
# A critical dimension of the NSF's Rules of Life Program -

## *A Field in Revolution:*

The impact of discovering the invisible force of the Earth's microbiomes

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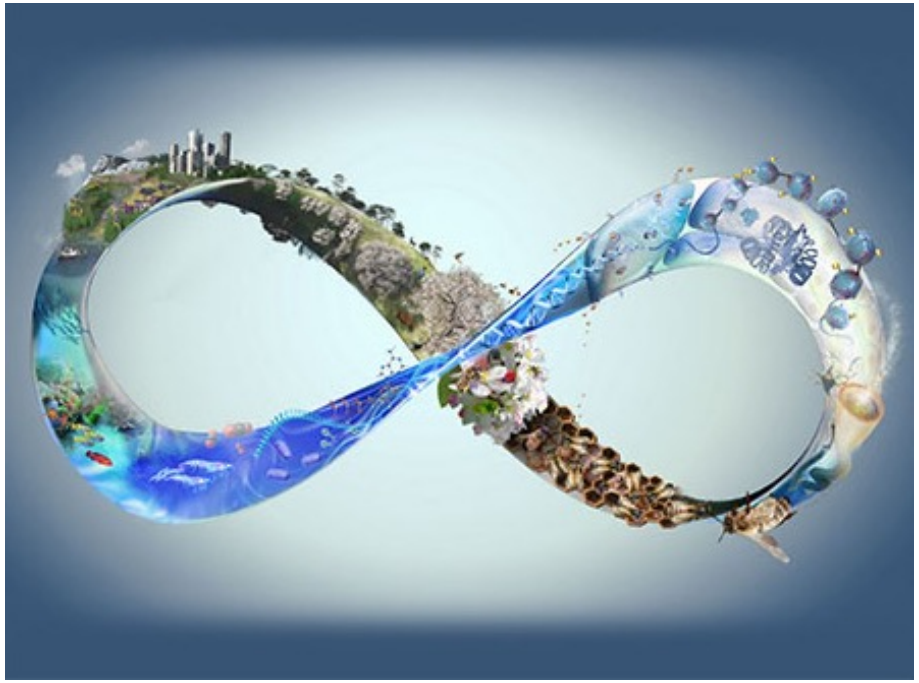
Division of Biology and Biological Engineering
California Institute of Technology
Division of Biosphere Sciences and Engineering
Carnegie Institution for Science

- What is the revolution all about?
- Why is it particularly important now?

## The NSF ‘Rules of Life’ Program

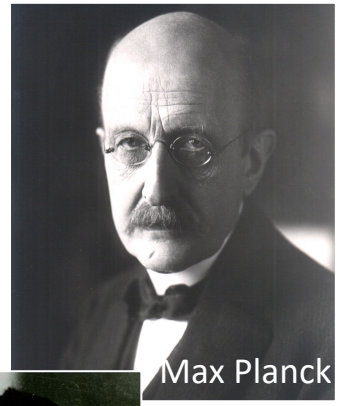


*[From the NSF website]*

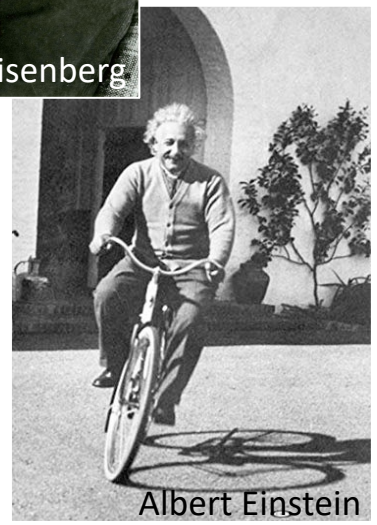
- To enable discoveries that will allow us to better understand…interactions and identify causal, predictive relationships across…scales
- To develop research tools and infrastructure
- To train the next generation of researchers
- And to foster collaboration and convergent research across the Foundation

# A “SEA CHANGE”…
# Driven by a better understanding of life’s diversity

- *The basis of this revolution, and why it is critical*


Max Planck


Werner Heisenberg


Albert Einstein

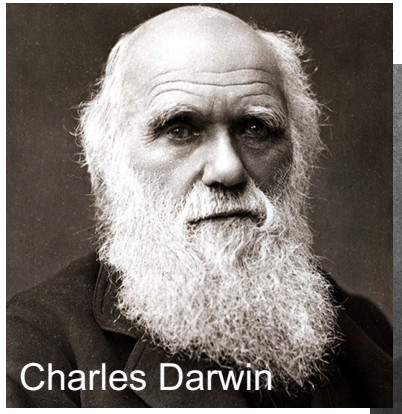
"True revolutions in science involve more than spectacular discoveries and rapid advances in understanding. They also change the concepts on which the subject is based. Such fundamental transformation took place in physics during the first thirty years of this [the 20th] century, culminating in what has been called the Golden Age of Physics. As a result, the physicist's world view has been radically and irreversibly altered."

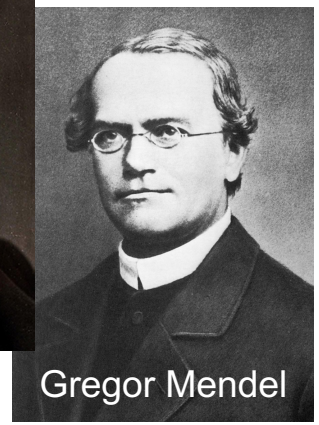
- Paul Davis,
Introduction to *Physics and Philosophy* by Werner Heisenberg, 1958

Revolutions in Biology - When biologists' "…world view has been radically and irreversibly altered"

*Mid-19th Century*

Evolutionary biology
& the 'Modern Synthesis'


Charles Darwin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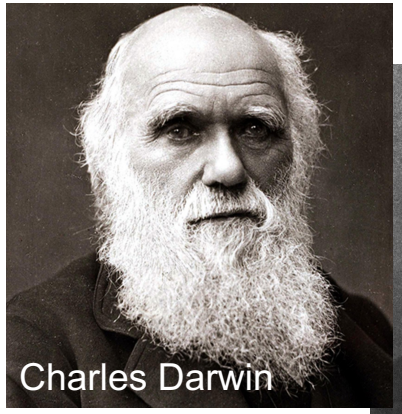
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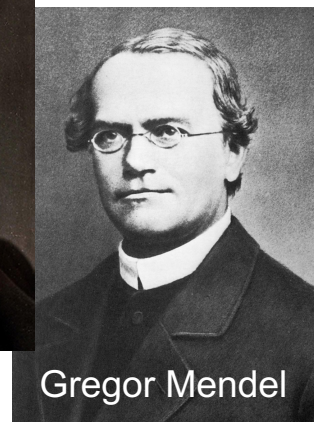
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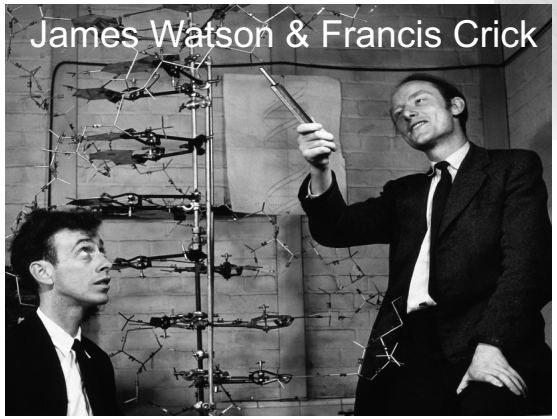
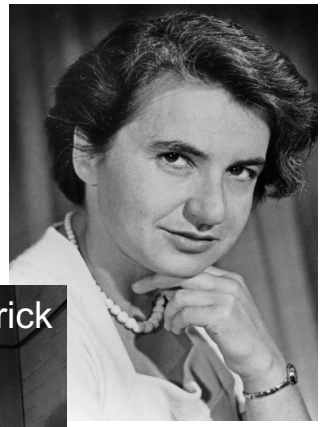
*Mid-20th Century*

DNA as the genetic material


James Watson & Francis Crick


Rosalind Franklin

In both cases, a marriage of theory & mechanism

Revolutions in Biology - When biologists' "…world view has been radically and irreversibly altered"

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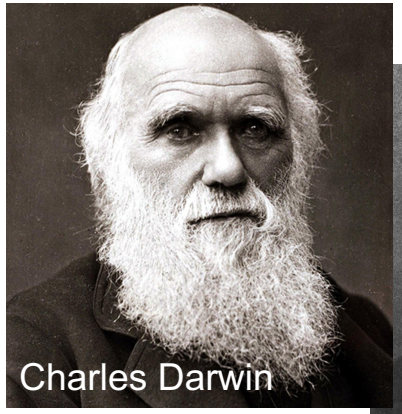
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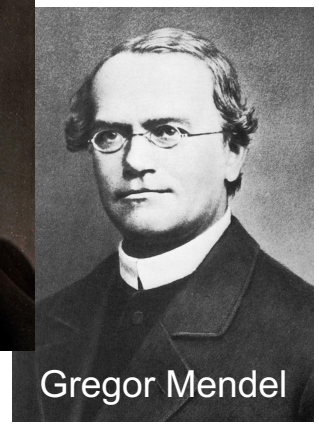
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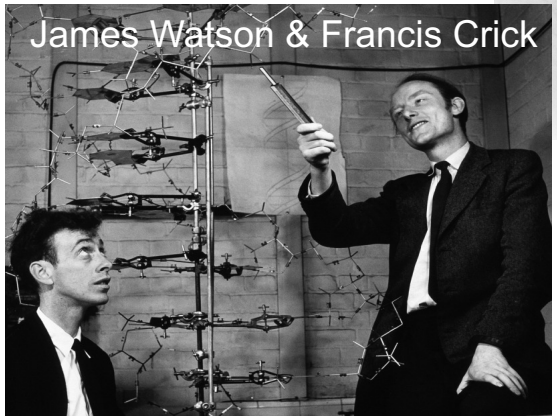
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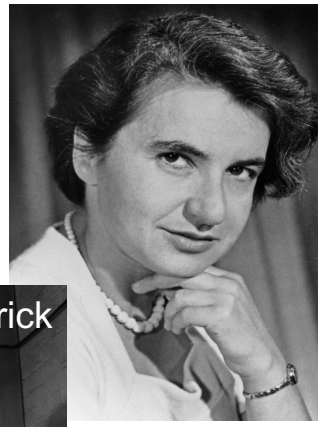

Rosalind Franklin

In both cases, a marriage of theory & mechanism

**WHAT IS THE 21st CENTURY REVOLUTION IN BIOLOGY ALL ABOUT AND HOW DID WE GET HERE?**

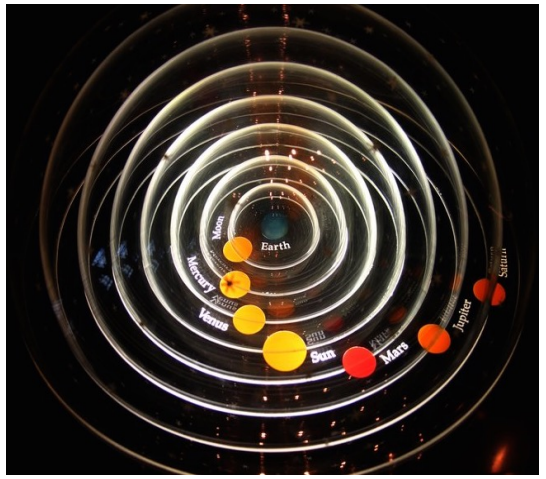
***A TECHNOLOGICAL BREAKTHOUGH***

# *Revolution through Technological Breakthrough – a New 'Lens'*

## ASTRONOMY

**Copernicus**

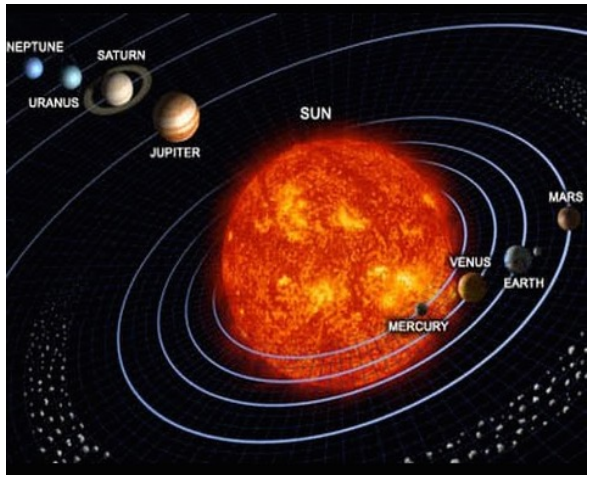
Geocentrism 600 BCE to ~1600




**Galileo**

*The telescope*

Heliocentrism ~1600 to the present



*Revolution through Technological Breakthrough – a New 'Lens'*

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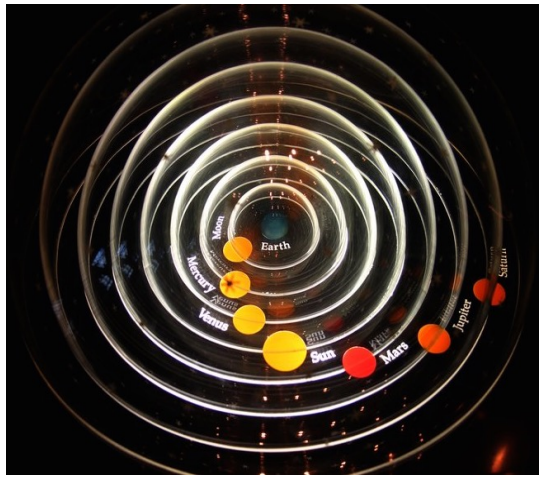


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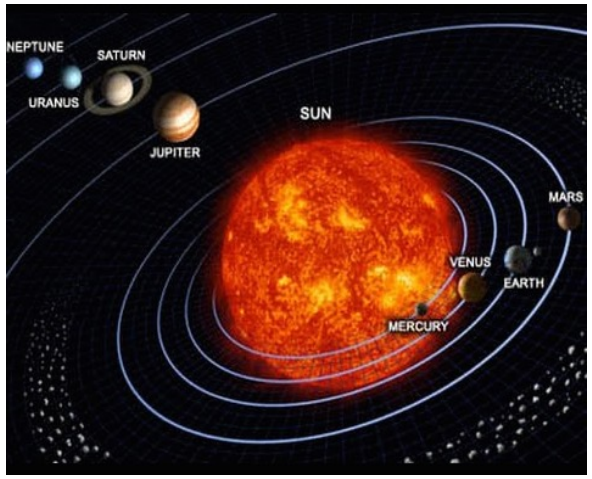


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**THIS INVENTION CHANGED OUR VIEW OF THE *UNIVERSE*,**
**AND OUR VIEW OF OUR *POSITION* IN THE UNIVERSE.**

*Revolution through Technological Breakthrough – a New 'Lens'*

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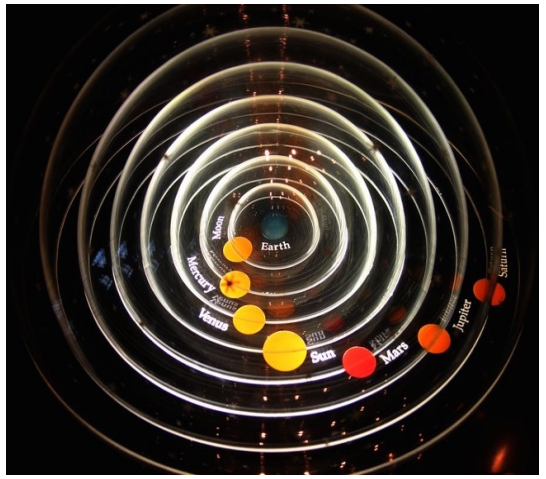


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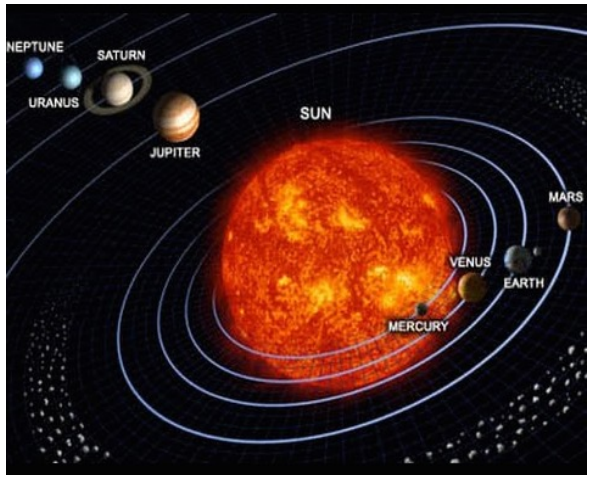


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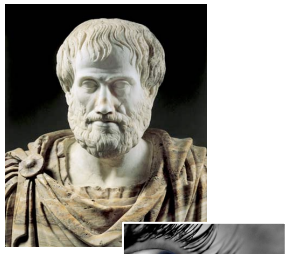
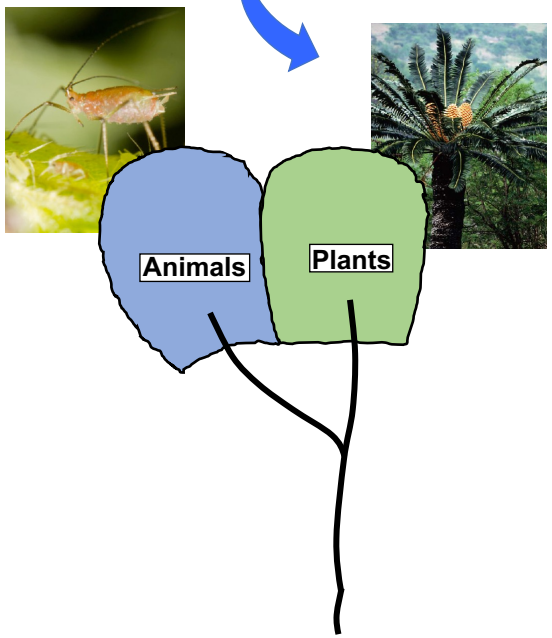
WHAT IS BIOLOGY'S CURRENT REVOLUTION?

# For over 2000 years, biologists organized the biosphere **optically**



**Aristotle**
**384-322 BCE**



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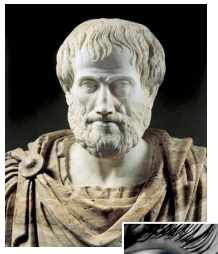

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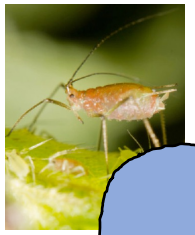
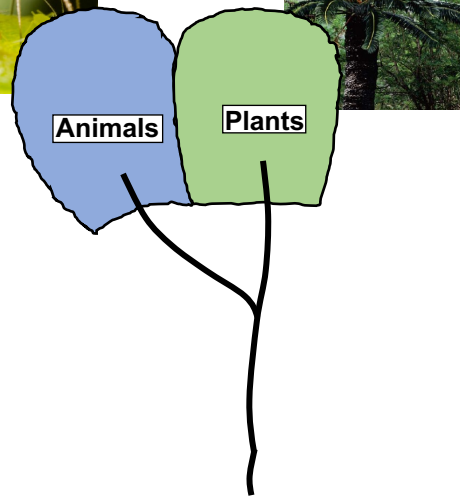
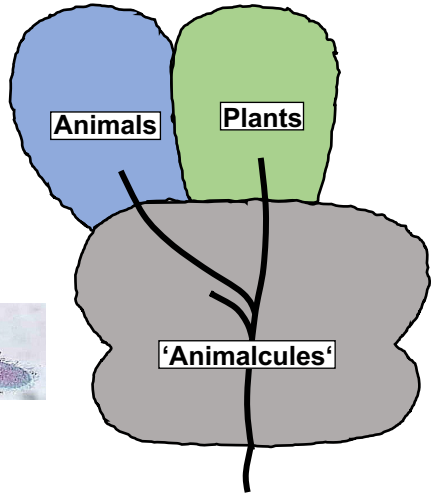





**Antonie van Leeuwenhoek**
**1632-1723**

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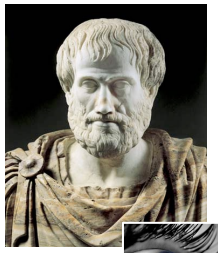

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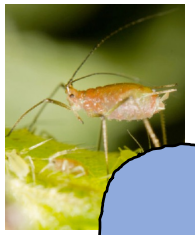

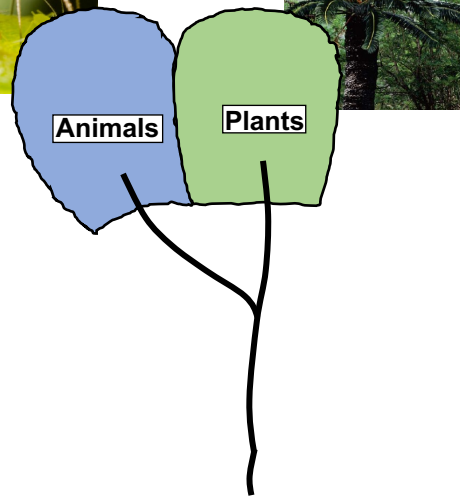


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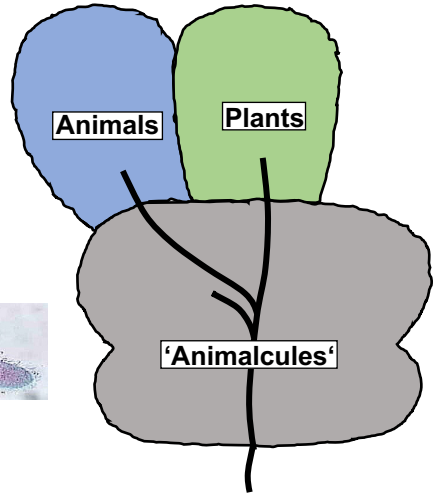
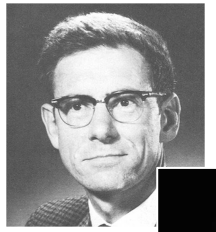
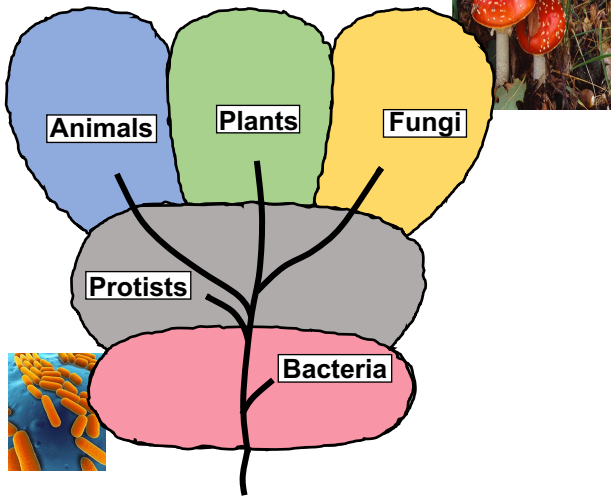


**Robert Whittaker**
**1920-1980**

*[electron microscope]*






The 'FIVE KINGDOM' Model
*[1969-2008 and beyond]*

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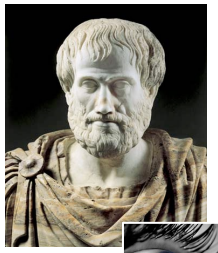

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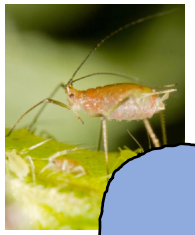

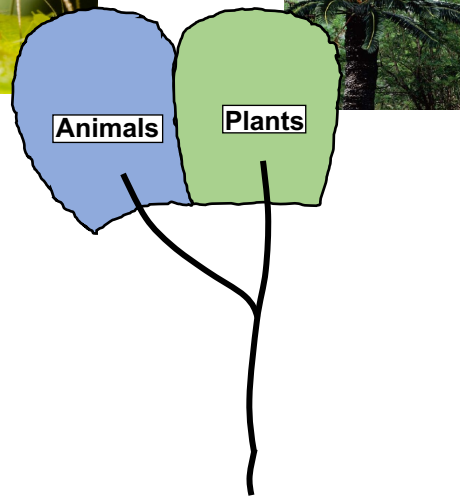


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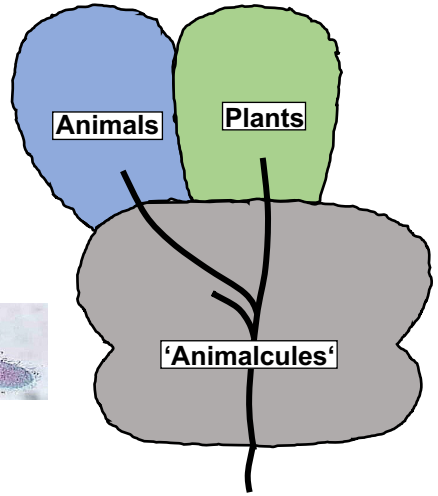
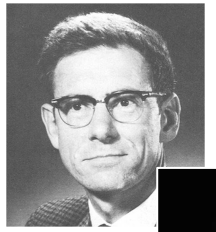
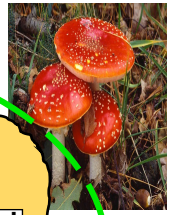


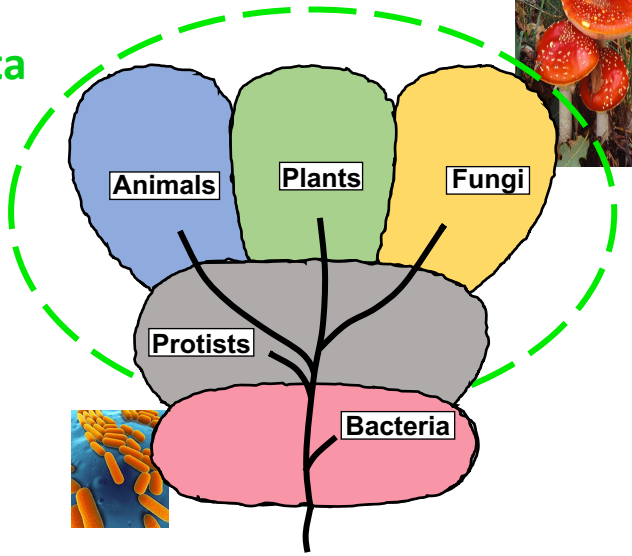



**Robert Whittaker**
**1920-1980**

*[electron microscope]*

**Eukaryota**
**+ a nucleus**








The 'FIVE KINGDOM' Model
*[1969-2008 and beyond]*

*To get an accurate picture*, biologists needed an entirely new method, one that is a more direct reflection of our relatedness… **OUR GENES**.

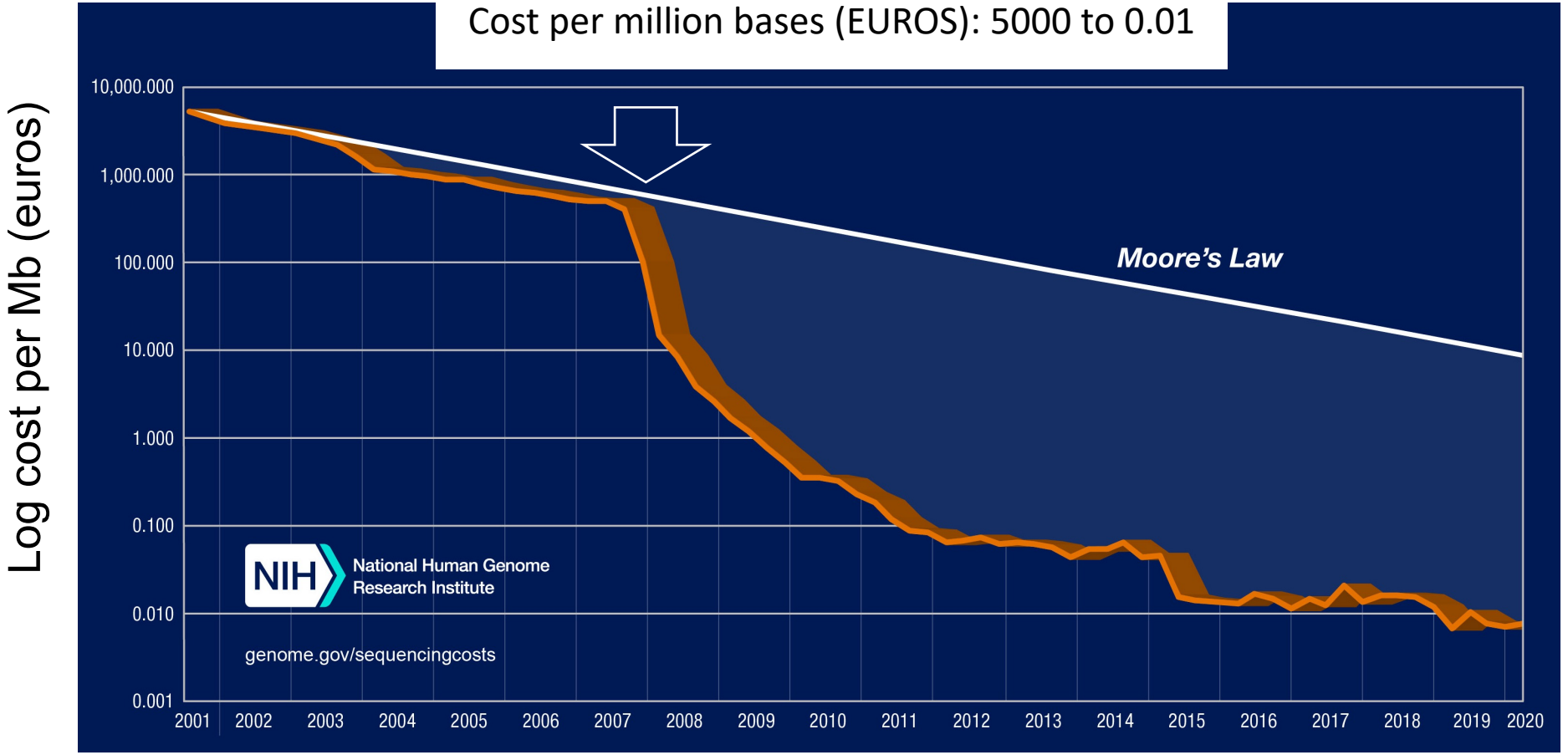
Carl Woese
1928-2012


*Woese's Idea: (late 1970s)*

*Use genetic sequences to determine relatedness –*
*the more similar the sequence, the more closely related*

*but…. sequencing was slow and expensive!*

A technological breakthrough – 'Next Generation Sequencing',
obtaining sequences is now *FAST AND CHEAP* – A WIDE FRONTIER IS OPENED!




2008

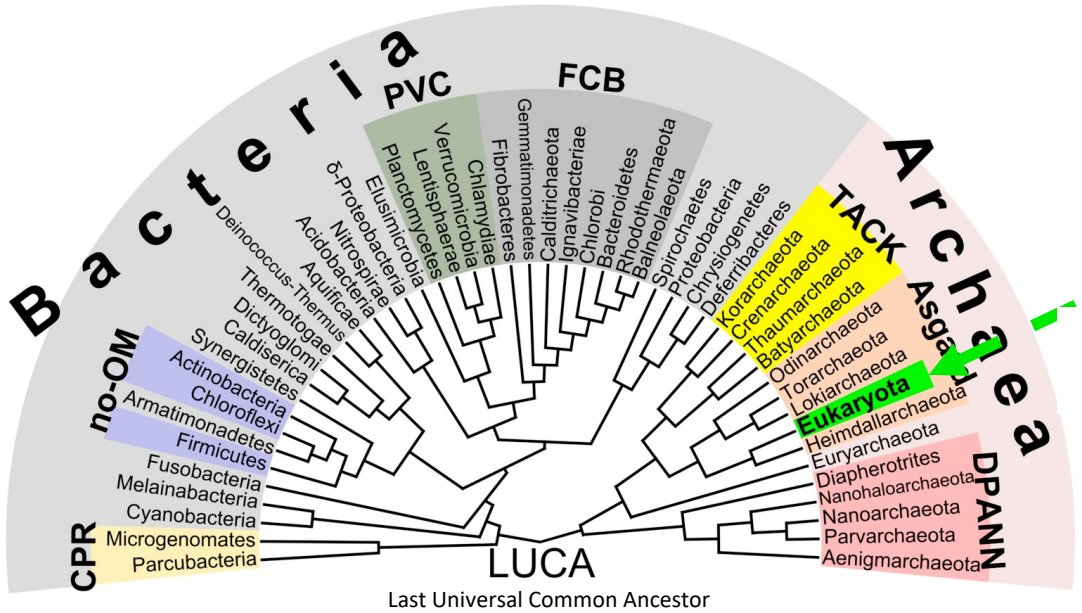
*14 years*

*30+ years after Carl Woese*

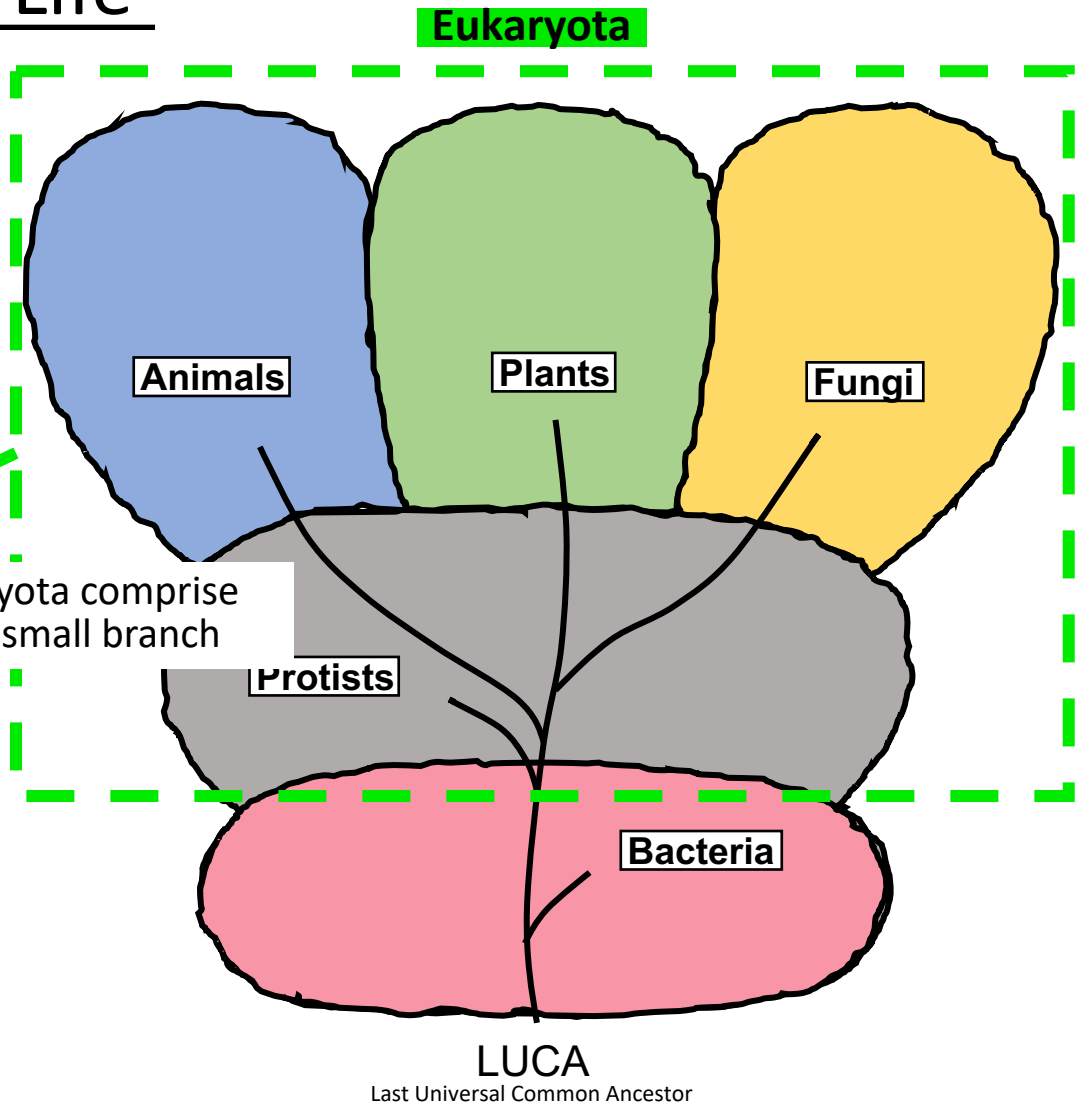
# *WHAT HAVE WE LEARNED THUS FAR?*

# The biggest change in our view of the biosphere since Darwin!
# - A world we couldn't have known

## The 'Tree of Life'




The Eukaryota comprise only one small branch



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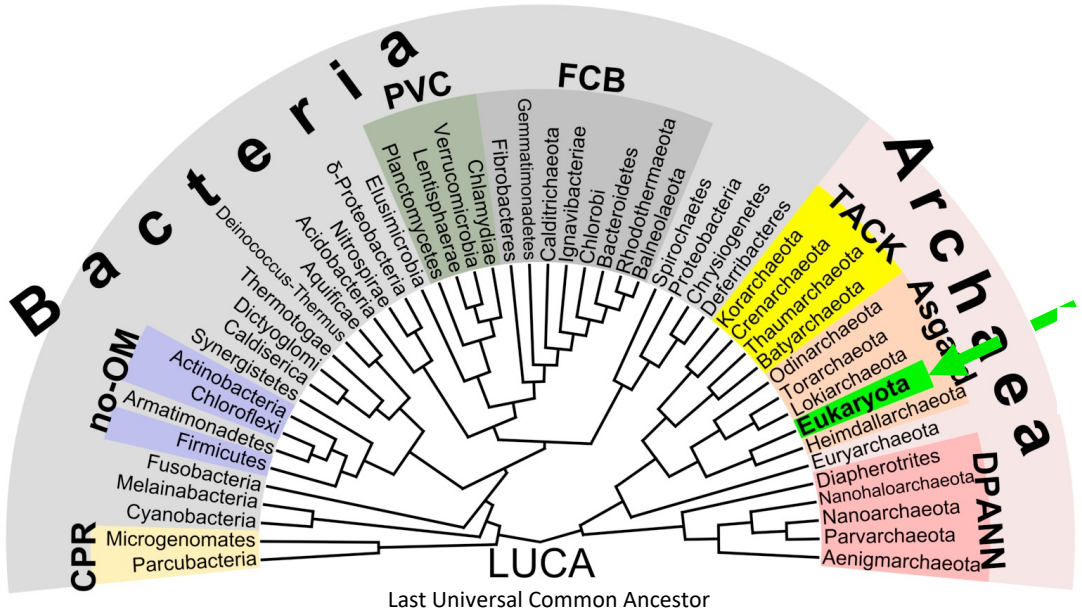


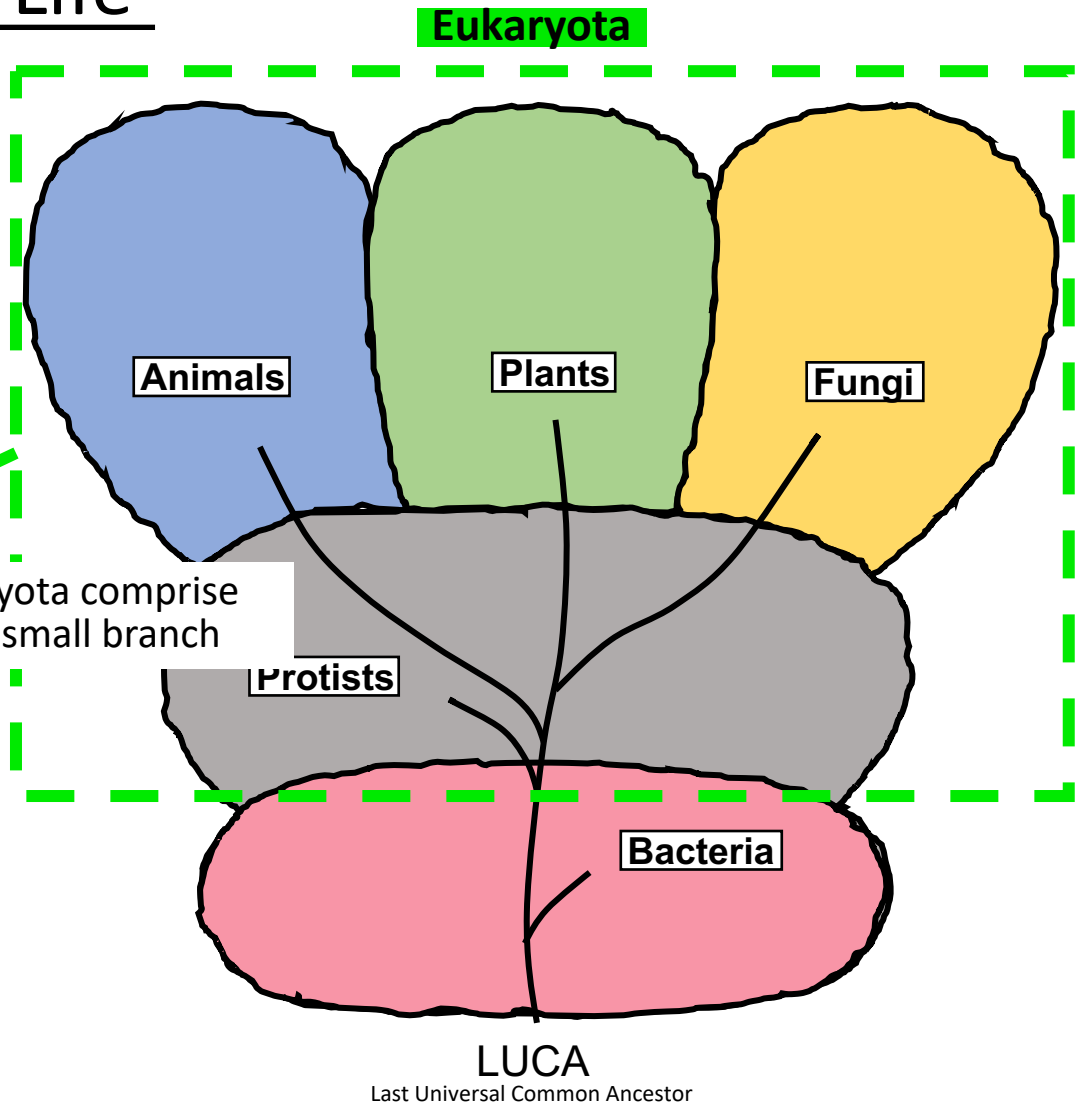


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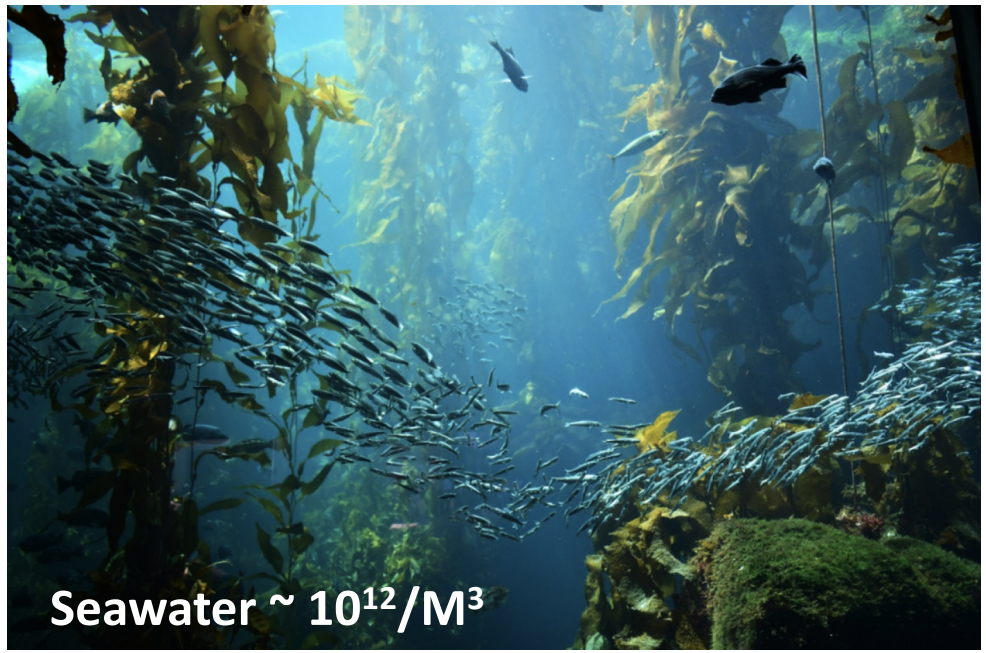
**THE DIVERSITY OF LIFE IS OVERWHELMINGLY MICROBIAL.**

# MICROBES ARE HIGHLY ABUNDANT…and they are everywhere.




Aquatic

Active, viable, persistent

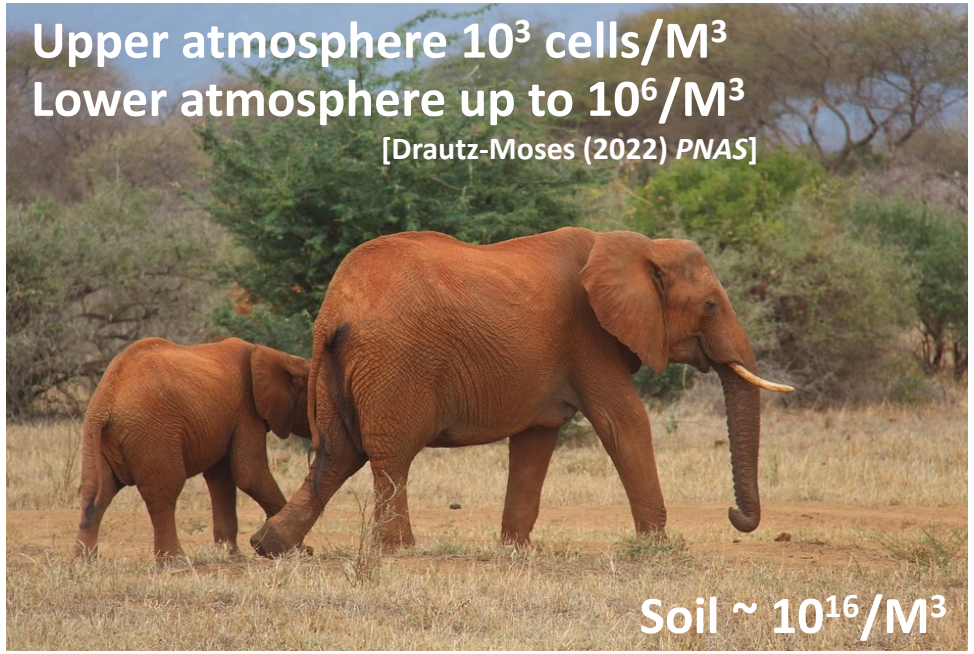
*water*

*soil*

*atmosphere*

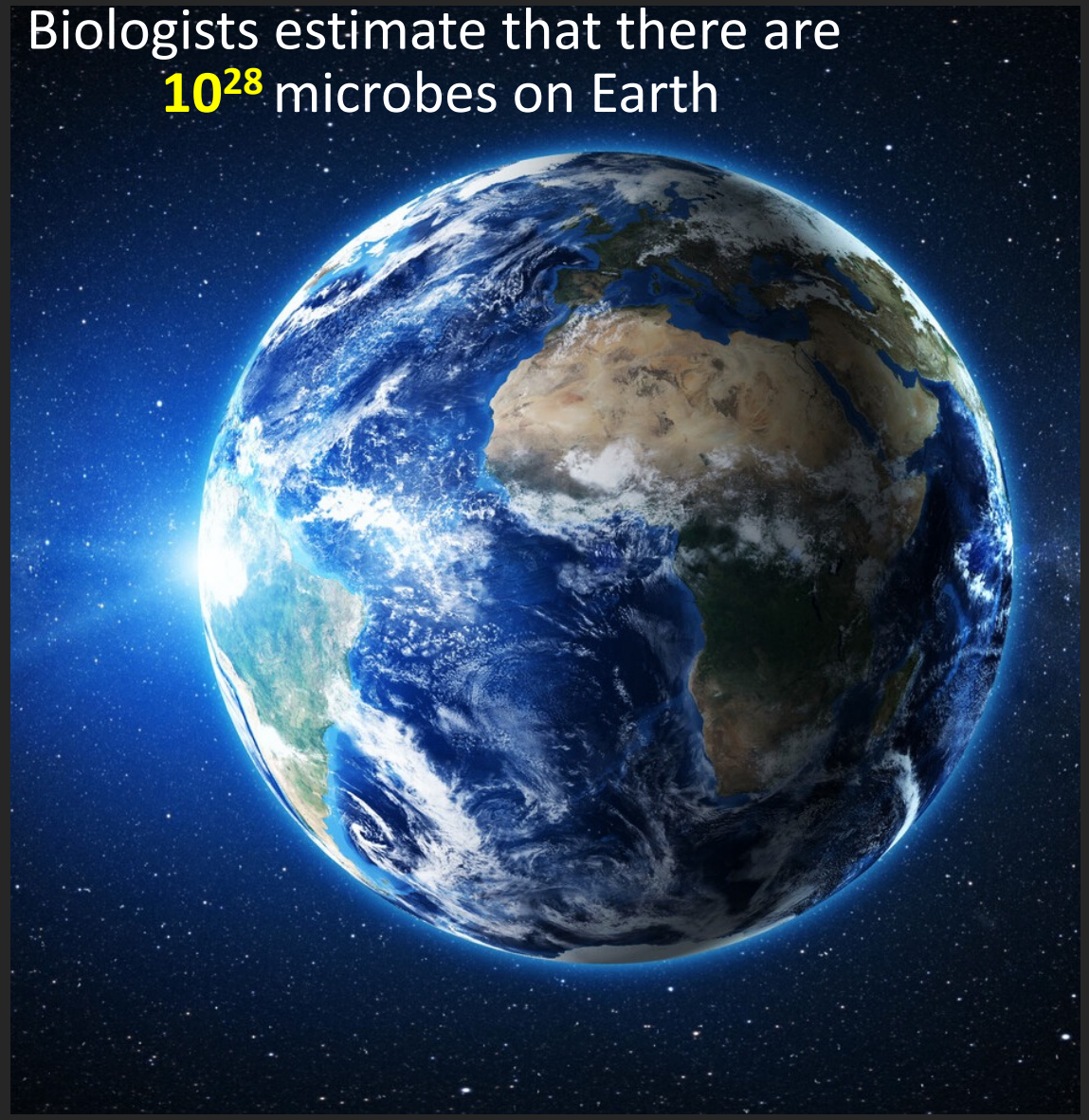
Inactive, non-viable ephemeral

Terrestrial



Astronomers estimate that there are $10^{24}$ stars in the sky

Biologists estimate that there are $10^{28}$ microbes on Earth



*Revolution through Technological Breakthrough – a New 'Lens'*

## ASTRONOMY

**Copernicus**

~ 60 years →

*[1540's – early 1600s]*

**Galileo**

**THIS INVENTION CHANGED OUR VIEW OF THE *UNIVERSE*,**
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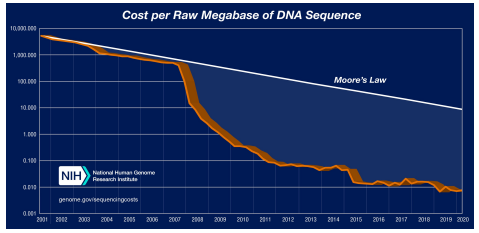
## BIOLOGY

**Carl Woese**

~ 30 years →

*[1970's – early 2000s]*

**'Next-Gen' Sequencing**




**THIS 'INVENTION' CHANGED OUR VIEW OF THE *BIOSPHERE*,**
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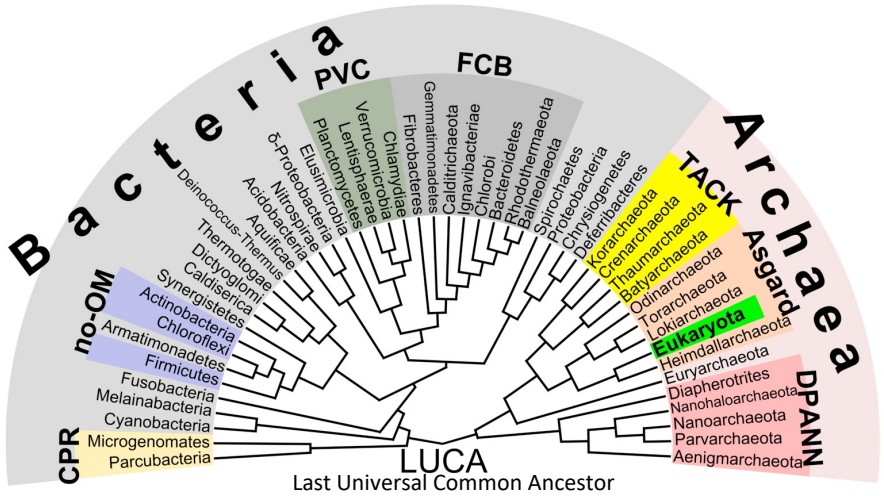
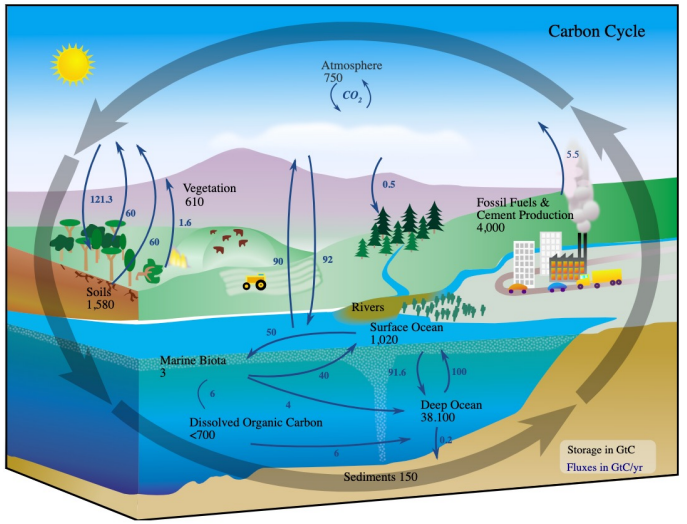
The activities of microbes drive the form and function of the biosphere, and are pivotal in shaping
the health of all sectors of the biosphere.




The impact of the phenomenal diversity of microbes and the ecological implications of this diversity continue to reshape the field of biology.

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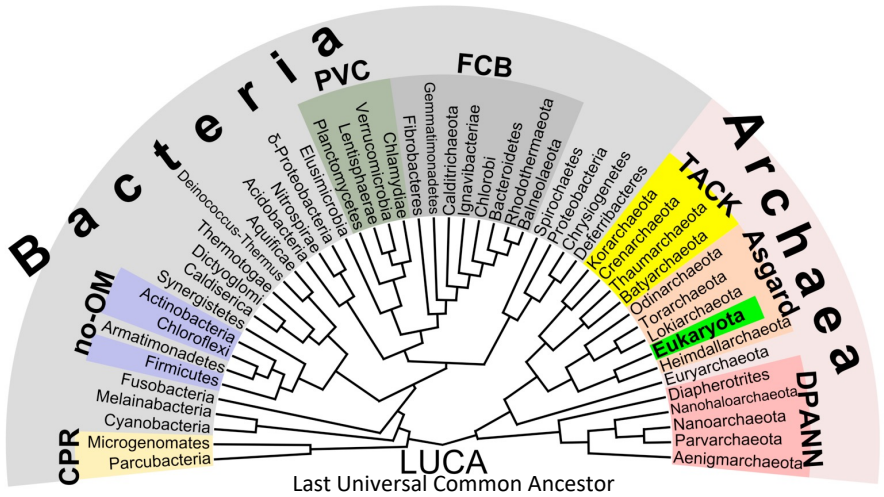


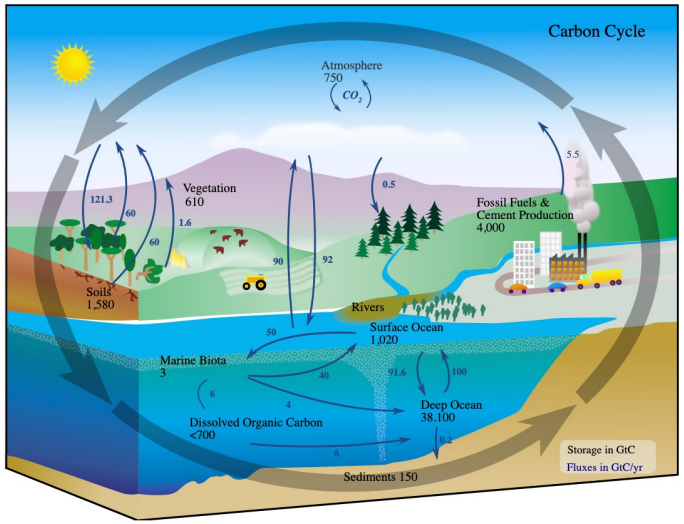


The impact of the phenomenal diversity of microbes and the ecological implications of this diversity continue to reshape the field of biology.

**A FEW EXAMPLES…**

Impact on a wide spectrum of biological research

## References in Europe PMC to 'microbiome' and '…'

**(through 1 August 2023)**

| | Total # | % last 3.5 years |
|---|---|---|
| 'soil' | 23,039 | 64 |
| 'plant' | 34,287 | 64 |
| 'ecology' | 26,564 | 67 |
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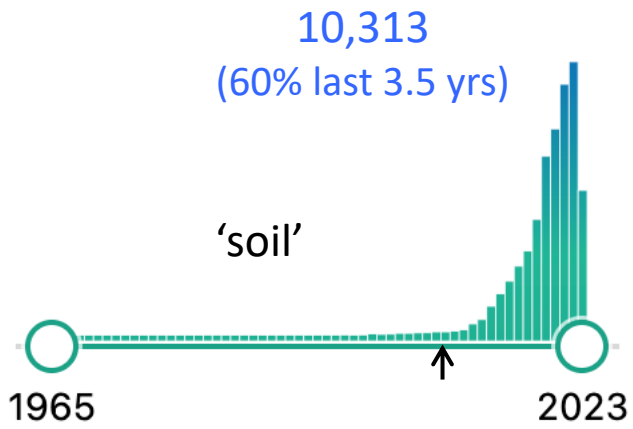
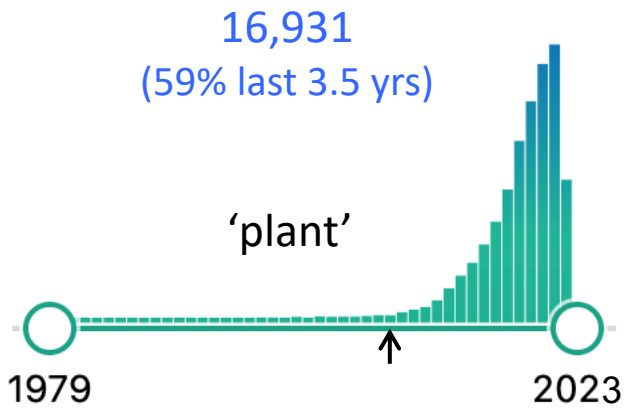
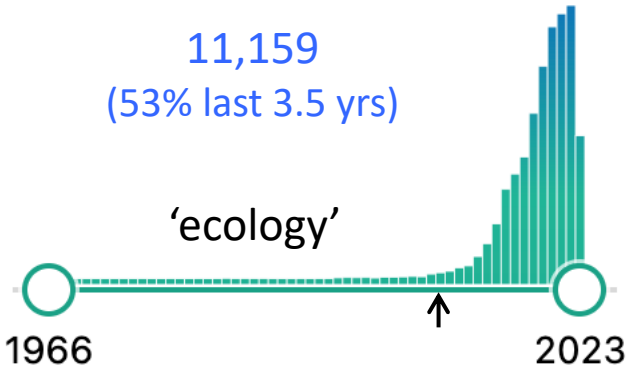
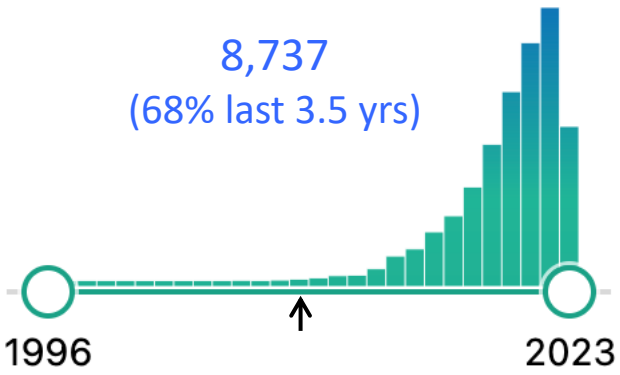


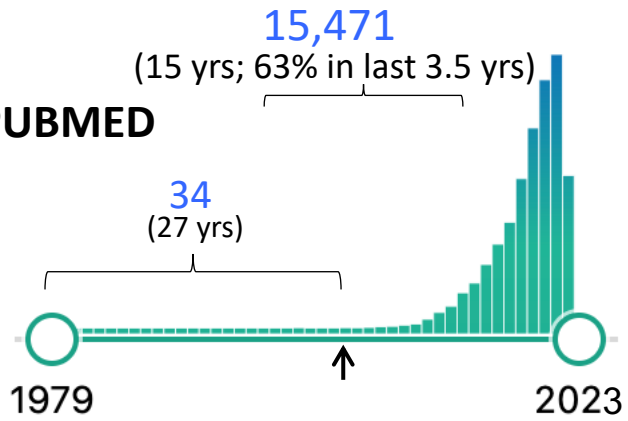

[ ↑ = 2008 ]

# ‘microbiome’ + ‘cancer’

**Europe PMC**

| Total # | % last 3.5 years |
|---|---|
| 48,699 | 64 |

**PUBMED**



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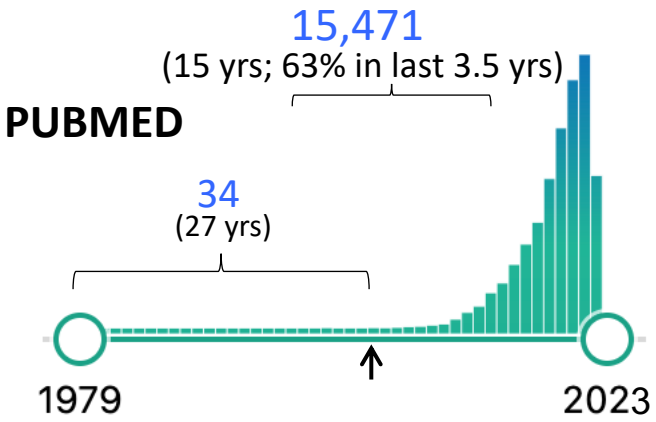
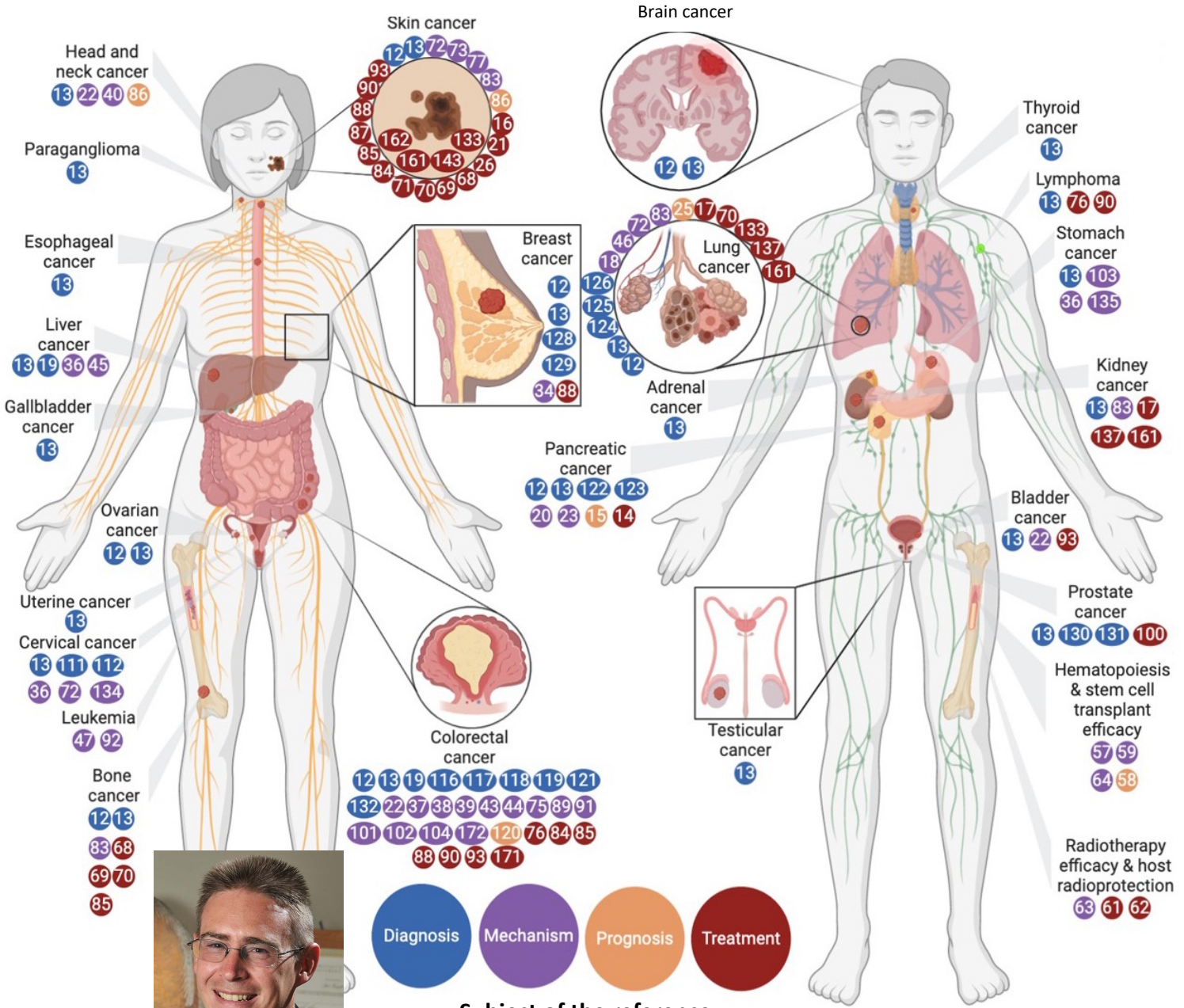



Sepich-Poore *et al.* (2021) **The microbiome & human cancer.** *Science* 371:eabc4552.

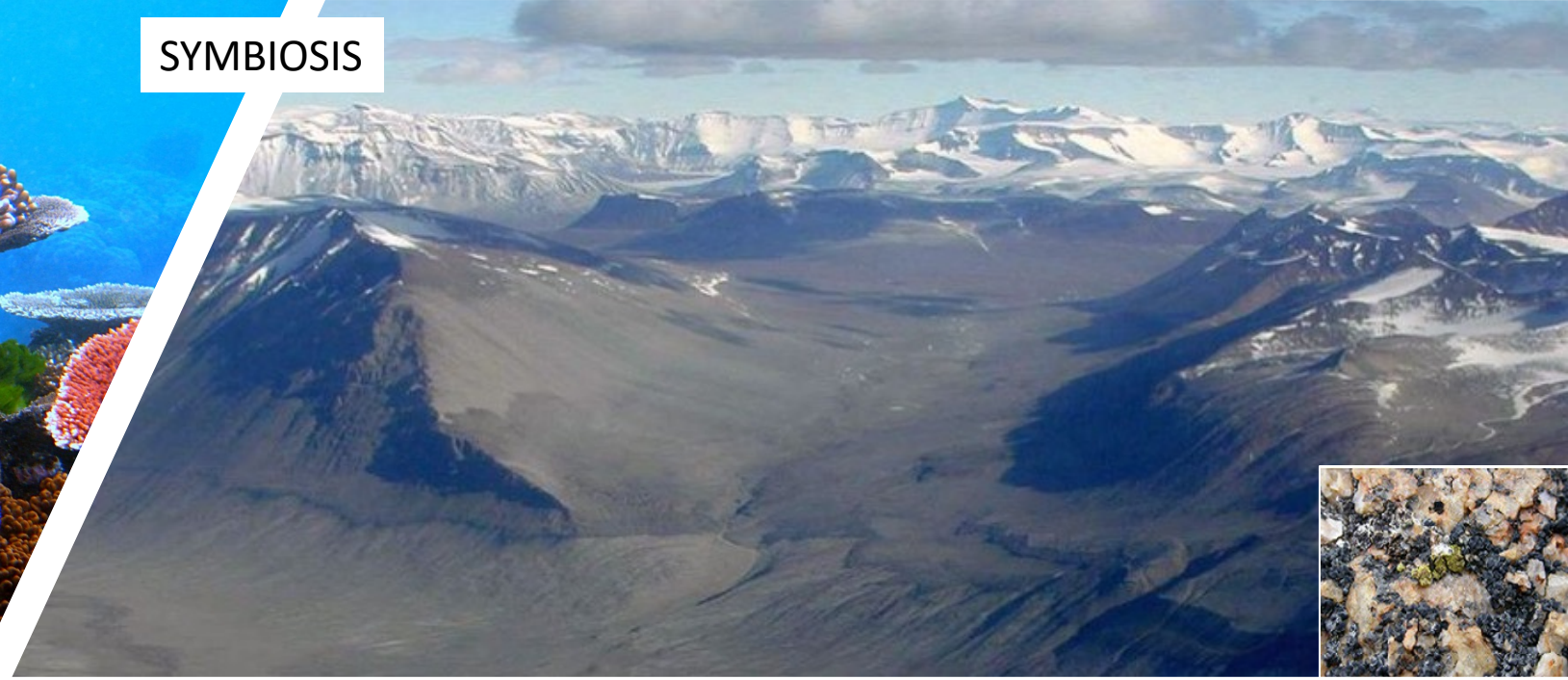
Sepich-Poore et al. (2022) **Cancer’s second genome.** *Bioessays* 44:e2100252.



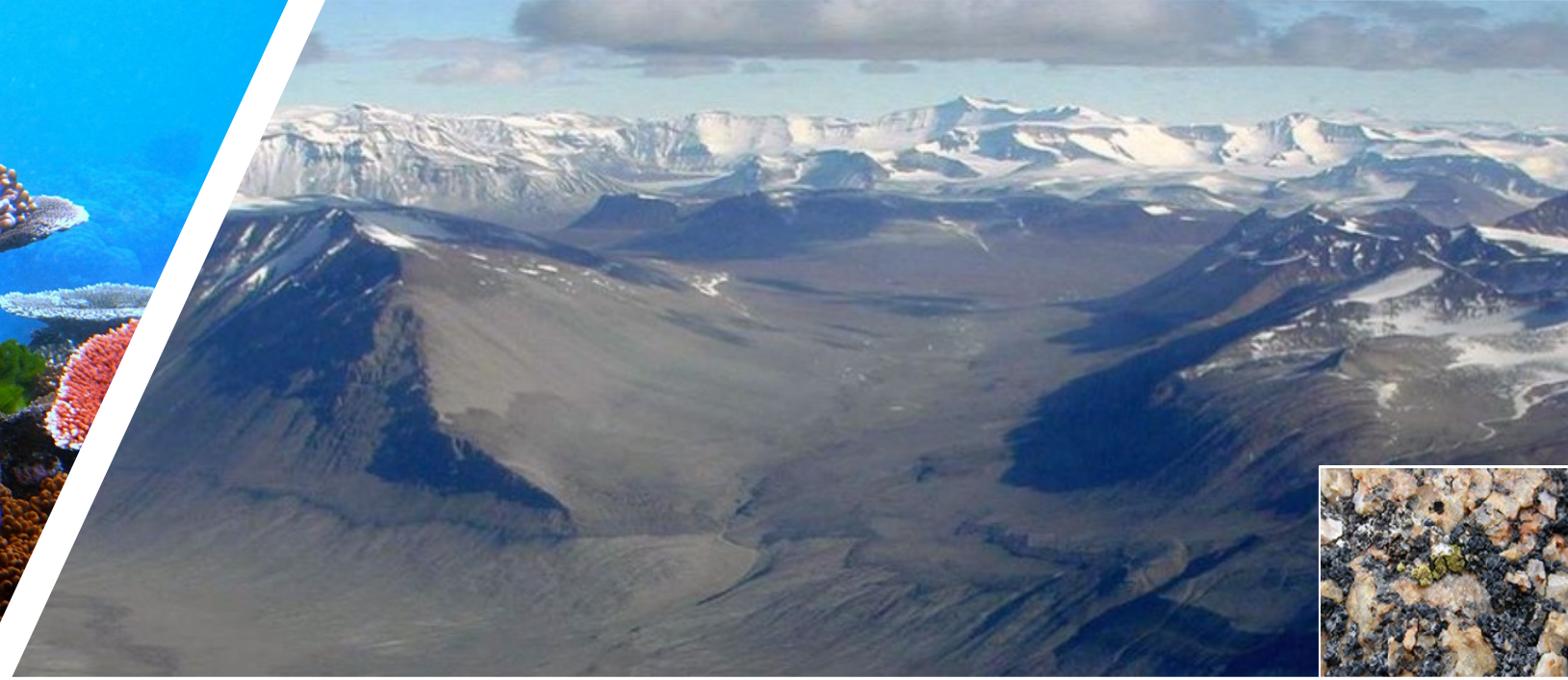

Rob Knight, UC San Diego – next week

This phenomenon of microbial integration occurs at the level of an individual organism – **ecosystems are ‘nested’**.

# SYMBIOSIS





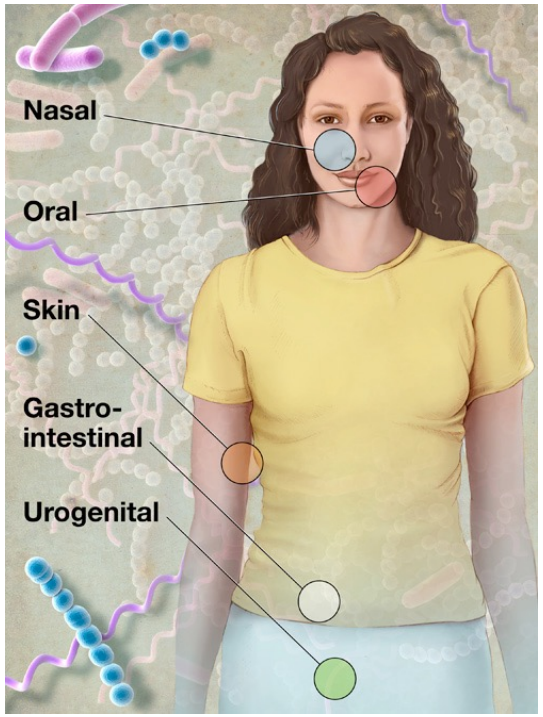


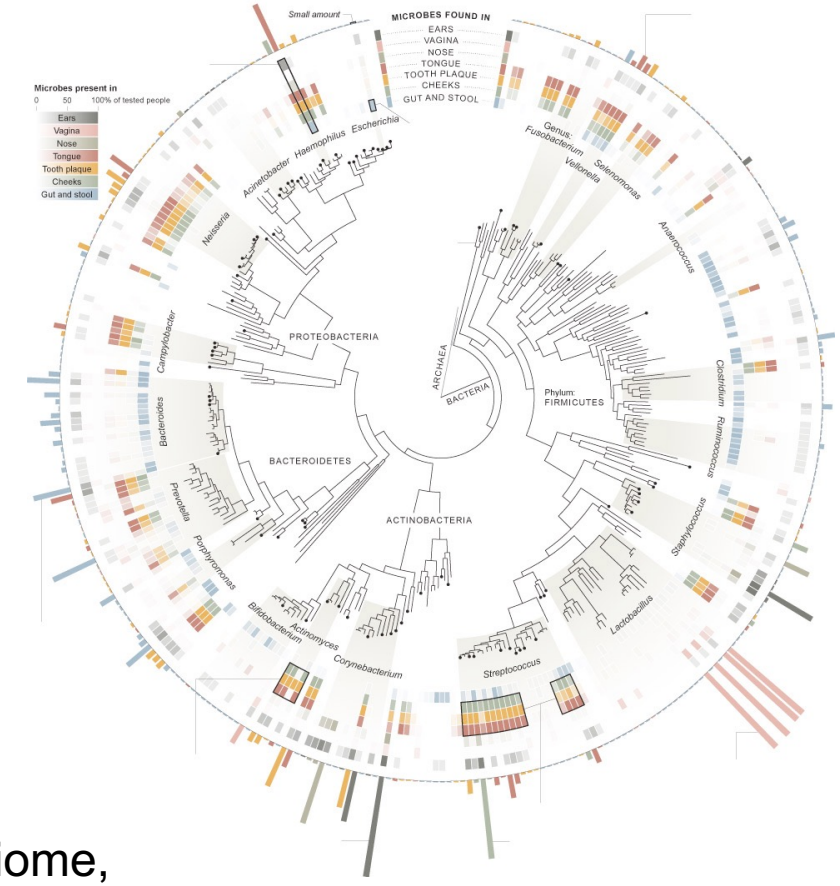


Symbiosis runs large sectors of the biosphere

# The healthy human is a nested ecosystem.

$10^{13}$ human cells




$10^{13}$ - $10^{14}$ cells in our microbiome, comprising 100s -1000s of species

*Tree of microbial species in and on our bodies*

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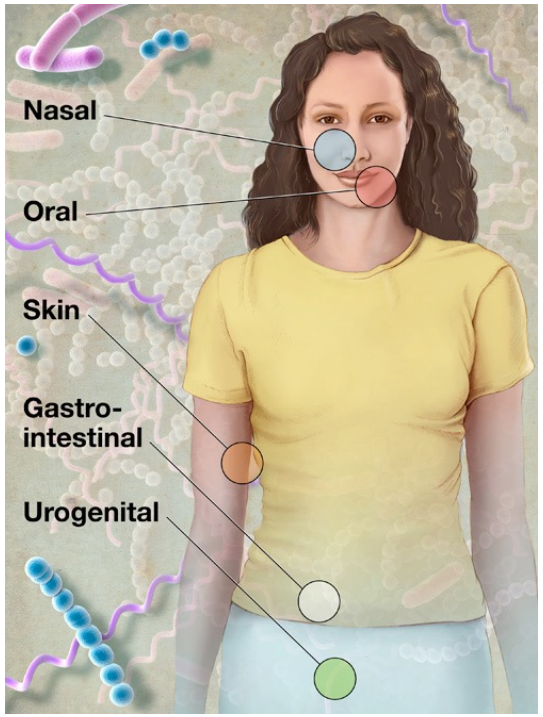
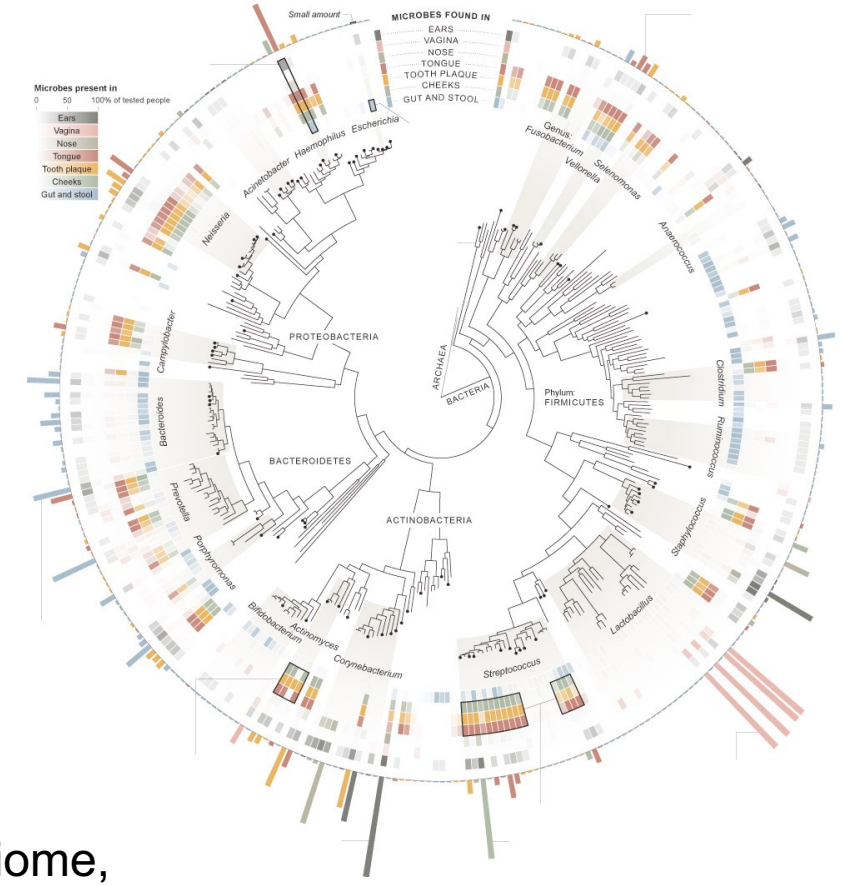


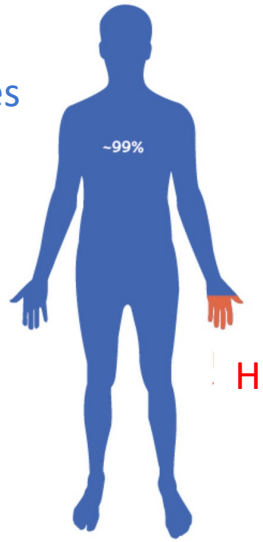




*Tree of microbial species in and on our bodies*

$10^{13}$ - $10^{14}$ cells in our microbiome, comprising 100s -1000s of species

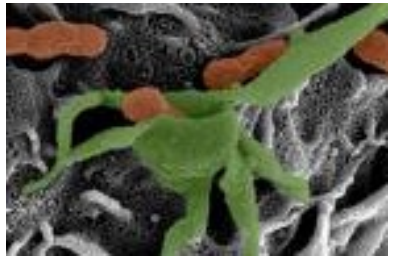
Proportion of unique genes in the human body

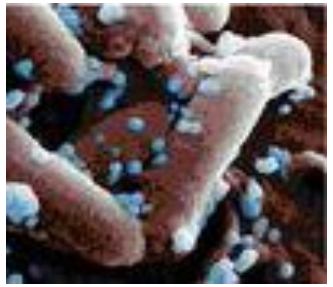
Microbial genes
~2,000,000




Human genes
~23,000

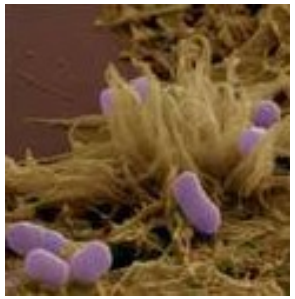
**Only about 1% of the genes are human.**





## A formidable challenge:

Integrating this critical new knowledge
into our conceptual framework
of biological sciences

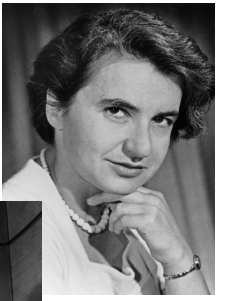


# Why is integrating these ideas difficult?

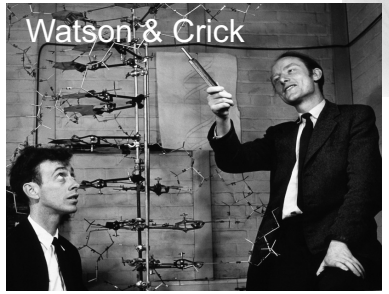
To address all the implications of the *20th century revolution*, biology went into deep 'silos', i.e., specializations.

This 'silos' are reflected in the structures of departments at institutes, universities, funding agencies, etc.

DNA as the genetic material



Franklin



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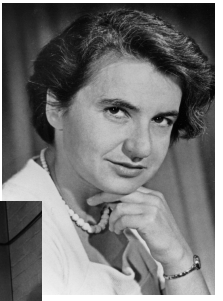

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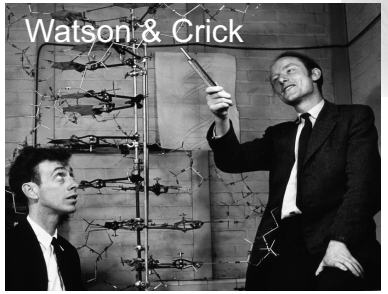


*Hierarchy of Life*

- biosphere
- ecosystem
- community
- population

ECOLOGY

- organism
- organ system
- organ
- tissue

ORGANISMAL BIOLOGY

- cell
- organelle

CELL BIOLOGY

- molecule
- atom

MOLECULAR BIOLOGY

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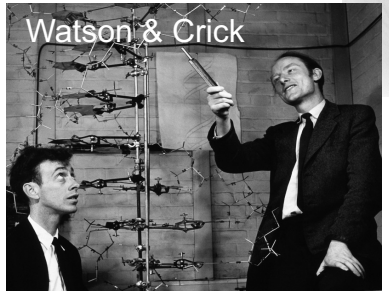


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MOLECULAR BIOLOGY

*An example:* In the US, a college student can receive an undergraduate degree in biology (BS, Bachelor of Science) with a single lecture on the microbial world.

# A CONCEPTUAL CHALLENGE – microbes as partners in health

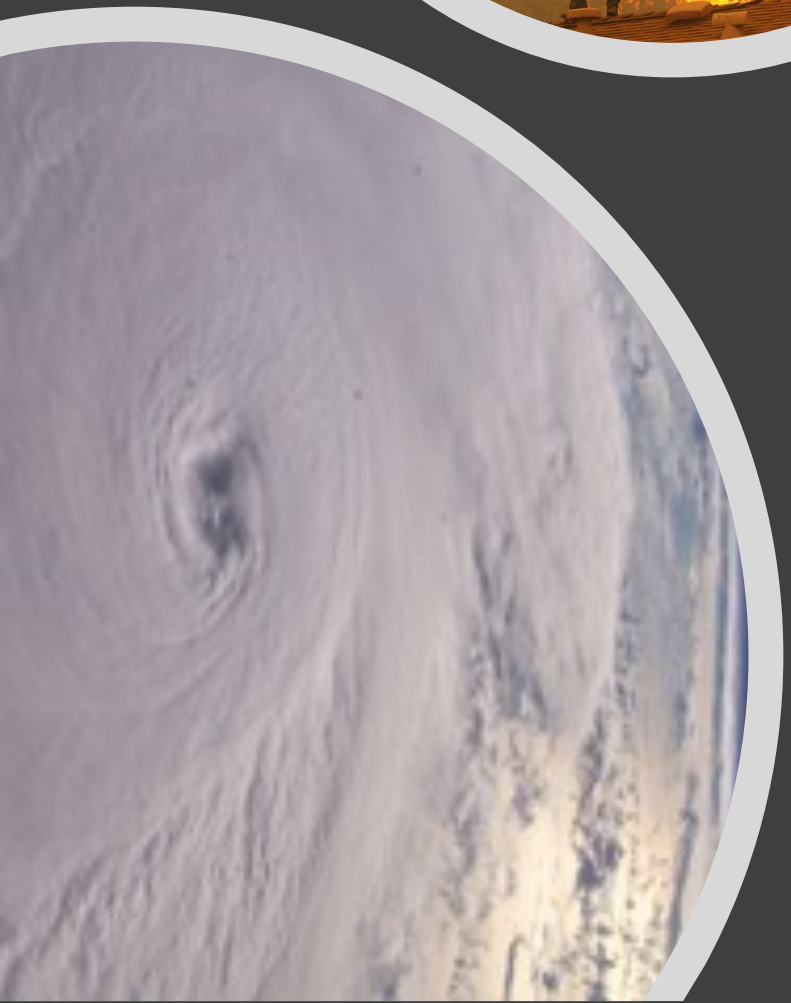
**Pathogenic Microbiology**

**Robert Koch (1843 - 1910) and others**

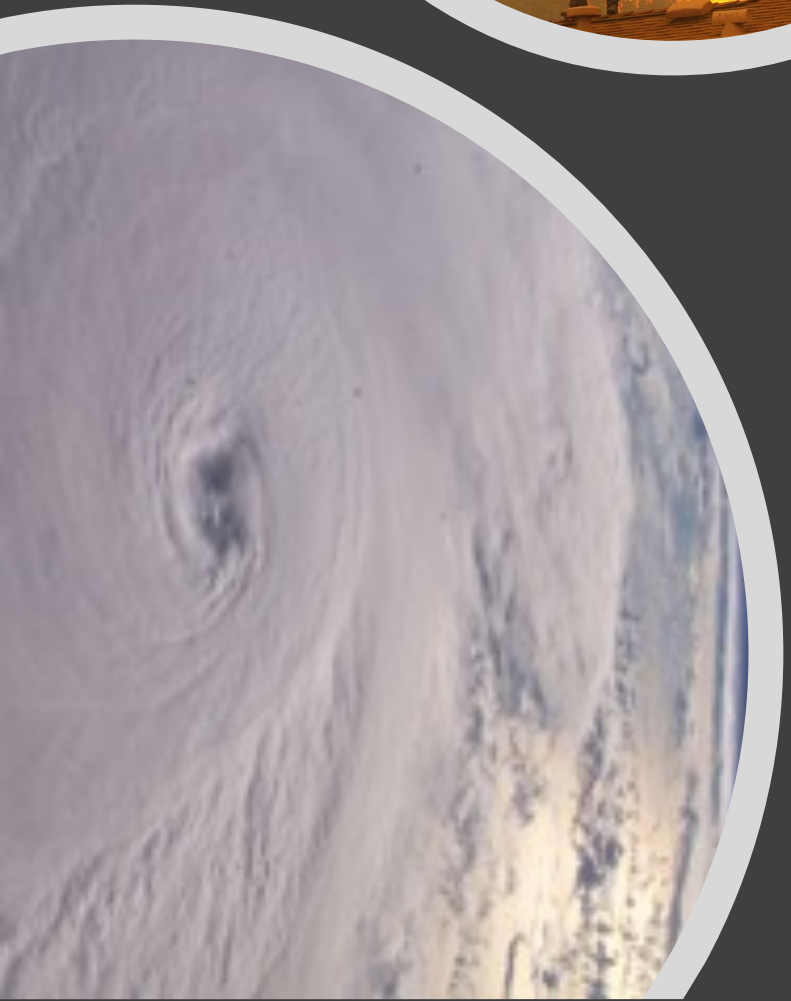
**Environmental Microbiology**

**Sergei Winogradsky (1856 - 1953) and others**

**?**



Why this so important at this time?

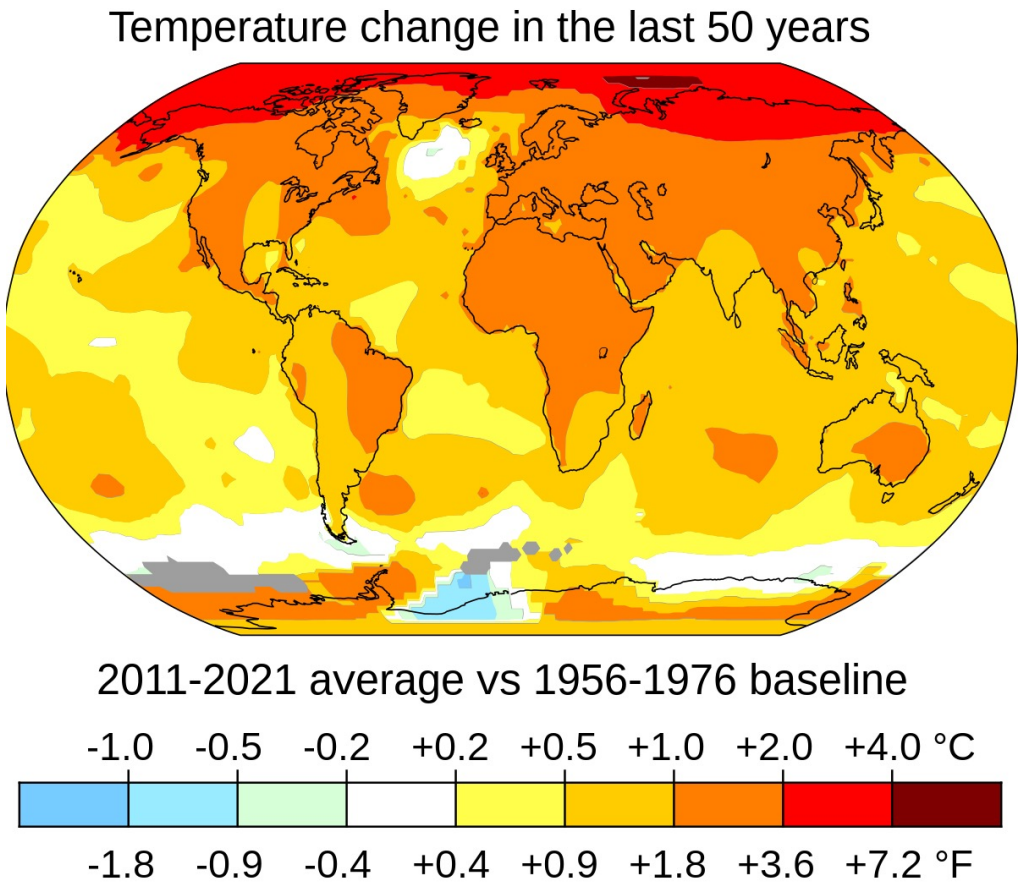


Why this so important at this time?

*A CLIMATE CRISIS!*

# *A CLIMATE CRISIS!*

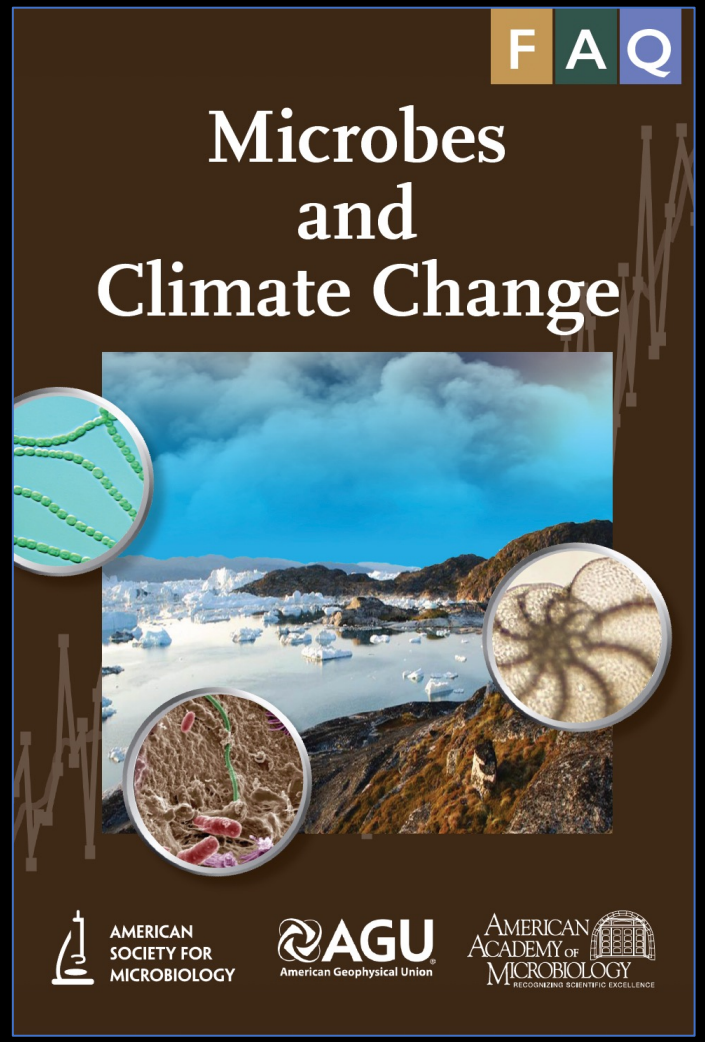
## PUSHING THE REVOLUTION FORWARD IS CRITICAL.




***We <u>cannot</u> be effective and creative with solutions if we don't have an accurate concept of the structure and function of the biological world.***

Failures to integrate:

AMERICAN SOCIETY FOR MICROBIOLOGY




*Only about microbes…*

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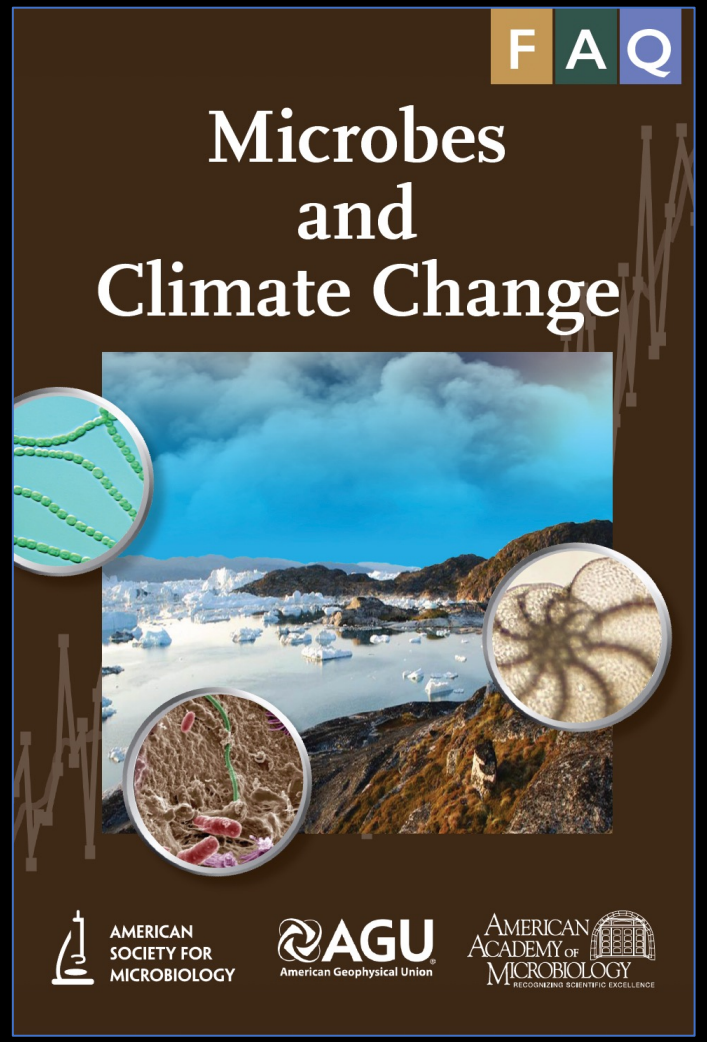
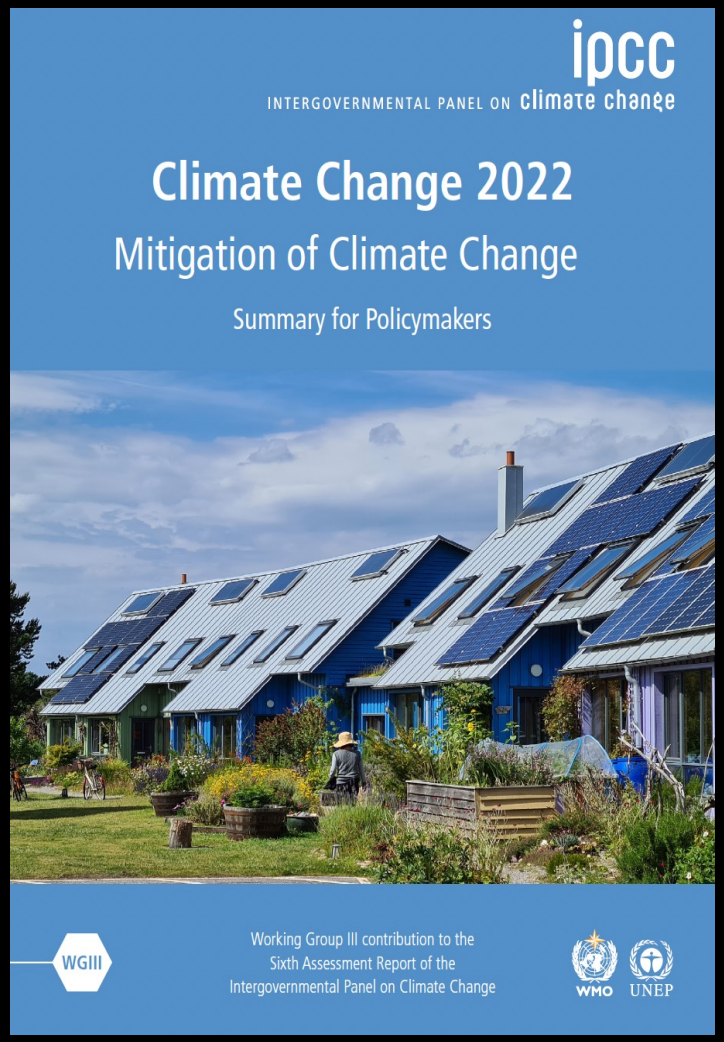


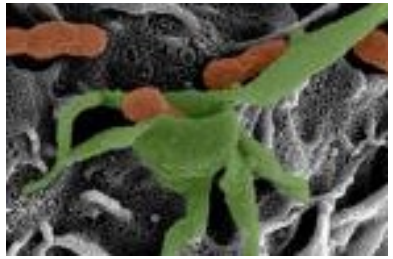

*Only about microbes…*

NATIONAL ACADEMY OF SCIENCES




*Nothing about microbes…*

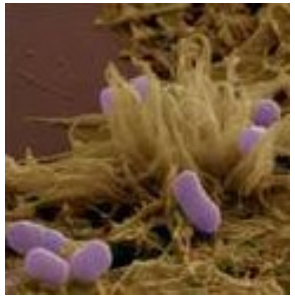
# Shaping the Change in Our Conceptual Framework

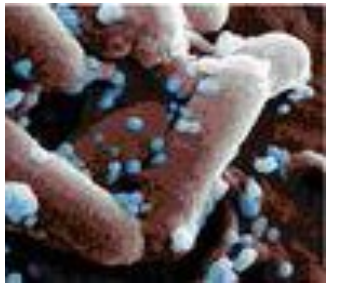


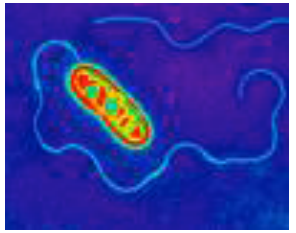
***Some Goals/Strategies:***

***1. Integrate macro-and microbiology unifying biology's conceptual framework***

- allows us to know what's critical for life processes on Earth







# But…change is happening!

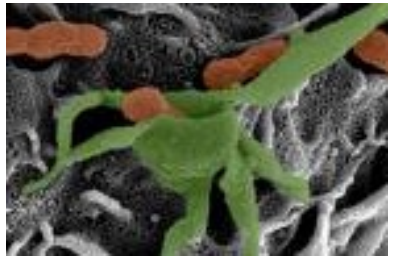
Reforestation including natural microbiomes

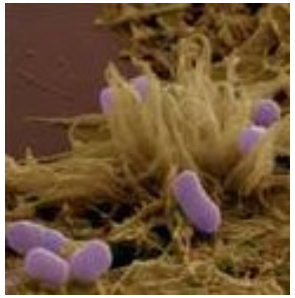
Preventing coral bleaching by genetic engineering

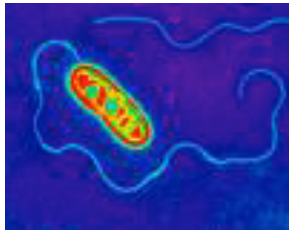

Kour D, Yadav AN (2022) Bacterial mitigation of drought stress in plants: Current perspectives and future challenges. *Curr Microbiol* 79:248.

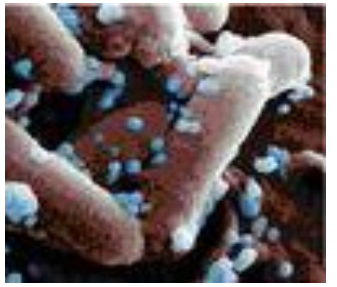
Li, J *et al.* (2023) Experimental temperatures shape host microbiome diversity and composition. *Glob Chang Biol* 29:41-56.

# Shaping the Change in Our Conceptual Framework









***Some Goals/Strategies:***

***1. Integrate macro-and microbiology unifying biology's conceptual framework***

- allows us to know what's critical for life processes on Earth

2. ***Engage physical scientists, mathematicians, anthropologists, sociologists, etc.***

- global problems – biological (food, health, energy, ecological environment)
- solutions across the sciences and humanities

# Mahalo nui loa!

[Hawaiian - Thank you very much]

The Hawaiian Bobtail Squid –
*Euprymna scolopes*

Its Luminous Bacterial Partner -
*Vibrio fischeri*