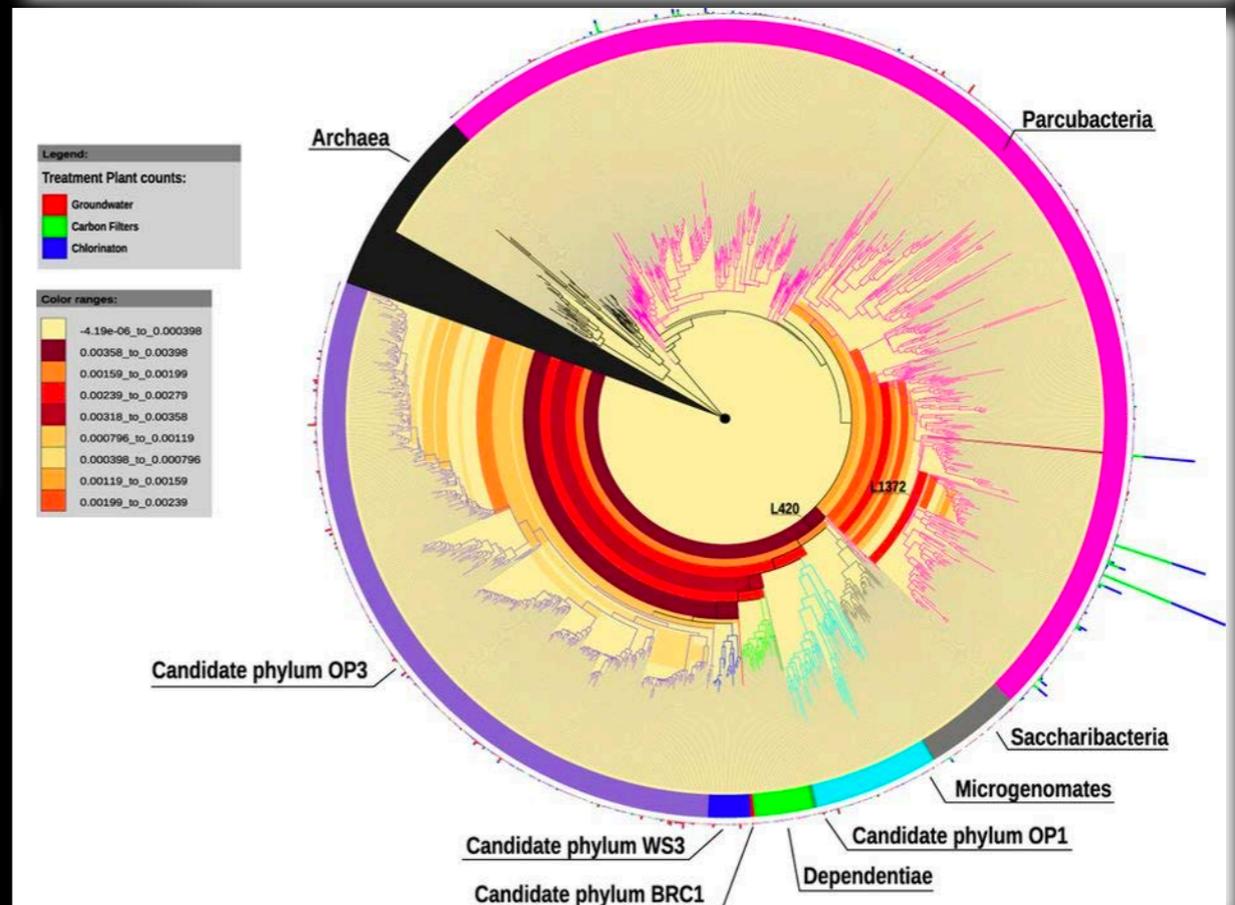
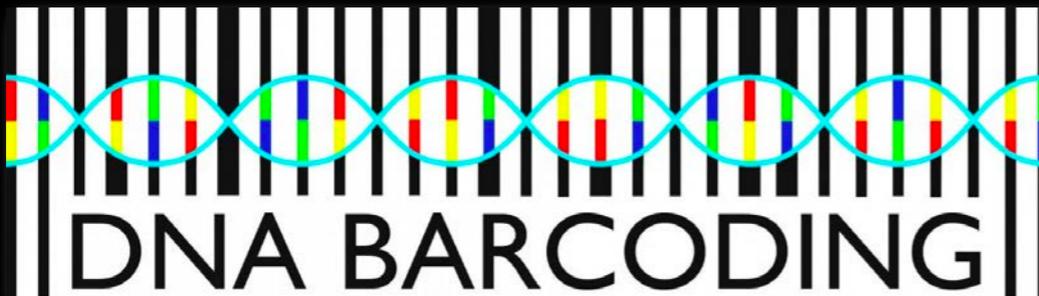
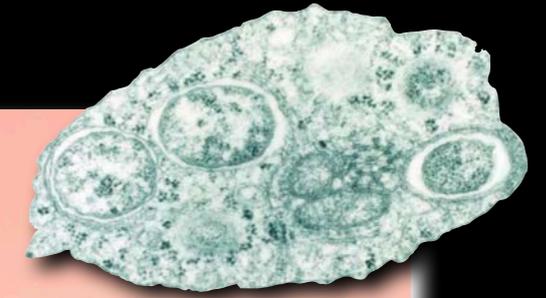


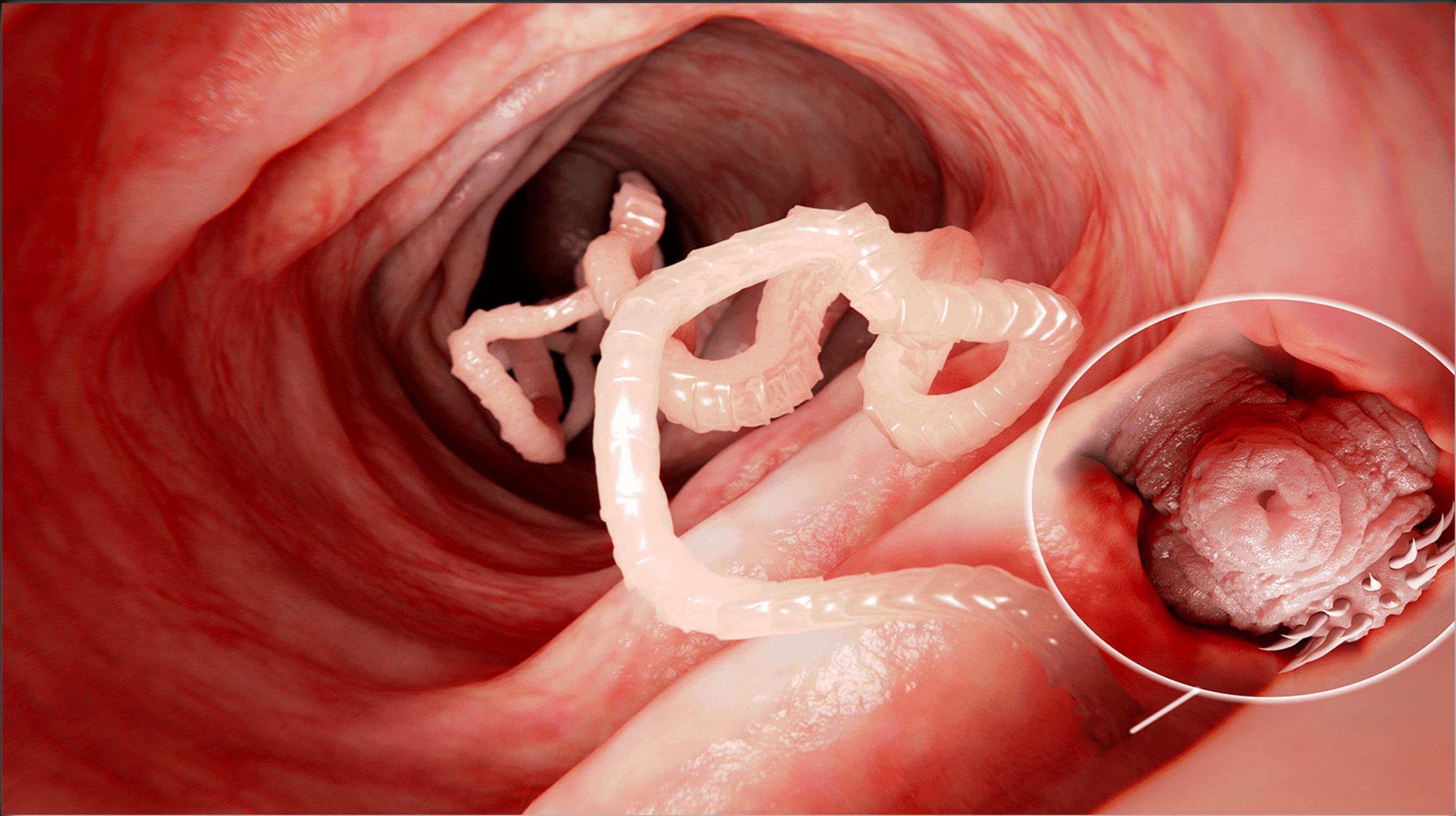
# The evolution of biological complexity: myths and truths

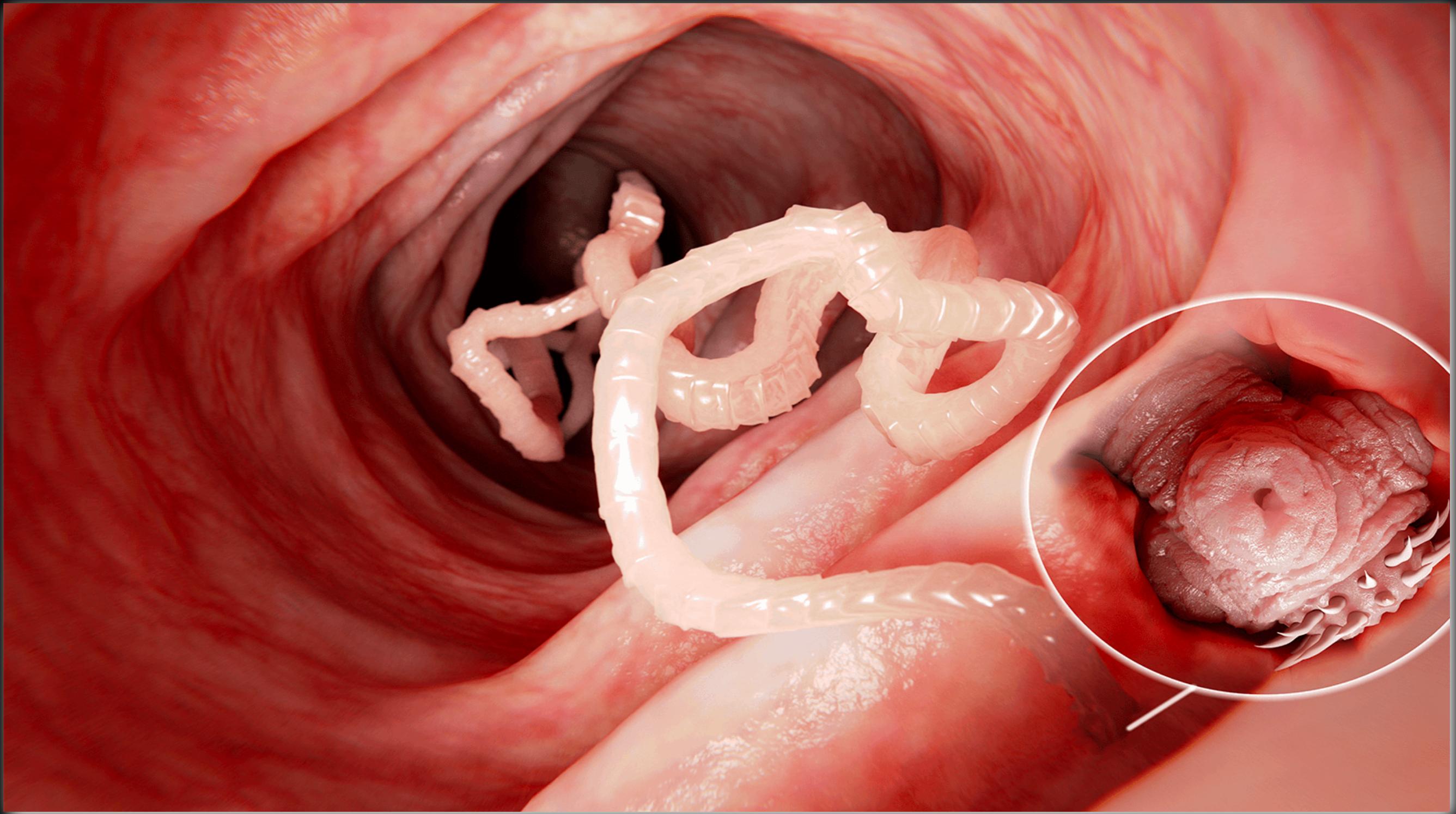
Maurizio Casiraghi, zoologist,  
ZooPlantLab, University of Milan-Bicocca



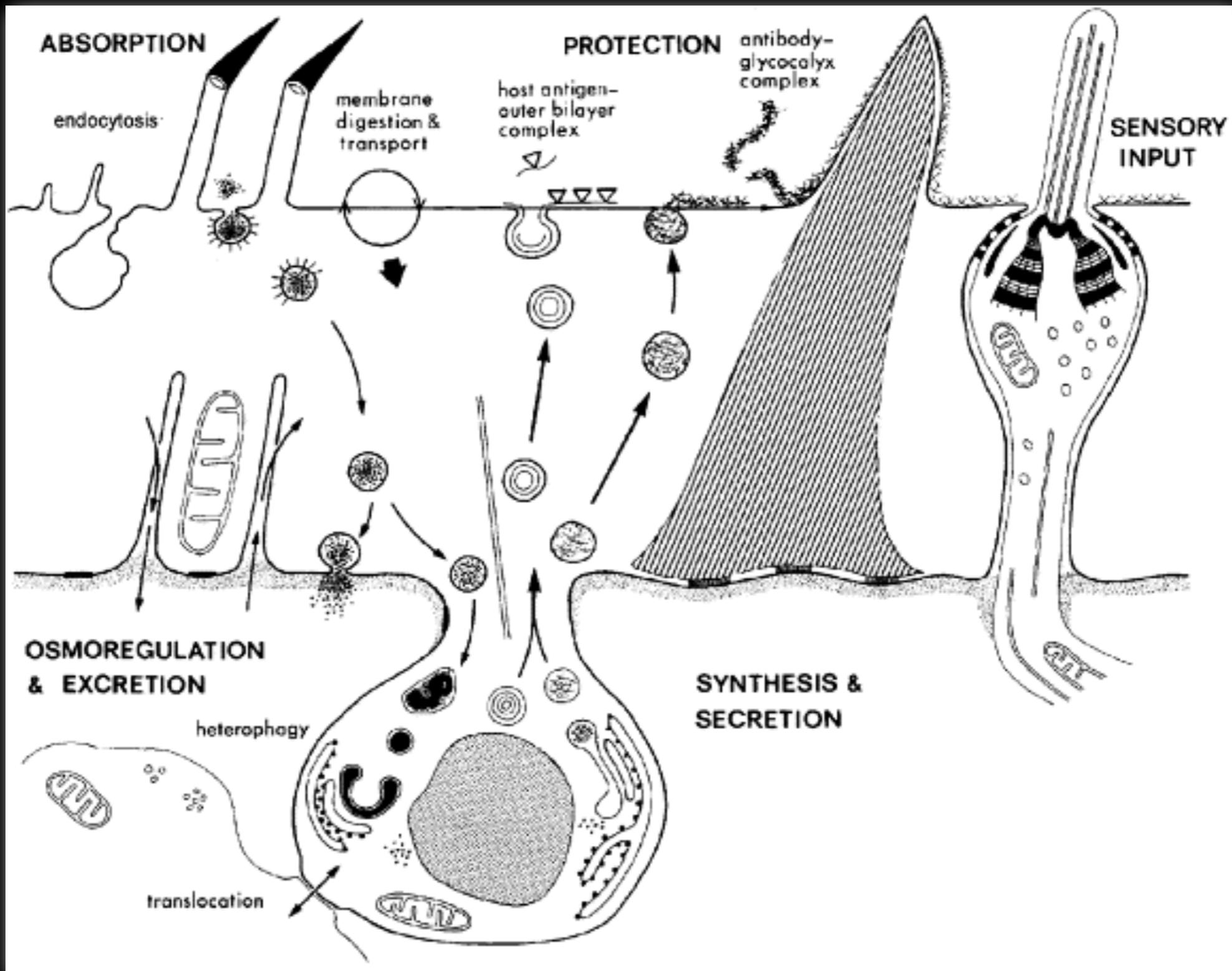
# My long journey







*“Taenia spp (tapeworms) are simple animals”*

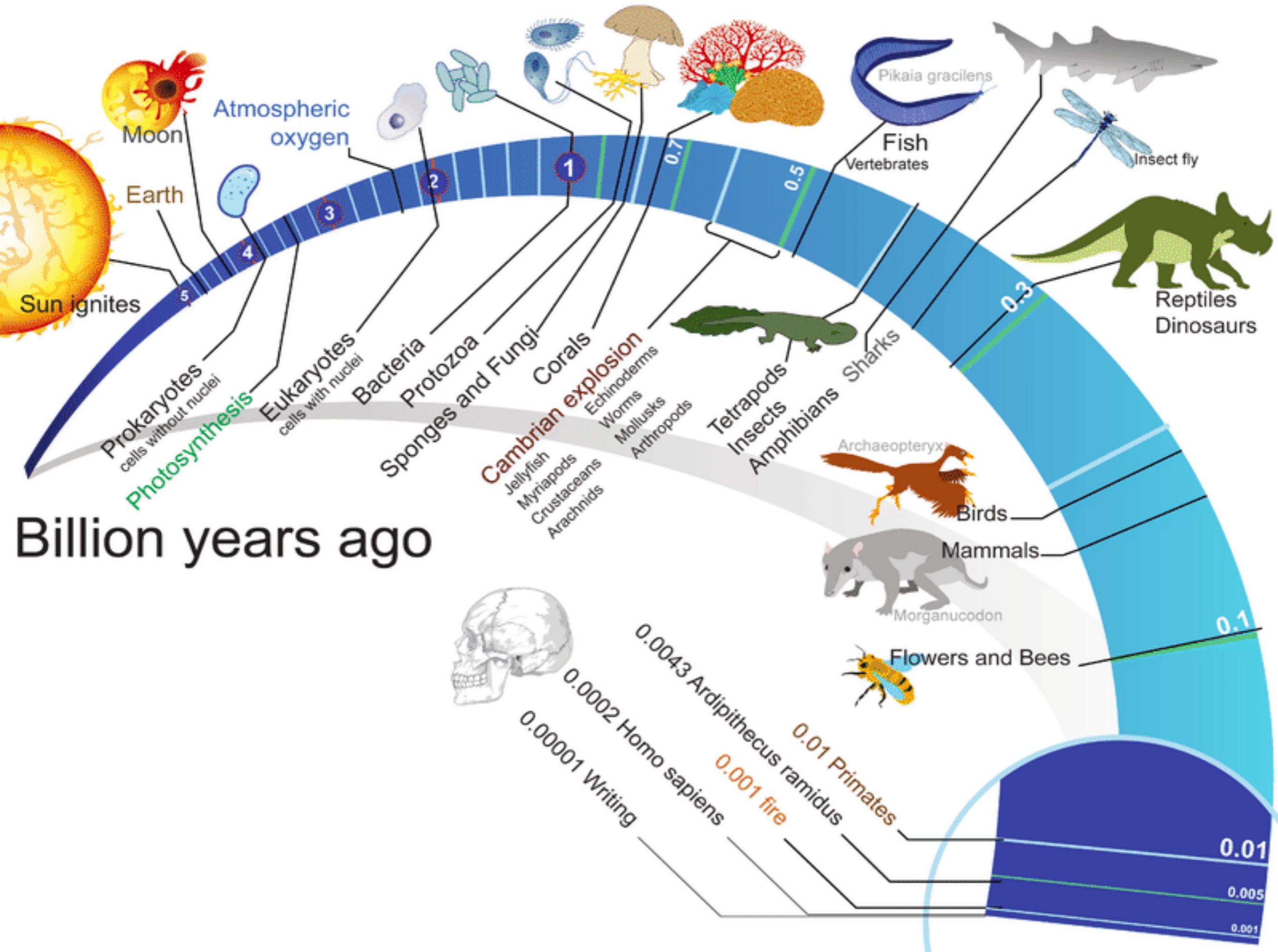


*Taenia* spp (tapeworms) tegument is really complex



So,  
tapeworms  
are simple  
or complex  
animals?

**The “slippery” concept  
of complexity in biology**



# The complex complexity

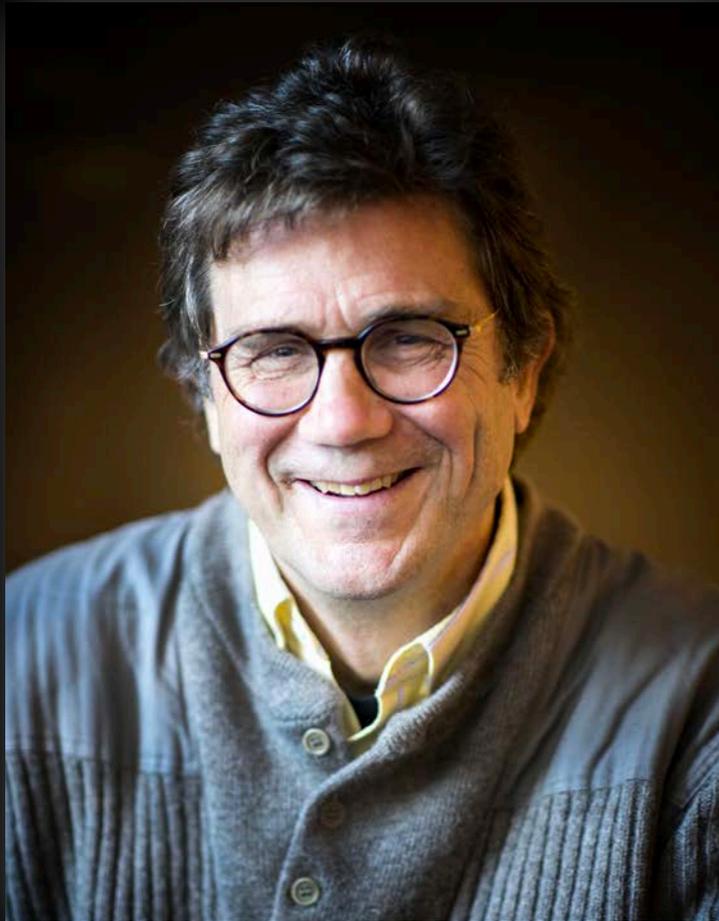
## **Trivial:**

life 3,2 billion years ago was  
simpler than life 300 mya

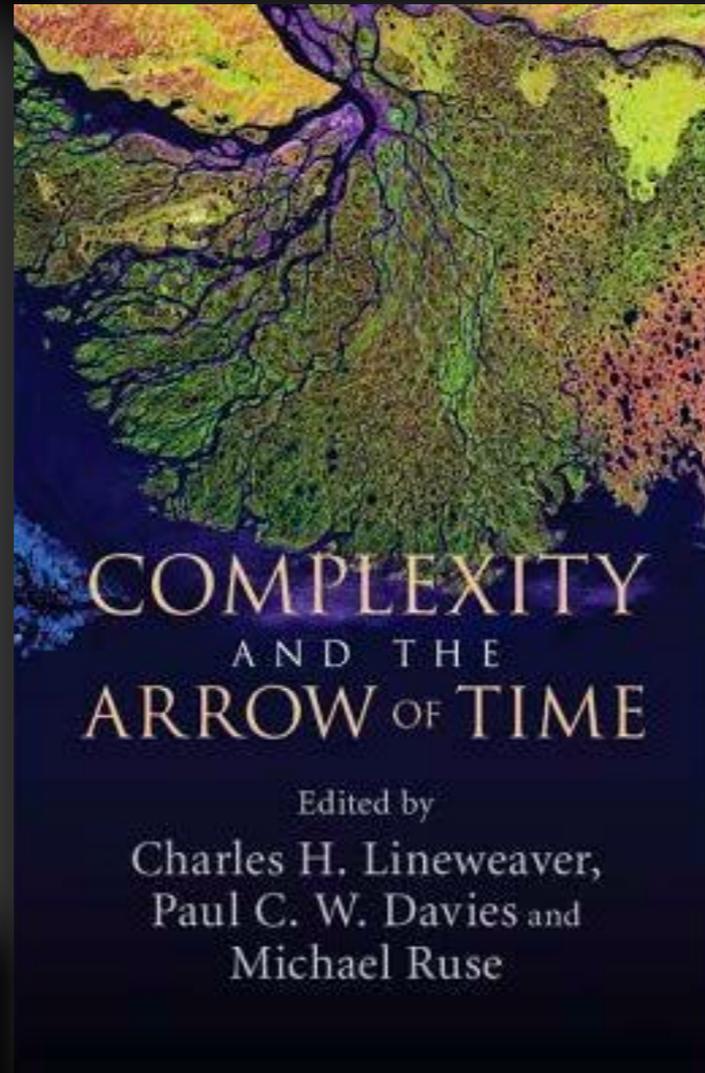
# The complex complexity

## Trivial:

life 3,2 billion years ago was simpler than life 300 mya



Charles Lineweaver



*...even without a definition or a way to measure it, isn't it qualitatively obvious that biological complexity has increased? Do we really need to wait for a precise definition to think about complexity and its limits?*



Simon Conway Morris

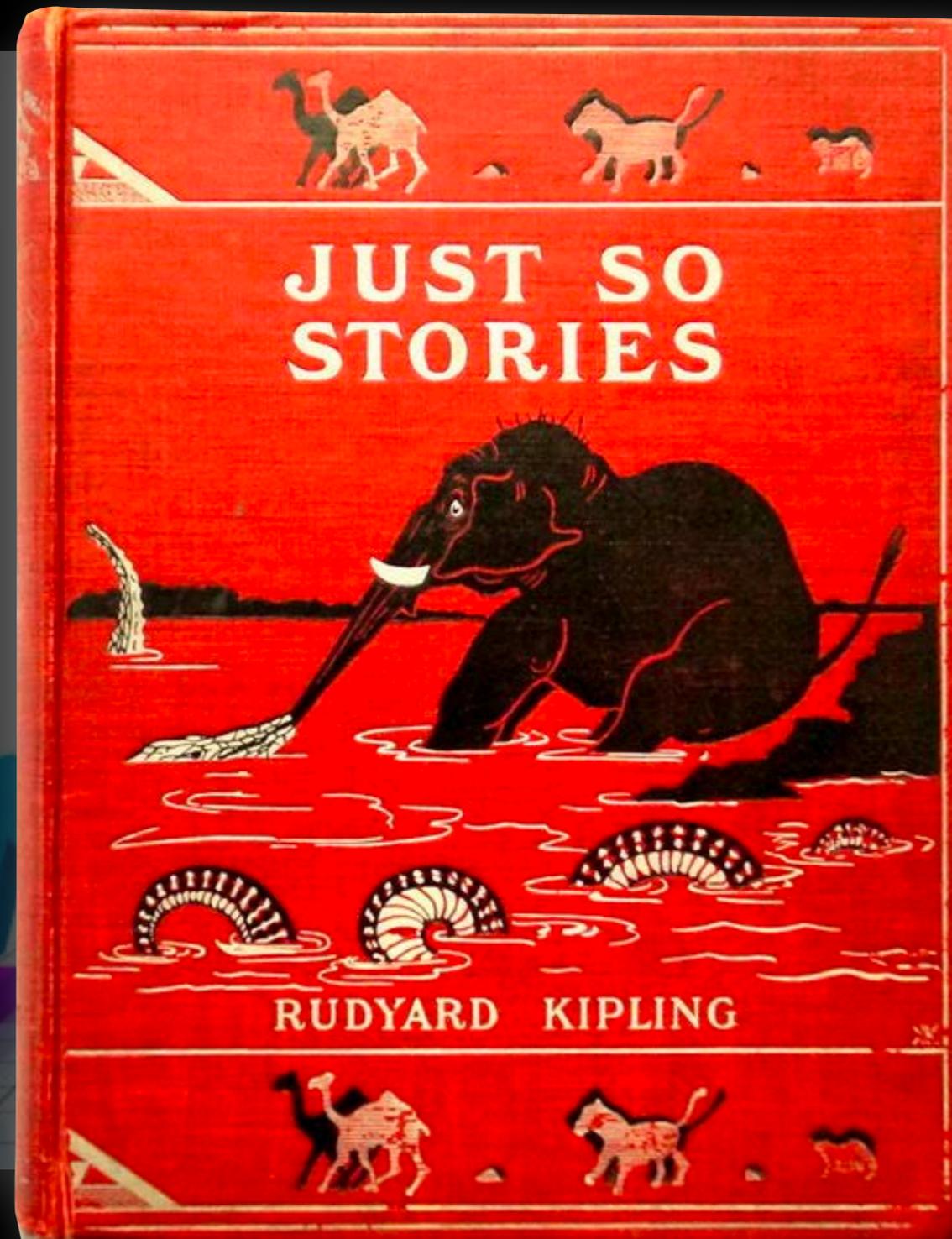
*“First there were bacteria, now there is New York”*



In some way complexity seems to increase in time



In some way complexity seems to increase in time





Mark A. Bedau

The evolution of complexity, 2009

*It is useful to distinguish three things:*

*(i) a **trend**, which is simply an observed directional change in some variable in some evolving system;*

*(ii) a **robust regularity**, which is a generic or non-accidental trend (perhaps with exceptions), a statistical “law” about the time dynamic of some variable;*

*(iii) a **mechanism or process**, that explains a trend, whether accidental or robust*



Mark A. Bedau

The evolution of complexity, 2009

*It is useful to distinguish three things:*

- (i) a **trend**, which is simply an observed directional change in some variable in some evolving system;*
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- (iii) a **mechanism or process**, that explains a trend, whether accidental or robust*

*So far we have simply been observing that **there is a trend** of increasing complexity of the most complex organisms. This observation does not necessarily imply that the trend is a robust regularity; it might simply be an accident. Nor is any particular mechanism or process implicated as the explanation of that trend.*

***Our starting point is merely the observation of a trend.***

**Arrow of time**

**Natural selection**

**Complexity**

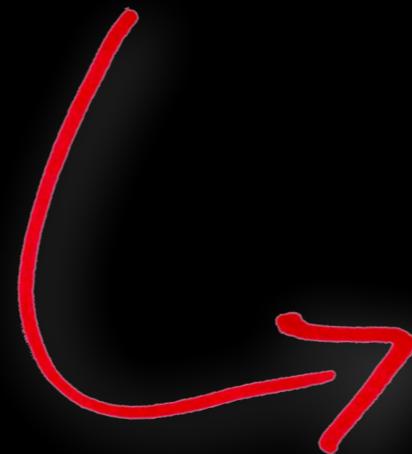
**Arrow of time**



*Natural selection  
during time...*

**Natural selection**

*...led to the increase of  
complexity in living beings*



**Complexity**

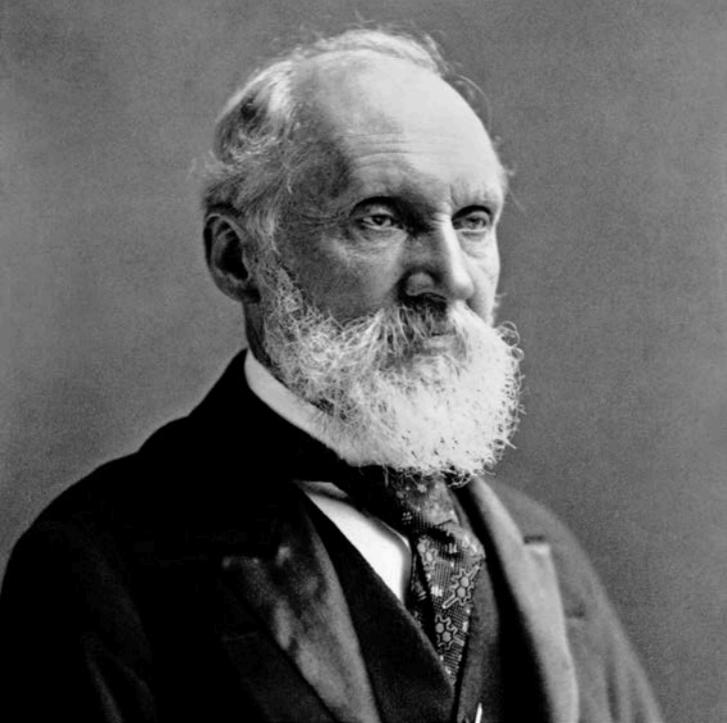
**is this true?**

**is this a rule,  
not only a trend?**

is this true?

is this a rule,  
not only a trend?

*Can you measure it?*



William T. "Lord" Kelvin

The Six Gateways of Knowledge,  
Presidential Address to the Birmingham  
and Midland Institute,  
Birmingham, 3 oct 1883

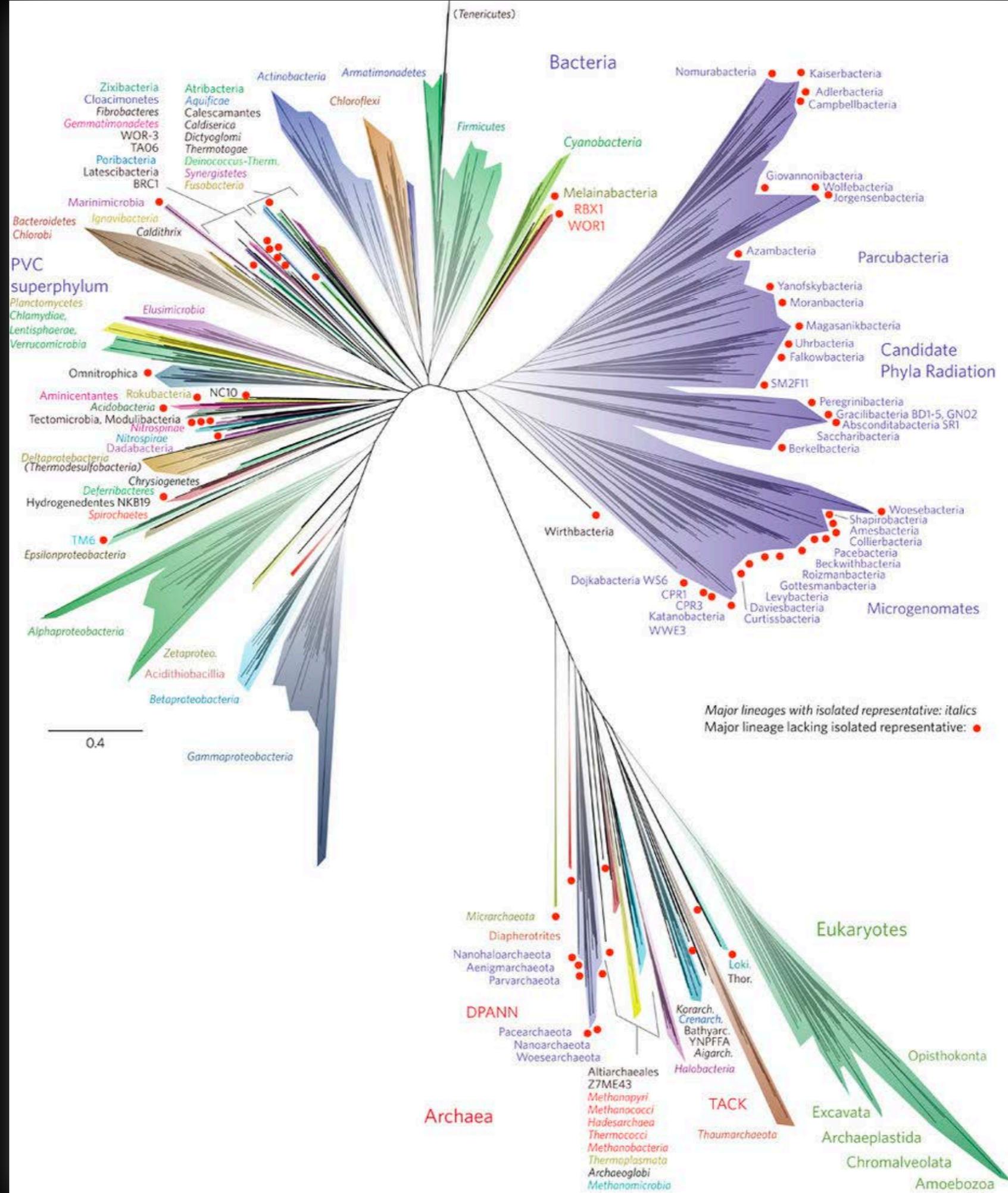
*. . .when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely in your thoughts advanced to the stage of science, whatever the matter may be.*

# Complexity and the arrow of time

If natural selection has forced complexity to increase, how then to explain the fact that the oldest living organisms of today (i.e. those having been exposed to natural selection for the longest time) are the most simpler?

Why haven't all living things raised themselves to the same level as man?

Bacteria, for example, are probably “no more complex” today than their ancestors 3.000 million years ago

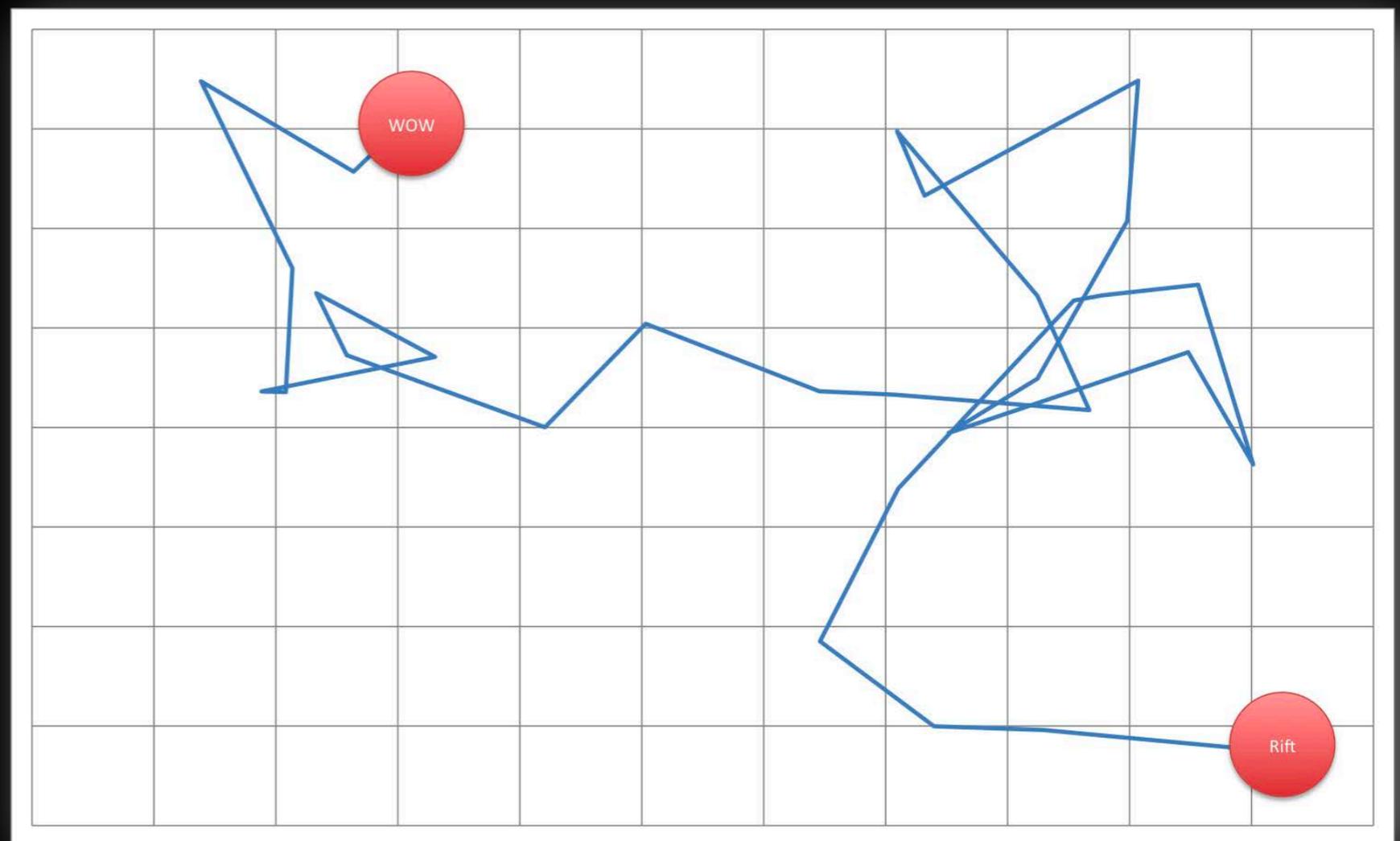




Stephen Jay Gould

# Evolution of a species in complexity

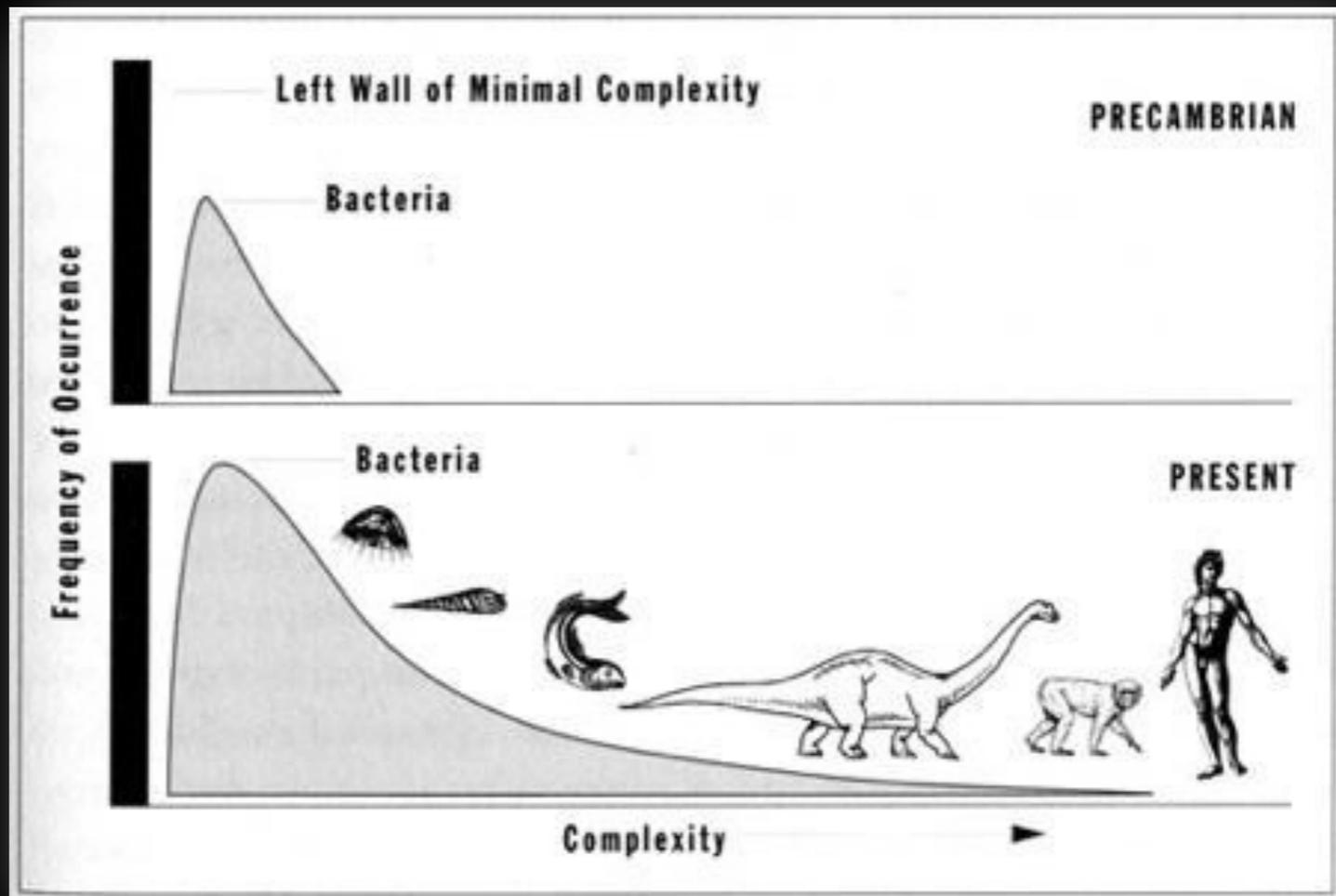
The drunkard's walk





Stephen Jay Gould

# The “left wall” of minimal complexity



S.J. Gould, The Evolution of Life on Earth, Scientific American, October, 1994.

# Tendency towards diversity



Stephen Jay Gould

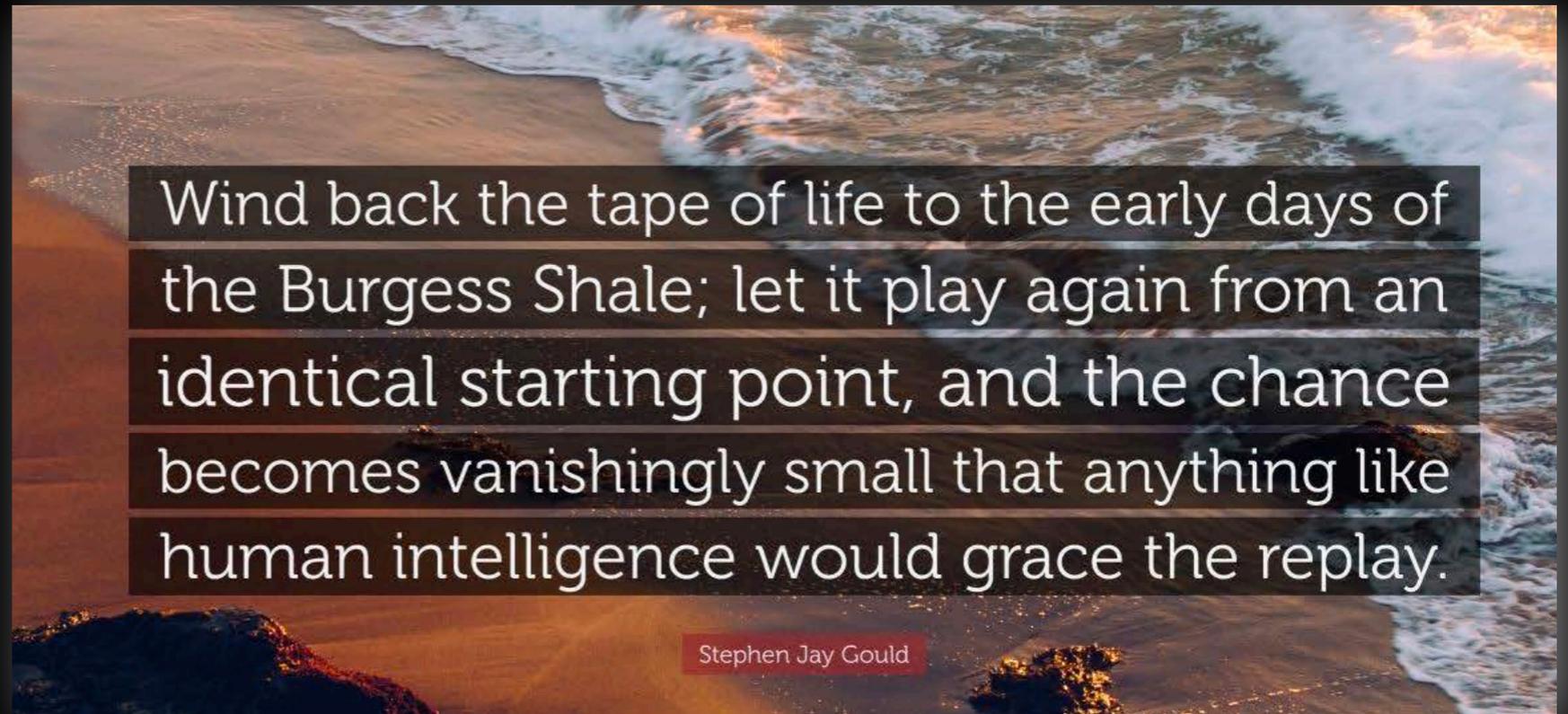
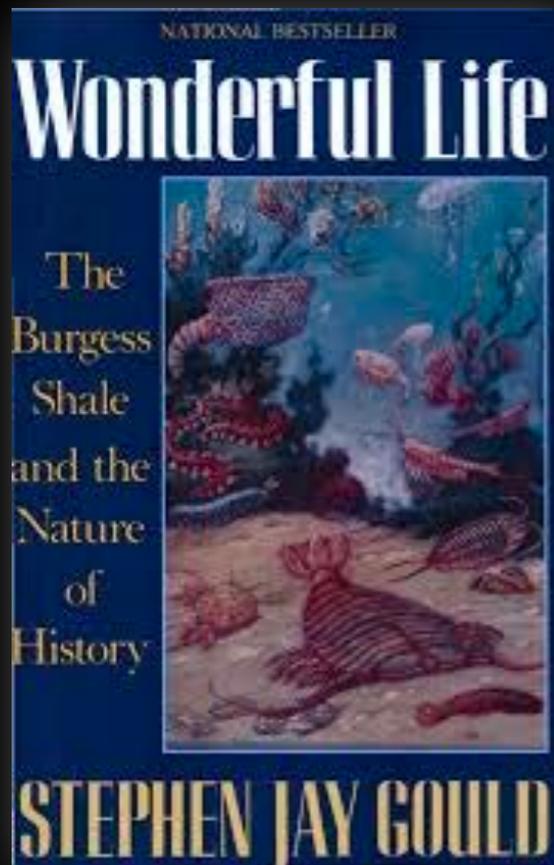




# Test the arrow of complexity hypothesis

*“Replaying the tape of life”*

Stephen Jay Gould  
Wonderful life (1989)



Wind back the tape of life to the early days of the Burgess Shale; let it play again from an identical starting point, and the chance becomes vanishingly small that anything like human intelligence would grace the replay.

Stephen Jay Gould



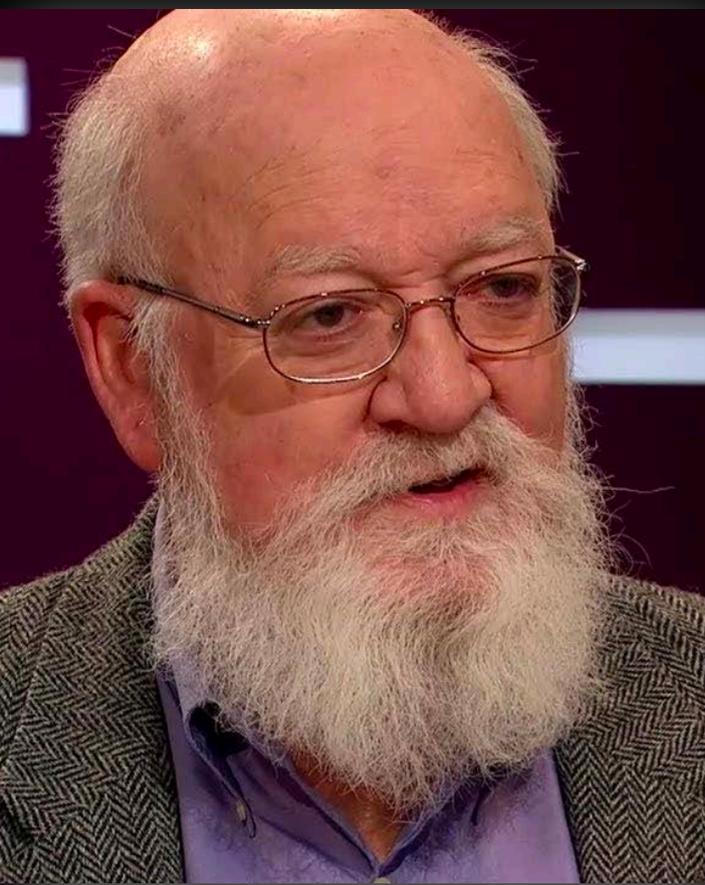
# Test the arrow of complexity hypothesis

*“Replaying the tape of life”*

Stephen Jay Gould

Wonderful life (1989)

Gould emphasizes that the evolution  
of life is a contingent historical  
process and is thus not law-like



Daniel C. Dennett

Darwin's dangerous idea (1995)

# The arrow of complexity exists

Dennett argues that complexities such as tools and language offer such obvious adaptive advantage that the stochastic process of natural selection would *almost inevitably* discover them



**ok, ok, but what is  
complexity  
(in biology, at least!)?**

# Complexity

Etymology: Lt, *complexus*, folded together, entangled or embracing

A scientific theory which asserts that some systems display behavioral phenomena that are completely inexplicable by any conventional analysis of the systems' constituent parts. These phenomena, commonly referred to as emergent behaviour, seem to occur in many complex systems involving living organisms, such as a stock market or the human brain.

Encyclopaedia Britannica

# Complexity

Something complex is characterized both by **distinctions** and by **connections**.  
Something becomes more complex the more distinctions and connections it has.

A scientific theory which asserts that some systems display behavioral phenomena that are completely inexplicable by any conventional analysis of the systems' constituent parts. These phenomena, commonly referred to as emergent behaviour, seem to occur in many complex systems involving living organisms, such as a stock market or the human brain.

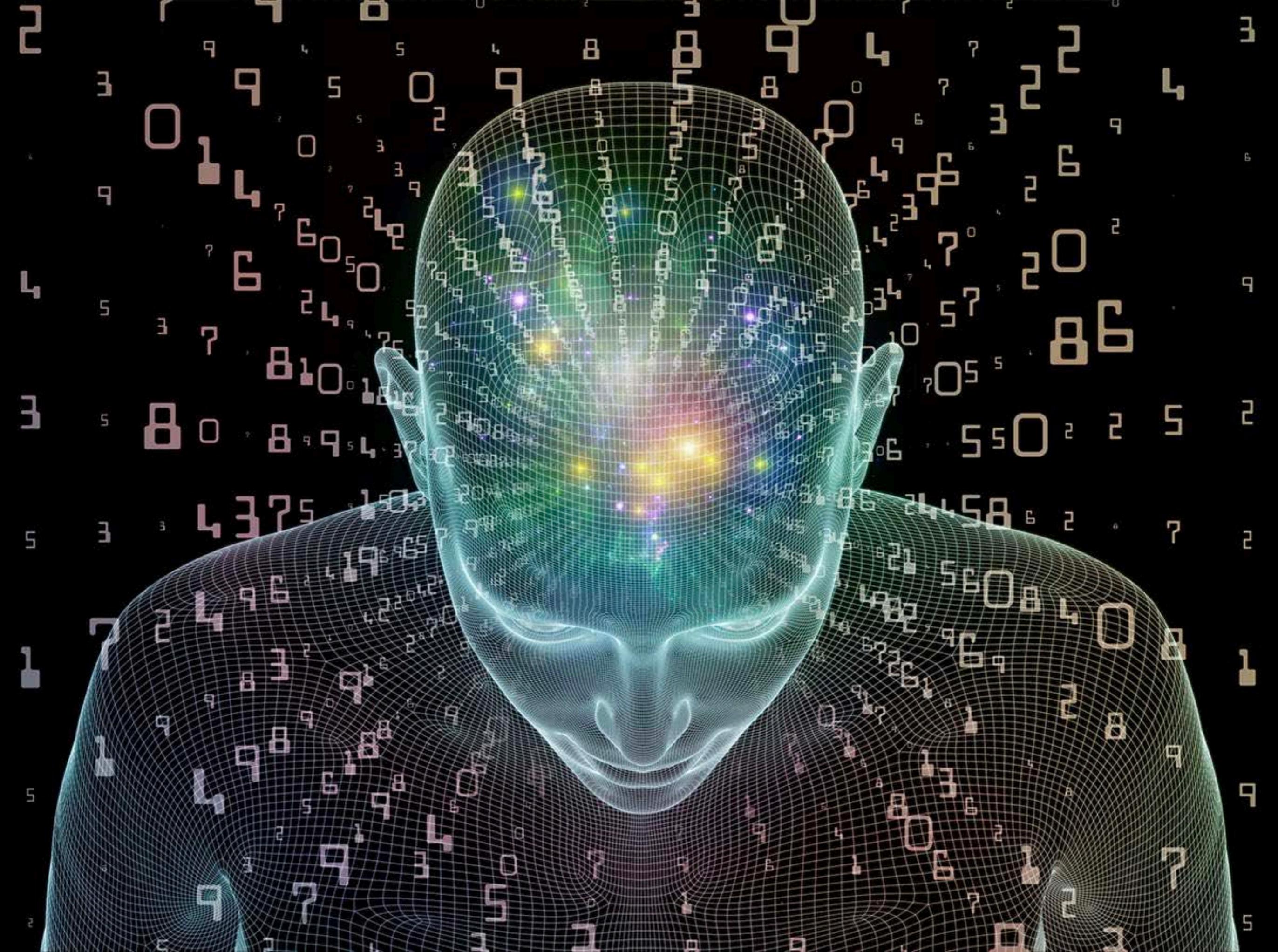
# Complexity

Something complex is characterized both by



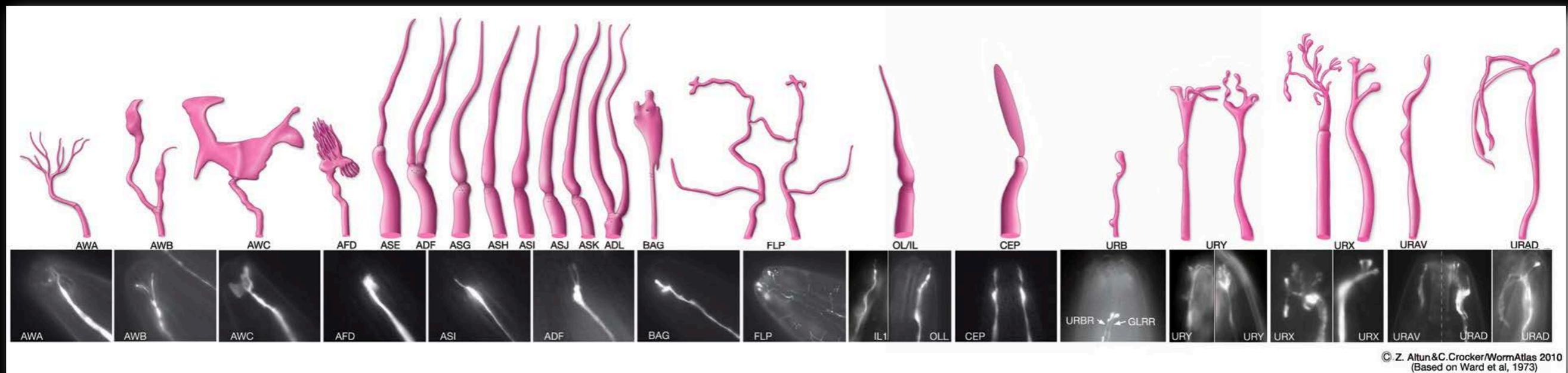
A  
beh  
com  
pl  
s

splay  
by any  
These  
viour,  
ving  
ain.



# WormBase

...if you are an animal model used in hundreds of labs worldwide, long 1 mm and you are constituted by 959 cells, things can be easier...



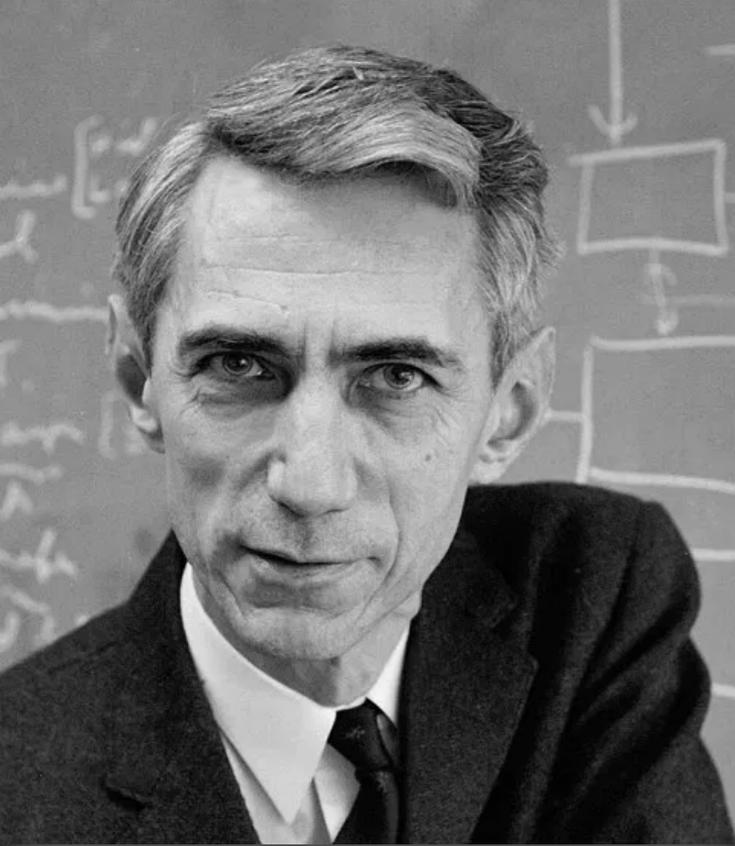
...in almost all the other cases you need proxy



Richard Dawkins  
Human chauvinism (1997)

A crab is morphologically more complex than a millipede because, if you wrote a pair of books describing each animal down to the same level of detail, the crab book would have a higher word-count than the millipede book. The millipede book would describe a typical segment then simply add that, with listed exceptions, the other segments are the same. The crab book would require a separate chapter for each segment and **would therefore have a higher information content**

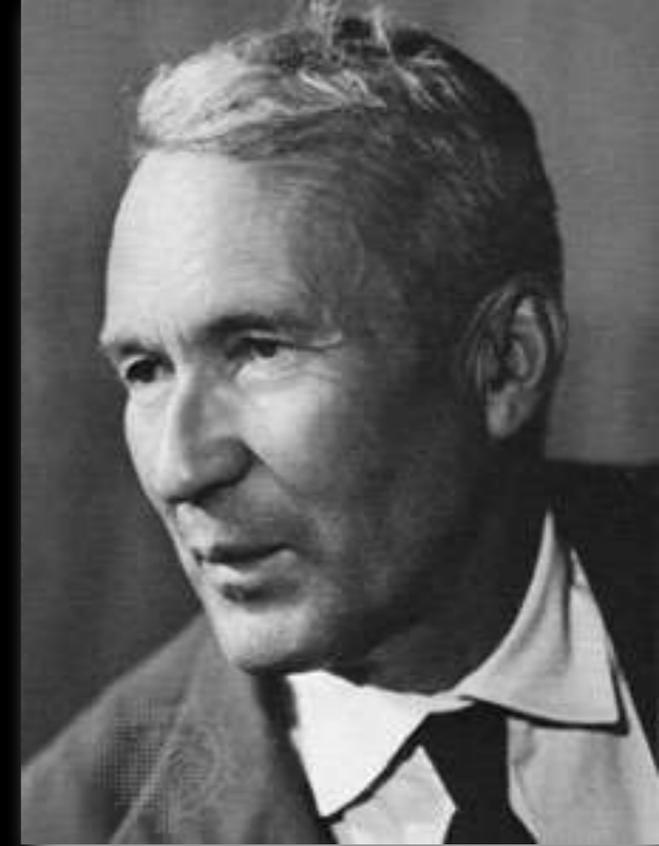




Claude E. Shannon

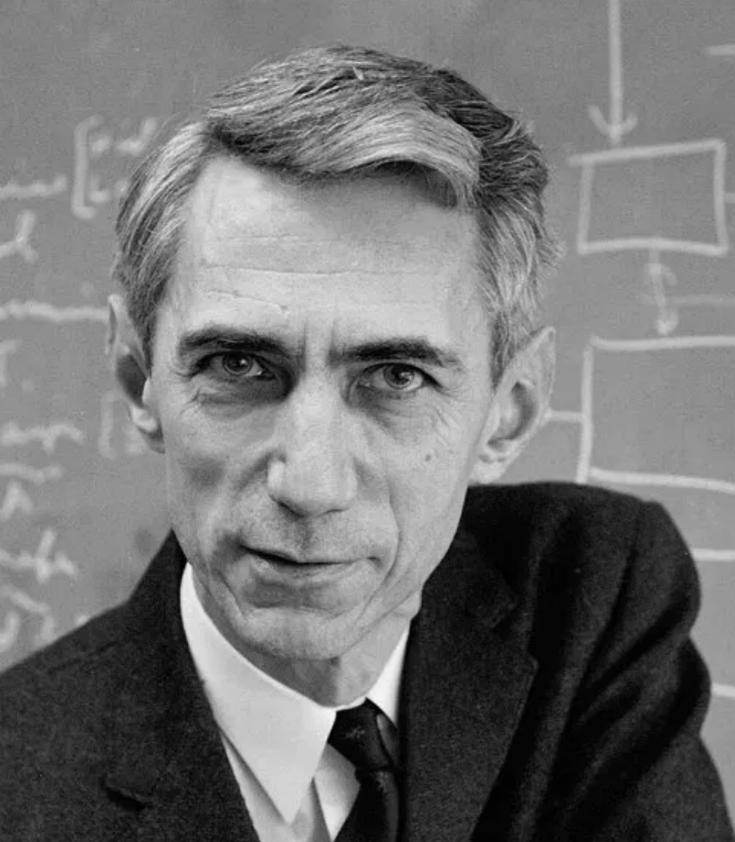
Information Theory, 1948

Both theories aim at providing a means for measuring 'information'. They use the same unit to do this: **the bit**. In both cases, the amount of information in an object may be interpreted as the length of a description of the object.



Andrej N. Kolmogorov

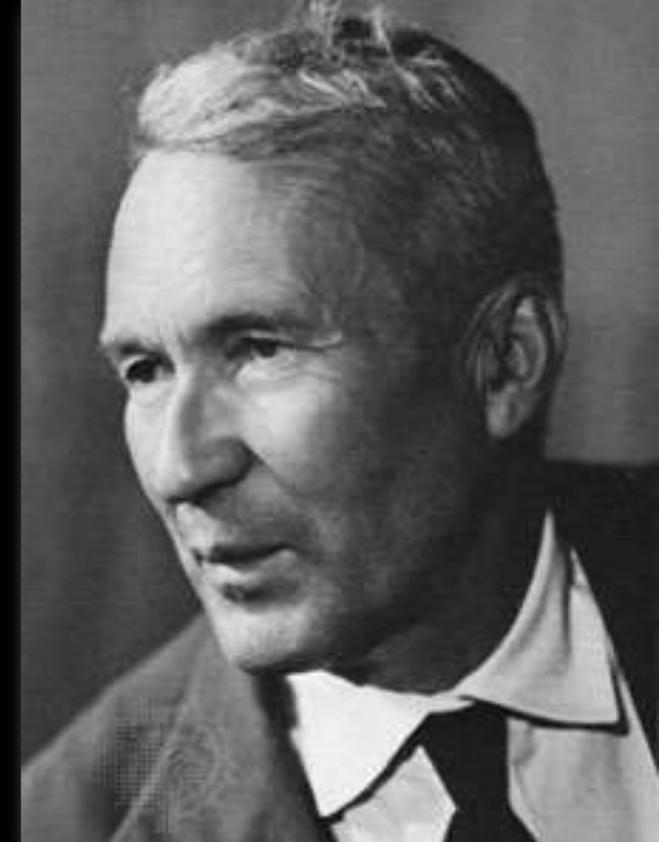
Complexity Theory, 1960-64



Claude E. Shannon

Information Theory, 1948

Both theories aim at providing a means for measuring 'information'. They use the same unit to do this: **the bit**. In both cases, the amount of information in an object may be interpreted as the length of a description of the object.



Andrej N. Kolmogorov

Complexity Theory, 1960-64

In the Shannon approach we are interested in the minimum expected number of bits to transmit a message from a random source of known characteristics through an error-free channel

In Kolmogorov complexity we are interested in the minimum number of bits from which a particular message or file can effectively be reconstructed: the minimum number of bits that suffice to store the file in reproducible format

From here there is a lot of math to use these parameters, but I would like to avoid it now.  
We can focalize our attention “on the bit”

## Shannon Information and Kolmogorov Complexity

Peter Grünwald and Paul Vitányi\*

July 22, 2010

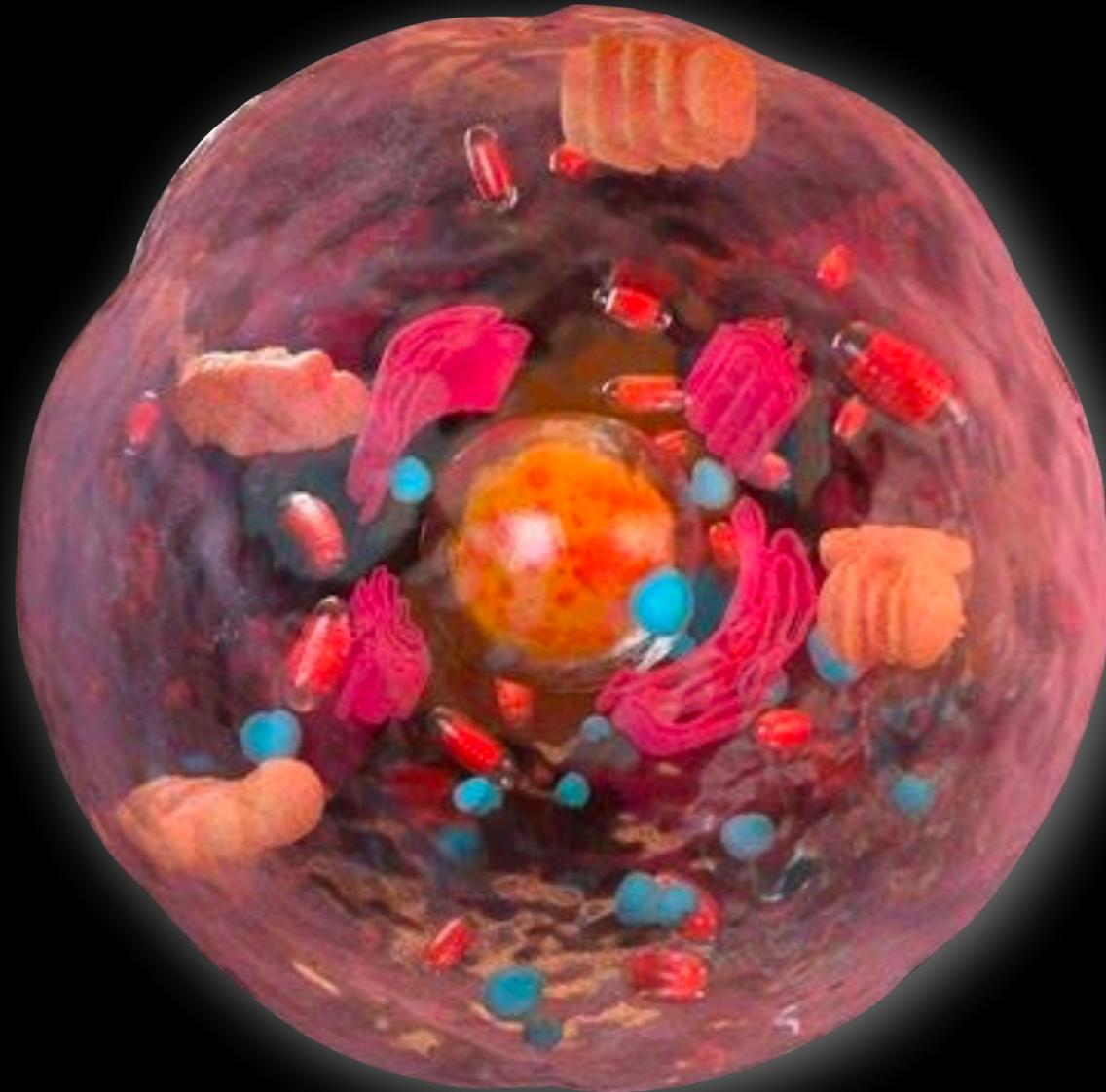
# Proxy 1: size

For the first 2,500 million years of life on Earth, most species rarely exceeded 1 mm in size and were generally much smaller (on average 5  $\mu\text{m}$ )



# Proxy 1: size

For the first 600-800 million years of eukaryotic life, while considerably larger, still ranged on average about 40-200  $\mu\text{m}$  in size



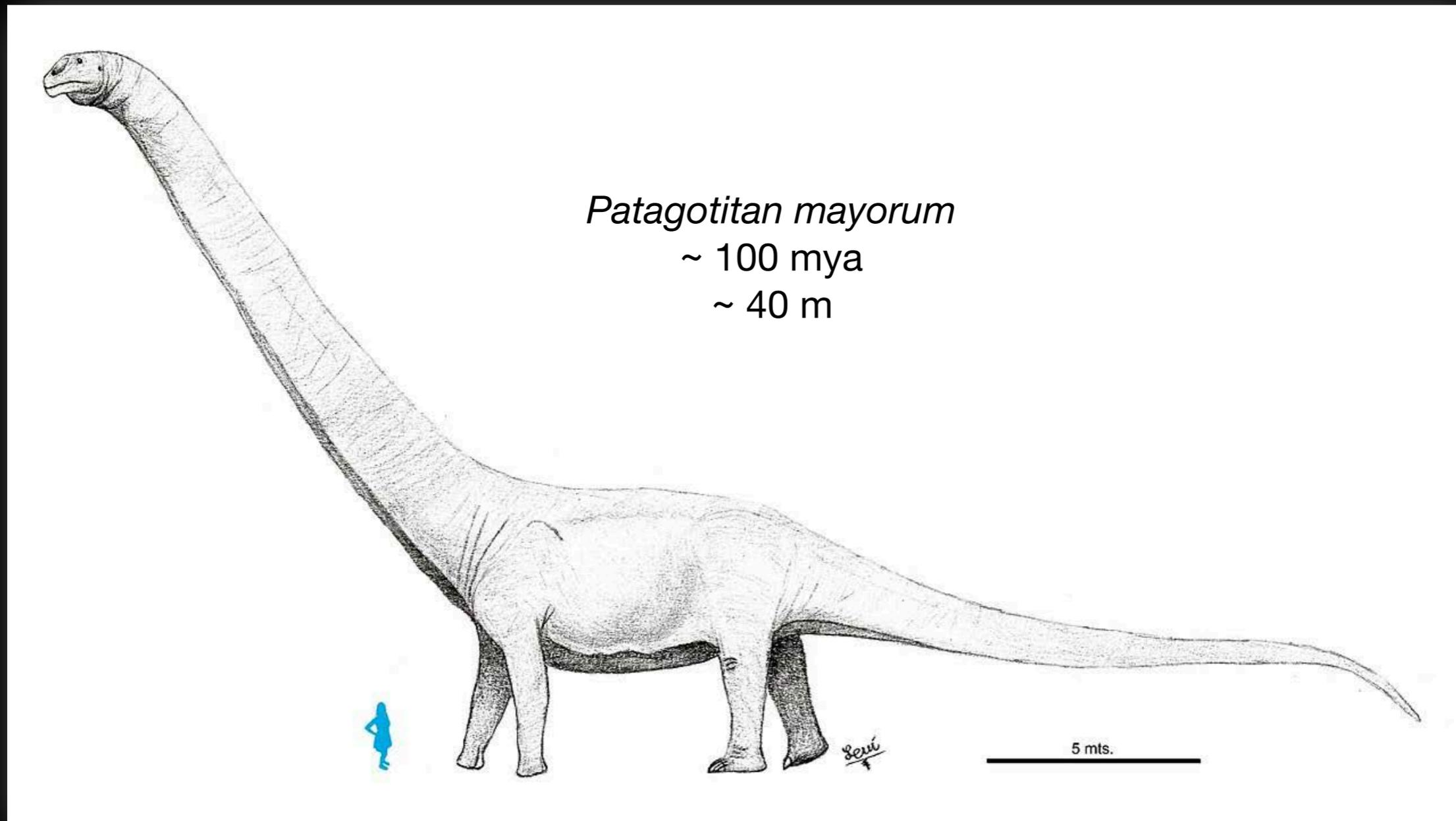
# Proxy 1: size

The increase in size is related to multicellularity, but it was significant after the Cambrian explosion (543 mya)



# Proxy 1: size

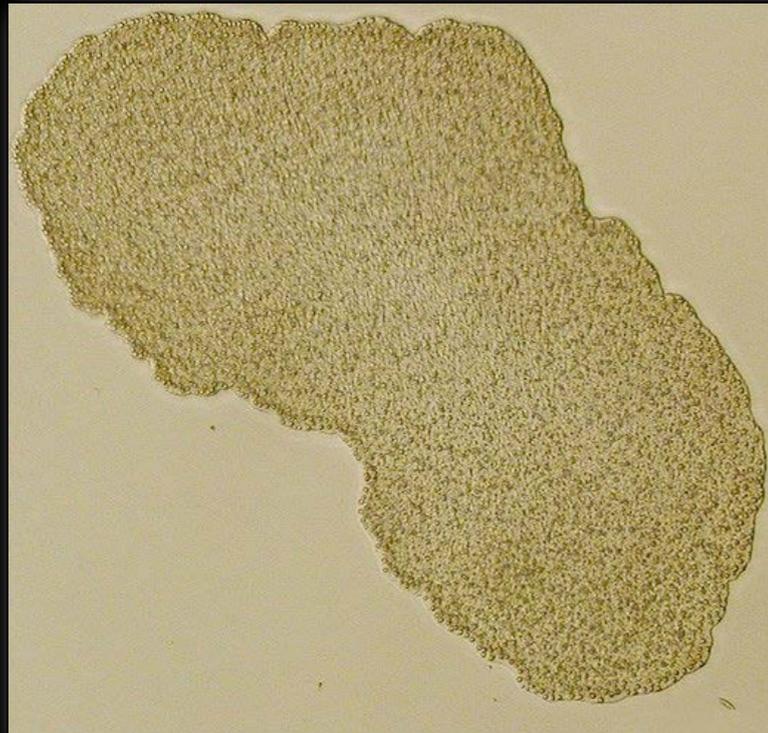
But since the Cambrian explosion (543 mya) the body size does not increased regularly



# Proxy 1: size



# Proxy 2: cell # and types



**$10^3$  cells, 6 types**

*Trichoplax adherens*,  
phylum Placozoa  
0,5 mm



**$10^3$  cells, 20 types**

*Caenorhabditis elegans*,  
phylum Nematoda  
1 mm



**$10^4$  cells, 30 types**

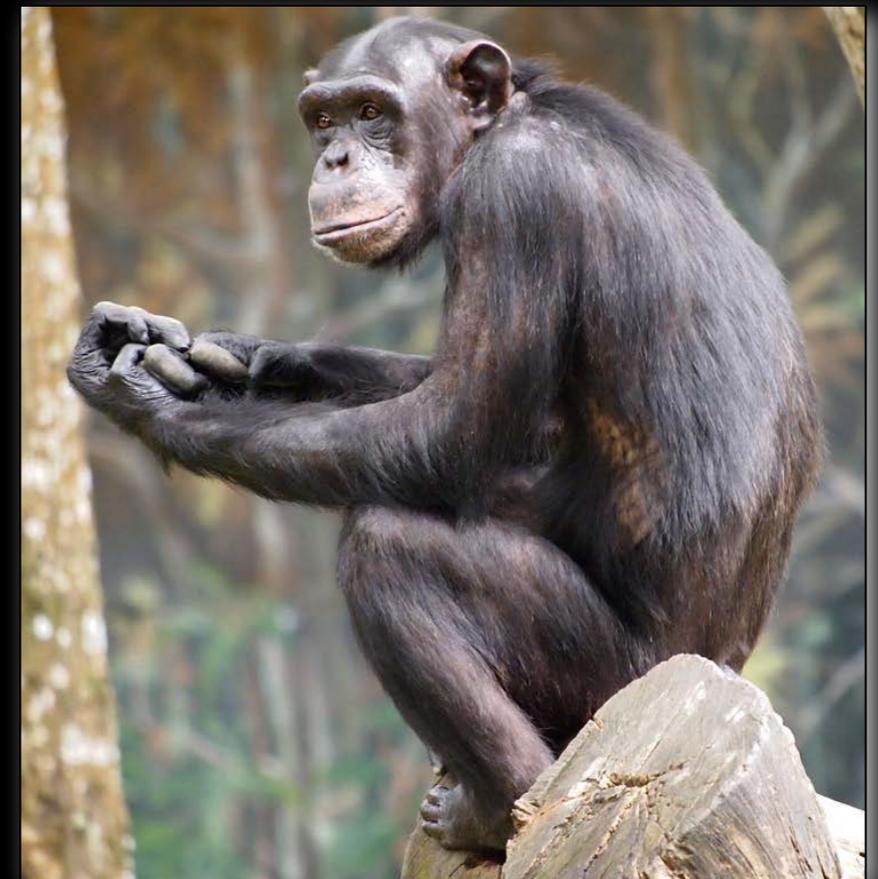
*Macrostomum hystericinum*,  
phylum Platelminta  
1-5 mm

# Proxy 2: cell # and types



**$10^{13}$  cells, is ~200 types**

*Columba livia*,  
phylum Chordata  
25 cm



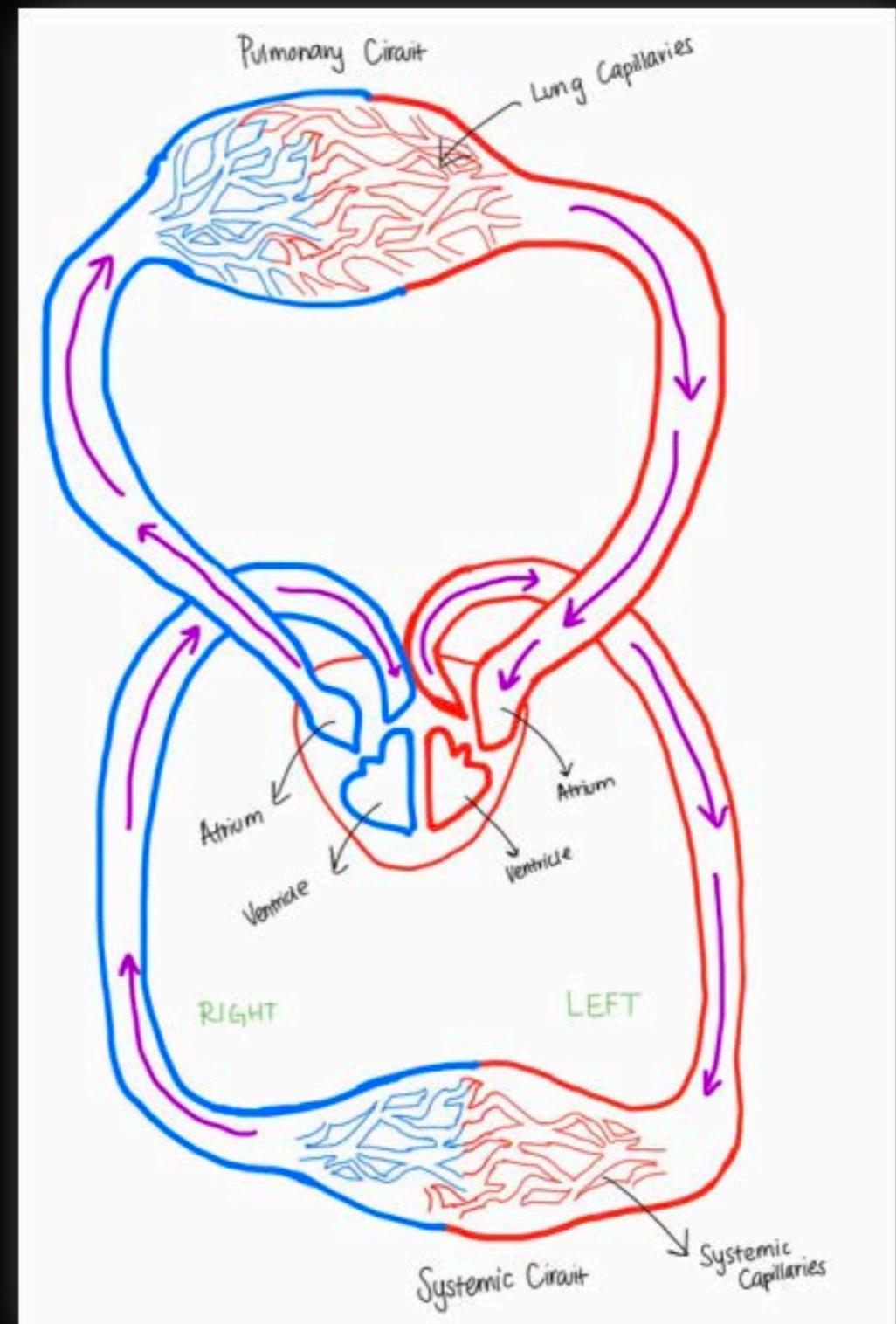
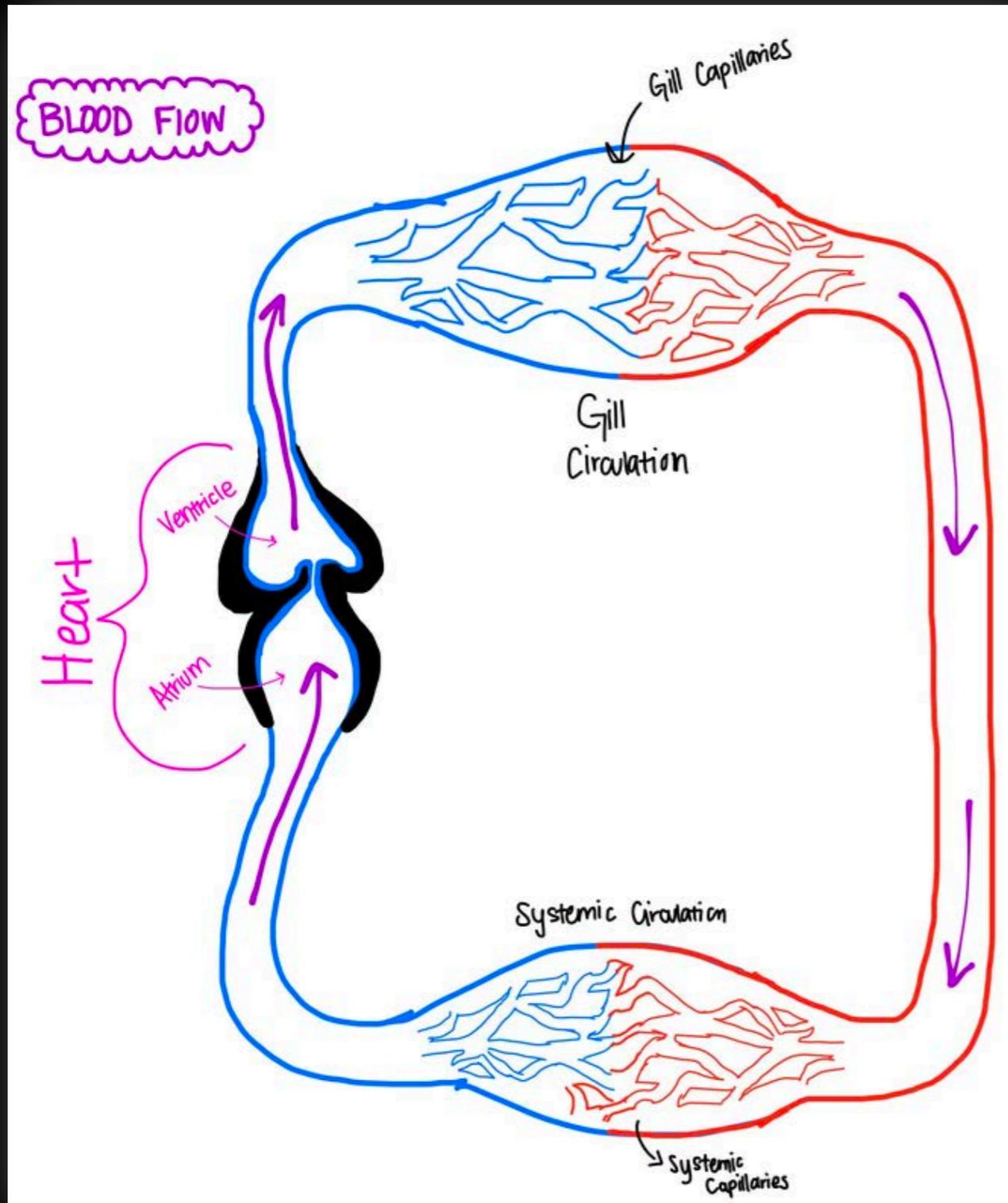
**$10^{14}$  cells, is ~200 types**

*Pan troglodytes*,  
phylum Chordata  
up to 1,5 m

# Proxy 2: cell # and types



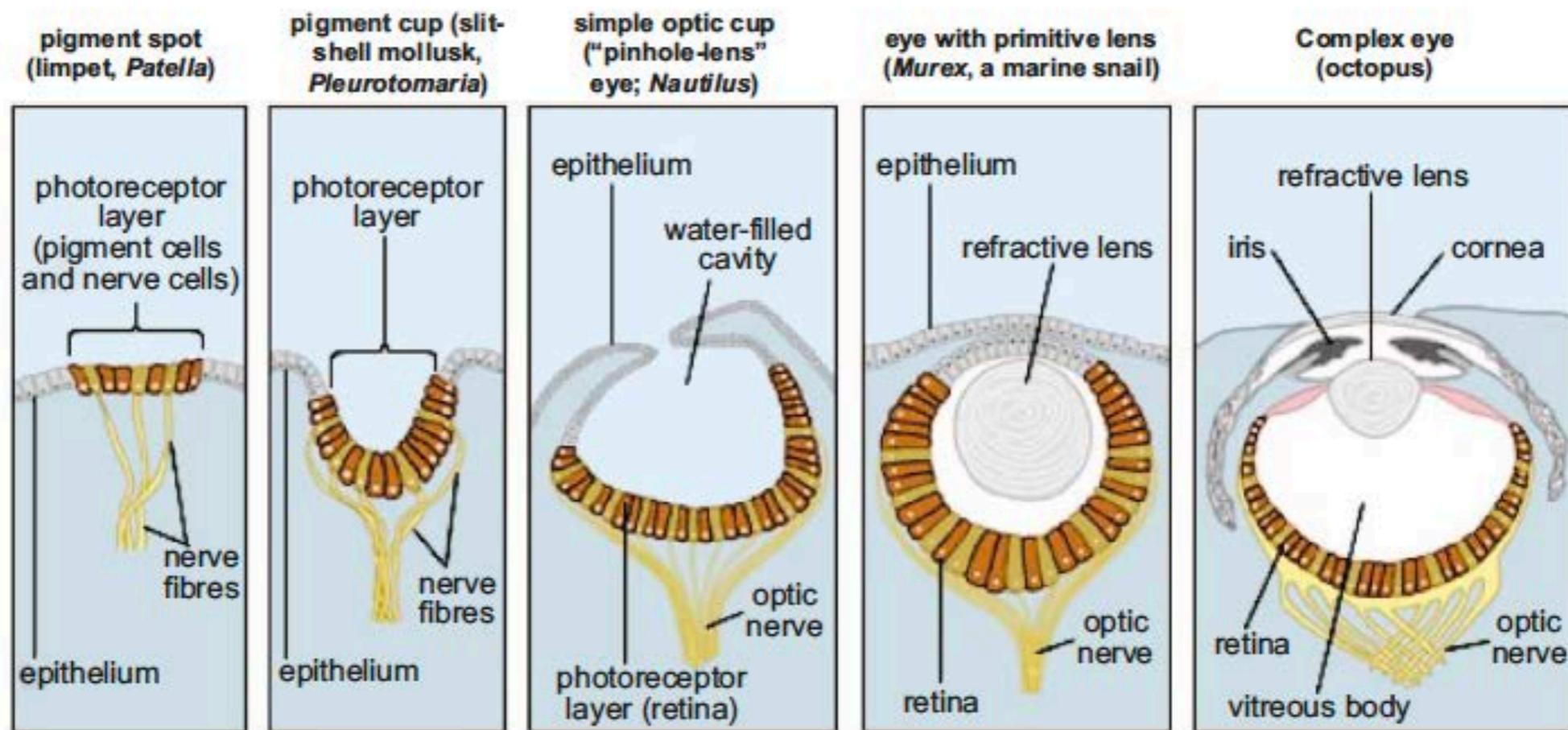
# Proxy 3: organ complexity



# Proxy 3: organ complexity

Darwin's greatest discovery: Design without designer

Francisco J. Ayala\*



**Fig. 1.** Steps in the evolution of eye complexity in living mollusks. The simplest eye is found in limpets (far left), consisting of only a few pigmented cells, slightly modified from typical epithelial (skin) cells. Slit-shell mollusks (second from the left) have a slightly more advanced organ, consisting of some pigmented cells shaped as a cup. The octopus eye (far right) is quite complex, with components similar to those of the human eye such as cornea, iris, refractive lens, and retina. (Adapted from "Evolution, The Theory of." By courtesy of Encyclopaedia Britannica, Inc.)

# Proxy 3: organ complexity



# Proxy 3: organ complexity



...but still



# Proxy 4: diversity vs. disparity



10.356 species



5.852 species

# Proxy 4: diversity vs. disparity

Birds are more diverse than mammals



10.356 species



5.852 species

# Proxy 4: diversity vs. disparity

The disparity in mammals is higher than the disparity in birds



Eggs, similar morphology

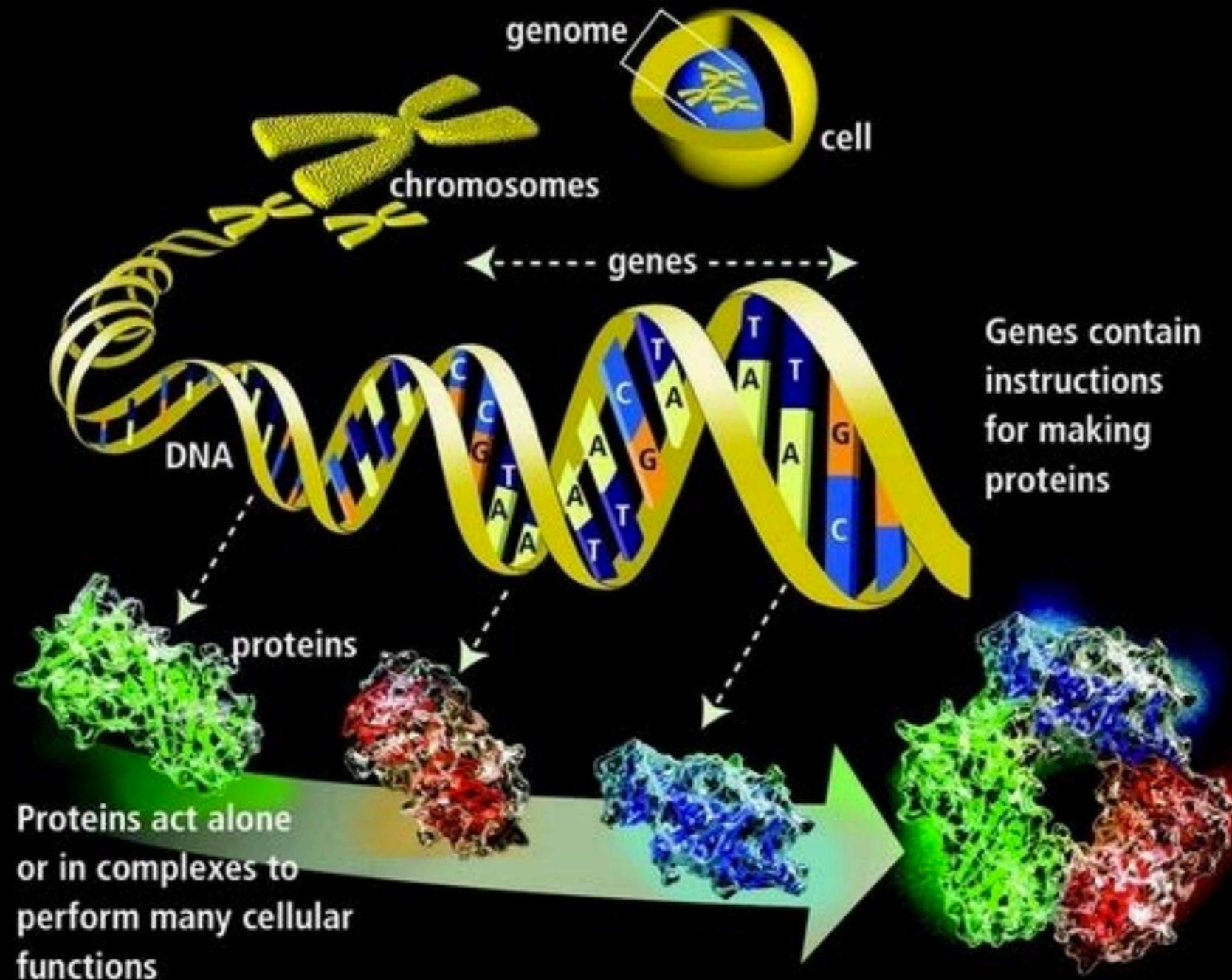


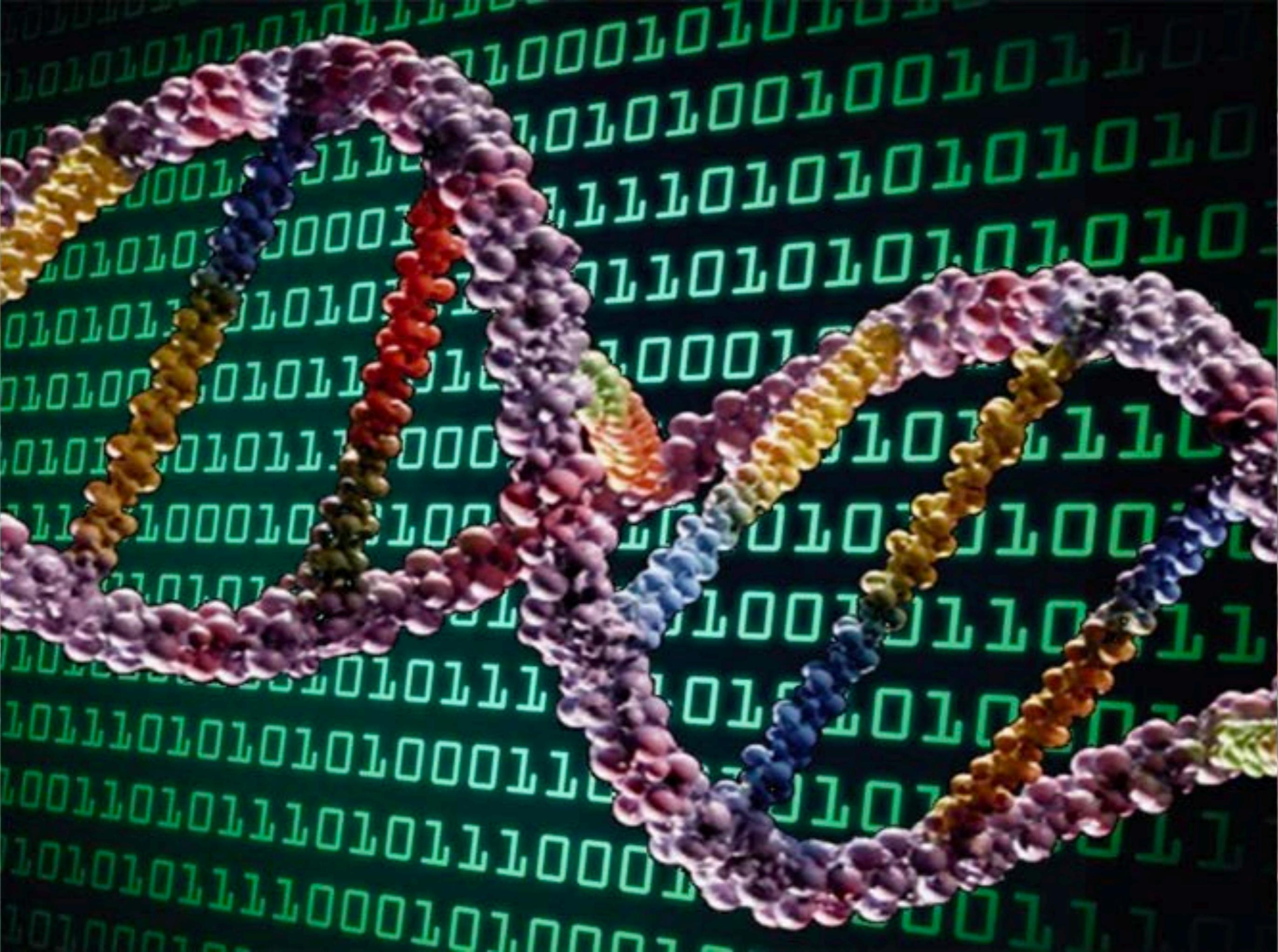
Eggs, placentas,  
more morphotypes

# Proxy 4: diversity vs. disparity



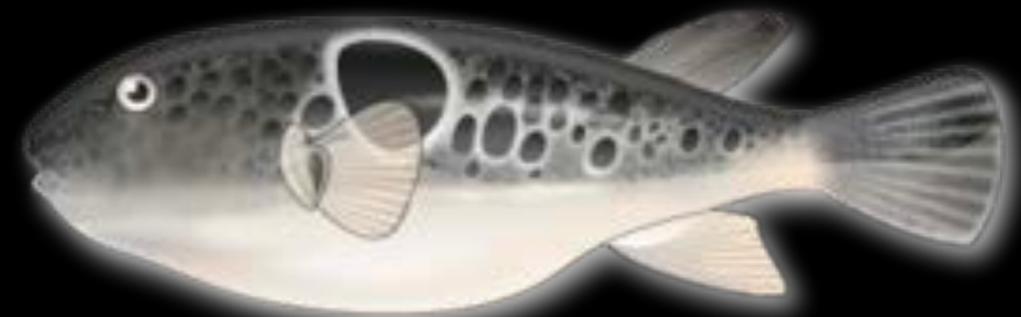
# Proxy 5: DNA - Genomes



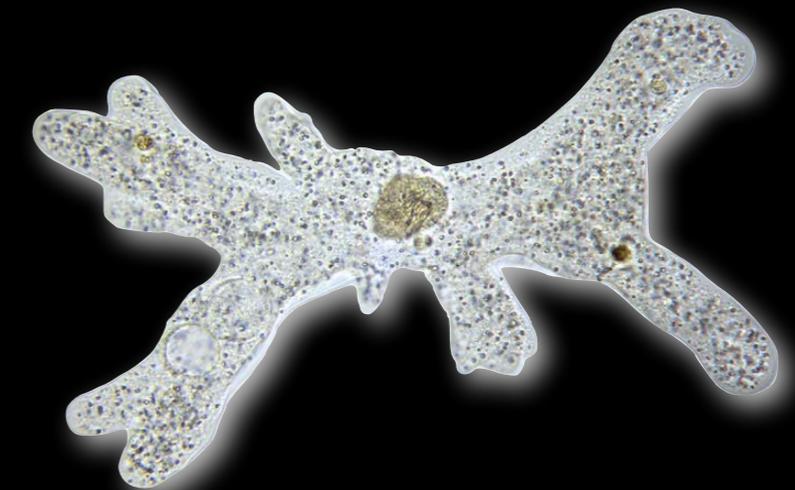


# Genomes - size

genome of pufferfish  
(*Takifugu rubripes*)



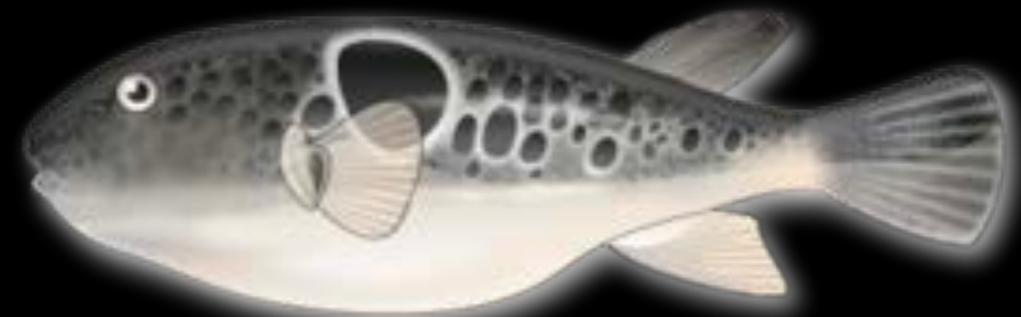
genome of man  
(*Homo sapiens*)



genome of protist (*Chaos chaos*  
sometimes confused  
with *Amoeba proteus*)

# Genomes - size

genome of pufferfish  
(*Takifugu rubripes*)

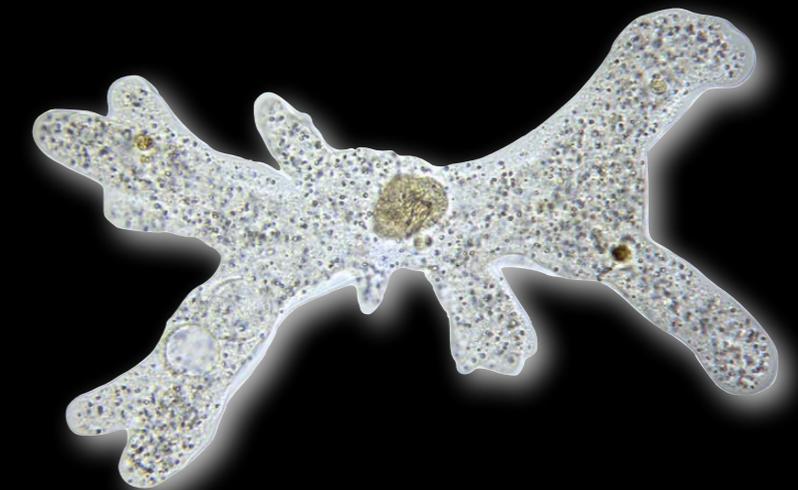


genome of man  
(*Homo sapiens*)

BIG

SMALL

expected

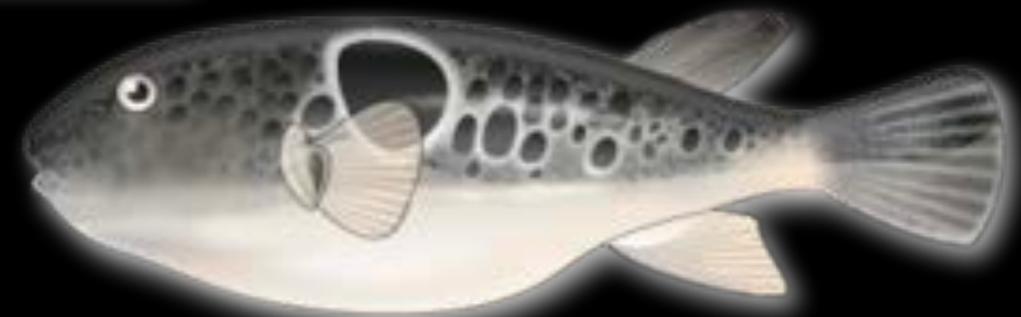


genome of protist (*Chaos chaos*  
sometimes confused  
with *Amoeba proteus*)

# Genomes - size

**10X**

genome of pufferfish  
(*Takifugu rubripes*)



BIG

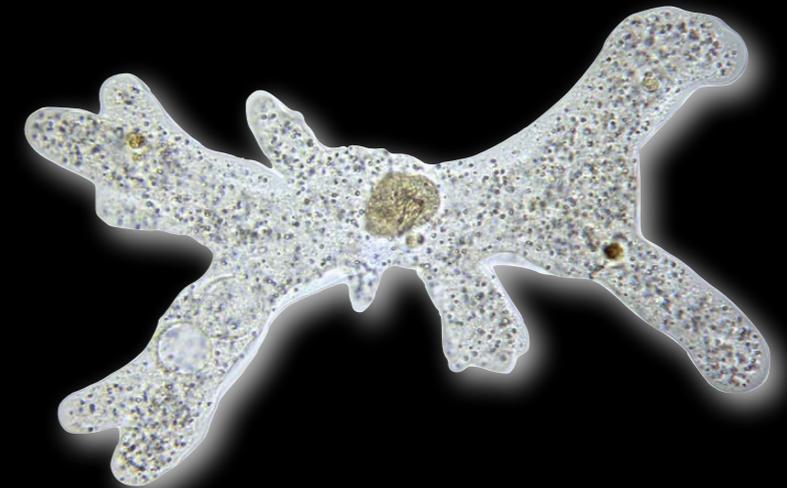
SMALL

realised



genome of man  
(*Homo sapiens*)

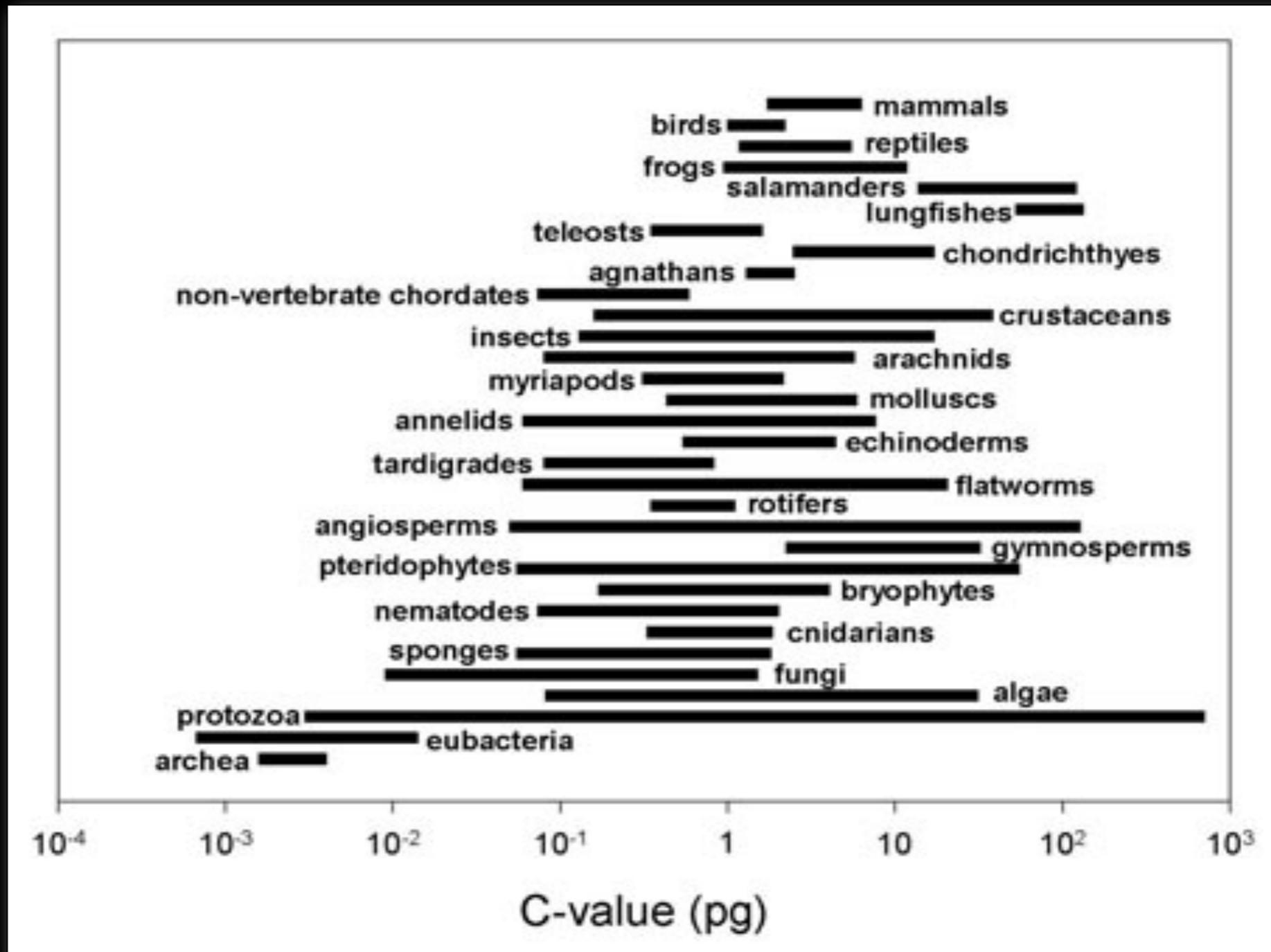
**1X**



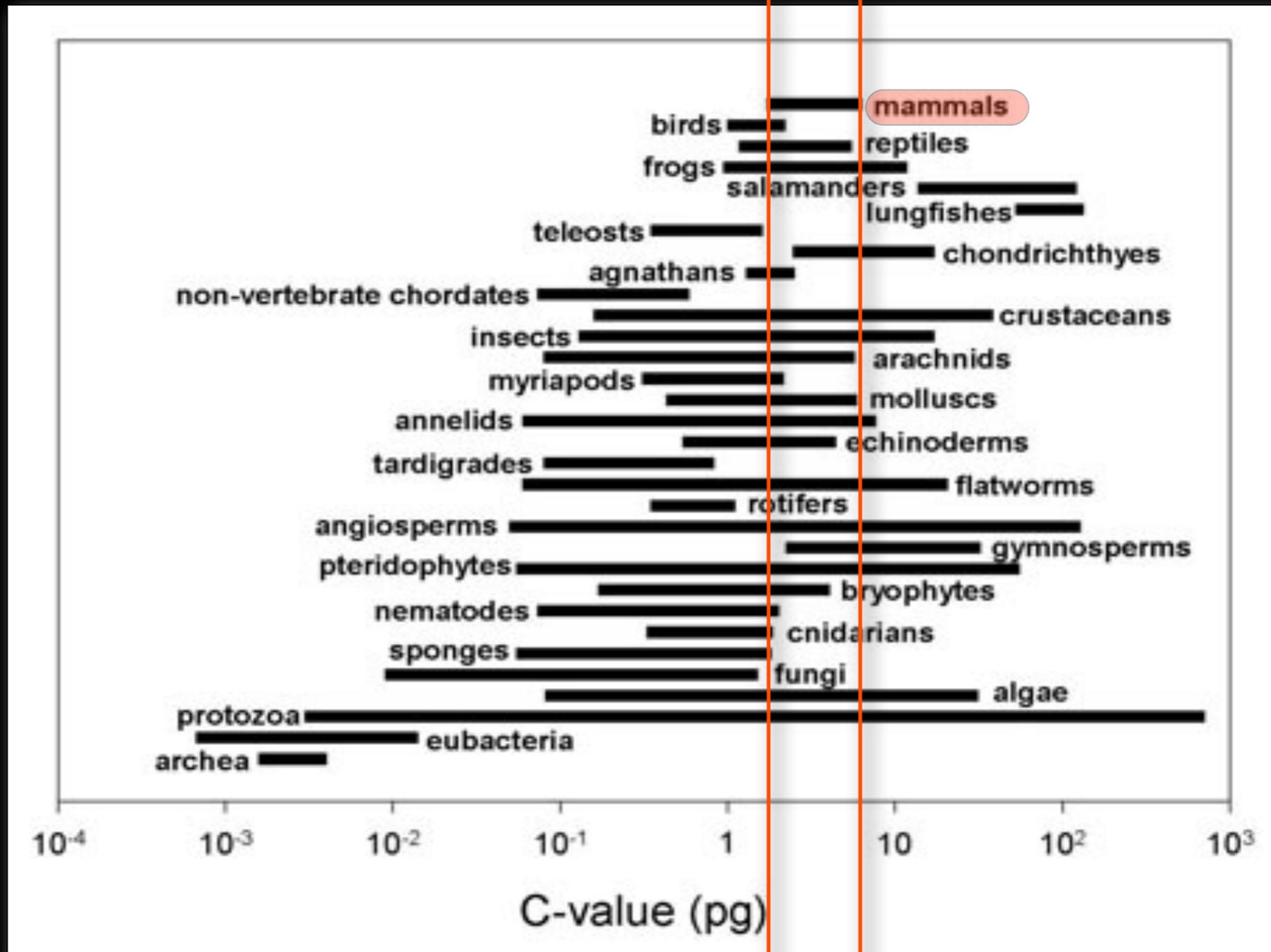
genome of protist (*Chaos chaos*  
sometimes confused  
with *Amoeba proteus*)

**400X**

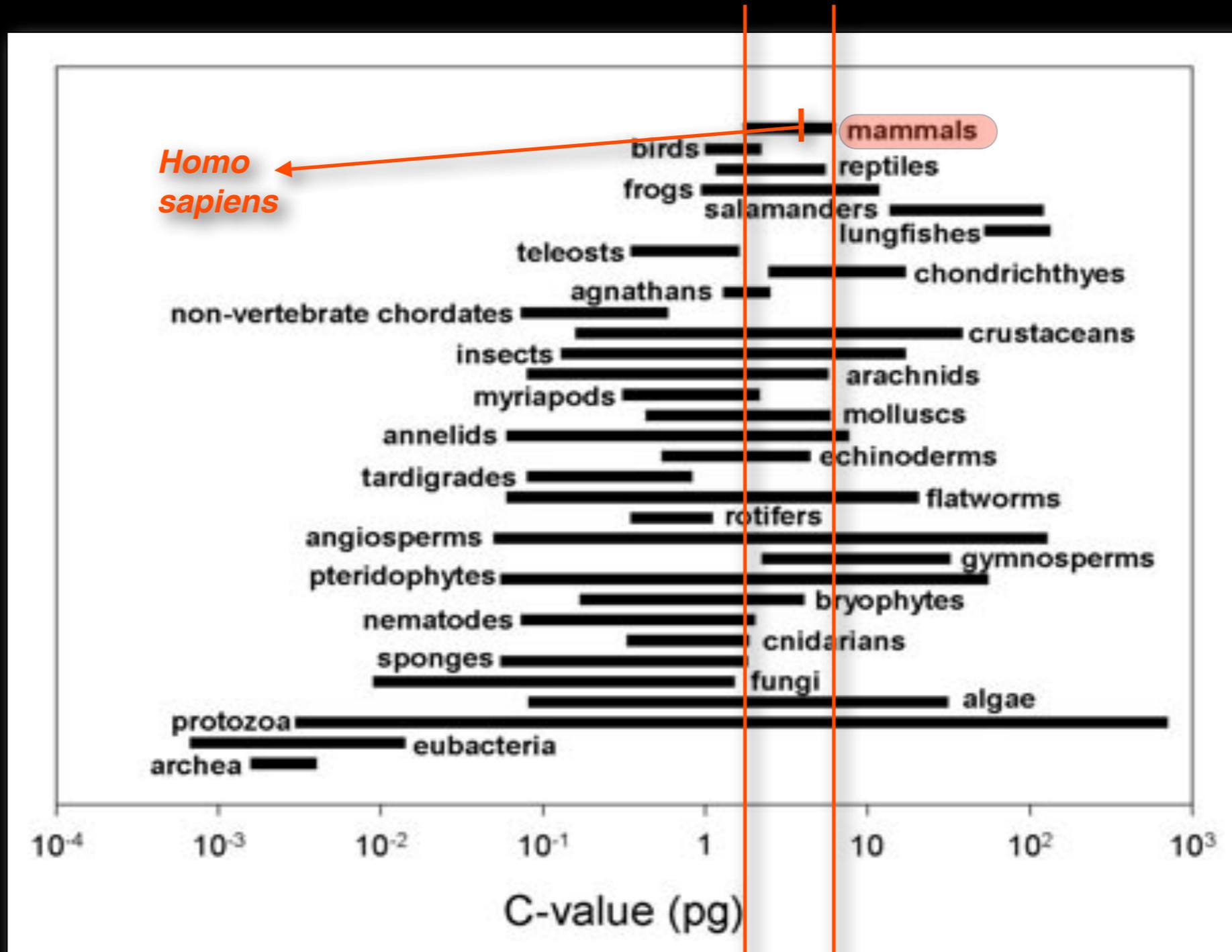
# Genomes - size



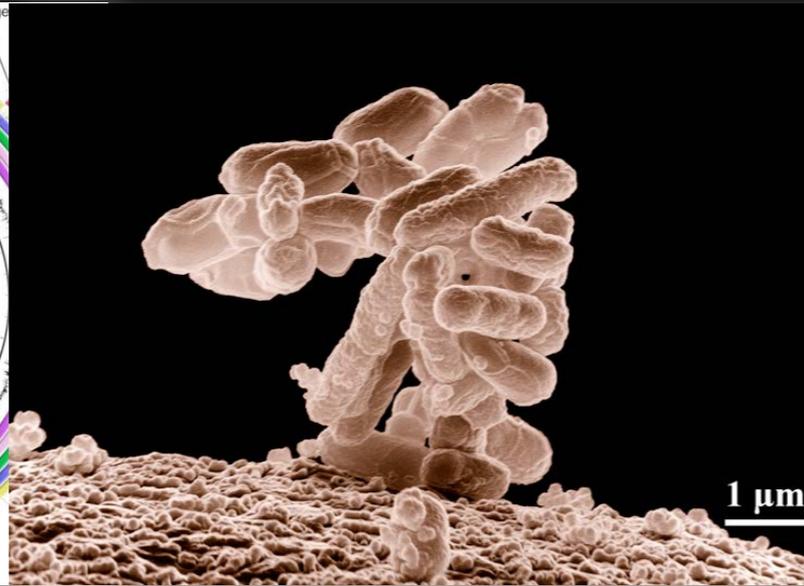
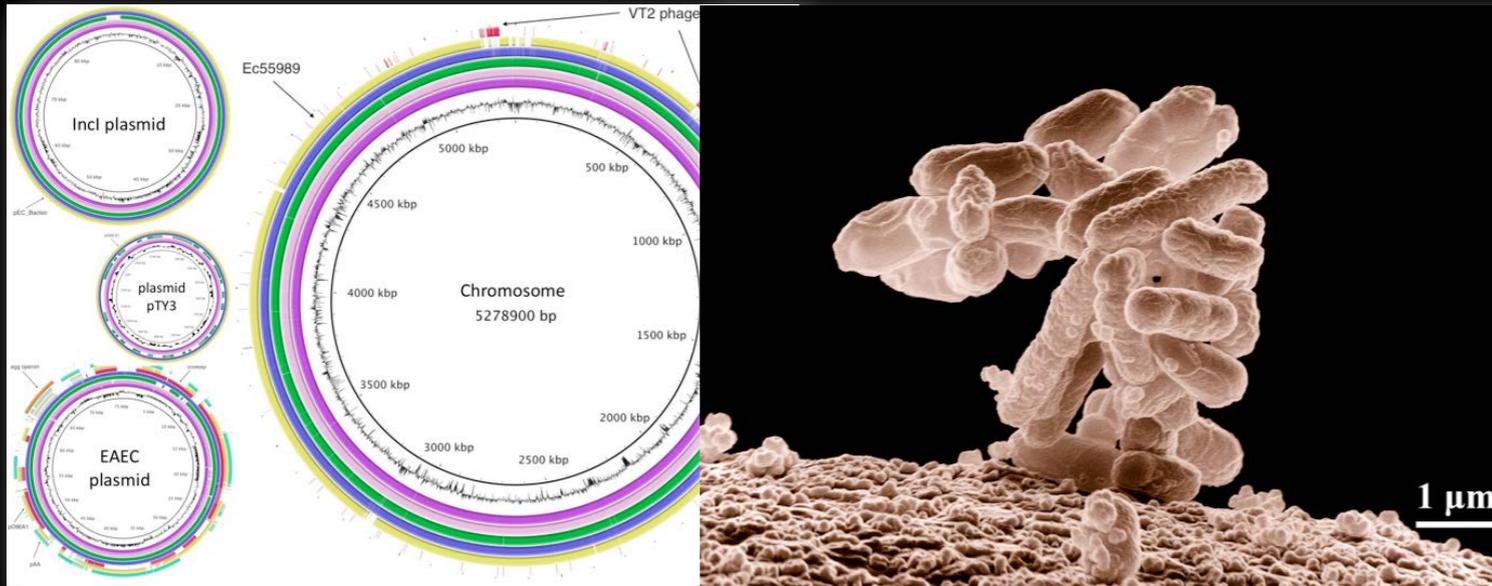
# Genomes - size



# Genomes - size



# Genomes - chromosome #



*Escherichia coli*,  
1 chromosome and some plasmids.



*Ophioglossum reticulatum*,  
720 chromosomes (n).  
One of the highest value  
for a living being

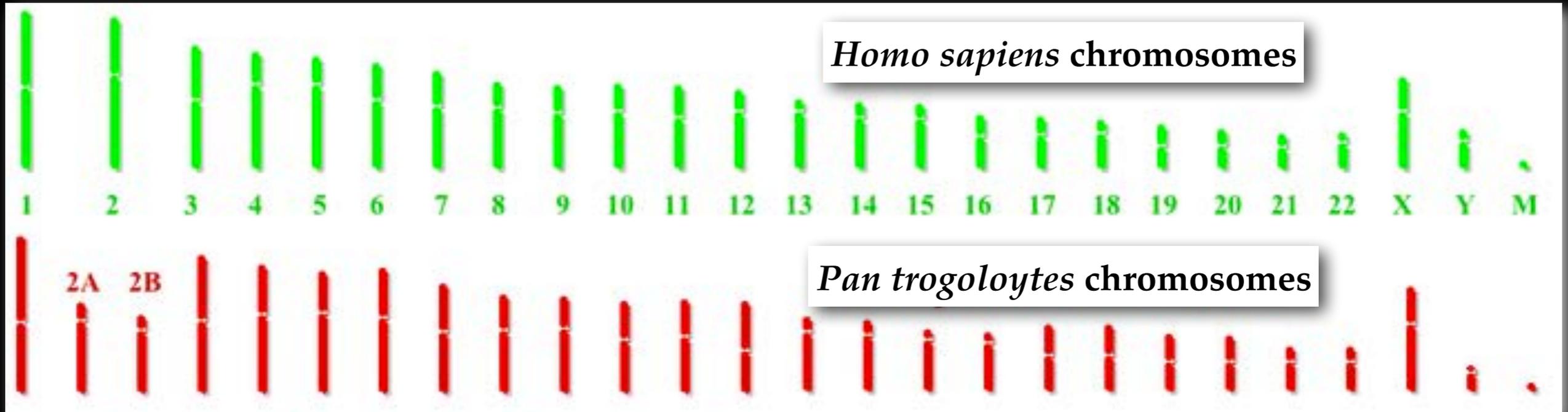
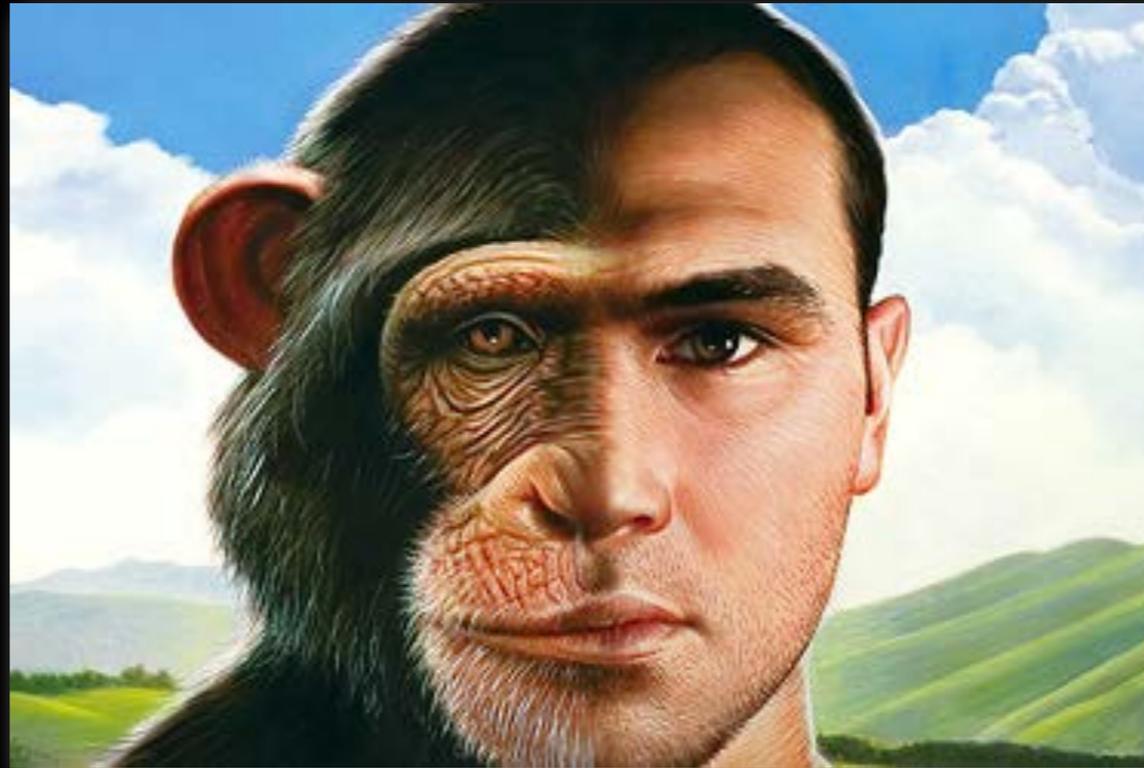
*Homo sapiens*,  
23 chromosomes (n)



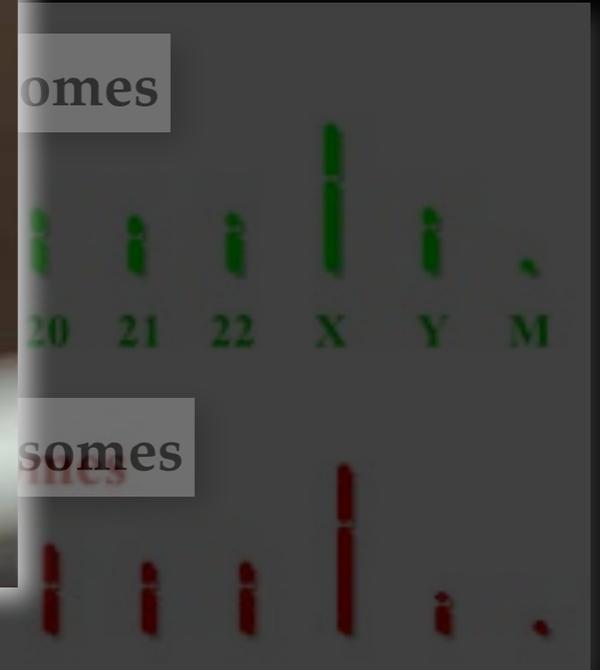
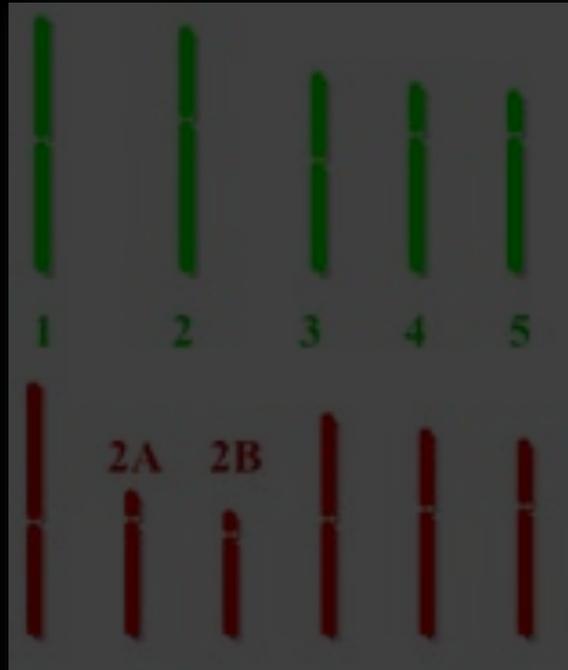
*Polyommatus atlanticus*,  
223 chromosomes (n).  
One of the highest value  
among metazoans



# Genomes - chromosome #



# Genomes - chromosome #



# Genome sizes vs gene #

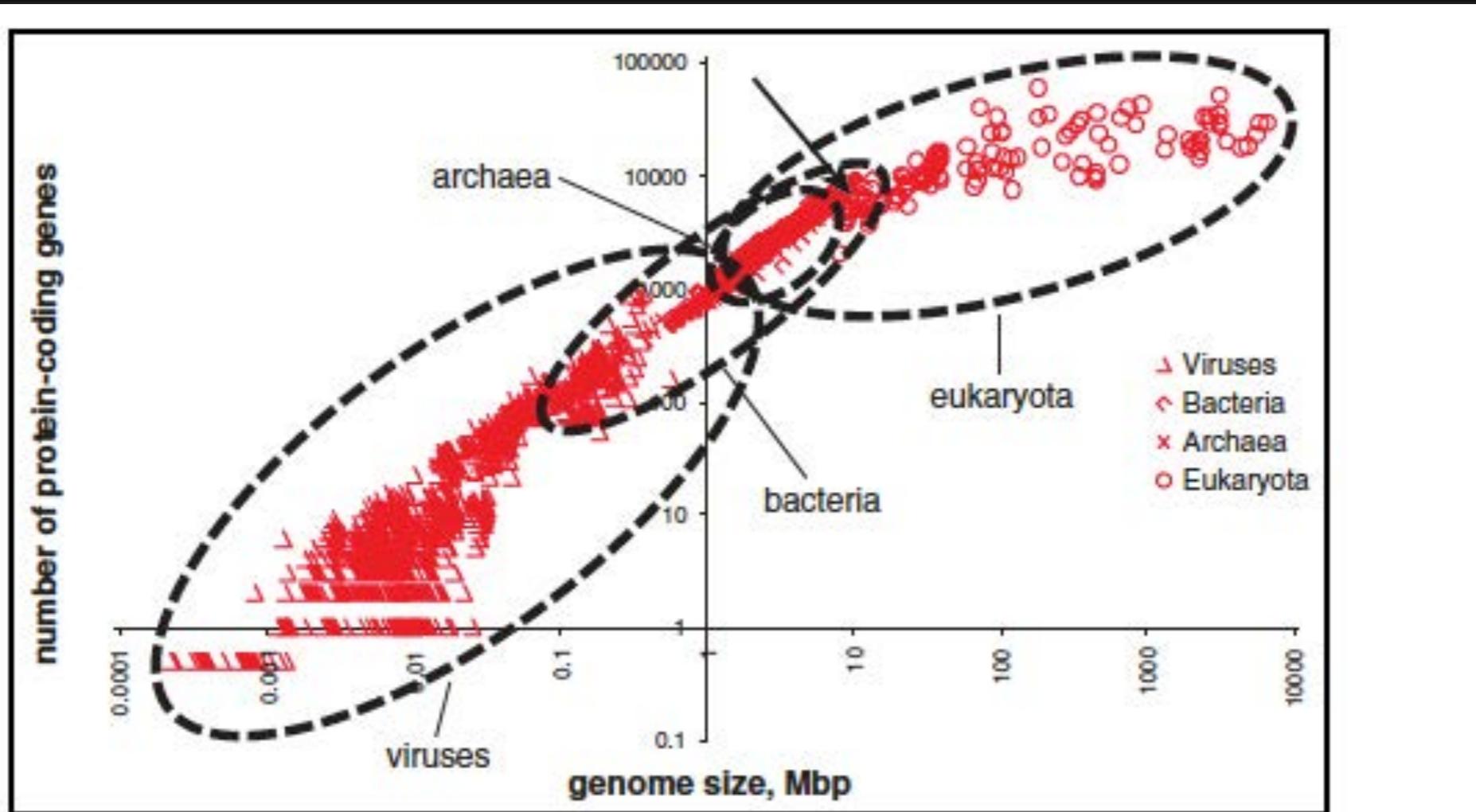
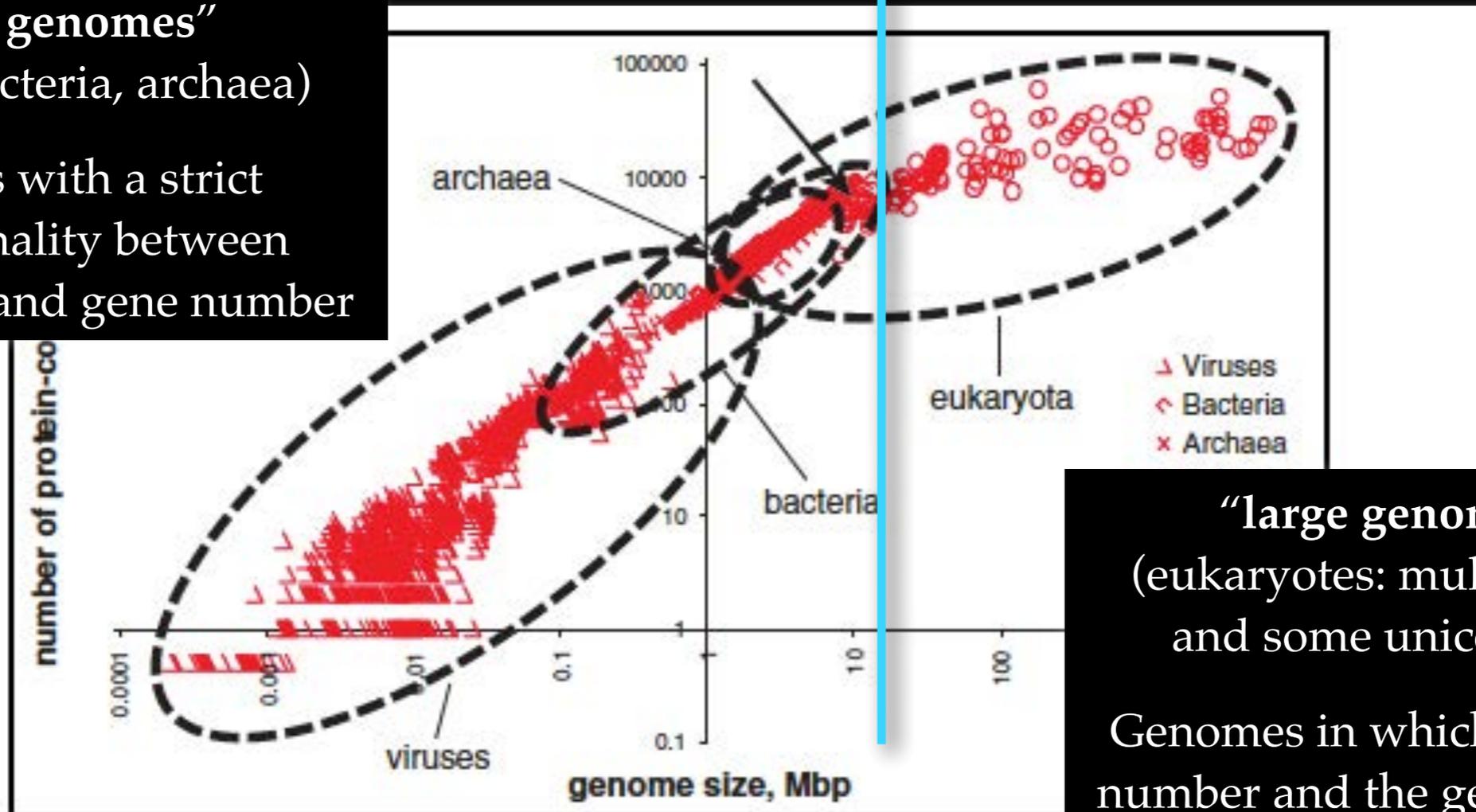


Figure 3-2 The total size of the genomes and the number of genes in viruses, bacteria, archaea, and eukaryotes. Data comes from the NCBI/Genomes website. The plot is in double logarithmic scale. Mbp stands for mega base-pairs. The arrow points to the change in the slope of curve that corresponds to the transition from "small" to "large" genomes.

# Genome sizes vs gene #

“small genomes”  
(viruses, bacteria, archaea)

Genomes with a strict  
proportionality between  
genome size and gene number

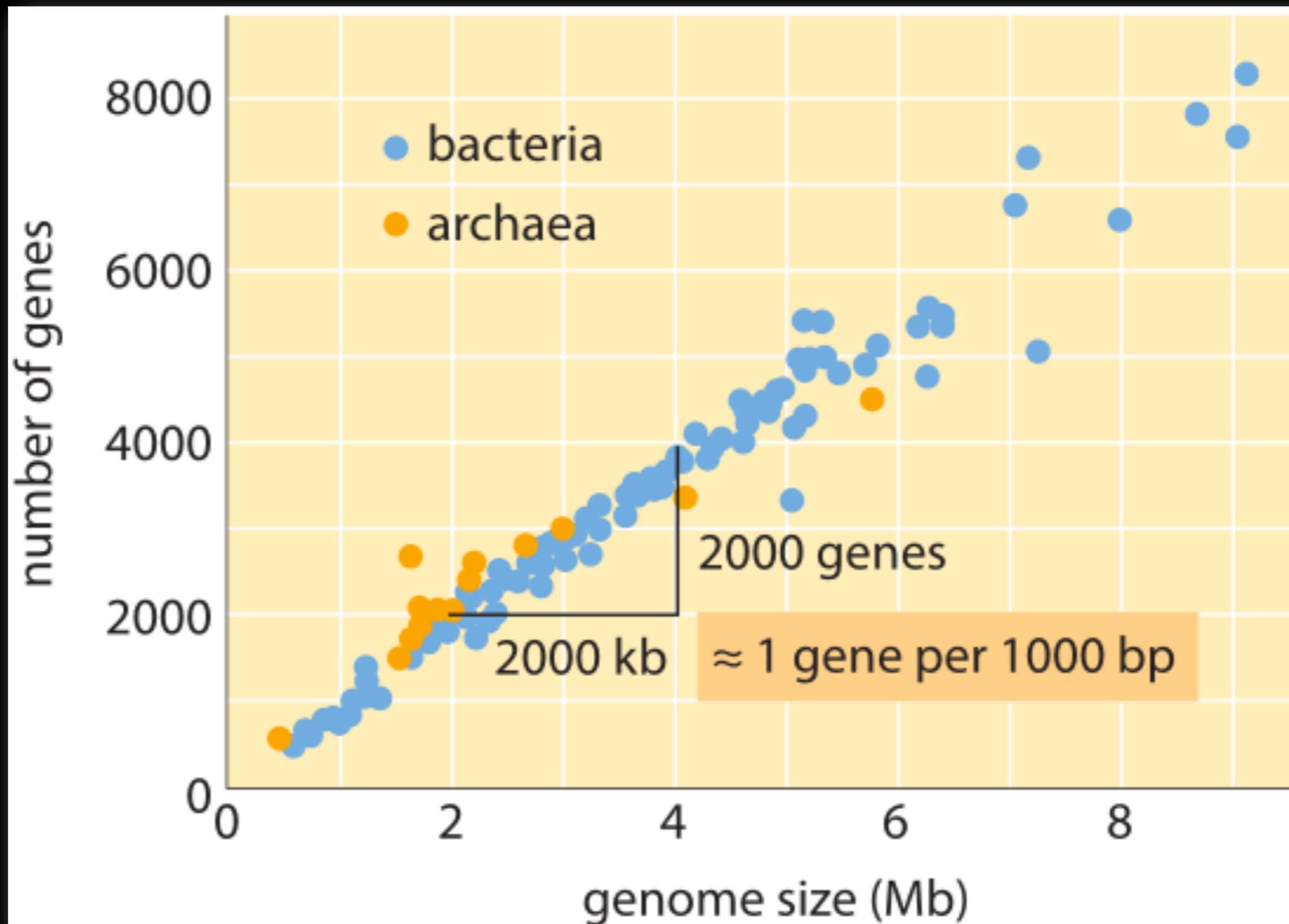


“large genomes”  
(eukaryotes: multicellular  
and some unicellular)  
Genomes in which the gene  
number and the genome size  
are decoupled

Figure 3-2 The total size of the genomes and the number of genes in viruses, bacteria, archaea, and eukaryotes. Data comes from the NCBI/Genomes website. The plot is in double logarithmic scale. Mbp stands for mega base-pairs. The arrow points to the change in the slope of curve that corresponds to the transition from “small” to “large” genomes.

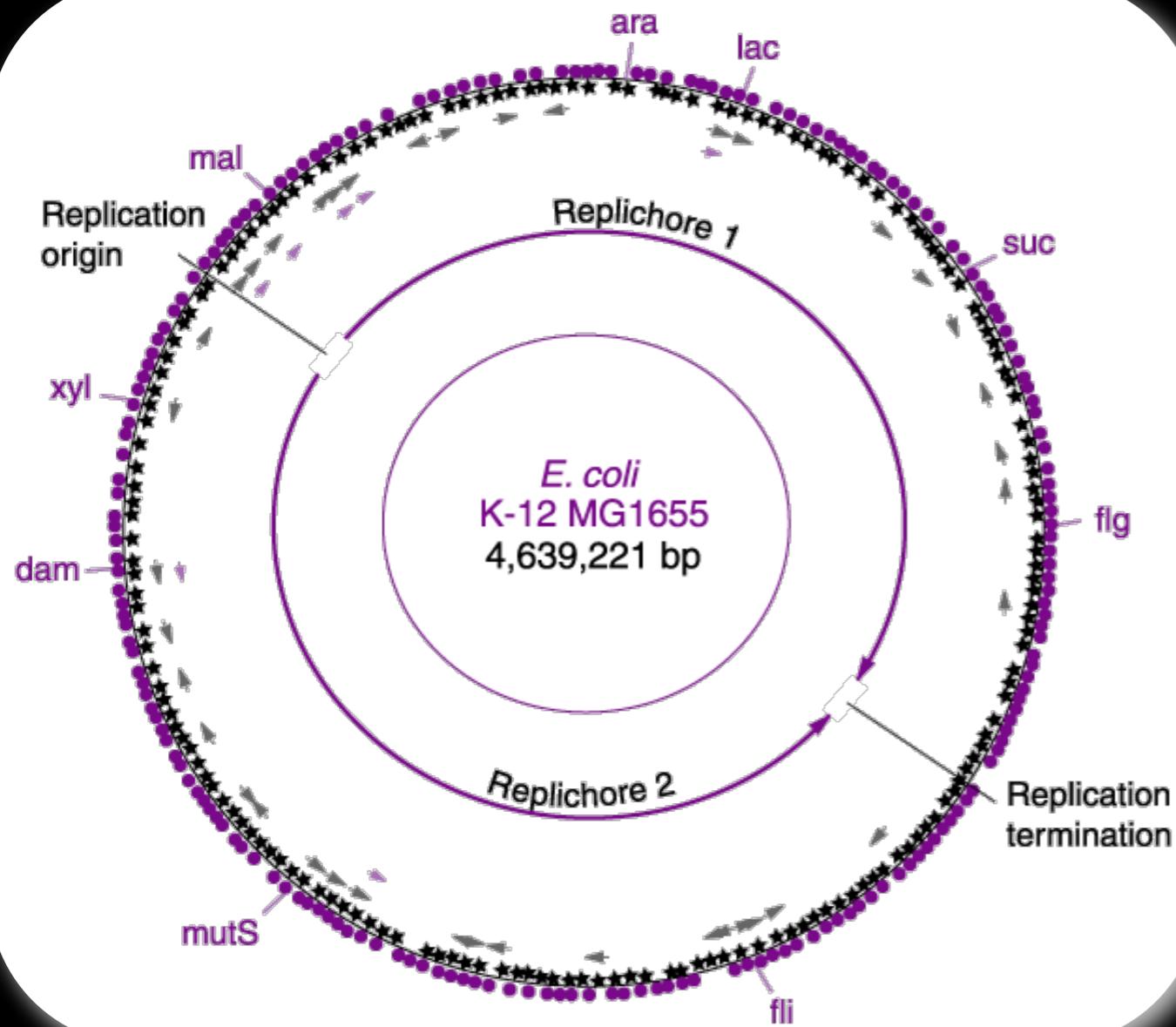
# Genome sizes vs gene #

“prokaryotes”



# Genome sizes vs gene #

“prokaryotes”

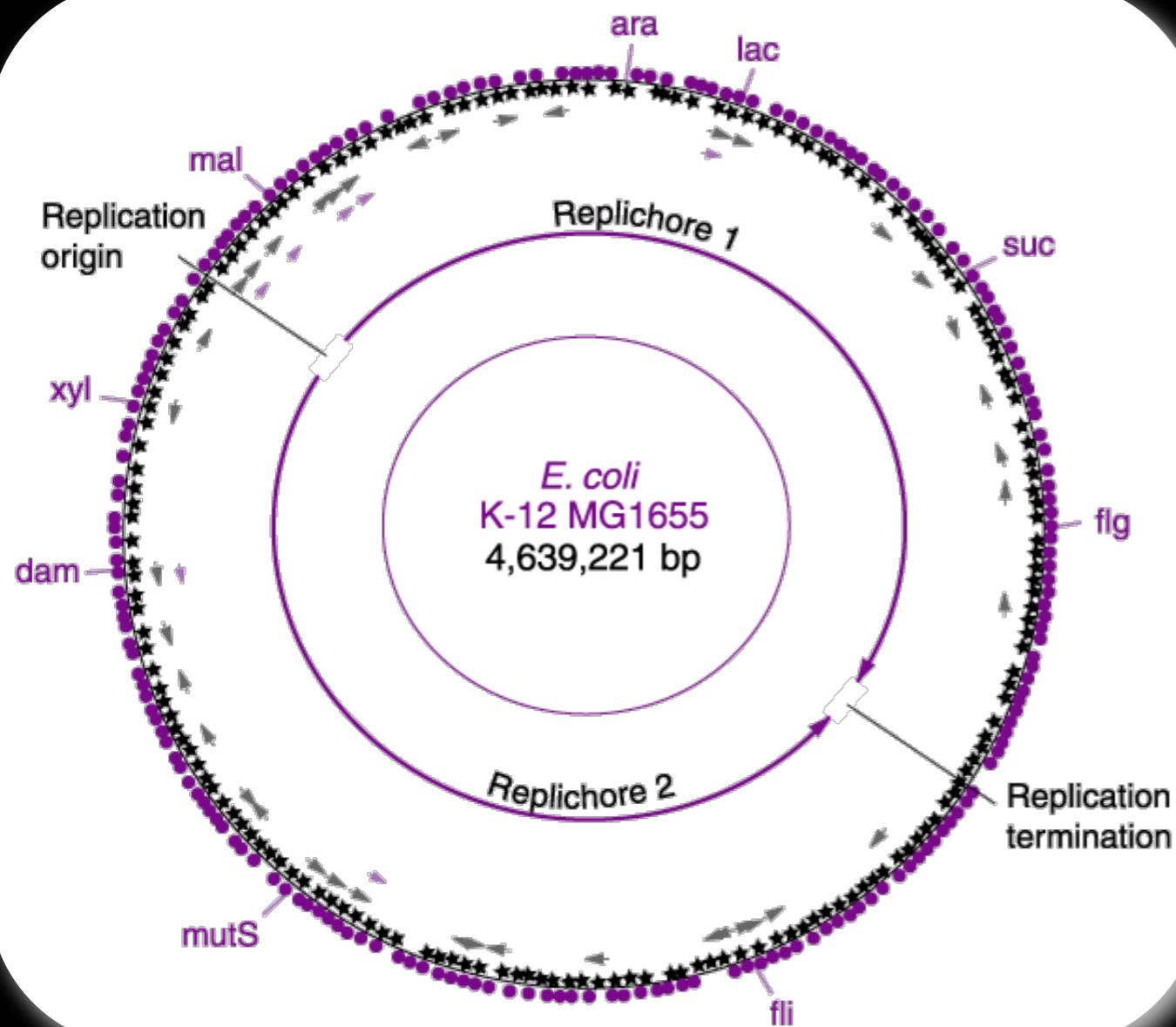


1997:  
K-12 MG1655  
the reference  
*E. coli* genome

4288 protein-  
coding genes  
annotated

# Genome sizes vs gene #

“prokaryotes”



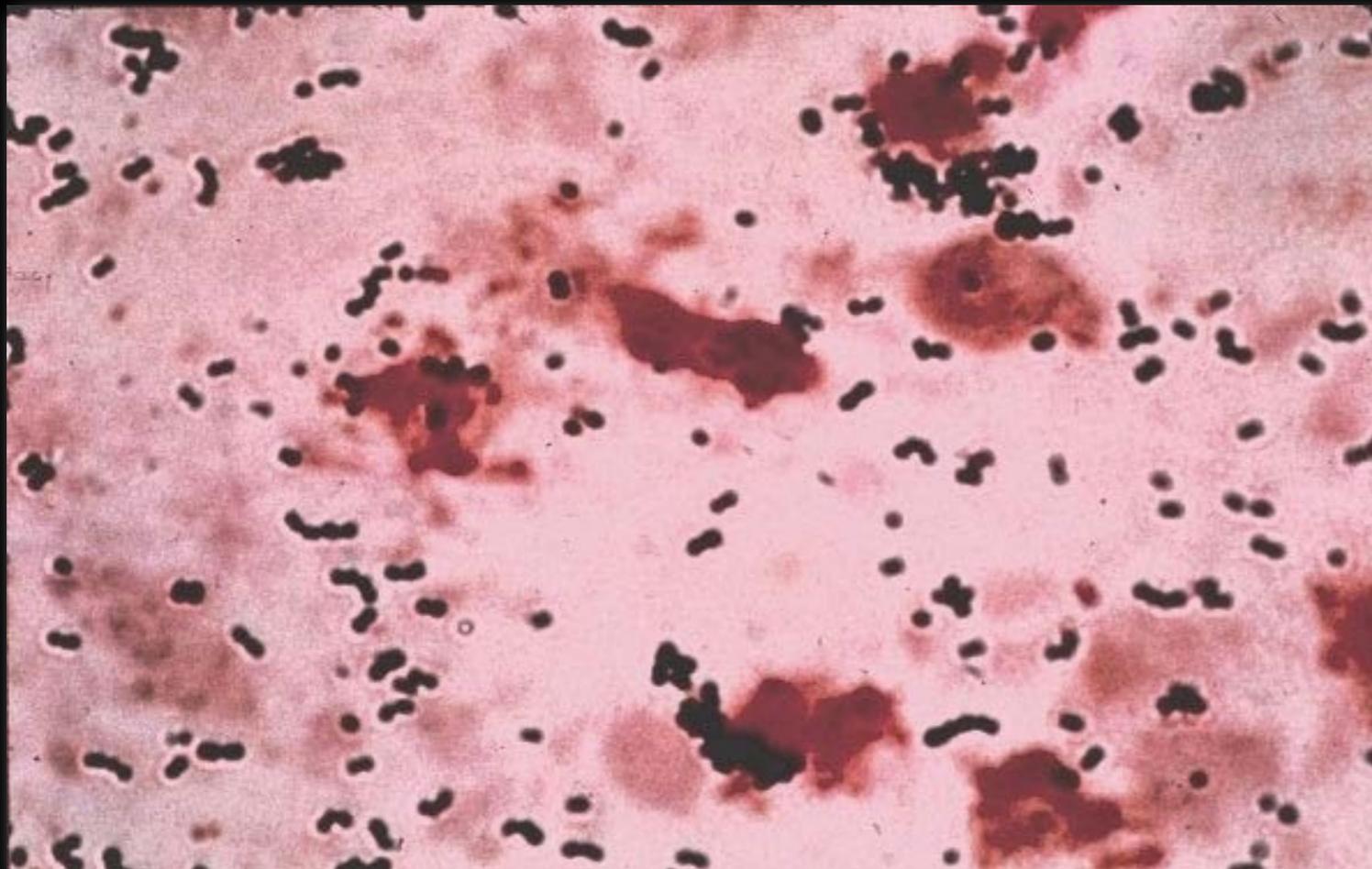
Rather soon it was clear that bacterial strains can be very different in their “behaviour”, physiology, biochemistry and so on...

But, what about their genomes?

- [ ] Strain:AW330
- [ ] Strain:BW25113
- [ ] Strain:D31
- [ ] Strain:DH5 alpha
- [+] Strain:E. coli (4)
- [ ] Strain:EMG2
- [ ] Strain:K-12 P2
- [ ] Strain:Lemo21(DE3)
- [ ] Strain:MC1061
- [ ] Strain:MH594
- [ ] Strain:RP437
- [+] Strain:RS2 (1)
- [ ] Strain:S26 r1e
- [ ] Strain:S26r1e
- [ ] Strain:S26R1e
- [ ] Strain:S26rde
- [ ] Strain:TG1
- [ ] Strain:W185
- [ ] Strain:WA803
- [ ] Strain:YA027
- [ ] Strain:ZYCY10P3S2T

# Genome sizes vs gene #

“prokaryotes”



*Streptococcus agalactiae*,  
Gram Positive bacteria

The genomes of 6 strains  
were completely sequenced  
(plus 2 already known).  
Gene prediction: about 3.500

Tettelin et al, 2005. PNAS

# Genome sizes vs gene #

## “prokaryotes”

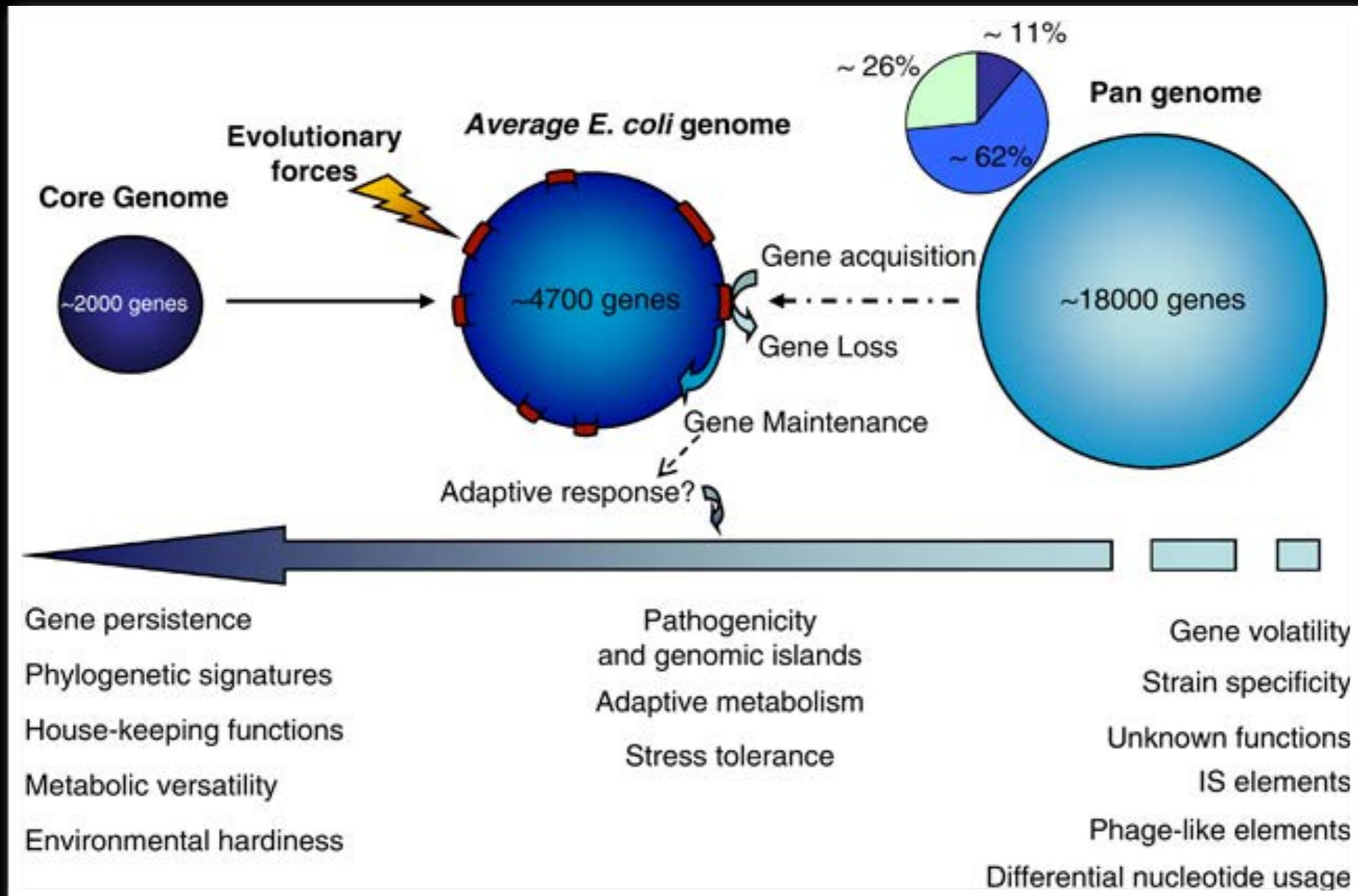
80% of the genome conserved, but 20% varies among different genomes

Comparative analysis of the six newly sequenced genomes and the two genomes already available in the databases suggests that a bacterial species can be described by its “pan-genome” (pan, from the Greek word  $\pi\alpha\nu$ , meaning whole), which includes a core genome containing genes present in all strains and a dispensable genome composed of genes absent from one or more strains and genes that are unique to each strain.

*Streptococcus agalactiae*,  
Gram Positive bacteria

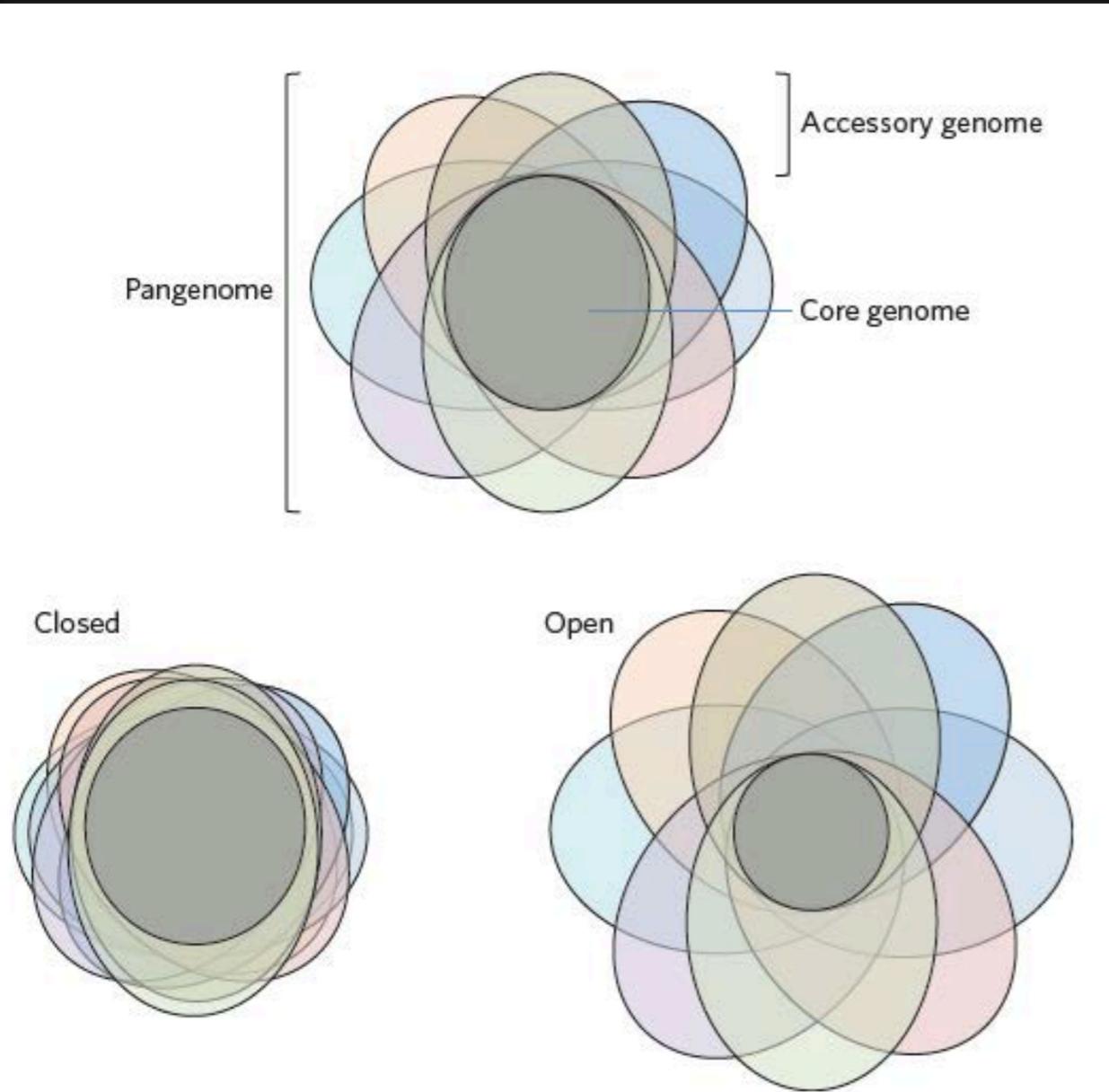
# Genome sizes vs gene #

## “prokaryotes”



# Genome sizes vs gene #

## “prokaryotes”



Up to 2019 there are at least 50 species of “prokaryotes” with a pangenome

**Figure 1 | Schematic representation of pangenomes as Venn diagrams.** Species differ in the sizes of their pangenomes, with larger, more open pangenomes correlating with larger long-term effective population sizes and the ability to migrate.

# Genome sizes vs gene #

## “prokaryotes”

MICROBIAL GENOMICS

RESEARCH ARTICLE

McCarthy and Fitzpatrick, *Microbial Genomics* 2019;5  
DOI 10.1099/mgen.0.000243

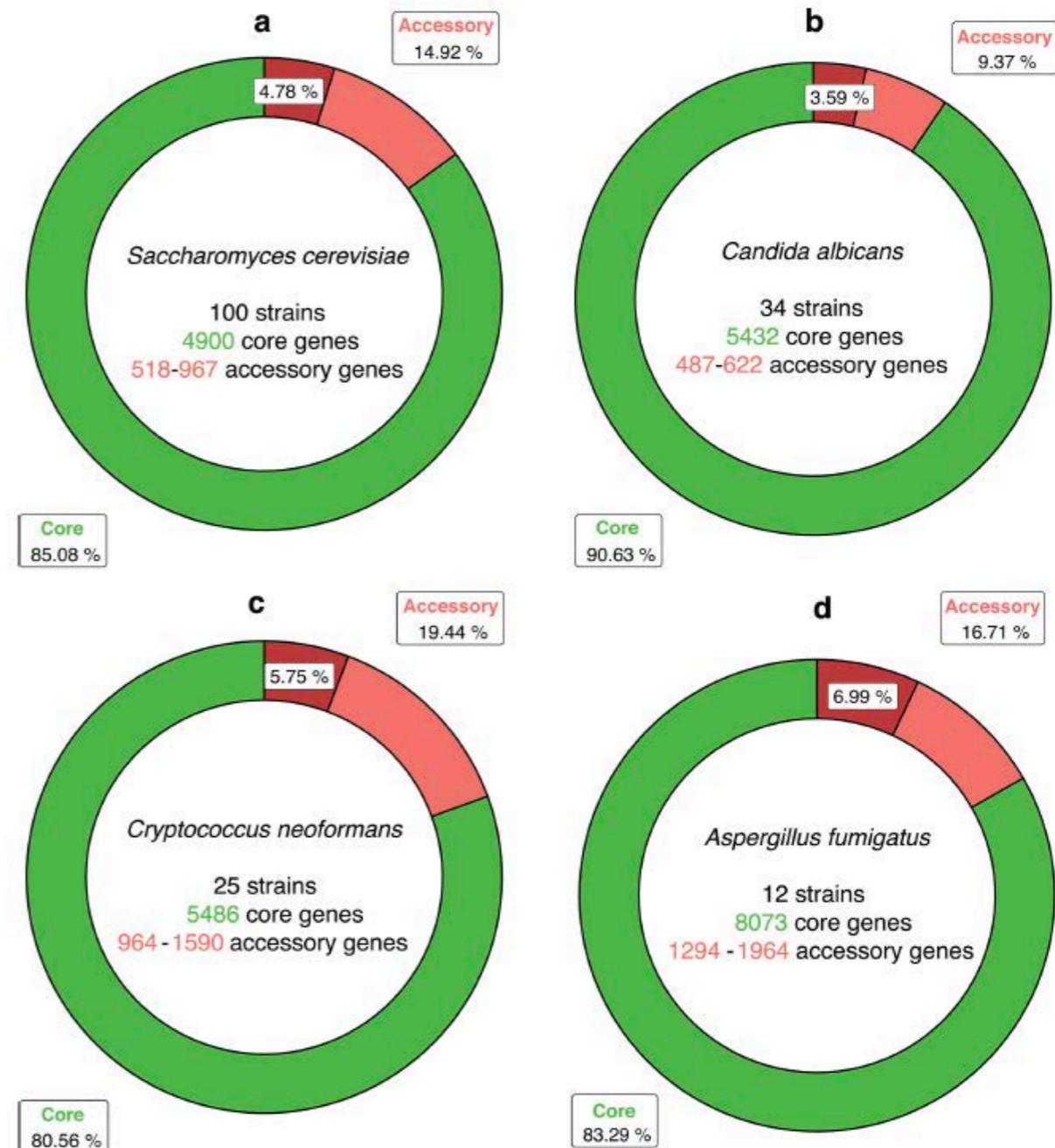


## Pan-genome analyses of model fungal species

Charley G. P. McCarthy<sup>1,2</sup> and David A. Fitzpatrick<sup>1,2,\*</sup>

### Abstract

The concept of the species ‘pan-genome’, the union of ‘core’ conserved genes and all ‘accessory’ non-core genes across all strains of a species, was first proposed in prokaryotes to account for intraspecific variability. Genomes have been extensively studied in prokaryotes, but evidence of species pan-genomes has also been documented in eukaryotes such as plants and fungi. Using a previously published methodology based on sequence homology and microsynteny, in addition to bespoke pipelines, we have investigated the pan-genomes of four model species: *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans* var. *grubii* and *Aspergillus fumigatus*. Between 90% of gene models per strain in each of these species are core genes that are highly conserved across all species, many of which are involved in housekeeping and conserved survival processes. In many of the remaining ‘accessory’ gene models are clustered within subterminal regions and may be involved in pathogenesis and antimicrobial resistance. Analysis of the ancestry of species core and accessory genomes suggests that fungi evolve by strain-level innovations such as gene duplication as opposed to wide-scale horizontal gene transfer. This study lends further supporting evidence to the existence of species pan-genomes in eukaryote taxa.



**Fig. 6.** Pan-genomes of four fungal species. (a) *Saccharomyces cerevisiae*, (b) *Candida albicans*, (c) *Cryptococcus neoformans* var. *grubii*, (d) *Aspergillus fumigatus*. The ring charts represent the total number of gene models in pan-genome complements expressed as a proportion of total pan-genome size. Sections in dark-red represent duplicated core gene models in the accessory genome.

**Figure 1 | Schematic representation of pangenomes as Venn diagrams.** Species differ in the sizes of their pangenomes, with larger, more open pangenomes correlating with larger long-term effective population sizes and the ability to migrate.

# Genome sizes vs gene #

“prokaryotes”

prokaryote  
pangenomes

prokaryote  
genomes



# Genome sizes vs gene # eukaryotes

eukaryote with the  
smaller genome

80,000 times

eukaryote with the  
larger genome

“prokaryotic” genome  
with the lowest  
number of genes

100 times  
(bacteria, less in archaea)

“prokaryotic” genome  
with the largest  
number of genes

# Genome sizes vs gene # eukaryotes



*Homo sapiens*  
Chordata  
Genome: 3,2 Gb



*Amoeba dubia*  
"Protozoan"  
Free living organism  
Genome: 690 Gb

# Genome sizes vs gene # eukaryotes

Species and Common Name	Estimated Total Size of Genome (bp)*	Estimated Number of Protein- Encoding Genes*
<i>Saccharomyces cerevisiae</i> (unicellular budding yeast)	12 million	6,000
<i>Trichomonas vaginalis</i>	160 million	60,000
<i>Plasmodium falciparum</i> (unicellular malaria parasite)	23 million	5,000
<i>Caenorhabditis elegans</i> (nematode)	95.5 million	18,000
<i>Drosophila melanogaster</i> (fruit fly)	170 million	14,000
<i>Arabidopsis thaliana</i> (mustard; thale cress)	125 million	25,000
<i>Oryza sativa</i> (rice)	470 million	51,000
<i>Gallus gallus</i> (chicken)	1 billion	20,000–23,000
<i>Canis familiaris</i> (domestic dog)	2.4 billion	19,000
<i>Mus musculus</i> (laboratory mouse)	2.5 billion	30,000
<i>Homo sapiens</i> (human)	2.9 billion	20,000–25,000

# Genome sizes vs gene #

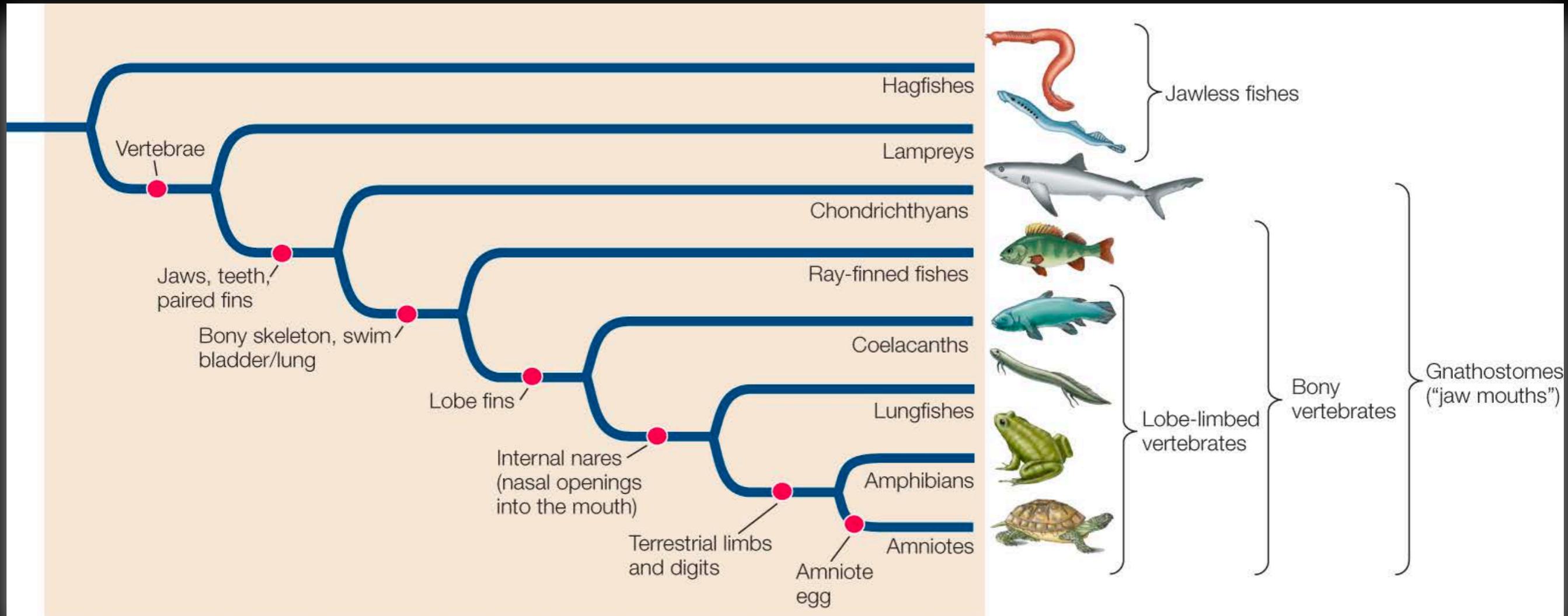
eukaryotes





# Complexity and evolutionary novelties

# Novelties





Massimo Pigliucci

**Massimo Pigliucci pointed out that novelties are structures, functions or a combination of them not present before, but in any case their correct identification is not easy because a modification of precedent structures, functions or an exaptation is not an evolutionary novelty**

Philosophy of Science, 75 (December 2008) pp. 887–898.

## What, if Anything, Is an Evolutionary Novelty?

Massimo Pigliucci†‡

The idea of phenotypic novelty appears throughout the evolutionary literature. Novelties have been defined so broadly as to make the term meaningless and so narrowly as to apply only to a limited number of spectacular structures. Here I examine some of the available definitions of phenotypic novelty and argue that the modern synthesis is ill equipped at explaining novelties. I then discuss three frameworks that may help biologists get a better insight of how novelties arise during evolution but warn that these frameworks should be considered in addition to, and not as potential substitutes of, the modern synthesis.

**1. Introduction.** “Evolutionary novelty” has been a recurring term in the evolutionary biology literature (Nitecki 1990). There is a palpable tension among biologists whenever evolutionary novelties are considered for discussion, with a common fear that the concept will be used as a wedge to undermine the modern synthesis (MS) constituting the currently accepted view of evolutionary theory. Ever since Goldschmidt (1940) professed dissatisfaction with the MS’s ability to explain variation across species, his “hopeful monsters” have repeatedly reared their ugly heads and have consistently been beaten back by defenders of the orthodoxy.

Yet, evolutionary novelties persist as a fascinating problem for theorists and experimentalists alike, a problem that has been taken seriously enough to become a major stated goal of a whole field of investigation, known as “evo-devo” (for evolution and/of development). Despite great progress over the past decade at finally incorporating development in the modern

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‡Thanks to Jonathan Kaplan for organizing a PSA symposium on evolutionary novelties, as well as to Jonathan, Alan Love, and Alirio Rosales for critical readings of the manuscript. The National Science Foundation (grant IOB-0450240) supported the development of these ideas.

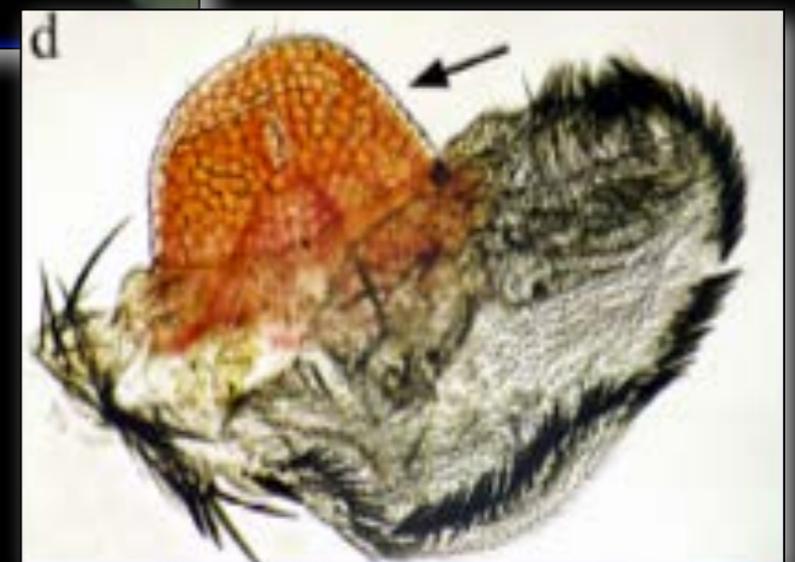
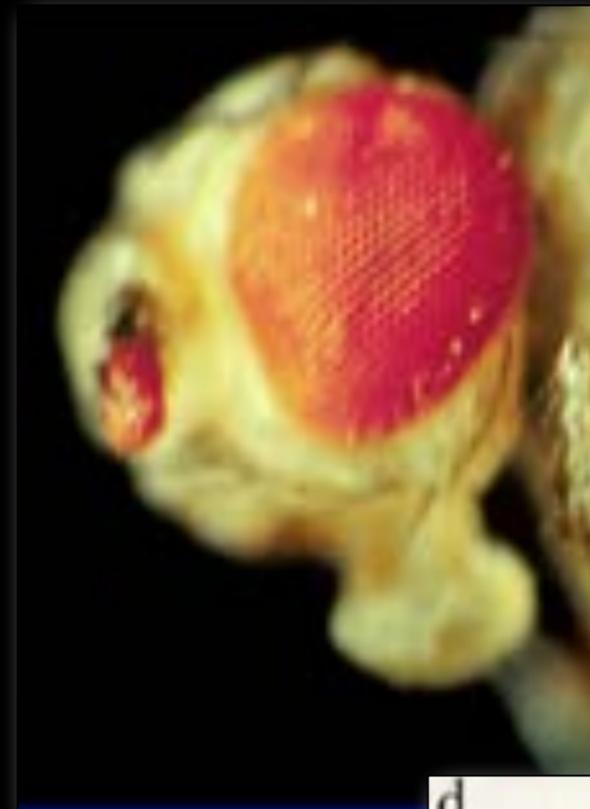
Philosophy of Science, 75 (December 2008) pp. 887–898. 0081-8248/2008/7505-0088\$10.00  
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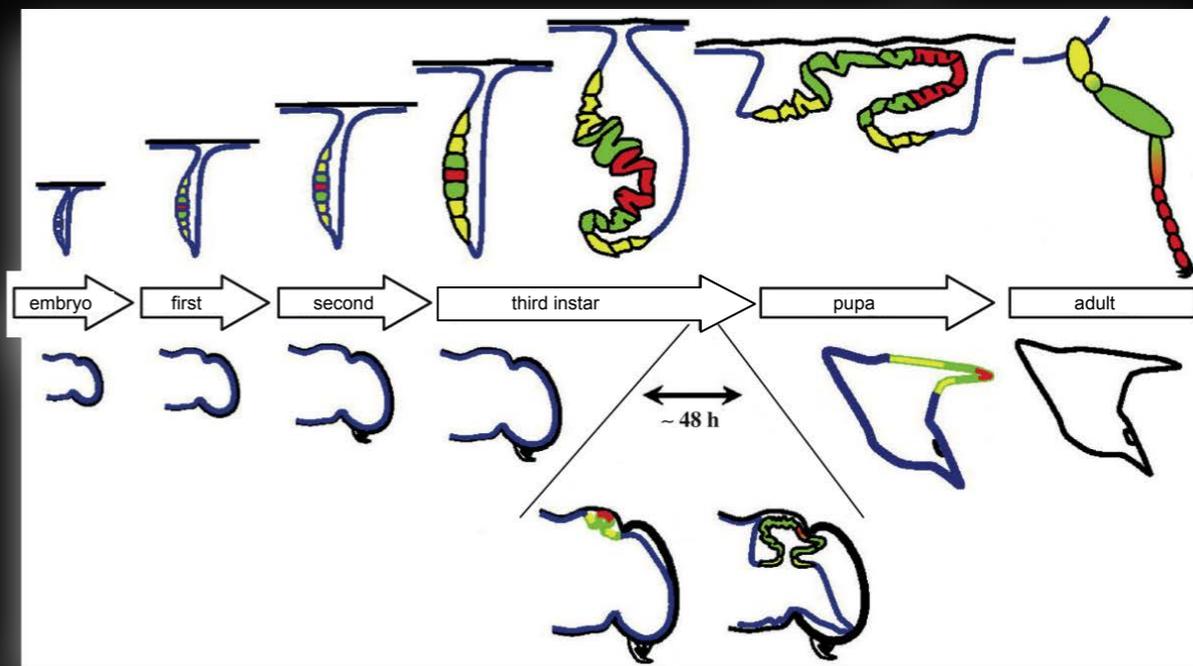


*eyeless*: master gene for compound eye in drosophila

*Pax6*: master gene for vertebrate eye in mouse

The genes can be switched  
and here mouse *Pax6* is  
inducing ectopic compound  
eyes in *Drosophila*



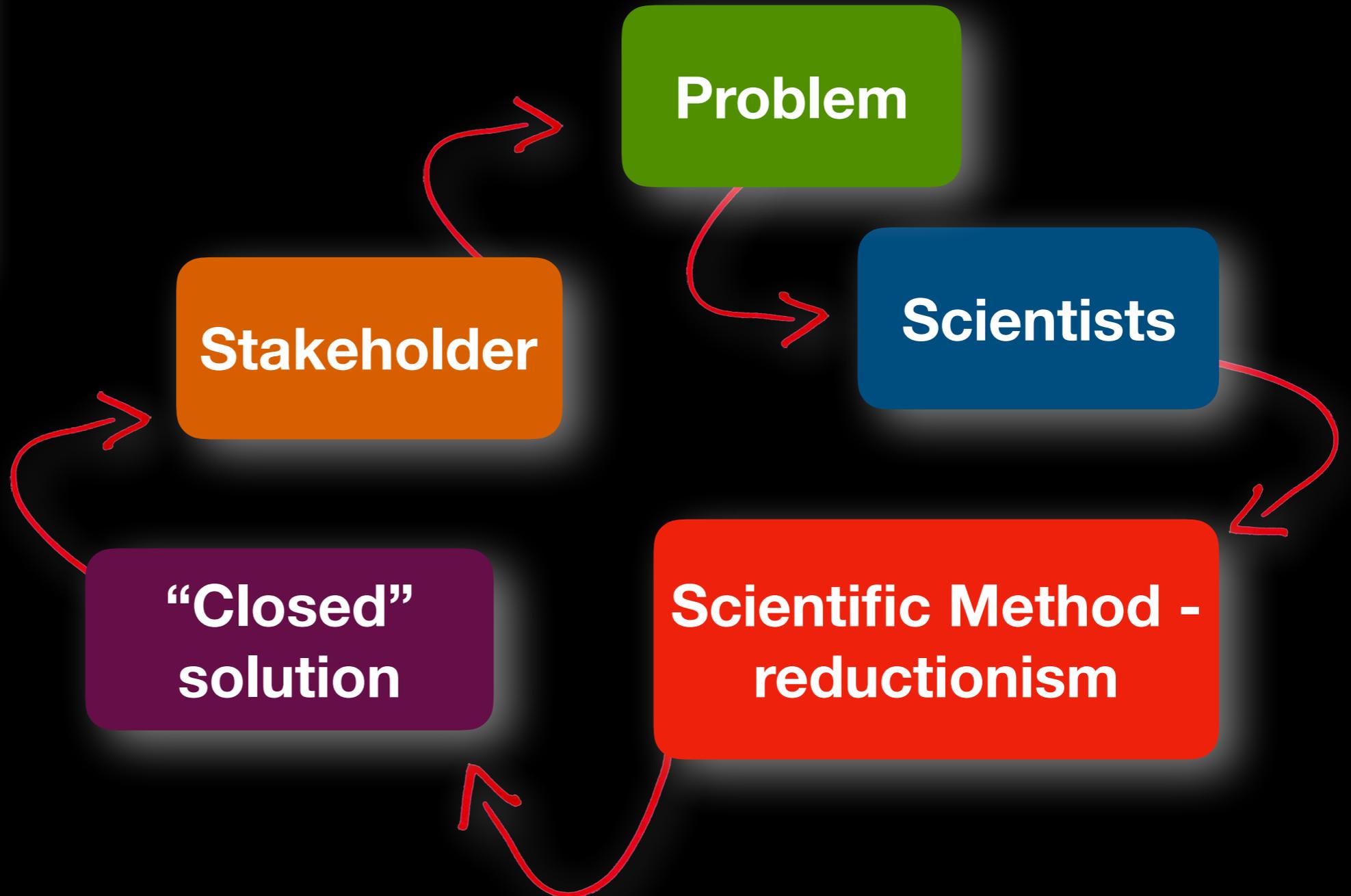
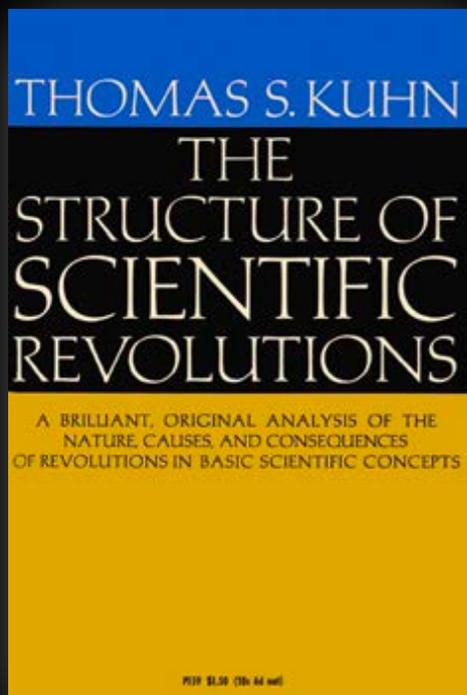


# Complexity and science

# Normal science



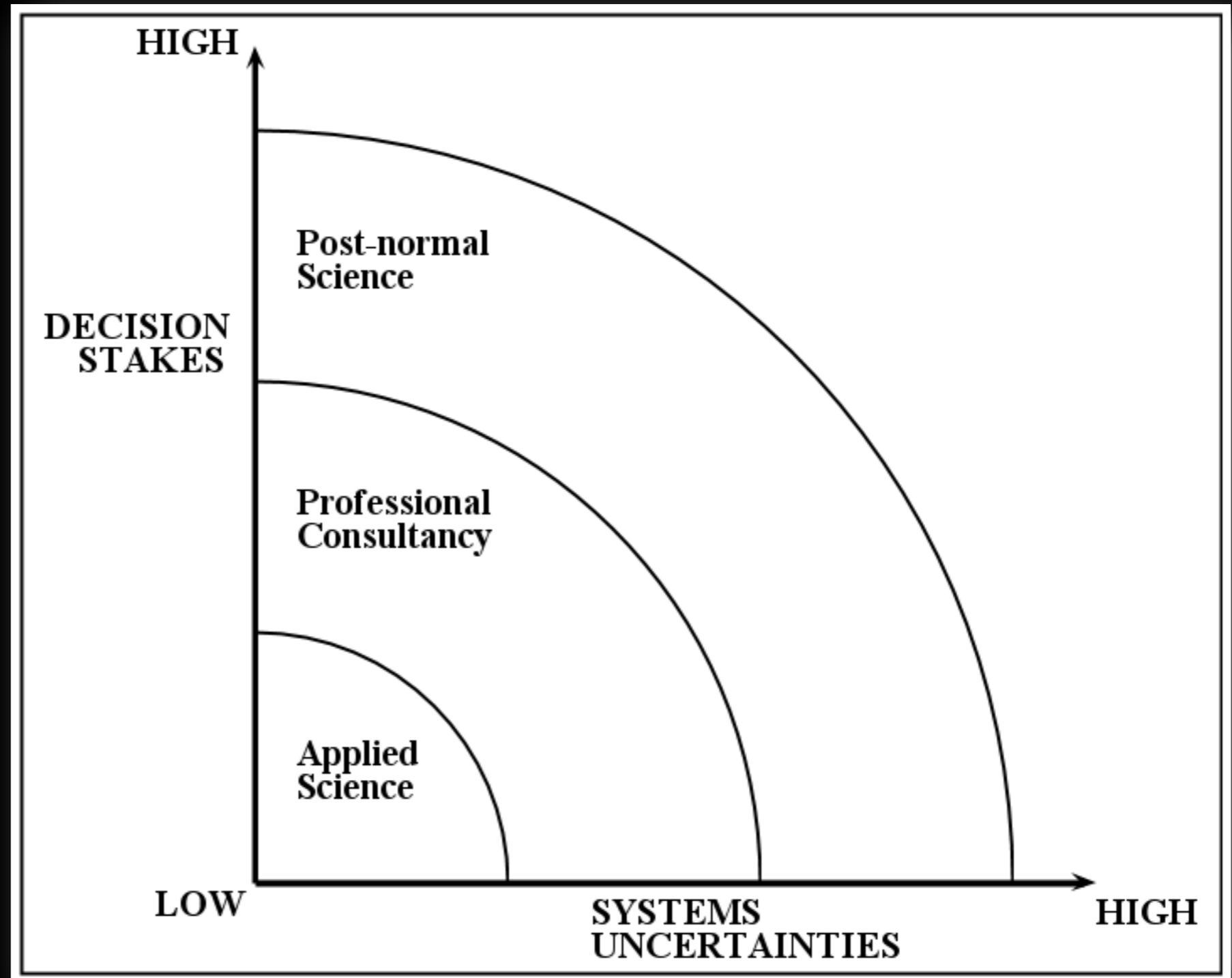
Thomas S. Kuhn



# Post-normal science



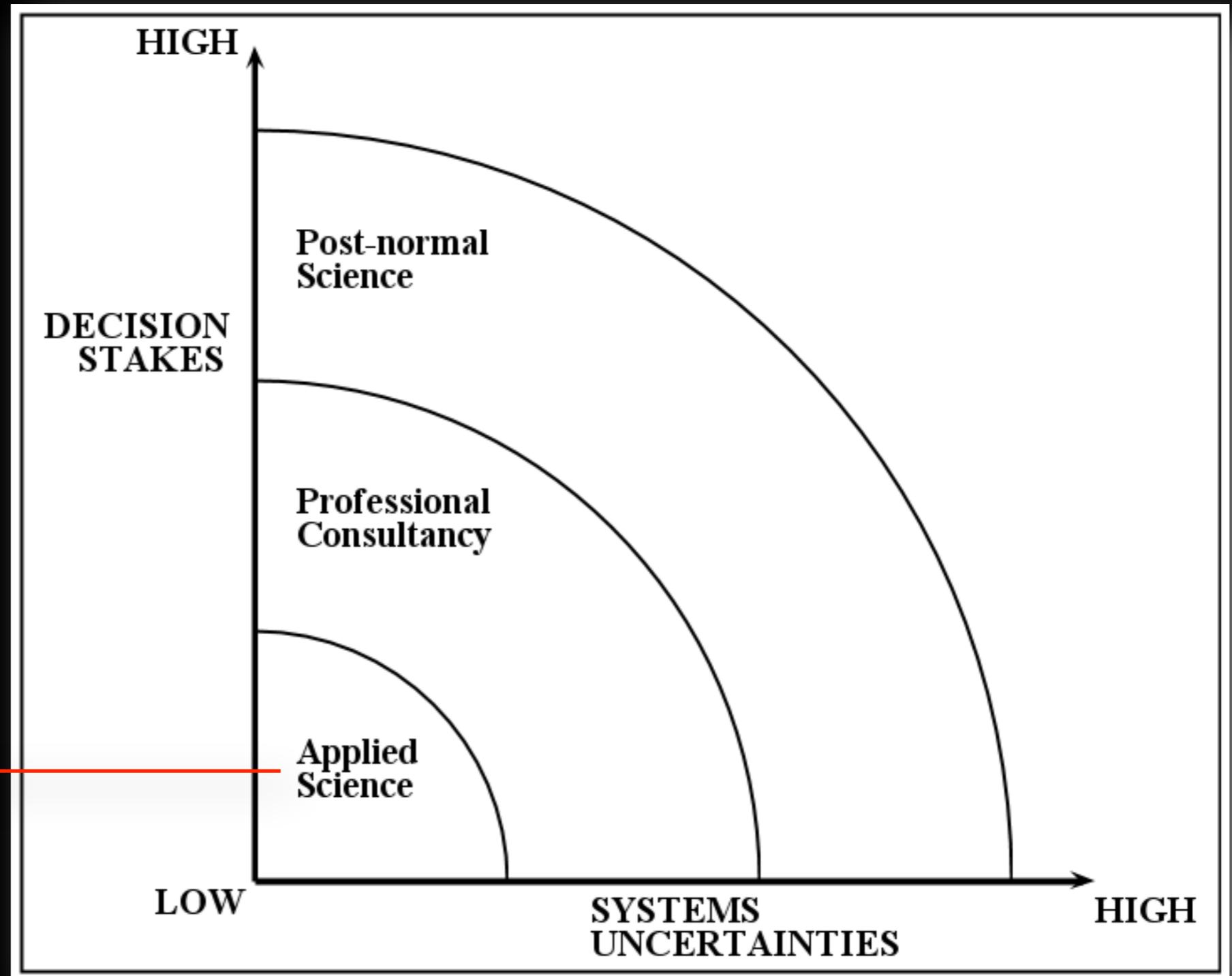
Silvio Funtowicz  
Jerome Ravez



# Post-normal science



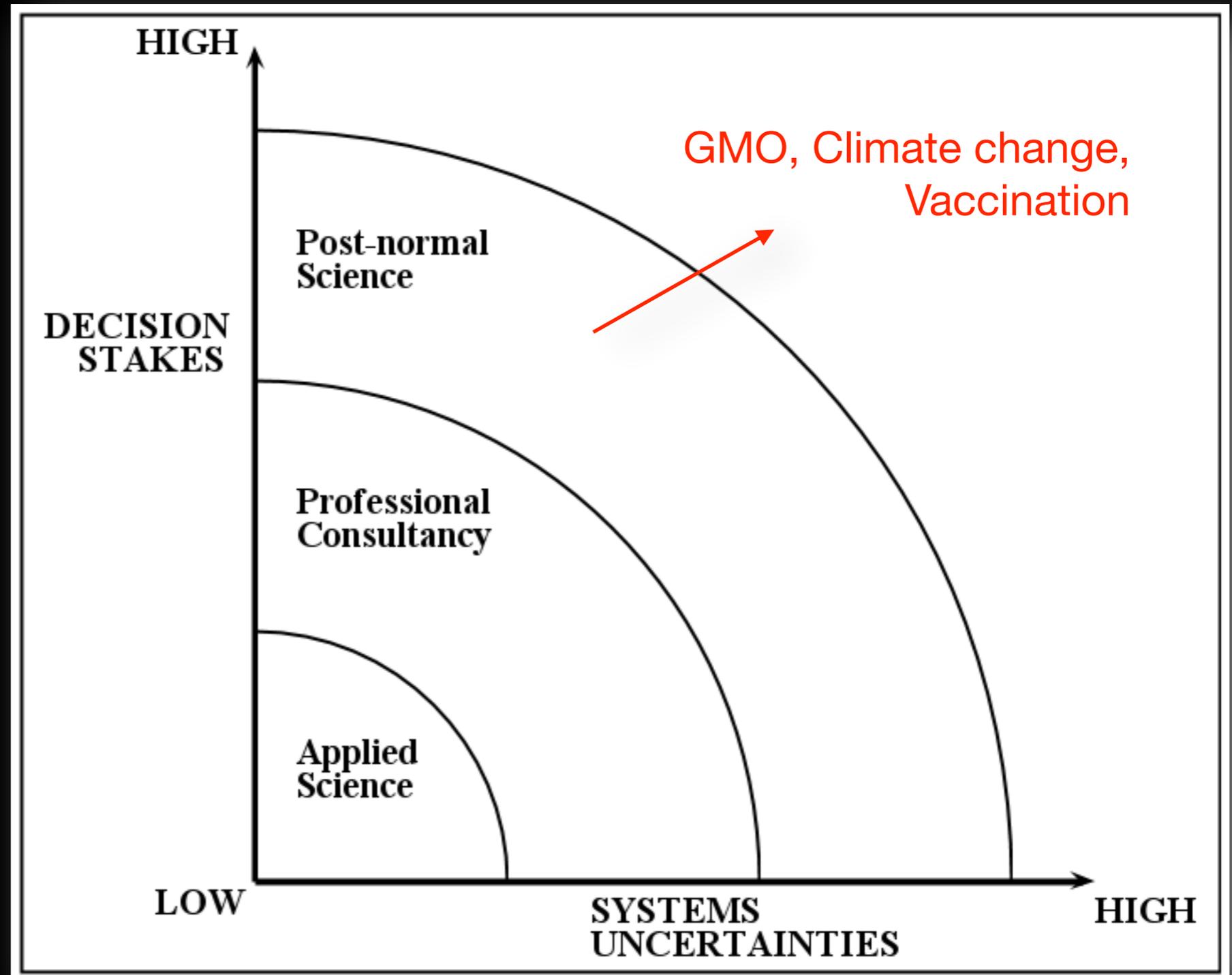
Silvio Funtowicz,  
Jerome Ravez

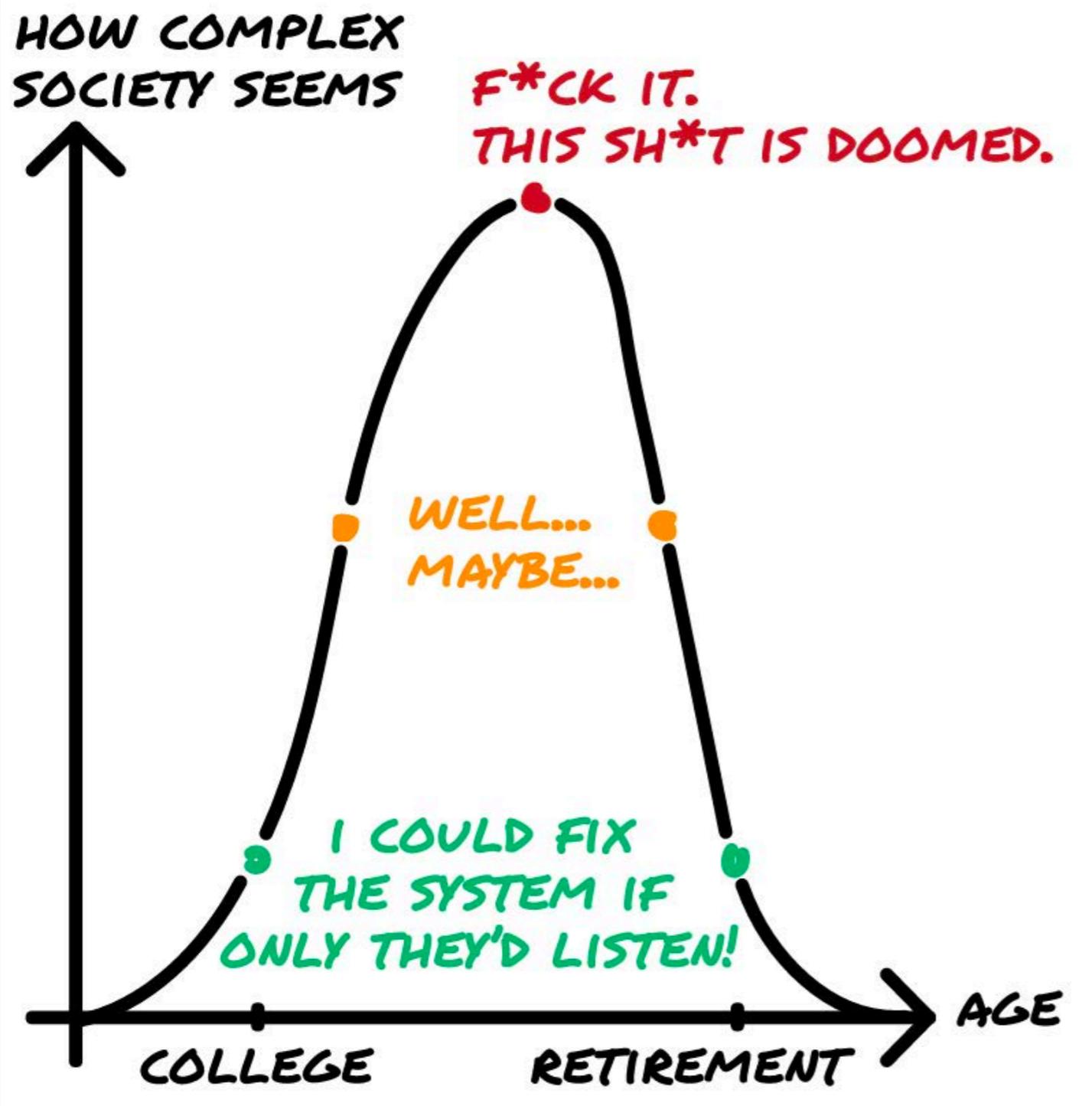


# Post-normal science



Silvio Funtowicz,  
Jerome Ravez





Thanks