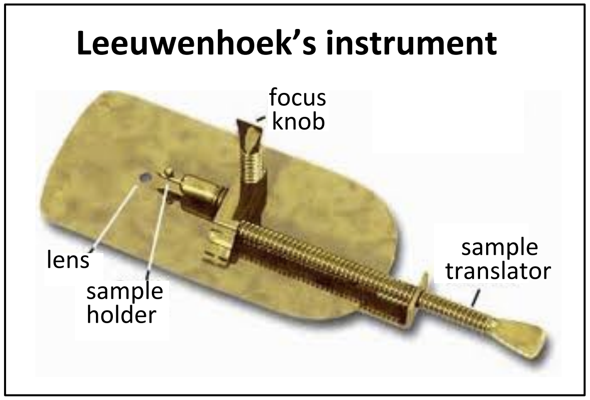

Animals in a Bacterial World:
A New Imperative for the Life Sciences
Margaret McFall-Ngai
University of Wisconsin-Madison
and California Institute of Technology

Anton van Leeuwenhoek – The Father of Microbiology

[1632-1723]

October 9, 1676



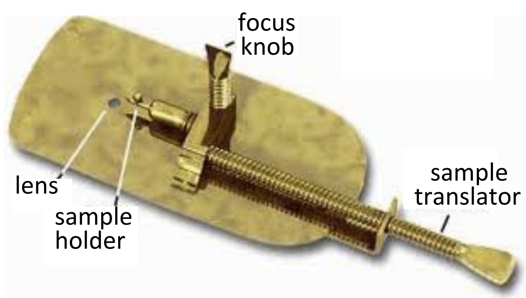
Anton van Leeuwenhoek – The Father of Microbiology

[1632-1723]

October 9, 1676

1683 – DISCOVERED BACTERIA IN CHEEK SWAB 'ANIMICULES'

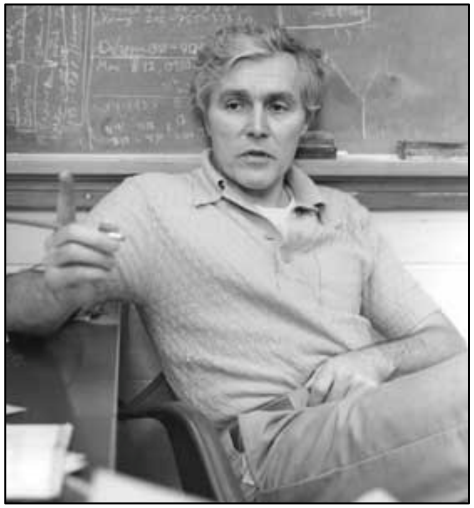
Leeuwenhoek's instrument



Two questions arose:

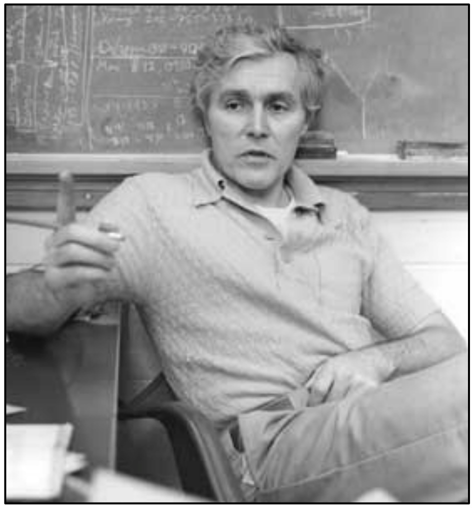
1) What are they?
2) What are they doing?

FAST FORWARD ~300 years ……………………….1977



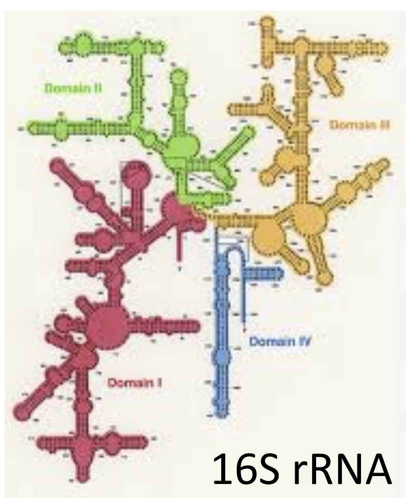
Carl Woese (b. 1928)

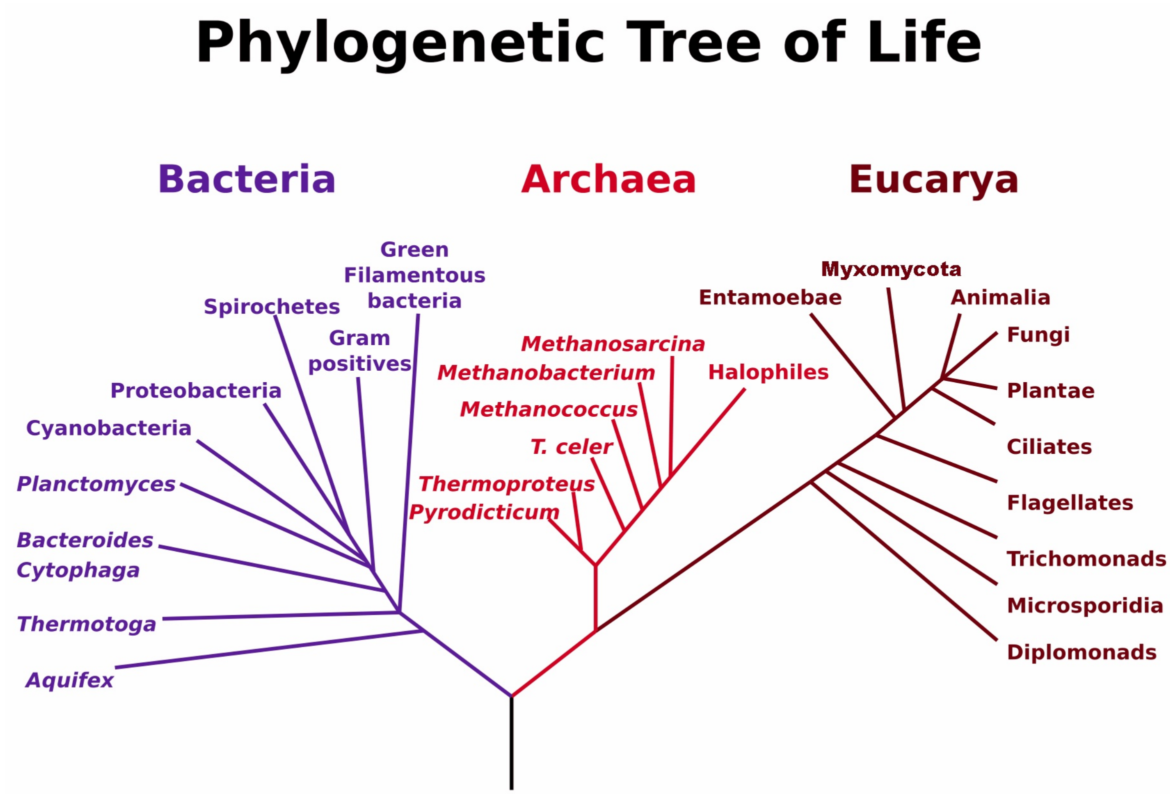
FAST FORWARD ~300 years ……………………..1977



Carl Woese (b. 1928)

Woese's 'Instrument'





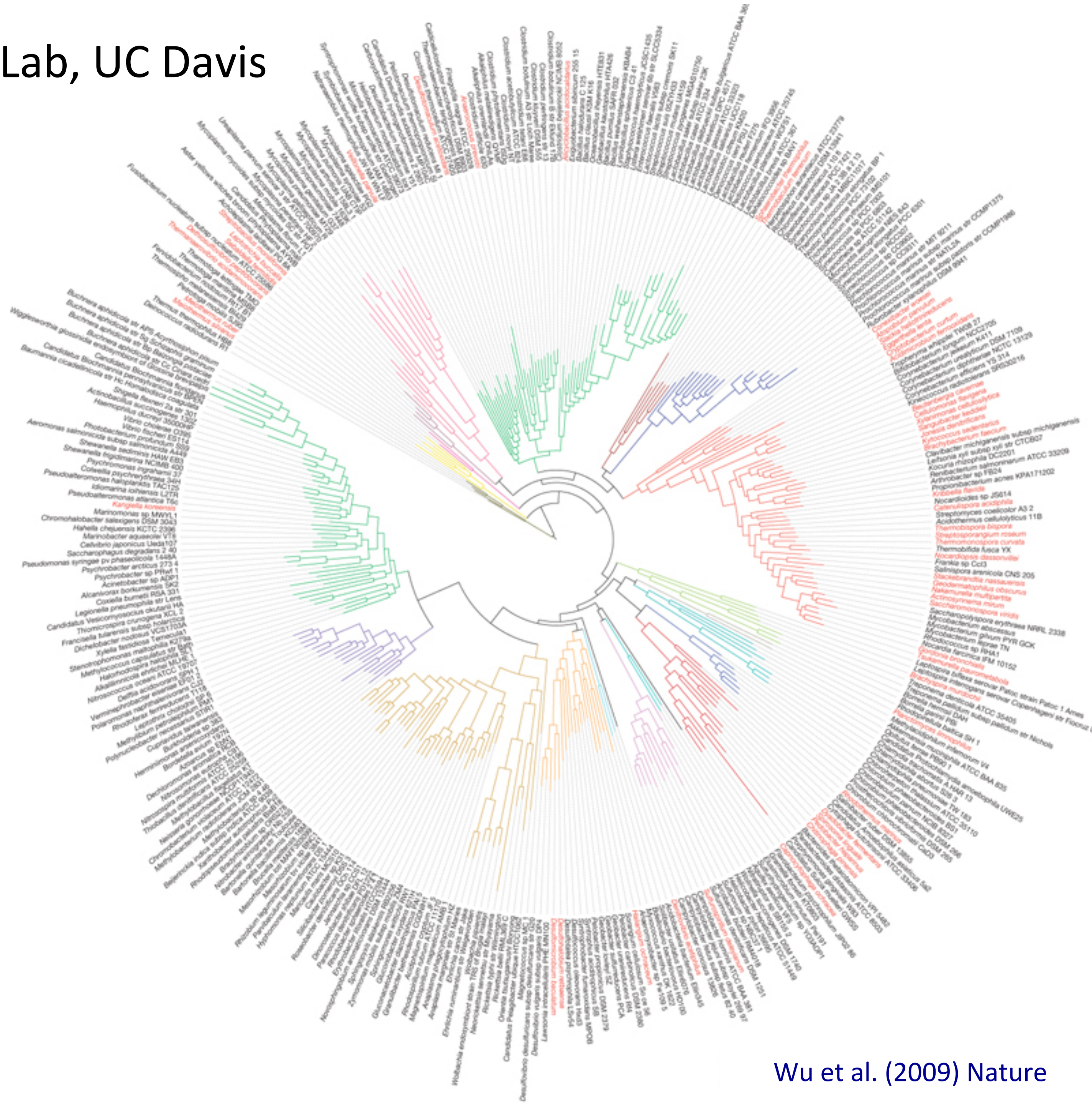
Woese *et al.* (1990) *PNAS* 87 (12): 4576–9.

Jonathan Eisen's Lab, UC Davis

PCR!!!!

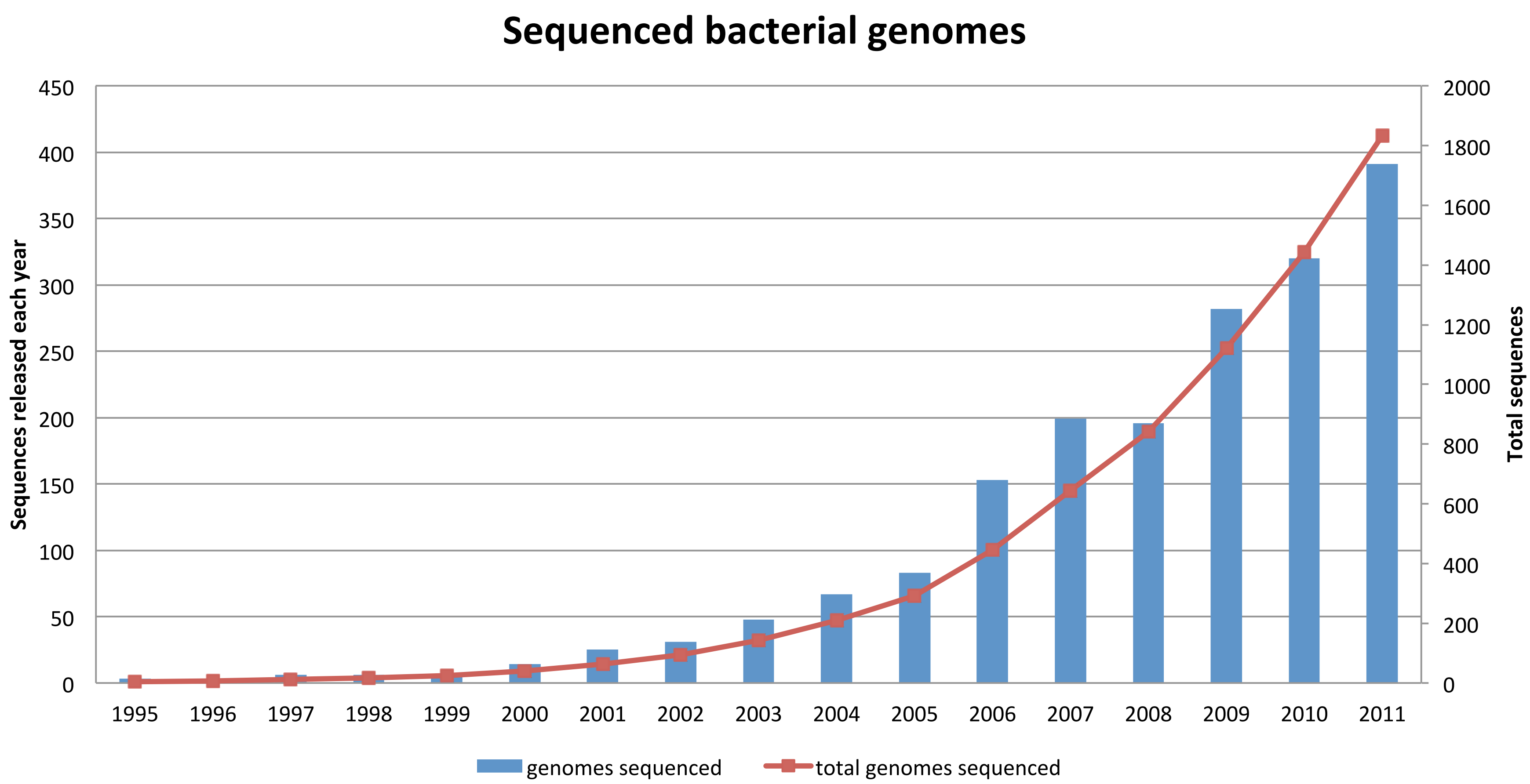
Kary Mullis

Science 1985



Wu et al. (2009) Nature

Heading to the '$1' genome



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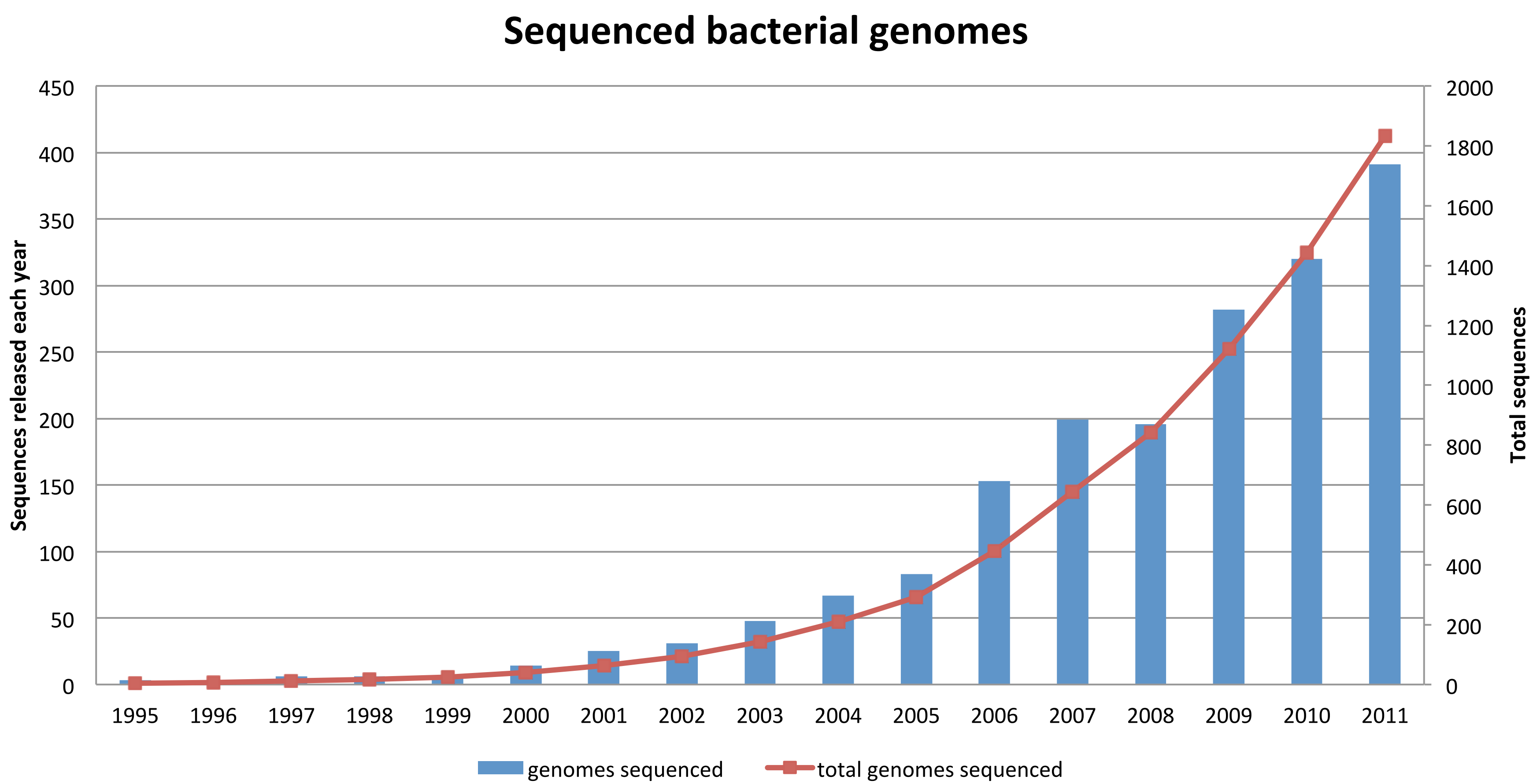

Cyrus Chothia (*Nature*, 1992) - predicted no more than 1,000 protein families

Pfam (Protein family database -Wellcome Trust Sanger Institute – est. 1998)

--as of Nov. 2011 ~14,000 protein families; discovery rate of 2-3 new families/day

Lesson from these data:

THE VAST DIVERSITY OF THE BIOSPHERE
IS IN THE MICROBIAL WORLD.

How will these new insights change biology?

How will these new insights change biology?

NESCent
National Evolutionary Synthesis Center

Catalysis Meeting:

"The origin and evolution animal-microbe interactions"

October 23-27, 2011

[One slice - focus was animal-bacteria]

Acknowledgments

National Evolutionary Synthesis Center (NESCent) Catalysis Meeting – Oct 23-27, 2011

Participants:

Thomas Bosch	Cell biologist/symbiosis	Christian Albrechts U, Kiel, Germany
Hannah Carey	Digestive physiology/immunology	U Wisconsin-Madison
Bernie Degnan	Evolution of development	U Queensland, Australia
Tomislav Domazet-Loso	Genomics	Ruder Boskovic Institute, Croatia
Angela Douglas	Symbiosis	Cornell U
Nicole Dubilier	Chemoautotrophy/oceanography	Max Planck Inst, Bremen, Germany
Gerard Eberl	Lymphoid tissue development	Pasteur Institute, Paris, France
Tadashi Fukami	Systems ecology	Stanford U
Scott Gilbert	Ecology of development	Swarthmore College
Michael Hadfield	Larval biology	U Hawaii
Ute Hentschel	Sponge biology/microbiology	U Wuerzburg, Germany
Nicole King	Animal origins/genome evolution	UC Berkeley
Staffan Kjelleberg	Microbial ecology/biofilms	U New South Wales, Australia
Andrew Knoll	Paleontology	Harvard U
Natacha Kremer	Evolution of symbiosis	U Wisconsin-Madison
Sarkis Mazmanian	Immunology/mammalian-microbe	California Inst Technol
Jessica Metcalf	Bioinformatics	U Colorado-Boulder
Margaret McFall-Ngai	Animal-bacterial associations	U Wisconsin-Madison
Ken Nealson	Bacterial physiology/geomicrobiology	U Southern California
Naomi Pierce	Ecology/evolution of interactions	Harvard U
John Rawls	Host-microbe interactions in the gut	UNC Chapel Hill
Ann Reid	Science policy	American Academy of Microbiology
Mary Rumpho	Lateral gene transfer, organelles	U Maine
Edward Ruby	Microbial metabolic pathways	U Wisconsin-Madison
Jon Sanders	Evolutionary biology/symbiosis	Harvard U
Diethard Tautz	Genomics	Max Planck Inst, Plon, Germany
Jennifer Wernegreen	Evolutionary biology	Duke U

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Five groups explored the effects of bacteria on animals and animals on bacteria in the following contexts:

ANIMALS ⟺ BACTERIA

Origins

*Andrew Knoll
Ute Hentschel
Nicole King
Ken Nealson
Jon Sanders

Ecology

*Nicole Dubilier
Tadashi Fukami
Staffan Kjelleberg
Naomi Pierce
Ann Reid

Genomics

*Jennifer Wernegreen
Tomislav Domazet-Loso
Jessica Metcalfe
Mary Rumpho
Diethard Tautz

Development

*Thomas Bosch
Bernard Degnan
Scott Gilbert
Natacha Kremer
John Rawls

Communication

*Ned Ruby
Hannah Carey
Angela Douglas
Gerard Eberl
Sarkis Mazmanian

*Group leader

1 History/Context

3 Origins

*Andrew Knoll
Ute Hentschel
Nicole King
Ken Nealson
Jon Sanders

2 Ecology

*Nicole Dubilier
Tadashi Fukami
Staffan Kjelleberg
Naomi Pierce
Ann Reid

4 Genomics

*Jennifer Wernegreen
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ANIMALS ⇔ BACTERIA

5 Development

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John Rawls

6 Communication

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Sarkis Mazmanian

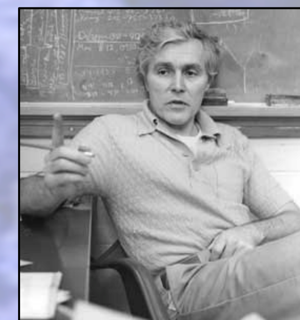
7 Summary/Horizons

Two impediments to integration of microbiology into other areas of biology:

- technical
- conceptual

1680

?



1980

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- **- technical**
- **- conceptual**

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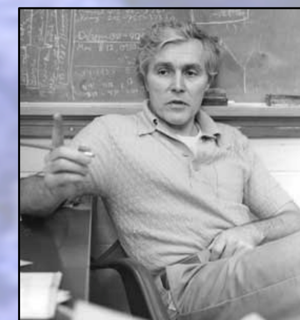
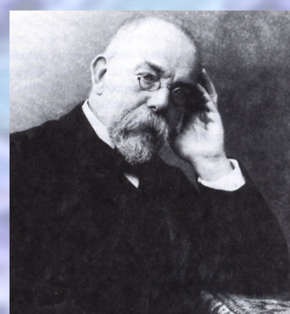


1980



Pathogenic Microbiology

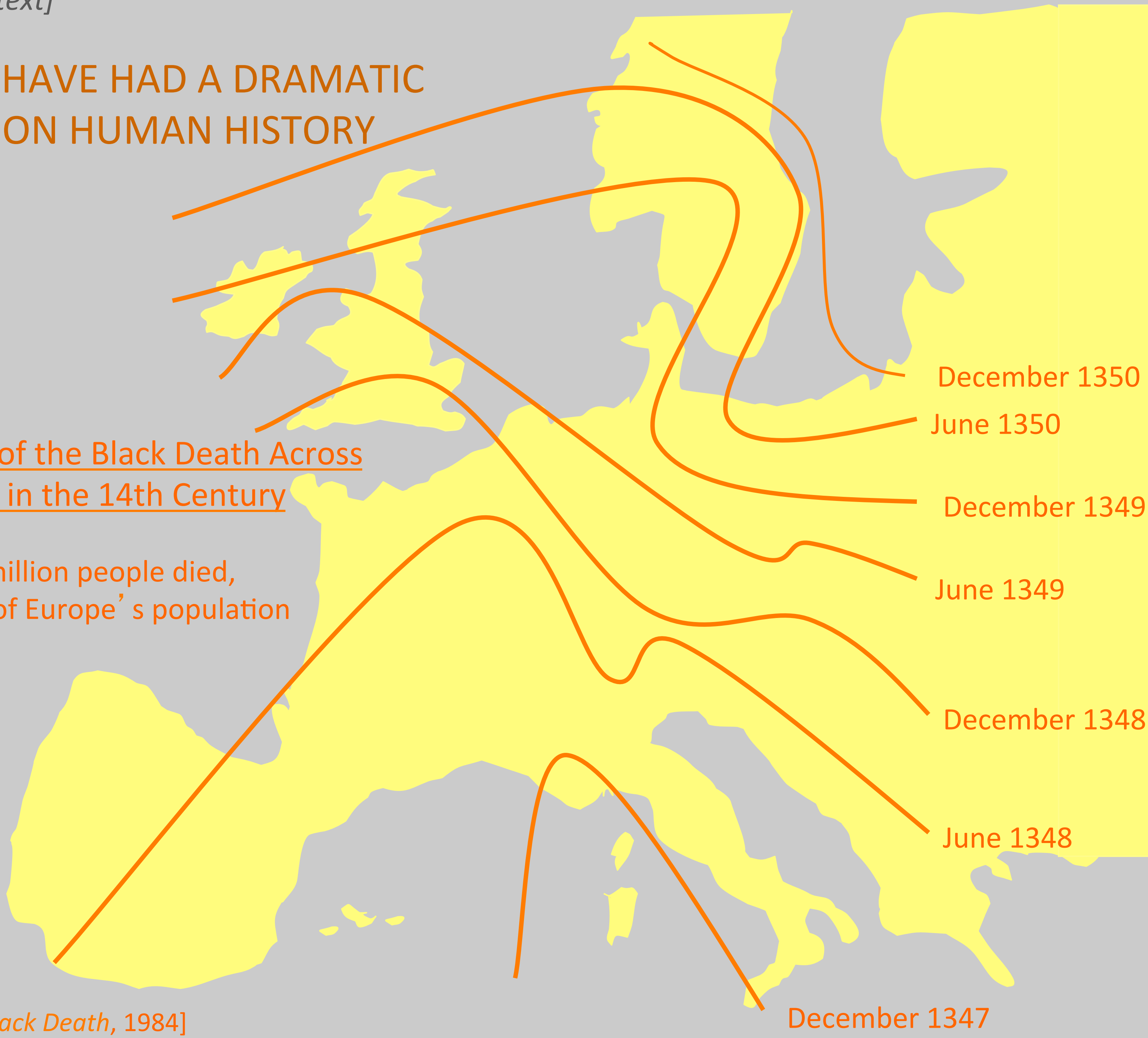
Robert Koch (1843-1910)
and others

Animal biology

Environmental Microbiology

Sergei Winogradsky (1856 - 1953)
and others

MICROBES HAVE HAD A DRAMATIC IMPACT ON HUMAN HISTORY



The Spread of the Black Death Across Europe in the 14th Century

20 million people died,
30-50% of Europe's population

[G. Twigg, *The Black Death*, 1984]

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- **technical**
- **conceptual**

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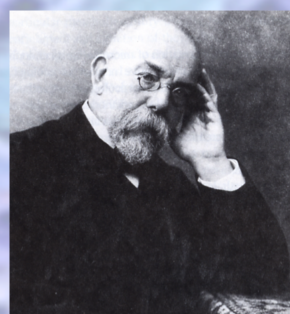

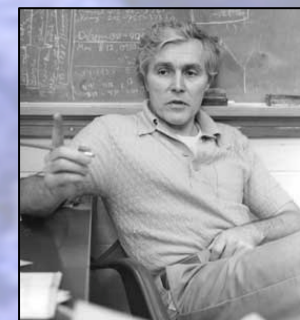

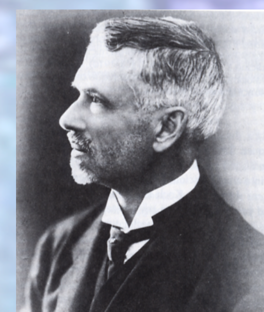

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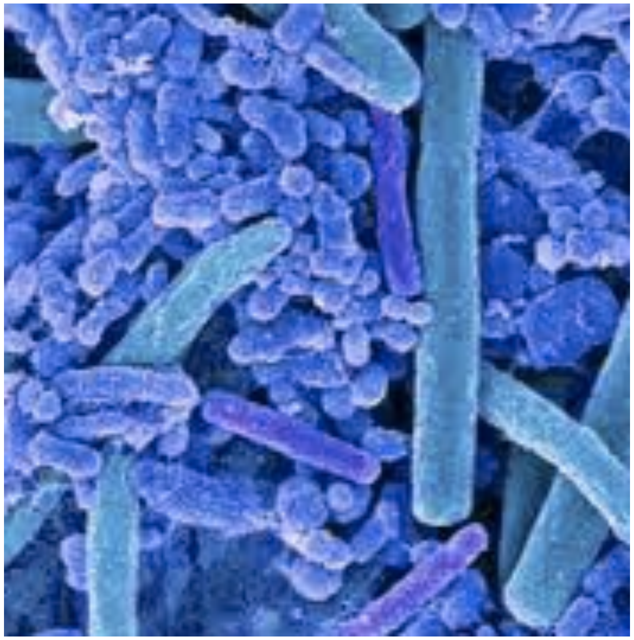
Summary/Horizons

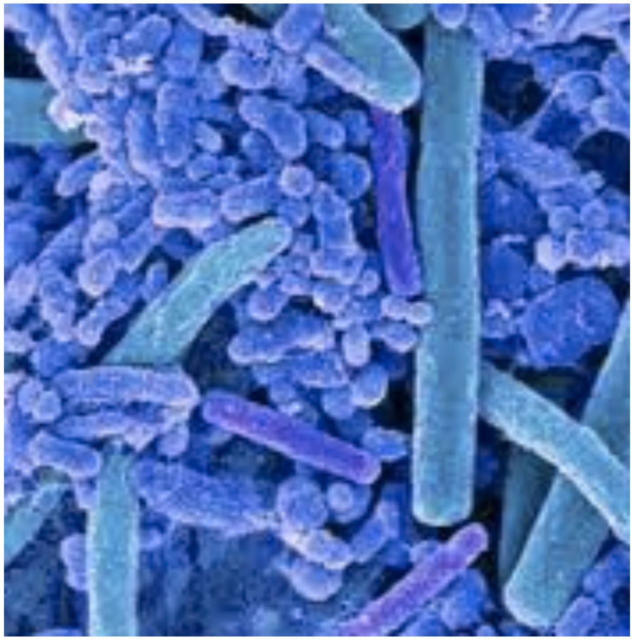
Traits

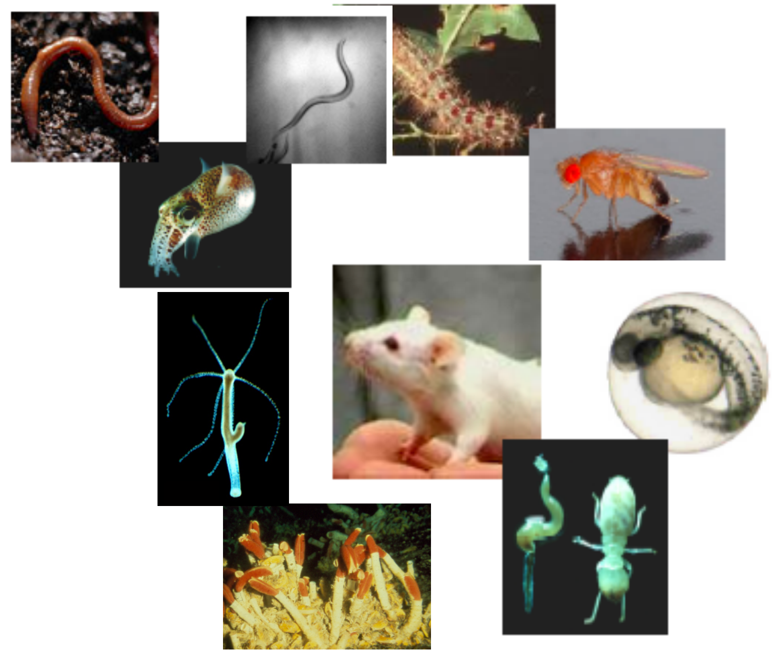


Microbes

Small (~0.2 - ~750 µm; aver 2 µm)
Short generation times (<10 min)
Large population sizes
Propensity *for* horizontal gene transfer (pangenome limitless)

Traits





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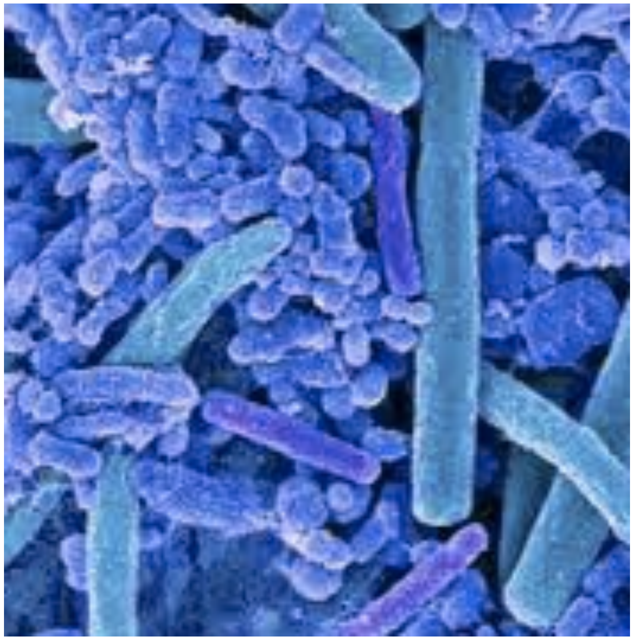
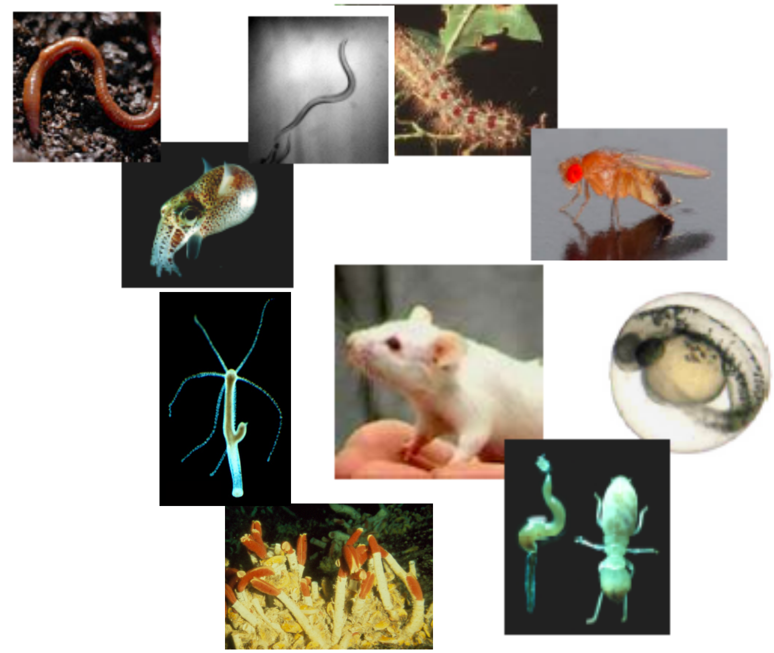
Large (80 µm to 30 m; aver mm-cm)
Long generation times (days – decades)
Small population sizes
Propensity *against* horizontal gene transfer

Traits





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Long generation times (days – decades)
Small population sizes
Propensity *against* horizontal gene transfer

By partnering with one another, animals and bacteria increase their scope.

Examining all components and levels of an ecosystem

Above- and below-ground impacts of introduced predators in seabird-dominated island ecosystems

Fukami et al. (2006) *Ecology Letters* 9:1299-1307

Compared offshore islands of New Zealand
- rat-free vs. rat-invaded

Measured:

vegetation density
seabird abundance
litter invertebrates
soil invertebrates and microbiota
soil nutrients and chemistry

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Measured:

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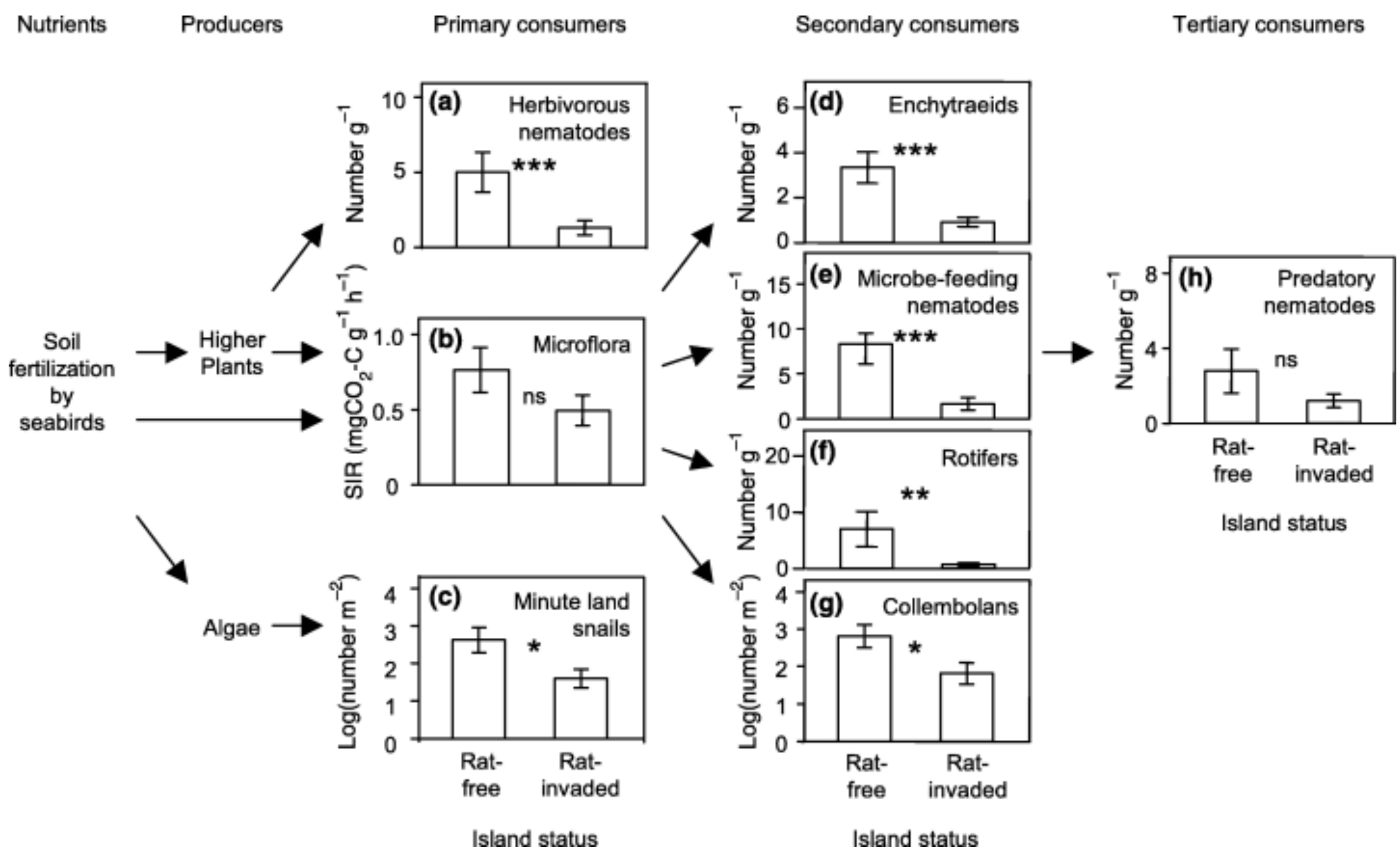
soil invertebrates and microbiota
soil nutrients and chemistry

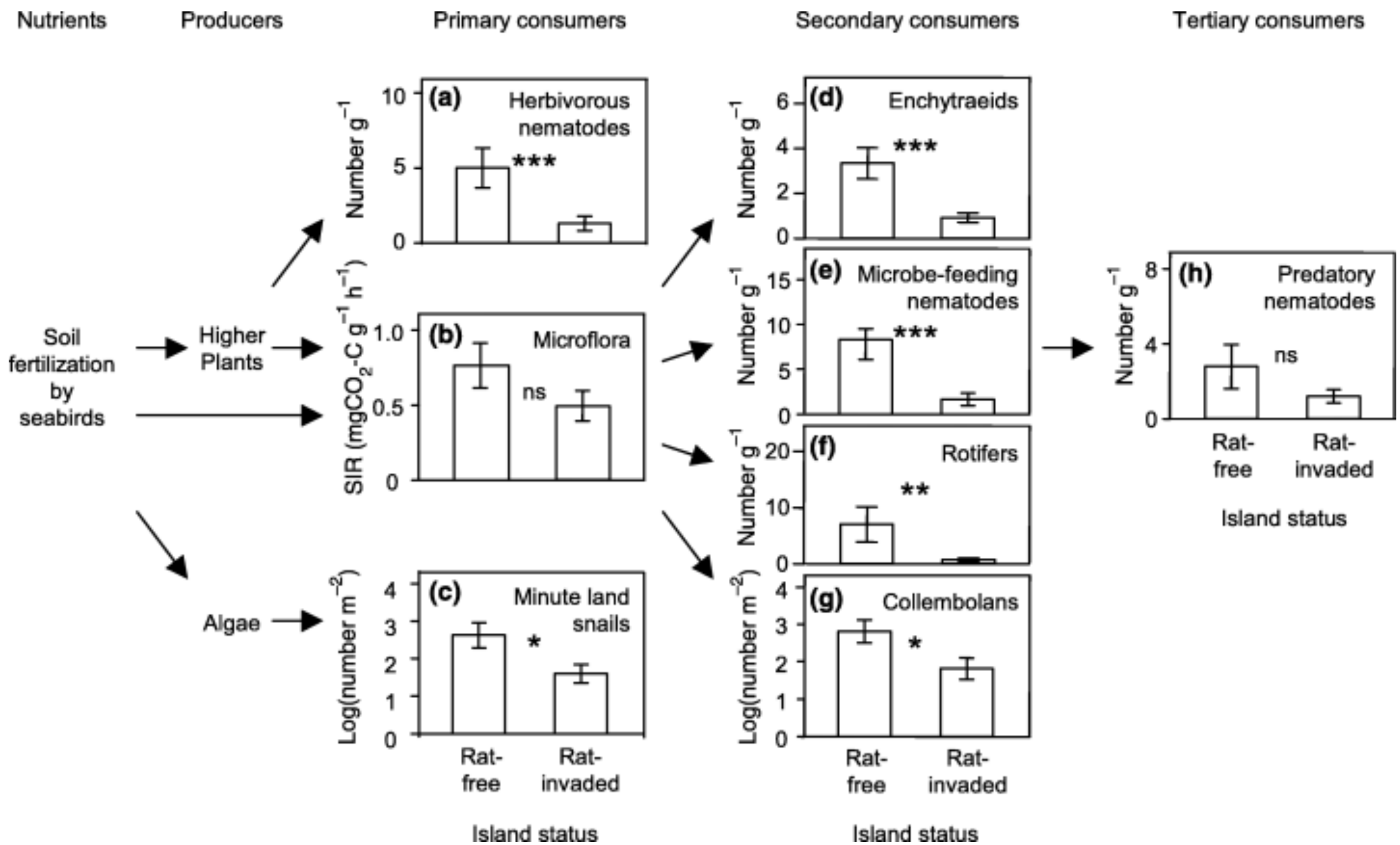
Seabird abundance down 24-fold on rat-invaded islands

Disrupting sea-land nutrient transport (guano deposition on the island)

Cascading effects

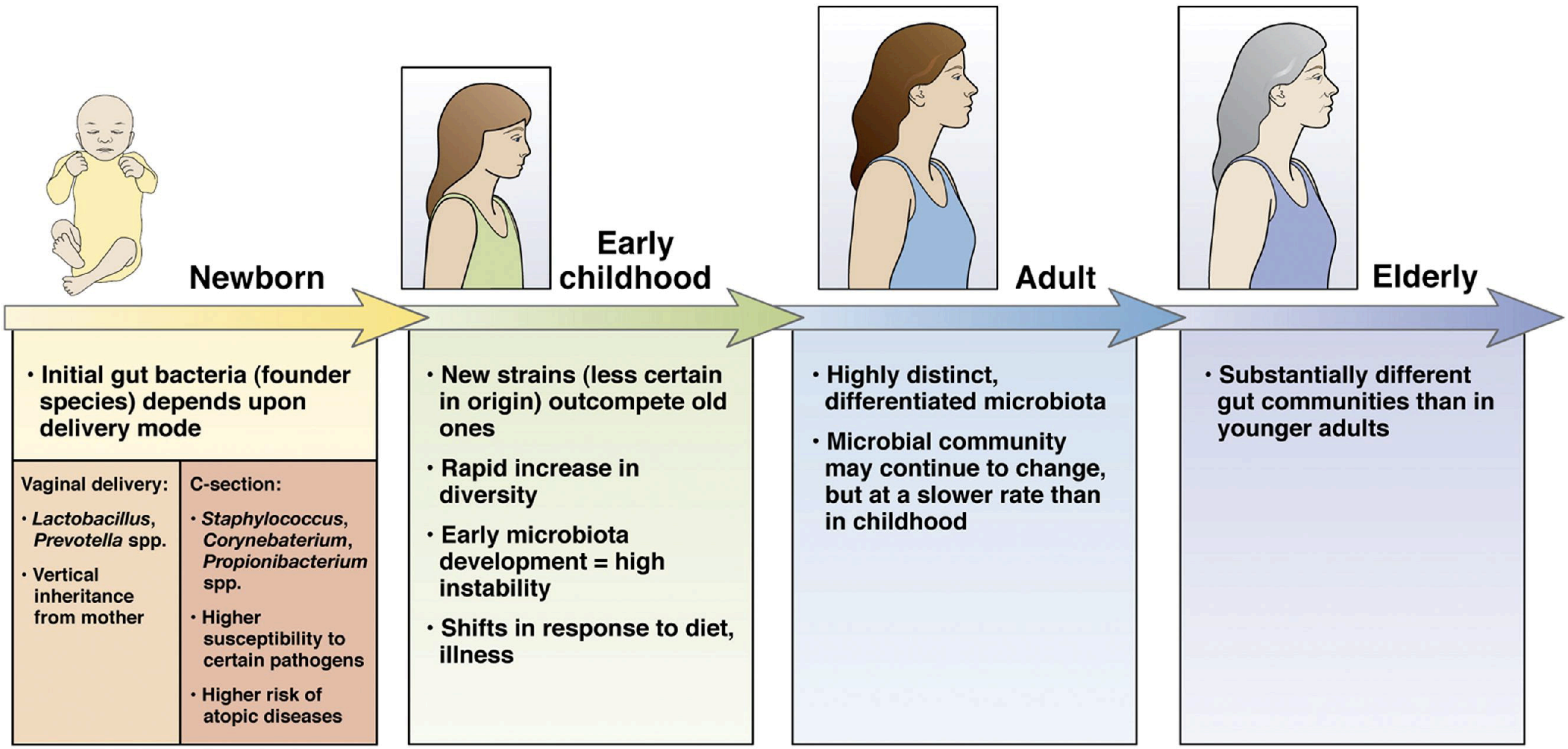


Cascading effects



Soil on rat-invaded islands:
nutrients – down 20-60%
pH up ~2 units (4.8 to 6.6)

Symbioses – classic nested ecosystems



Dominguez-Bello (2010) *Proc Natl Acad Sci USA 107: 11971-5 & (2011) Gastroenterology* 140:1713-9.

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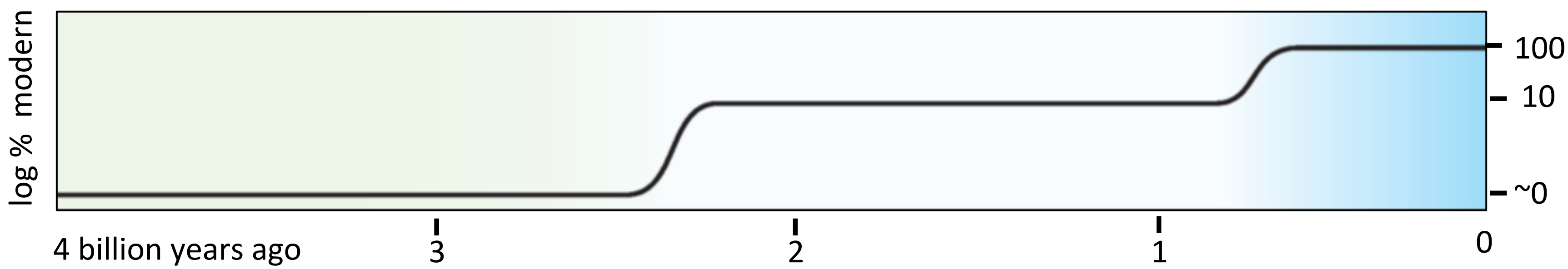
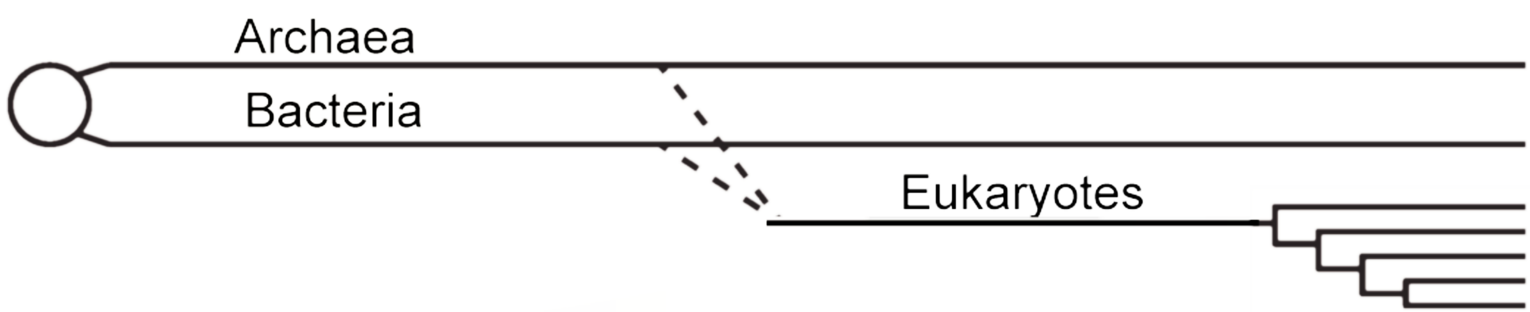
Summary/Horizons

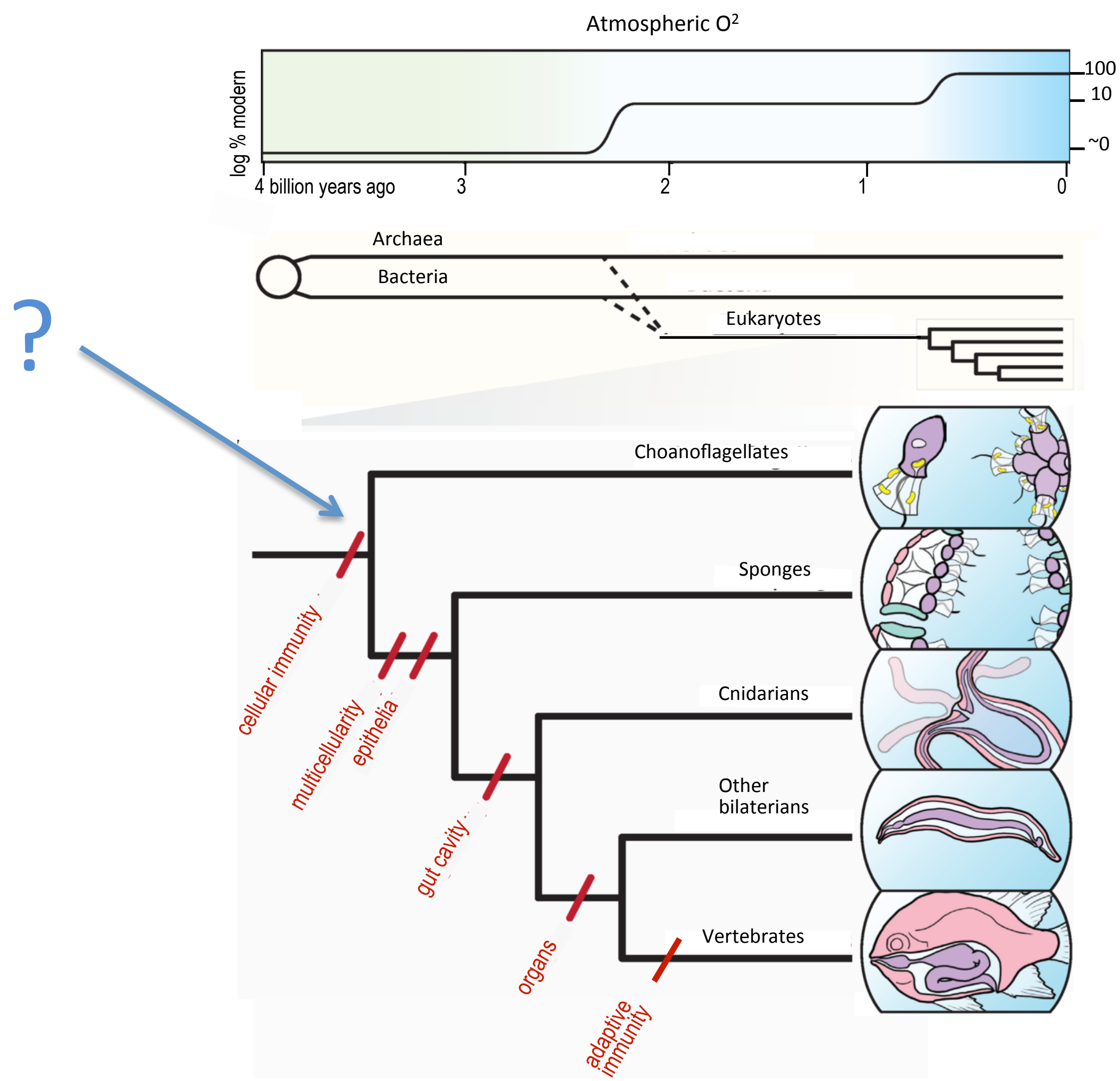
When and how did these complex ecosystems evolve?

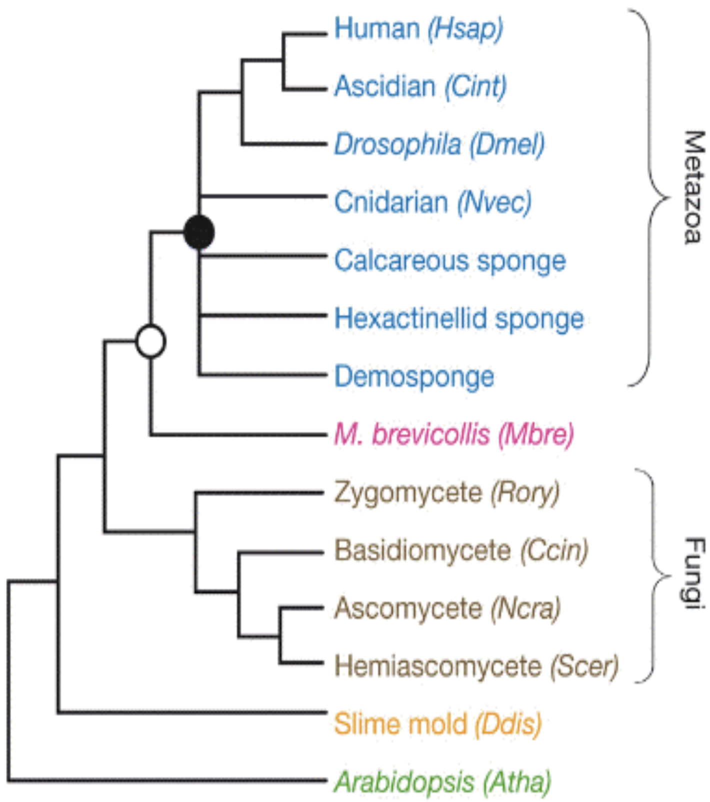
Changes in atmospheric oxygen levels correlate with major radiations

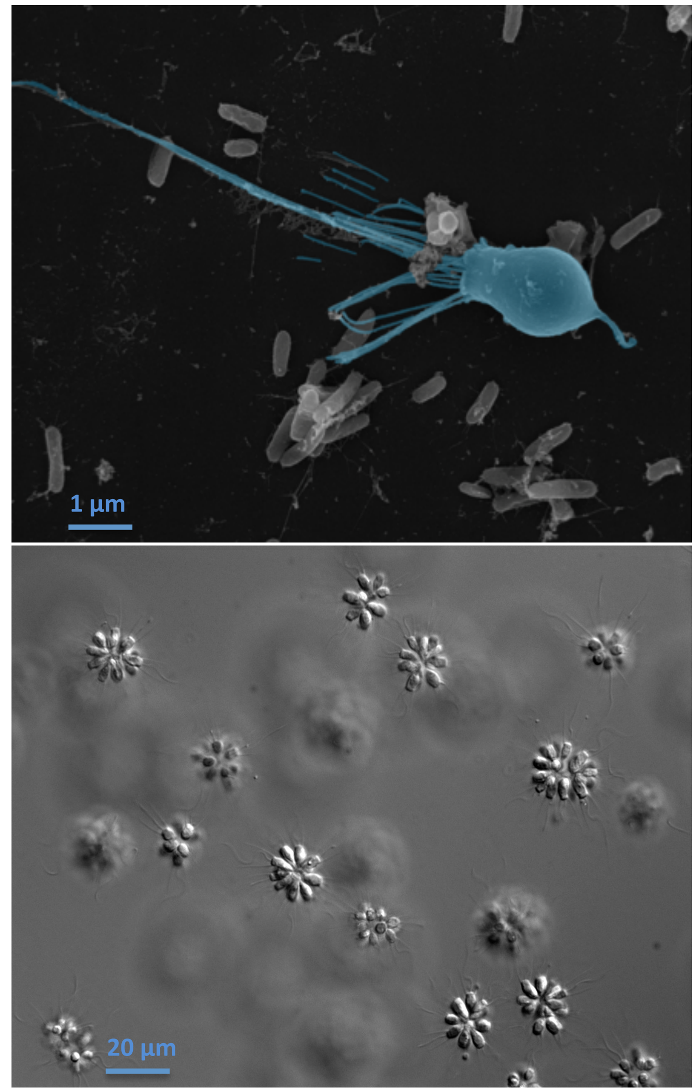




Any evidence for bacteria participating in the evolution of multicellularity?

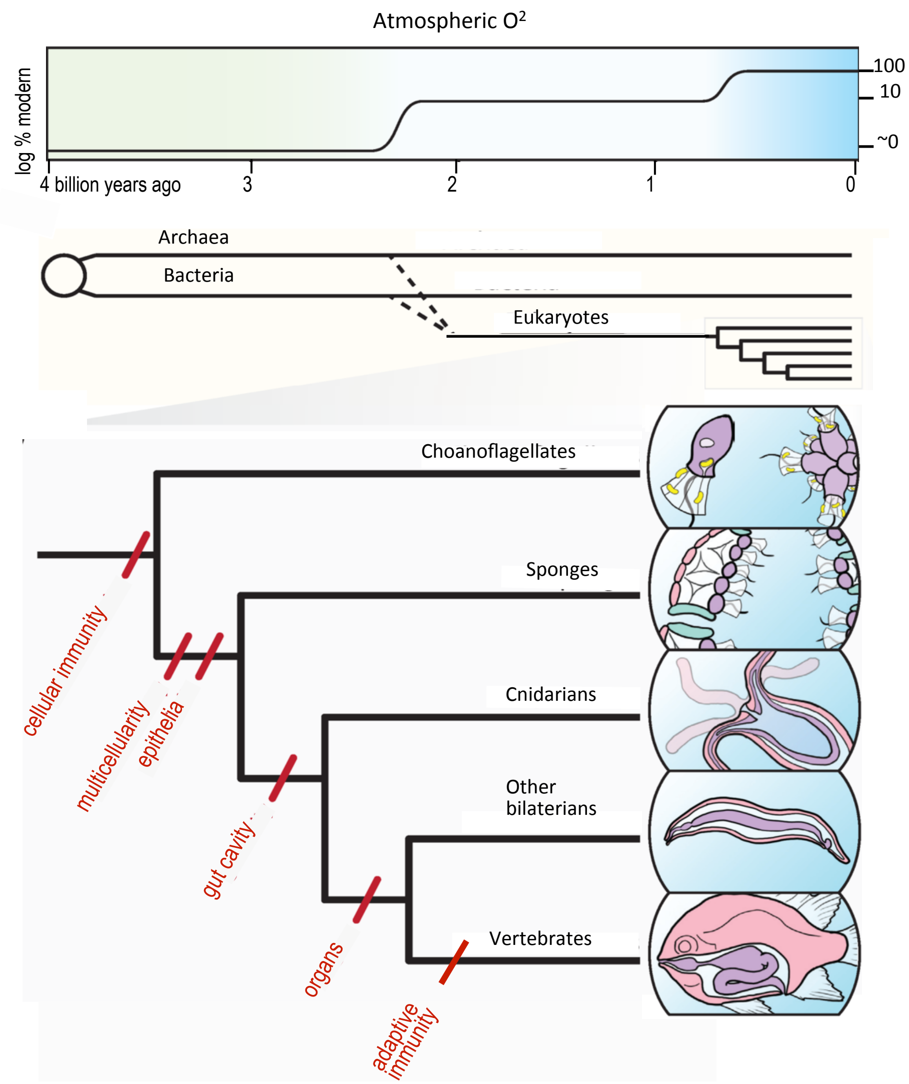






Fairclough, Dayel and King (2010) Curr Biol 20:R875-6.

Any evidence for bacteria driving major milestones in animal evolution?



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Summary/Horizons

Is there a genomic signature?

Perhaps you aren't the person you think you are.

The 'Ecosystem'

Victoria Orphan, Prof. Caltech

Host:bacterial partners -

1:10 cell number (10^{13} host cells/10^{14} bacterial cells)
1:1 gene number (30,000 in 10^{13}/3,000 in 10^{14})
1:200 gene diversity

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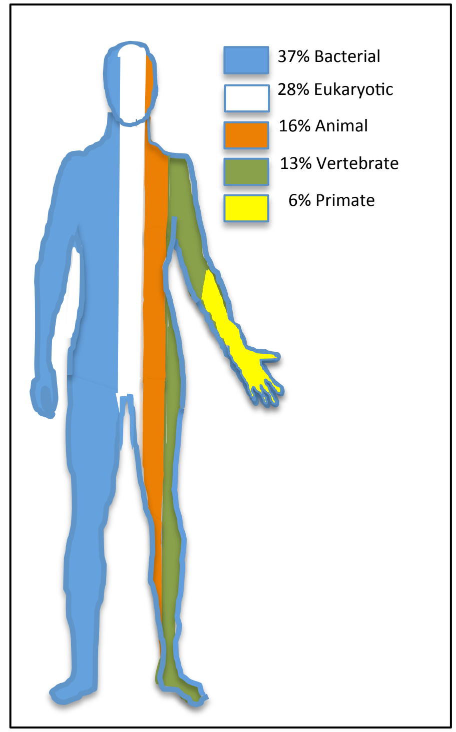
Origin of host genes



Host:bacterial partners -

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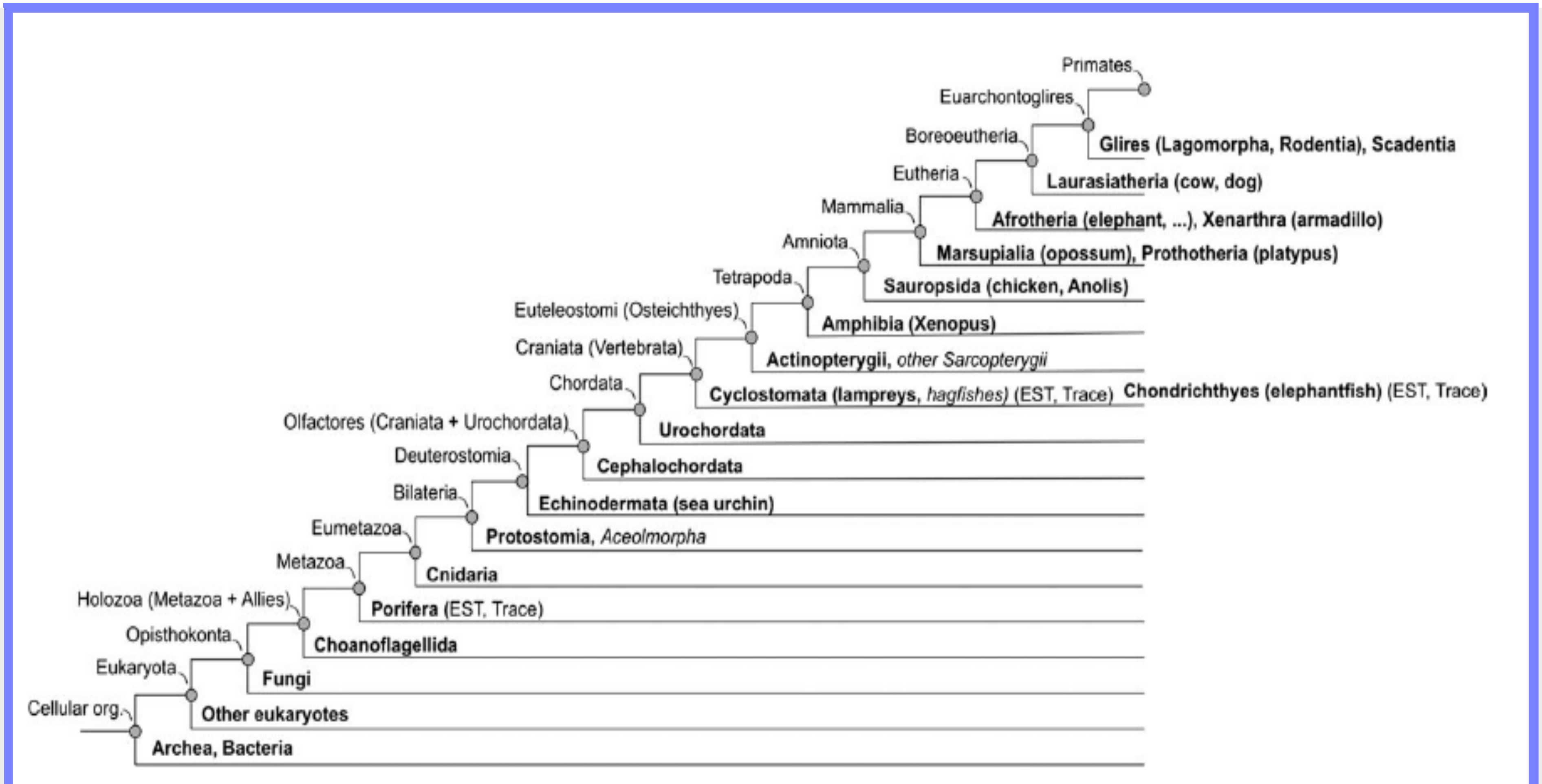
The evolutionary trajectory to humans in 19 steps -

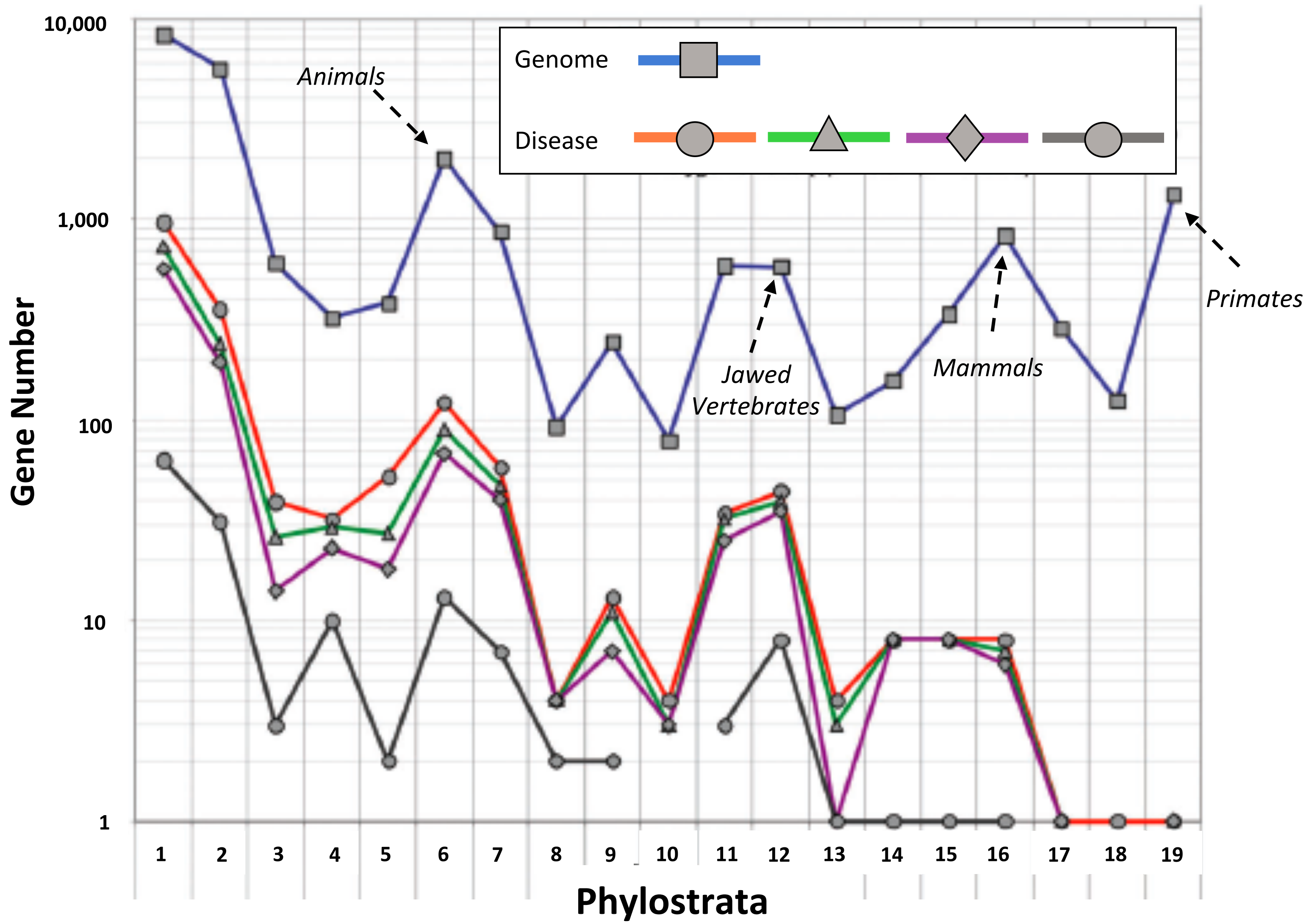
Question: At which steps in evolution did the human genes evolve?

Method: All available proteins sequences were used to create a phylographic framework, within which the positions of human protein sequences (~23, 000) were identified.



(Domazet-Loso and Tautz, 2008)

Origin of Human Genes/Genes Associated with Human Genetic Disease
(1,760/22,937)



(Domazet-Loso and Tautz, 2008)

ANIMALS ⟺ BACTERIA

Effects on bacterial gene evolution:

Examples:

1. Extreme genome reduction in the intracellular symbionts of insects

2. Diversification of metabolic pathways in response to host niche

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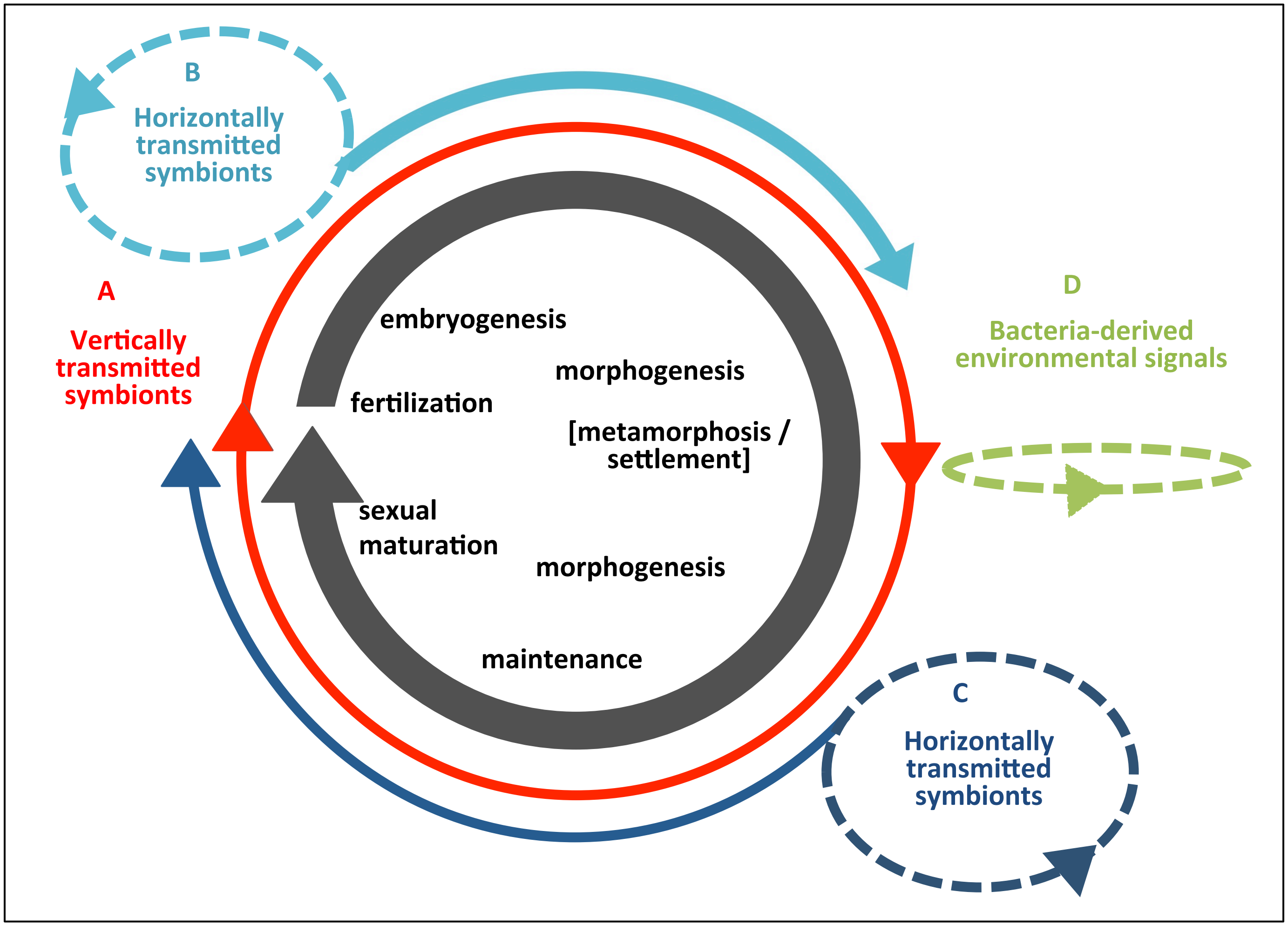
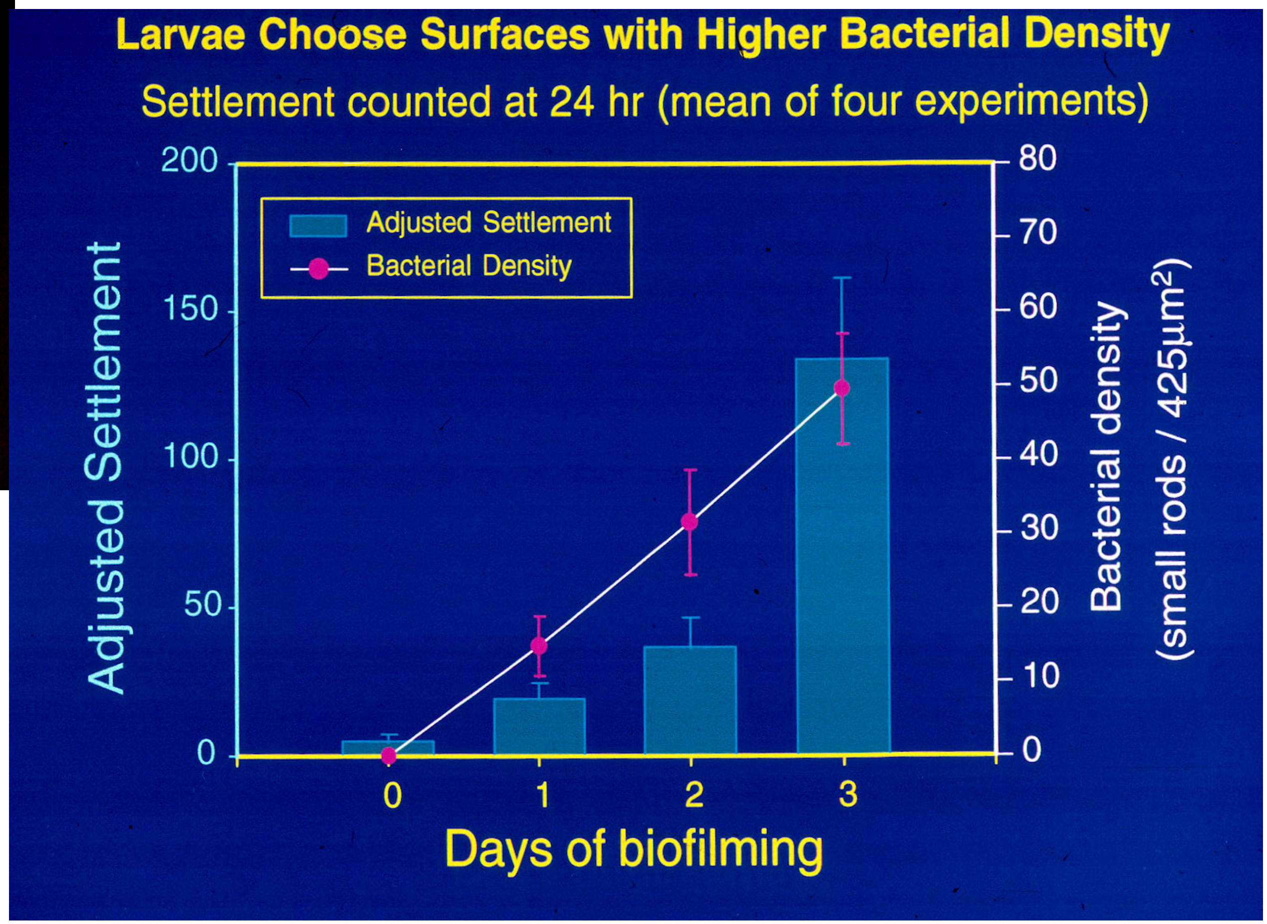
Summary/Horizons

Bacteria influence animal development at many levels, egg to mature adult.

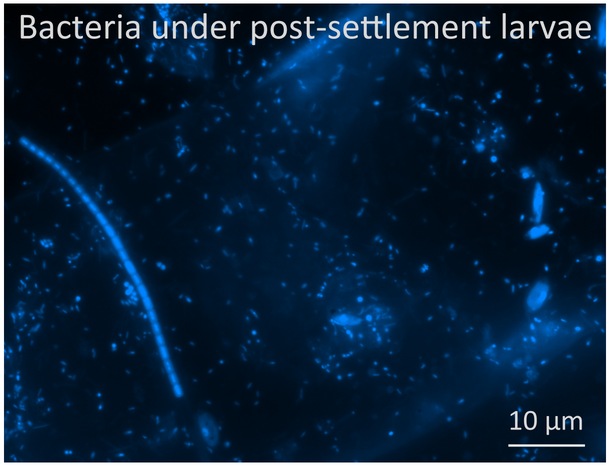


Many, if not most marine invertebrate larvae that settle on hard substrates require bacterial biofilms for settlement and/or metamorphosis.

Hydroides elegans



Hadfield (2011) *Annu Rev Mar Sci* 3:453.



IDENTIFYING THE MECHANISM

Hadfield (Ying Huang) and Callahan lab:

Identified a bacterial species, *Pseudoalteromonas luteoviolacea*, that is a strong inducer of metamorphosis.

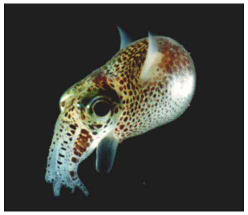
Through transposon mutagenesis, they identified mutants defective in induction of larval settlement.

Obtained full genome sequence of *P. luteoviolacea*.

Defined genes essential for induction of larval settlement
(4 genes critical; e.g., adhesins, biofilm formation, type VI secretion).

Huang, Callahan & Hadfield (in press) *Scient Rep*

<u>Symbiont induction of host tissue development - evolutionarily conserved processes</u>



Euprymna scolopes -Vibrio fischeri light organ symbiosis

MAMPs (peptidoglycan monomer and LPS) from the gram-negative symbiont induces epithelial development. [Koropatrick et al. (2004) *Science*]

after MAMPs inductive signal delivered at 12 h

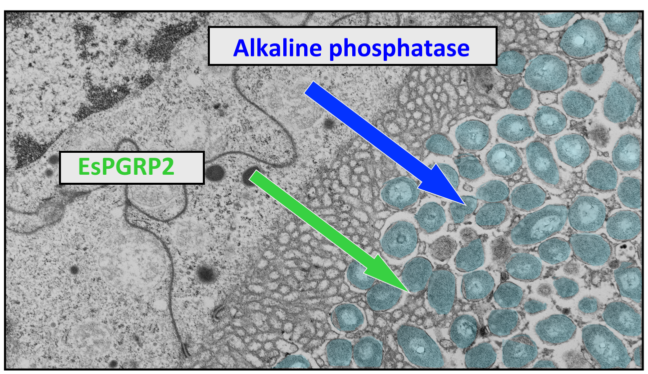
Taming of the MAMPs

PGN monomer — X

LPS — X

[Troll et al. (2010) *Env Microbiol]*
[Leulier - drosophila]

[Rader et al. (In prep)]
[Guillemin - zebrafish]



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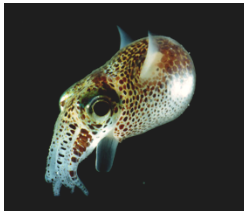

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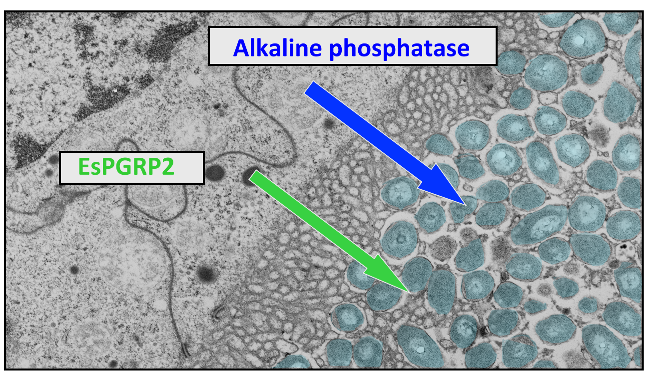

Mus musculus - gut consortial symbiosis

MAMPs (peptidoglycan monomer) from the gram-negative component of the consortium induces GALT development.
[Bouskra et al. (2008) *Nature*]

Taming of the MAMPs -

modulation of MAMPs/PRR activity

See Eberl and Boneca (2010)
Curr Opin Immunol

1
History/Context

3
Origins

*Andrew Knoll
Ute Hentschel
Nicole King
Ken Nealson
Jon Sanders

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*Nicole Dubilier
Tadashi Fukami
Staffan Kjelleberg
Naomi Pierce
Ann Reid

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Tomislav Domazet-Loso
Jessica Metcalfe
Mary Rumpho
Diethard Tautz

ANIMALS ⟺ BACTERIA

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Development

*Thomas Bosch
Bernard Degnan
Scott Gilbert
Natacha Kremer
John Rawls

6
Communication

*Ned Ruby
Hannah Carey
Angela Douglas
Gerard Eberl
Sarkis Mazmanian

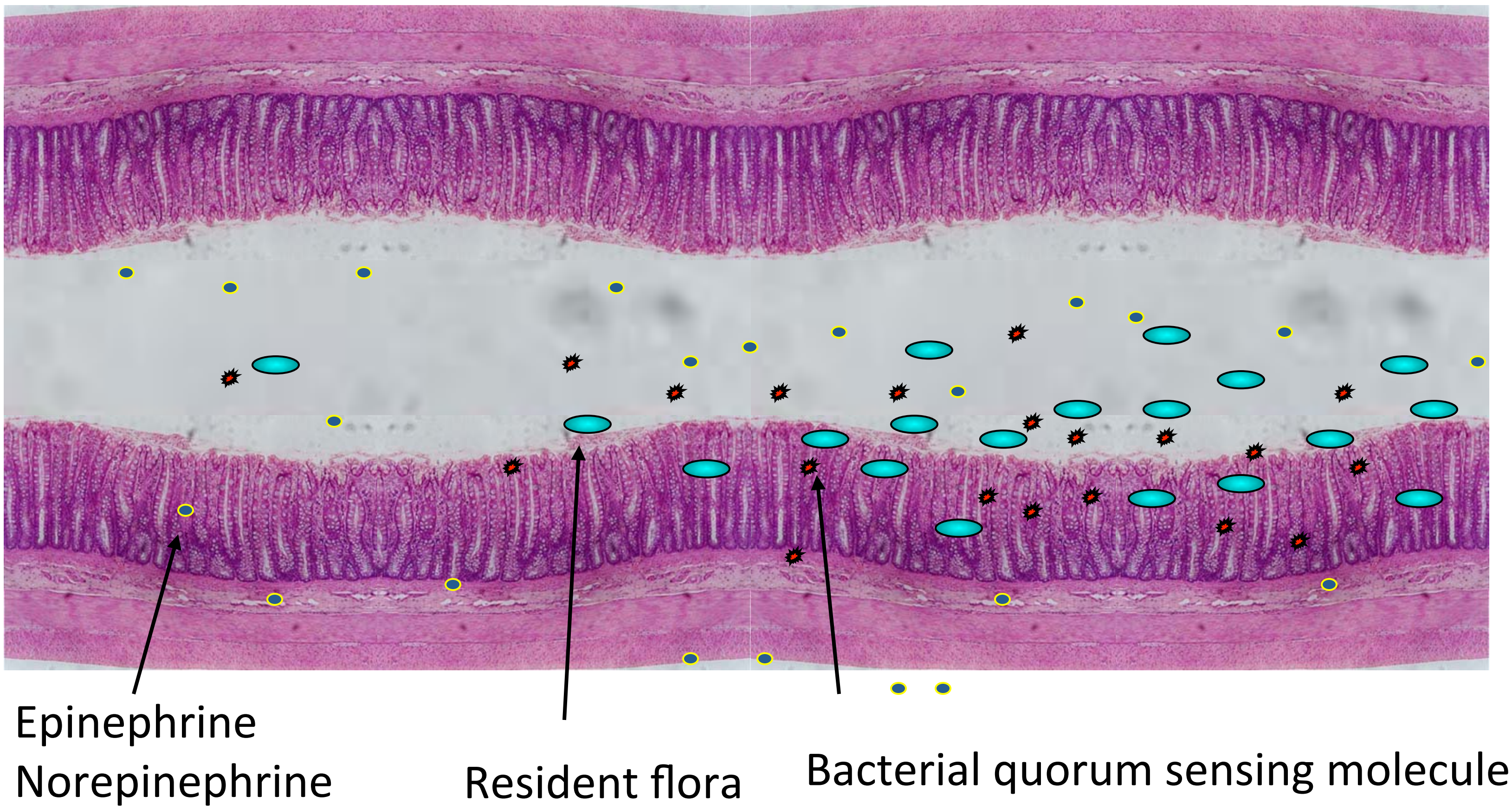
7
Summary/Horizons

Until recently –
no mechanism for bacterial communication known.

Quorum sensing – bacterial pheromones, both intra- and interspecific; bacteria respond when at high density.

The hormones epinephrine and norepinephrine control:

- **intestinal motility**
- **ion channel activity**
- **mucosal immune system**
- ***have a molecular structure very similar to a bacterial quorum-sensing molecule.***

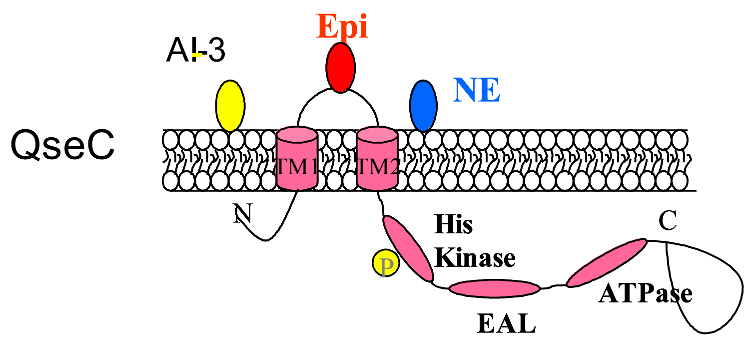


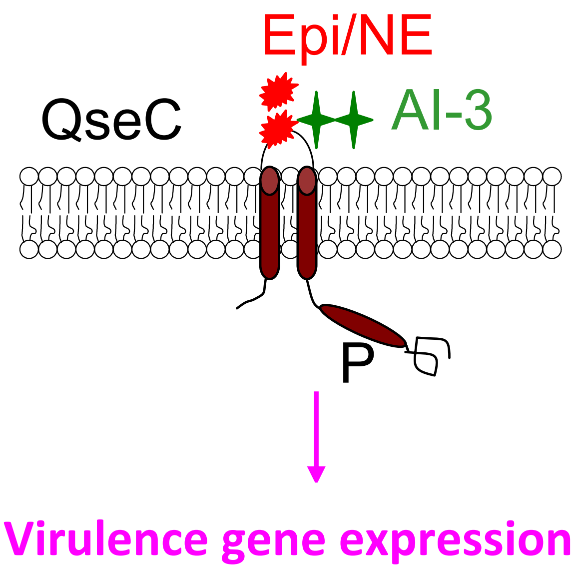
Courtesy of V Sperandio, UT Southwestern

Clarke et al. PNAS 2006

Bacterial adrenergic receptor: QseC

- QseC is an inner membrane bacterial adrenergic receptor (Histidine kinase). QseC responds to the bacterial signal AI-3 *and* to the host signals epinephrine and norepinephrine





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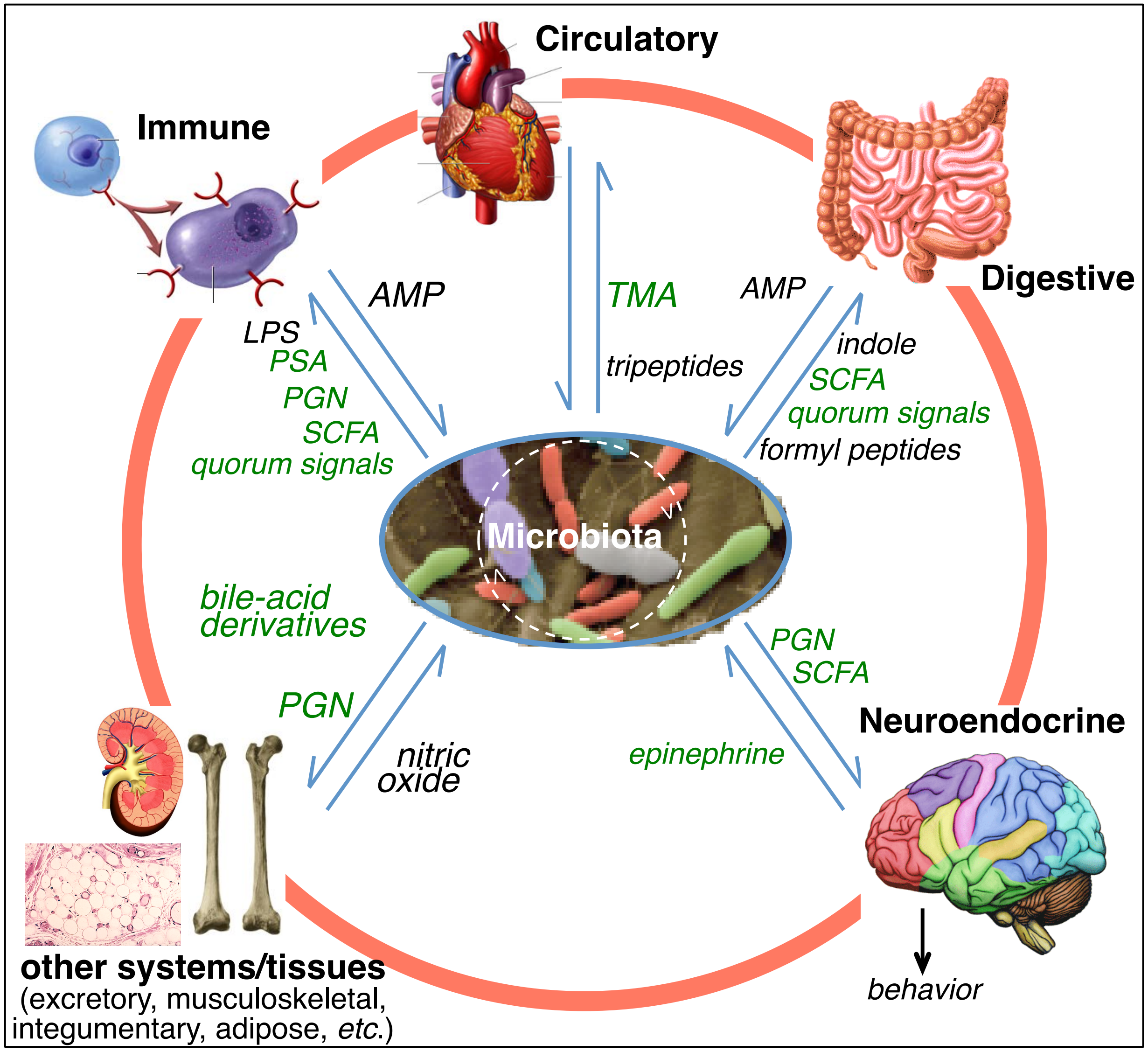
Mammalian microbiota have profound effects on host biology:



METABOLOMICS

Biologists are discovering
the 'mammalian-microbial co-metabolome'

Analysis of the small biomolecules in the
body fluids (blood, sweat, tears, urine)

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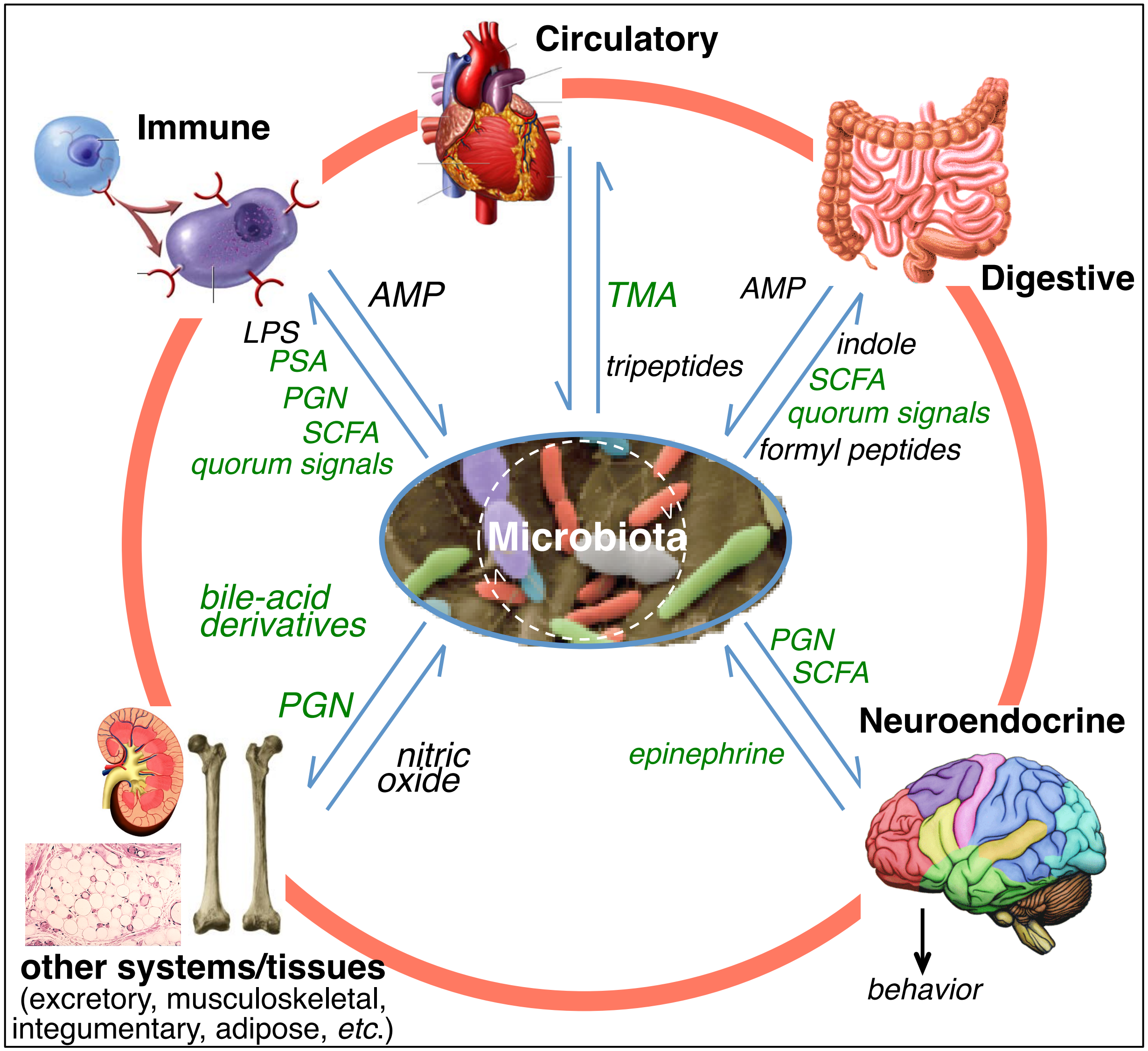
A large proportion of a mammal's metabolic signature is determined by the activity of the resident microbiota.

Every cell in the body of an animal is affected.

Mammalian microbiota have profound effects on host biology:



What about other animals?

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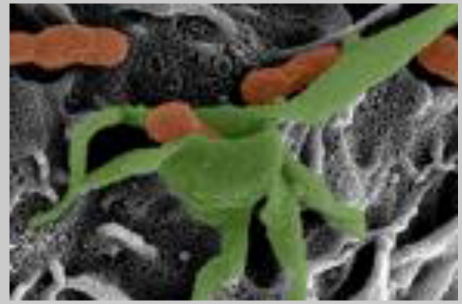


New technology has revealed that animals are deeply imbedded in the microbial world, and all aspects of an animal's biology are likely to be affected.





Lynn Margulis 1938-2011

The Challenge – Intellectual Silos

<u>The structure of</u>:

- departments and research institutes at universities

- professional societies

- funding agencies

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Be bold - Make bridges with microbiologists.
[currently mainly a biomedical focus]

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Challenge the funding agencies to support the developing frontiers.
[not enough for such a vast horizon]

Thanks for listening to our story!

NESCent Catalysis Mtg. Group