכחות בסמינר**

Website

- http://borensteinlab.com/courses/TAU_CS_3116_B_19/

- Print your slides before class
- Send me your slides after class



TAU CS 0368-3116-01
Seminar in Computational Methods in Metagenomics and Microbiome Research

Instructor: Elhanan Borenstein (elbo [a t] tauex.tau.ac.il)
Schedule: Wednesdays, 13:00-15:00, Ornstein 110.

The human microbiome – the diverse ensemble of microorganisms that live in and on the human body – is an incredibly complex ecosystem with a tremendous impact on our health. Recent years have witnessed a revolution in our ability to profile the microbiome across multiple functional levels, driven by exciting advances in high-throughput next generation technologies that can assay the composition of species, genes, transcripts, proteins, and metabolites in the microbiome. Importantly, however, such 'meta-genomic' technologies also pose daunting and unique computational challenges that cannot be addressed by traditional bioinformatic and genomic analysis methods. In this seminar, we will cover some of the key algorithms recently developed for processing and analyzing such metagenomic data and for accurately mapping the composition of the microbiome and its role in human health.

The seminar is open for both BSc and MSc students.

No prior knowledge in biology is required – all necessary background in biology will be given in the first meetings!

News:

» **Follow this website for news and updates.**

Lectures and Resources:
(Note: Links to resources will become live as the course progresses)

Week	Date	Topic	References	Speaker	Slides
1	Feb 27	Introduction; Seminar logistics; Background: Microbes, microbiomes, metagenomics	1,2	Borenstein	Slides
2	Mar 6	Taxonomic and functional profiling of the microbiome	3,4	Borenstein	Slides
3	Mar 13		-	-	
4	Mar 20		-	-	
5	Mar 27		-	-	
6	Apr 3		-	-	
7	Apr 10		-	-	
8	May 1		-	-	
9	May 15		-	-	
10	May 22		-	-	
11	May 29		-	-	
12	Jun 5		-	-	
13	Jun 12		-	-	

References:

1. Cho, I. & Blaser, M. J. The human microbiome: at the interface of health and disease. Nat. Rev. Genet. 13, 260–270 (2012).
2. Gilbert, J. A. et al. Current understanding of the human microbiome. Nat. Med. (2018). doi:10.1038/nm.4517
3. Quince, C., Walker, A. W., Simpson, J. T., Loman, N. J. & Segata, N. Shotgun metagenomics, from sampling to analysis. Nat. Biotechnol. (2017). doi:10.1038/nbt.3935
4. Noecker, C., McNally, C. P., Eng, A. & Borenstein, E. High-resolution characterization of the human microbiome. Transl. Res.

Resources

» *Ten Simple Rules for Making Good Oral Presentations (Philip E Bourne; Paper).*
» *Designing effective scientific presentations (Susan McConnell; Video).*
» *How To Give a Good Talk (Uri Alon; Paper).*

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Giving a Good Talk

- Partly innate but largely an acquired skill
  - Practice makes perfect
- Part science, but also part art
  - Lots of resources, rules, dos and don’ts, best practice guidelines
  - … but, every rule has exceptions
  - If it works, it works

Identity 2.0 Keynote

https://www.youtube.com/watch?v=RrpajcAgR1E

Presentation – General Tips

- Be clear!!!!
  - If your audience comes out of the talk with a feeling that you are really smart but they didn't really get what you talked about, you failed in your mission !
- Grab your audience's attention (and don't lose it)
- Structure your talk
  - Have a clear beginning, middle, and end
  - Section your talk and highlight transitions (verbally and via slides)
  - Use a 'home slide'
- Provide *intuition*, *examples*, clear *definitions*
- Use mostly slides, and the board sparingly
- Make contingencies in case you're out of time

The 3 Rules of a Good Presentation

- Rehearse your talk!

- Rehearse your talk!
- Rehearse your talk (and time it)!
- A few other rules/suggestions:
  - Record yourself and listen
  - Present to friends and family
  - Know your next slide (even if you use ‘presenter mode’)
  - Write down some of the your script
  - But don’t over rehearse

Slide Design: Dos and Don’ts 1

- Use the slide’s real-estate wisely
- Avoid clutter (and be generous with white space)
- If you are not going to take the time to explain it, don’t include it
  - (e.g., image panels, labels, equations)
- Avoid text-heavy slides (like this one)
- Try to include a simple image on every slide
- Use available space but avoid narrow margins (like this one).

Slide Design: Dos and Don’ts 2

- Be (very) mindful about fonts
  - *Prefer easy to read fonts*
  - Size!!!
- Be (even more) mindful about colors
  - Think about visibility, contrast
  - Remember the color-blinds
- Be mindful about animation
  - Too much (or too animated) can be distracting
  - But often animation is a powerful tool
  - Build your slide progressively (example: plots)
- Be consistent in titles, visuals, colors, etc.
- Don’t be sloppy

Presentation – Resources

- Philip E Bourne's "Ten Simple Rules for Making Good Oral Presentations" (paper)

  https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.0030077

- Susan McConnell's "Designing effective scientific presentations" (video)

  https://www.youtube.com/watch?v=Hp7Id3Yb9XQ

- Uri Alon's "How To Give a Good Talk" (paper)

  http://www.weizmann.ac.il/mcb/UriAlon/sites/mcb.UriAlon/files/uploads/nurturing/howtogiveagoodtalk.pdf

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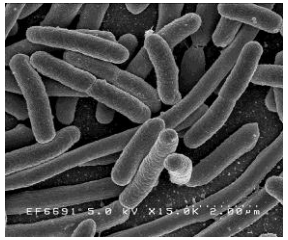
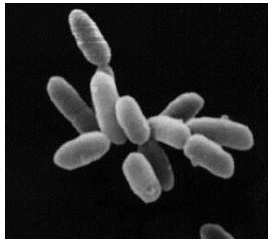
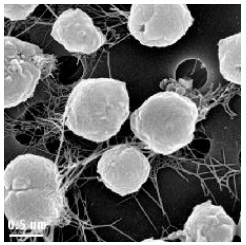


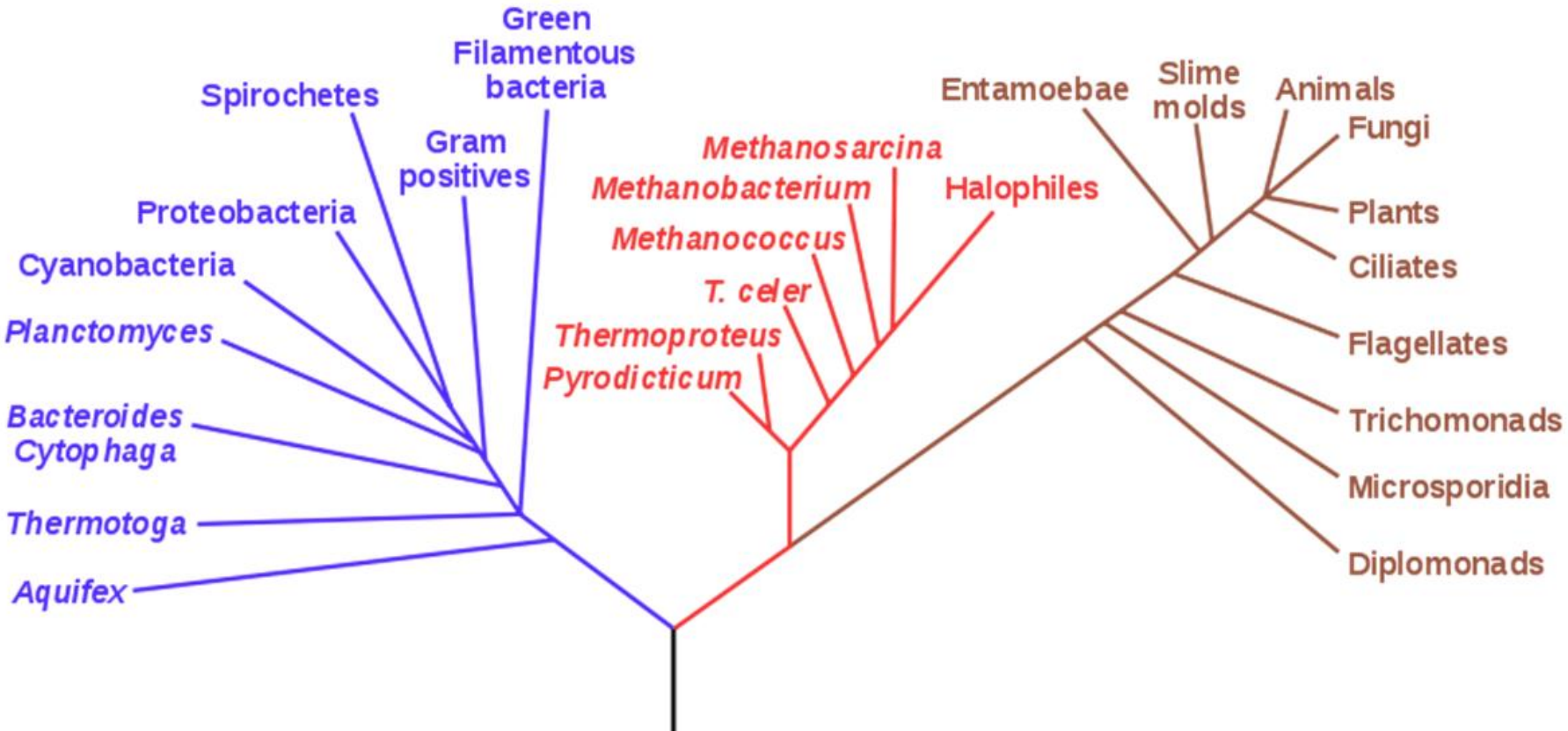




Prokaryote

Bacteria

Archaea

Eukaryota



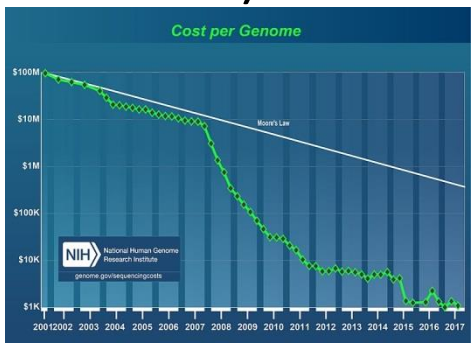
Why microbes?

Why Microbes? A Big Data Perspective

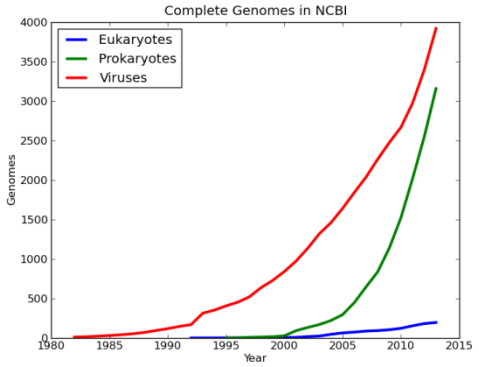
- Most abundant organisms on earth
  - 1 gram of soil: 10^{10}-10^{11} microbes
  - 1 nonillion microbes in the oceans

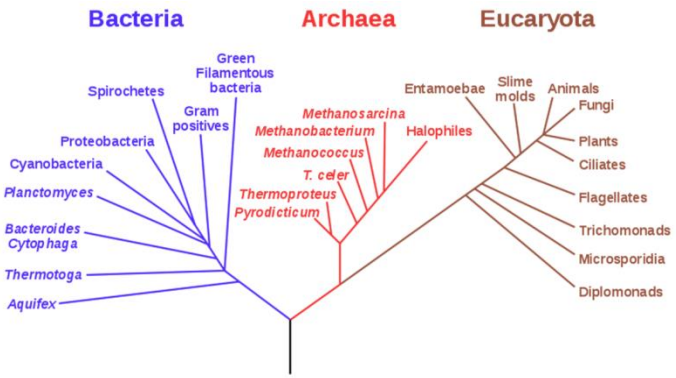
    (1 nonillion = 1000000000000000000000000000000)

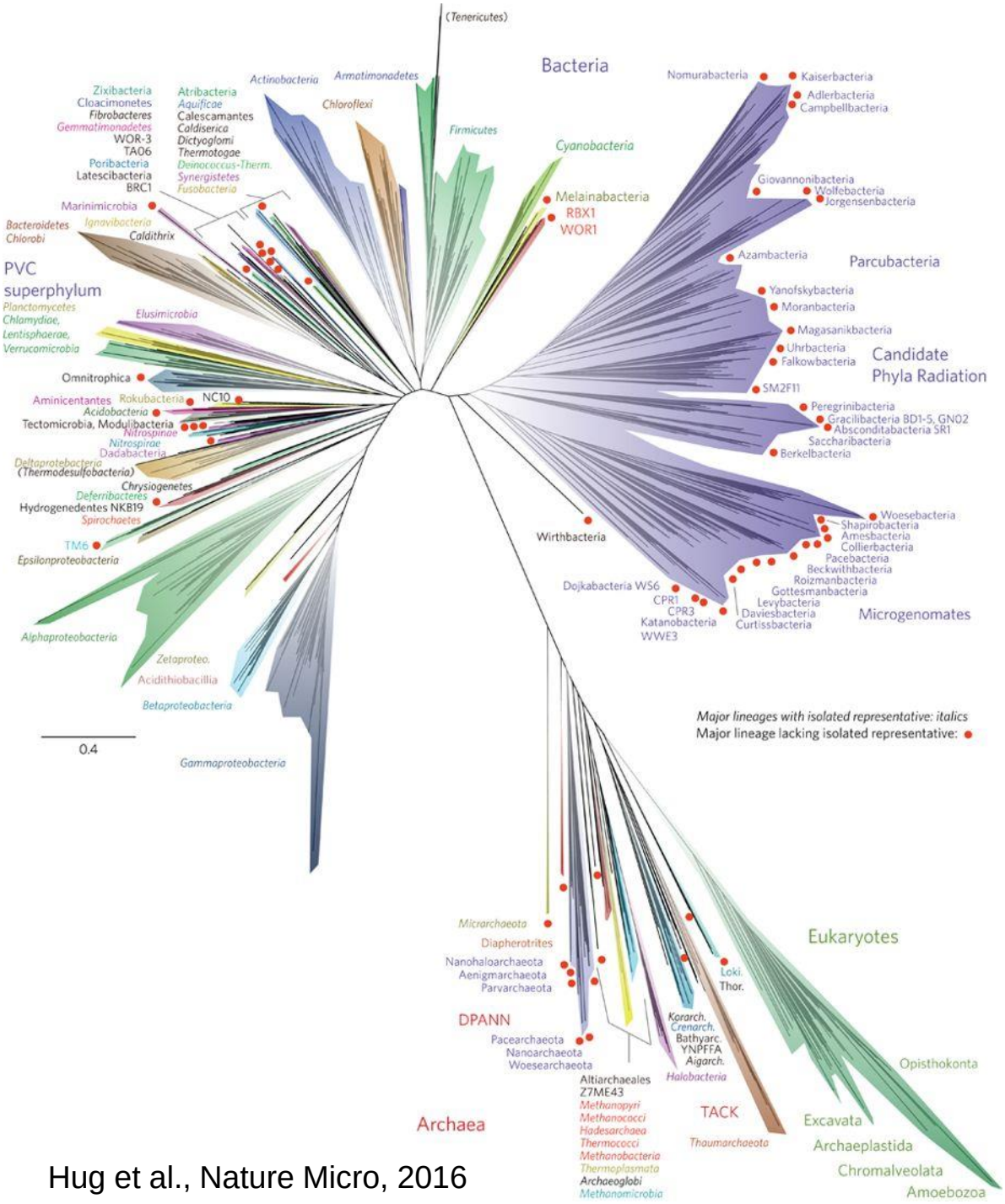
    (= 240 billion )



- Most diverse organisms on earth
  - Soil (1g): 6,000-50,000 species
  - In total: 10^{8}-10^{9} species (and maybe 10^{12})

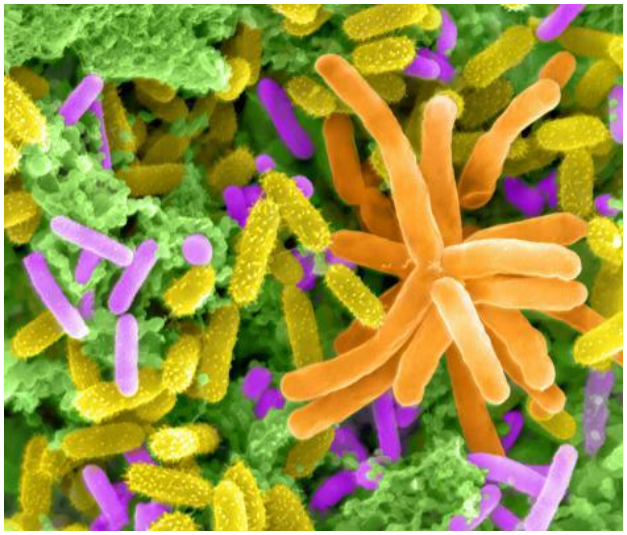


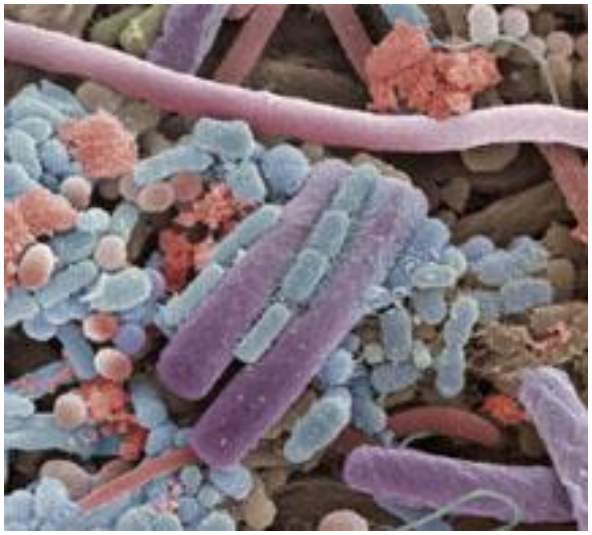


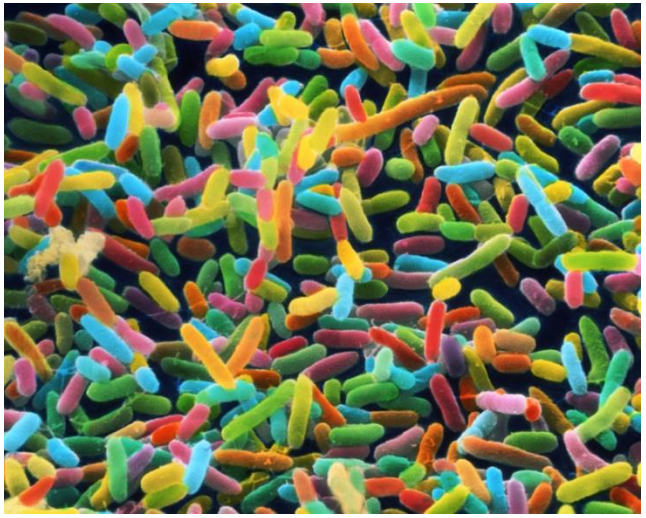
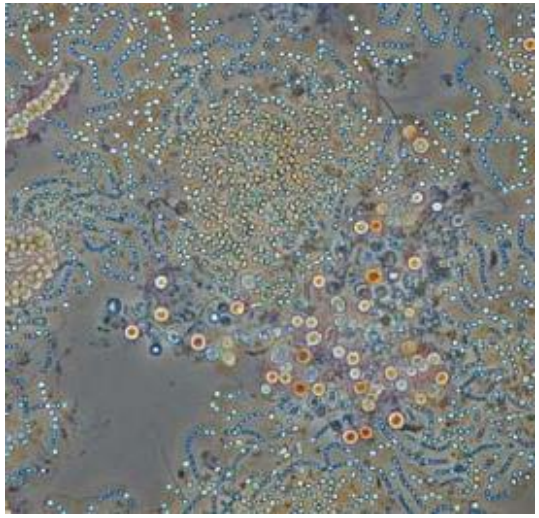


Hug et al., Nature Micro, 2016

Microbial communities

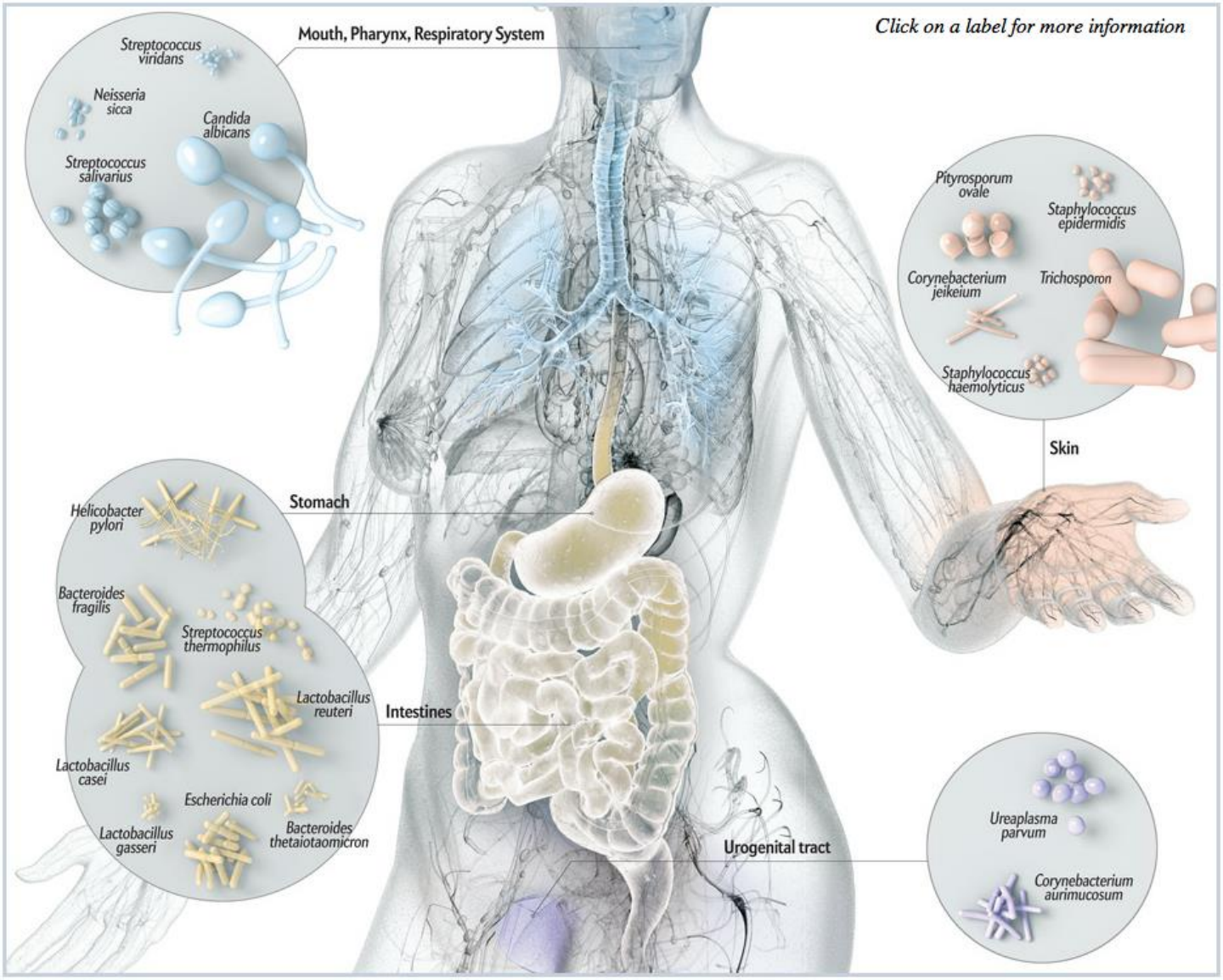




Microbes live in the darndest places

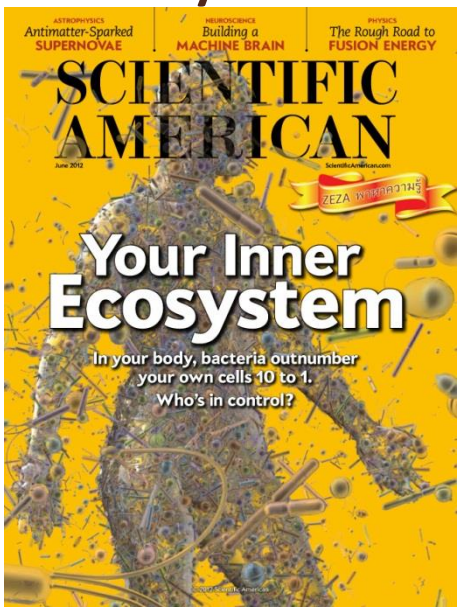
The Human Microbiome

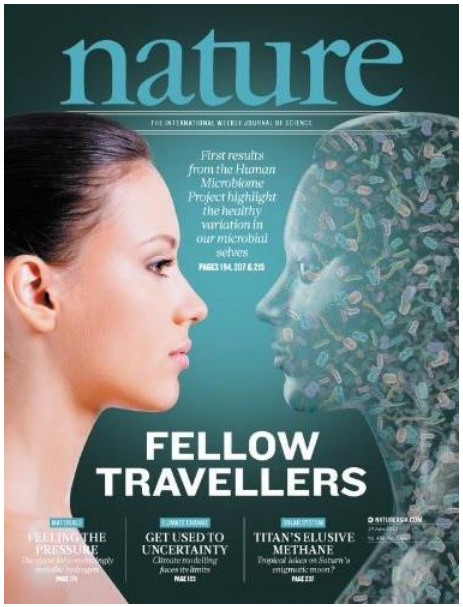


Scientific American

The Human Microbiome:

Our inner ecosystem



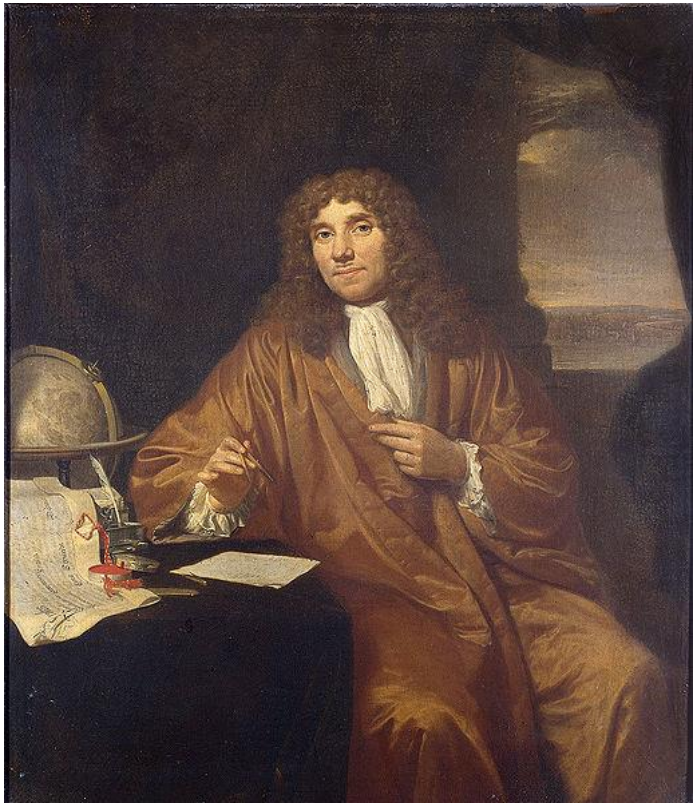


THE NATIONAL MICROBIOME INITIATIVE

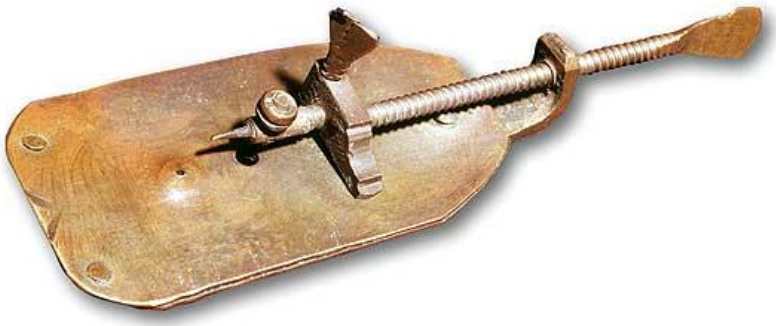
1. **Supporting interdisciplinary research** to answer fundamental questions about microbiomes in diverse ecosystems.
2. **Developing platform technologies** that will generate insights and help share knowledge of microbiomes in diverse ecosystems and enhance access to microbiome data.
3. **Expanding the microbiome workforce** through citizen science and educational opportunities.

New Public and Private Investments in Microbiome Research

The Father of Microbiology

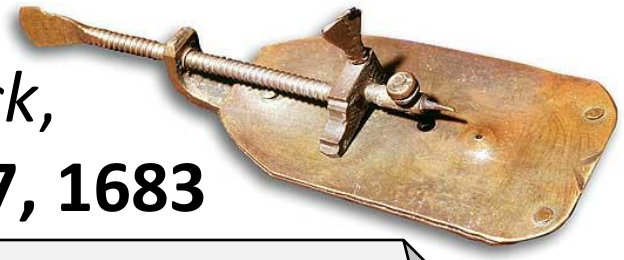


Antony van Leeuwenhoek (1632–1723)



Big fleas have little fleas,
Upon their backs to bite 'em,
And little fleas have lesser fleas,
and so, ad infinitum.

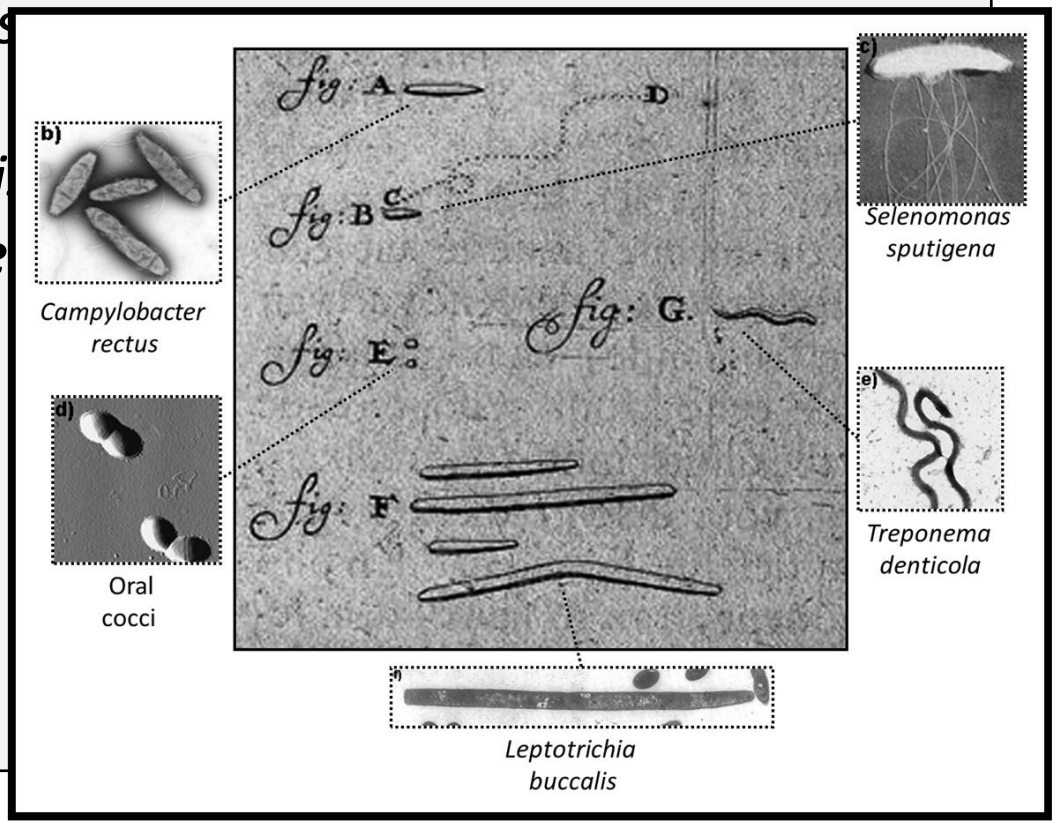
Jonathan Swift

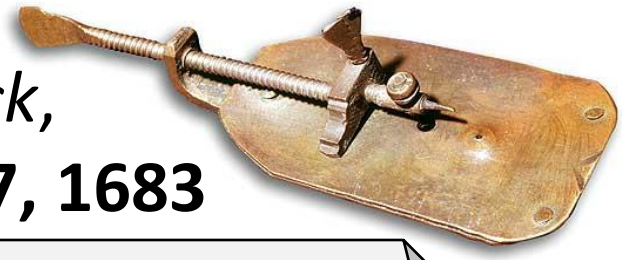


A Letter from *Mr. Anthony Leuwenhoeck*, to the *Royal Society of London*, **Sept. 17, 1683**

*"**Though my teeth are kept usually very clean**, yet when I view them in a magnifying glass, I find growing between them a little white matter, as thick as wetted flour: in this substance though I could not perceive any motion, I judged there might probably be living creatures*

I therefore took some of thi
surprize perceived that the
many small living animals,
***strangely** …*





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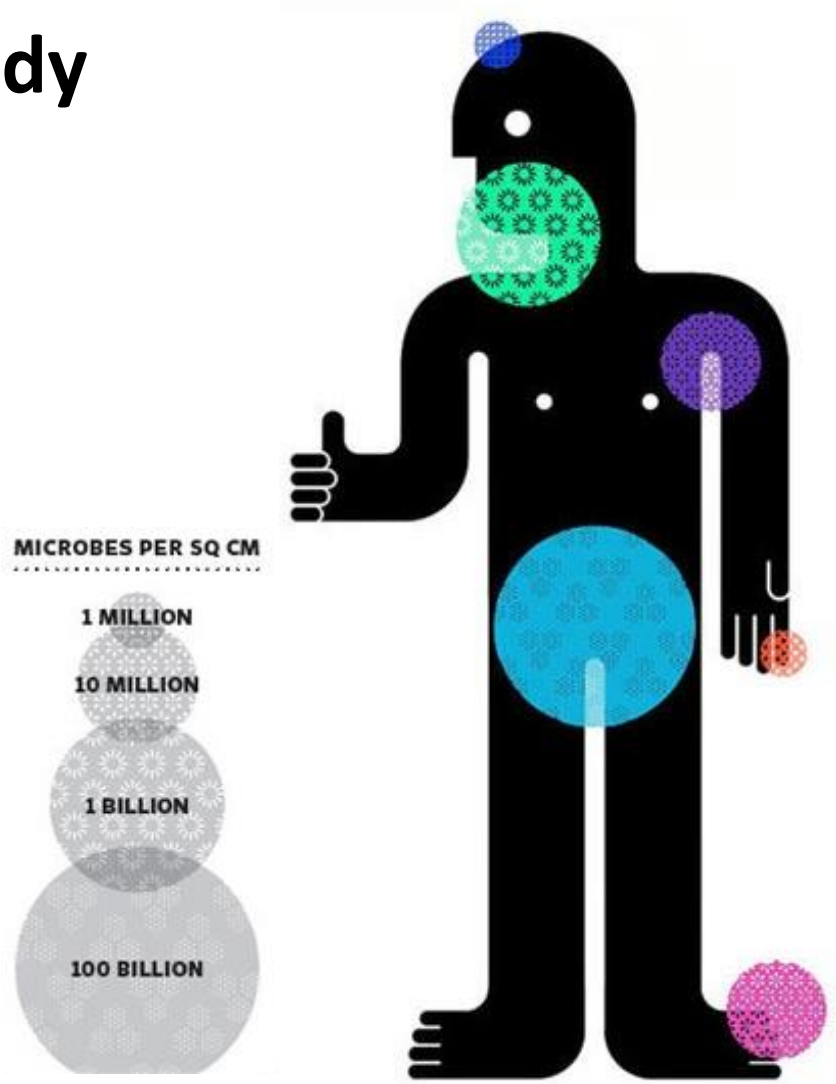
*I therefore took some of this flour … and then **to my great surprize perceived that the aforesaid matter contained very many small living animals, which moved themselves very strangely** …*

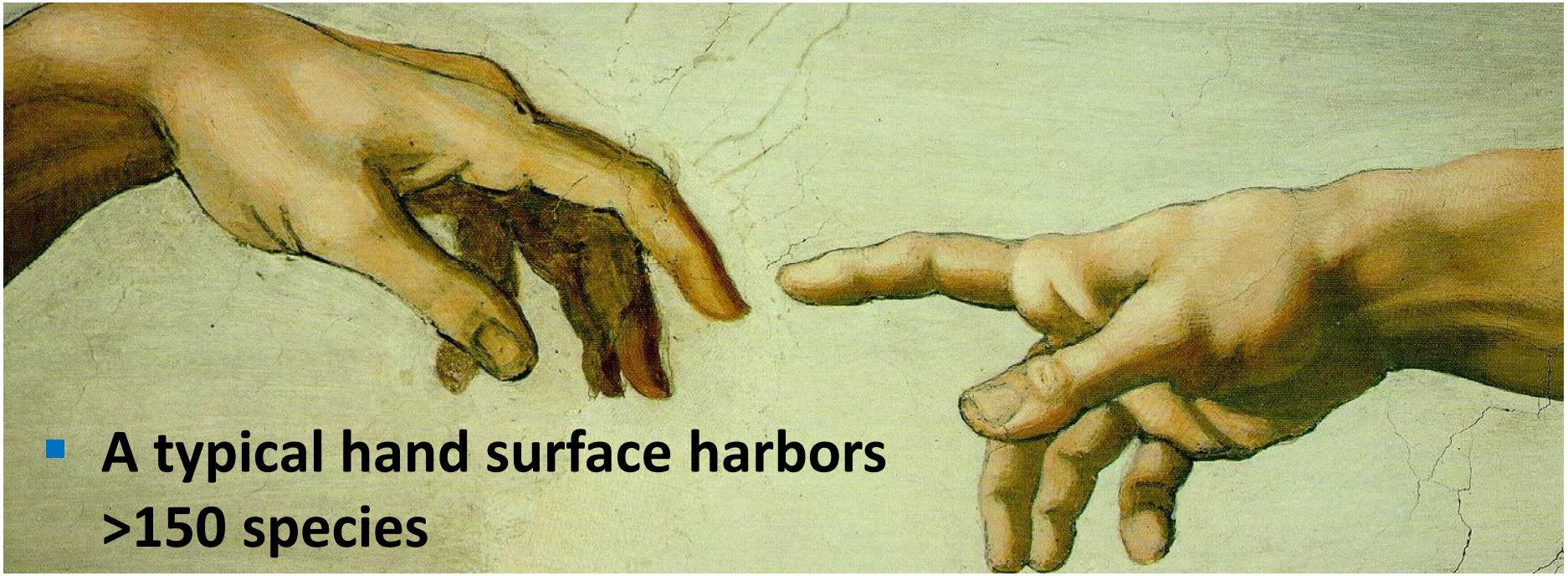
The number of these animals in the scurf of a man's teeth are so many, that I believe they exceed the number of men in a kingdom. …"

We are mostly microbes!

~90% of the cells in our body are non-human



WIRED MAGAZINE: 16.03

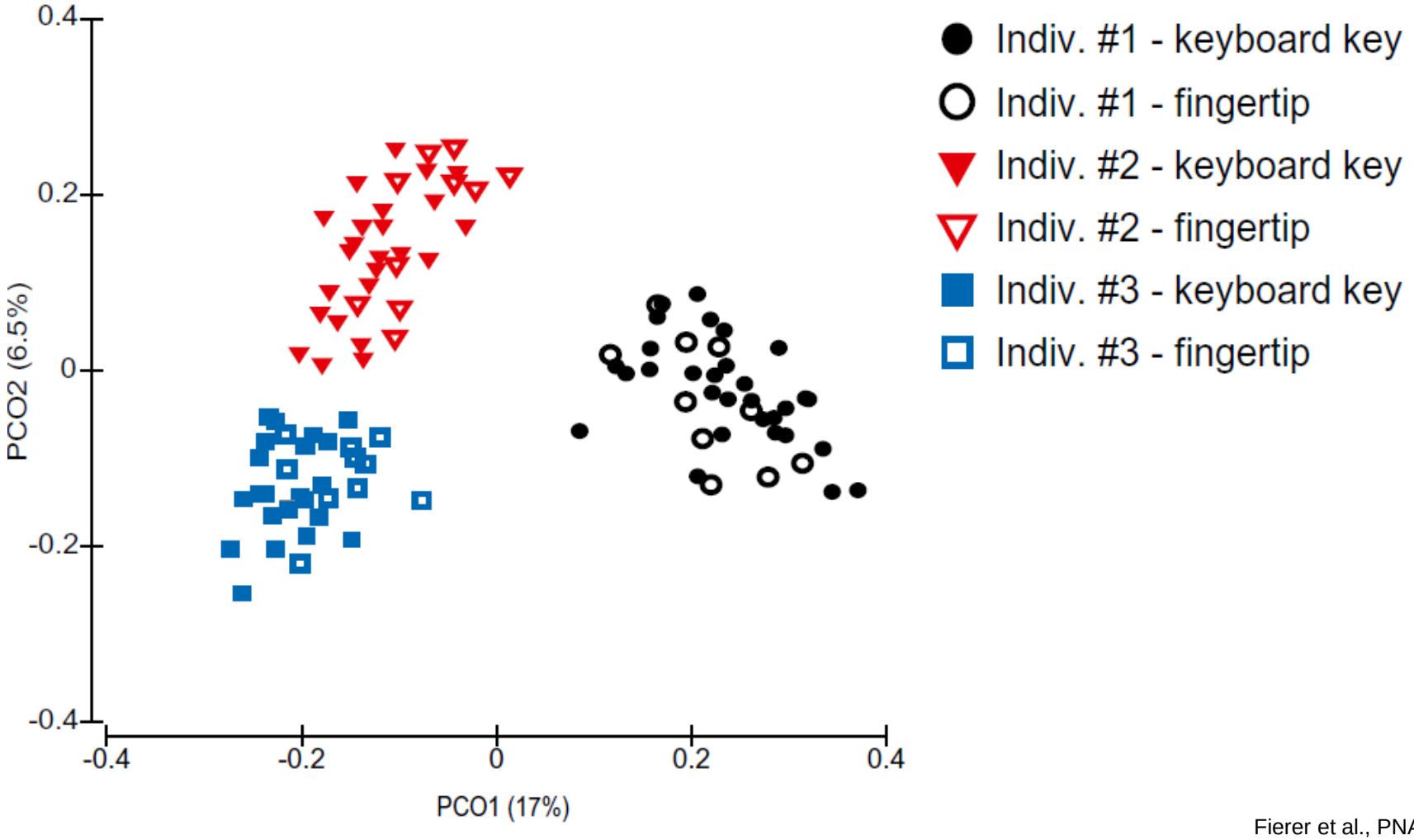


- **A typical hand surface harbors >150 species**

- Hand washing affects composition (but not diversity)
- Women have significantly higher diversity than men
- Your left hand shares only ~17% of its species with your right hand
- Your hand shares only ~13% of its species with the hand of the person next to you

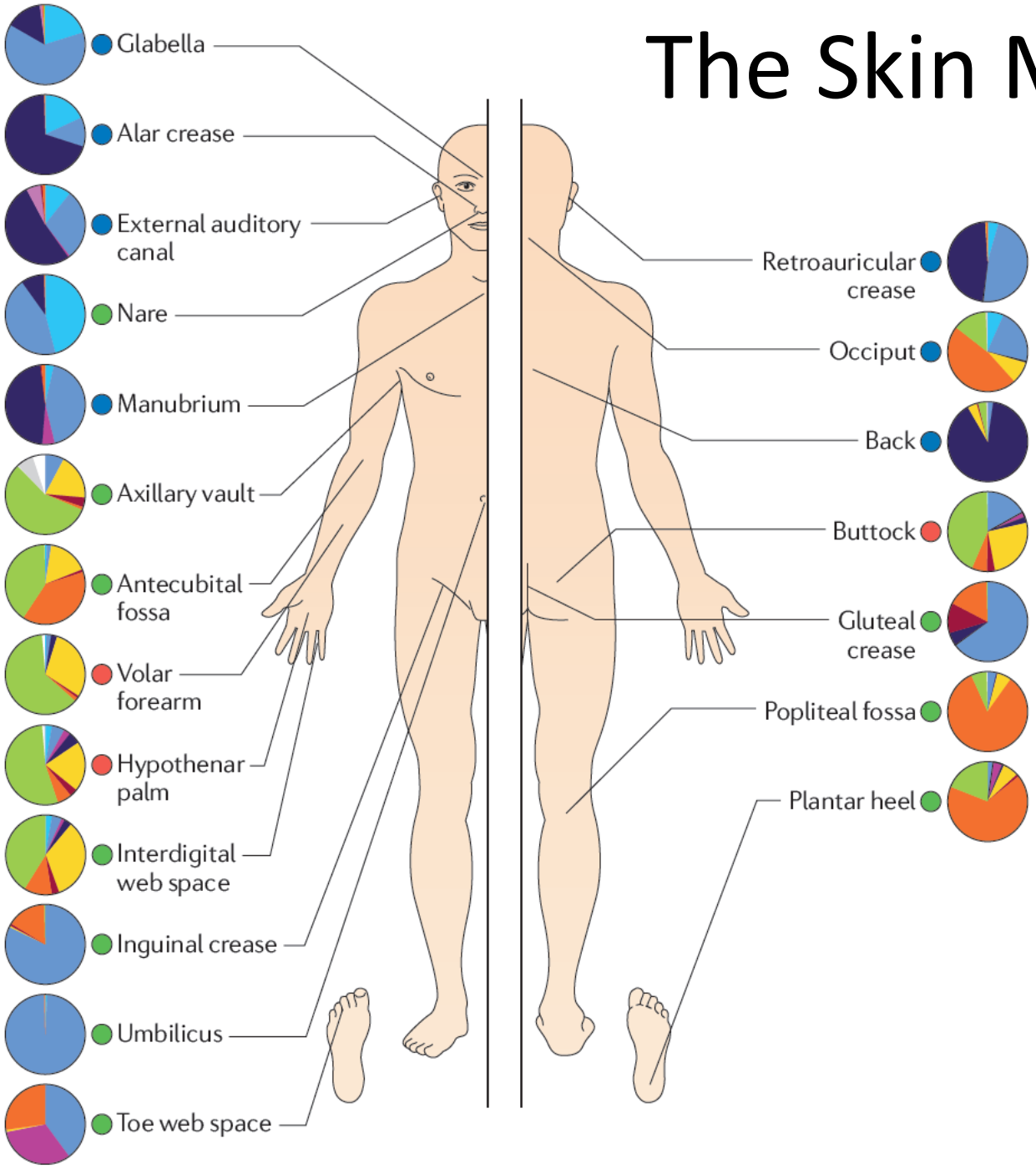
Fierer et al., PNAS, 2008

A Microbiome Fingerprint



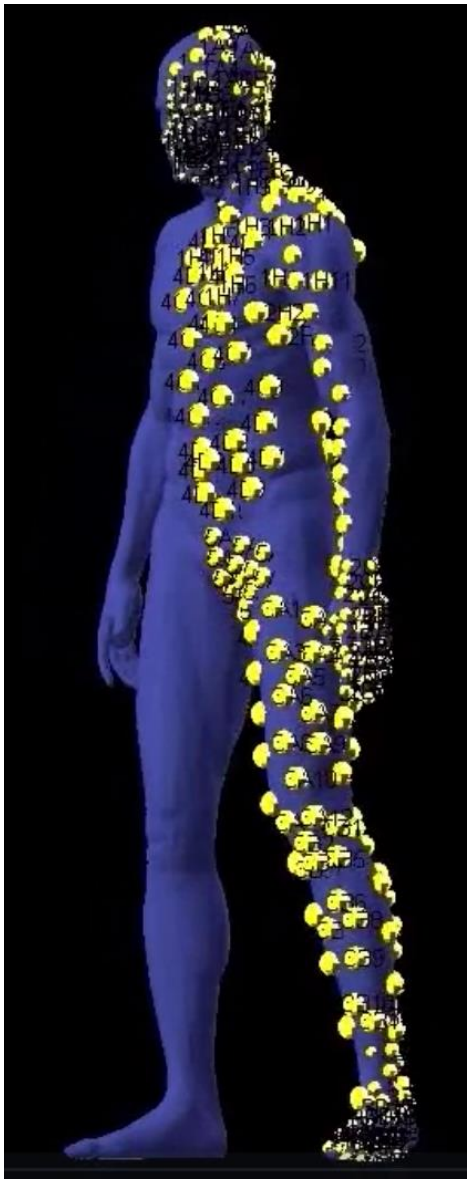
Fierer et al., PNAS, 201

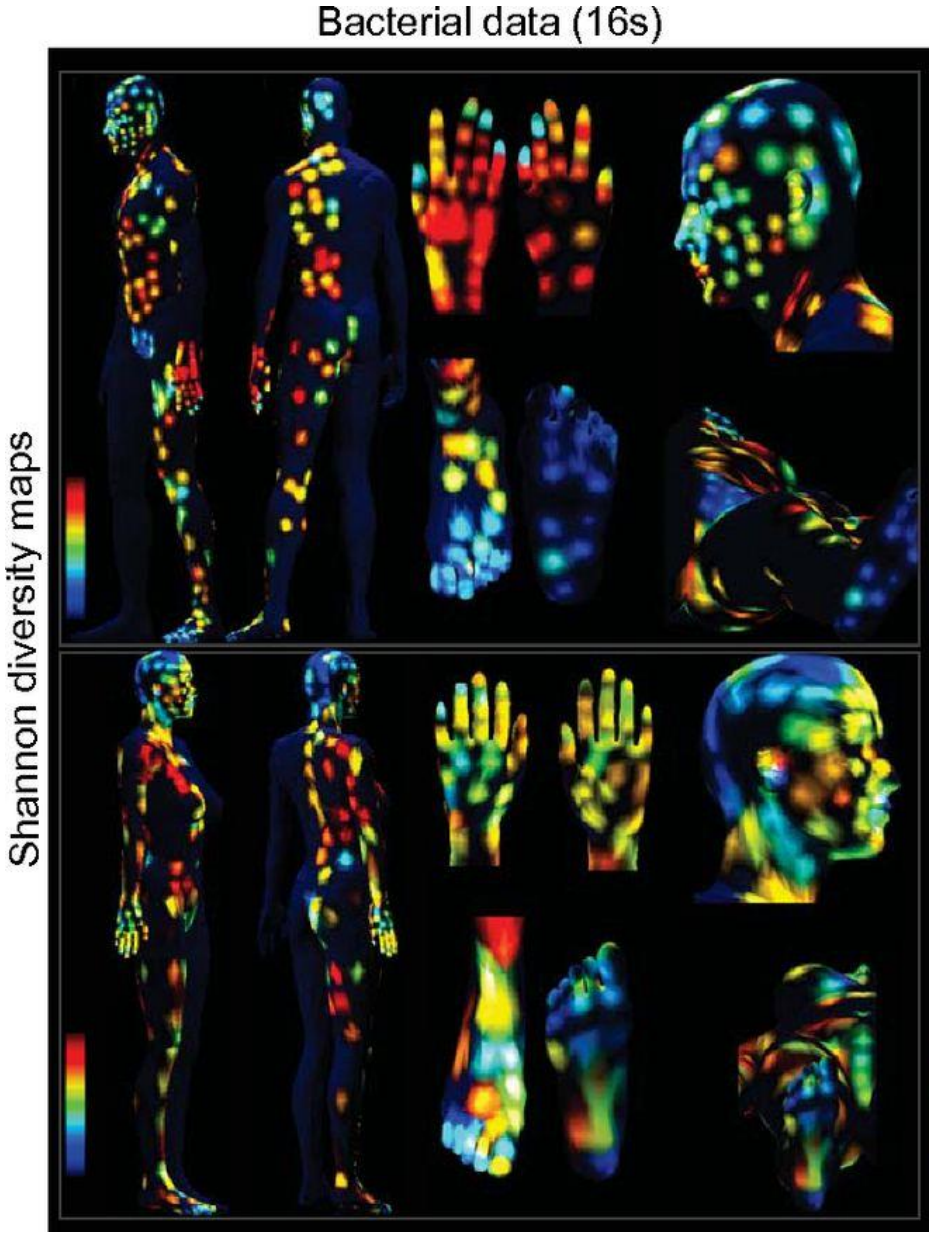
The Skin Microbiome



Grice and Segre Nature Rev Micro, 2011

Hi-Resolution Skin Microbiome Survey

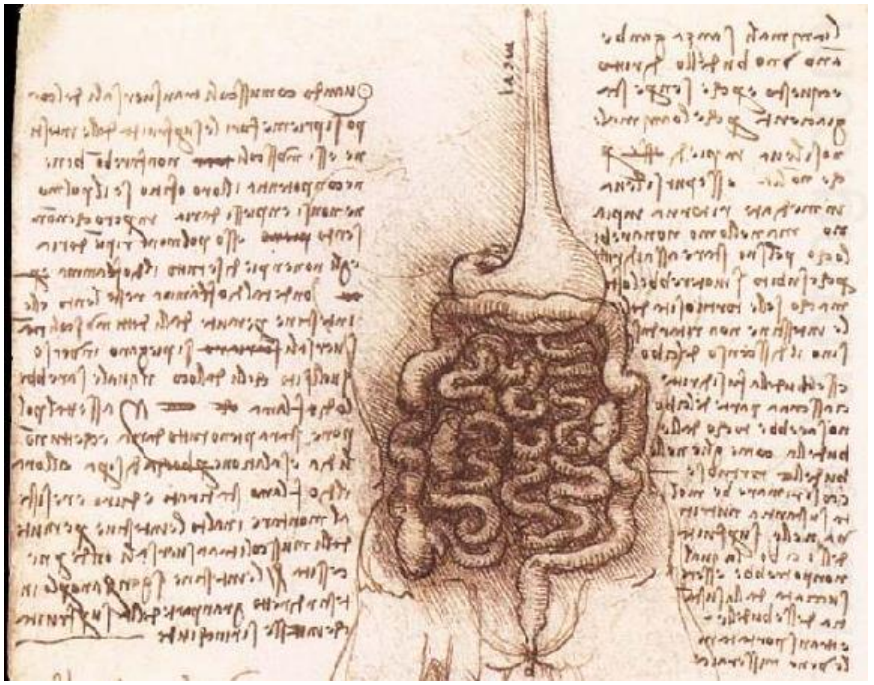




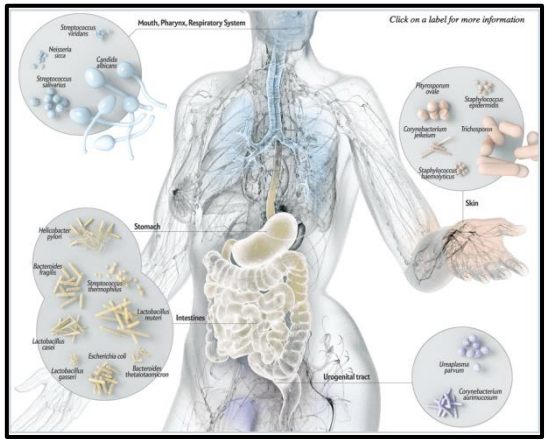
Amina Bouslimani et al. PNAS 2015

The Human Gut Microbiome

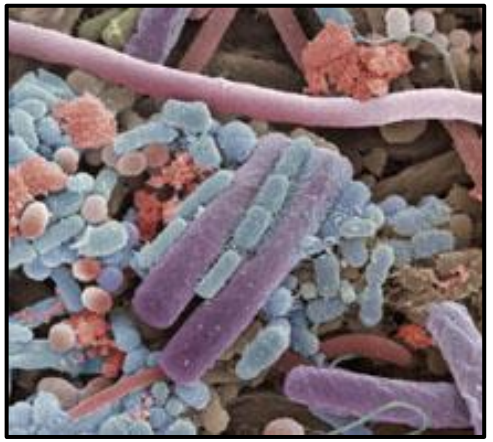
- **Hundreds of species!**
- **100 trillion microbes!**
  (weighing ~3-4lb)
- **150x more genes**
  (~3,300,000)
- **Commensal**
  - Harvests energy from diet
  - Reduces exposure to toxins
  - Primes the immune system
  - Resists pathogens



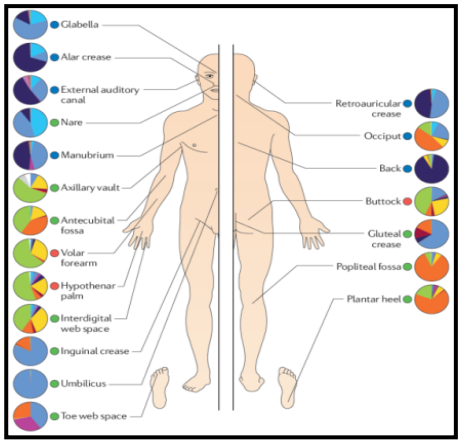
The Human Microbiome 2018



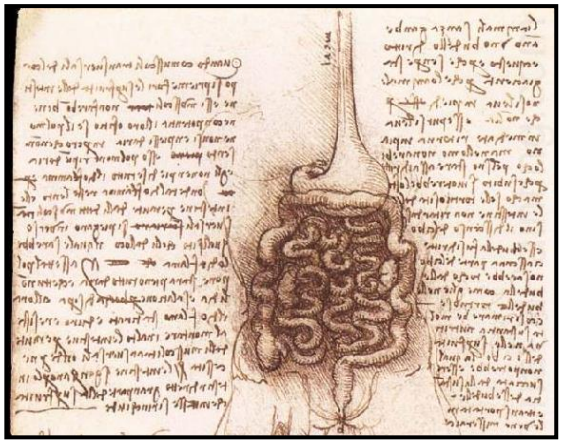
We are mostly microbes



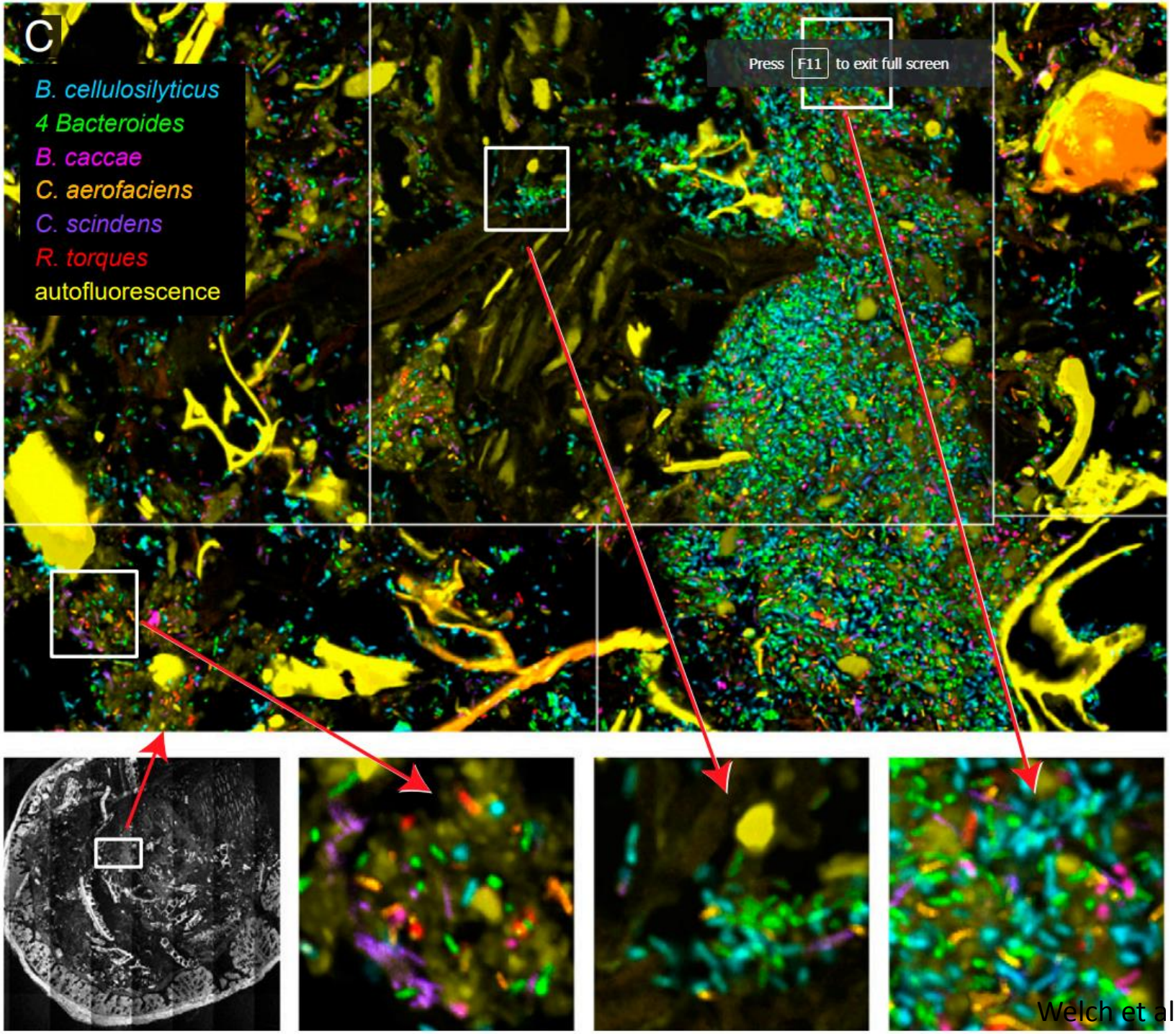
Complex and diverse



Highly variable

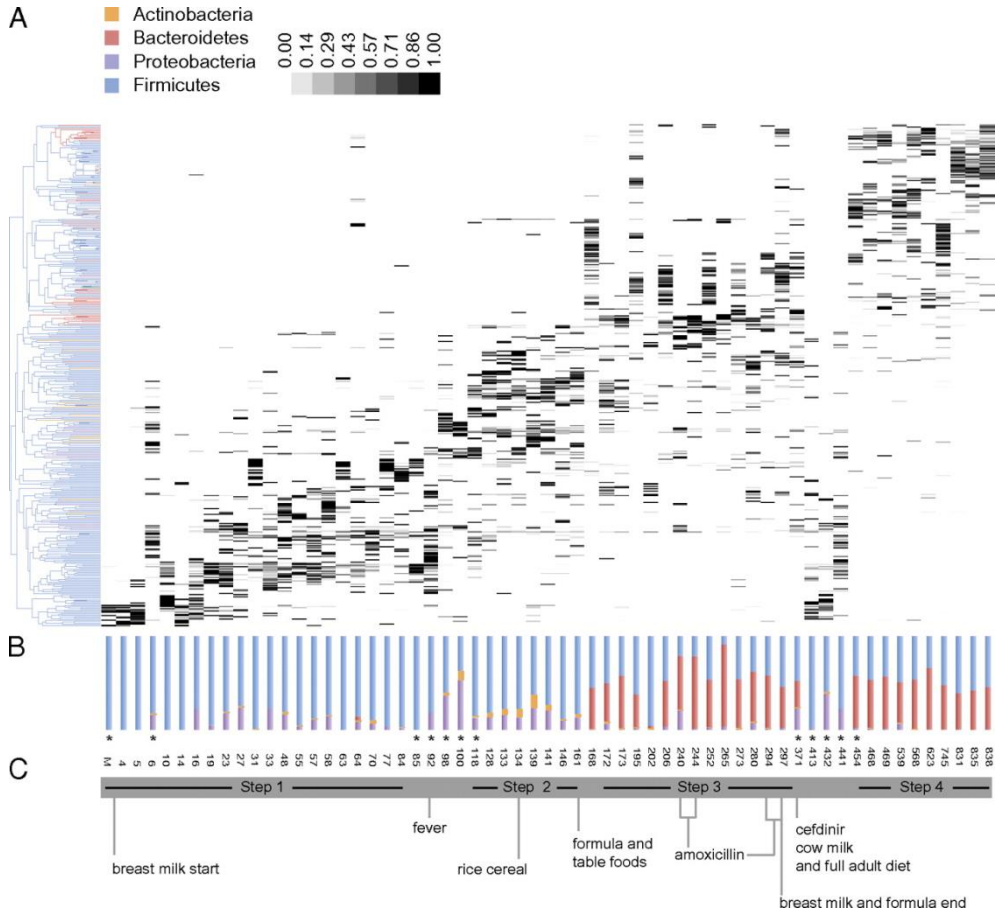


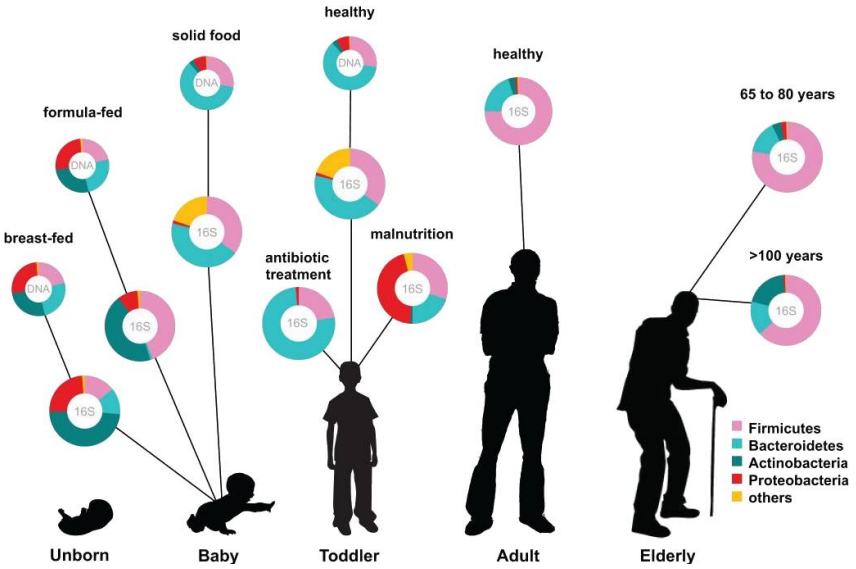
Crucial processes

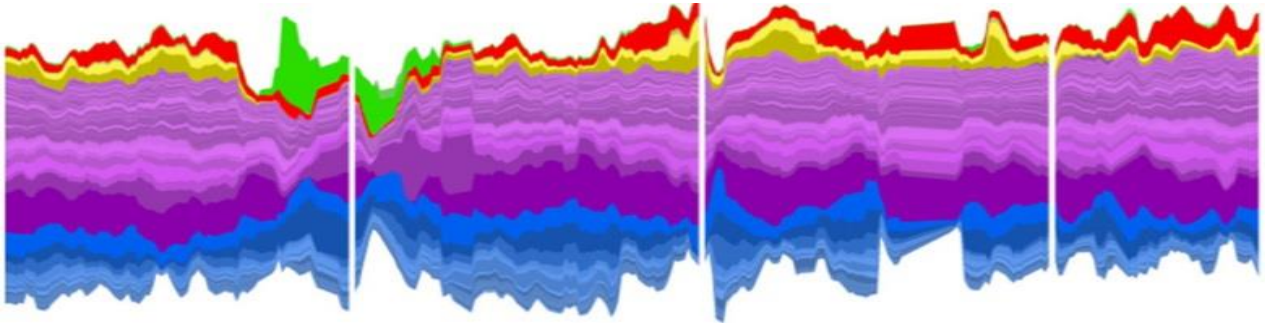


Welch et al., 2017

Microbiome Variation Over Time

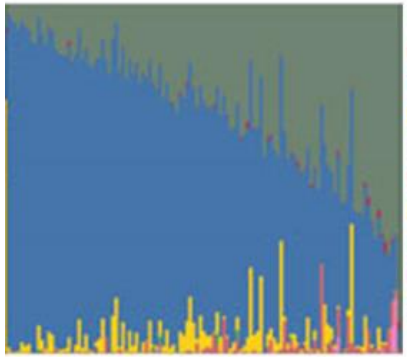




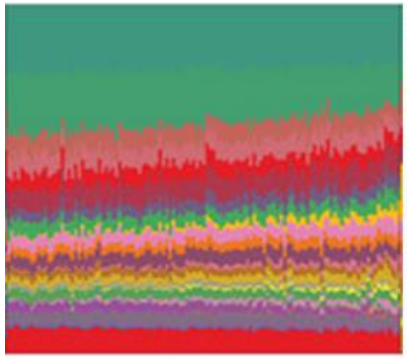


Jeremy E. Koenig, 2010
Ottman et al., 2012
David et al., 2014

Microbiome Variation Across Hosts

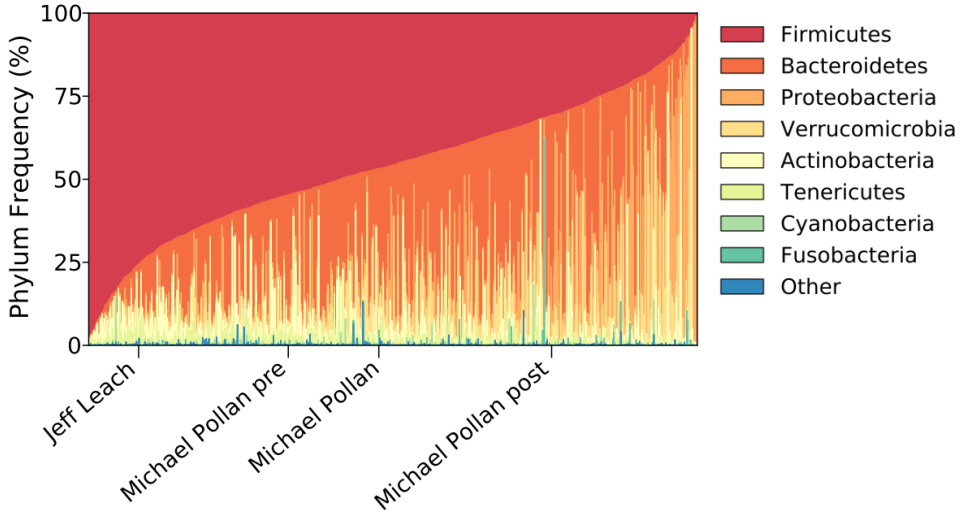


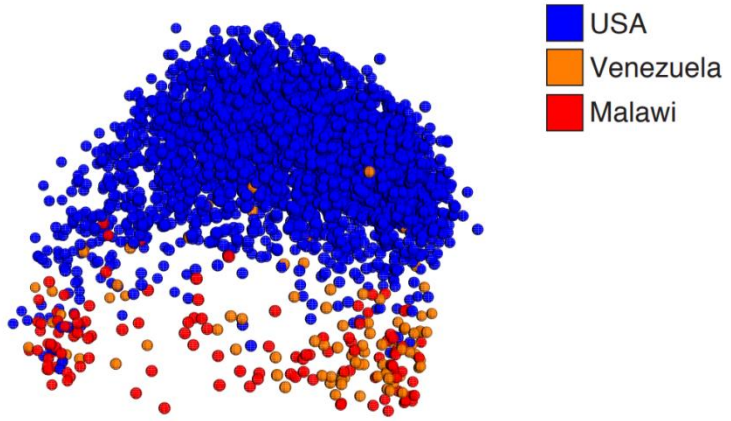
Firmicutes
Actinobacteria
Bacteroidetes
Proteobacteria
Fusobacteria
Tenericutes
Spirochaetes
Cyanobacteria
Verrucomicrobia
TM7



Central carbohydrate metabolism
Cofactor and vitamin biosynthesis
Oligosaccharide and polyol transport syste
Purine metabolism
ATP synthesis
Phosphate and amino acid transport system
Aminoacyl tRNA
Pyrimidine metabolism
Ribosome
Aromatic amino acid metabolism

Stool

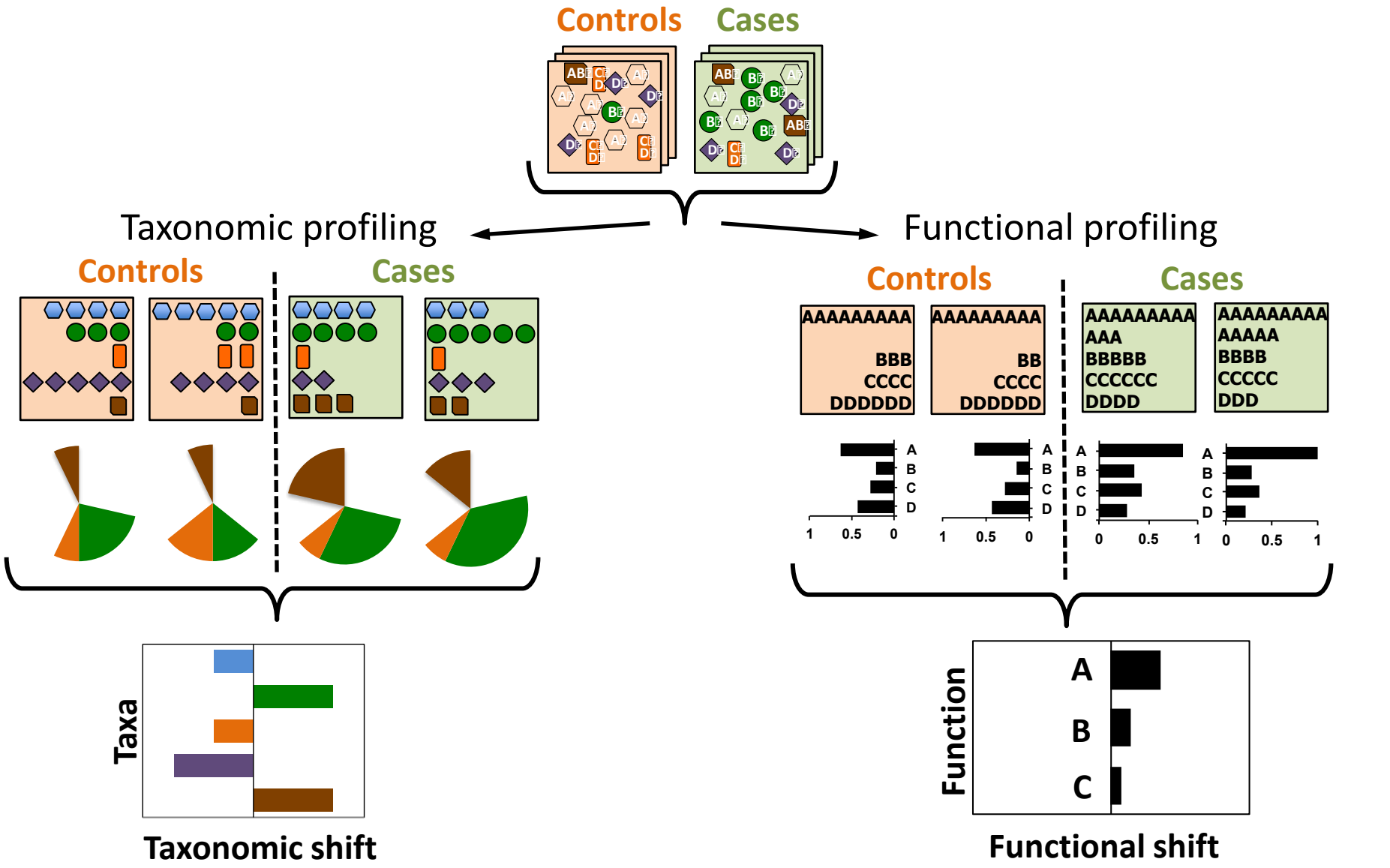




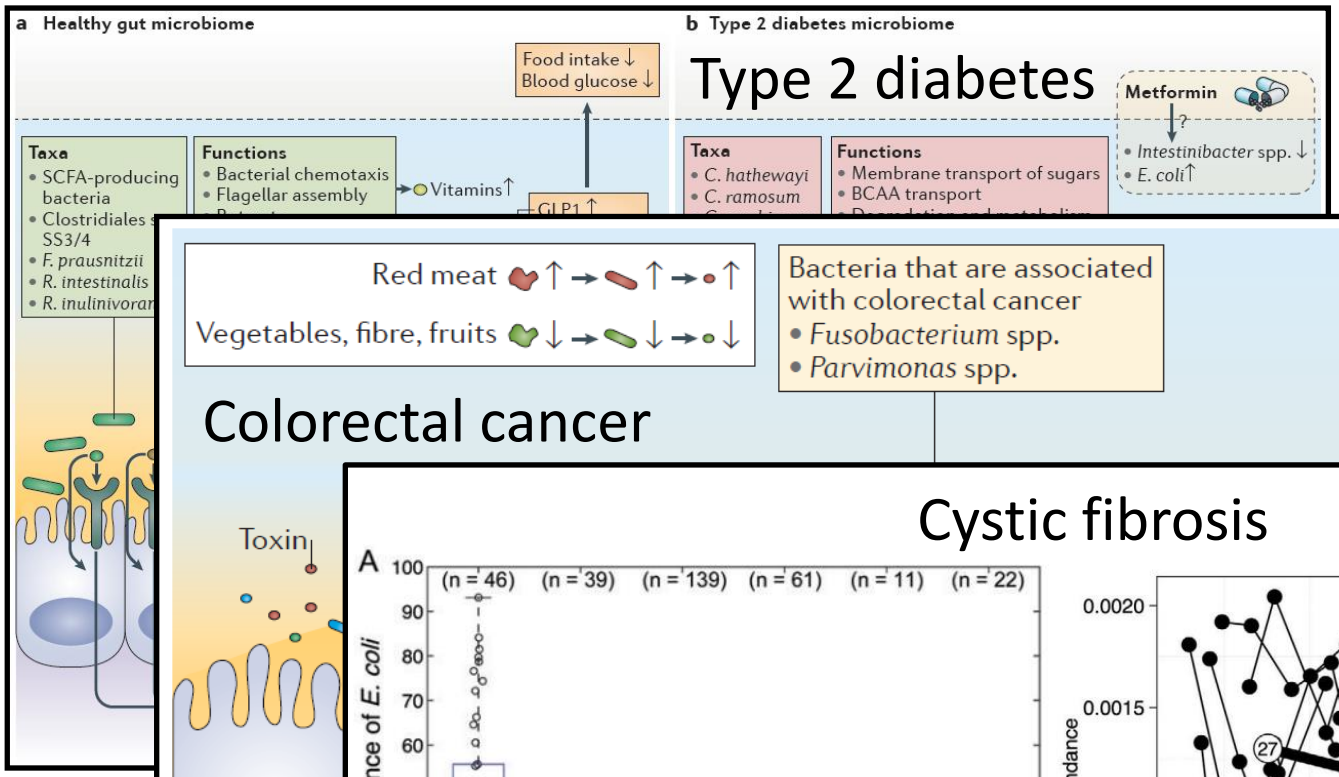
Human Microbiome Project HMP Consortium, Nature, 2012

American Gut Project

Metagenome-wide association studies



Metagenome-wide association studies



Hoffman et al., 2014, Manor et al., 2016
Wang and Jia, Nature Rev Micro, 2016

Association with disease

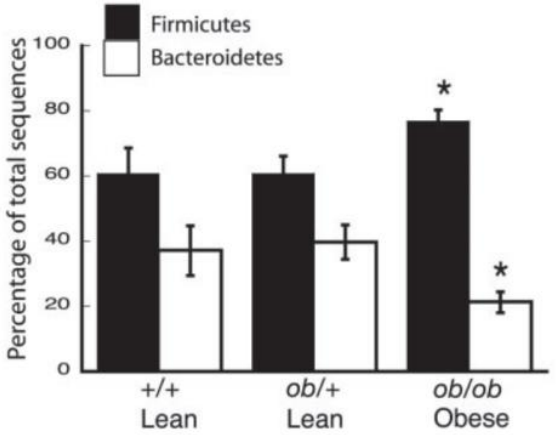
- **Obesity**
- **T2 Diabetes**
- Hay fever
- Arthritis
- Autism
- Asthma
- **colorectal cancer**
- Metabolic disorder
- Rheumatoid arthritis
- Alzheimer's disease
- **Liver cirrhosis**
- Crohn's disease
- Chronic fatigue syn’
- Multiple sclerosis
- Cardiovascular diseases
- Ulcerative colitis
- Diarrhea
- Depression
- Anxiety
- Gastric ulcers
- Malnutrition
- **Cystic fibrosis**
- Celiac disease

Hoffman et al., 2014, Manor et al., 2016
Wang and Jia, Nature Rev Micro, 2016

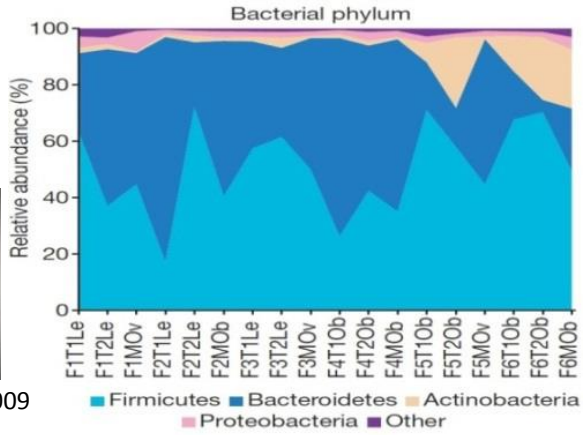
Cause or Effect

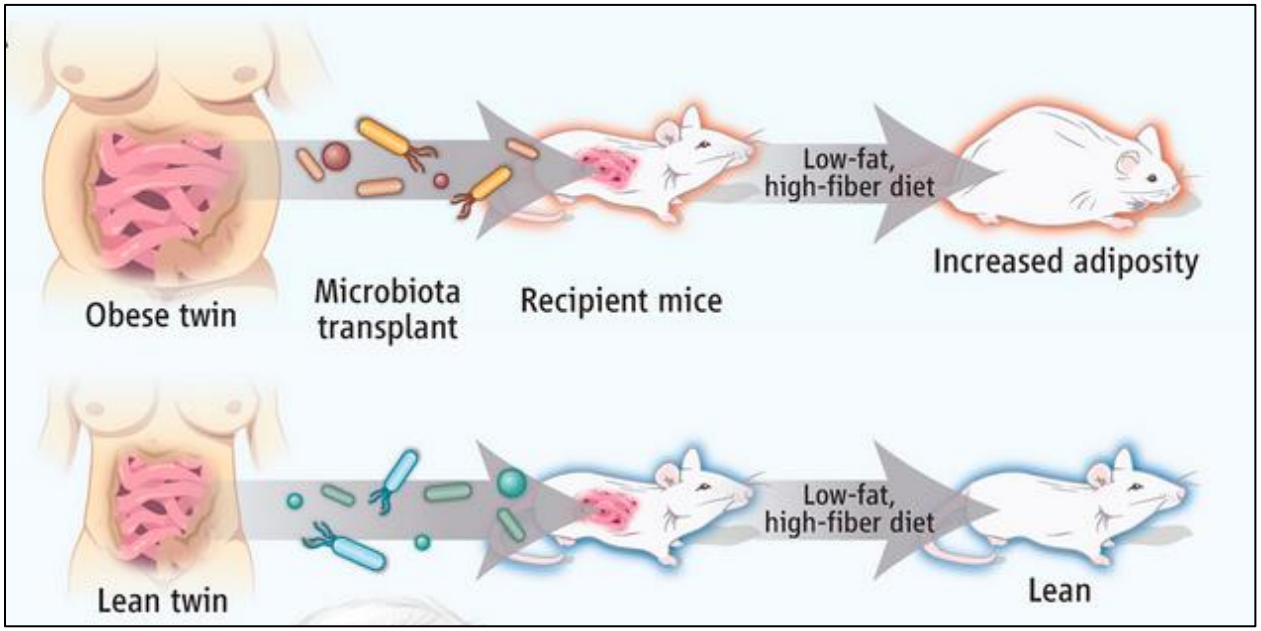
- Obesity

Ley et al., PNAS, 2005



Turnbaugh et al., 2009





Ridaura et al. *Science*, 2013

Next Class:

From Significance to (Computational) Challenges

Outline

About the Seminar

Tips for Giving a Good Talk

A *Very* Brief Background about Microbes, Microbiomes, and Metagenomics

Q&A