‘Realism’ and ‘Instrumentalism’ in models of molecular evolution

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Galileo

Overview

sites free to vary

summing sources of error

‘rates’ of molecular evolution

estimates of time intervals

do we know anything? (flat priors)

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Human/chimp divergence

1) *Ramapithecus* = 12Ma → HC = 5±1Ma

But *Ramapithecus* in Asia, HCG in Africa.

Is 18-20Ma a better estimate for divergence?

2) *Ramapithecus* = 18Ma → HC = 7.5±1.5Ma

Or should we combine uncertainties?

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In this case, I would rather not – leave it as a conditional estimate – need both.

sites free to vary

	rate $k_{aa} \times 10^9$/yr
- fibrinopeptides	8.3
- lysozyme	2.0
- hemoglobin α	1.2
- cytochrome c	0.3
- histone H4	0.01

Dickerson, 1971

explained the differences by the proportion of sites ‘free to vary’.

change of function should show a rate change

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realism

we use a tiny fraction of the information in the data

Alignment original sequence order	Reordered Alignment shuffled/reordered
AIIFLNSALGPSPELFPIILATKVL	ASAGPSPPATPLLIIIIILLFFNEKV
AIMFLNSALGPPTELFPVILATKVL	ASAGPPTPATPLLIMVILLFFNEKV
SIMFLNHTLNPTPELFPIILATETL	SHTNPTPPATPLLIMIILLFFNEET
TILFLNSSLGLQPEVTPTVLATKTL	TSSGLQPPATPLLILTVLVTFNEKT
TLLFLNSMLKPPSELFPIILATKTL	TSMKPPSPATPLLLLIILLFFNEKT
ALLFLNSTLNPPTELFPLILATKTL	ASTNPPTPATPLLLLLILLFFNEKT
AILFLNSFLNPPKEFFPIILATKIL	ASFNPPKPATPLLILIILFFFNEKI

c columns

c! alignments

If c = 1000, we use ≈ 1/ 1000! of the information

sites change

X-ray crystallographers: the strongest conclusion we have is that the same sites in different species may be fixed, in others they are variable.

Molecular Phylogeneticists: Our methods (such as the Gamma distribution) assume sites are in the SAME rate class across the entire tree (AND, we only need one parameter- so there).

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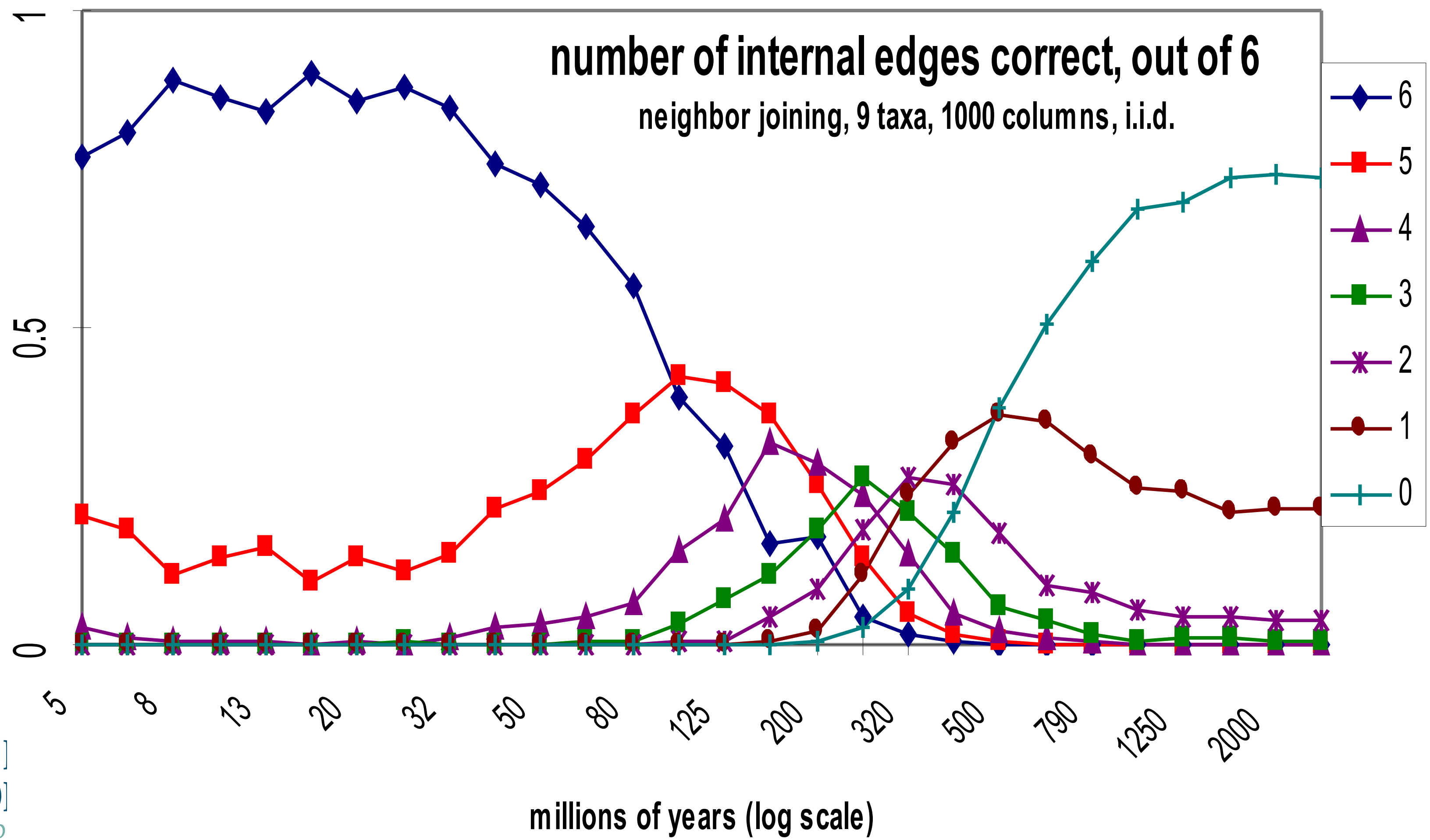
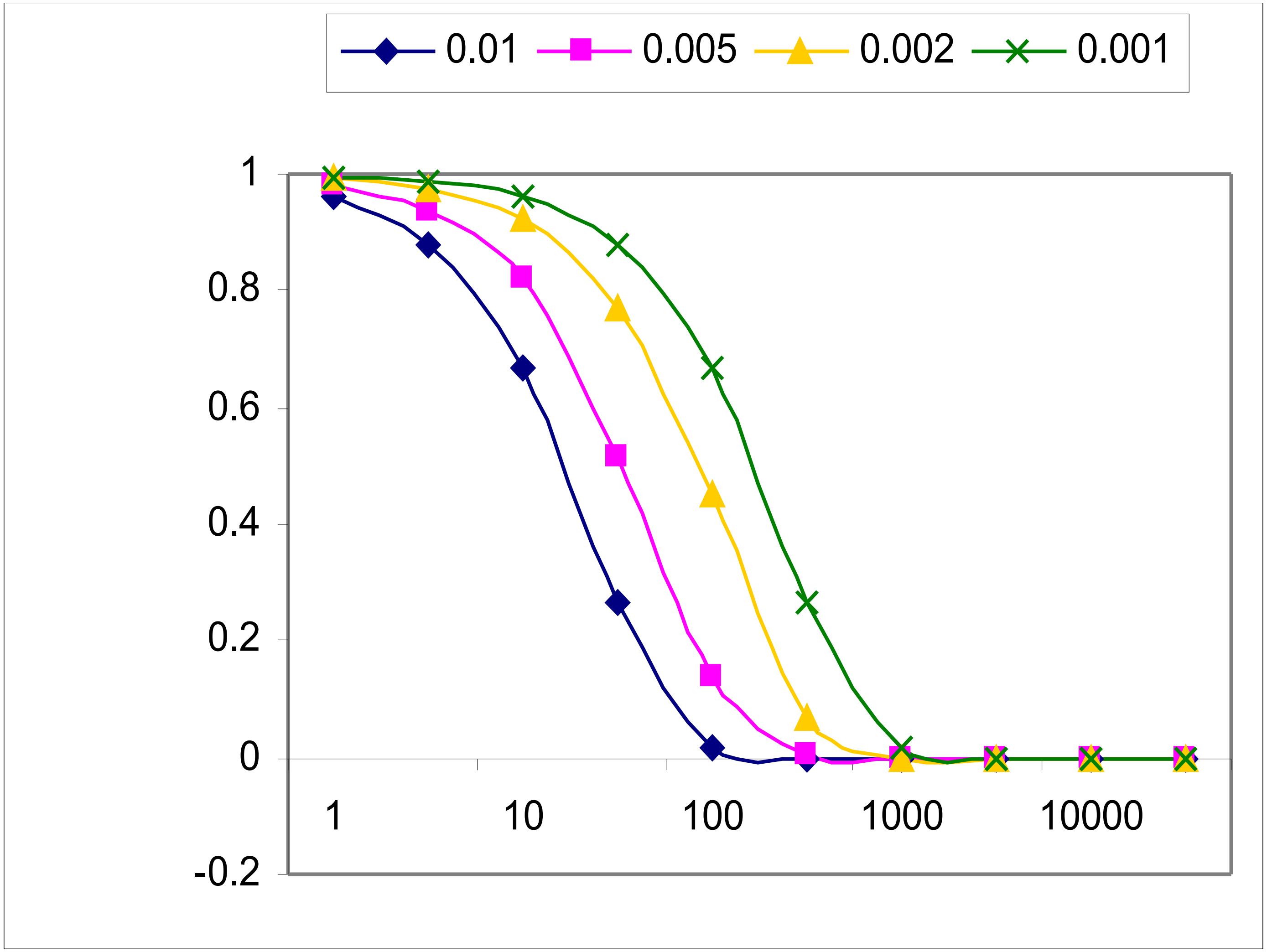
simulation results with standard model



Calculated results, $\Delta \leq ¼ + ne^{-qt}$



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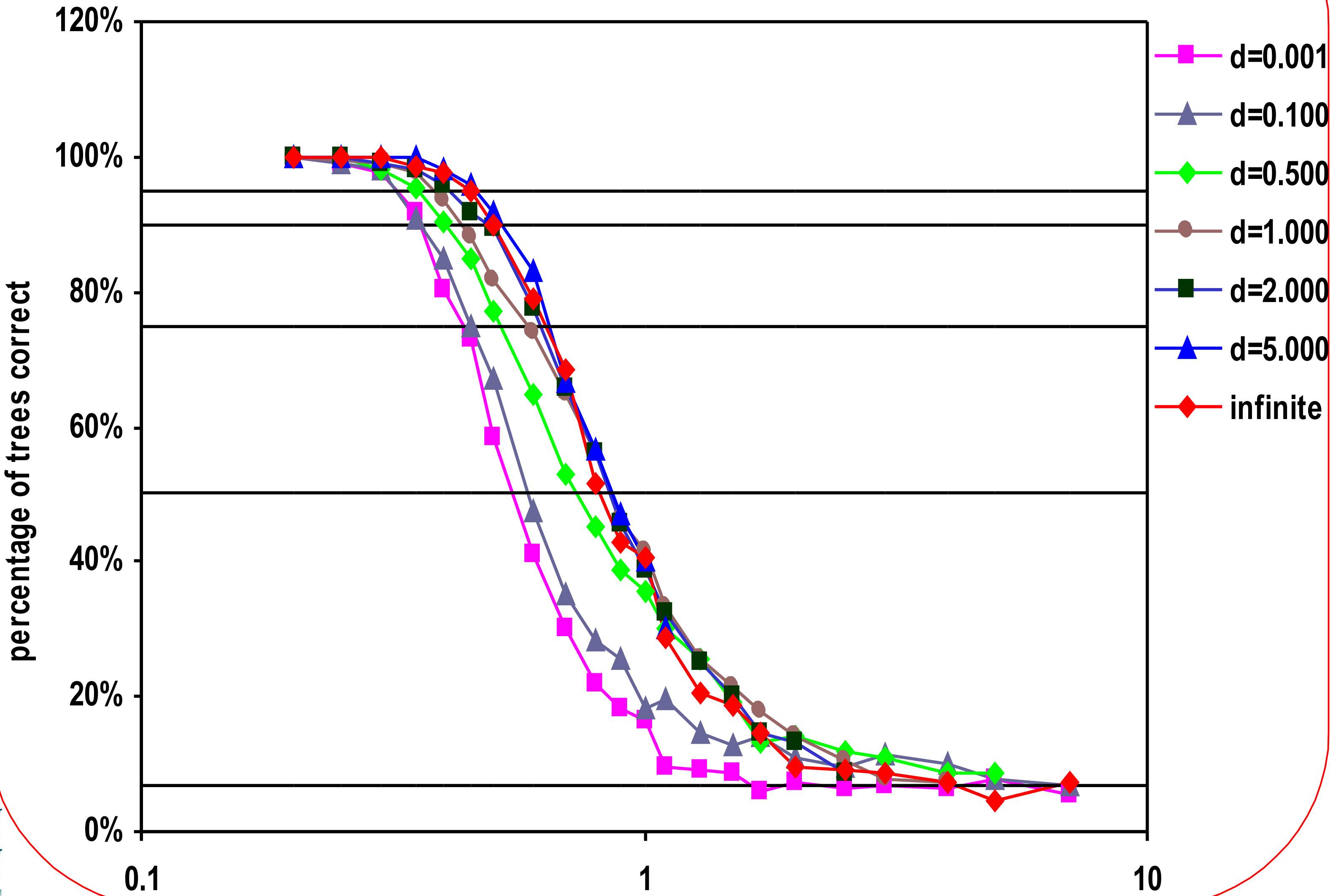
simulation results with covarion model



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do ‘rates’ exist !!!

We go ON

and ON

and ON

and ON

About ‘molecular clocks’.

Should we??

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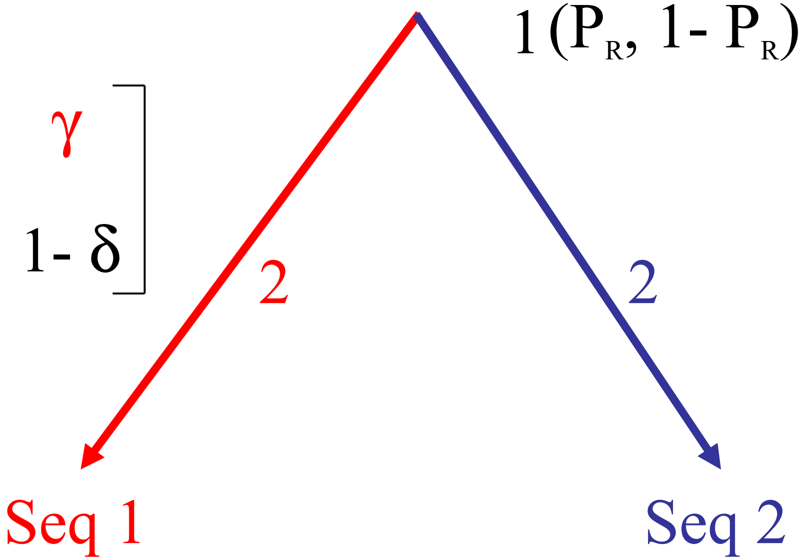
not enough information to recover the full model

$$\begin{bmatrix} 1-\gamma & \gamma \\ \delta & 1-\delta \end{bmatrix}$$



$1\ (P_R,\ 1-P_R)$ *composition at root*

5 required,

3 available

two taxa, two codes

Seq 1 --

Seq 2 --

$$\text{Seq 1}\quad \begin{array}{c} R \\ Y \end{array}\begin{bmatrix} \alpha & \beta \\ \gamma & * \end{bmatrix}$$

$$\begin{array}{cc} R & Y \end{array}$$

Seq 2

Divergence matrix, $F_{i,j}$

1	2	
R	R	α
R	Y	β
Y	R	γ
Y	Y	*

Three independent parameters estimated

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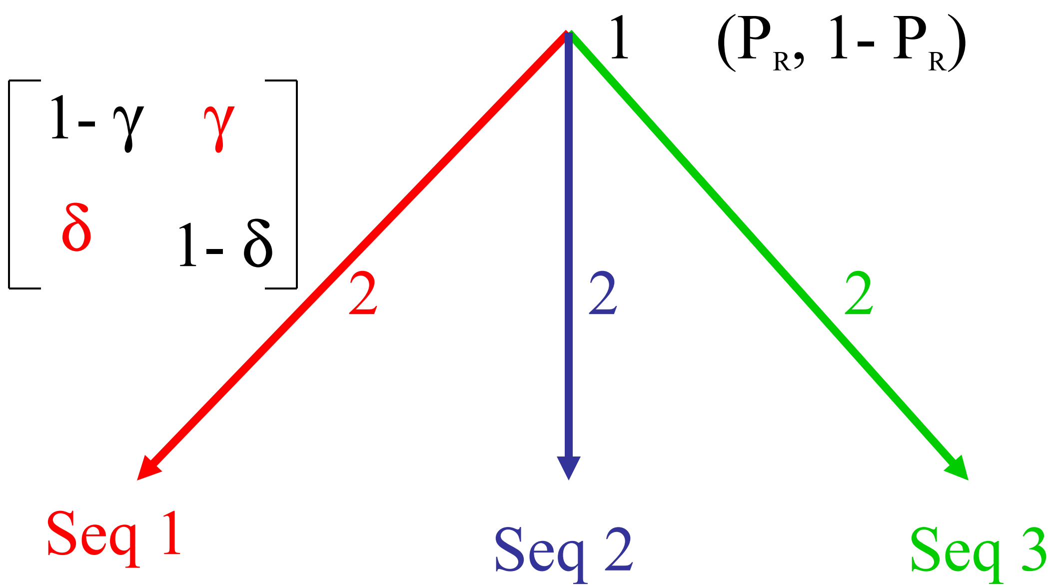
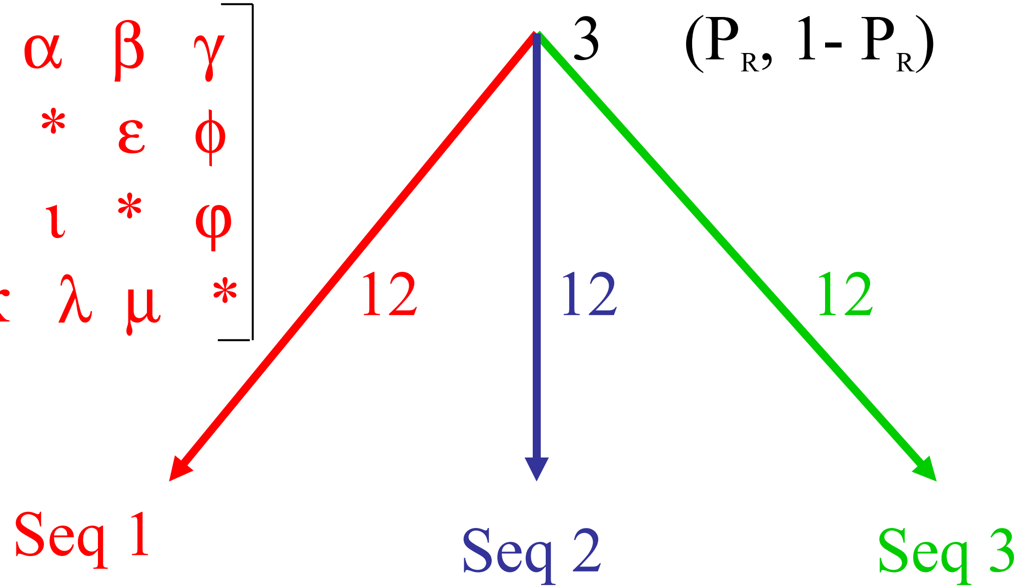
three taxa



7 required

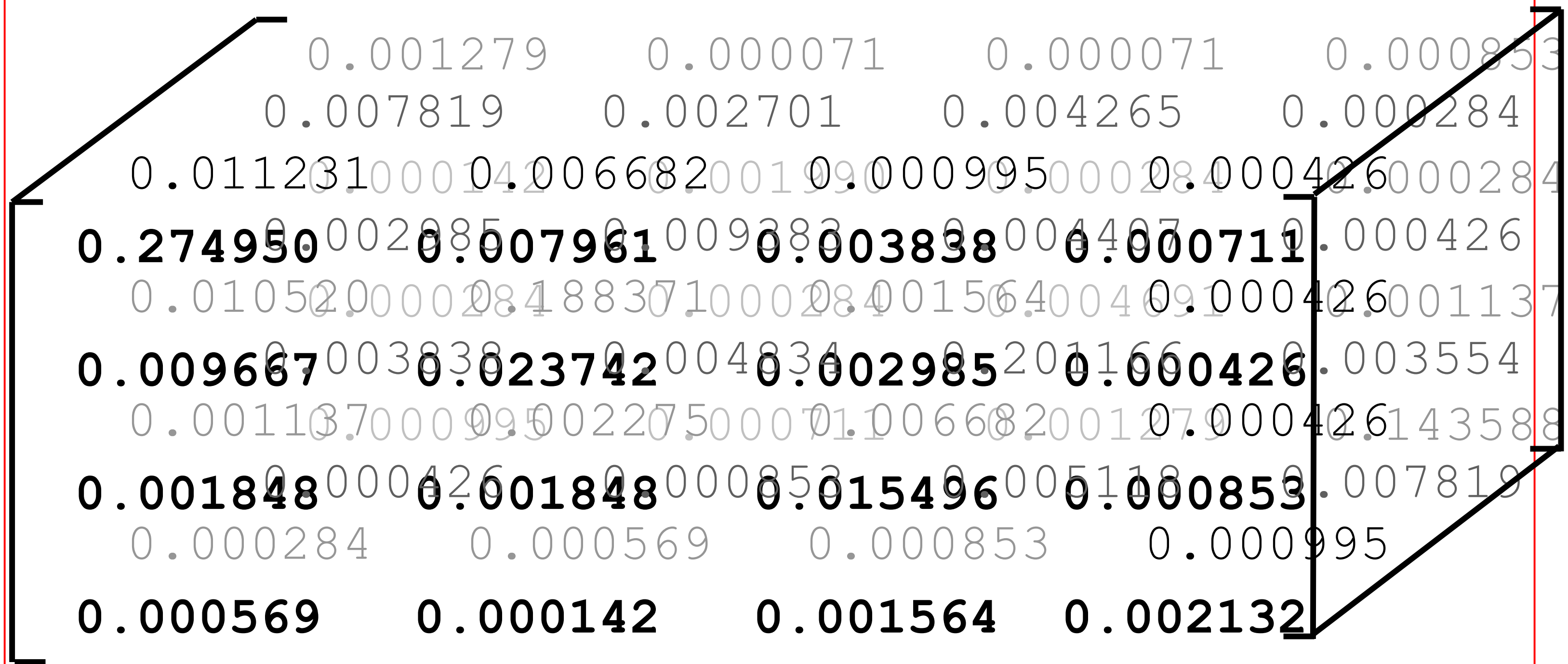
four character states

$$\begin{bmatrix} * & \alpha & \beta & \gamma \\ \delta & * & \varepsilon & \phi \\ \eta & \iota & * & \varphi \\ \kappa & \lambda & \mu & * \end{bmatrix}$$



39 required

tensor, 3D matrix



64 – 1 = 63 values, but a sparse matrix!

primary diagonal

Gymnure, Mole and Shrew

T	**T**	**0.274950**	0.007961	0.003838	0.000711
T	C	0.009667	0.023742	0.002985	0.000426
T	A	0.001848	0.001848	0.015496	0.000853
T	G	0.000569	0.000142	0.001564	0.002132
C	T	0.011231	0.006682	0.000995	0.000426
C	**C**	0.010520	**0.188371**	0.001564	0.000426
C	A	0.001137	0.002275	0.006682	0.000426
C	G	0.000284	0.000569	0.000853	0.000995
A	T	0.007819	0.002701	0.004265	0.000284
A	C	0.002985	0.009383	0.004407	0.000426
A	**A**	0.003838	0.004834	**0.201166**	0.003554
A	G	0.000426	0.000853	0.005118	0.007819
G	T	0.001279	0.000071	0.000071	0.000853
G	C	0.000142	0.001990	0.000284	0.000284
G	A	0.000284	0.000284	0.004691	0.001137
G	**G**	0.000995	0.000711	0.001279	**0.143588**
		T	**C**	**A**	**G**

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secondary diagonals

		Gymnure (moon rat)	Mole,	Shrew	
T	T	**0.274950**	0.007961	0.003838	0.000711
T	C	0.009667	**0.023742**	0.002985	0.000426
T	A	0.001848	0.001848	**0.015496**	0.000853
T	G	0.000569	0.000142	0.001564	**0.002132**
C	T	**0.011231**	0.006682	0.000995	0.000426
C	C	0.010520	**0.188371**	0.001564	0.000426
C	A	0.001137	0.002275	**0.006682**	0.000426
C	G	0.000284	0.000569	0.000853	**0.000995**
A	T	**0.007819**	0.002701	0.004265	0.000284
A	C	0.002985	**0.009383**	0.004407	0.000426
A	A	0.003838	0.004834	**0.201166**	0.003554
A	G	0.000426	0.000853	0.005118	**0.007819**
G	T	**0.001279**	0.000071	0.000071	0.000853
G	C	0.000142	**0.001990**	0.000284	0.000284
G	A	0.000284	0.000284	**0.004691**	0.001137
G	G	0.000995	0.000711	0.001279	**0.143588**
		T	**C**	**A**	**G**

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moon rat, 1+2

T	0.955	0.148	0.087	0.028
C	0.025	0.803	0.025	0.009
A	0.018	0.043	0.876	0.076
G	0.002	0.006	0.012	0.887
	T	C	A	G

T	.955 ±.004	.150 ±.013	.087 ±.009	.029 ±.008
C	.025 ±.003	.800 ±.014	.025 ±.005	.009 ±.003
A	.018 ±.003	.044 ±.006	.877 ±.011	.077 ±.011
G	.002 ±.001	.006 ±.002	.012 ±.002	.886 ±.015
	T	C	A	G

therefore we believe in symmetric models

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mole, shrew and moon rat

mole

	T	C	A	G
T	0.976	**0.062**	0.021	0.013
C	0.017	0.931	0.020	0.007
A	**0.006**	0.006	0.948	**0.012**
G	0.001	0.001	0.010	0.968

shrew

	T	C	A	G
T	0.977	**0.038**	0.024	0.011
C	0.020	0.951	0.020	0.003
A	**0.002**	0.009	0.942	**0.011**
G	0.001	0.001	0.015	0.976

moon rat

	T	C	A	G
T	0.955	**0.148**	0.087	0.028
C	0.025	0.803	0.025	0.009
A	**0.018**	0.043	0.876	**0.076**
G	0.002	0.006	0.012	0.887

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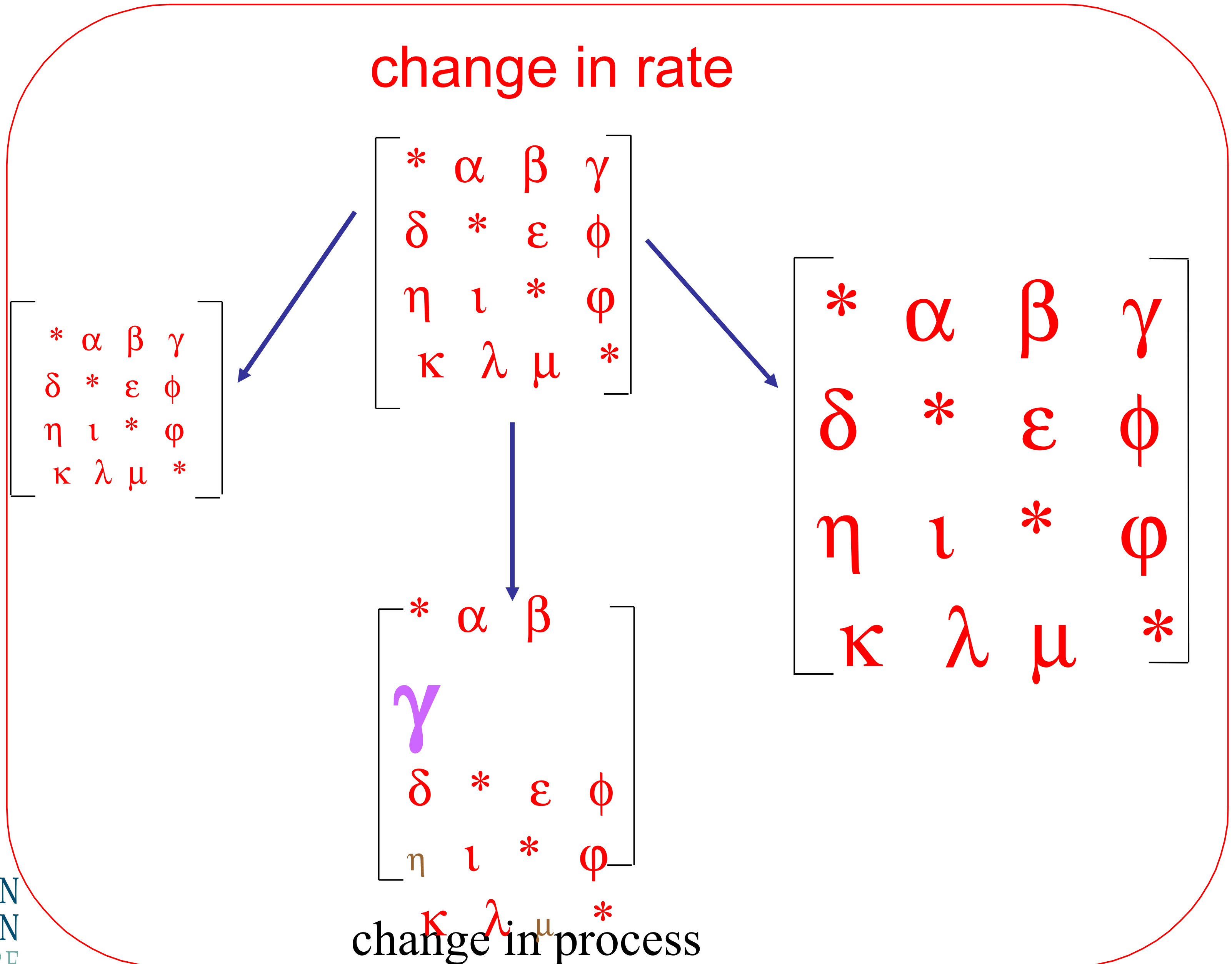
change in rate
* α β γ
δ * ε ϕ
η ι * φ
κ λ μ *
* α β γ
δ * ε ϕ
η ι * φ
κ λ μ *
* α β γ
δ * ε ϕ
η ι * φ
κ λ μ *
* α β
γ
δ * ε ϕ
η ι * φ
κ λ μ *
change in process

do we know anything?

the curse of ‘flat priors’

the ‘we know nothing syndrome’

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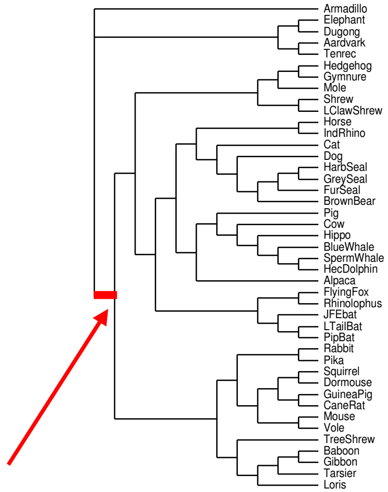
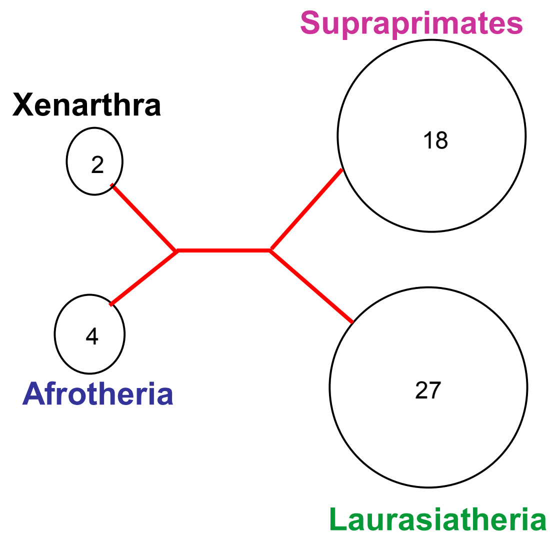
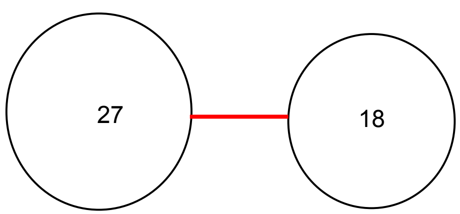
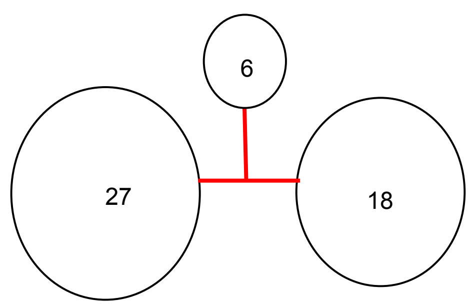




binary trees, b(n) = (2n-5)!!
= 1 x 3 x 5 x 7 … 2n-5.

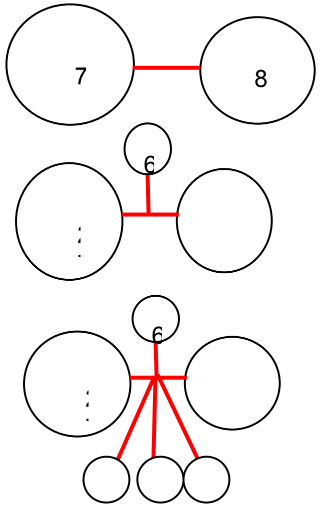




5.68×10^{-18}

binary trees, $b(n) = (2n-5)!!$

$= 1 \times 3 \times 5 \times 7 \ldots 2n-5.$

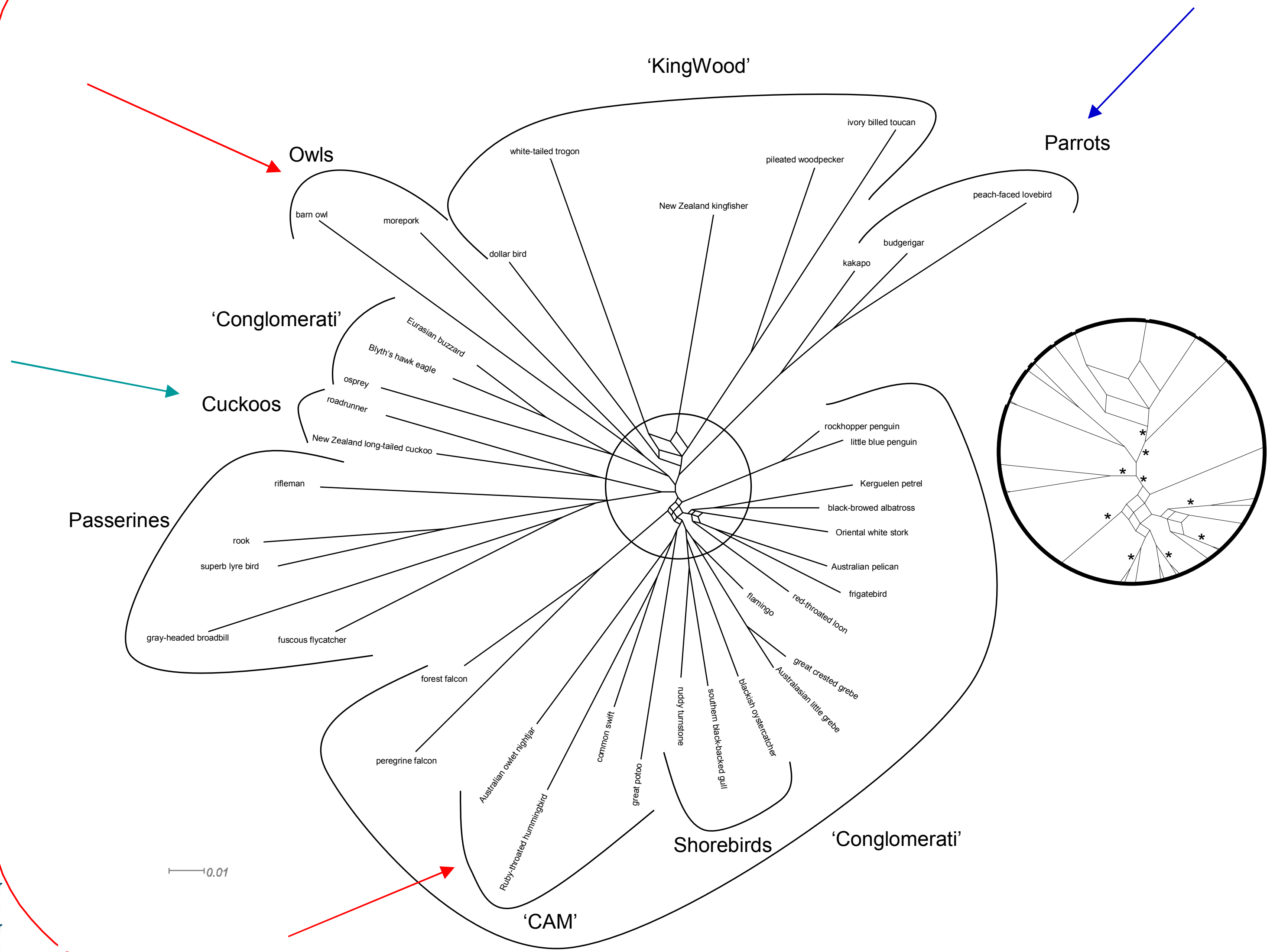


$b(n_1+1).b(n_2+1) / b(n_t)$

$b(n_1+1).b(n_2+1).b(n_3+1) / b(n_t)$

$b(n_1+1).b(n_2+1) \ldots b(n_i+1) / b(n_t)$

40 birds



'KingWood'
Owls
Parrots
'Conglomerati'
Cuckoos
Passerines
Shorebirds
'CAM'
'Conglomerati'
ivory billed toucan
white-tailed trogon
pileated woodpecker
New Zealand kingfisher
peach-faced lovebird
barn owl
morepork
dollar bird
budgerigar
kakapo
Eurasian buzzard
Blyth's hawk eagle
osprey
roadrunner
New Zealand long-tailed cuckoo
rifleman
rook
superb lyre bird
gray-headed broadbill
fuscous flycatcher
rockhopper penguin
little blue penguin
Kerguelen petrel
black-browed albatross
Oriental white stork
Australian pelican
frigatebird
flamingo
red-throated loon
great crested grebe
Australasian little grebe
blackish oystercatcher
southern black-backed gull
ruddy turnstone
great potoo
common swift
Ruby-throated hummingbird
Australian owlet nightjar
peregrine falcon
forest falcon
0.01

$$P(n,k) = \frac{R(k) \times B(n-k+1)}{B(n)}$$

probability with *n* taxa of observing a prespecified clade of size *k*.

with $n = 40$ and

$k = 2$, $P \approx 0.013$ cuckoo,roadrunner

$k = 3$, $P \approx 0.0026$ parrots

$k = 4$, $P \approx 7.12 \times 10^{-6}$,

$k = 5$, $P \approx 5.84 \times 10^{-8}$.

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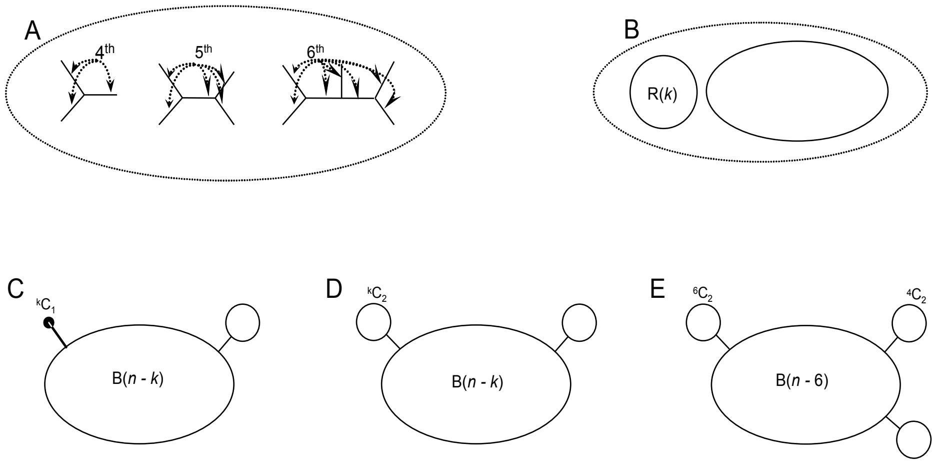

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potoo, owlet-nightjar, owl, barn owl, swift, hummingbird (6)

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Where next in Phylogeny?

allow realism in phylogeny

set the biological question

we have some bad failures

we need a range of alternatives

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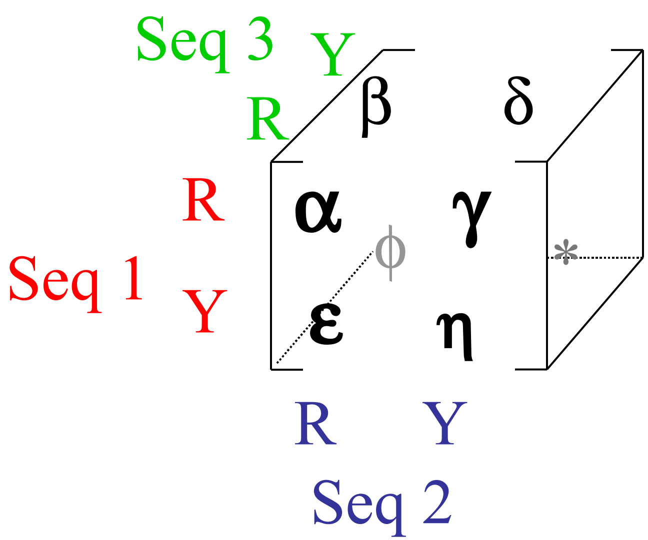
Belief is the curse of the thinking class

tensor, 2-states

Seq 1 ----------------R--
Seq 2 ----------------R--
Seq 3 ----------------R--



R R R α
R R Y β
R Y R γ
R Y Y δ
Y R R ε
Y R Y ϕ
Y Y R η
Y Y Y *
1 2 3

7 available !