



Why Philosophy of Microbiology?



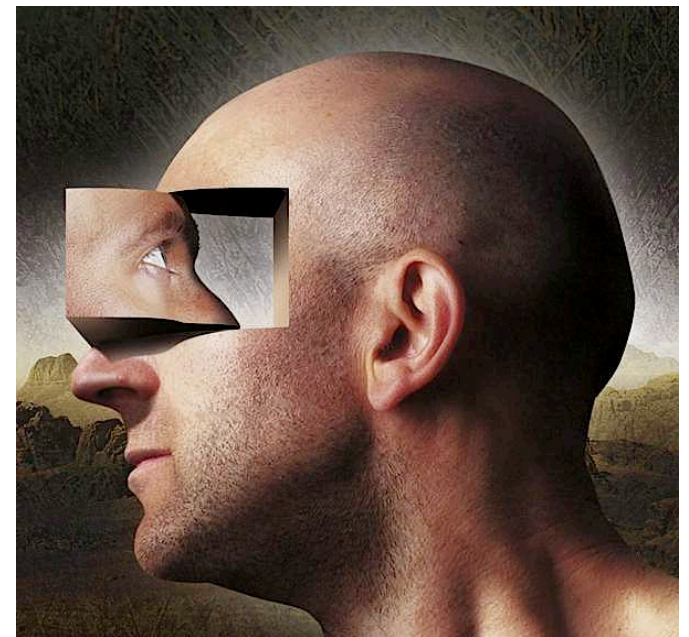
- Philosophy of science
  - Philosophy of biology
    - Philosophy of microbiology

What is any philosophy of science?

Not just ethics, nor even mostly ethics

Not wild speculation and fantasy

Not anti-science or anti-empirical



Examining the arguments, conceptual resources, and knowledge-producing strategies scientists use in their science

Who does philosophy of science?

1. Philosophers
2. Scientists

What is the nature of the chemical bond?





# Why (on Earth) philosophy of microbiology?

Excellent list of reasons:

- From the microbes' side
- From the microbiology side
- From the philosophy side





## Some specific issues in microbiology that are philosophical

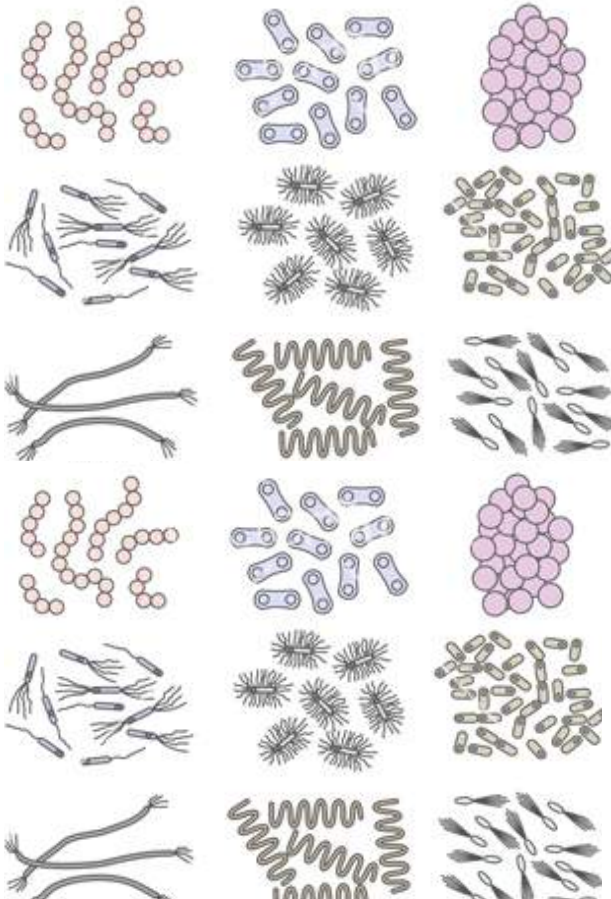
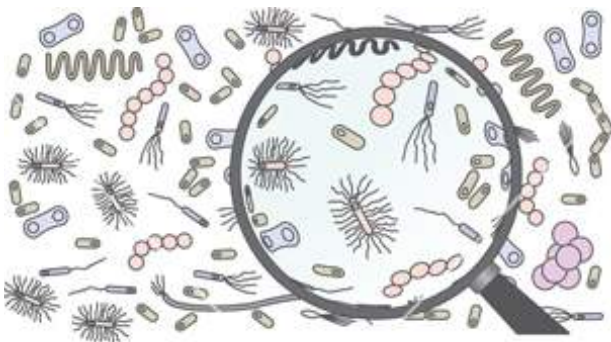
- Species concepts
- Tree of life concepts and methods
- Microbial model systems (my Bordeaux project)



Note:

Microbes = prokaryotes + eukaryotes





# The many philosophical woes of prokaryote species concepts

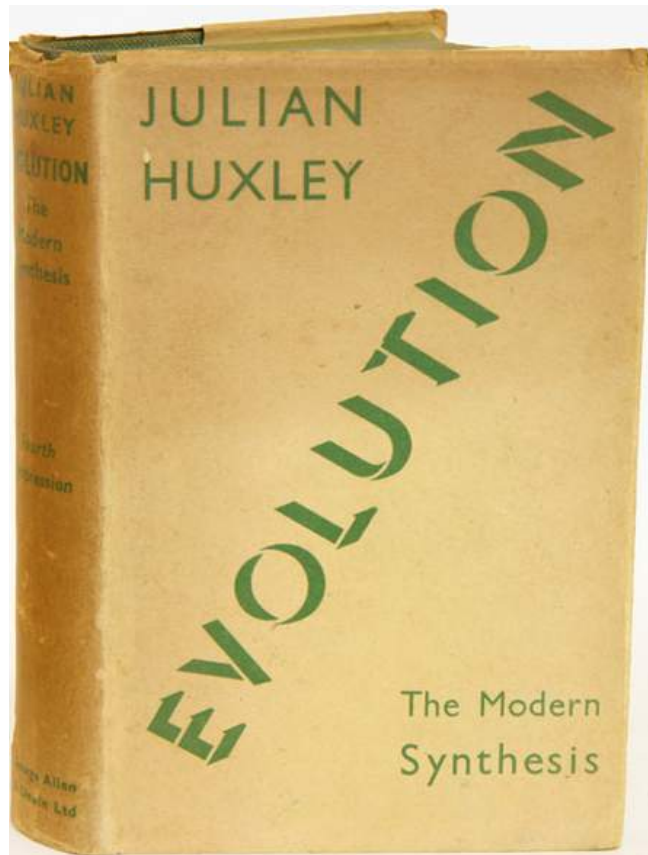
- Crucial to phylogeny, biodiversity counts etc.
- Meant to capture something real in nature (only rank meant to do so)
- Meant to be universal

However:

- Dominant concept devised for animals
- Multiple competing concepts
- Different scientific conclusions reached when different species concepts used
- Pragmatic not 'natural'?

# Modern synthesis of evolution

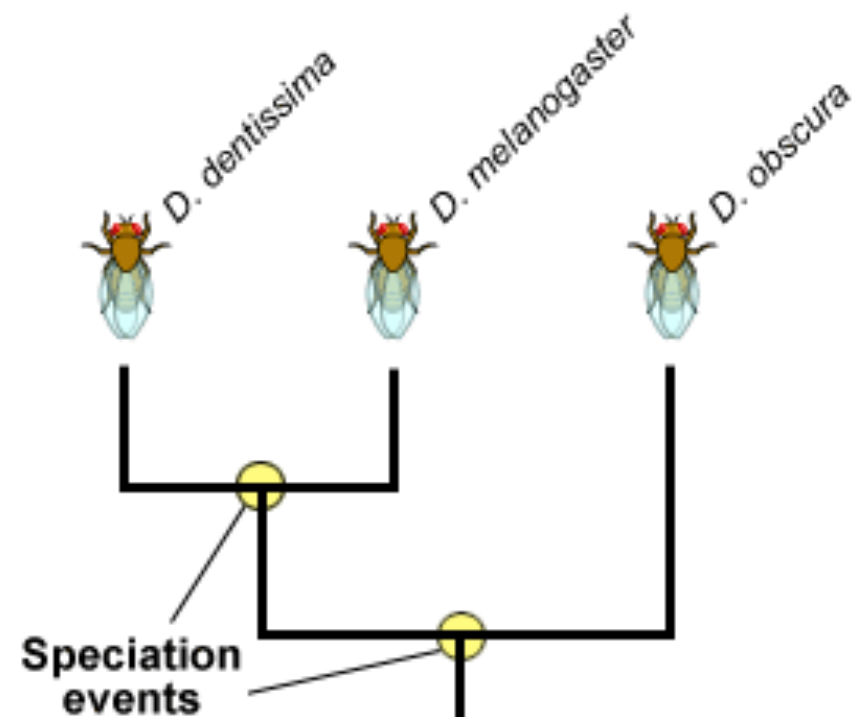
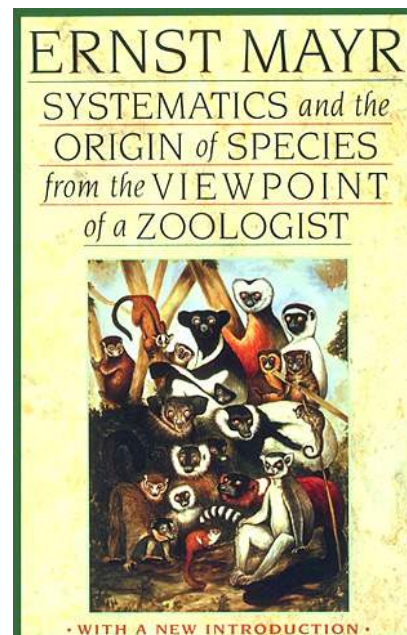
‘Bacteria have their own evolutionary rules. ... the processes of variation, heredity and evolution in **bacteria are quite different** from the corresponding processes in multicellular organisms’ (Huxley 1942, pp. 126, 131-132).



# Evolution without species?

**'Only sexually reproducing organisms qualify as species** and some other terminology, for instance paraspecies, will have to be found for uniparentally reproducing forms' (Mayr 1942; 1987, pp. 165, 145)

And evolution without species is unimaginable; for the modern synthesis, speciation just *is* the major pattern produced by natural selection.



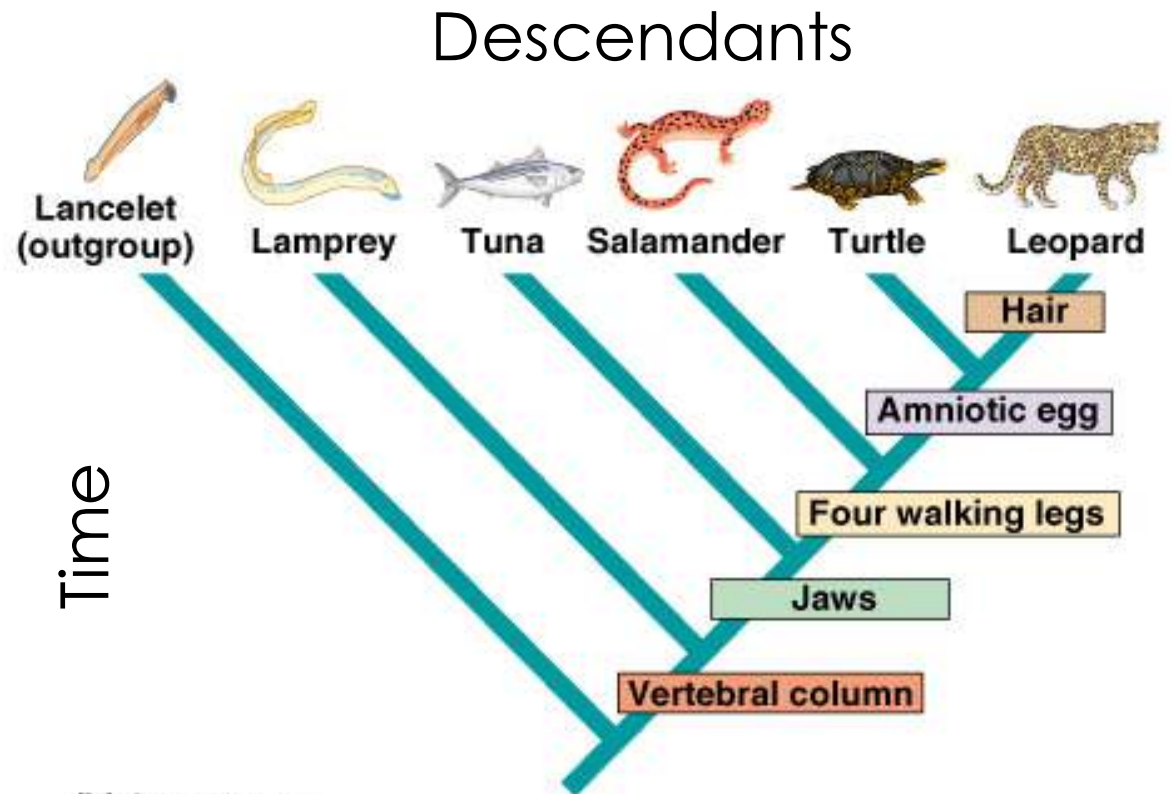


# Reconstructing speciation patterns = phylogeny

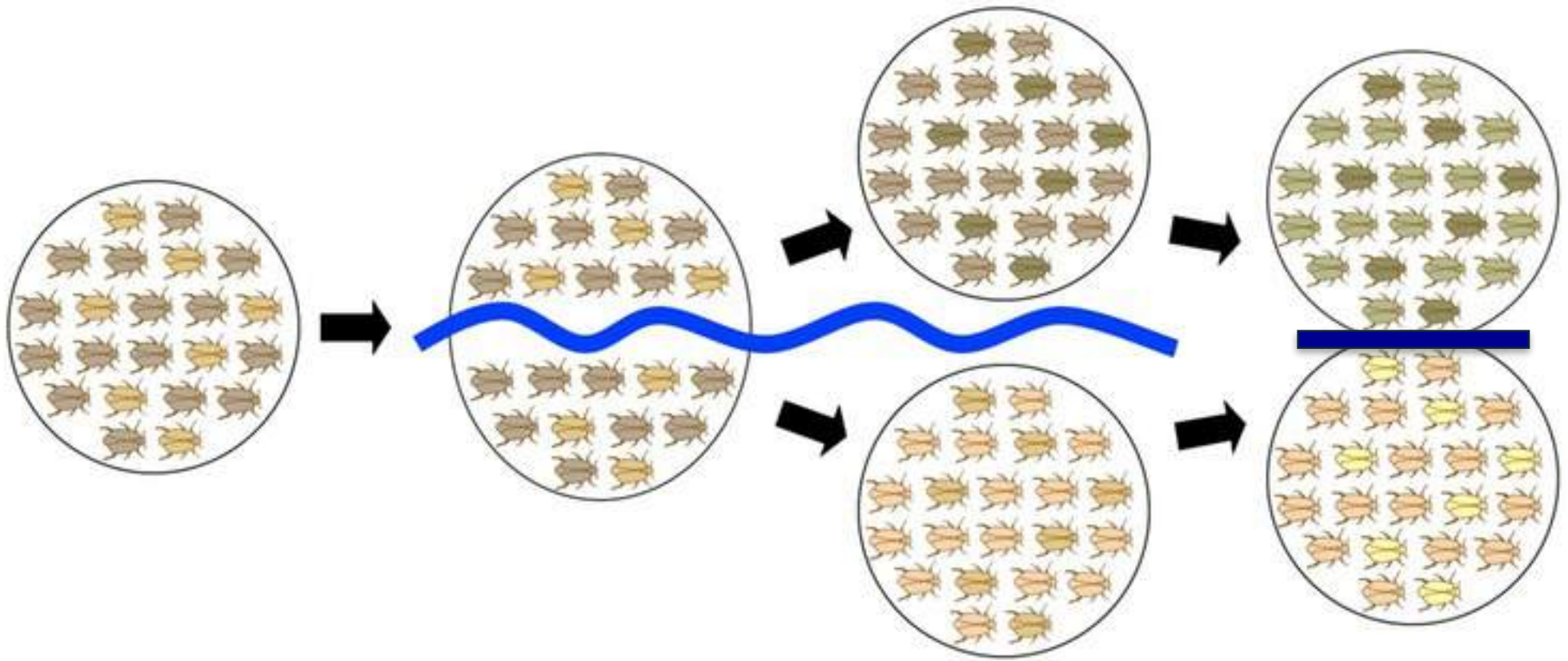
CHARACTERS	TAXA					
	Lancelet (outgroup)	Lamprey	Tuna	Salamander	Turtle	Leopard
Hair	0	0	0	0	0	1
Amniotic (shelled) egg	0	0	0	0	1	1
Four walking legs	0	0	0	1	1	1
Jaws	0	0	1	1	1	1
Vertebral column (backbone)	0	1	1	1	1	1

(a) Character table

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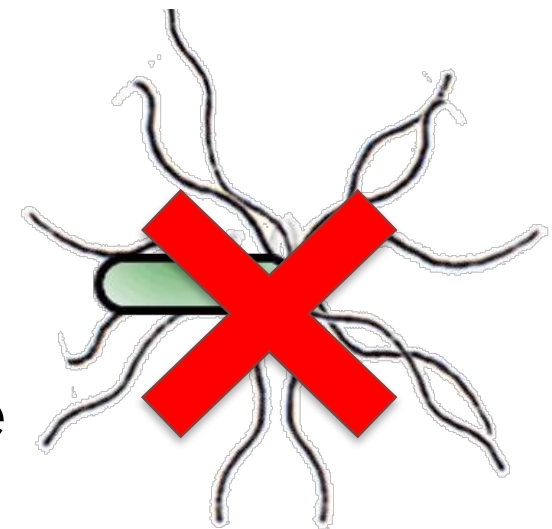


(b) Cladogram

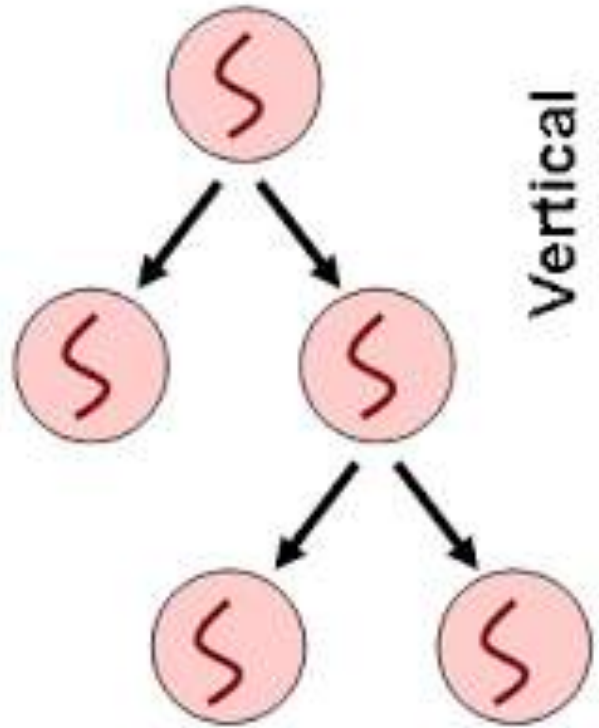


Major processes of speciation

~~Geographic~~ isolation,  
~~reproductive~~ isolation, divergence

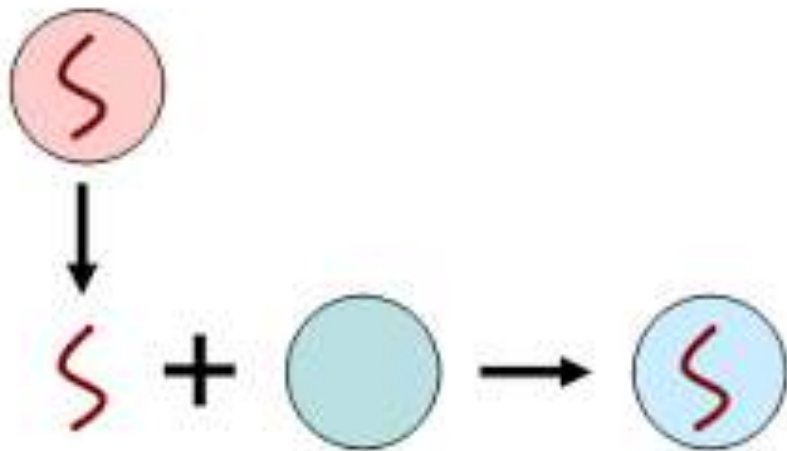




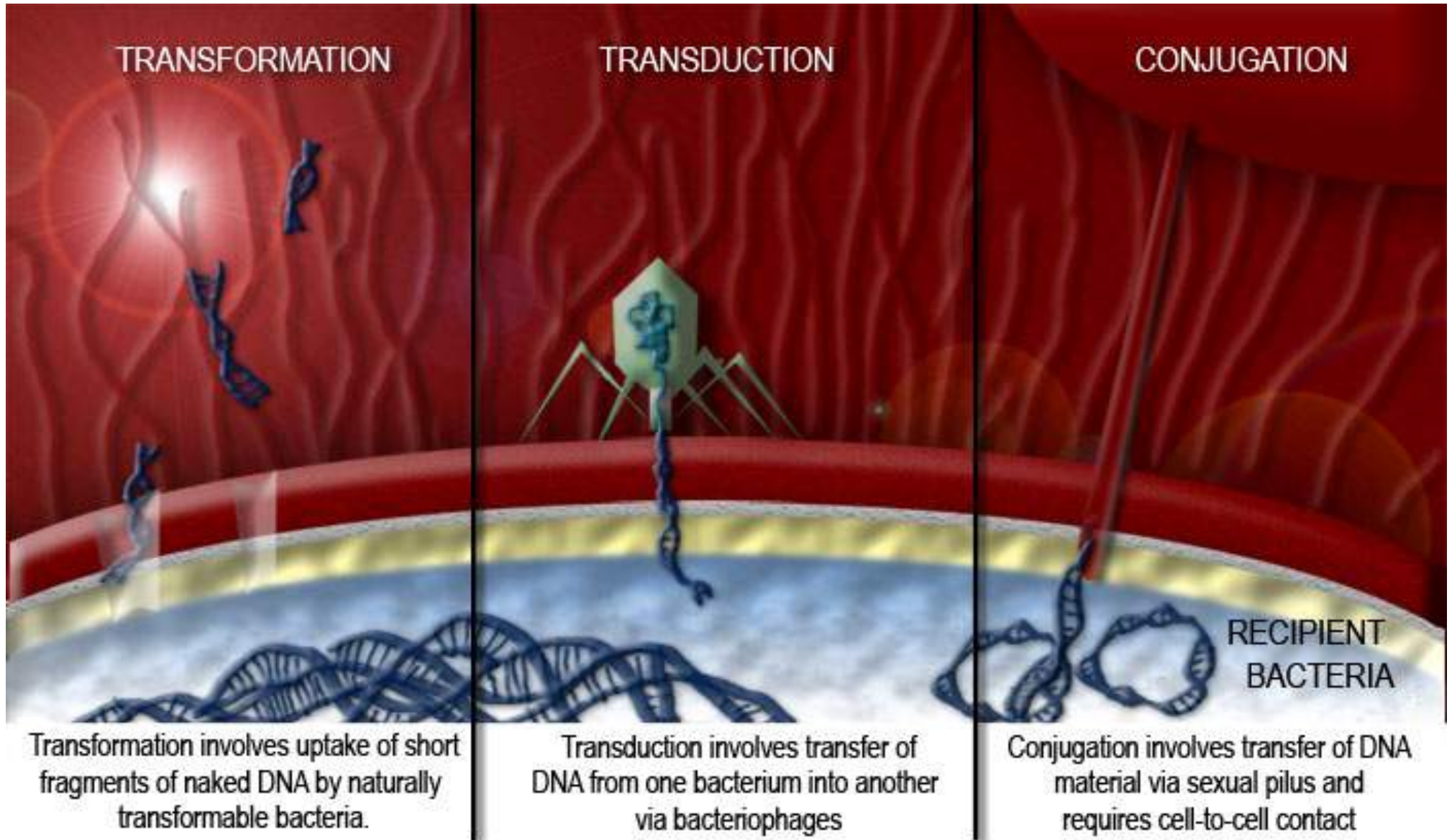


Not just divergence +  
vertical inheritance

Horizontal  
'inheritance' too



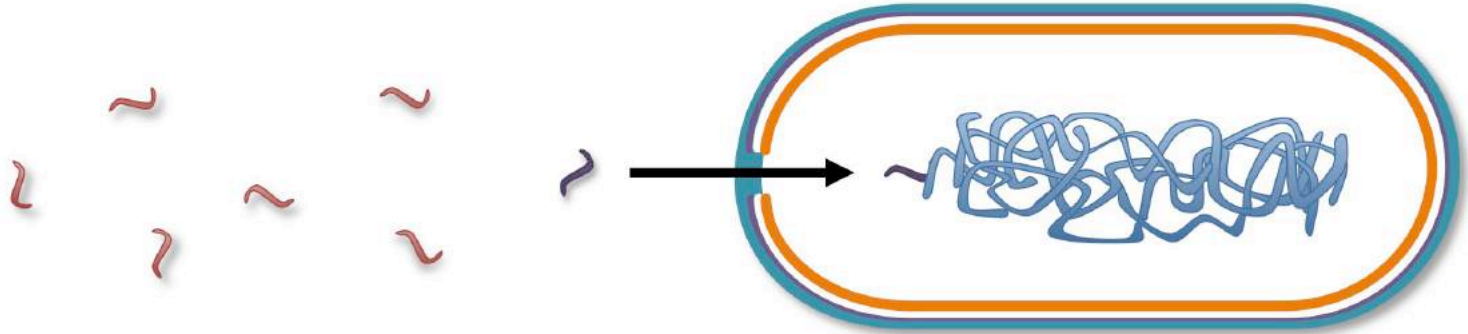
Lateral/horizontal  
acquisition of  
'foreign' genetic  
material (LGT)



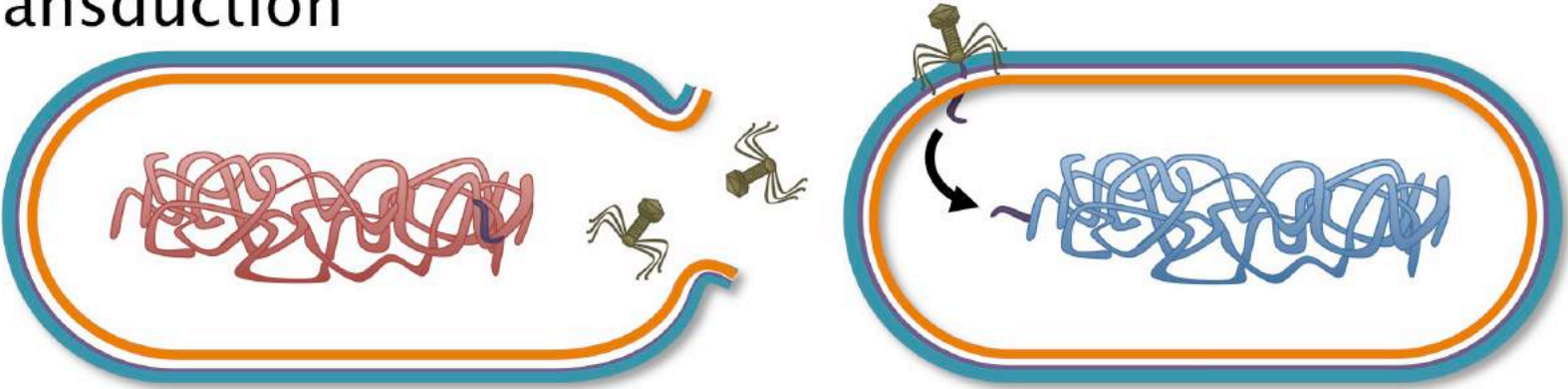
## Mechanisms of lateral gene transfer (LGT)



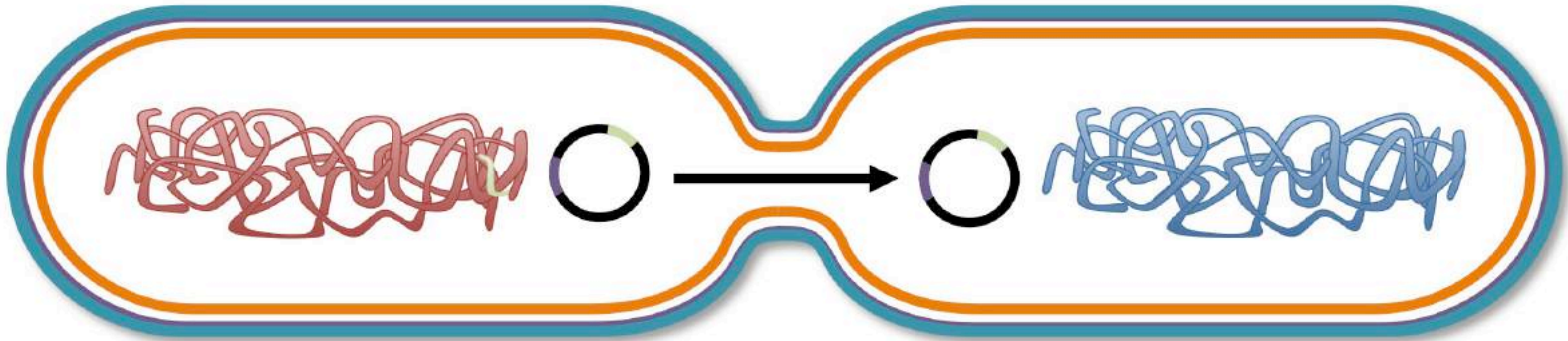
# Transformation

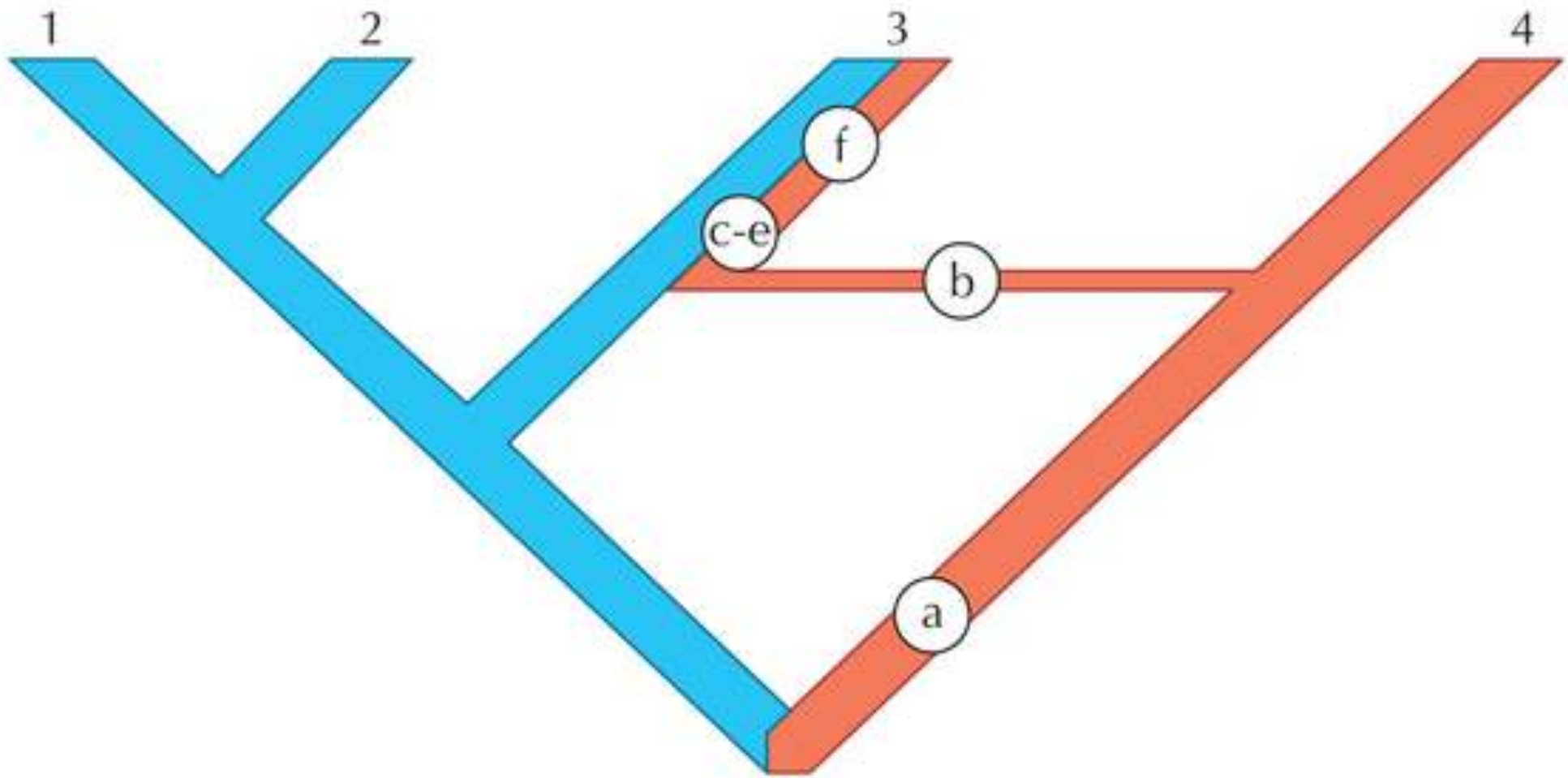


# Transduction



# Conjugation

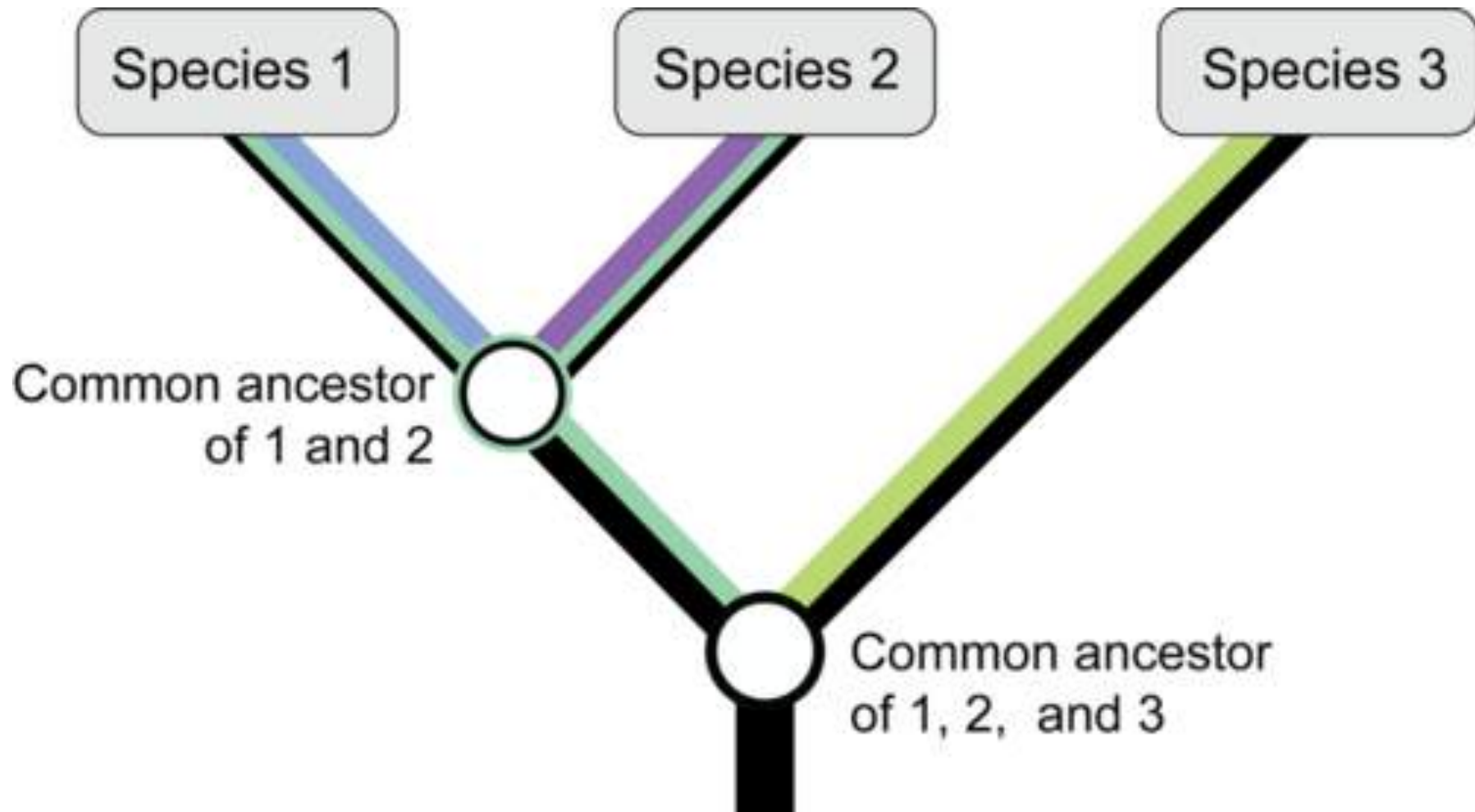


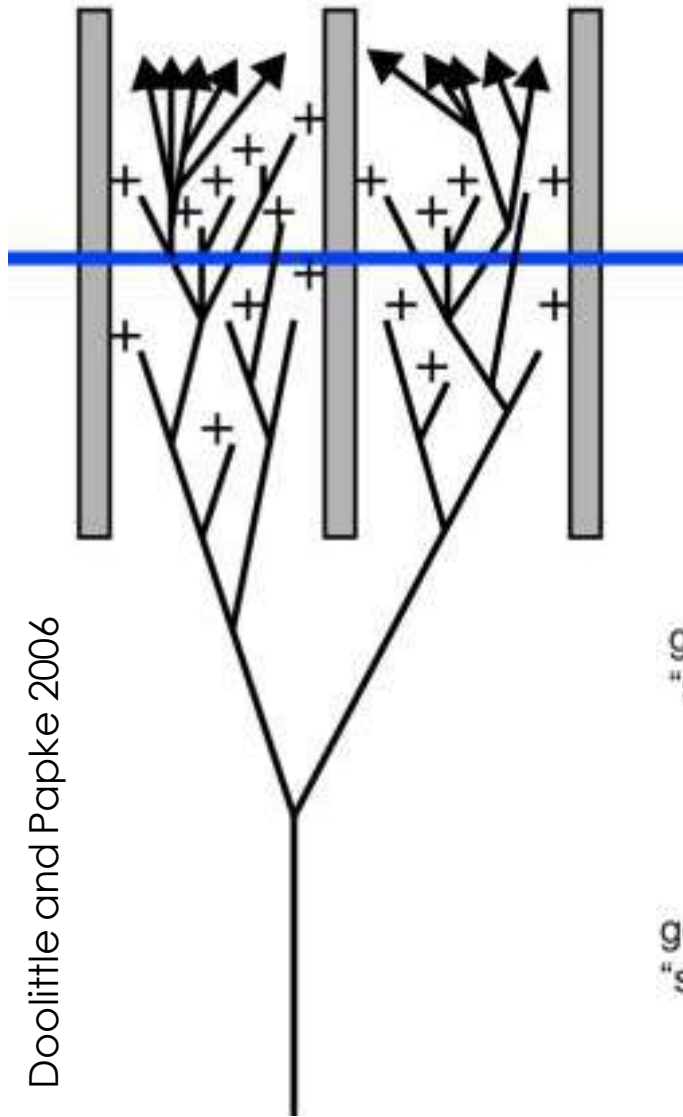


Big problem for reconstruction of species relationships (phylogeny)



# Phylogenetic species

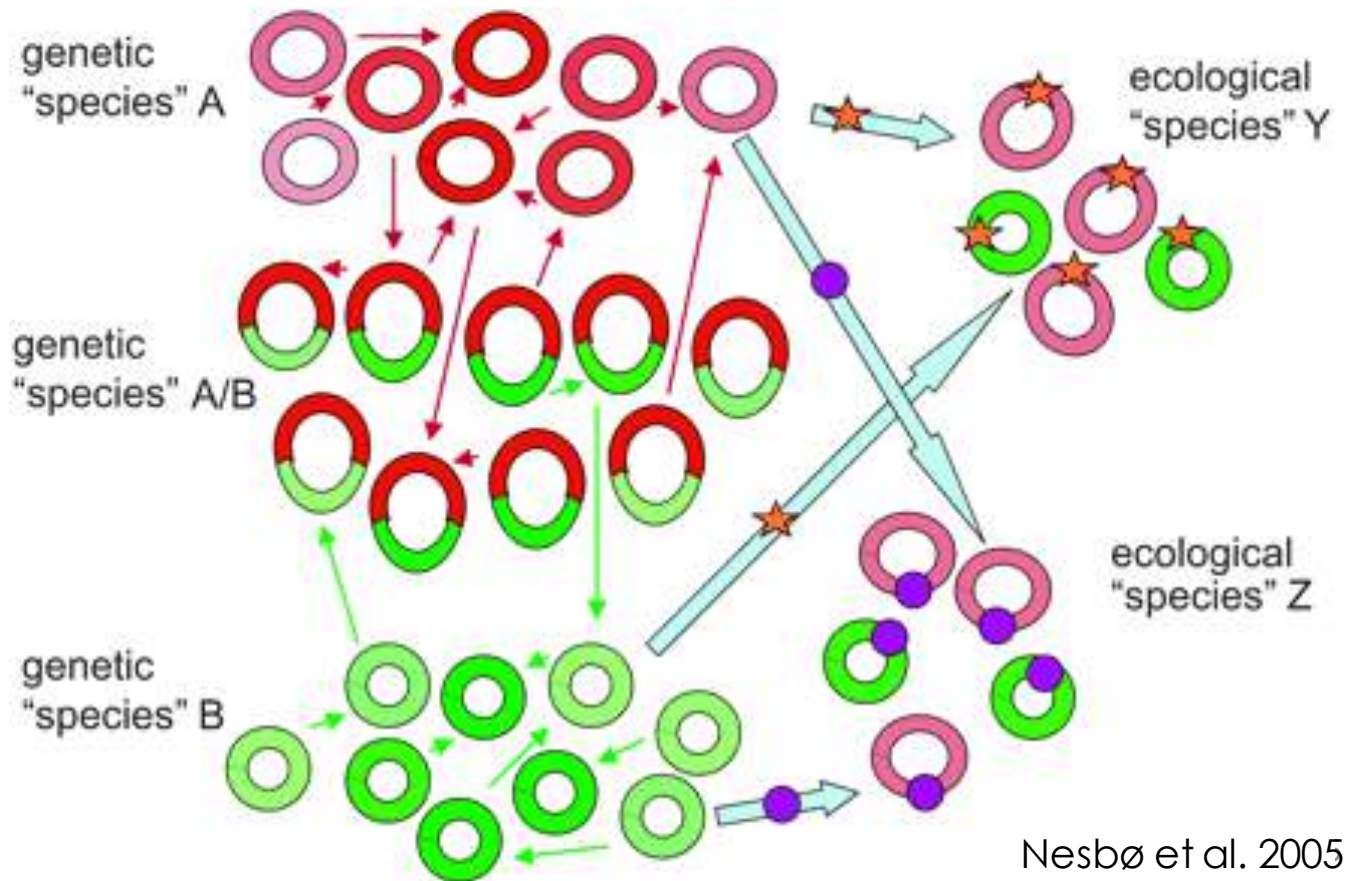




Doolittle and Papke 2006

# Ecotypes or ecological species

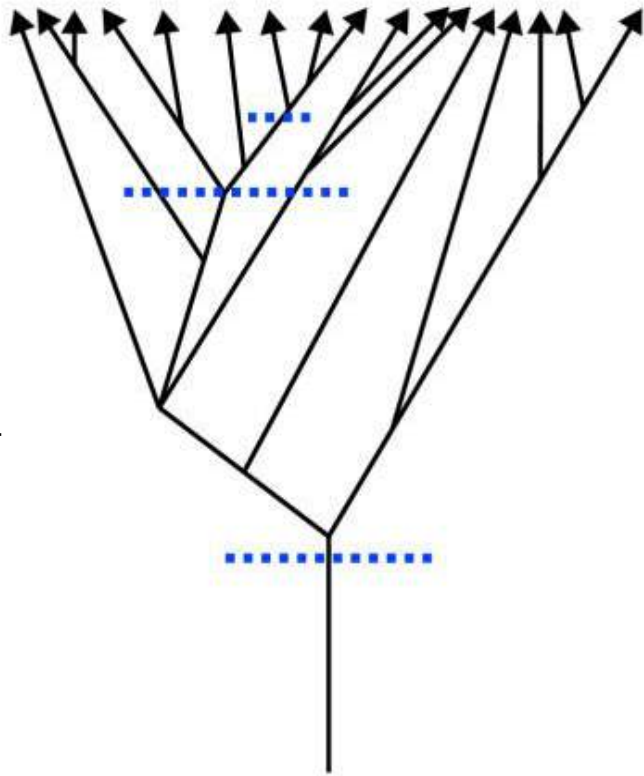
Genetically cohesive clonal lineages, **ecologically distinct**, mostly **non-recombining** (Cohan 2002)



Nesbø et al. 2005



Doolittle and Papke 2006



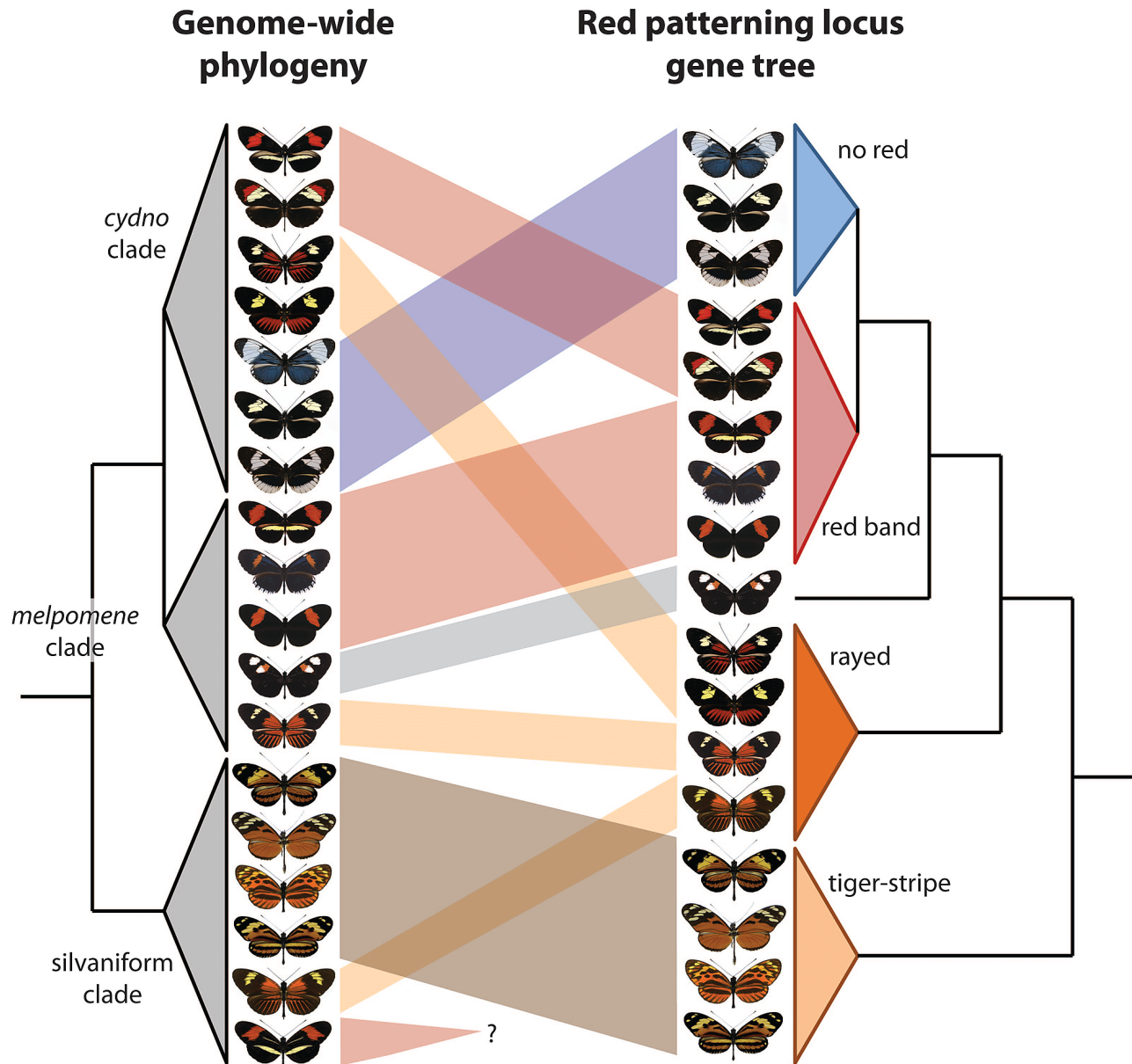
## Polyphasic species

A method of diagnosis and verification, not a concept (Stackebrandt et al. 2002)

Consensus classification: combines biochemical and other phenotypic data with genetic data and phylogenetic inferences (from genes)

Conceptual concession: Multiple processes operating to different degrees in different groups of microorganisms. No one-size-fits-all concept. Only true for prokaryotes?

# *Heliconius* butterfly hybridization



'Species are poorly differentiated way-stations in a continuous hierarchy of biodiversity, rather than discrete and fundamental units' (Mallet 2005, p. 229 – clause order reversed).

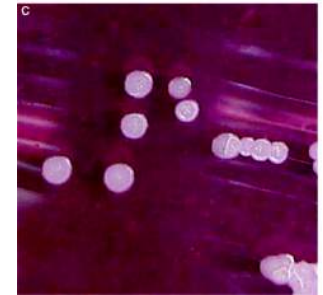


# Conceptual and practical tensions

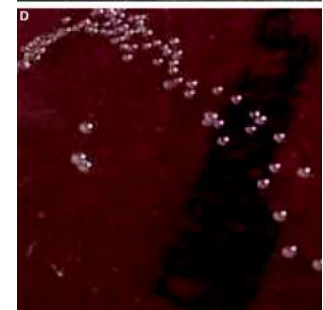
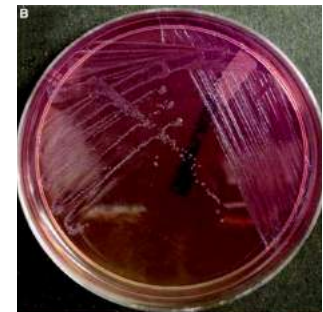
*Burkholderia mallei* and *Burkholderia pseudomallei*: causes of different diseases (glanders versus melioidosis), but similarly antibiotic resistant

Multilocus sequence analysis: '*B. mallei* is a clone of *B. pseudomallei* that, on population genetics grounds, should not be given separate species status' (Godoy et al. 2003).

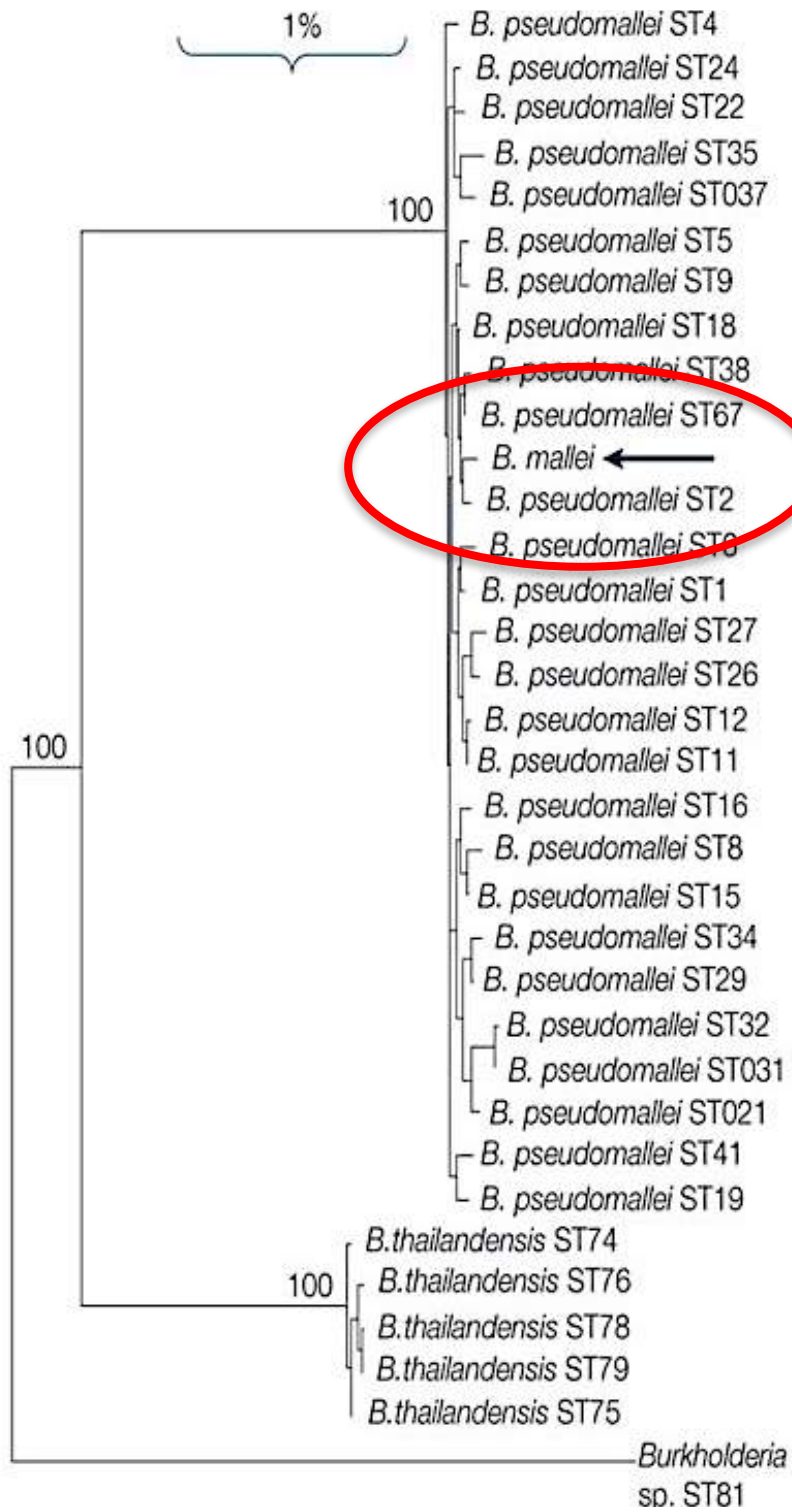
**But** *B. mallei* has a much smaller genome, is ecologically distinct, and has a separate evolutionary trajectory – heading to extinction: a 'species within a species'? (Hanage et al. 2006)



Glass et al.  
2009



Gevers et al. 2005



*B. mallei*



*B. pseudomallei*



*B. thailandensis*

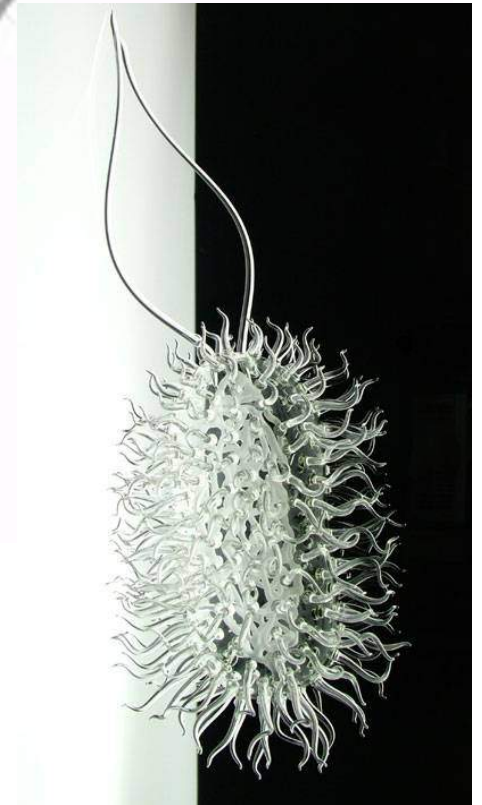
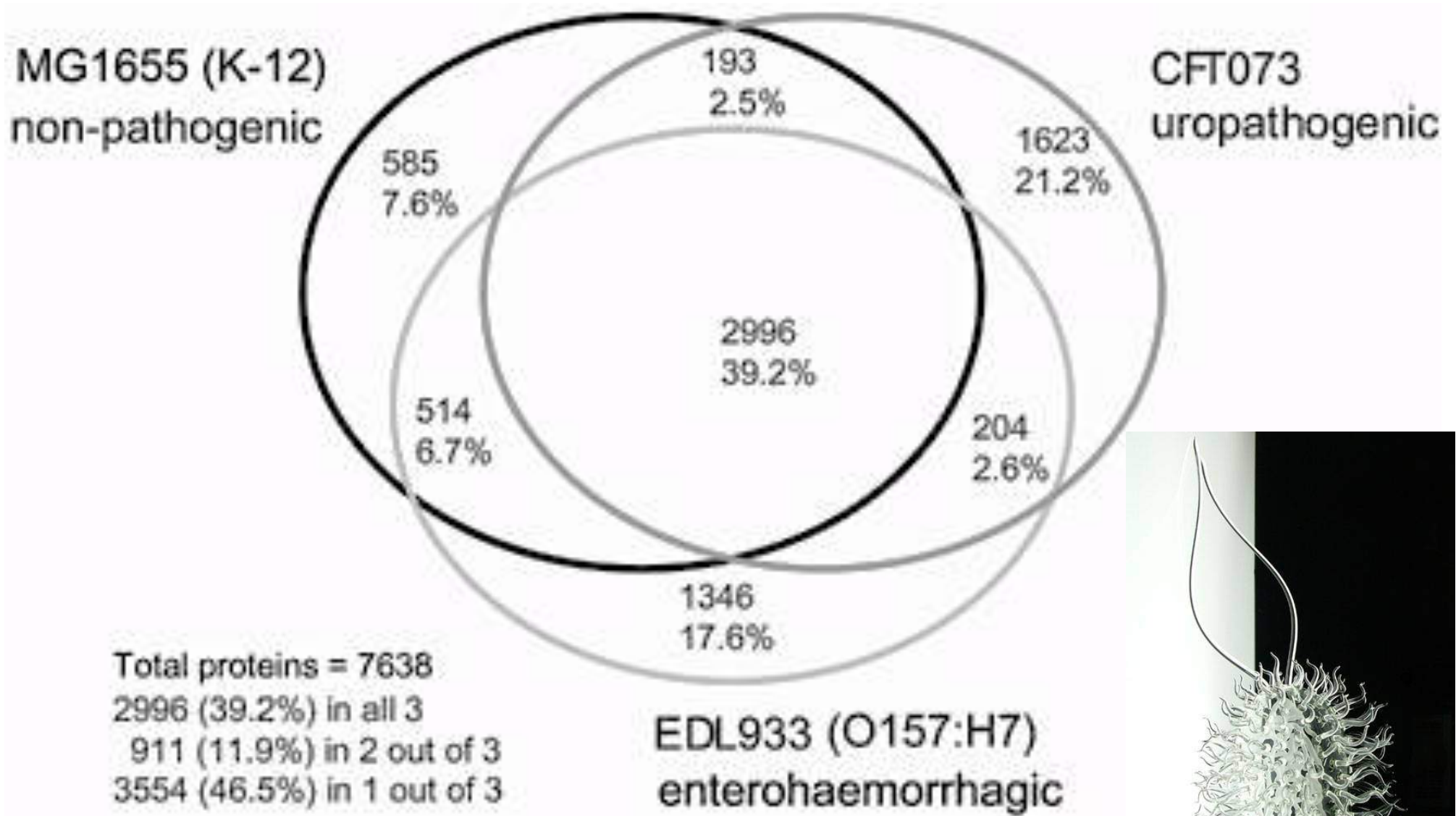


*B. oklahomensis*

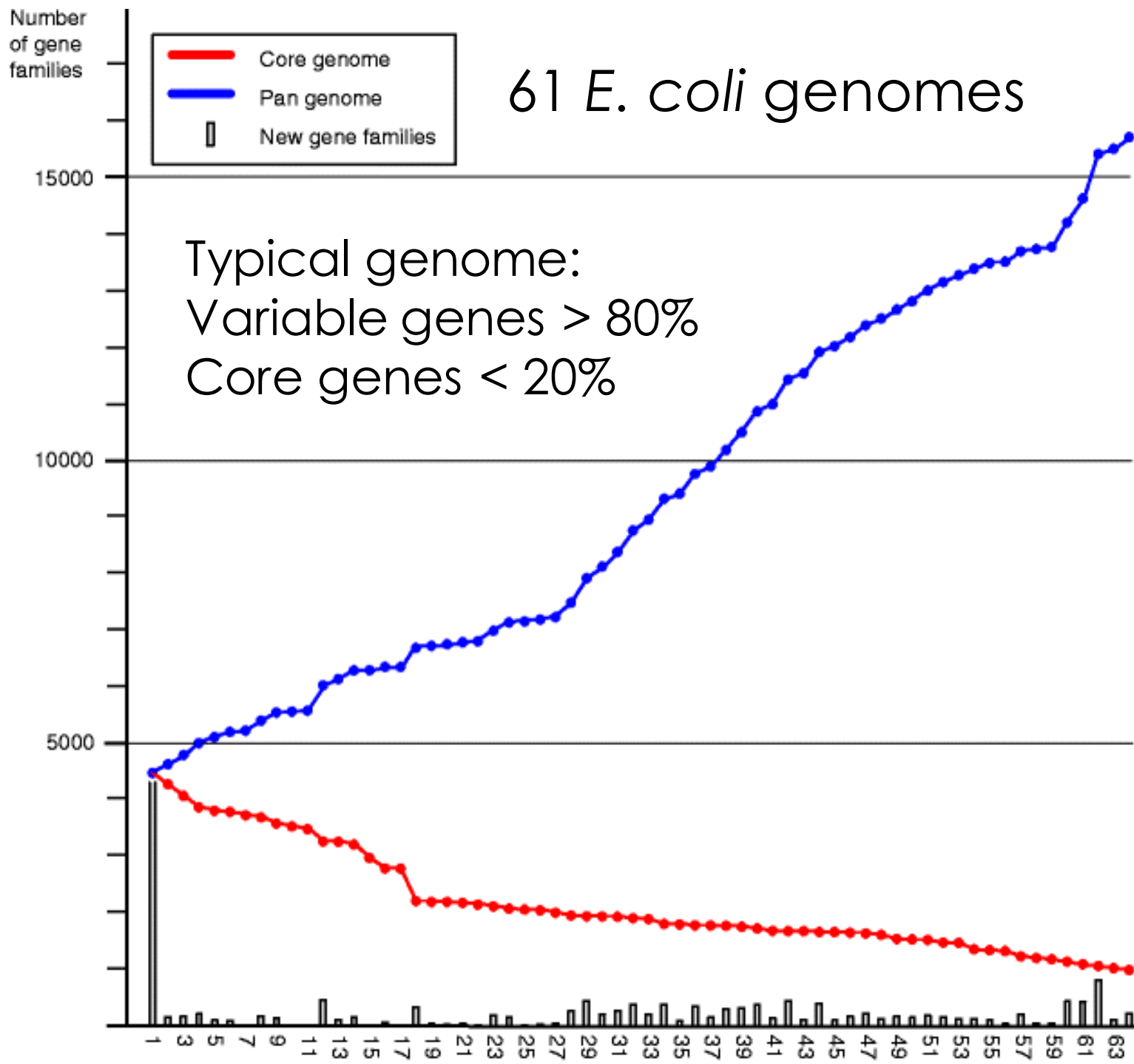
1

Hanage et al. 2006





Genomic (and phenotypic) variation within one 'species': *E. coli* (Welch et al., 2002)



- 1: *Escherichia coli* 0157:H7 str. EC4196
- 2: *Escherichia coli* 0157:H7 str. EC4113
- 3: *Escherichia coli* 0157:H7 str. EC508
- 4: *Escherichia coli* 0157:H7 str. EC4501
- 5: *Escherichia coli* 0157:H7 str. EC4076
- 6: *Escherichia coli* 0157:H7 str. EC4115
- 7: *Escherichia coli* 0157:H7 str. EC4042
- 8: *Escherichia coli* 0157:H7 str. EC4486
- 9: *Escherichia coli* 0157:H7 str. EC869
- 10: *Escherichia coli* 0157:H7 str. EC4206
- 11: *Escherichia coli* 0157:H7 str. EC4401
- 12: *Escherichia coli* 0157:H7 str. EDL933
- 13: *Escherichia coli* 0157:H7 str. TW14588
- 14: *Escherichia coli* 0157:H7 str. Sakai
- 15: *Escherichia coli* 0157:H7 str. EC4045
- 16: *Escherichia coli* 0157:H7 str. LANL ECF
- 17: *Escherichia coli* 0157:H7 str. LANL ECA
- 18: *Escherichia coli* K12 str. DH10B
- 19: *Escherichia coli* K12 str. MG1655
- 20: *Escherichia coli* K12 str. W3110
- 21: *Escherichia coli* K12 str. DH1
- 22: *Escherichia coli* BW2952
- 23: *Escherichia coli* ATCC8739
- 24: *Escherichia coli* B REL606
- 25: *Escherichia coli* BL21 (DE3 Korea)
- 26: *Escherichia coli* BL21 (DE3 AU)
- 27: *Escherichia coli* BL21 (DE3 DOE)
- 28: *Escherichia coli* HS
- 29: *Escherichia coli* SE11
- 30: *Escherichia coli* IAI1
- 31: *Escherichia coli* 65989
- 32: *Escherichia coli* E24377A
- 33: *Escherichia coli* O26:H11 str. 11368
- 34: *Escherichia coli* O127:H6 str. E2348/69
- 35: *Escherichia coli* O103:H2 str. 12009
- 36: *Escherichia coli* O111:H- str. 11128
- 37: *Escherichia coli* O103 Oslo
- 38: *Escherichia coli* SMS-3-5
- 39: *Escherichia coli* UMN026
- 40: *Escherichia coli* 53638
- 41: *Escherichia coli* IAI39
- 42: *Escherichia coli* UT189
- 43: *Escherichia coli* S88
- 44: *Escherichia coli* CFT073
- 45: *Escherichia coli* SE15
- 46: *Escherichia coli* 535
- 47: *Escherichia coli* ED1a
- 48: *Escherichia coli* F11
- 49: *Escherichia coli* APECO1
- 50: *Escherichia coli* E110019
- 51: *Escherichia coli* E22
- 52: *Escherichia coli* B7A
- 53: *Escherichia coli* 101-1
- 54: *Shigella flexneri* 2a 2457T
- 55: *Shigella flexneri* 2a 301
- 56: *Shigella flexneri* 5 8401
- 57: *Shigella boydii* CDC 3083-94
- 58: *Shigella boydii* Sb227
- 59: *Shigella sonnei* Ss046
- 60: *Escherichia fergusonii* ATCC 35469
- 61: *Escherichia albertii* TW07627
- 62: *Salmonella enterica* Typhimurium LT2
- 63: *Shigella dysenteriae* Sd197
- 64: *Shigella dysenteriae* 1012

***E. coli* pan-genome 10,131 genes**

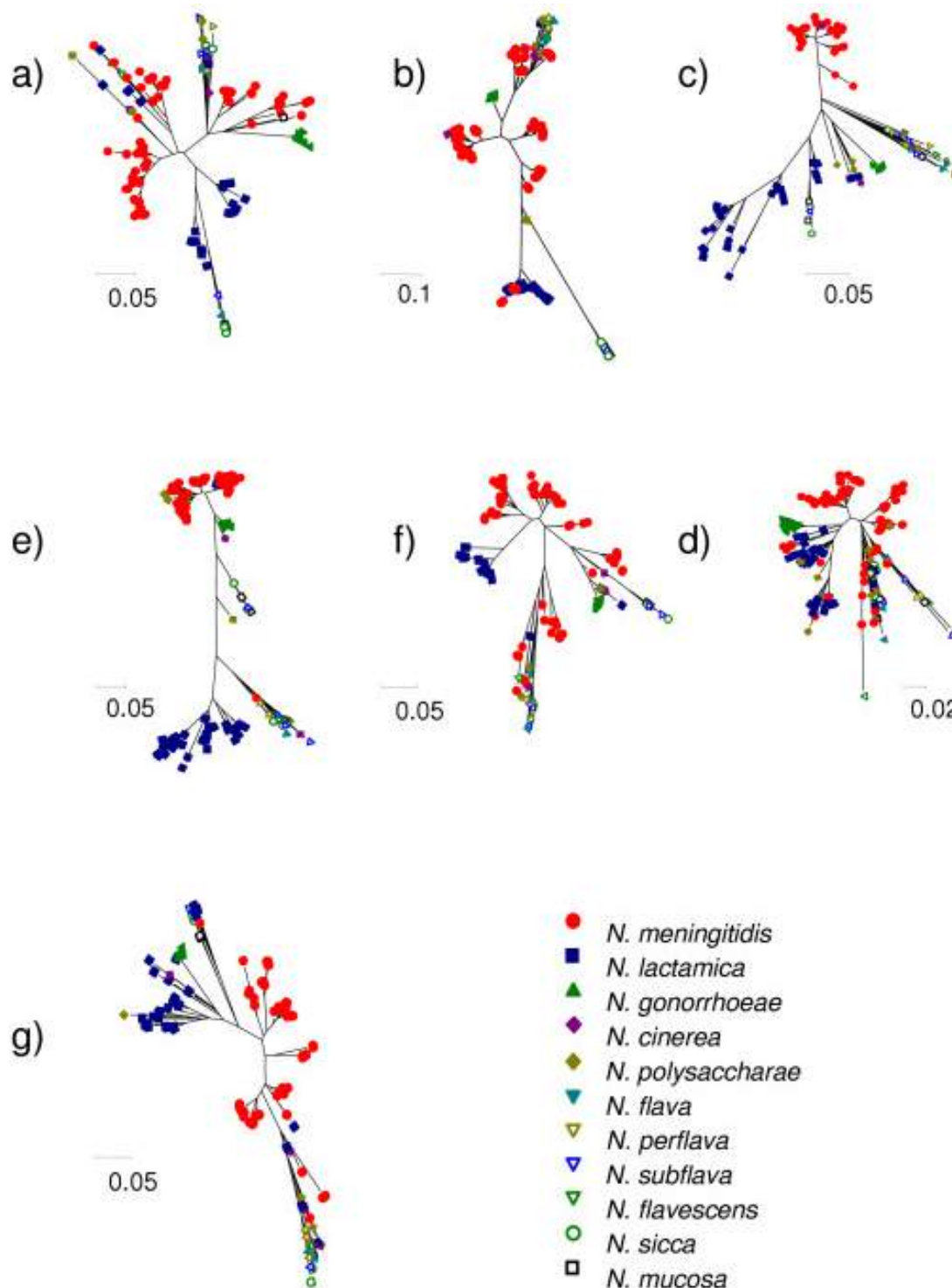
**Average *E. coli* genome has 4,721 genes**

**Core genome 2,167 genes**

One species?

The core genome is less than 50% of the genes of any 'strain' (not considered to be a species) of *E. coli* (Hendrickson 2009)

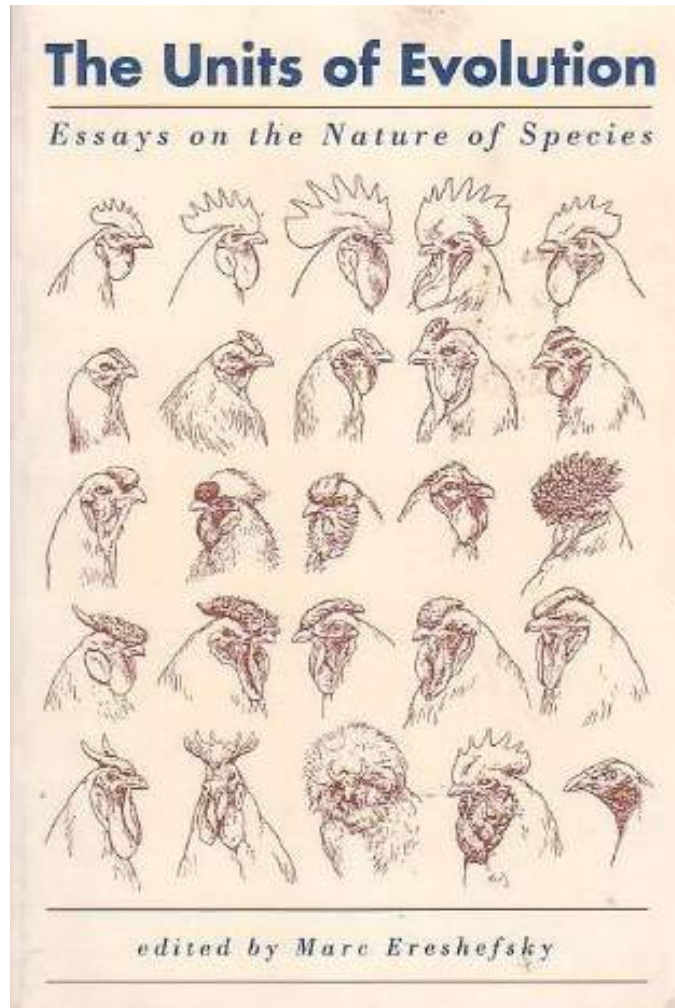




Different genes,  
different histories:  
**fuzzy species**

‘Species clusters are not ideal entities with sharp and unambiguous boundaries; instead they come in multiple forms and ... may be fuzzy and indistinct’ (Hanage et al. 2005, p. 6)

# Pluralism re species concepts



What are the ramifications of accepting species concept pluralism?

Anything goes?

Human created, not created by nature/evolution? Non sequitur

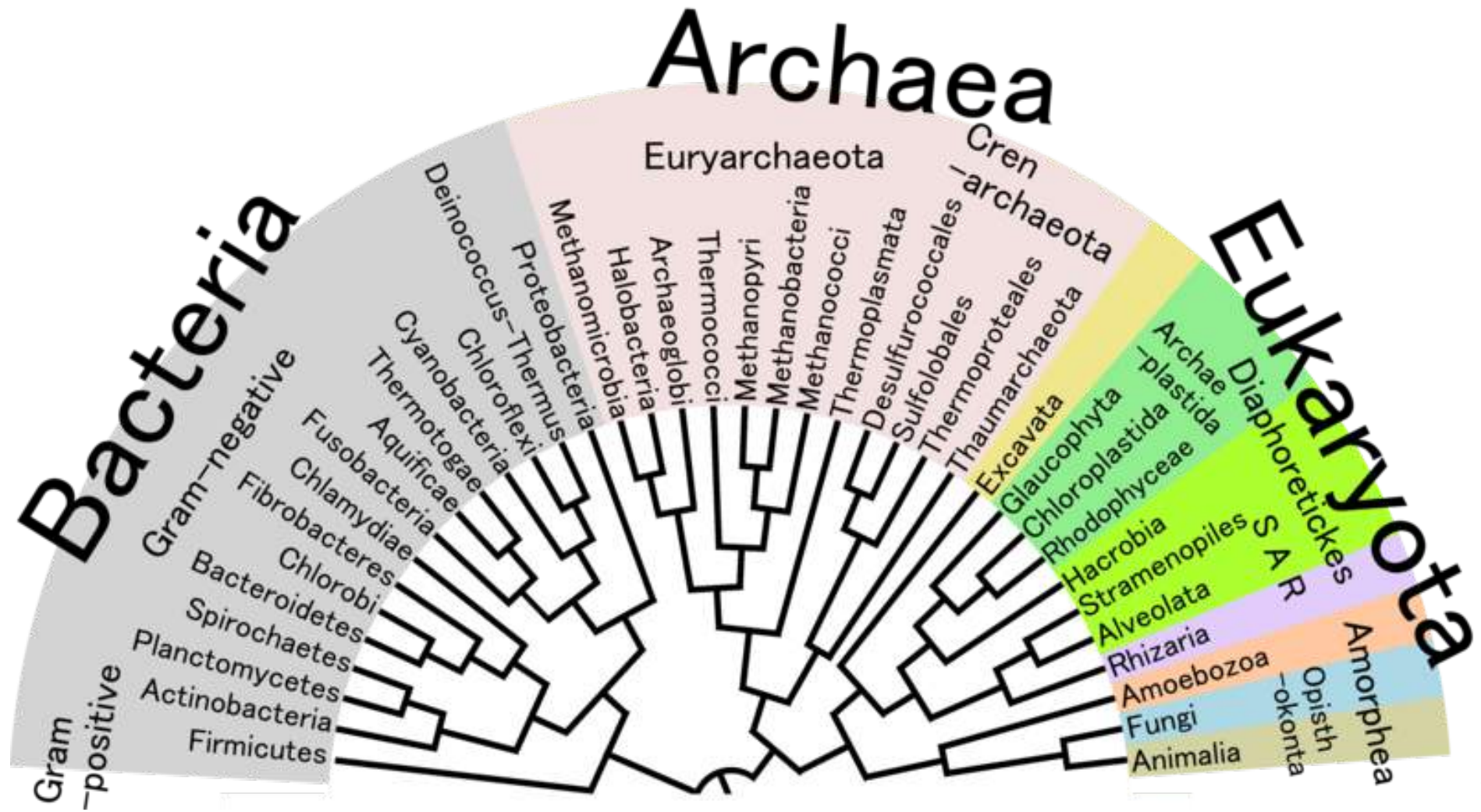
Is it a disaster for biology/medicine to have a plurality of concepts?

Different explanatory aims: epidemiological, ecological, evolutionary, taxonomic

Lots of philosophical questions ...

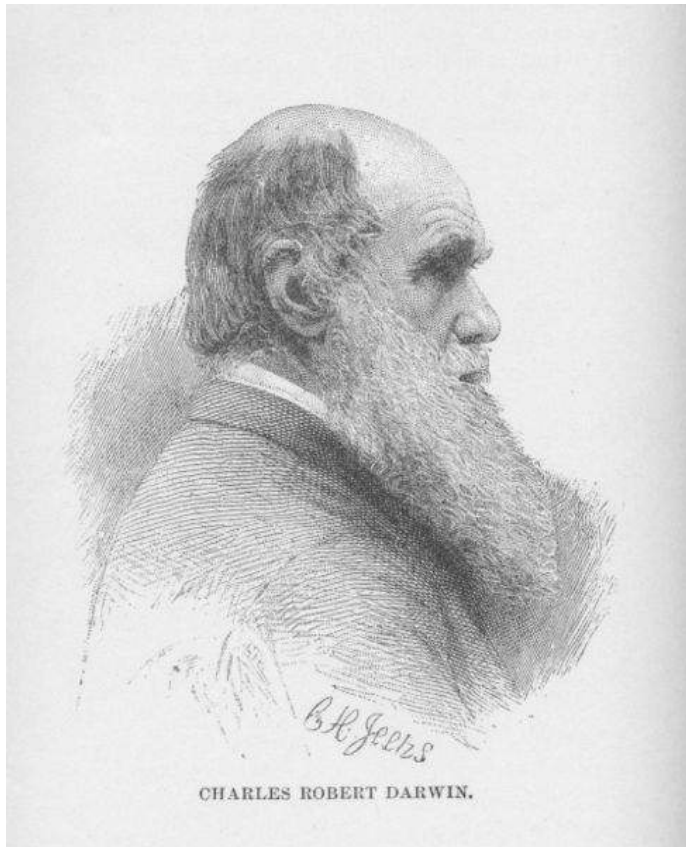
# Tree of Life (TOL)

From species to trees  
Tree of life = tree of species?



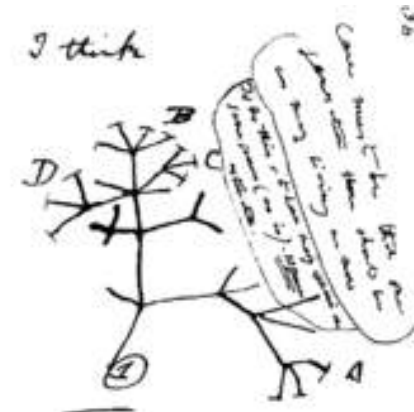


## Darwin and the tree of life



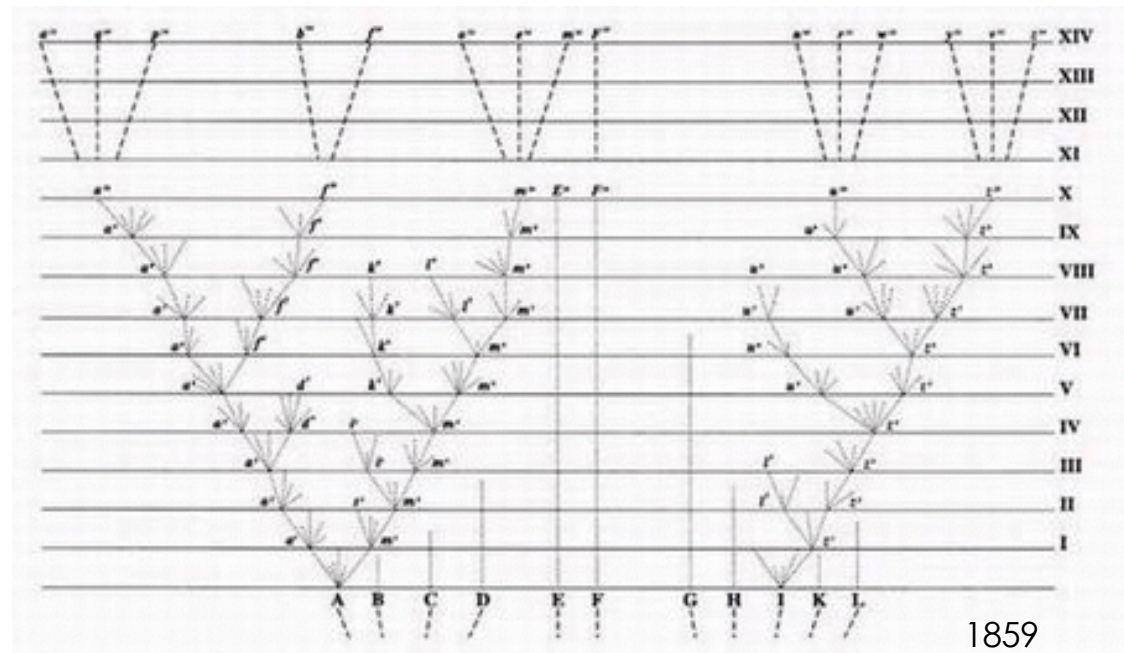
‘The affinities of all the beings of the same class have sometimes been **represented by a great tree.** I believe this simile largely speaks the truth. The green and budding twigs may represent **existing species**; and those produced during each former year may represent the long succession of **extinct species**’ (1859, p 129).

‘As limbs give rise by growth to fresh buds, and these, if vigorous, branch out and overtop on all sides many a feebler branch, so by generation I believe it has been with **the great Tree of Life**, which fills with its dead and broken branches the crust of the earth, and covers the surface with its ever branching and beautiful ramifications’  
 (1872, pp. 171-2)

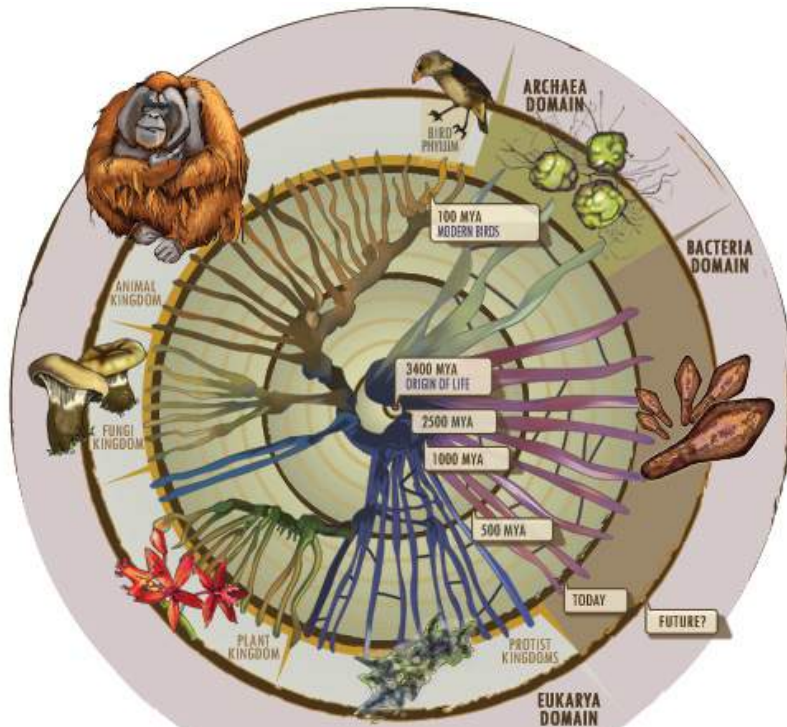


*I think*  
 Then between A & B. various  
 size of relation. C & B. the  
 first predation, B & D  
 rather greater distinction  
 then former would be  
 formed. - binary relation

1837



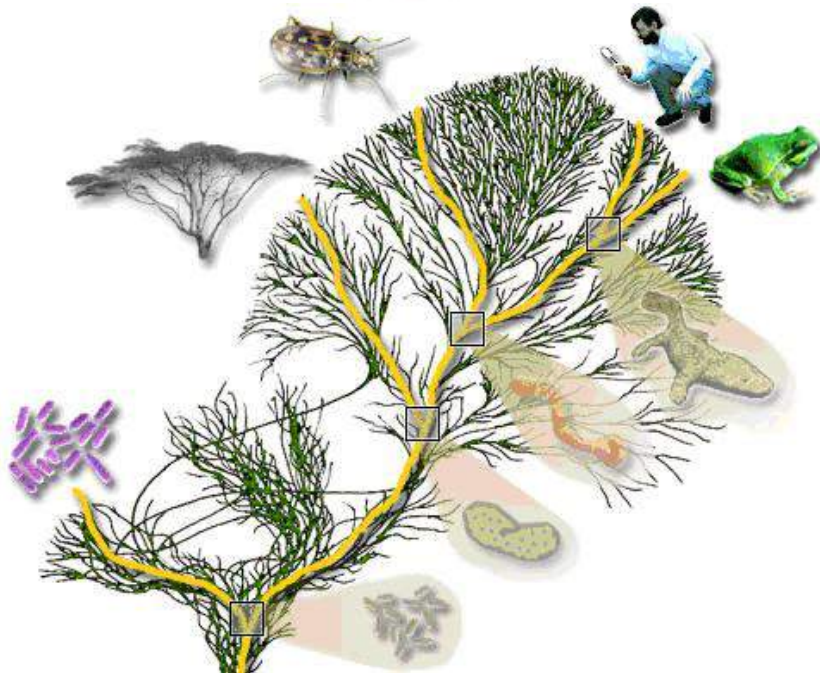
1859



Picou and Pollock 2009

## Universal molecular TOL

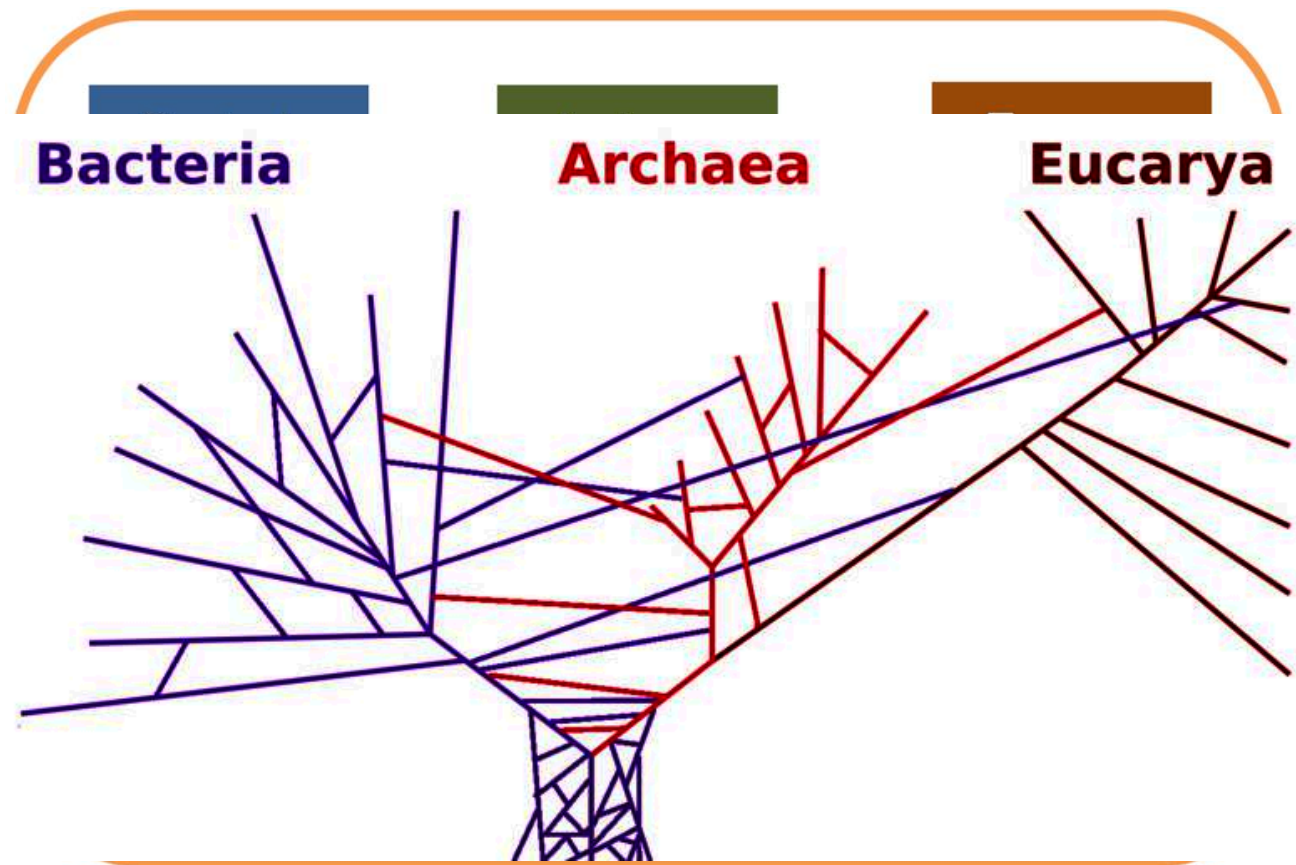
‘The Tree of Life represents the phylogeny of all organisms, i.e., the history of organismal lineages as they change through time. It implies that different species arise from previous forms via descent, and that **all organisms**, from the smallest microbe to the largest plants and vertebrates, **are connected by the passage of genes along the branches of the phylogenetic tree that links all of Life**’ ([www.tolweb.org](http://www.tolweb.org))





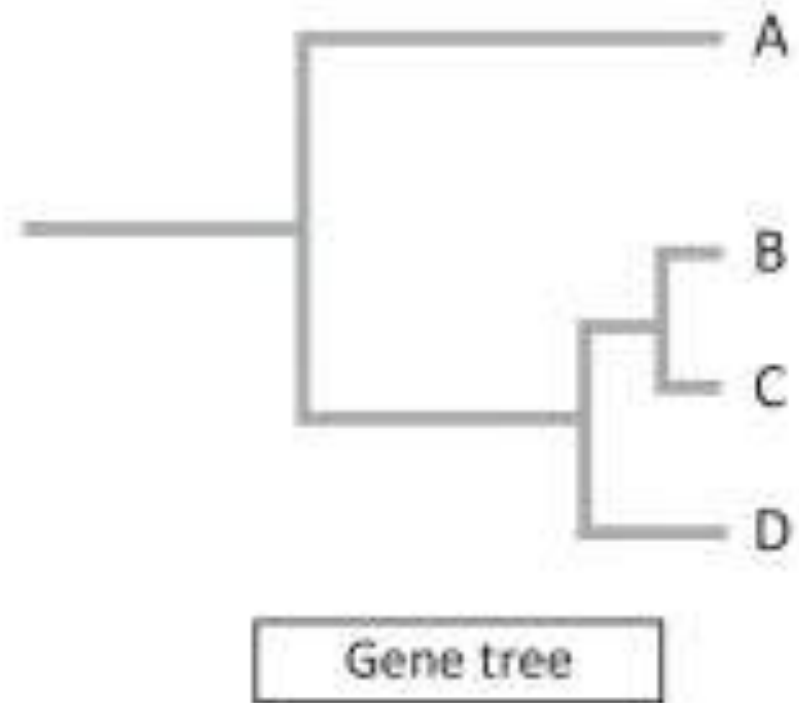
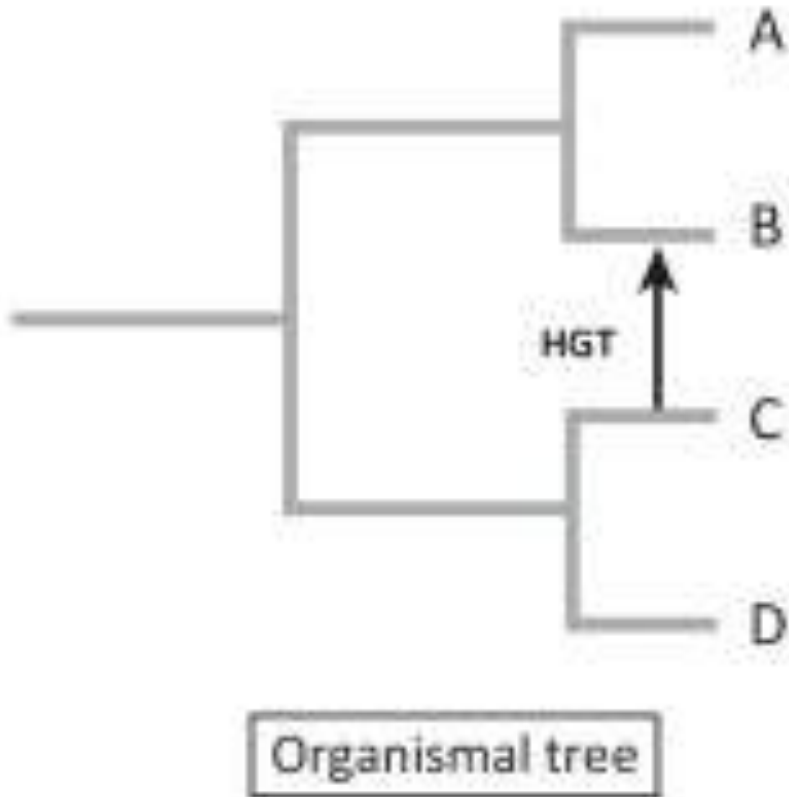
## Phylogeny and gene trees

Salvation for microbiology!  
Or is it?



Incongruence due to promiscuous, rampant gene transfer. The demise of the tree of life?

Seems not.  
What's going on?



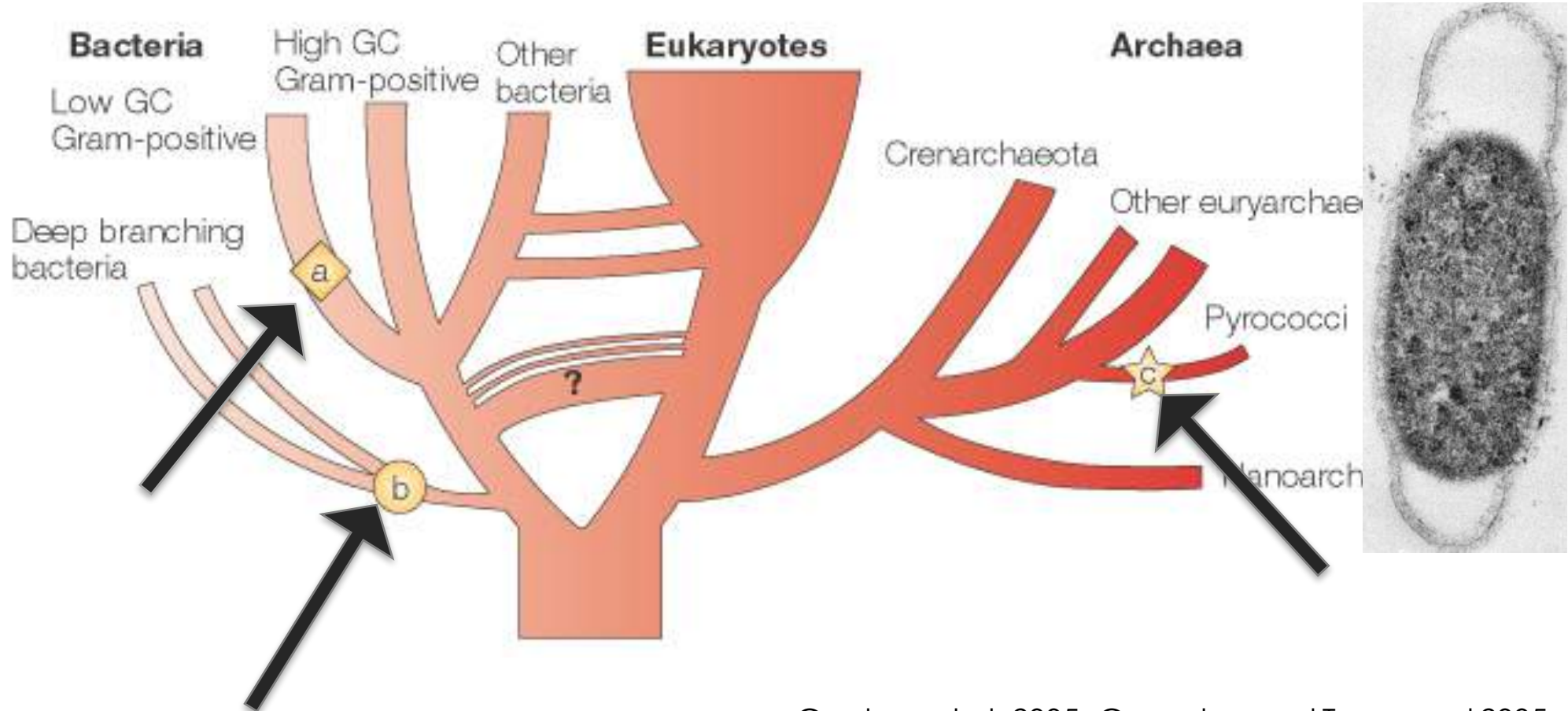
Incongruence due to LGT

# Placing *Thermotoga maritima* in the tree of life

a = according to 'concordant' genes

b = according to ribosomal genes and genome data

c = according to 'phylogenetically discordant' genes

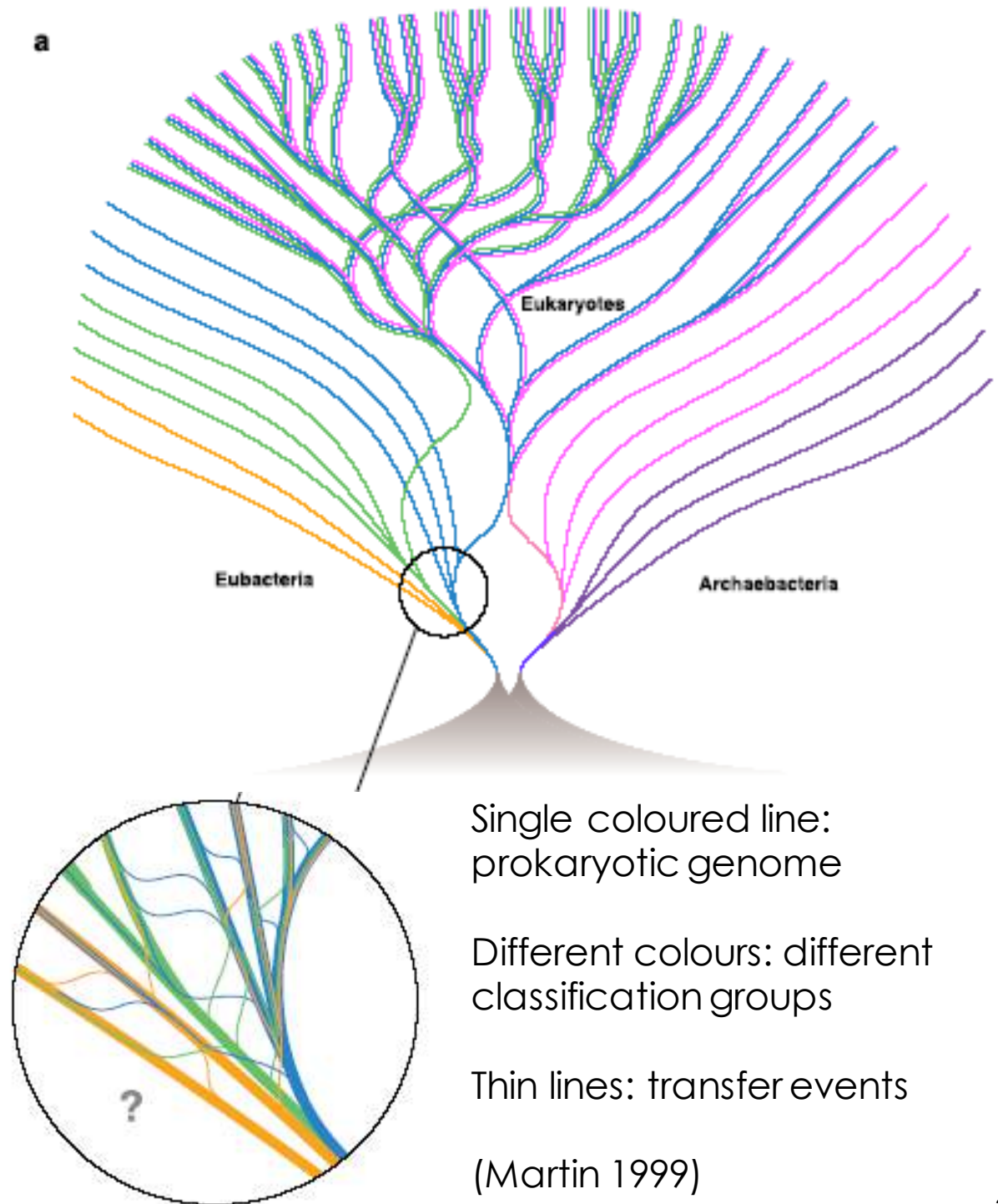




# Tree of genomes

Lateral gene transfer is widespread and evolutionarily significant

The closer you look, the worse it gets!



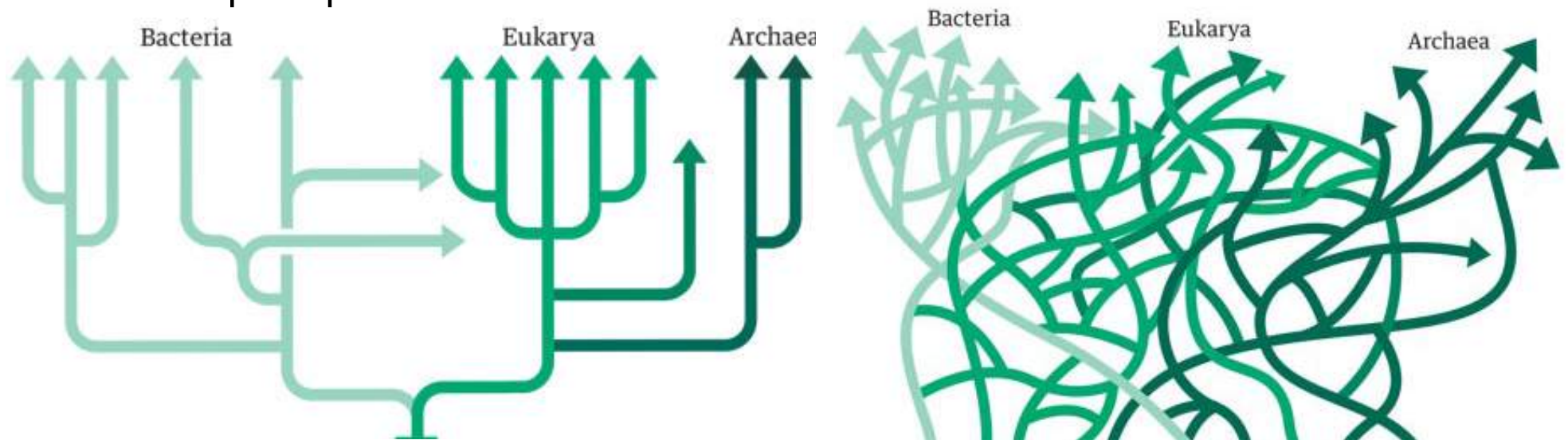
# Different processes and patterns for prokaryotes

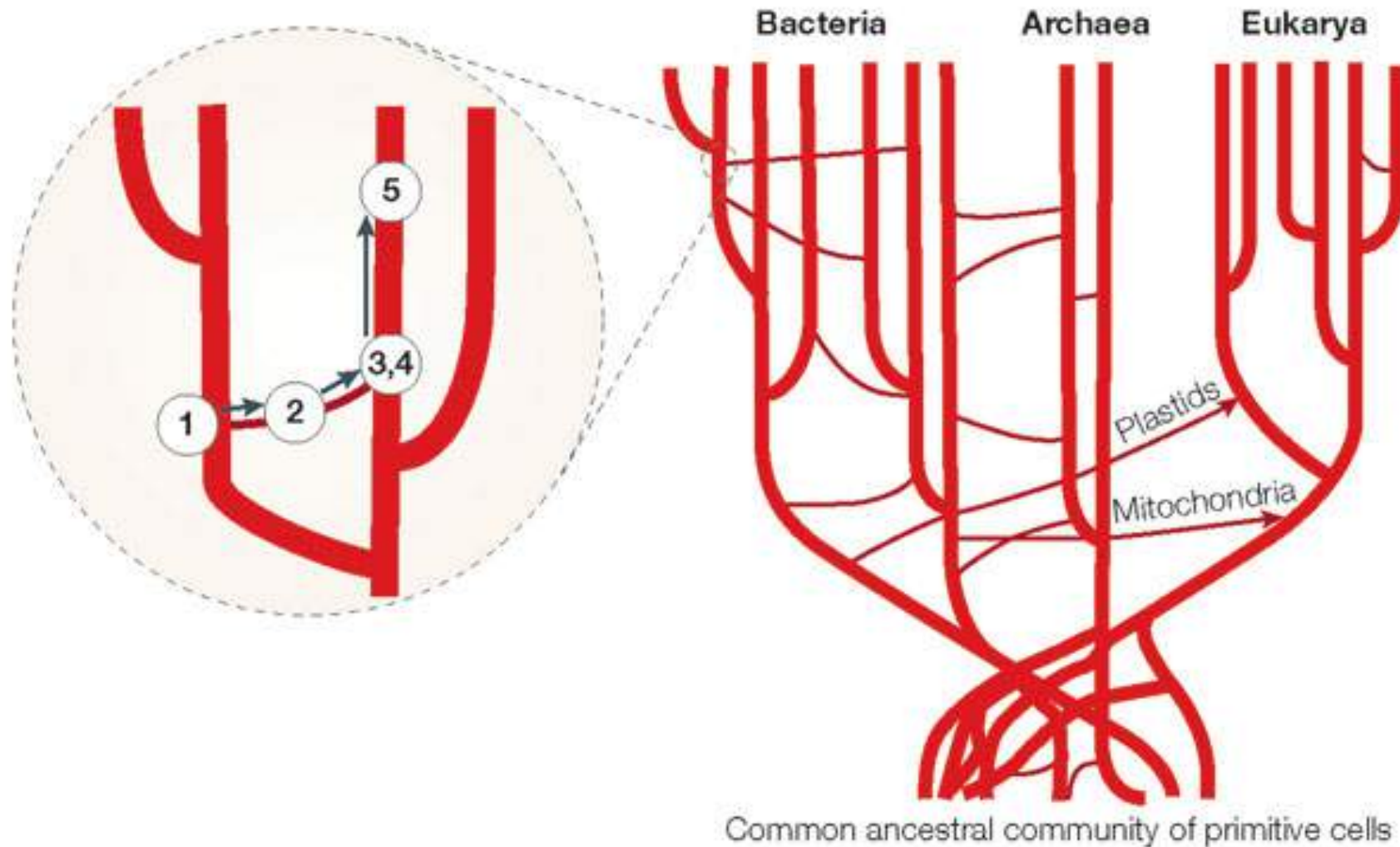
Major differences in mechanisms of genetic variation

- Lateral gene transfer is not sexual reproduction
  - Unidirectional (non-reciprocal recombination)
  - Partial recombination of genomes

Patterns in prokaryotic evolution

- Not structured exclusively by bifurcations
- Often extensively reticulated
- Multiple patterns

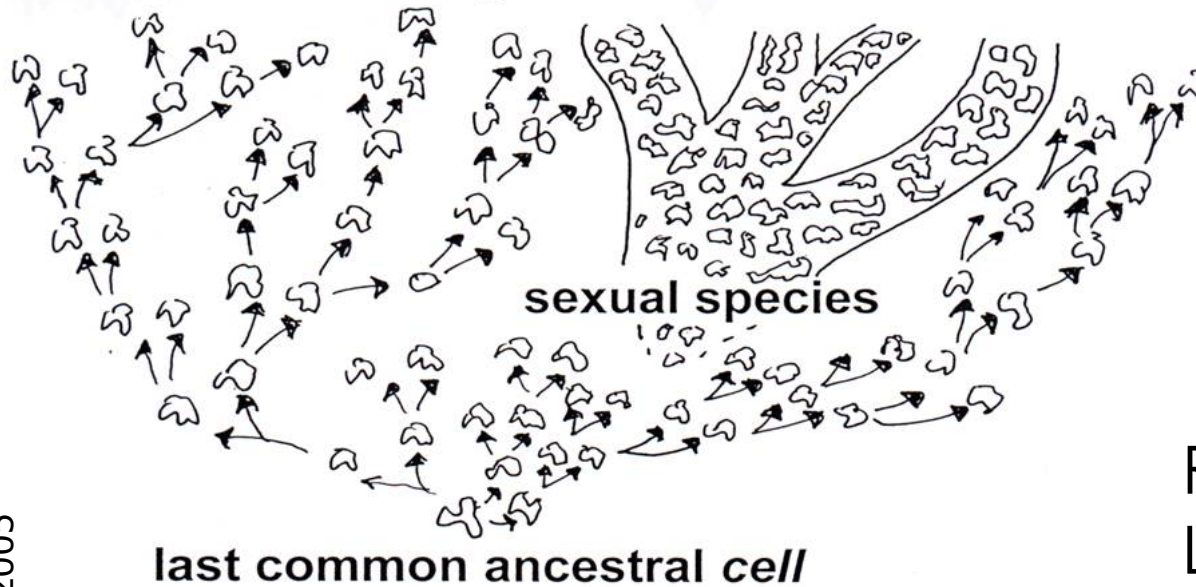




Response 1: LGT is '**just a complication** that leaves the basic tree structure intact' (e.g., Smets and Barkay 2005, p. 676, paraphrased).

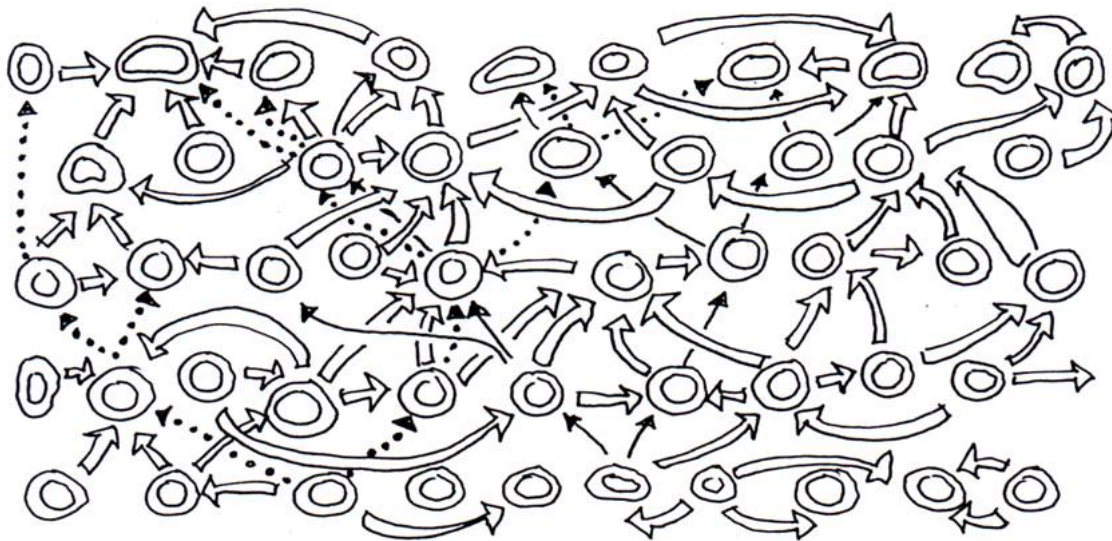


## Tree of Organisms



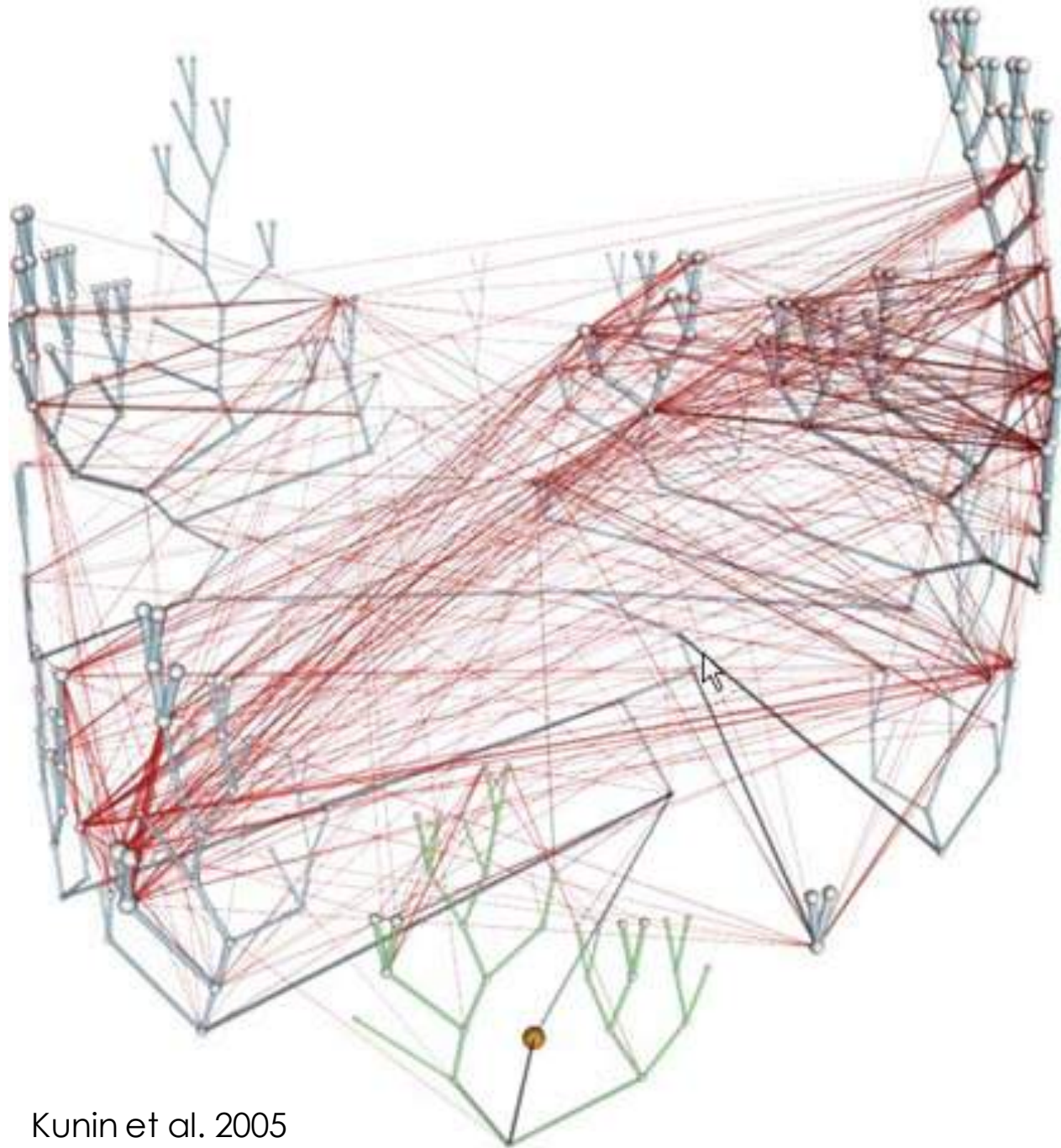
Doolittle 2005

## Web of Genomes



Response 2:  
LGT destroys all hope  
of reconstructing the  
**tree** of life (e.g.,  
Doolittle 2005)

But it opens the door  
to another view ...



## Net of life

Branches & vines:  
representing  
vertical *and*  
horizontal  
transmission

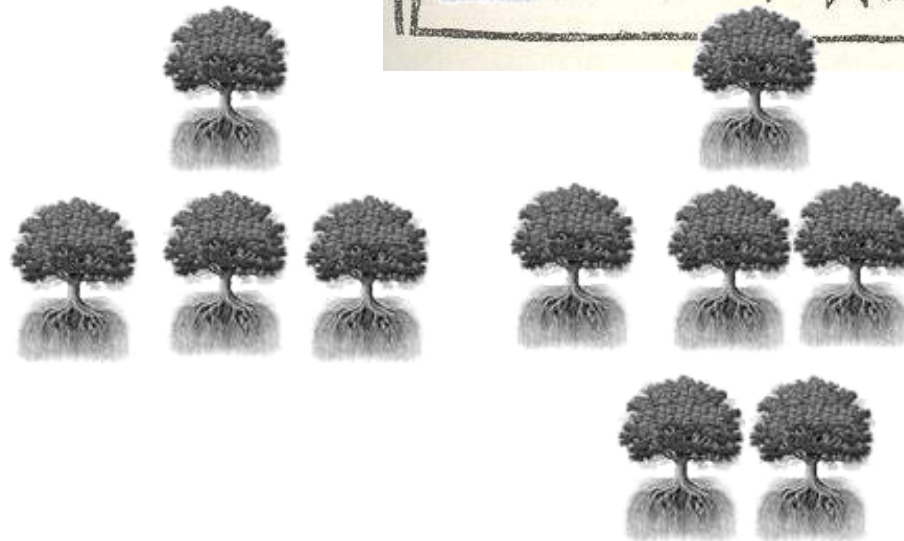
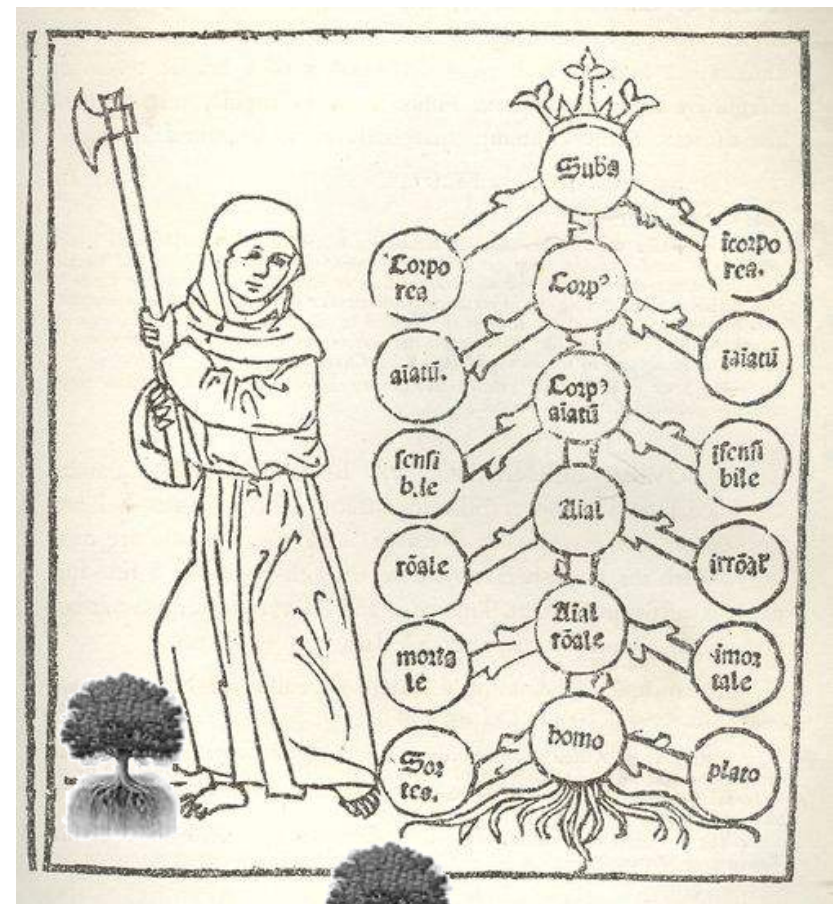
Trees are special  
networks; not all  
networks are trees



What scientific role is the tree of life (TOL) playing?

Not in regard to what it represents (evolution of species, genes, genomes, cells etc) but what it does in scientific practice

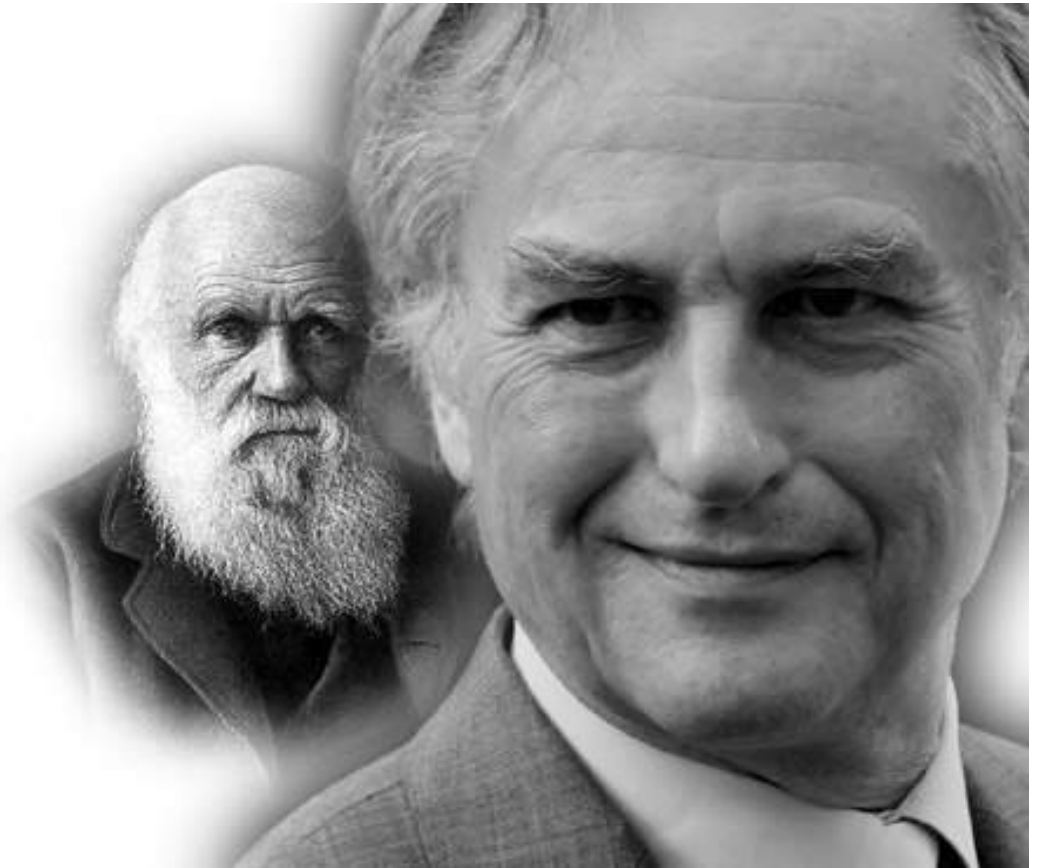
- An axiom
- A hypothesis
- A heuristic
- A model





## The TOL as an axiom

‘For there is, after all, one true tree of life, the unique pattern of evolutionary branching that actually happened. It exists. It is in principle knowable’  
(Dawkins 2003, p. 112)



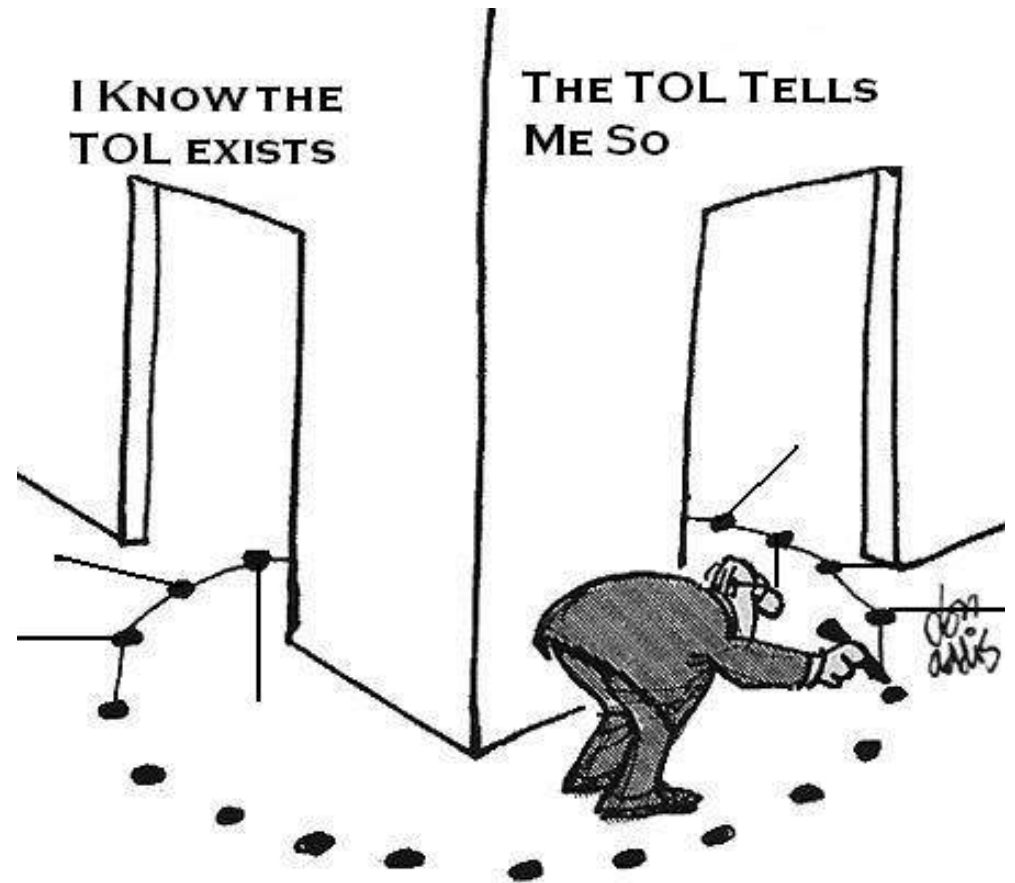
## TOL-axiom problems

A major assumption: can it be justified?

Circularity of justification and assumption

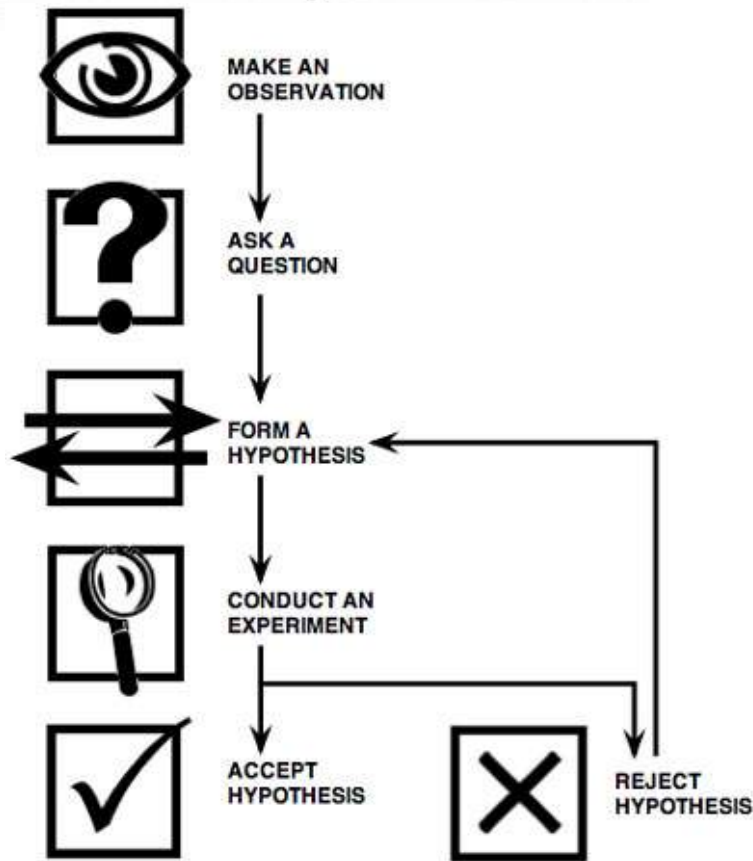
Is that really how the TOL has been used?

Good science is about testing hypotheses, isn't it?



**FAITH-BASED TREE LOGIC**

**because circular reasoning works**



## The TOL as a hypothesis

‘If LGT repeatedly contradicts Darwin’s hypothesis about the TOL, then the hypothesis has to be rejected. Continuing to use the TOL means that testability, verification and falsification have all been violated’ (Doolittle and Baptiste 2007, paraphrased).



But abandoning the TOL means abandoning phylogeny, doesn't it?

Problems of 'falsification': that's not how science works.

Why do the TOL and phylogeny persist?

Just a bad metaphor? Or something more constructive?



# The TOL as heuristic

For gaining broad knowledge, not testing narrow hypotheses



Carl Woese (1994, 1996): 'A phylogenetic articulating framework';  
'Darwin's dream' of a unified phylogeny

Nicolas Galtier (2009): 'The TOL is a conceptual tool ... irrespective of its existence in the real world'

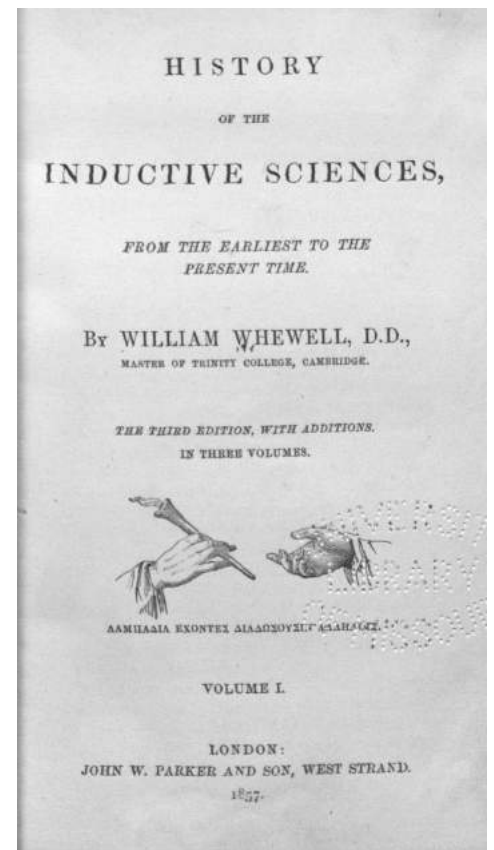
Ford Doolittle (2009): The TOL has a 'useful organizing function'

# William Whewell (1794-1866)

Early use of heuristic in English:

‘If you will not let me treat the Art of Discovery as a kind of Logic, I must take a new name for it, Heuristic’ (1860 letter, in *Todhunter* 1876, p. 418).

A heuristic is a ‘bond of unity by which the phenomena are held together’ so that the topic may be examined more closely and formally.





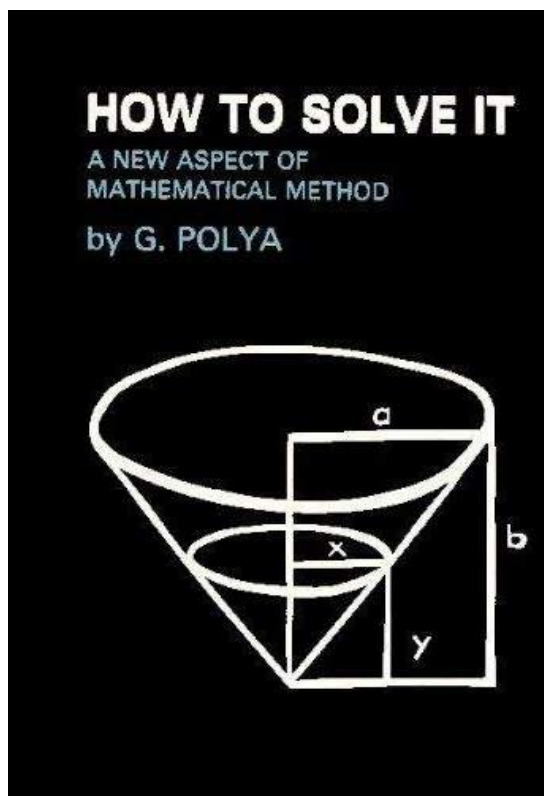


## George Pólya on heuristics

Heuristic reasoning is 'provisional and plausible only', aimed at discovering the solution to particular problems.

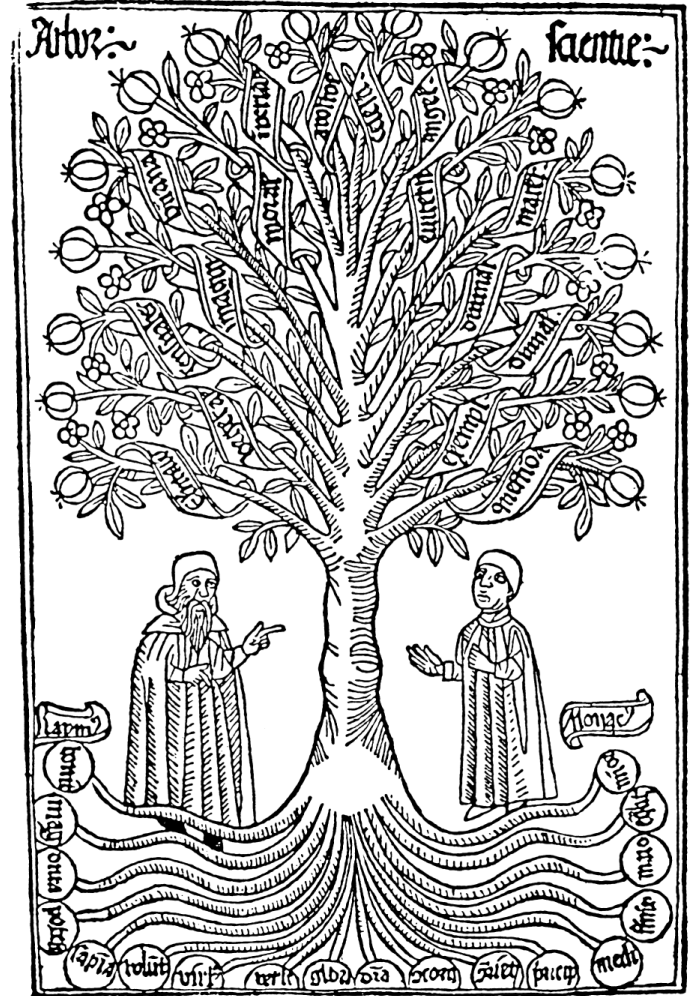
Heuristics, on the basis of induction or analogy, produce a partial solution that may become more complete.

By understanding heuristics, the mathematician will understand the methods of discovery (Pólya 1957; Romanycia and Pelletier 1985).



## The Tree of Life in Darwin : Aid = heuristic?

‘As it is difficult to show the blood-relationship between the numerous kindred of any ancient and noble family, even by the aid of a genealogical tree, and almost **impossible to do this without this aid**, we can understand the extraordinary difficulty which naturalists have experienced in describing, without the **aid of a diagram**, the various affinities which they perceive between the many living and extinct members of the same great natural class’ (Darwin 1859, p. 431 — emphases added).





Only for discovery? Move beyond the heuristic once you've got the correct theory?

That doesn't seem to be happening with the tree of life. It is a goal, an end point, for many evolutionary analyses.

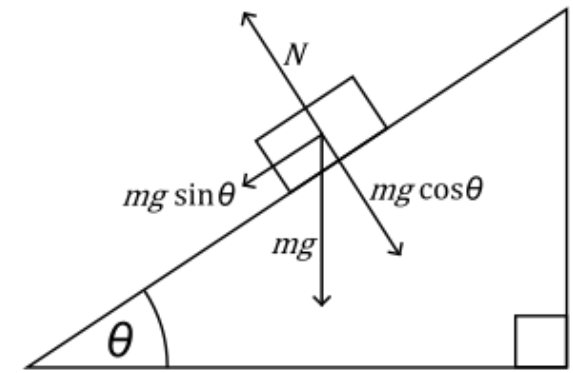
More trees and trees of life now than ever before.

And lots of optimism about **reconciliation** of incongruent branches and **resolution** of unknown branching patterns.

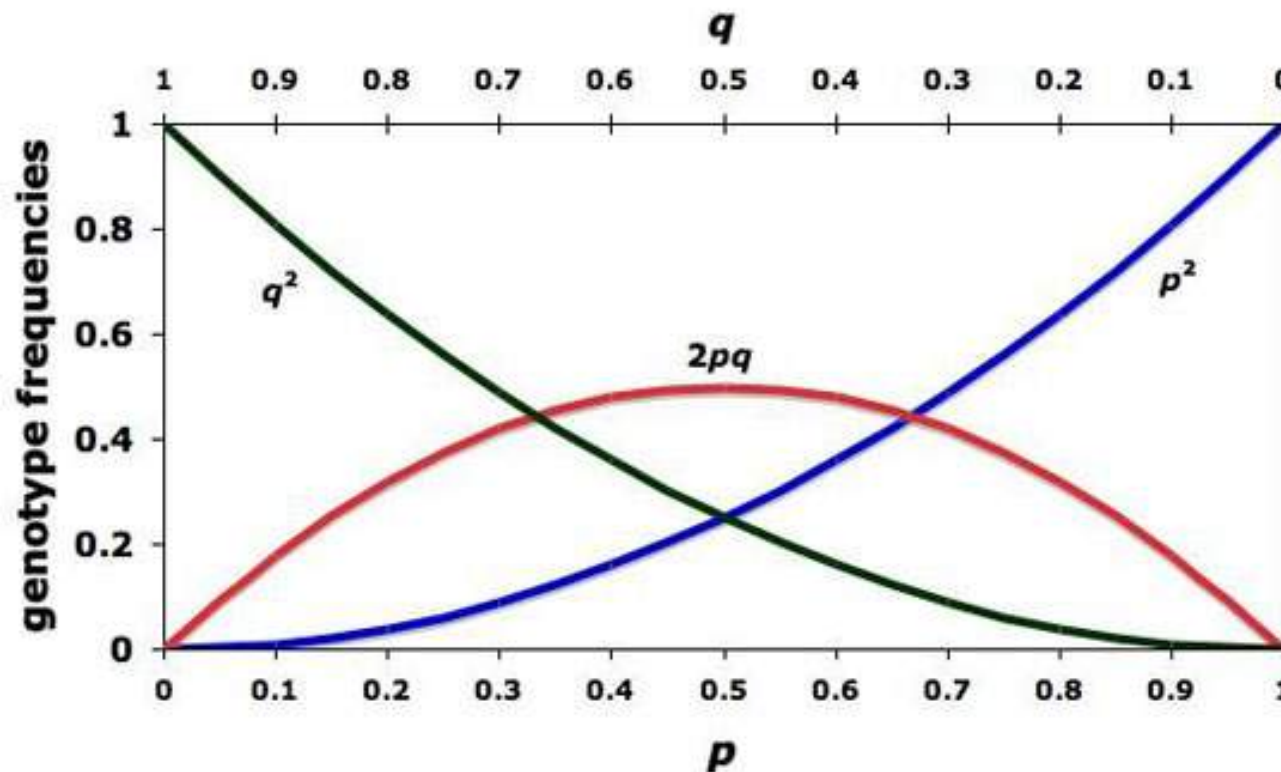


# The TOL as a model

What do models do?



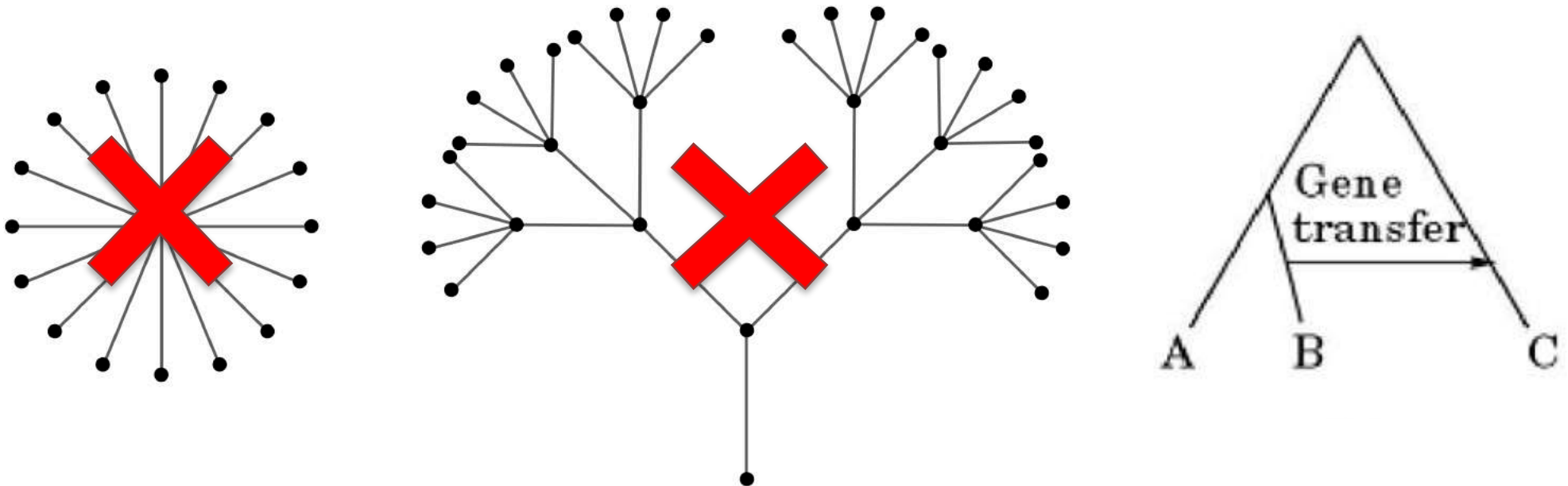
One well known characteristic of models is idealization: frictionless planes, infinite populations + random mating, etc



# Idealizations in tree-building

- Bifurcation only
- Monophyly
- Vertical descent

Phylogenetic trees are basically mathematical structures from graph theory (i.e., rooted binary trees).  
Do they truly *represent* evolutionary history?

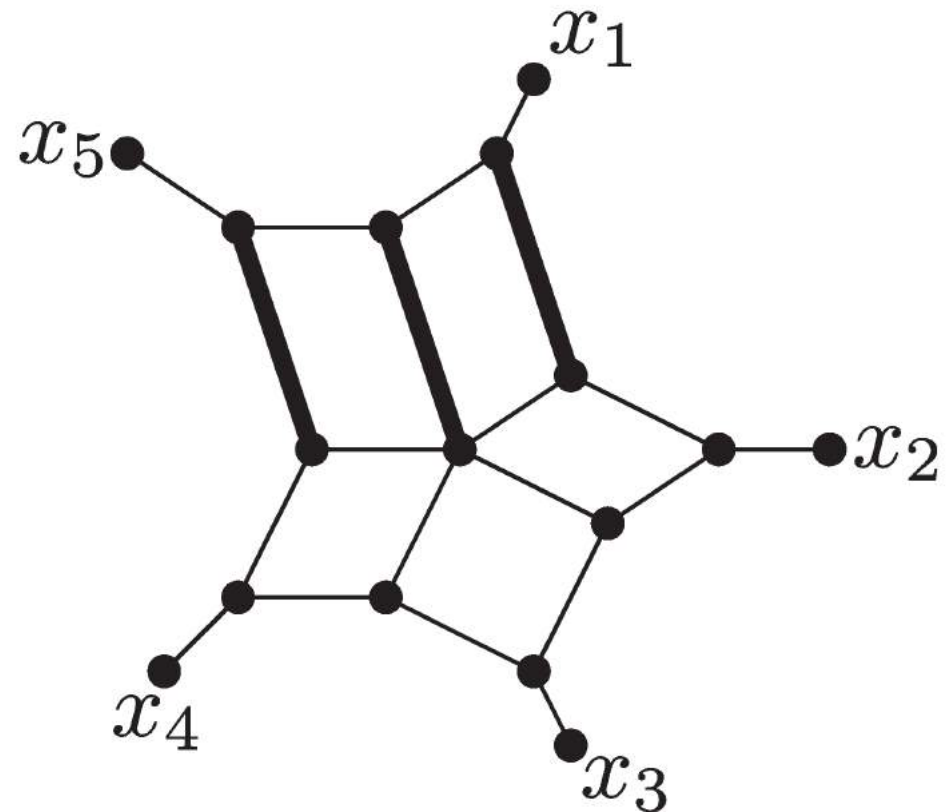


# Model idealization

A philosophical account of the tree of life and microbial phylogeny helps make sense of phylogeny continues despite 'falsification', and why tree-building flourishes and continues to be useful.

Plus, the idealizations of graph theory allow the construction of sophisticated networks of evolutionary history.

But there's more to microbes and models than phylogeny.



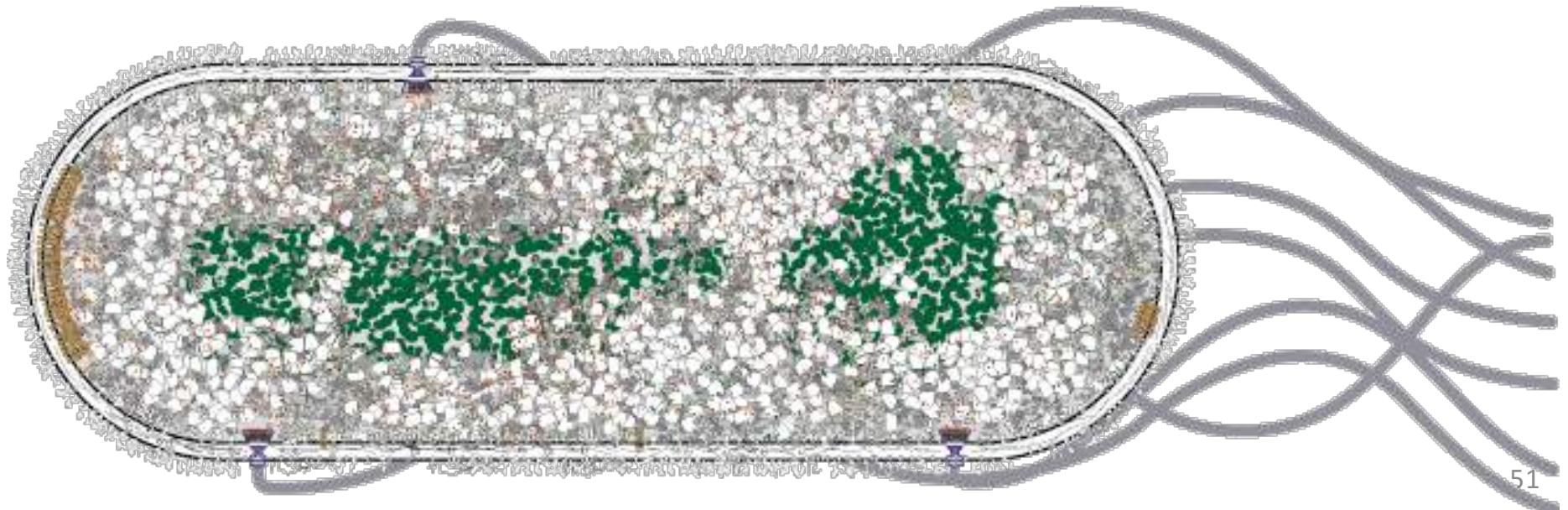


# Microbes as model systems

Astounding history of microbes modelling evolution, ecology, molecular biology, development, decision making (!)

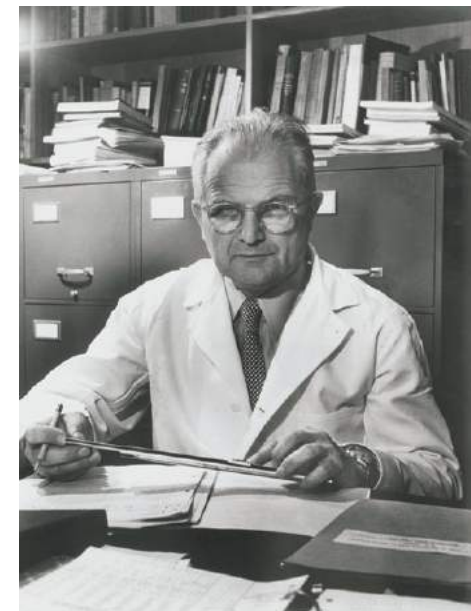
How do they work as 'model' systems?

Some historical ideas



‘By using as experimental material these microorganisms, which are **easy to handle**, biologists and biochemists are trying to unravel two of the most intricate puzzles of all living matter; namely, the mechanism of heredity, and the reproduction of living substances.’

‘Since the fundamental **laws of nature are general**, discoveries made by working with these minute organisms help us to understand the life processes of higher living beings’ (Demerec 1946, p. 217).





Not just mechanistic genetics, however

Also bacterial population biology (evolutionary)



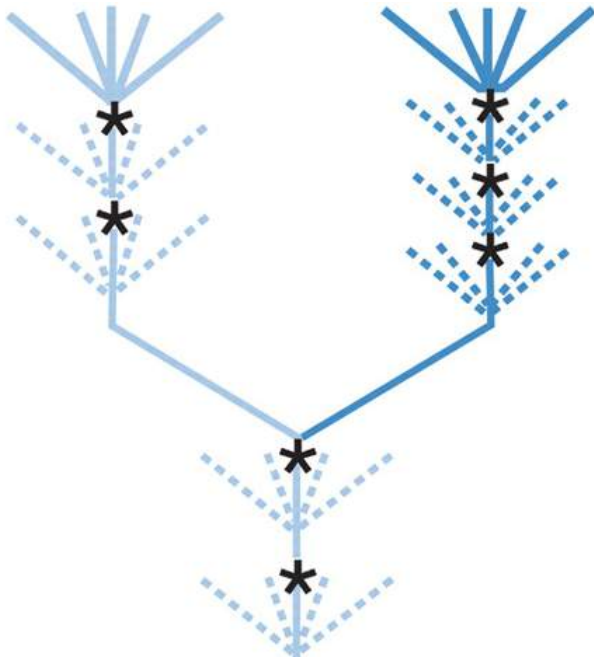
Bacteria are useful **because they are not sexual**: mutations = obvious

‘[In] non-sexual bacteria ... the immediate source of genetic variability resides in the capacity of the existing genotype to mutate, and not in the emergence of recombinant types’  
(Atwood et al. 1951, p. 345).



# The discovery of clonal or periodic selection

The phenomenon in which selection at one locus entails selection at all loci because of the absence of recombination.



Periodically, therefore, one clone in a population replaces all other variation in a selective sweep (Atwood et al. 1951a, 1951b)

Notable also for being genetic  
'experimental evolution':  
lab-based research demonstrating  
Darwinian evolutionary theory

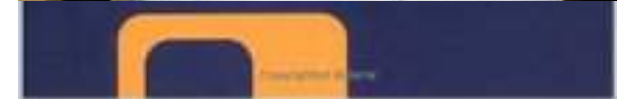
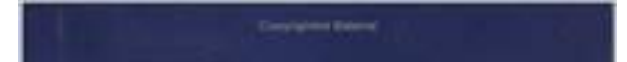
# Microbiological modern synthesis

Experimental evolution tracking genotypic as well as phenotypic change: 1960s+

Environmental manipulations to see if new metabolic capacities could evolve (e.g., Clarke, Lin, Mortlock, Levins, etc)

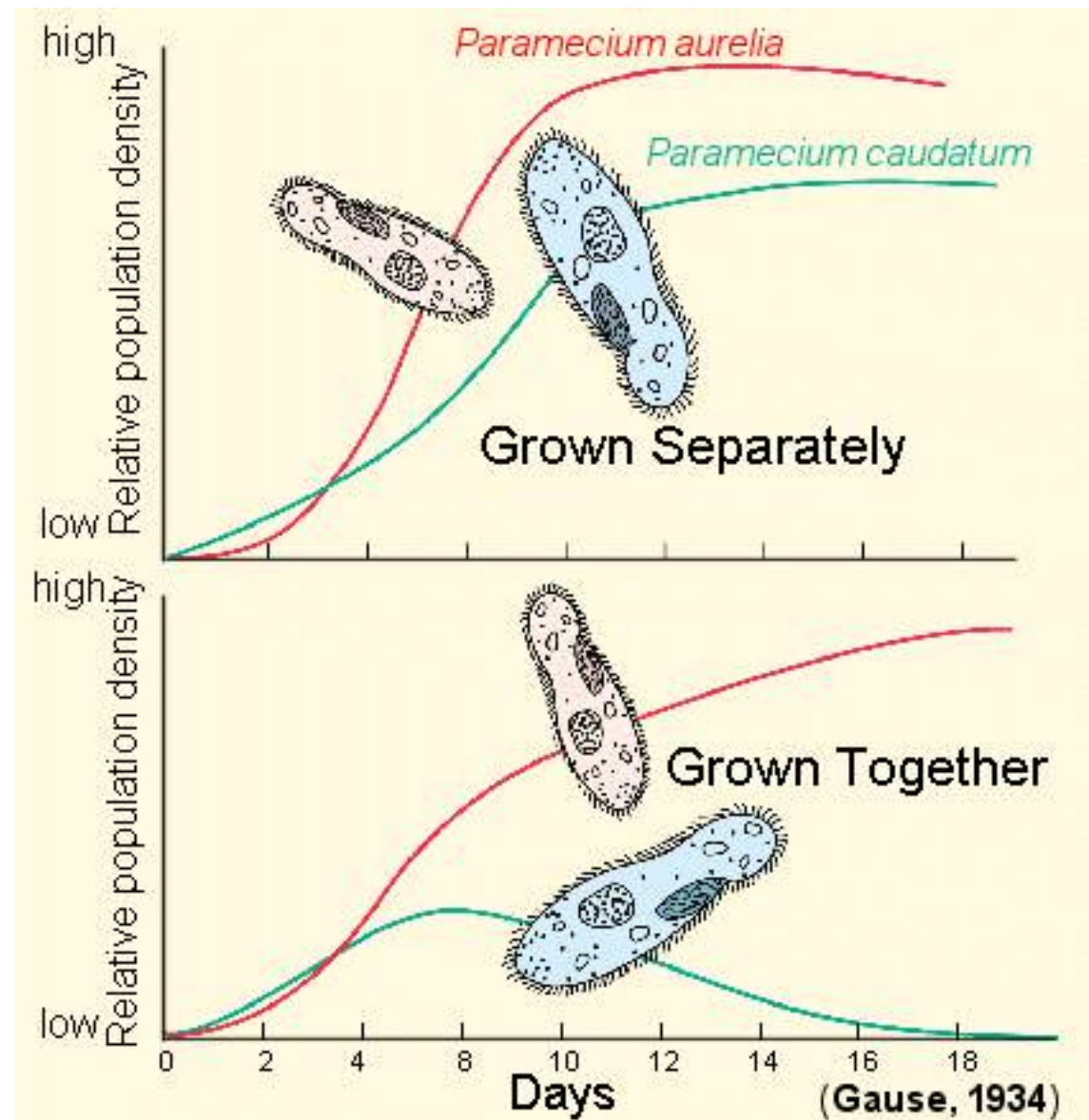
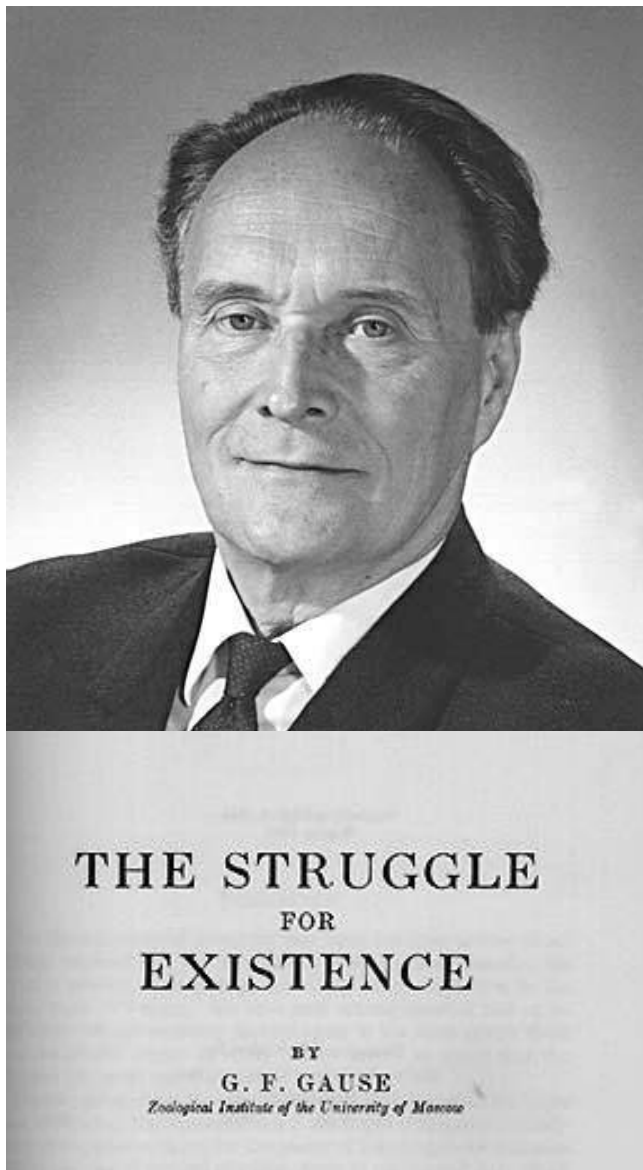
Insight into molecular mechanisms of evolution, and the 'optimality' of evolution

**Aim:** to make evolutionary theory not only testable but also predictive (Hall 1980; Levin and Lenski 1985).



# Experimental ecology

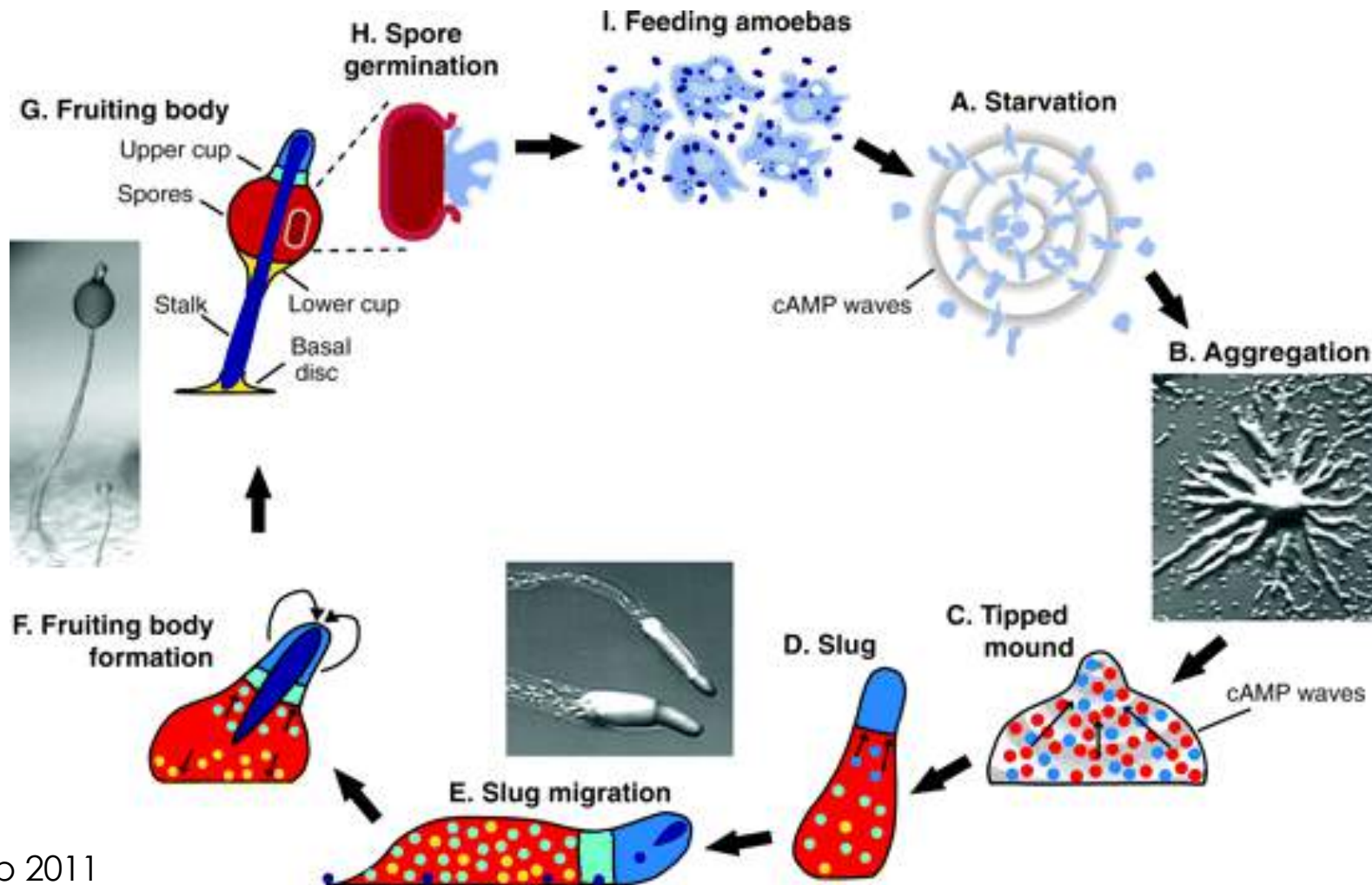
## Georgy Gause's 1934 principle of competitive exclusion





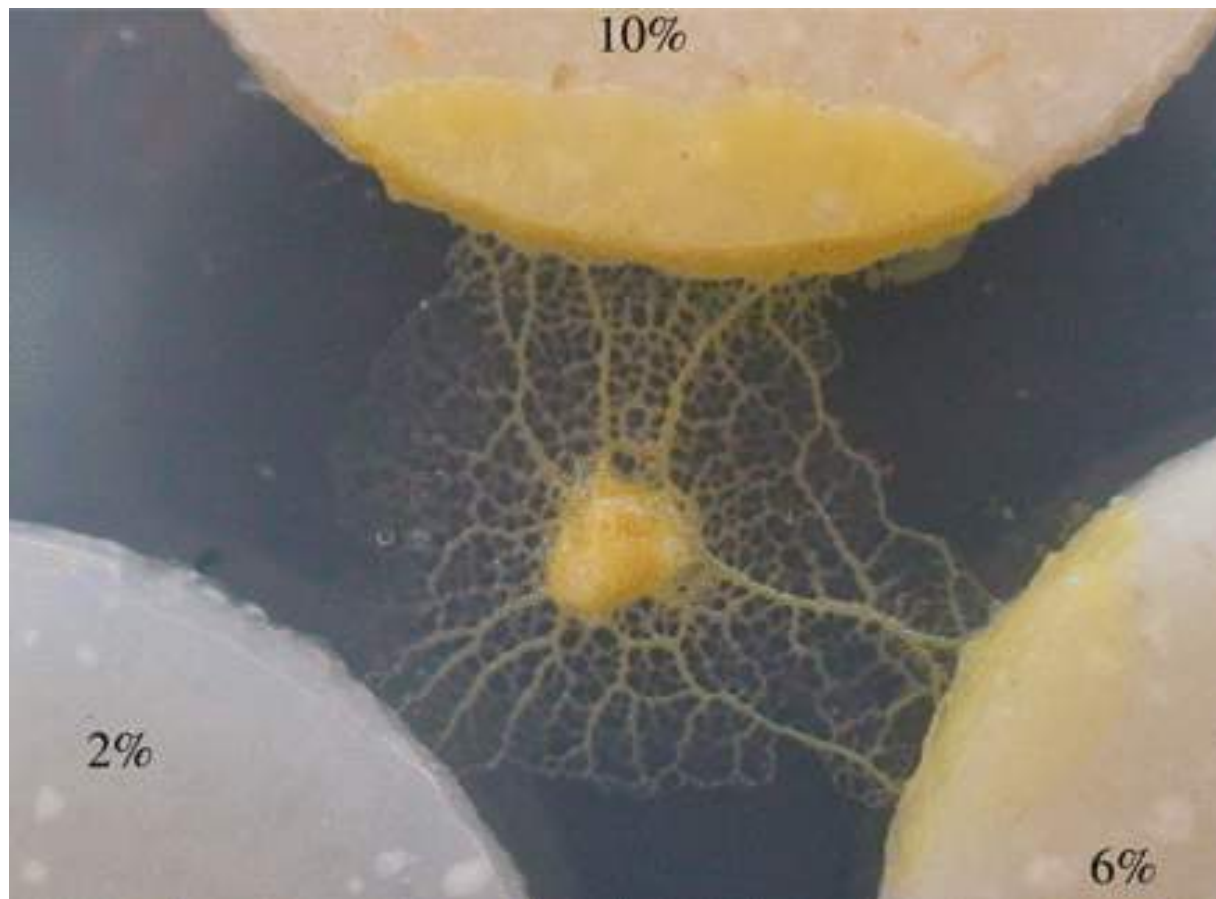
# Microbes as model systems for development

What? But they don't develop! They're only unicellular, aren't they?



# Microbes as decision-making model systems

*Physarum polycephalum*: preference valuation strategies, heuristics, speed-accuracy trade-offs (Latty and Beekman, 2011a, 2011b, 2015)





What do we learn about microbial model systems from these examples?

Tractable: they stand in for more complex, less manipulable systems

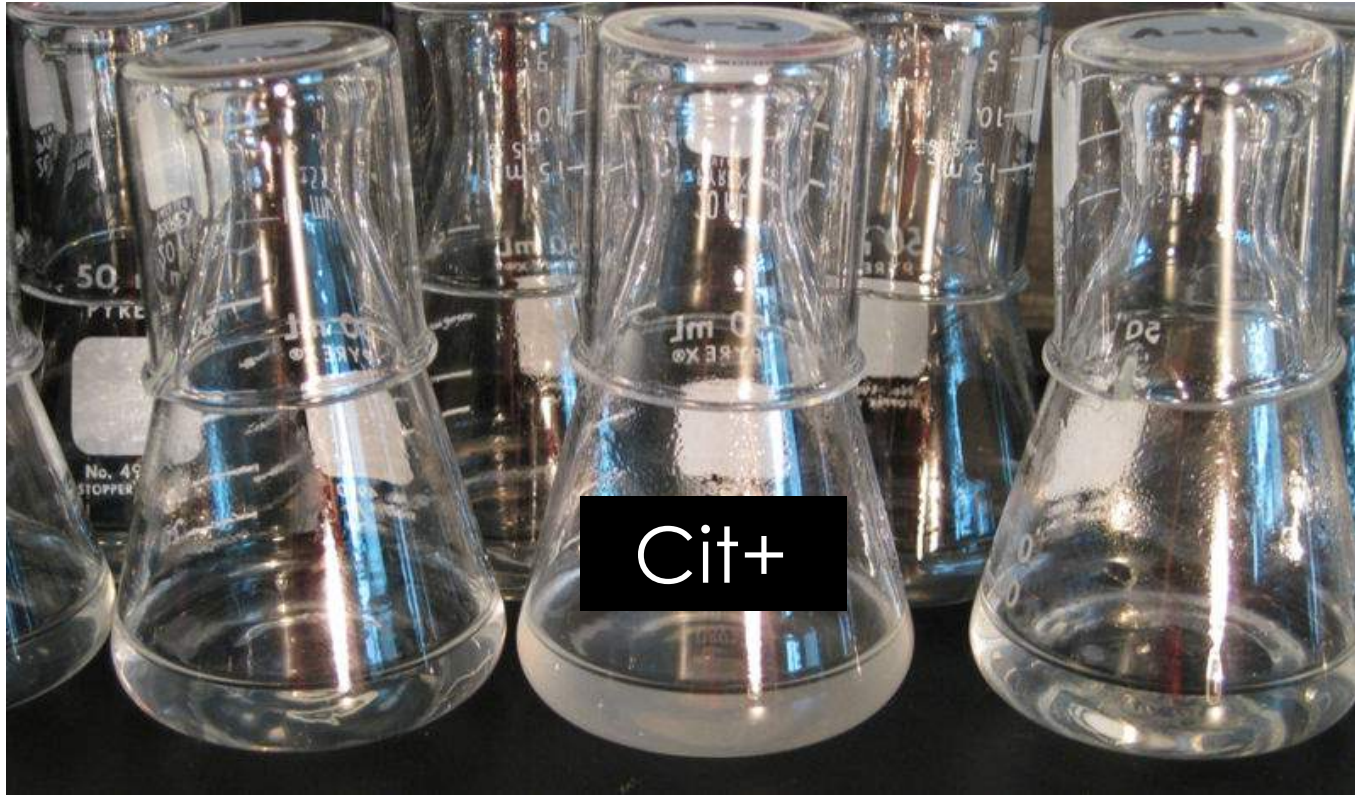
Representative: they are able to represent indirectly target features of other systems



# Model simplification

‘Laboratory model systems are not intended to be miniature versions of field systems, and laboratory ecologists do not intend to reproduce nature in a laboratory model system. Rather, the purpose of laboratory model systems is to **simplify nature so that it can be more easily understood**’ (Jessup et al. 2004, pp. 190-191)





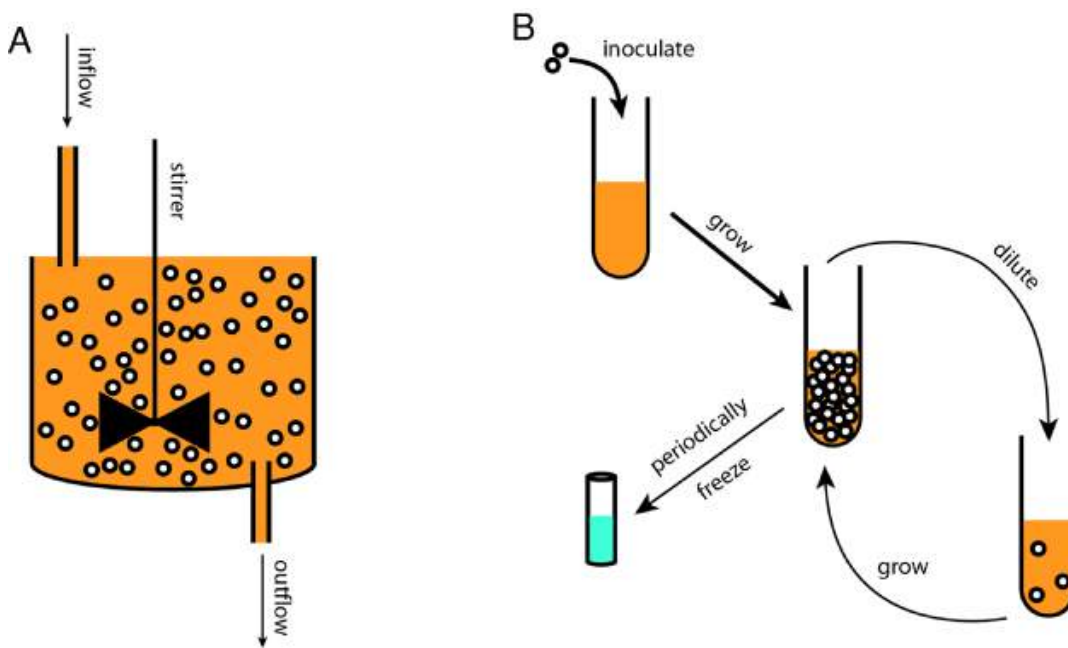
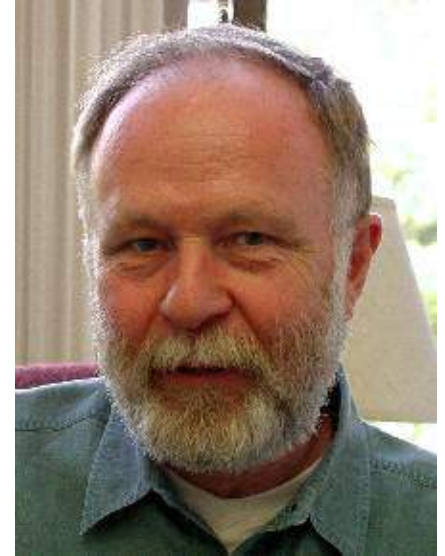
‘Experimental evolution does not seek to mimic specific systems in all their complexity. Instead, the microcosms are biological models in which researchers attempt to capture the essence of evolving systems in order to **shed light on general processes** that are expected to occur in all life’  
(Buckling et al. 2009, p. 827)



# Relationship to mathematical models?

Microbial model systems have properties similar to those of mathematical models: both are heuristics 'to show what is possible'

Microbial systems function as 'an intermediate between mathematical theory and field observations' (Dykhuisen & Davies 1980, p. 1213)



$$\frac{db}{dt} = b \frac{k_{\max} n}{k_n + n} - D b$$
$$\frac{dn}{dt} = D(n_o - n) - \beta b \frac{k_{\max} n}{k_n + n}$$

But microbes aren't really *models*, are they?

Philosophy of modelling:  
Material models, model  
organisms, model systems

Material models are not fully  
worked out in philosophy of  
modelling: attention to  
microbial model systems will  
help.

Doing so is part of my current  
research focus at Bordeaux.





Plus philosophy of microbiota research

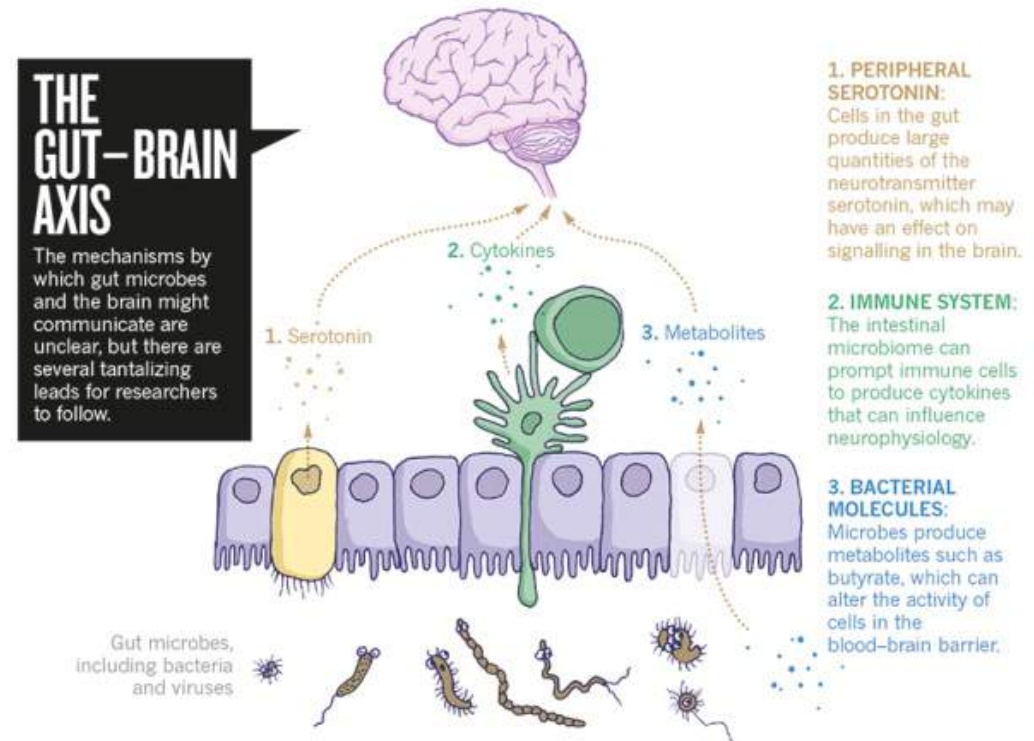
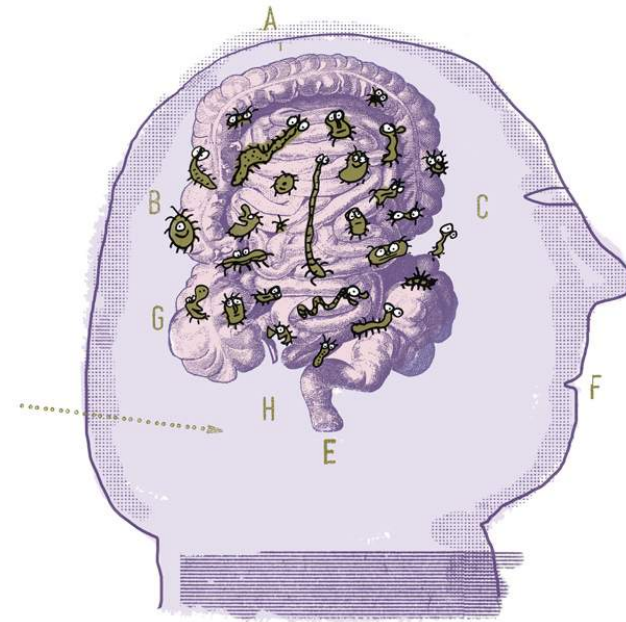
From correlation to causation

What does it take to establish explanations in microbiota research?

Are they causal explanations?

Are there non-causal explanations?

What do correlations do?





## Some philosophical conclusions about microbiology

Microbiology has deep philosophical issues running through it, for all of its history.

These philosophical issues are about the nature of things, and how knowledge about those things is produced and evaluated.

It's hard to get away from philosophy at basic levels of scientific assumption, and when scientific debates are occurring.



# Some microbiological implications for philosophy

Traditionally, philosophy of biology has not paid much attention to microbiology.

Worth remedying in what might be the microbiological era of the life sciences.

In the same way scientists do, philosophers might learn more about the world in general by focusing on microbes and microbiology.





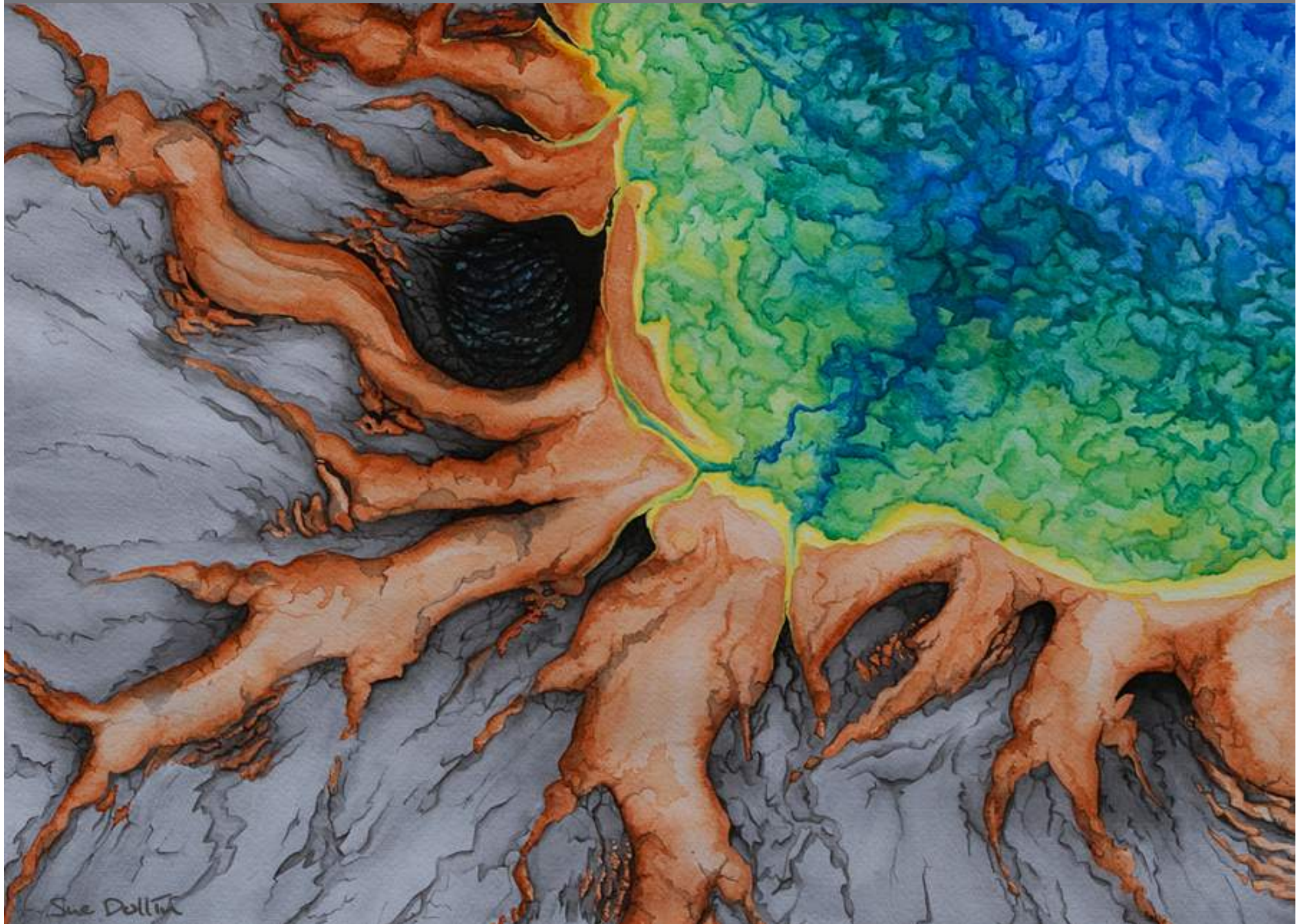
# Acknowledgements

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Grand Prismatic  
Spring





Sue Dollin