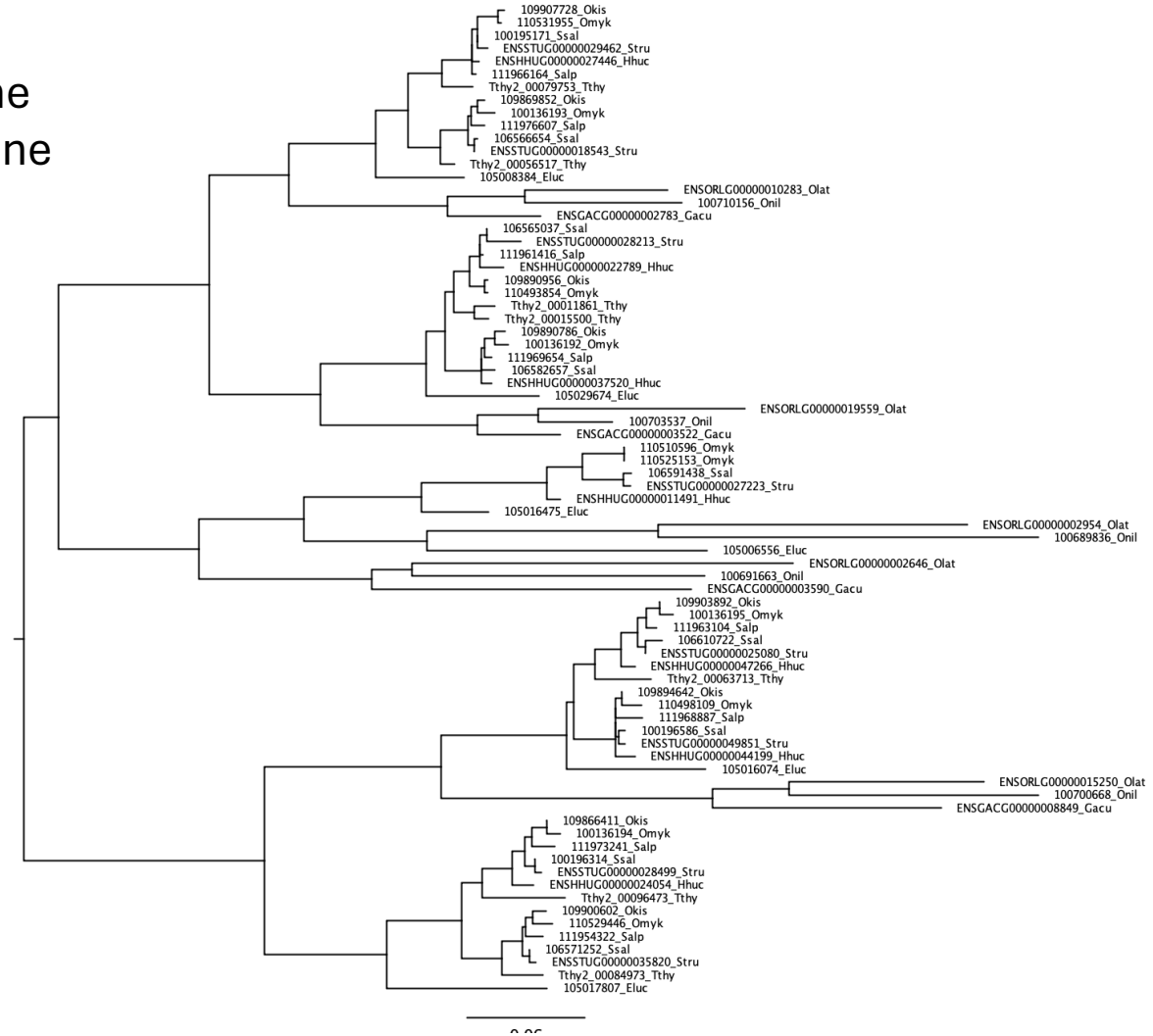
CAFE

Computational **A**nalysis of gene **F**amily **E**volution

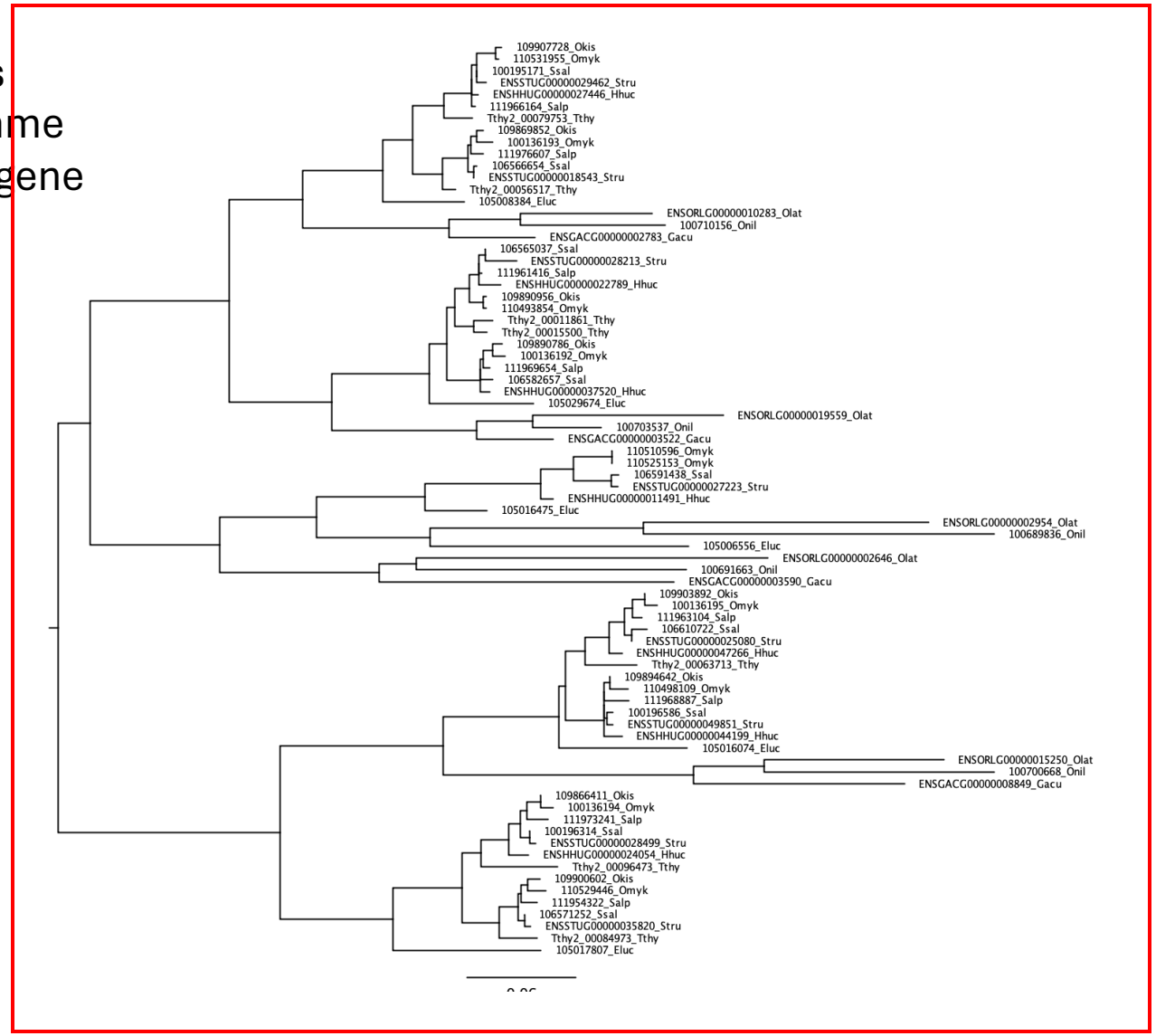
Gene family

Set of similar genes evolved from the same common ancestor gene



Gene family defined by orthofinder

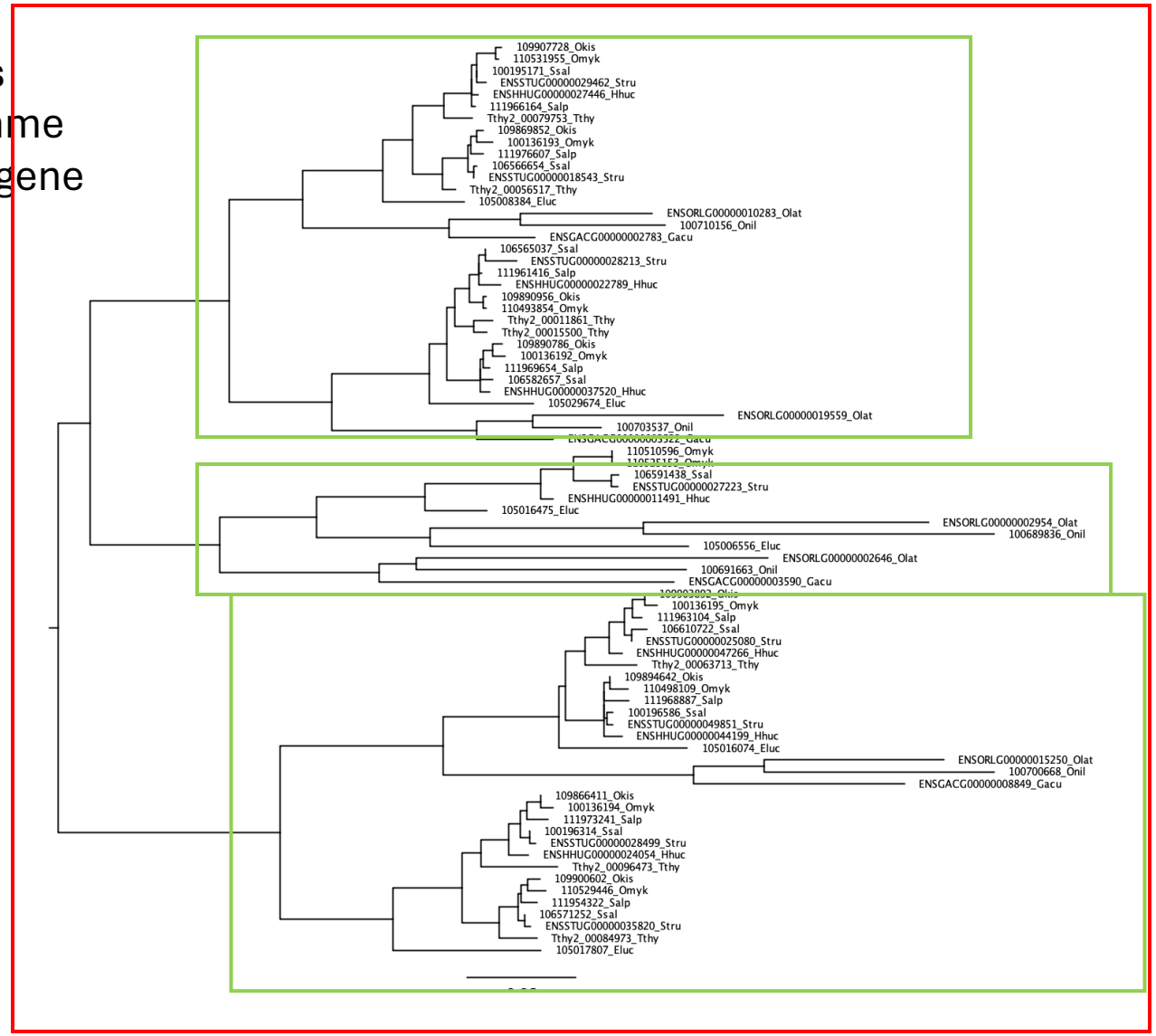
Set of similar genes evolved from the same common ancestor gene



OG: orthogroup

Gene family defined by orthofinder

Set of similar genes evolved from the same common ancestor gene

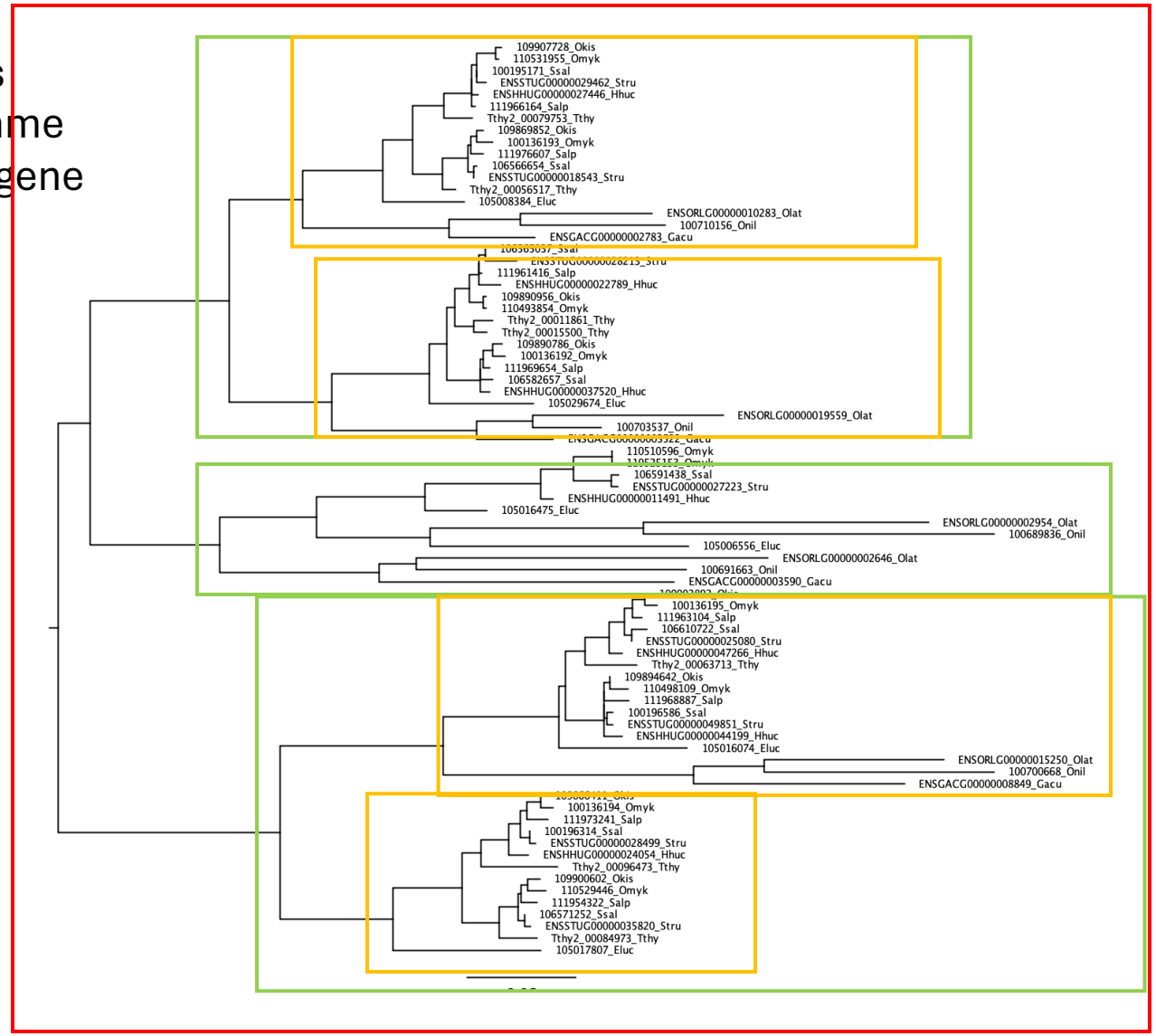


OG: orthogroup

HOG: N0

Gene family defined by orthofinder

Set of similar genes evolved from the same common ancestor gene



OG: orthogroup

HOG: N0

HOG: N1

Gene family defined by orthofinder

hierarchical orthogroups

orthogroups

gene family →

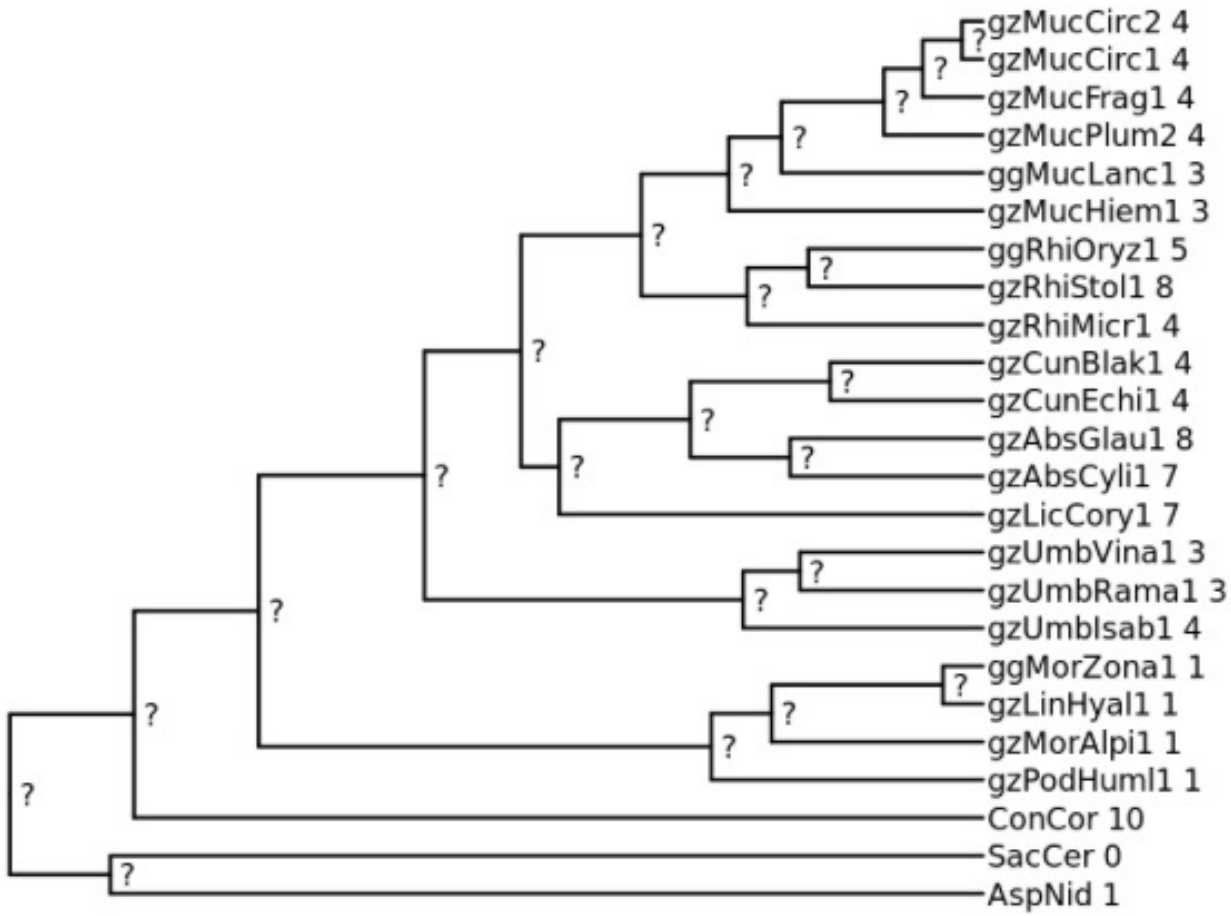
HOG	OG	AspNid.pep	ConCor.proteins	SacCer.proteins	ggMorZona1.proteins	ggMucLanc1.proteins	...
N0.HOG0000000	OG0000000	ANIA_05003		YPL230W, YMR182C	GGMOZO1EN_008077, GGMOZO1EN_001786	GGMULA1EN_008598, GGMULA1EN_000691, GGMULA1EN_000990, GGMULA1EN_007452	
N0.HOG0000001	OG0000000	ANIA_01251	CONCODRAFT_55634				
N0.HOG0000002	OG0000000						
N0.HOG0000003	OG0000000	ANIA_06195	CONCODRAFT_37485, CONCODRAFT_21796, CONCODRAFT_26205	YGL035C	GGMOZO1EN_000154, GGMOZO1EN_003935	GGMULA1EN_001958, GGMULA1EN_003830, GGMULA1EN_007797, GGMULA1EN_006125, GGMULA1EN_003642	
N0.HOG0000004	OG0000000			YER028C, YGL209W			
N0.HOG0000005	OG0000000						
N0.HOG0000006	OG0000000					GGMULA1EN_002316	
...							

Variation in the number of gene copies in each species for each gene family

HOG	OG	AspNid.pep	ConCor.proteins	SacCer.proteins	ggMorZona1.proteins	ggMucLanc1.proteins	...
N0.HOG0000000	OG0000000	1	0	2	2	4	
N0.HOG0000001	OG0000000	1	1	0	0	0	
N0.HOG0000002	OG0000000	0	1	0	0	0	
N0.HOG0000003	OG0000000	1	3	1	2	5	
N0.HOG0000004	OG0000000	0	0	2	0	0	
N0.HOG0000005	OG0000000	0	0	0	0	0	
N0.HOG0000006	OG0000000	0	0	0	0	1	
...							

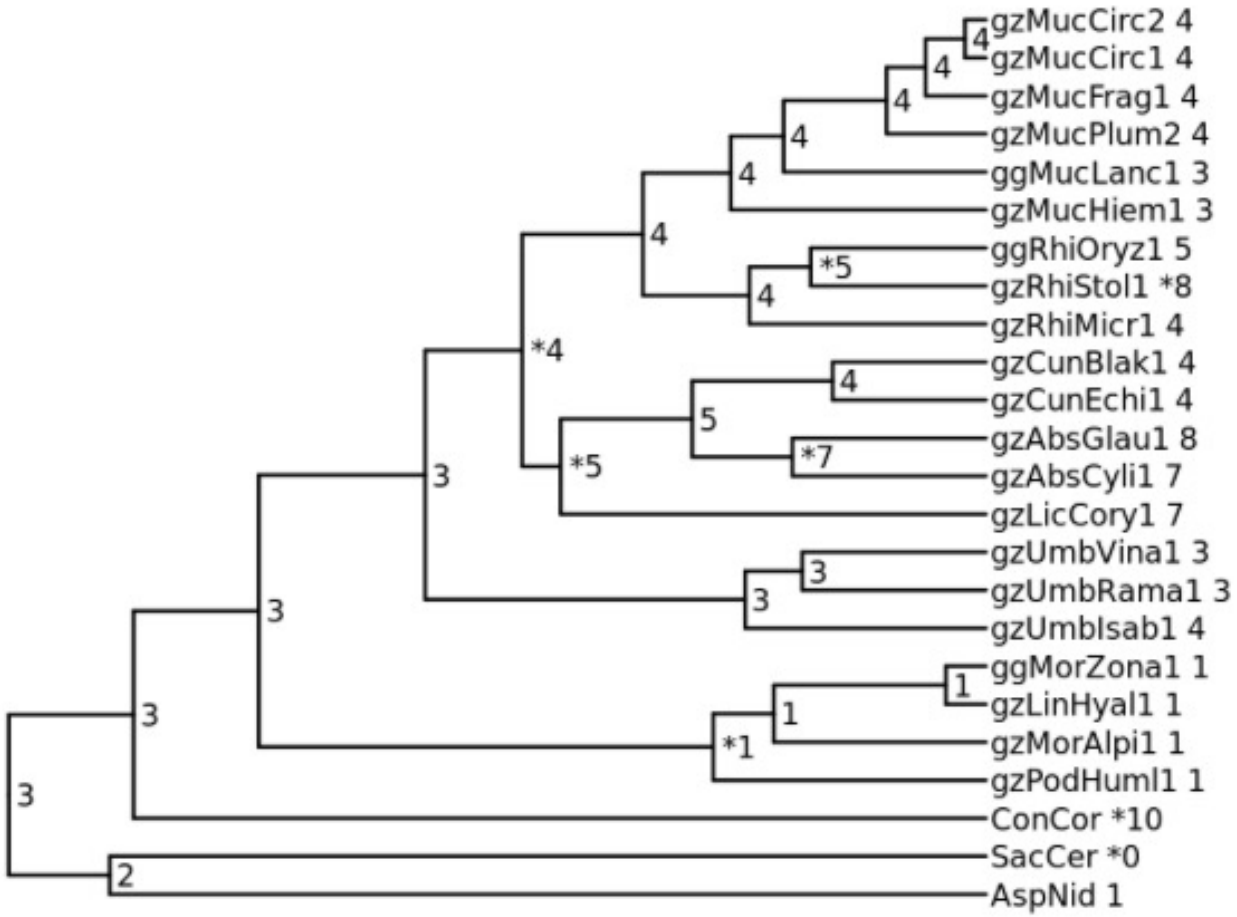
- How gene family sizes have evolved?
- Genes had been gained/lost randomly or under natural selection
- When the contractions/expansions happened?

CAFE estimates gene family size evolutions over a **phylogeny** using a **statistical model**



a gene family

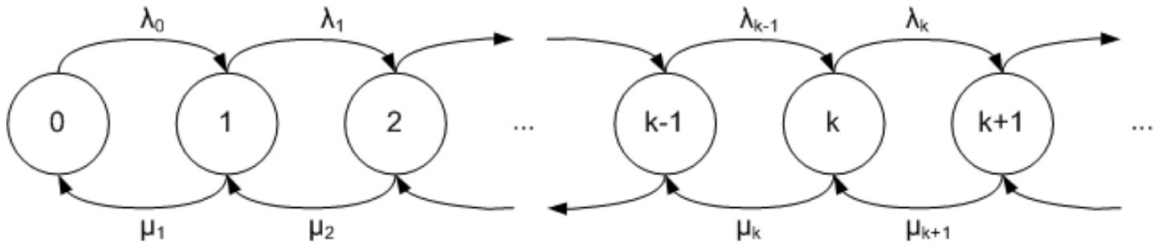
CAFE estimates gene family size evolutions over a **phylogeny** using a **statistical model**



a gene family

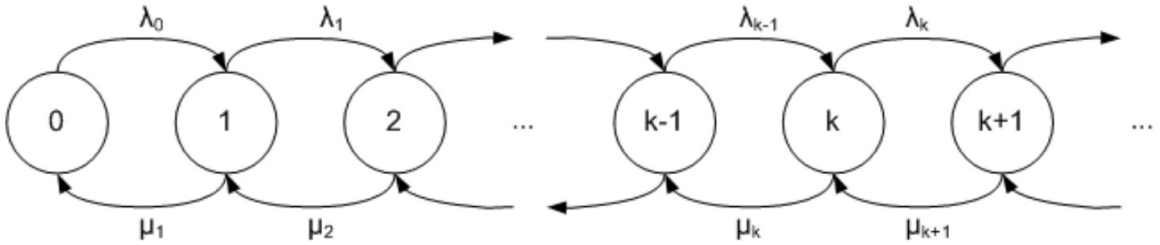
Statistical model

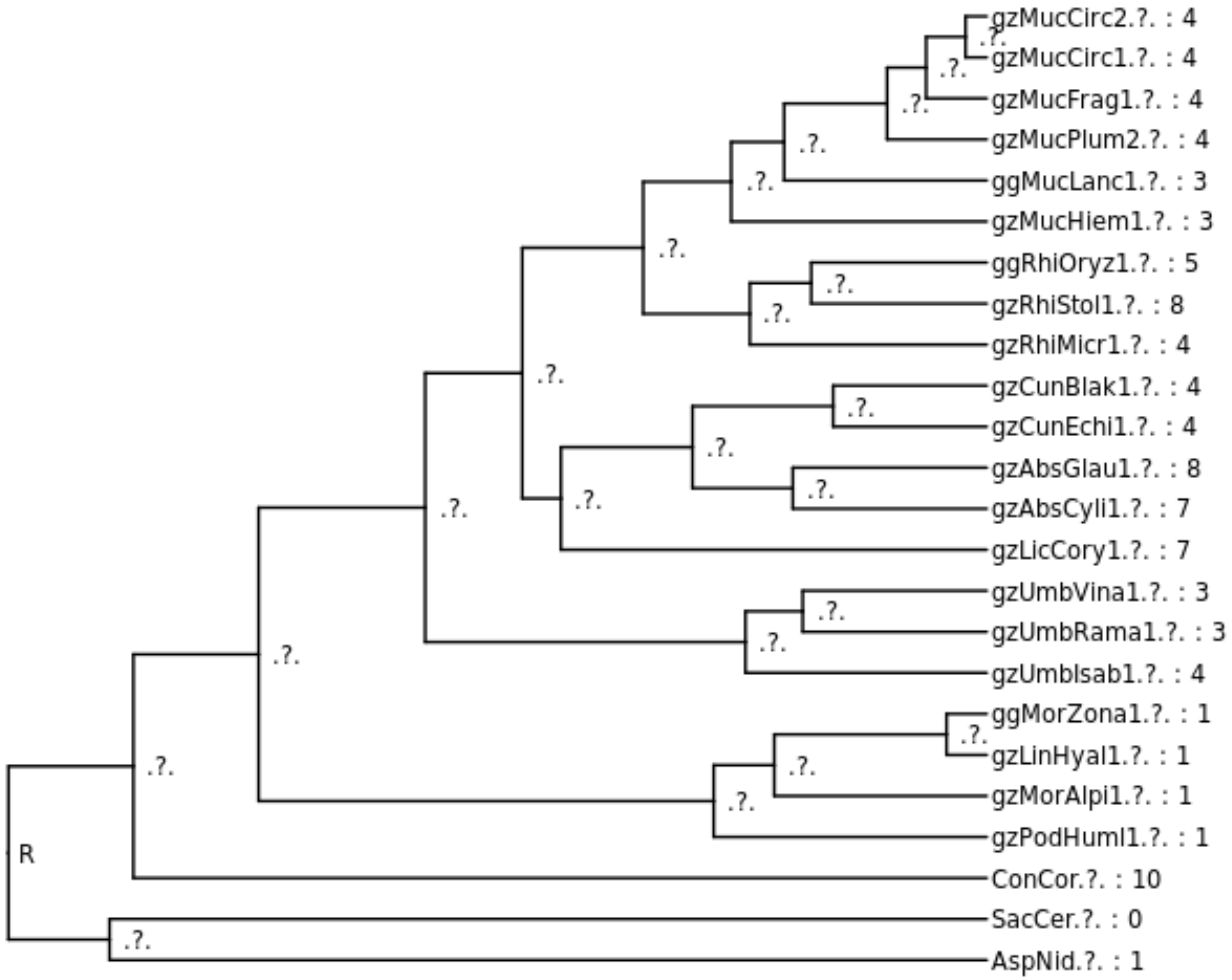
- Gene gain/loss process -> random **birth/death** model



the **rate** of gene gain/loss: $\lambda = \mu$

Conditional likelihood computation





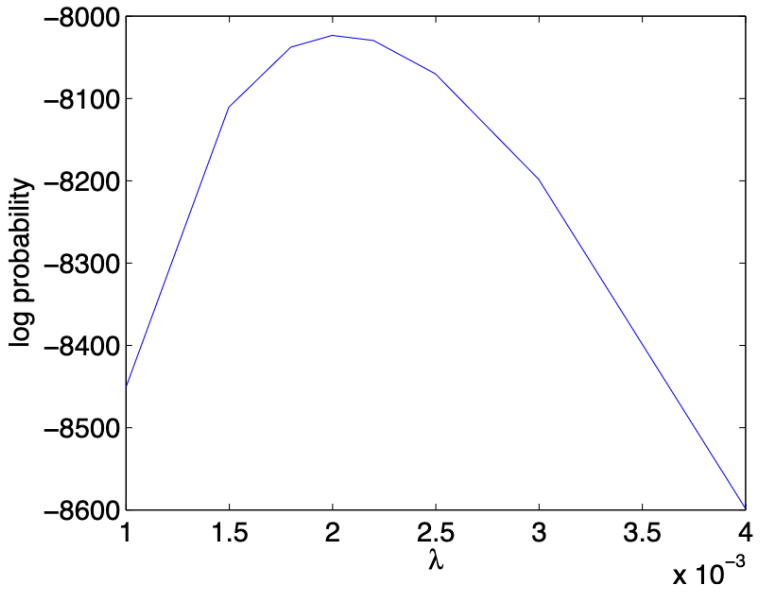
For each gene family, compute the likelihood of observing the gene family size for the leaf nodes, conditioned on the root size.

A likelihood function depends on :

- Tree toplogy
- branch lengths
- root size R
- gain/loss rate λ

Testing hypotheses about gene family evolution

Inferring λ



Maximum log likelihood

We have p-values conditioned on each value of the root node
➔ Choose the **largest** of these conditional p-values

➔ Significant p-value (ex. <0.05):
- unlikely gene families
- do not follow birth/death model
- have undergone unusual (*natural selection*) expansions or contractions

Identifying the unlikely branches

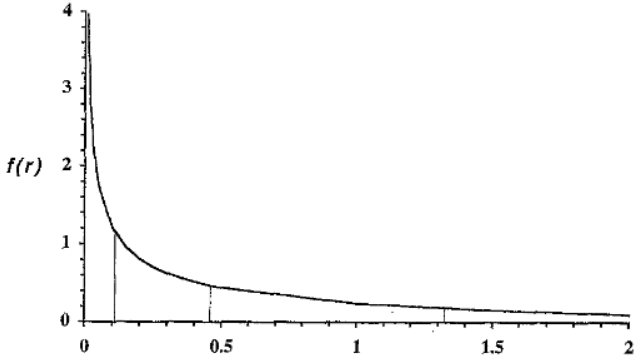
If **removal** of 1 branch results in a large p-value (compared to a threshold), i.e. the remaining trees cannot reject the birth/death model, then this branch may be responsible for violating the model.

Several versions of CAFE

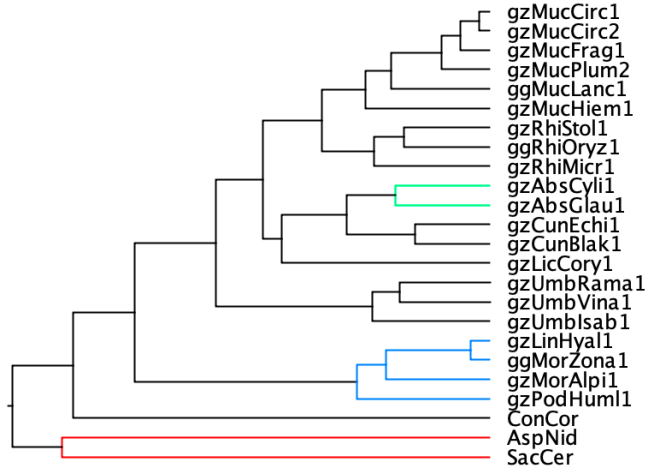
CAFE	• Hahn, M. W., T. De Bie, J. E. Stajich, C. Nguyen, and N. Cristianini. 2005. Estimating the tempo and mode of gene family evolution from comparative genomic data. *Genome Research* 15:1153–1160. • De Bie, T., N. Cristianini, J. P. Demuth, and M. W. Hahn. 2006. CAFE: a computational tool for the study of gene family evolution. *Bioinformatics* 22:1269–1271.
CAFE2	• Hahn, M. W., J. P. Demuth, and S.-G. Han. 2007. Accelerated rate of gene gain and loss in primates. *Genetics* 177:1941–1949. Genetics.
CAFE3,4	• Han, M. V., G. W. C. Thomas, J. Lugo-Martinez, and M. W. Hahn. 2013. Estimating Gene Gain and Loss Rates in the Presence of Error in Genome Assembly and Annotation Using CAFE 3. *Mol. Biol. Evol.* 30:1987–1997.
CAFE5	• Fábio K Mendes, Dan Vanderpool, Ben Fulton, Matthew W Hahn, CAFE 5 models variation in evolutionary rates among gene families, Bioinformatics, 2020

Advanced features in the new version

- Allow **rate variation** among families using gamma-distributed rate categories



- Allow different rates for **different branches** *using user-defined branch partition*



- Account **errors** in gene family counts (*should give an error model for each gene family*)

Running cafe5 on the fungi data

- Go to github page: https://github.com/ebp-nor/workshop-2024/blob/main/day2_genome_annotation/CAFE5.md