Mitochondrial ribosomes of the Last Eukaryotic Common Ancestor (LECA)

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For the discussion of science...

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Why have we gathered here? Sketch of the discussion

- Introduction

  Key concepts of:

  - Eukaryotic supergroup
  - Mitochondrial ribosome
  - Alphaproteobacteria
- Mitochondrial ribosome of the Last Eukaryotic Common Ancestor (LECA)
- Evolution of LECA in one of the supergroups
- [backup] Implications of LECA and the domains of life

We will be mostly following [1]

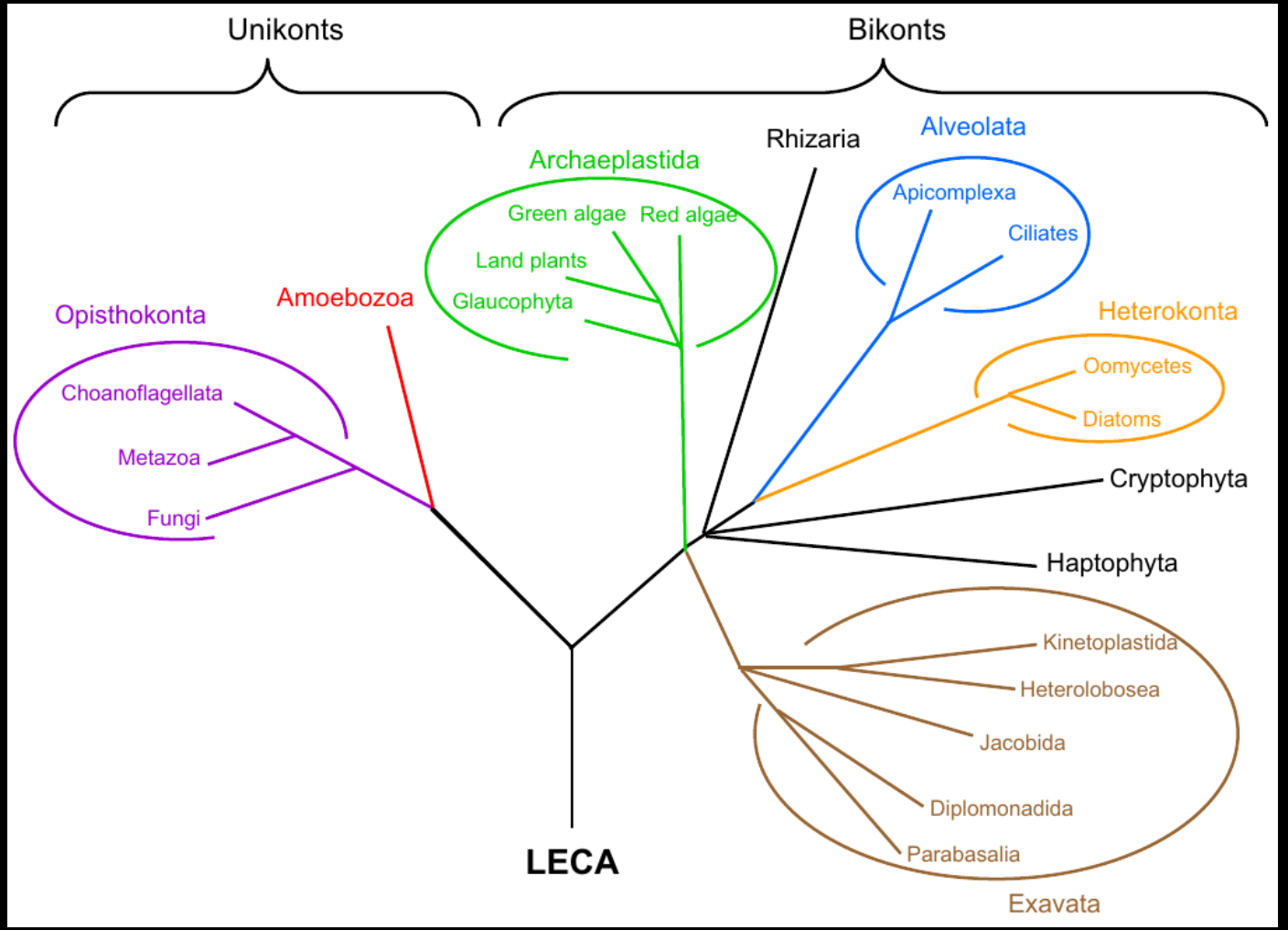
"What could be more interesting than the problem of Genesis?" – From, *The First Three Minutes* by Steven Weinberg

In this case, we eventually want to deal with the problem of

Eukaryogenesis

Eukaryotic supergroups

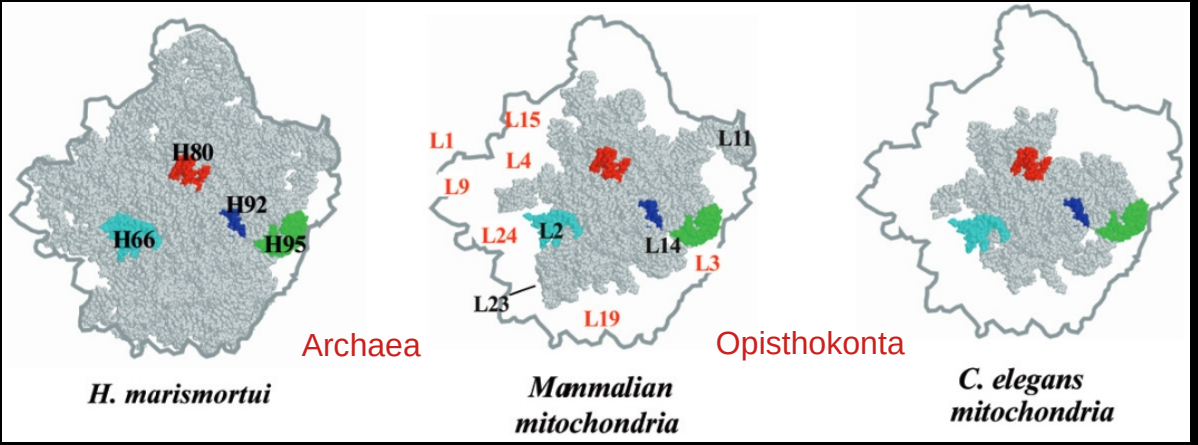
- Endosymbiotic events led to eukaryotes
- Genetic **reconstruction** is difficult
- Concept of supergroup and treat LECA as a “polytomy”
- 5/6 supergroups
- Each supergroup is monophyletic



From [1]

About Mitoribosomes

- Ribosomes inside a mitochondria
- Ribosomes – rRNA + Proteins
- Mitochondrial Ribosomal Protein (MRP)
- **Losses and translocation** of mitochondrial genes throughout its evolution
- Bacterial-specific MRP (Bt-MRP)
- Eukaryotic-specific MRP (Ek-MRP)
- Dynamic evolution compared to cytosolic ribosomes



coloured functional rRNA domains

based on crystal structure of bacterial 50S subunit – rRNA replaced by proteins

From [3]

- Bacteria – 57 MRP (cytosolic ribosome)
- 54 Bt-MRPs in the ancestor of mitochondria (known)
- Mammals and yeast: ~70–80 MRPs with ~20 Ek-MRP
- Kinetoplastids *Trypanosoma brucei* – 133 MRPs! (no homologues for 95 of these in other Eukaryotic lineages)

Now, we will mostly follow analysis done in [1] ...

- Analyzed 336 MRPs from a wide taxonomic sampling
- 38 complete nuclear and mitochondrial genomes (representatives from all 6 supergroups)
- Reconstruct mitoribosome of LECA
- Phylogenomic and proteomic techniques
- Look for homologues of various MRPs in each taxa
- Amitochondrites – have lost all MRPs in the host genome

Key objectives at the end is to:

- Gain insights into the origin and early evolution of Eukaryotes [via LECA]

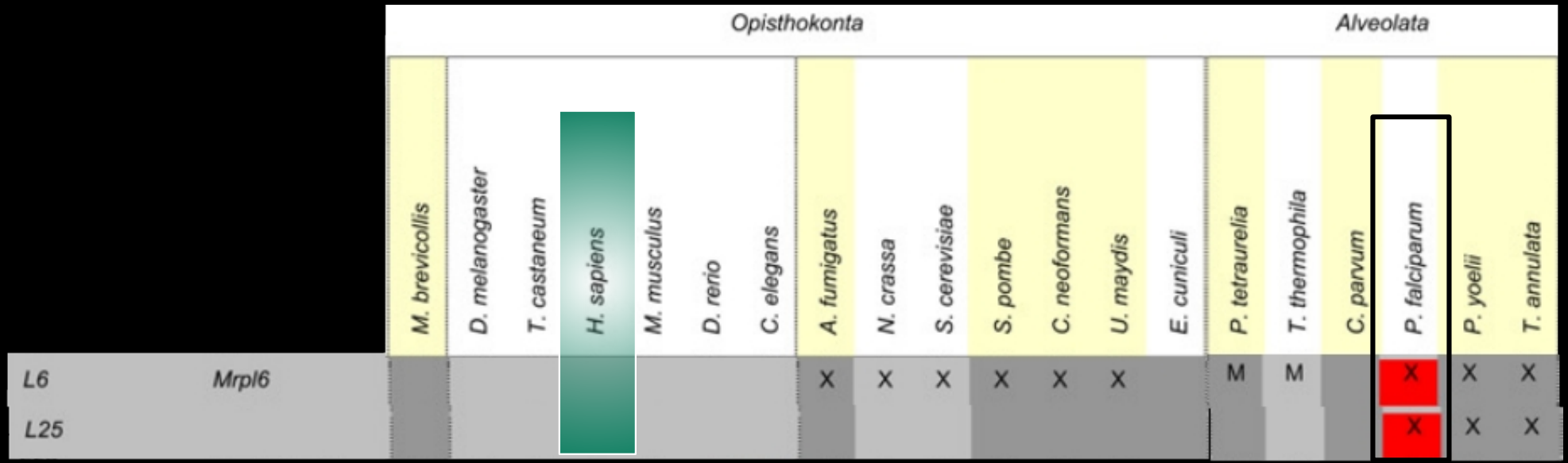
LECA mitoribosome reconstruction (1)

- Recruitment of Ek-MRPs, some are not homologous to cytosolic ribosomal proteins
- Naming convention: Lxx and Sxx refer to the large subunit and the small subunit in mammilian MRPs; of course analysis takes into account their homologues in other lineages

- 54 Bt-MRPs in the ancestor of mitochondria (deduced from the ribosome of alphaproteobacteria)

See the spreadsheet for a quick overview

Possible practical application from the analysis (specific targets for antimalarial treatment)



Better models and wider taxonomic sampling, there are no homologues of L6 and L25 in humans, but they are present in P. falciparum (which causes the most fatal case of malaria)

LECA mitoribosome reconstruction (2)

- Analyze fate of MRPs from the time of endosymbiosis event up to LECA
- Identified 22 MRPs previously unreported
- Ambiguity of protein “Ppe1” (MRP) in amitochondrites
- Absence of S20 in all eukaryotic genome – lost early in eukaryotic evolution

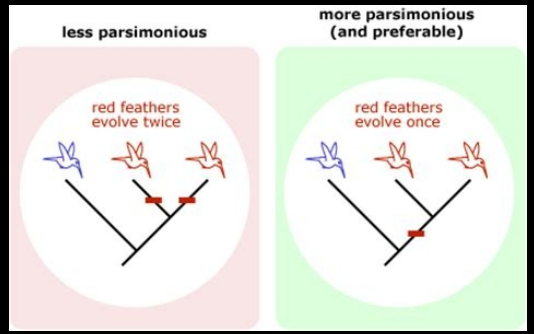
- 27 Bt-MRPs in Jacobid *Reclinomonas americana* (9 of which not found in any other mitochondrial genome)
- Minimum of 27 Bt-MRP in mitochondrial genome of LECA!
- 26 Bt-MRPs (= 54 – 1 – 27) not encoded in the mitochondrial genome, may have been transferred to the host nuclear genome prior to the divergence of major eukaryotic supergroups

- Mitoribosome of LECA had 18 MRPs more than alphaproteobacteria-like ancestor
- Novel Eukaryotic proteins were already accumulated
- Endosymbiosis happened before the evolution of LECA to major Eukaryotic supergroups

LECA reconstruction (1) + (2)

Considerable time elapsed between the endosymbiosis and the diversification of present-day eukaryotic lineages

Translocation of Bt-MRPs to the host nucleus occurred rapidly after endosymbiosis; independently in each supergroup



*independent and convergent translocation of Bt-MRP coding genes could also happen in each eukaryotic lineage
[perhaps less parsimonious and minimal genome considerations?]

To solve the decision tree – look at the “trends” in bacterial endosymbionts

Order and timing of transfer from the ancestral mitochondrial genome to the host nucleus by looking at bacterial endosymbionts involved in genomic reduction processes

Eukaryote	Endosymbiont	Genomic size (reduced) [Mb]	Protein-encoding genes	Comparison with 54 Bt-MRPs (missing ones)
Psyllids	**gammaproteobacteria *Candidatus Carsonella ruddii***	**0.16**	182	**14**
Cedar aphid, Cinara cedri	***Buchnera aphidicola str. Cc***	**0.42**	357	**0**
Cicada Diceroprocta semicincta	**alphaproteobacteria *Candidatus Hodgkinia cicadicola Dsem***	**0.14**	169	**14**
Blue-Green sharpshooter	**Flavobacterium *Candidatus Sulcia muelleri DMIN***	**0.24**	226	**6**

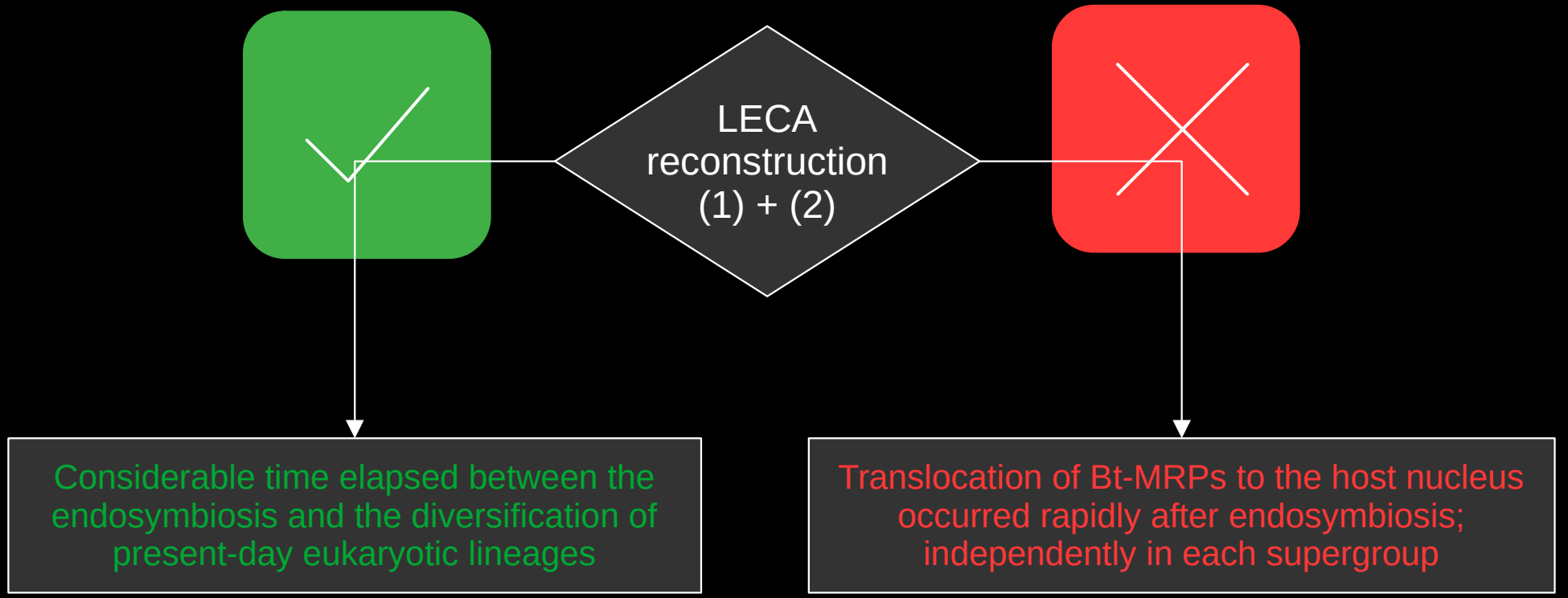
- In *B. aphidicola* no losses of ribosomal proteins – ribosomal proteins are among the last to be lost during genome reduction after endosymbiosis!
- 6 simultaneously missing in the three most reduced endosymbiont genome

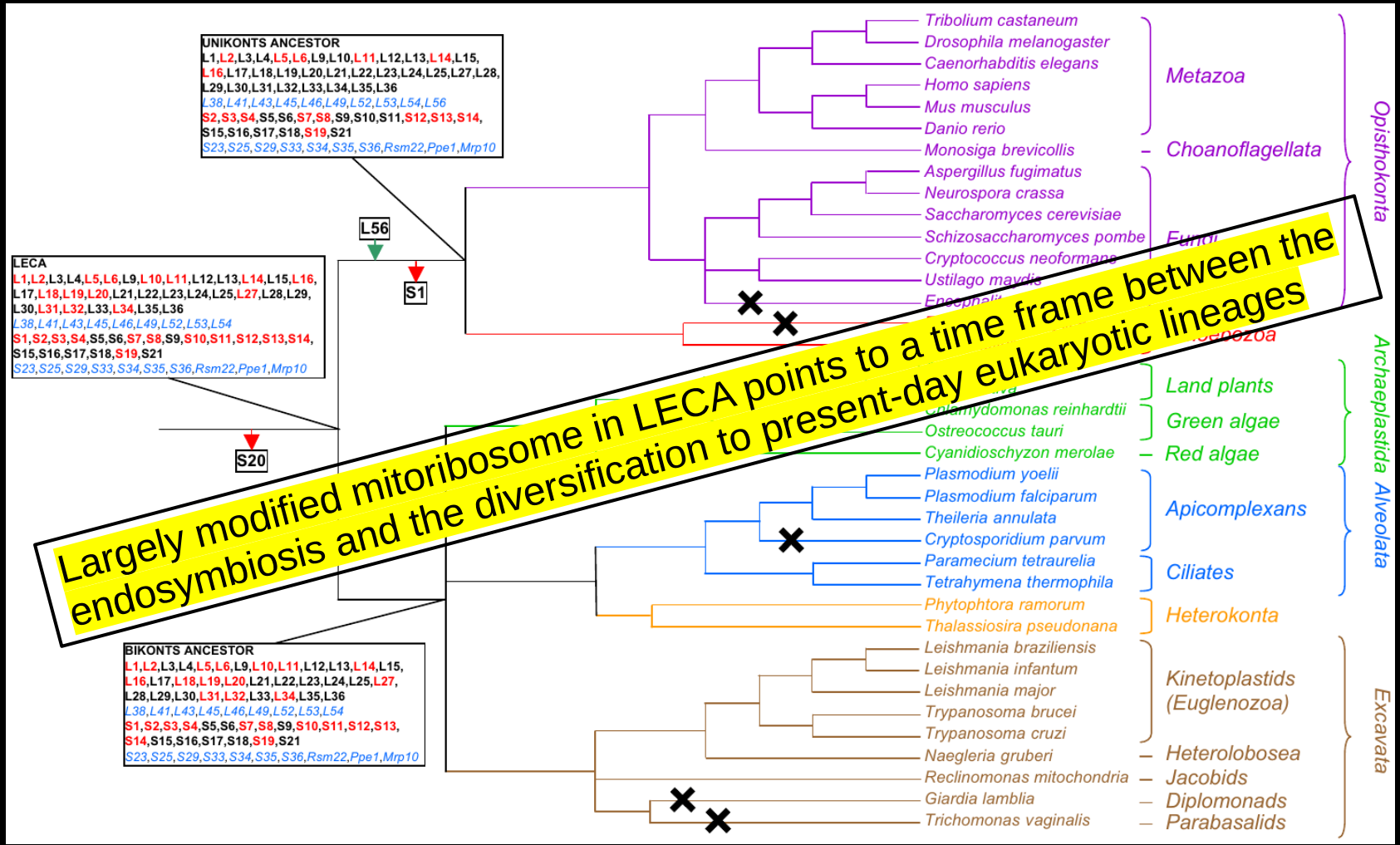
- 5 of the lost genes in three of the endosymbionts also missing in the inferred mitochondrial genome of LECA

- 3 additional protein losses in two of the smallest (reduced) genomes [C. ruddii and H. cicadicola]

	Candidatus carsonella ruddii	*Buchnera aphidicola* Cc	*Candidatus* Hodgkinia cicadicola Dsem	*Candidatus* Sulcia muelleri DMIN	*LECA*
LSU					
L9		YP_802912			
L23		YP_802886			
L24		YP_802877			
L29		YP_802880			
L30		YP_802870			
L34		YP_802584			M
L25		YP_802658		YP_003543201	
SSU					
S20		YP_802664		YP_003543343	
S21		YP_802610		YP_003543321	

Furthermore, 19 Ek-MRP (9 LSU + 10 SSU) in at least one representative of a Uniknot and a Bikont, and thus must have appeared before LECA


LECA
reconstruction
(1) + (2)
Considerable time elapsed between the endosymbiosis and the diversification of present-day eukaryotic lineages
Translocation of Bt-MRPs to the host nucleus occurred rapidly after endosymbiosis; independently in each supergroup



Reconstructed LECA!

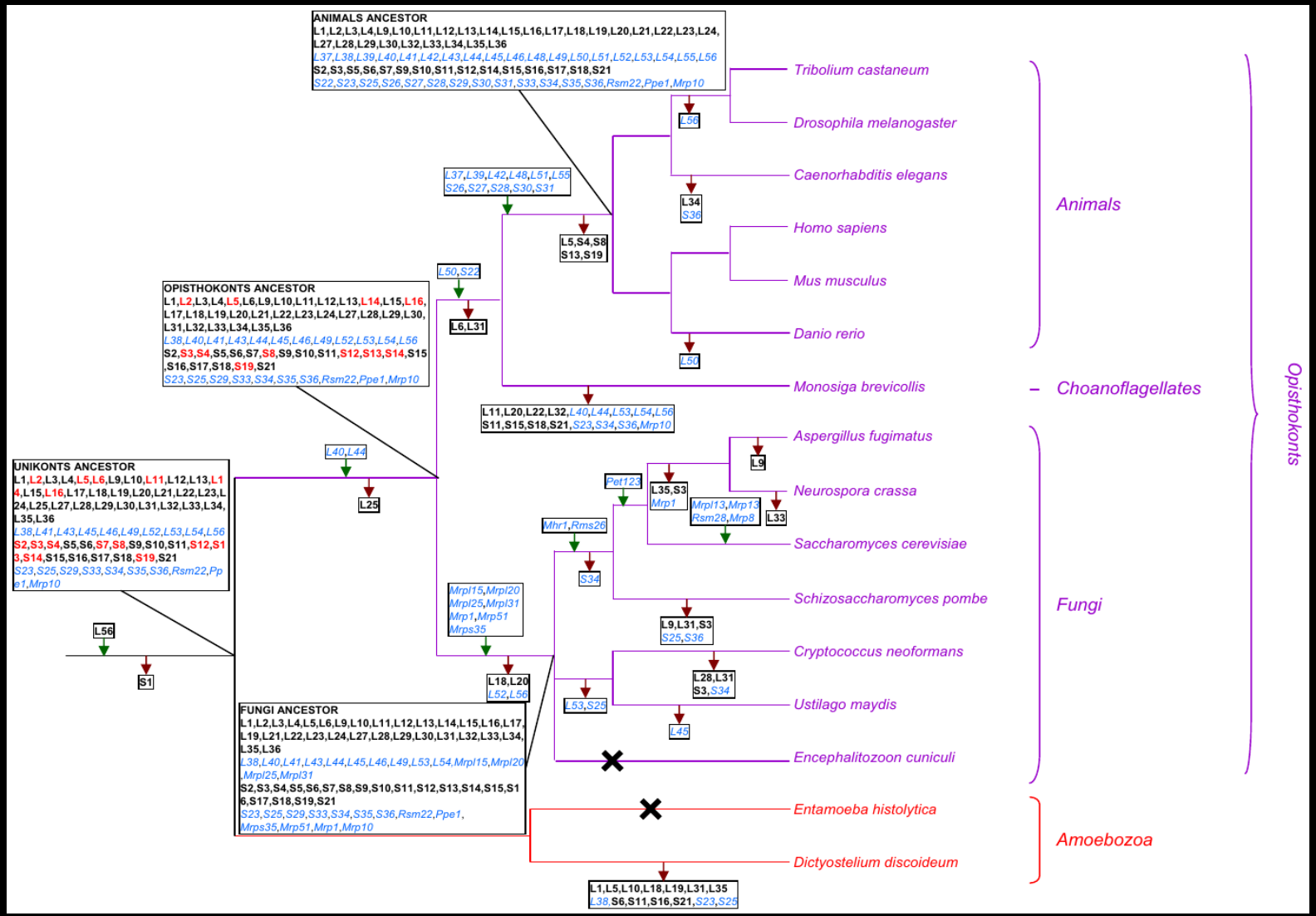
- 18 more proteins than the original alphaprotebacterial ribosome (i.e. +54 MRPs already)
- 26 Bt-MRPs may have already translocated to the nucleus

The inference shows that LECA mitoribosome must have at least 72 MRPs (42 LSU + 30 SSU); 72 = 54 – 1 + 19 i.e. 53 Bt-MRPs and 19 Ek-MRPs

Expanded to 33 SSU and 46 LSU (possibly 49), so 79 MRPs see [5]

Evolution in one of the supergroups (Opisthokonts)

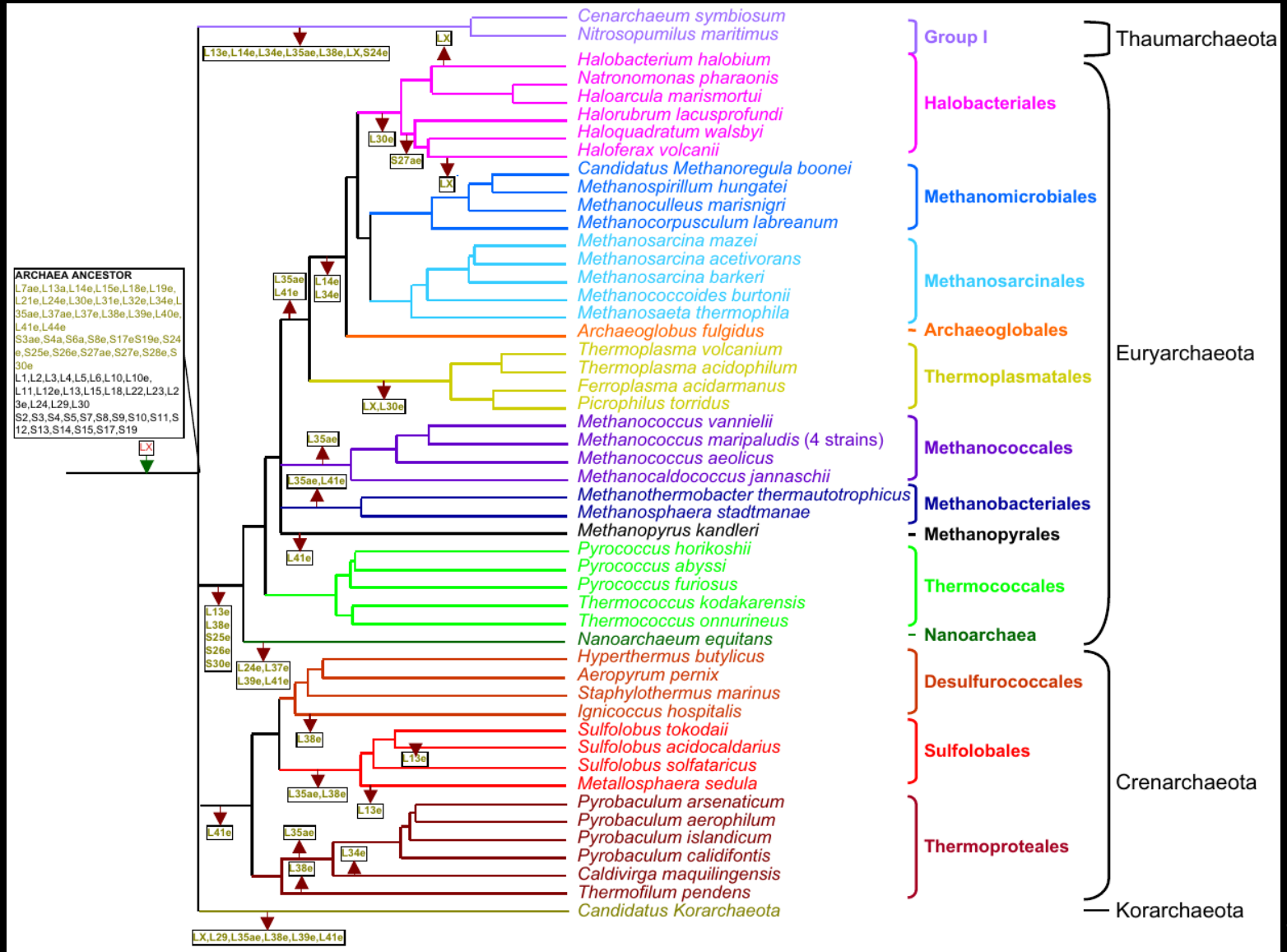
- Mitoribosomes of Unikonts and Bikonts are remarkably similar
- Only one gain (L56) and one loss (S1)
- Very rapid split or stationary phase in the evolution of mitoribosome
- Loss and gain constitute synapomorphies



Comparing with archaeal ribosomes

Dynamic and chaotic evolutionary history of archaeal ribosomal proteins

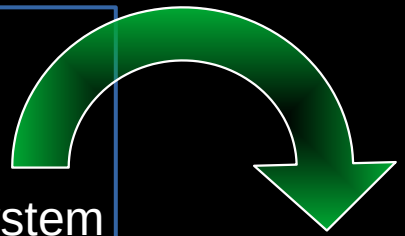
How many domains of life [2 or 3]?



Combing results of various other studies and after LECA reconstruction, we find:

LECA had (and what we definitely know by now)

- Mitochondrion
- Meiotic machinery
- Fully differentiated endomembrane system
- Phagocytosis
- Actinomyosin and tublin-based cytoskeletal system
- Large complement of motor proteins



And subsequently, many lineages simplified various cellular aspects and the driving reason behind diverse eukaryotic lineages (and perhaps helped some move towards a multicellular lifestyle)

Thanks to the sophisticated cell of LECA!

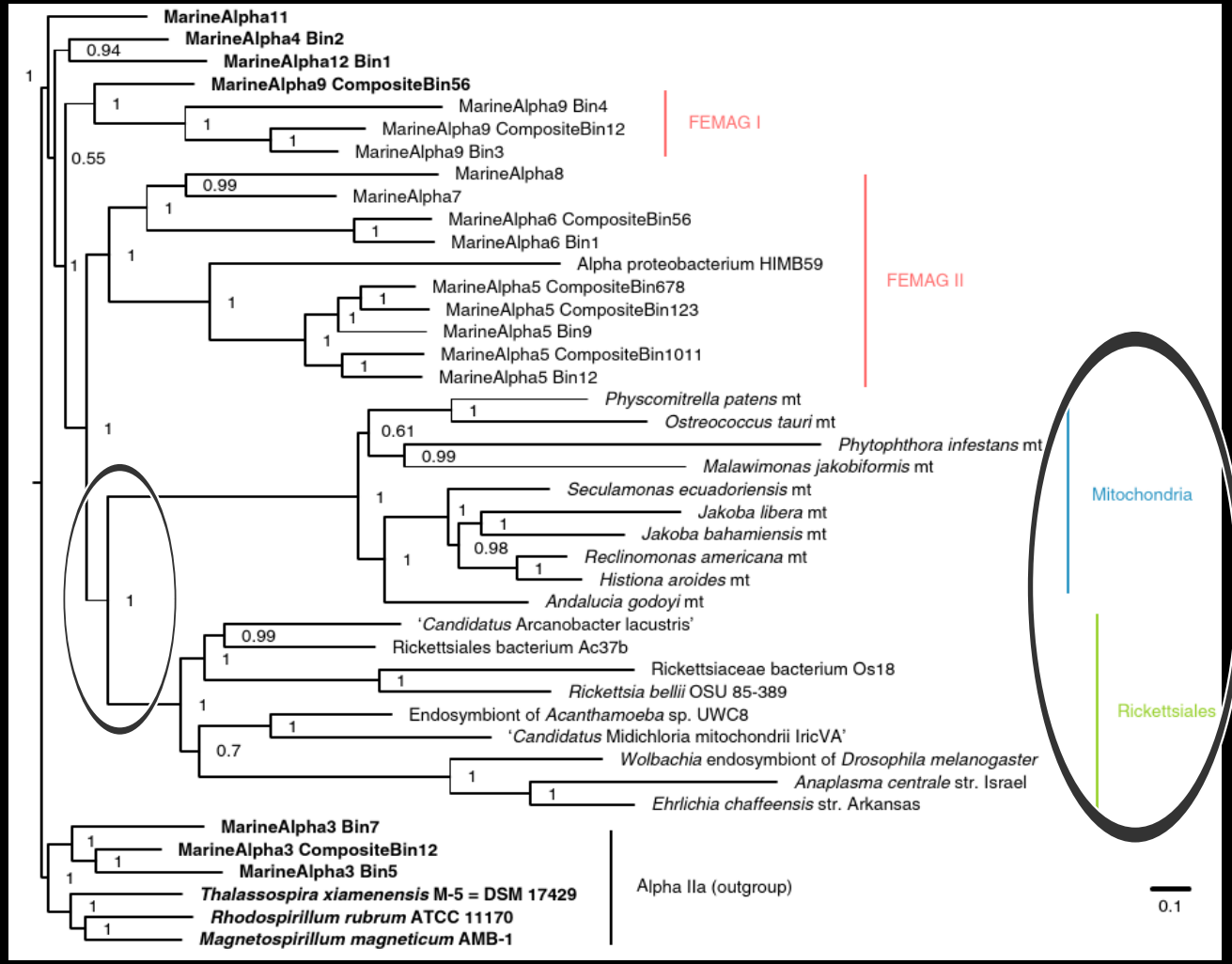
Moreover, there was a time frame between the endosymbiosis event and LECA

Backup/Additional (BA) slides

Alphaproteobacteria

- Diverse and ancient group of bacteria
- Most abundant and metabolically versatile group of bacteria on Earth
- Many live inside cells of other organisms, parasites

- Mitochondria originated from an alphaproteobacteria-like ancestor
- 57 proteins in its ribosome, must also be present in the alphaproteobacteria-like ancestor of mitochondria



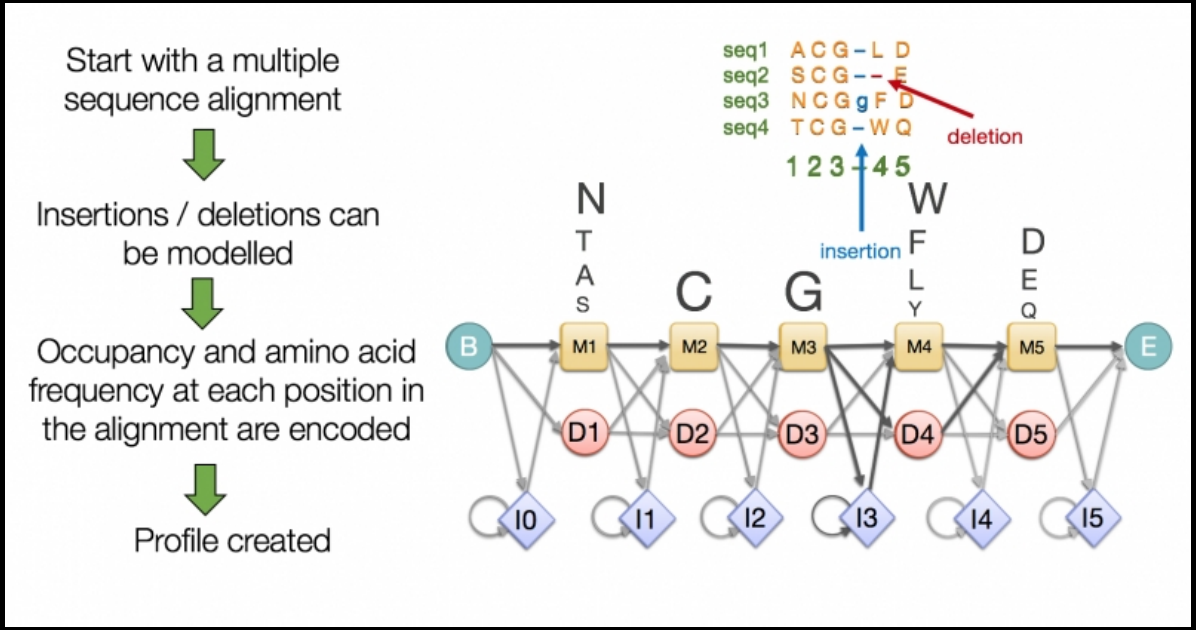
From [2]

Interesting class – amitochondriates

In 2016, a microbial eukaryote oxymonad *Monocercomonoides* sp. was found to have complete lack of mitochondria [secondary loss] & functions such as Fe-S cluster

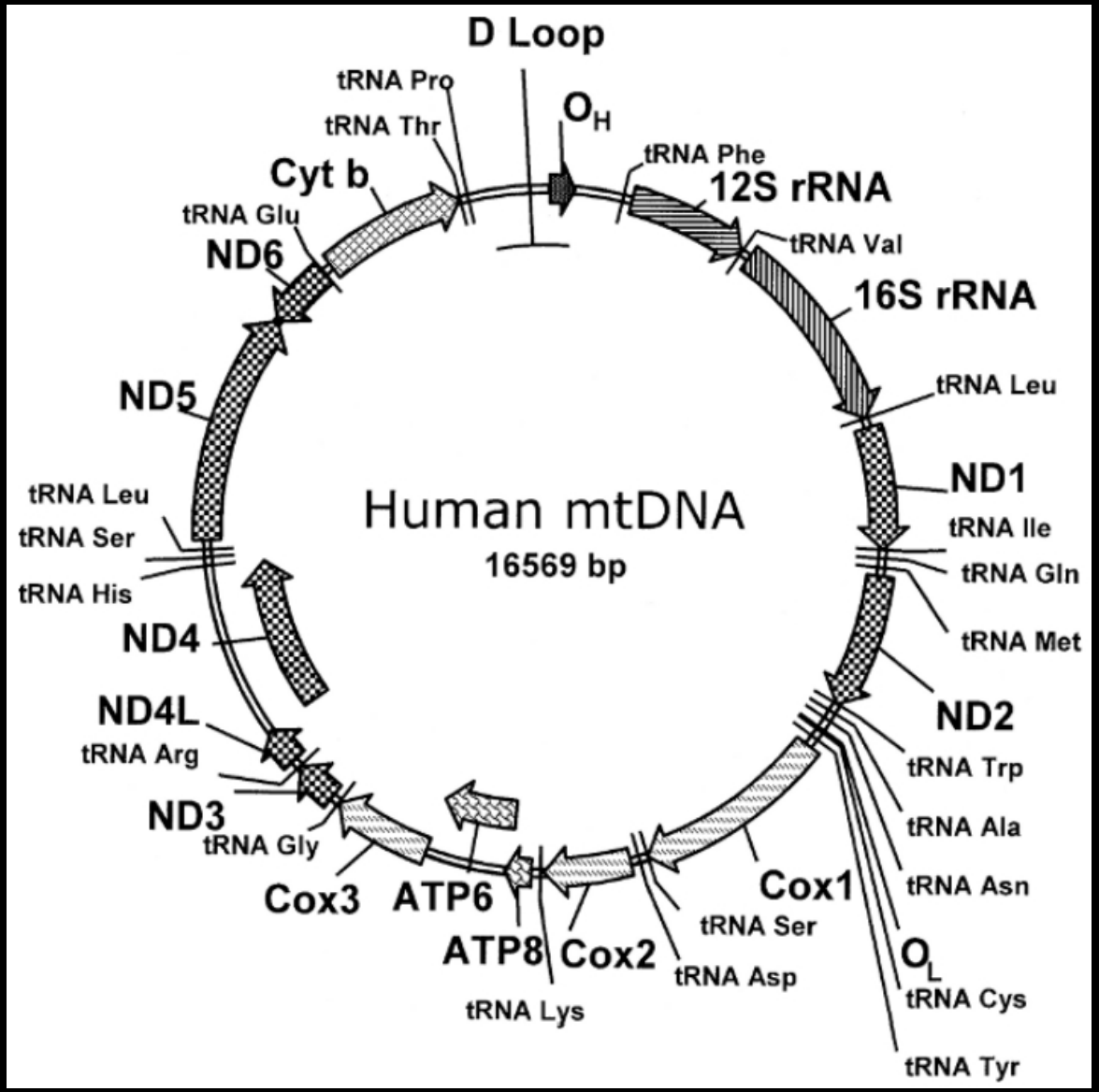
In 2020, first multicellular eukaryote was found which had no mitochondria organelle

About HMMER (for homologues)



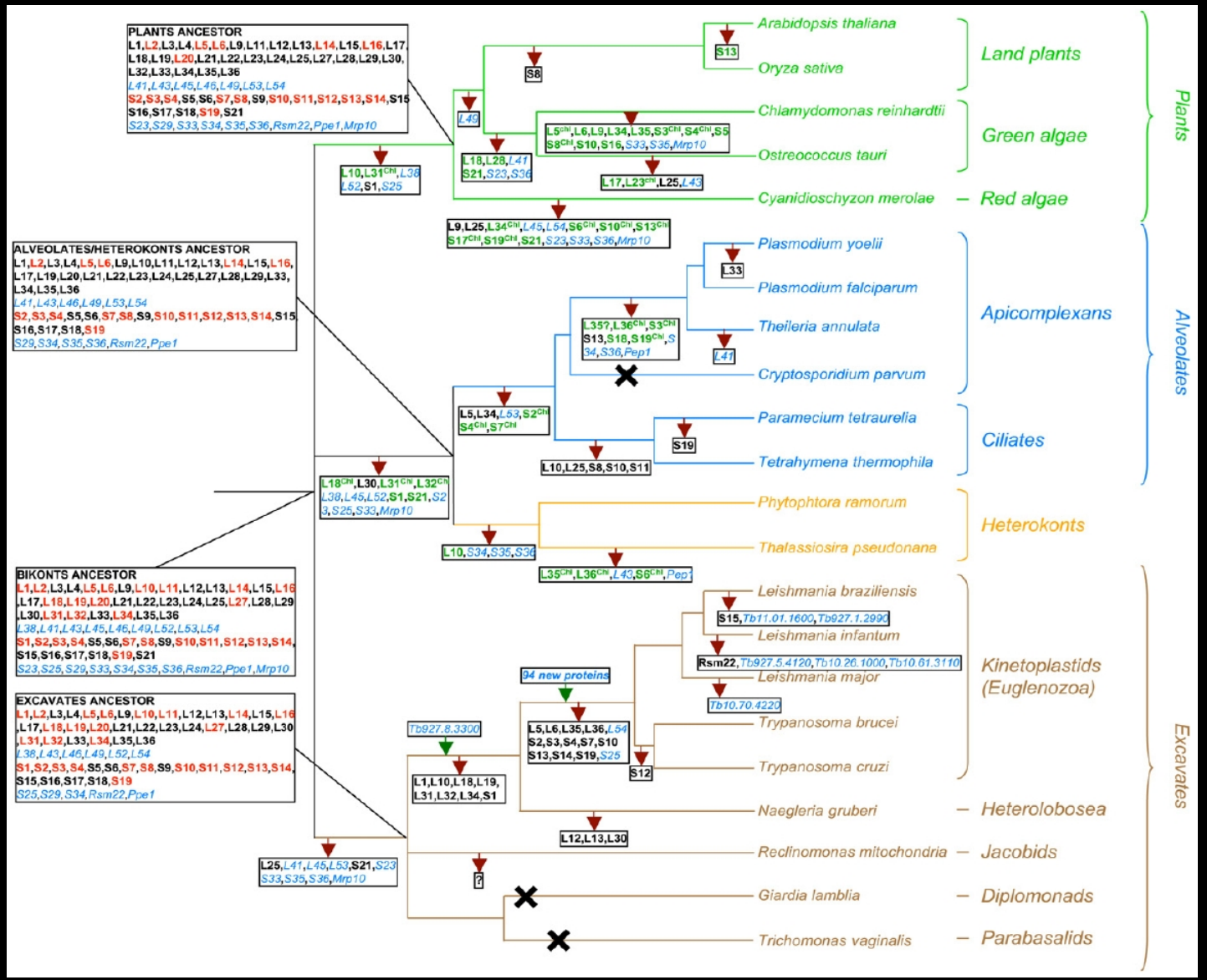
Human mitochondrial DNA

- Highly reduced genome
- Mostly tRNA and rRNA genes remaining
- Other genes **translocated** to the host nuclear genome
- Usually the case with most endosymbionts!



From [4]

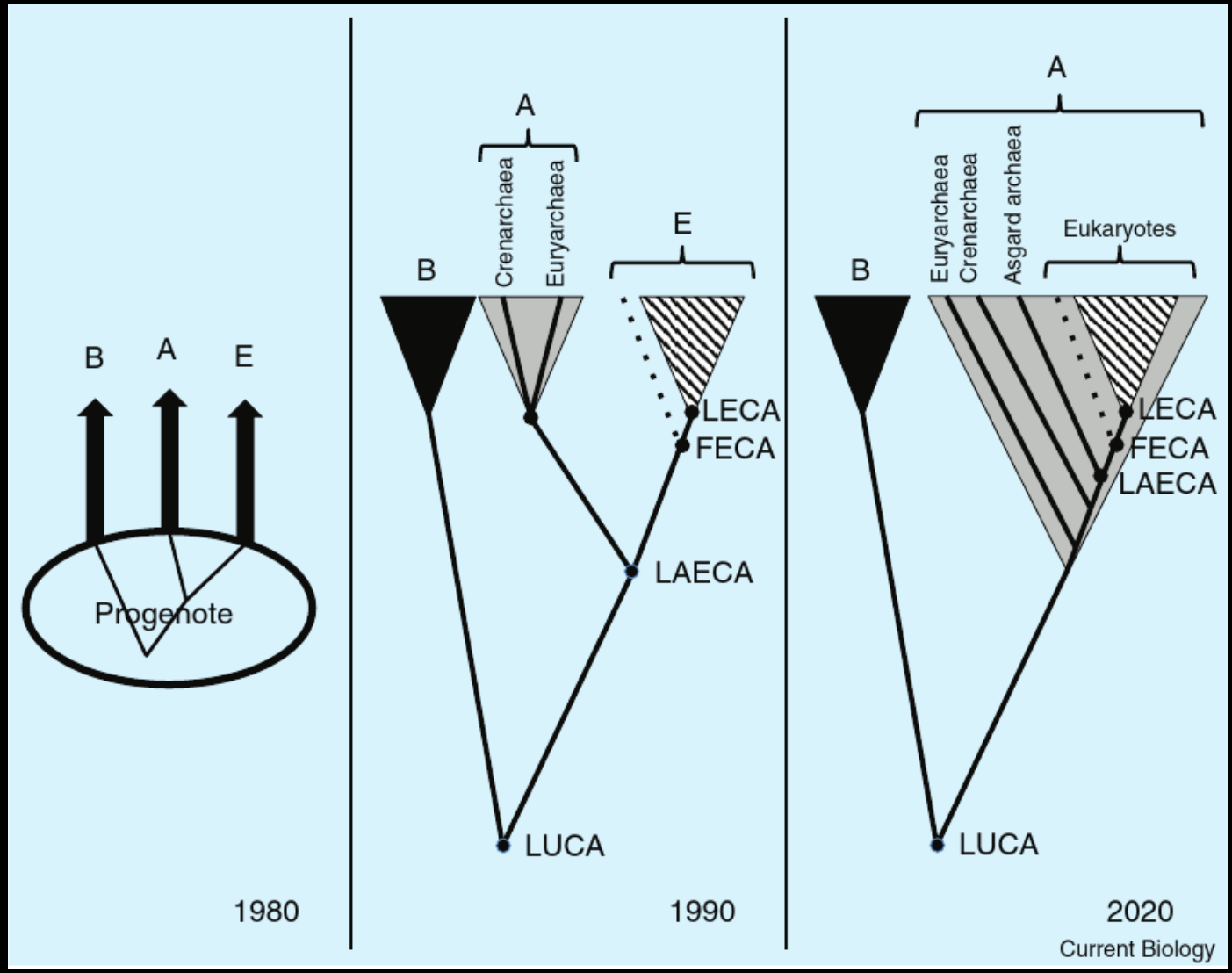
Evolution in Bikonts



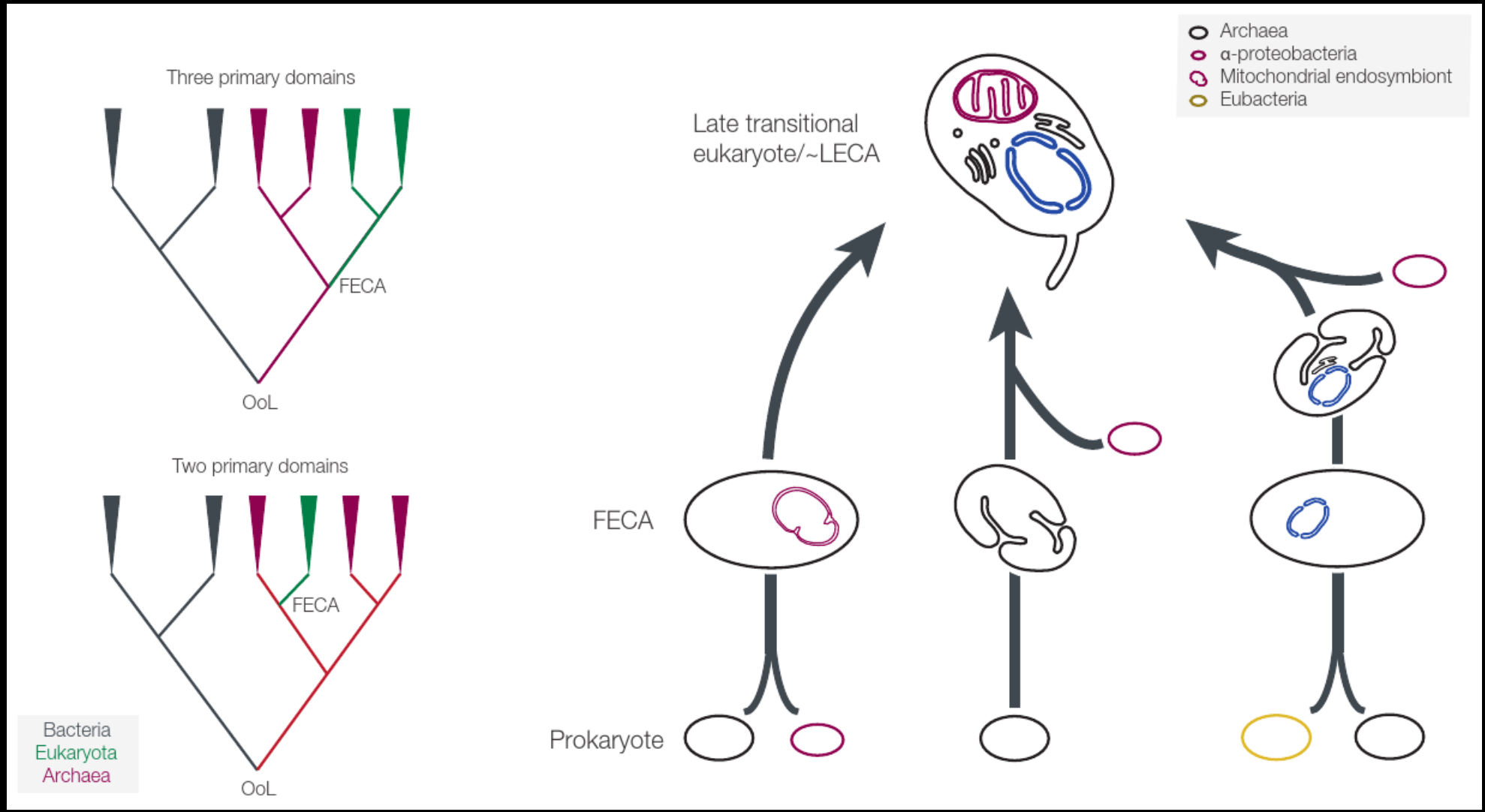
Domains of life

However, recent studies find that asgard archaeal-unique contributions to protein families of the LECA was only 0.3%

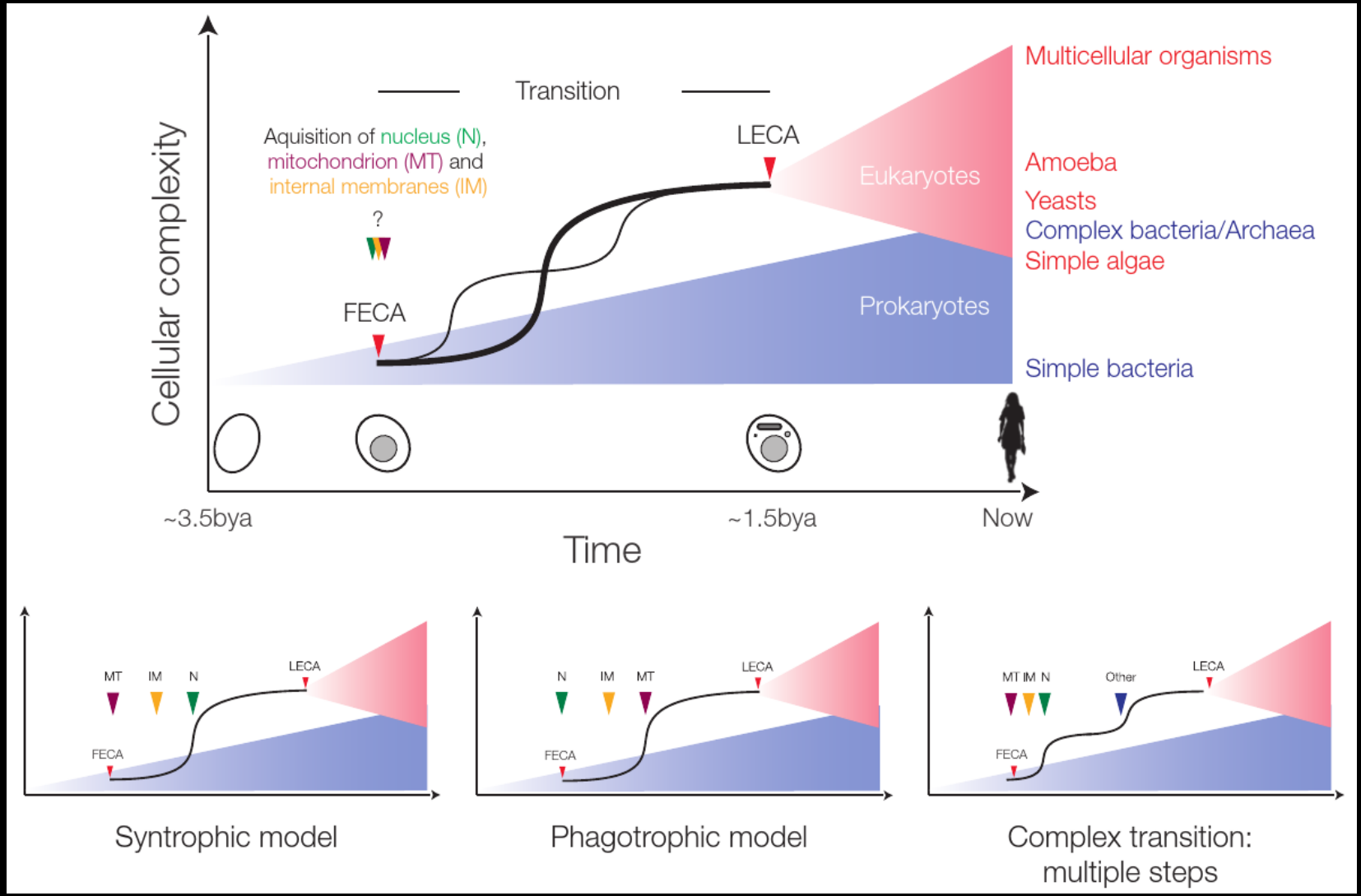
(see [6])



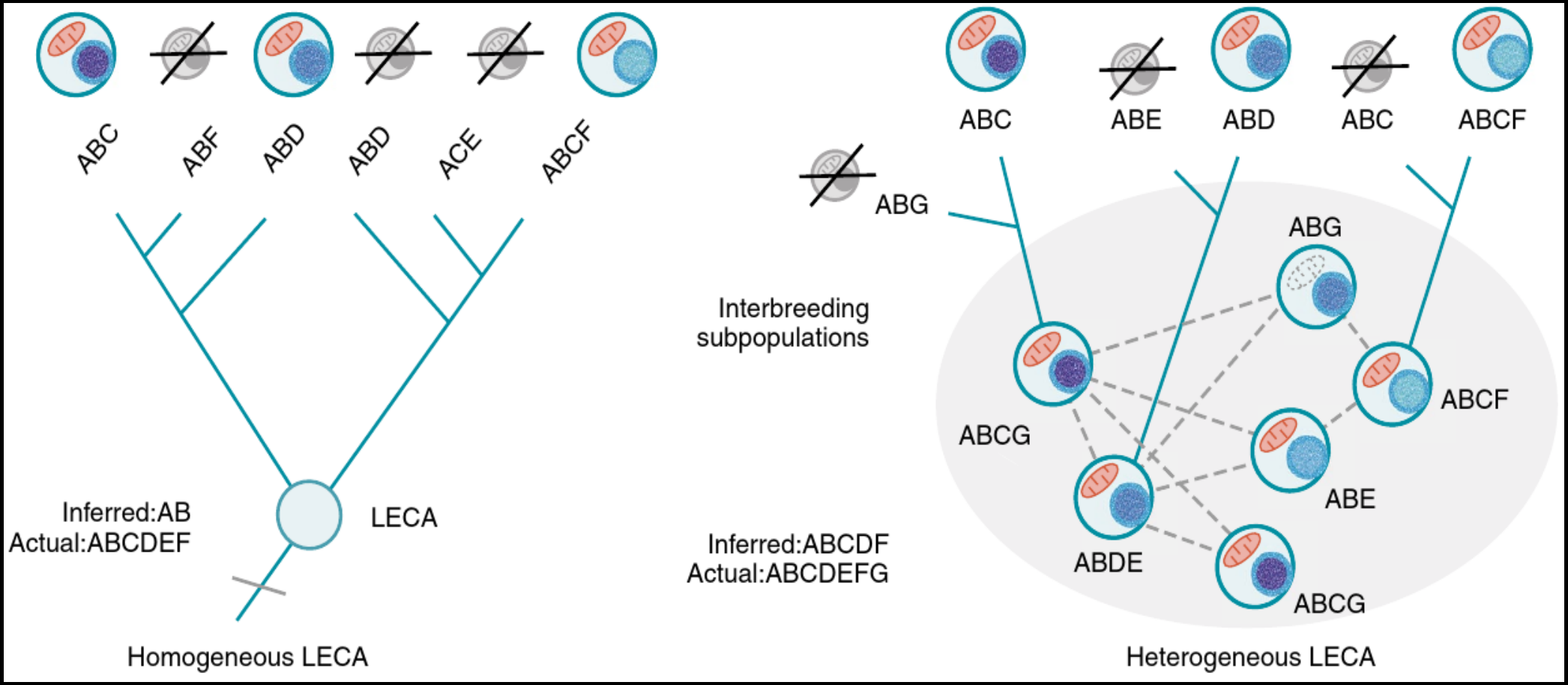
From [7]


Three primary domains
FECA
OoL
Two primary domains
FECA
OoL
Bacteria
Eukaryota
Archaea
Archaea
α-proteobacteria
Mitochondrial endosymbiont
Eubacteria
Late transitional
eukaryote/~LECA
FECA
Prokaryote

From [8]


Cellular complexity
Transition
Aquisition of nucleus (N), mitochondrion (MT) and internal membranes (IM)
?
LECA
FECA
Eukaryotes
Prokaryotes
Multicellular organisms
Amoeba
Yeasts
Complex bacteria/Archaea
Simple algae
Simple bacteria
~3.5bya
~1.5bya
Now
Time
MT IM N
LECA
FECA
Syntrophic model
N IM MT
LECA
FECA
Phagotrophic model
MT IM N
Other
LECA
FECA
Complex transition: multiple steps

From [8]


ABC
ABF
ABD
ABD
ACE
ABCF
Inferred:AB
Actual:ABCDEF
LECA
Homogeneous LECA
ABG
Interbreeding
subpopulations
Inferred:ABCDF
Actual:ABCDEFG
ABC
ABE
ABD
ABC
ABCF
ABG
ABCG
ABCF
ABE
ABDE
ABCG
Heterogeneous LECA

From [9]

References

[1] E. Desmond et al., "On the last common ancestor and early evolution of eukaryotes: reconstructing the history of mitochondrial ribosomes", Research in microbiology **162**, 53–70 (2011).

[2] L. Fan et al., "Phylogenetic analyses with systematic taxon sampling show that mitochondria branch within Alphaproteobacteria", Nature ecology & evolution **4**, 1213–1219 (2020).

[3] K. Watanabe, "Unique features of animal mitochondrial translation systems–The non-universal genetic code, unusual features of the translational apparatus and their relevance to human mitochondrial diseases", Proceedings of the Japan Academy, Series B **86**, 11–39 (2010).

[4] S. W. Schaffer and M. S. Suleiman, *Mitochondria: the dynamic organelle*, Vol. 2 (Springer, 2010).

[5] M. Valach et al., "An unexpectedly complex mitoribosome in Andalucia godoyi, a protist with the most bacteria-like mitochondrial genome", Molecular biology and evolution **38**, 788–804 (2021).

[6] M. Knopp et al., "The asgard archaeal-unique contribution to protein families of the eukaryotic common ancestor was 0.3%", Genome Biology and Evolution **13**, evab085 (2021).

[7] W. F. Doolittle, "Evolution: two domains of life or three?", Current Biology **30**, R177–R179 (2020).

[8] V. L. Koumandou et al., "Molecular paleontology and complexity in the last eukaryotic common ancestor", Critical reviews in biochemistry and molecular biology **48**, 373–396 (2013).

[9] M. A. OMalley et al., "Concepts of the last eukaryotic common ancestor", Nature ecology & evolution **3**, 338–344 (2019).