SUBSTITUTION MODELS

SHORT RECAP + MODELTEST PAPER DISCUSSION

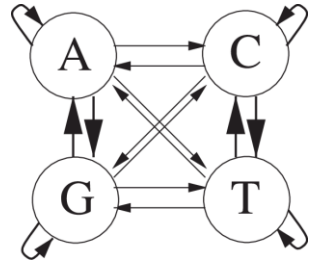
AARHUS
UNIVERSITY
DEPARTMENT OF MOLECULAR BIOLOGY AND GENETICS

EVOLUTIONARY THINKING 2023
WEEK 36

CALIN PANTEA
PHD STUDENT

EVENT MODELLING

- Basic nucleotide substitution models
- Appropriateness
- Gamma distribution
- Model selection (AIC and BIC)



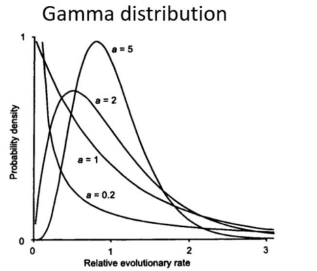
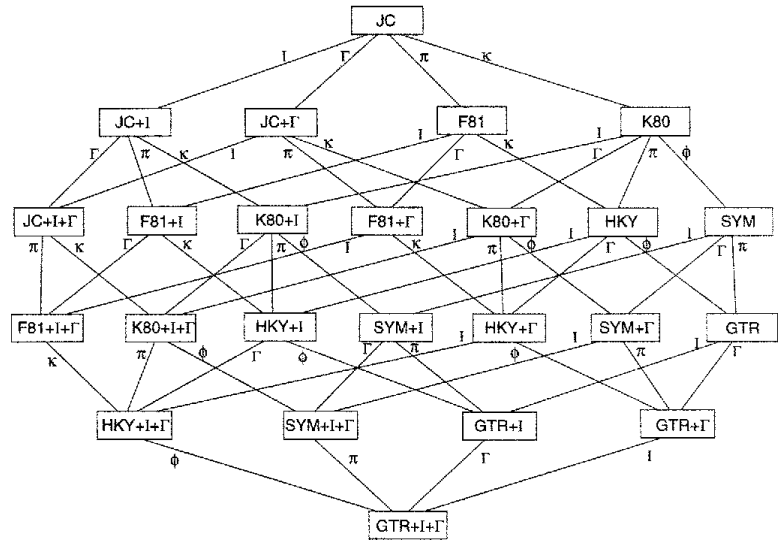


FIGURE 2.3. Gamma distributions of substitution rates among sites for different gamma parameters (α's).

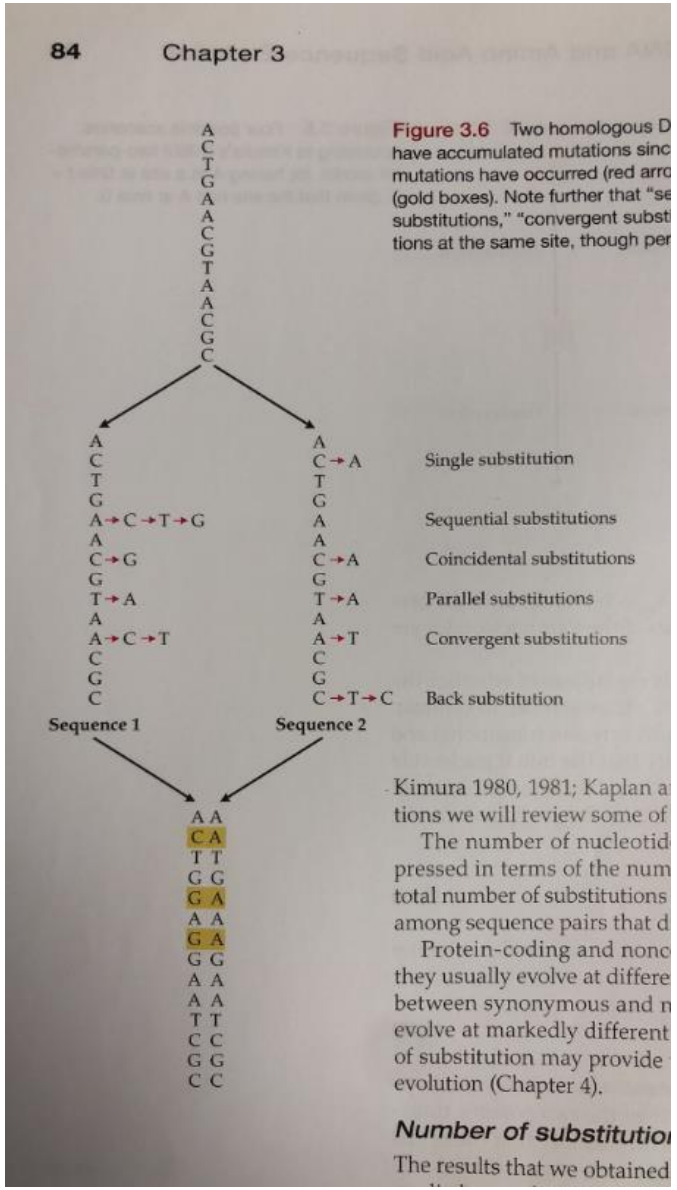


NUCLEOTIDE SUBSTITUTION

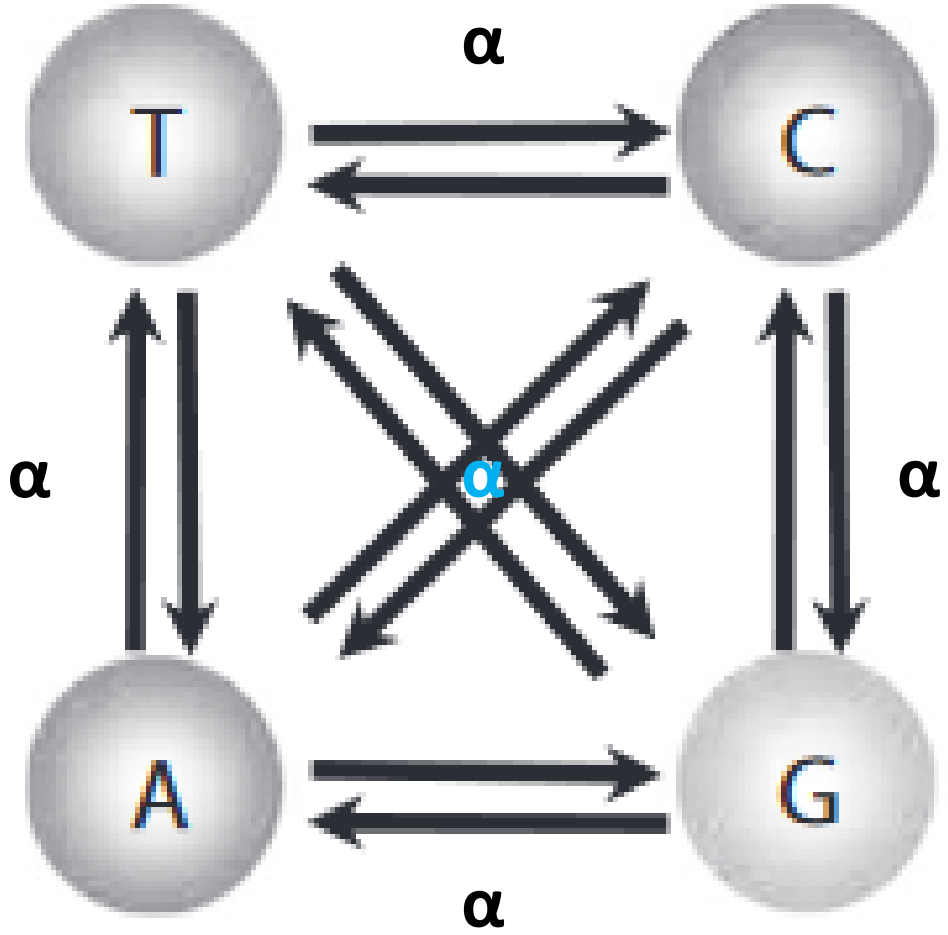
- divergent sequences

AGATGCTAGCATCGACTAGCATCAGCTGACCCCGCGCGCGCAT

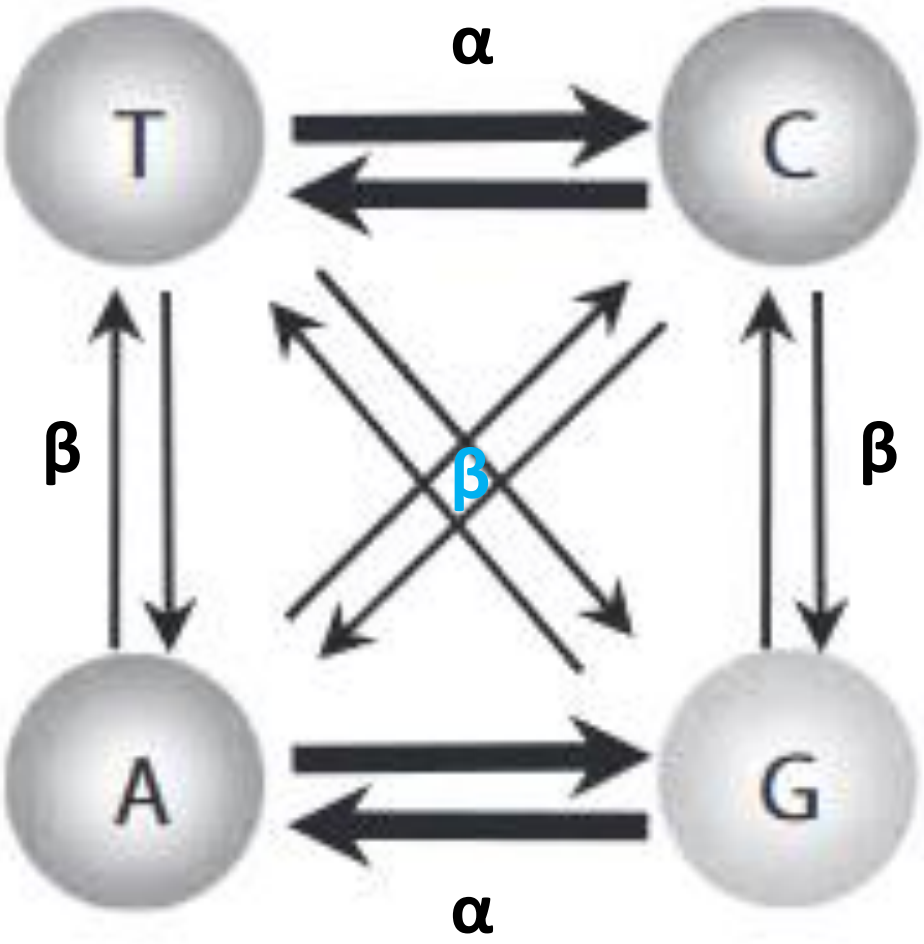
AGATAATAGCATCGACTAGCATCAGCGGACCCCGCGCGCGCAC



JUKES-CANTOR (JC69)



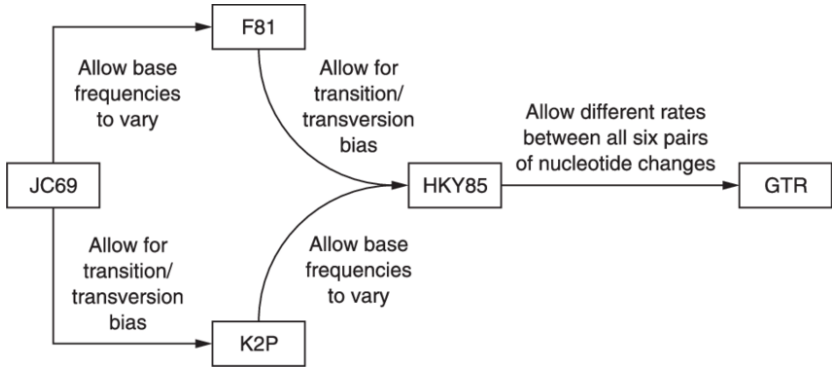
KIMURA (K2P)



OTHER MODELS

Which model is the best?

- Simple models
  - Few parameters (LOW sampling variance)
  - Perform poorly for large distance
- Complex models
  - Many parameters (LARGE sampling variance)
  - Better behaved for large divergence
  - Require LOTS of data
- What is the true patterns of substitution ?



Gamma distribution

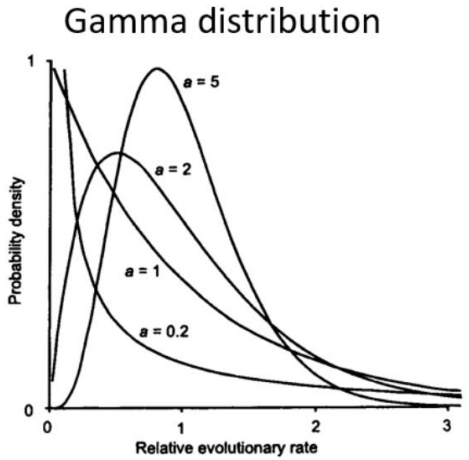
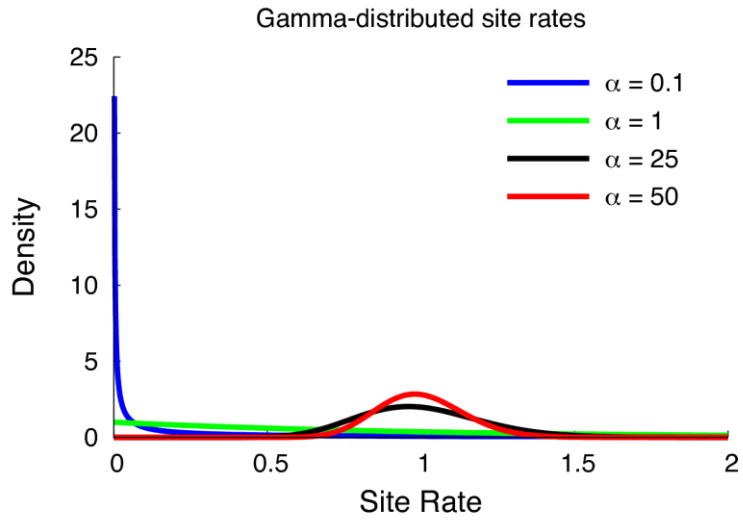


FIGURE 2.3. Gamma distributions of substitution rates among sites for different gamma parameters (*a*'s).



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  - Few paramete
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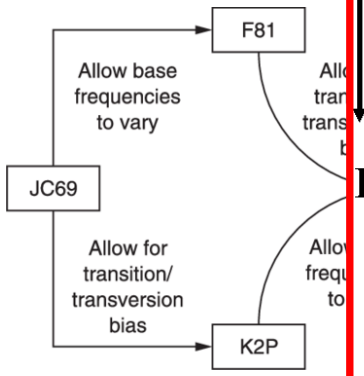
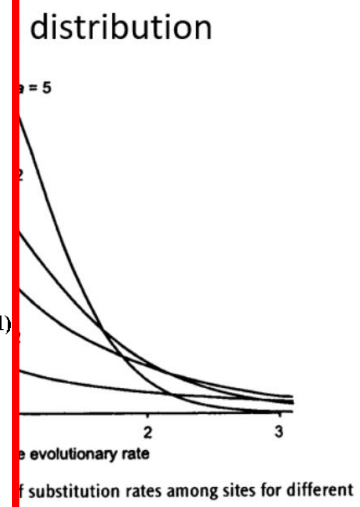
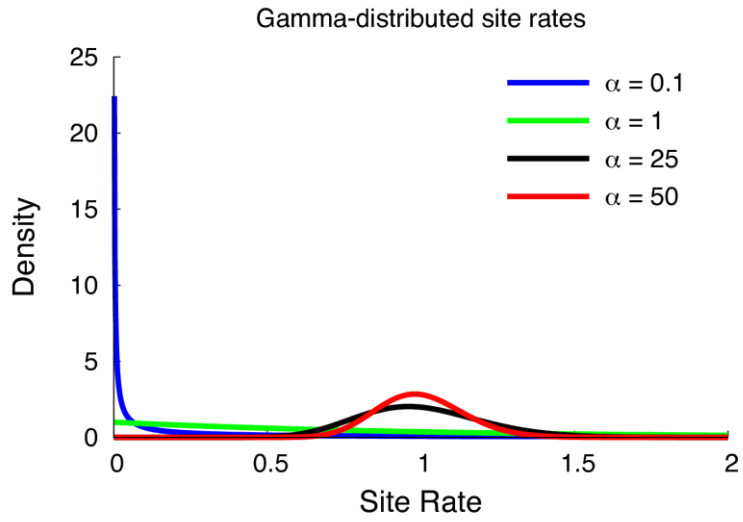
  - Require LOTS
- What is the tru



Model	Free parameters in the Q-matrix
GTR	**8** $a, b, c, d, e, \pi_A, \pi_C, \pi_G,$ $(a+b+c+d+e+f=1 \quad \pi_A+\pi_C+\pi_G+\pi_T=1)$
TN93	**5** $a=c=d=f, b=e, \pi_A, \pi_C, \pi_G,$ *(Ti/Tv ratio, Y/R ratio and and three frequencies since* $\pi_A+\pi_C+\pi_G+\pi_T=1$*)*
HKY85 → **F84**	**4** $a=b=c=d=1, \quad b=e=k, \pi_A, \pi_C, \pi_G,$ *(Ti/Tv ratio and only three frequencies since* $\pi_A+\pi_C+\pi_G+\pi_T=1$*)*
F81	**3** $a=c=d=f=b=e=f, \pi_A, \pi_C, \pi_G,$ *(only three nt frequencies since* $\pi_A+\pi_C+\pi_G+\pi_T=1$*)*
K80	**1** $a=b=c=d=1, \quad b=e=k, \quad \pi_A=\pi_C=\pi_G=\pi_T$ *(Ti/Tv ratio)*
JC69	**0** $a=b=c=d=e=f, \quad \pi_A=\pi_C=\pi_G=\pi_T$

Gamma distribution



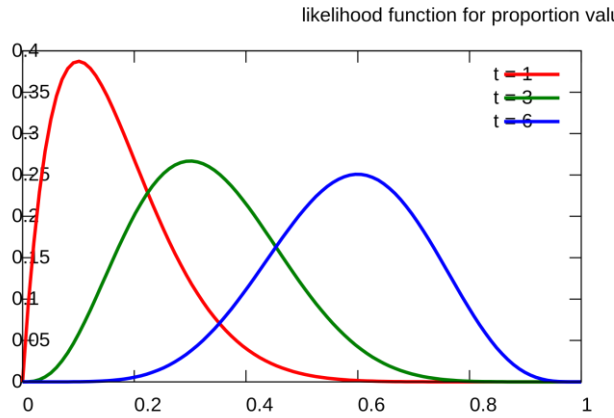


LIKELIHOOD FUNCTION AND MLE

Likelihood function

$\mathcal{L}(\theta \mid x)$

- describes the distribution of probabilities that a model fitted to data describes it well



MLE (maximum likelihood estimation) – maximum value of the likelihood function for model describing studied data

- basically – highest possible probability for the fitted model to really described the data

-> but more complex models are more prone to overfitting!

AIC AND BIC

k = number of model parametres; n = number of observations

Bayesian information criterion (BIC)

$$\mathrm{BIC} = k\ln(n) - 2\ln(\widehat{L})$$

- depends on sample size ‘n’
- can only be reliable as long as n >> k

Akaike information criterion (AIC)

$$\mathrm{AIC} = 2k - 2\ln(\hat{L})$$

- somewhat more permissive
- sometimes more reliable
- better choice than BIC for n!>>k

MODELTEST PAPER

- Introduces an early solution for substitution model choice: simple model likelihood pairwise comparison
- Old and plain; but still a solid early paper discussion resource
- Why?
  - Practice paper discussion
  - Insight into scientific thinking
  - Useful for exam mindset <and> future research work

Course week	Week number	Lecture Monday	Readings	TA Wednesday	TA Friday	Hand-ins
1	35	Origin of life substitution models	Yang, pp 1-23 and originoflife paper	Tree pretest exercise (pen and paper) Installing MEGA11	MEGA11 exercises: retrieve sequences, alignment and distance matrix	
2	36	Phylogenetic tree reconstruction	Yang pp 23-50, graur 165-178	Paper discussion: Modeltest paper, Yang problems	MEGA11 exercises: substitution models	
3	37	Trees continued plus Molecular clocks	Graur 165-209	Paper discussion: Zoonomia paper	Work on Hand in I	Hand-in I: Phylogenetic tree analysis
4	38	Student prestentations and work on hand in I	Yang 361-368	Paper discussion: HIV infection on a dental clinic	**Introduction to R using phylogenetics**	Hand-in I deadline
5	39	Basics of population genetics	NS 2,3, Charlesworth	Problems NS 1,2,3 Hand-in I correction	Wright-Fisher and Coalescent simulator exercises (R)	
6	40	The coalescent continued	NS 4,5,6, Ellegren paper	Problems NS 4,5,6	Problems NS 4,5,6	
7	41	Tests of neutrality	NS 7,8,9, Vicoso paper	Problems NS 7,8	**R exercise: detecting positive selection using dn/ds. Jeopardy**	Hand-in II: NORK
-	42	Autumn Break		Autumn Break	Autumn Break	Autumn Break
8	43	Incomplete lineage sorting	Mailund et al.	Paper discussion:Iker Rivas Gonzalez et al	Hand-in II correction	Hand-in II deadline
9	44	Comparative genomics and X chromosomes	Review	Paper discussion:	**Chatgbt driven phylogenetics exercise in R**	
10	45	Genome scans and primate genomics,	Marques-Bonet et al and Kuderna et al	Paper discussion: Gao et al.	**R exercise**	
11	46	Ancient DNA	Rasmussen et al.	Paper discussion: Green et al.	**Update: MEGA11 exercise with data**	
12	47	Genome evolution, mutation		Paper discussion: Bergeron et al	Ancient DNA exercise Work on Hand-in III	Hand-in III: Ancient DNA
13	48	Genome evolution, TE		Paper discussion: Hallast et al. Self-test	Self-test	Hand-in III deadline
14	49	Evaluation	none	Hand-in III correction/discussion	Summary of the exercises/discussion	

PAPER QUESTIONS

Group 1

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Martensen, René, au684546, 684546
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Saha, Anik, au746885, 746885
Thingholm, Malthe Skovmand, au599620, 599620

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Jensen, Sebastian Kjellerup Godske, au664538, 664538
Jørgensen, Søren, au643843, 643843

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Namsaraeva, Altana, au746258, 746258
Skov, Anna Kathrine Jensen, au646861, 646861

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Charlton, Chester Henry, au747556, 747556
Danger, Stinna Weisberg, au643227, 643227

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7-11

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Kongsgaard, Viktor, au661991, 661991
von Vegesack, Hans Carlo, au752686, 752686

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Sucipto, Abby Kurniawati, au747615, 747615
Wahab, Adam Faraldon, au667387, 667387

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Guo, Jiahui, au747088, 747088
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Nikolaidou, Eleni, au752666, 752666
Svenningsen, Laurids, au632957, 632957

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Gálfalvy, Nóra, au752687, 752687
Jørgensen, Carolina Ferreira, au590004, 590004
Ulstrup, Johan Christensen, au664823, 664823

YOUR QUESTIONS ABOUT PAPER QUESTIONS

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QUESTIONS ABOUT PAPER QUESTIONS

Google Docs

QUIZ TIME!

questions

and

feedback

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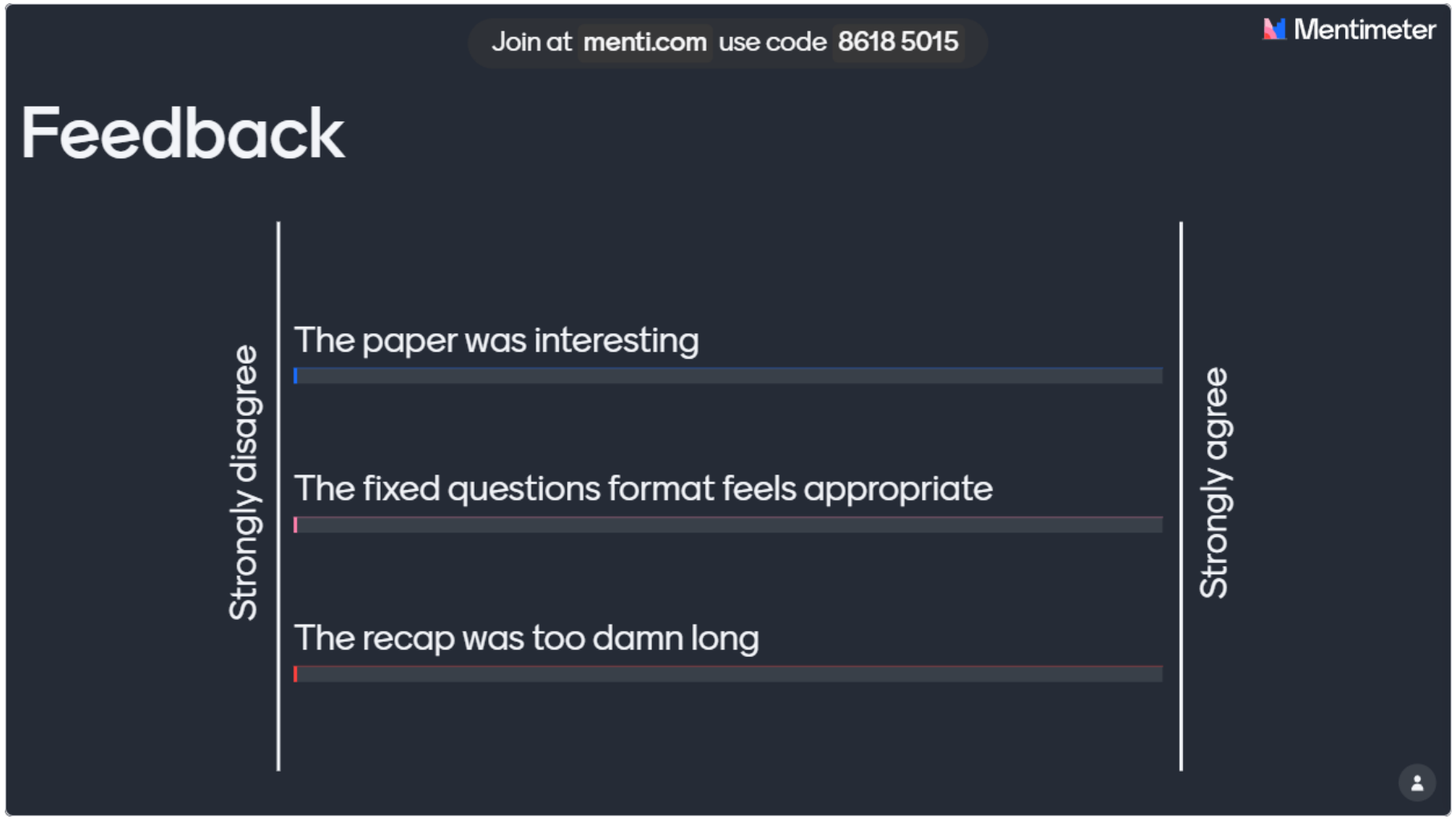


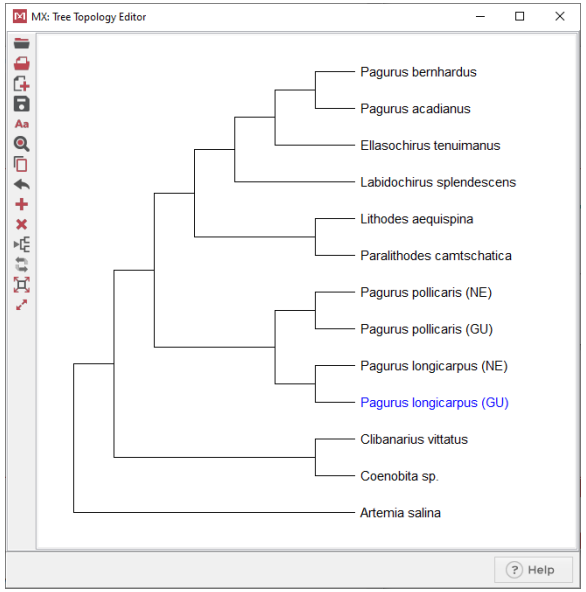
POTENTIAL LECTURE CHANGES

Monday 18th Sept (Week 38) – No lecture (Mikkel is away)

Possibly moved the week before, on Friday the 15th Sept!

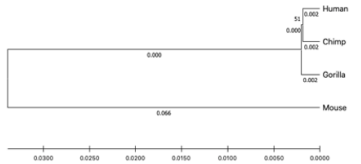
SEE YOU ON FRIDAY FOR SOME MORE DELIGHTFUL MEGA SHENANIGANS

MEGA tree building!



FOXP2

UPGMA



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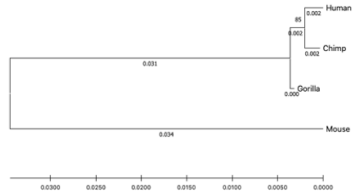

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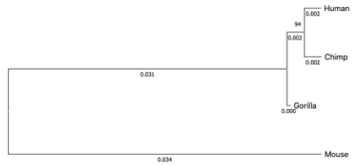

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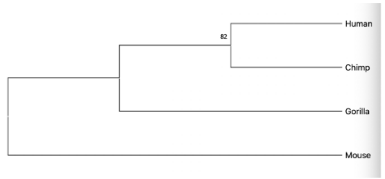

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