PoSeiDon

A Web Server for the Detection of Evolutionary Recombination Events and Positive Selection

Martin Hölzer

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Friedrich Schiller University Jena
RNA Bioinformatics and High Throughput Analysis

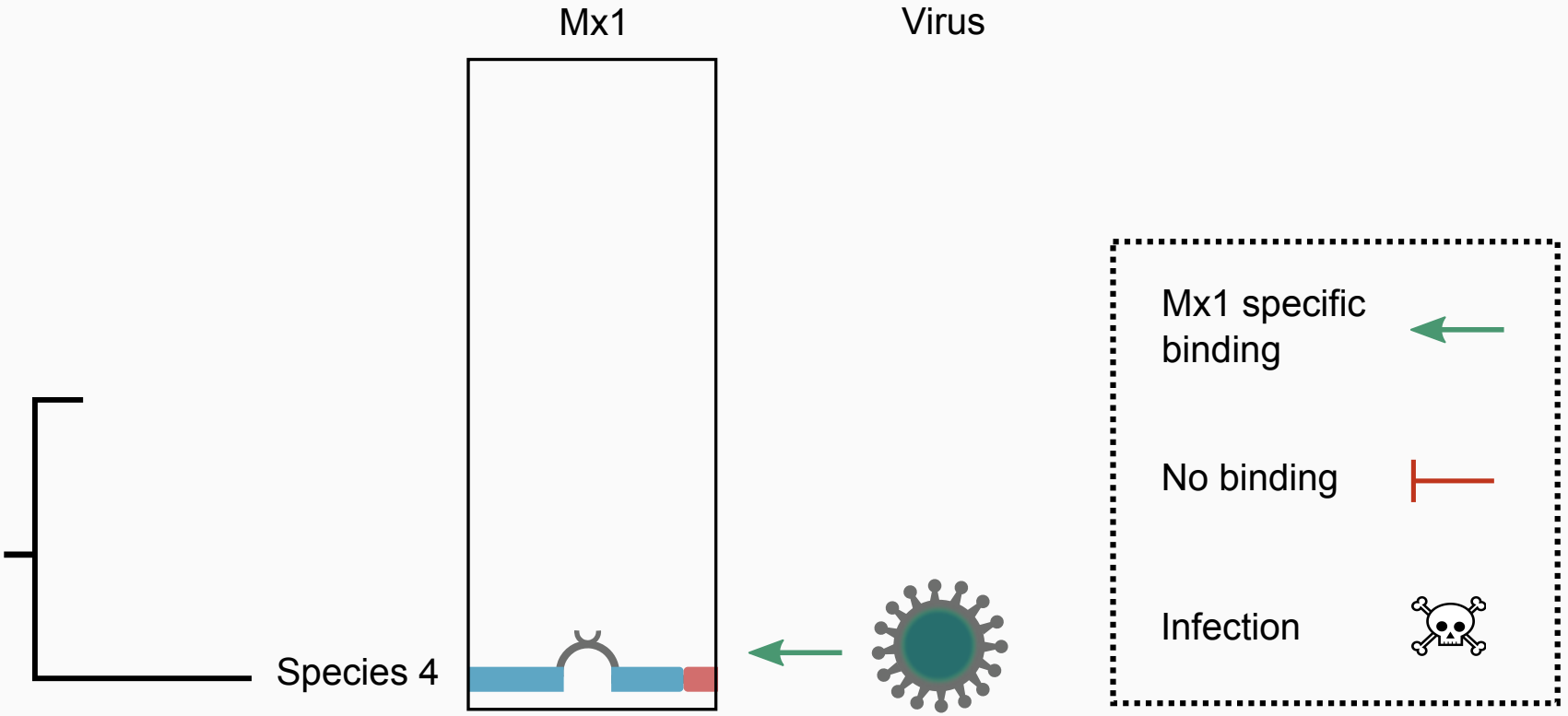
32nd TBI Winterseminar in Bled

Evolutionary Biology

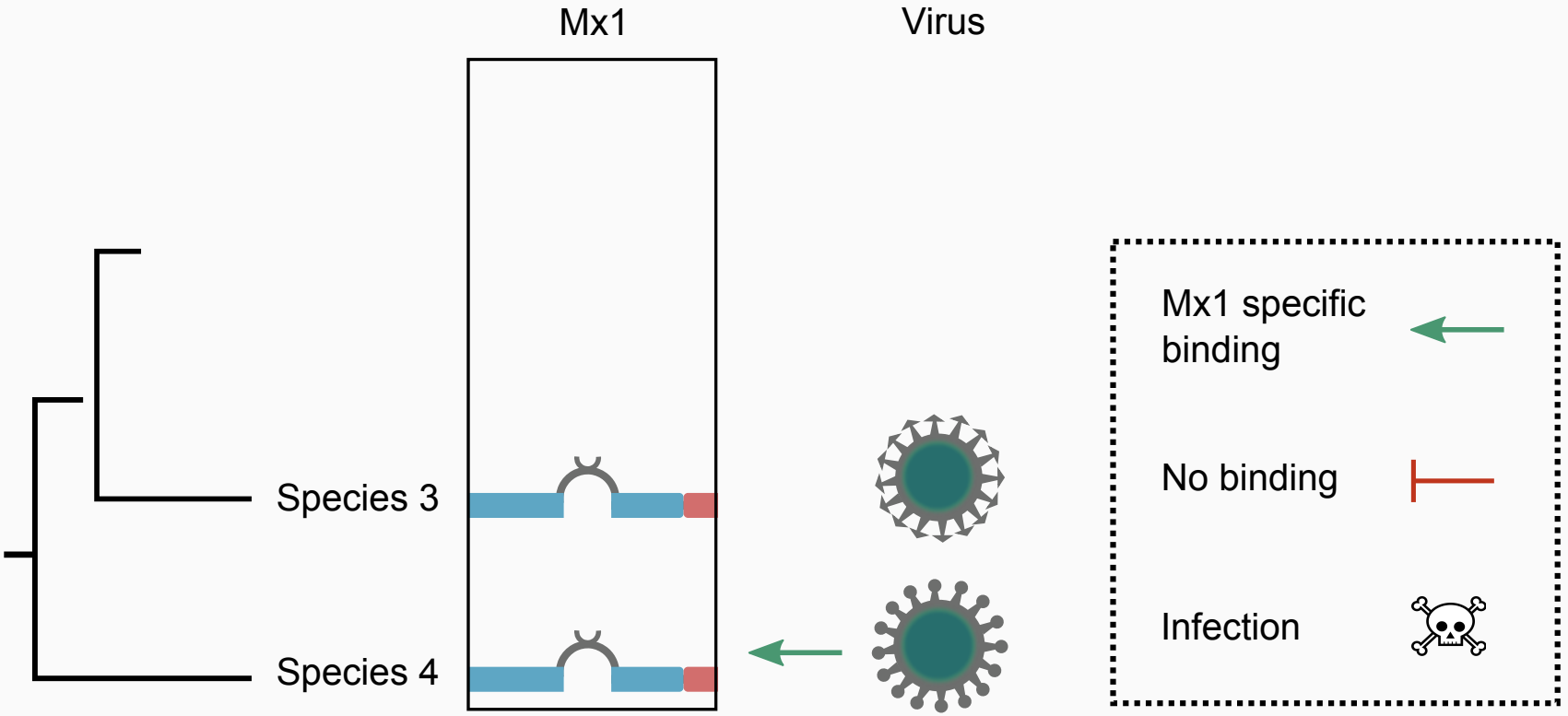
How do protein-coding genes evolve through time and in the various organisms that exist today?

Positive Selection

'Arms Race'


Mx1
Virus
Species 4
Mx1 specific binding
No binding
Infection

'Arms Race'


Mx1
Virus
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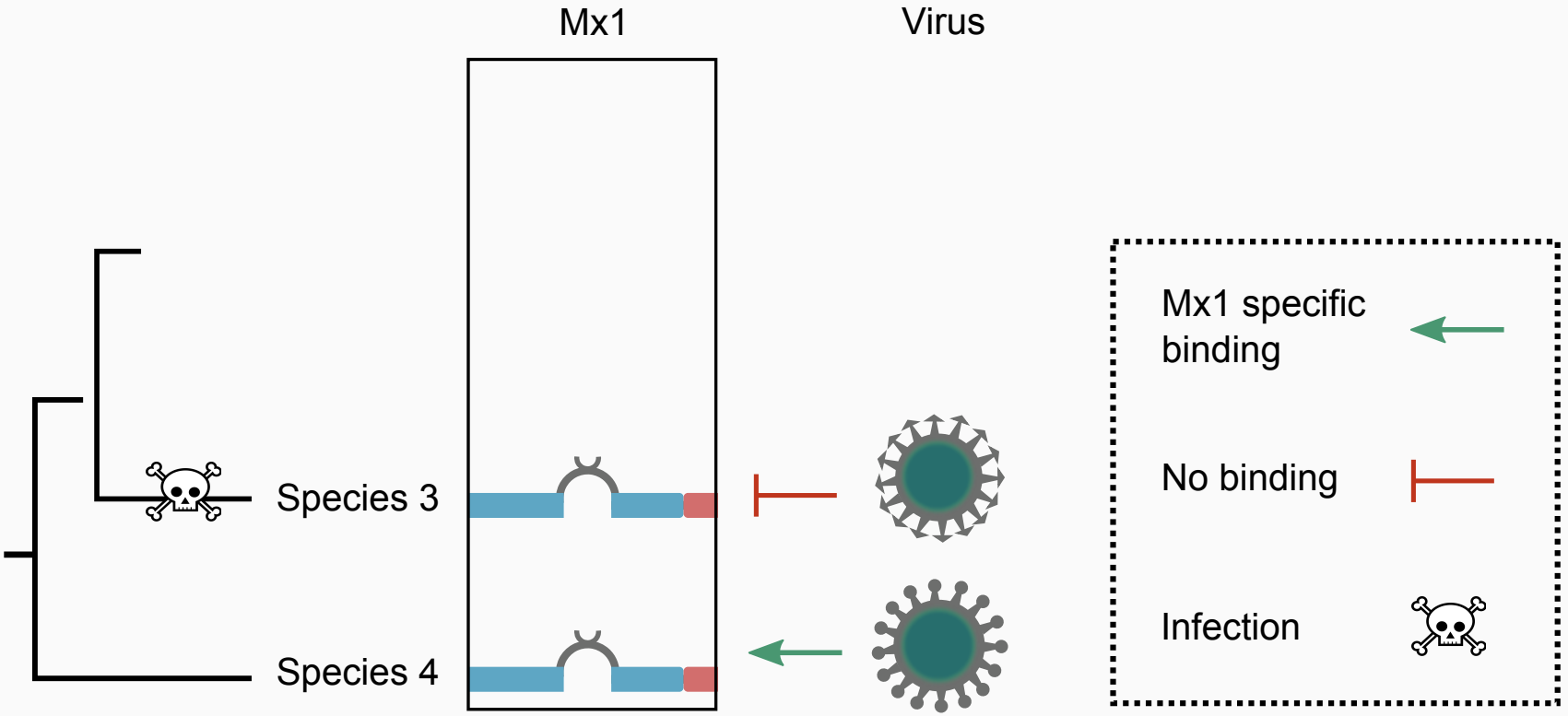
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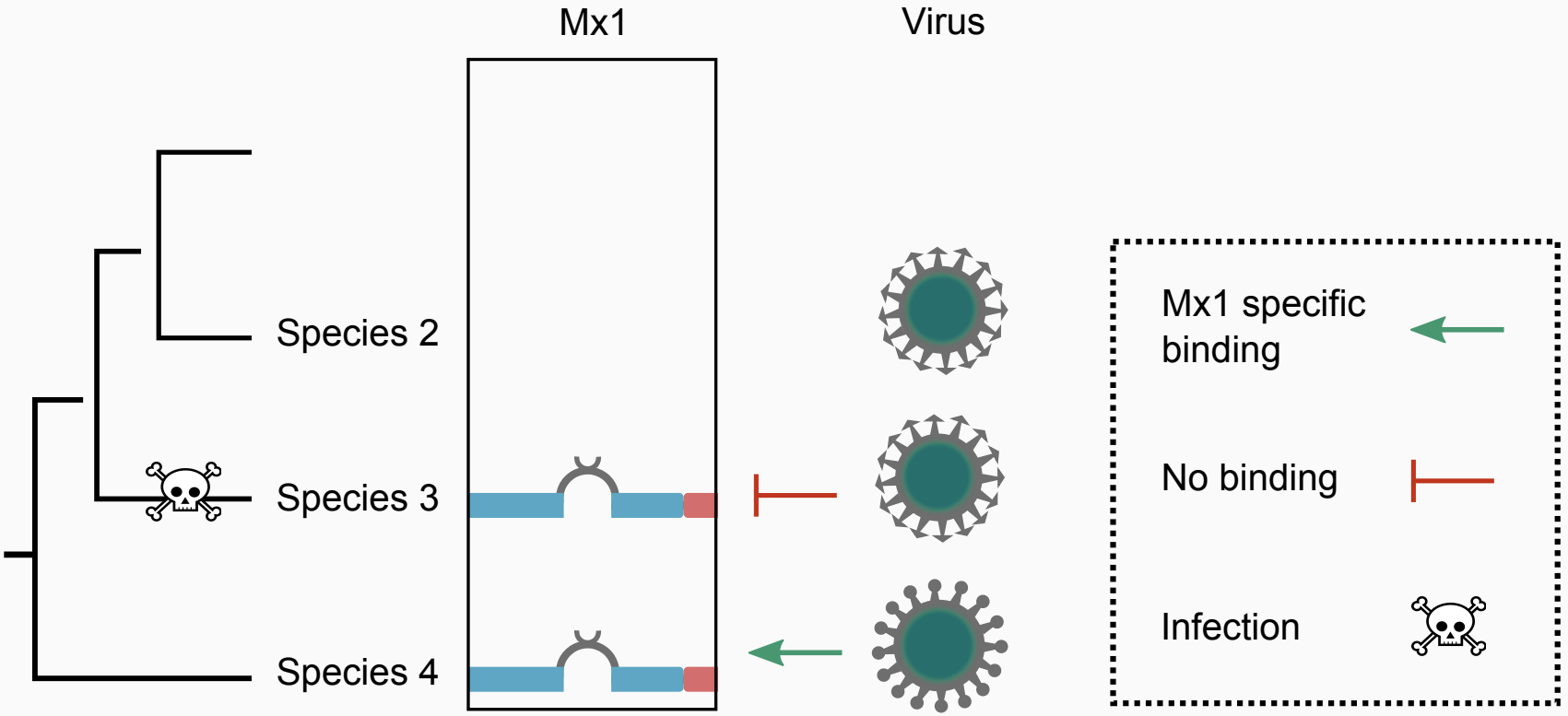
Mx1
Virus
Species 2
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Species 4
Mx1 specific binding
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Infection

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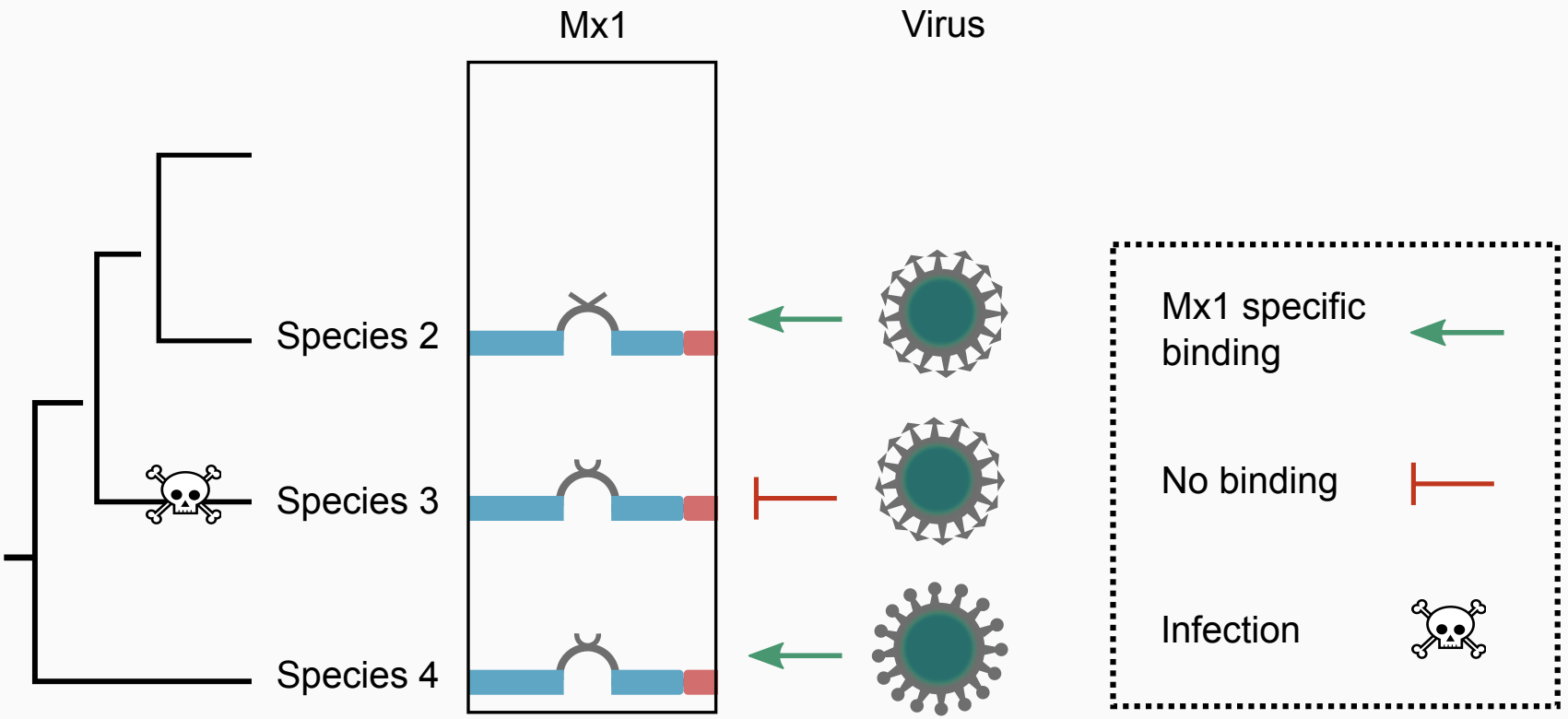
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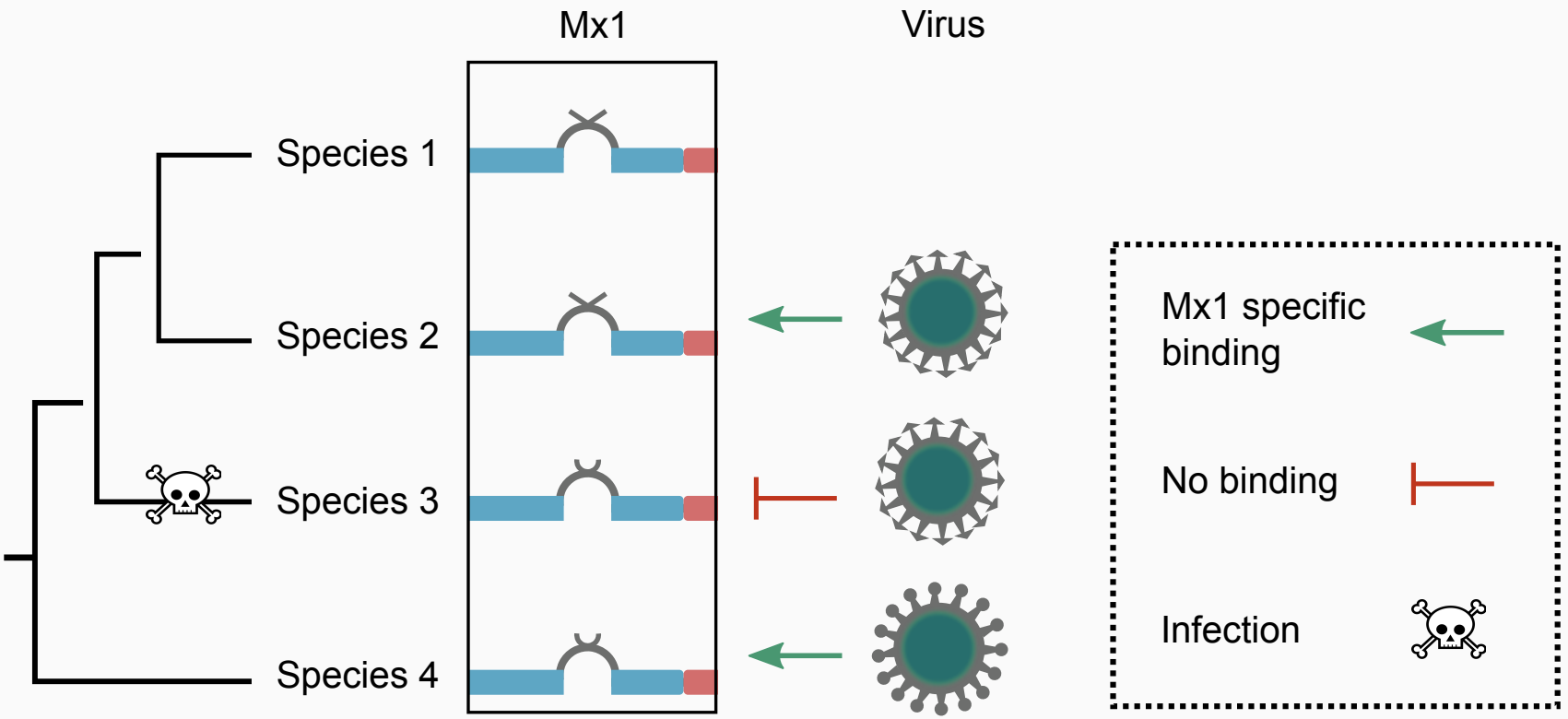
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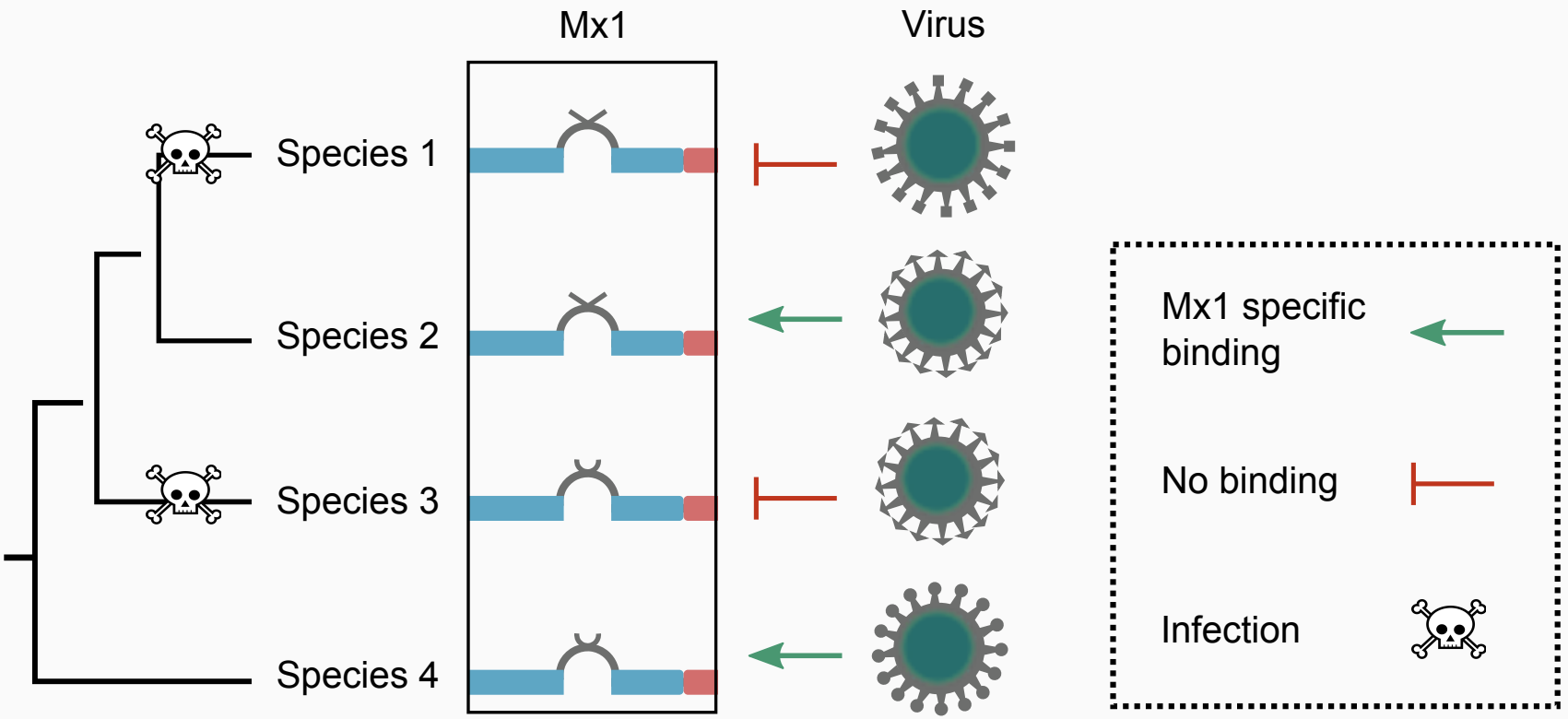
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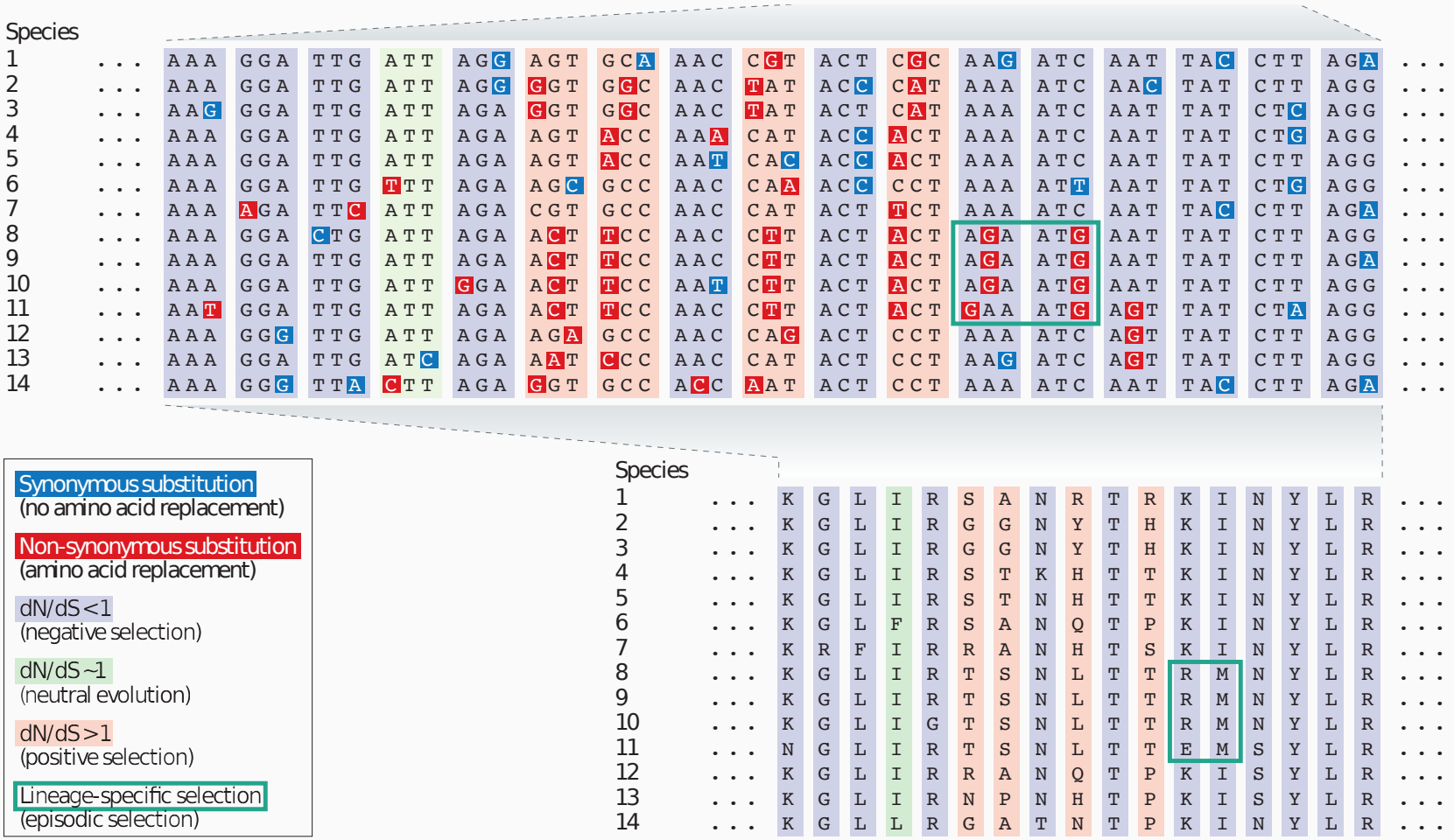
Co-Evolution and detecting natural selection



Sironi, Manuela, *et al.* "Evolutionary insights into host-pathogen interactions from mammalian sequence data." *Nature Reviews Genetics* 16.4 (2015): 224-236.

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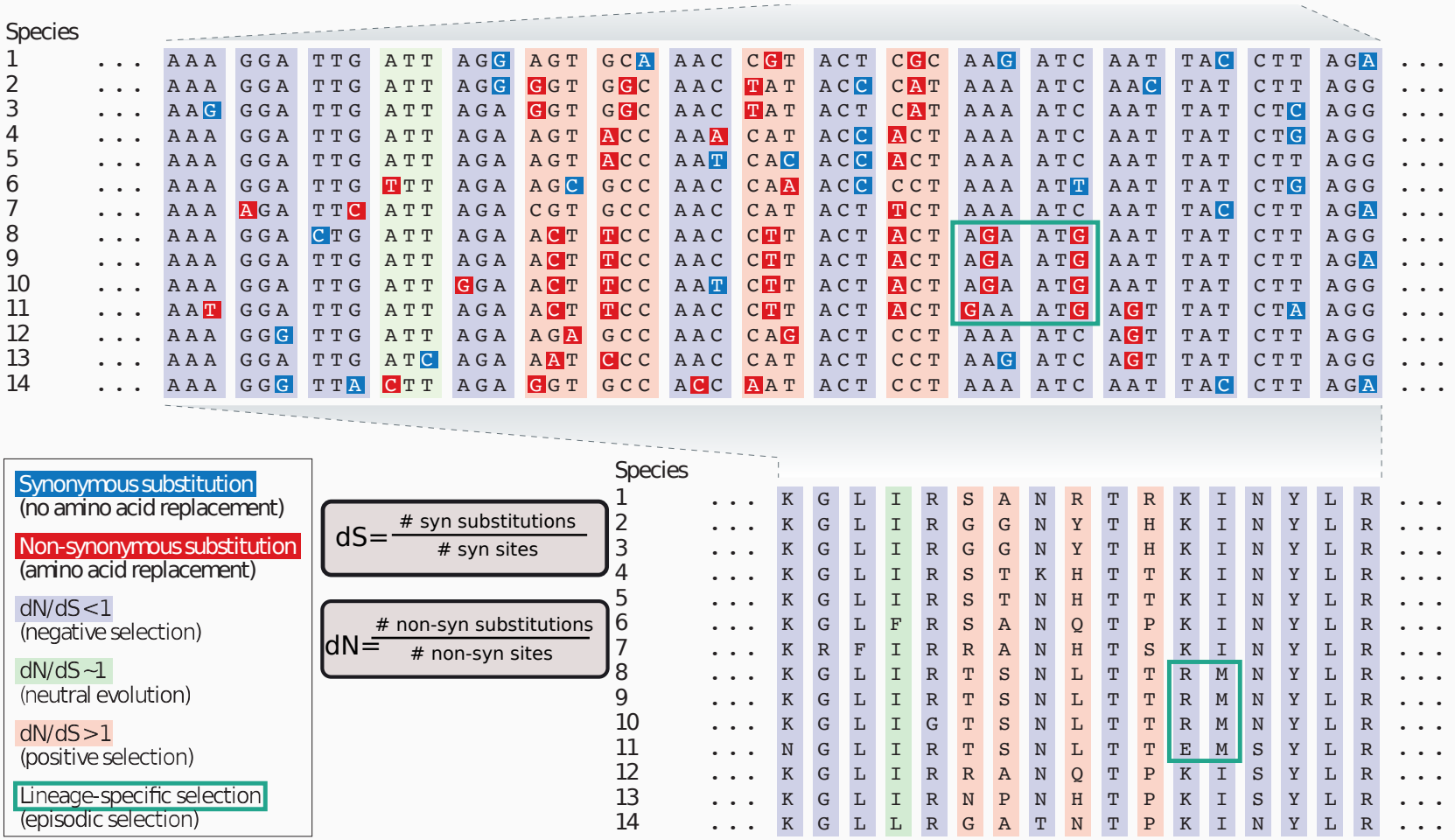

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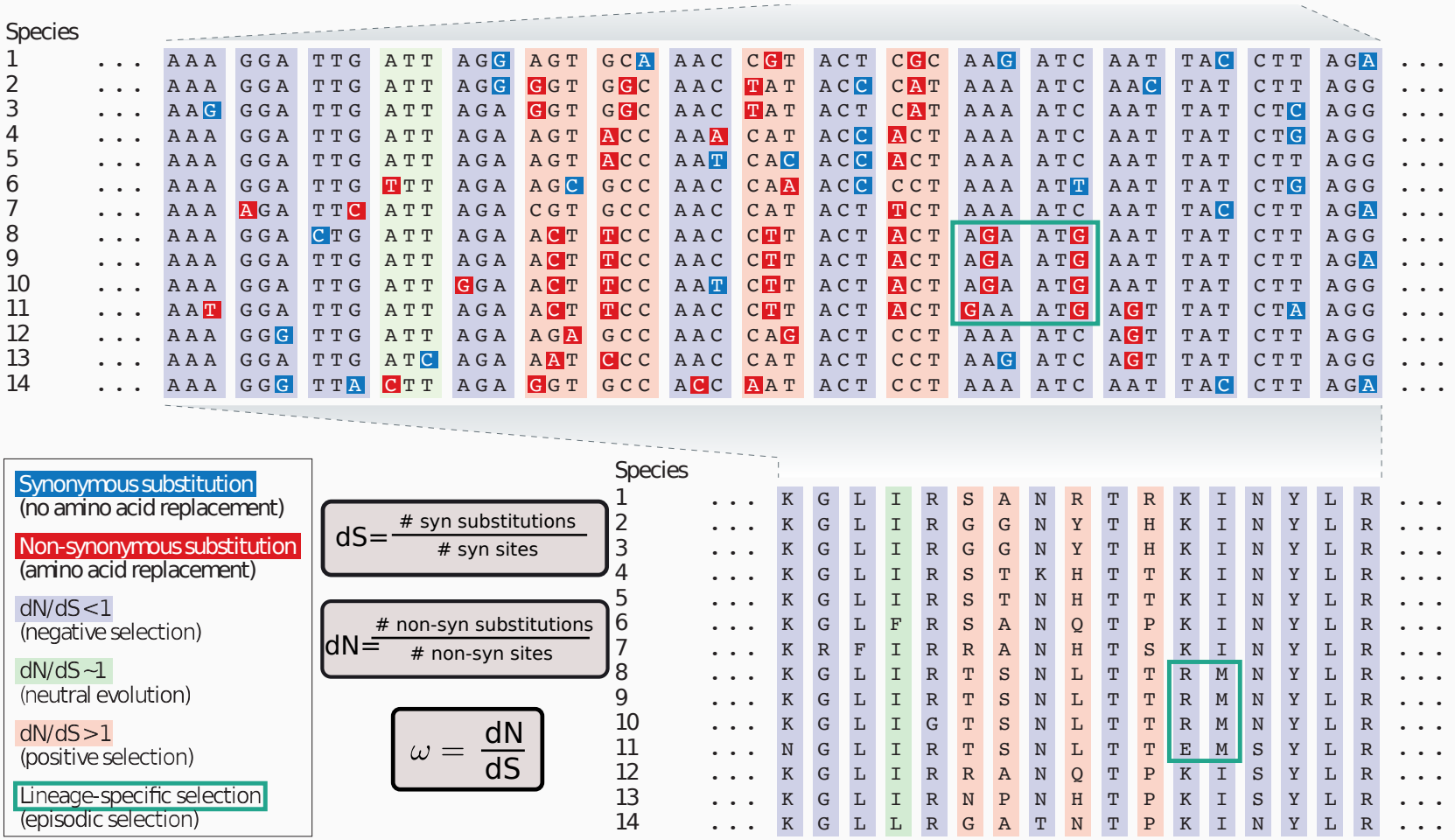

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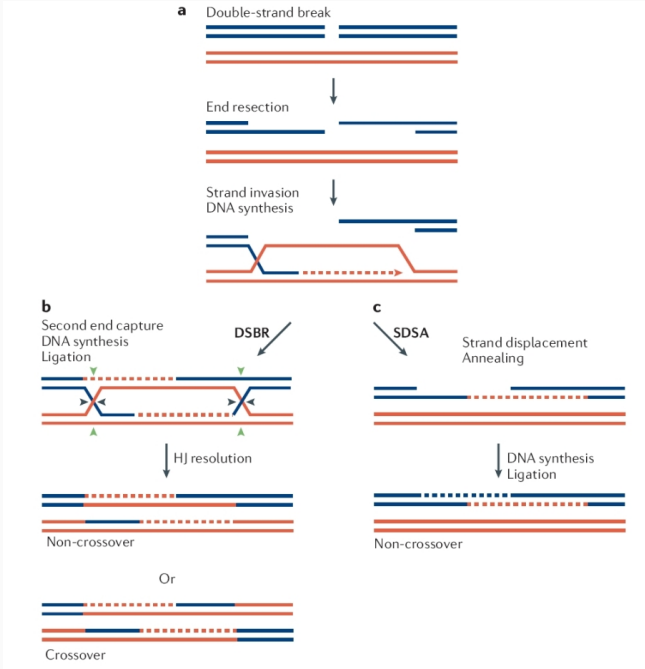
Recombination

Genetic Recombination

- Rearrangement of genetic information within and among DNA molecules
- If recombination, then possibly no unique tree topology can describe the evolutionary history of the whole sequence

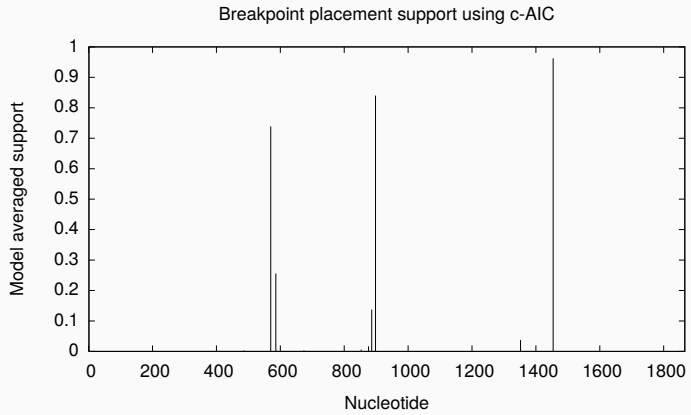


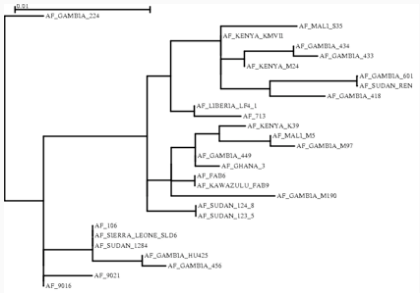
Clancy, S. (2008) "Genetic recombination." *Nature Education* 1(1):40

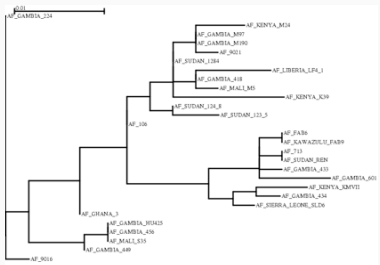
Genetic Recombination

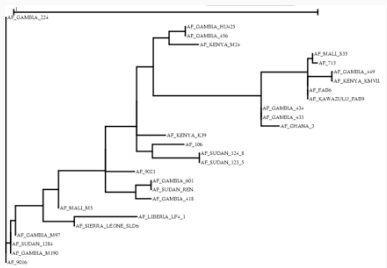
GARD found evidence of 3 breakpoints

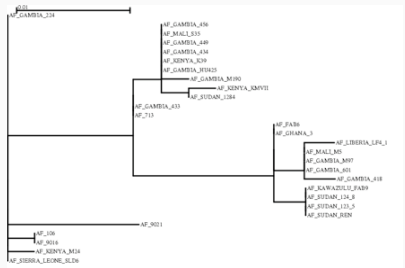
BPs	c-AIC	Δ c-AIC	Segments
0	7902.02		1-1866
1	7642.2	259.812	898
2	7518.5	123.708	724 1454
3	7424.64	93.8553	570 898 1454
4	7424.64	0	570 898 1454







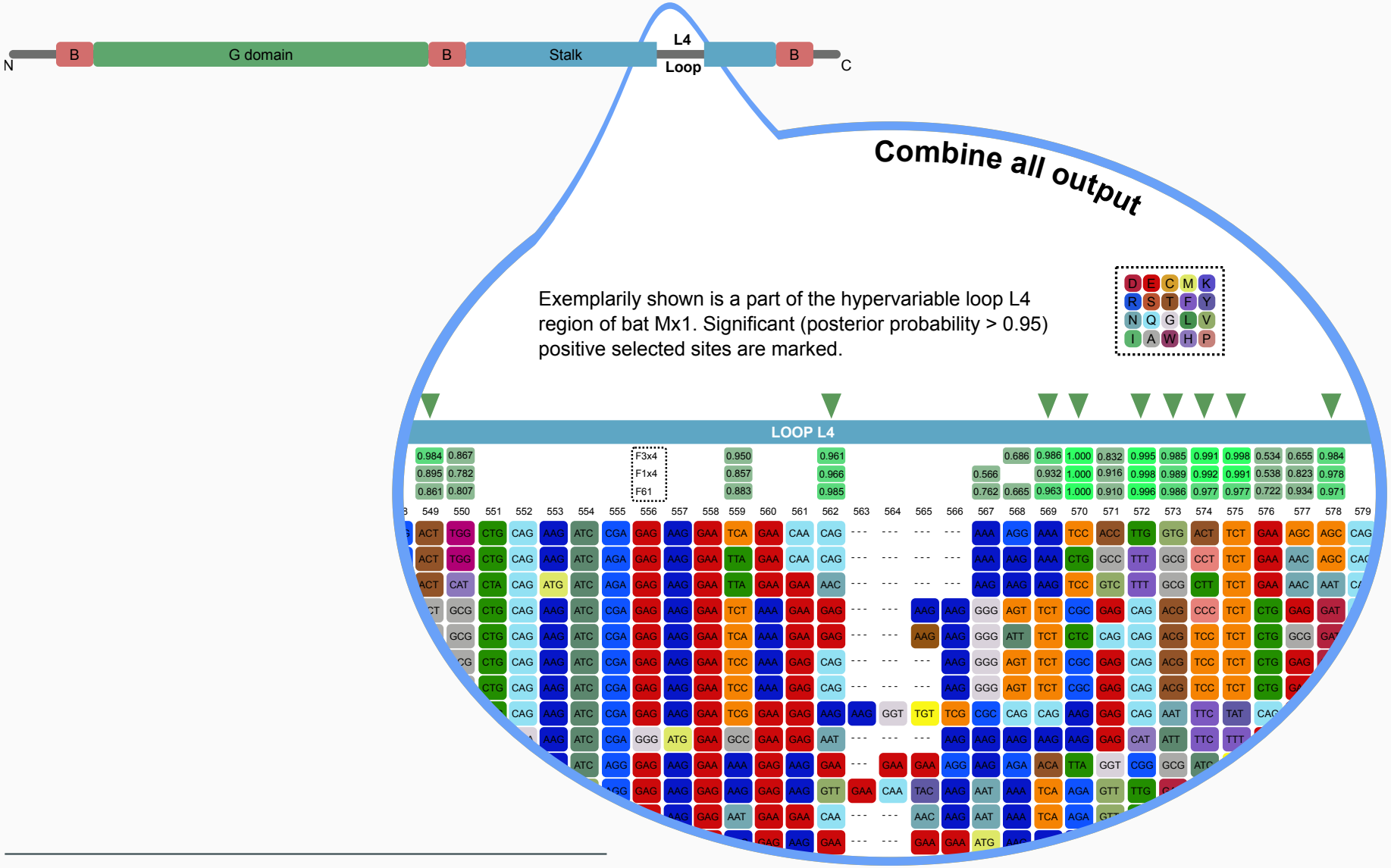




Pond, Sergei L. Kosakovsky, *et al.* "GARD: a genetic algorithm for recombination detection." *Bioinformatics* 22.24 (2006): 3096-3098.

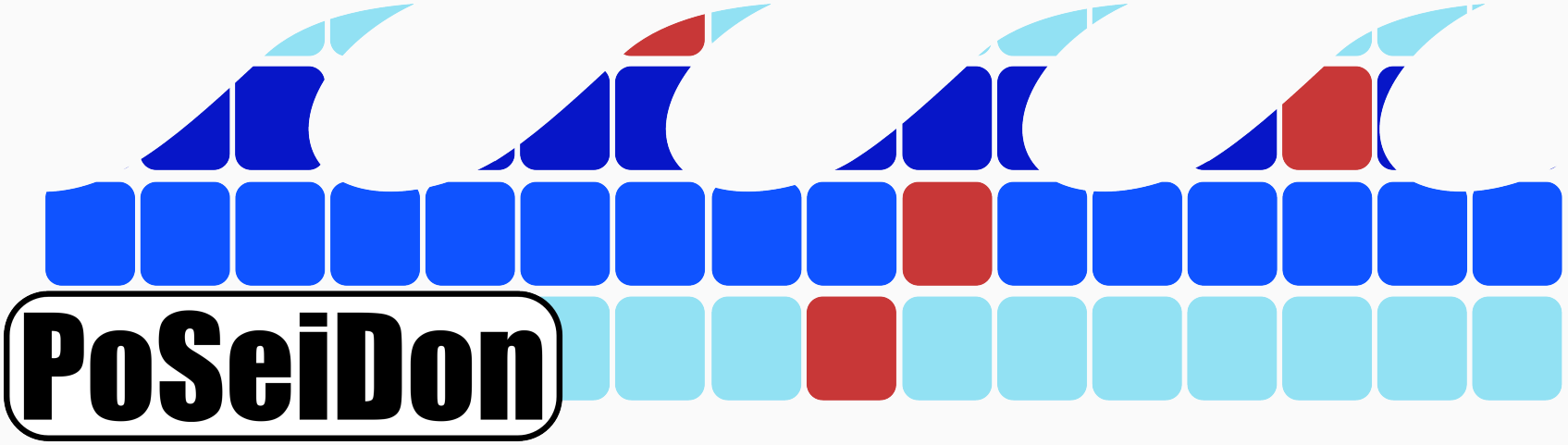
Previous Work

Positive Selection in bat MX1



Fuchs, Jonas *et al.*, "Evolution and antiviral specificity of interferon-induced Mx proteins of bats." Submitted.

Positive Selection Detection and Recombination Analysis



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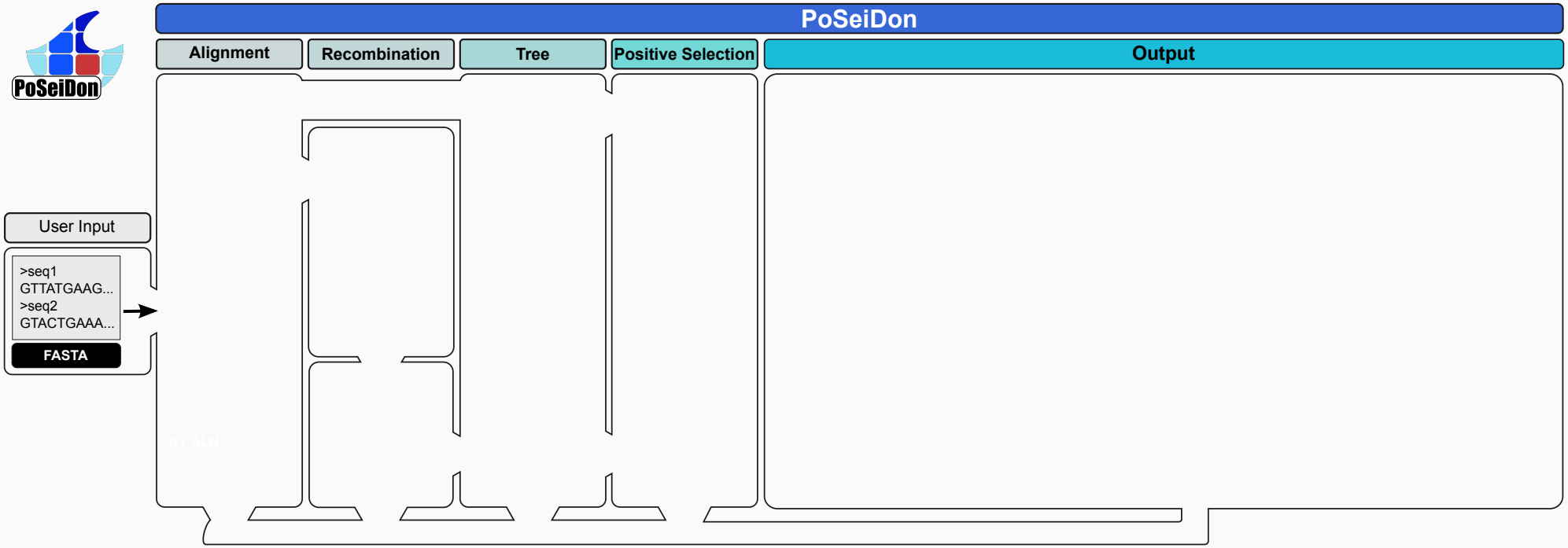

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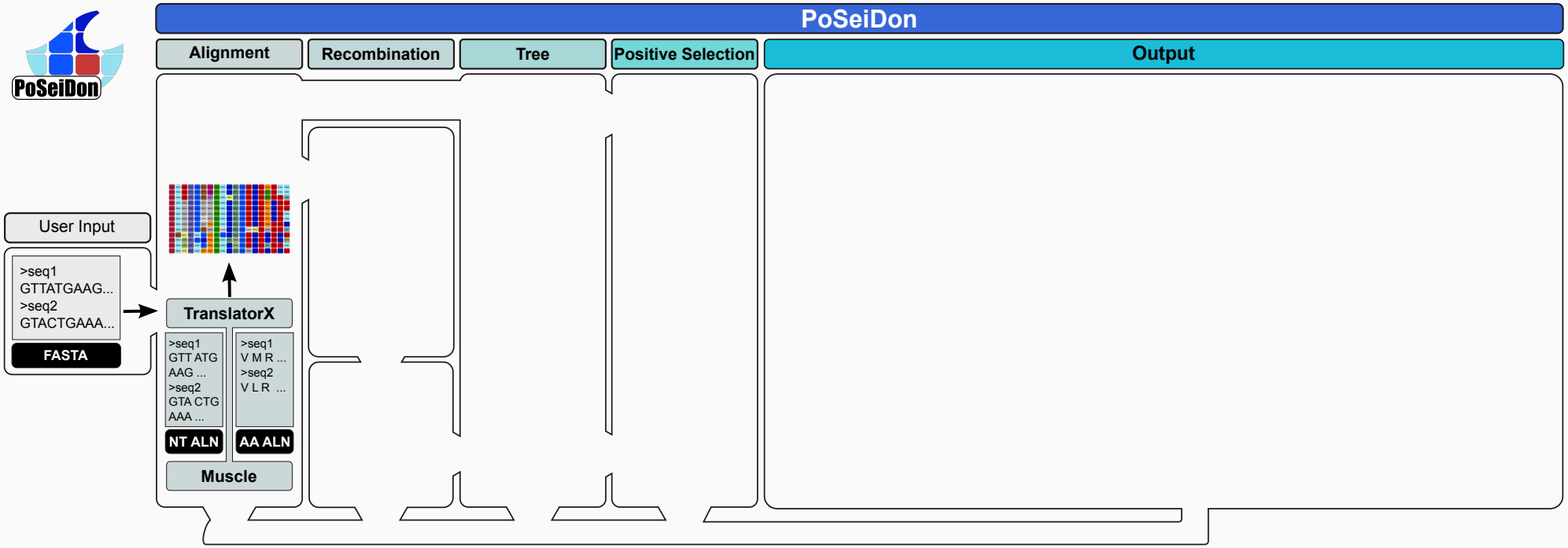

Abascal, Federico, Rafael Zardoya, and Maximilian J. Telford. "TranslatorX: multiple alignment of nucleotide sequences guided by amino acid translations." *Nucleic acids research* (2010): gkq291.

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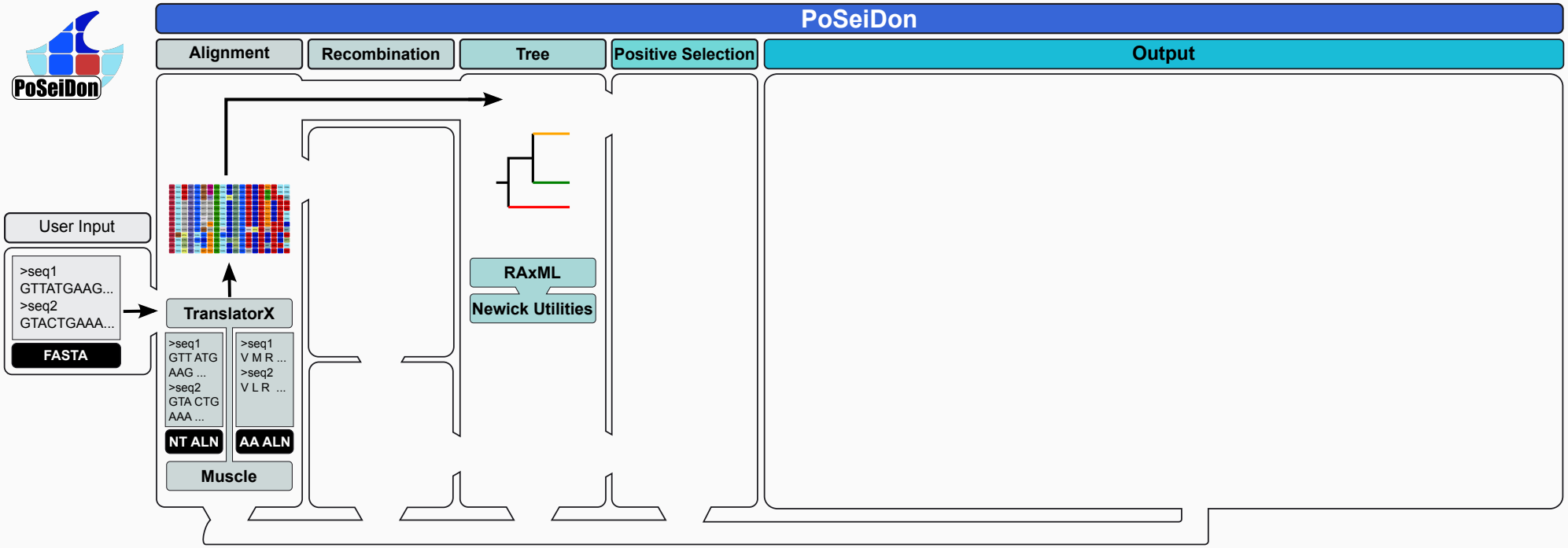

Stamatakis, Alexandros. "RAxML version 8: a tool for phylogenetic analysis and post-analysis of large phylogenies." *Bioinformatics* 30.9 (2014): 1312-1313.

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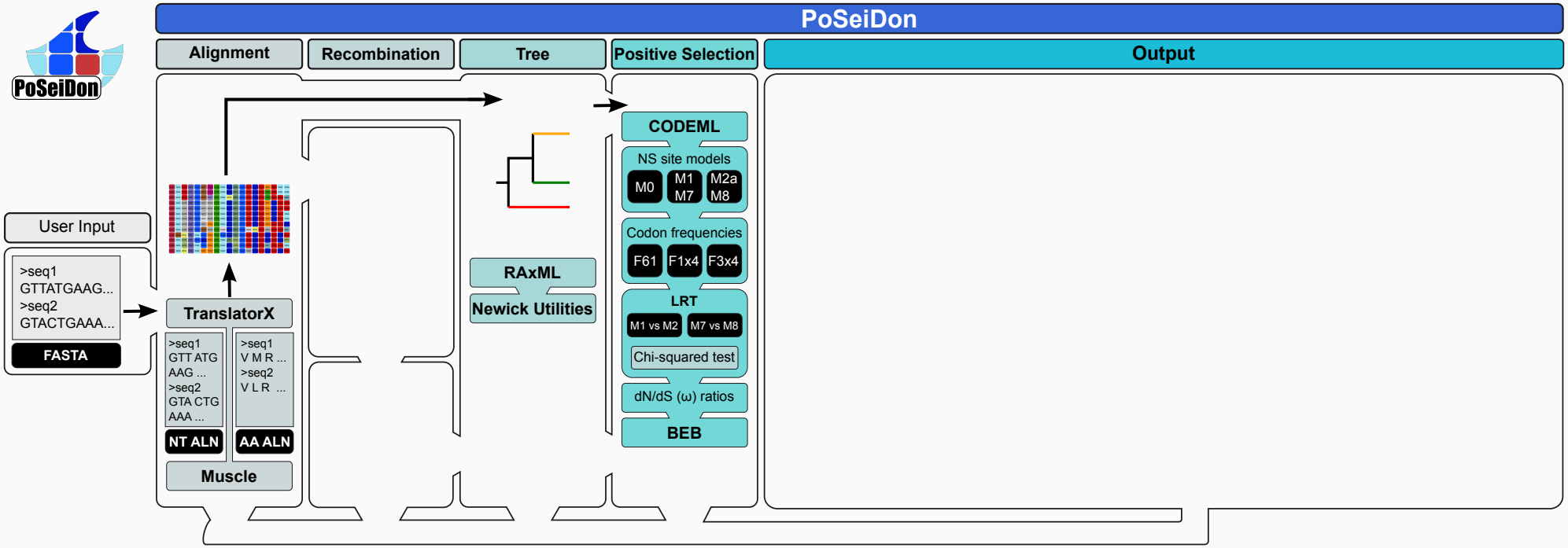

Yang, Ziheng. "PAML 4: phylogenetic analysis by maximum likelihood." *Molecular biology and evolution* 24.8 (2007): 1586-1591.

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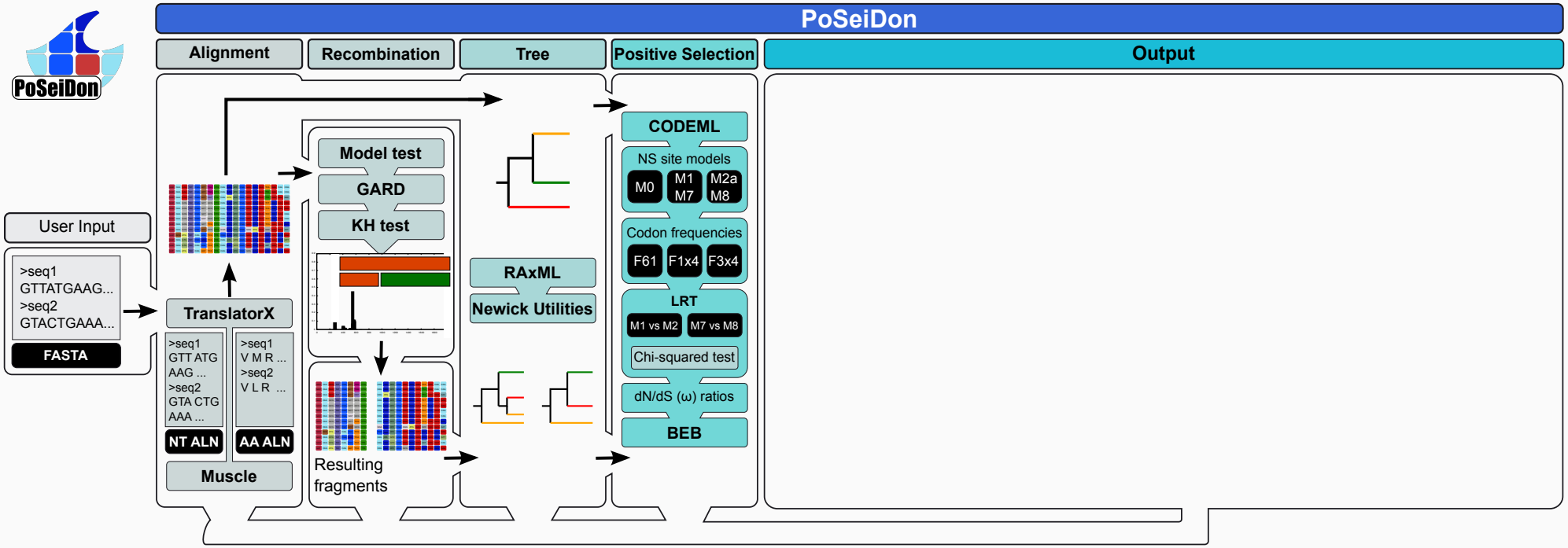

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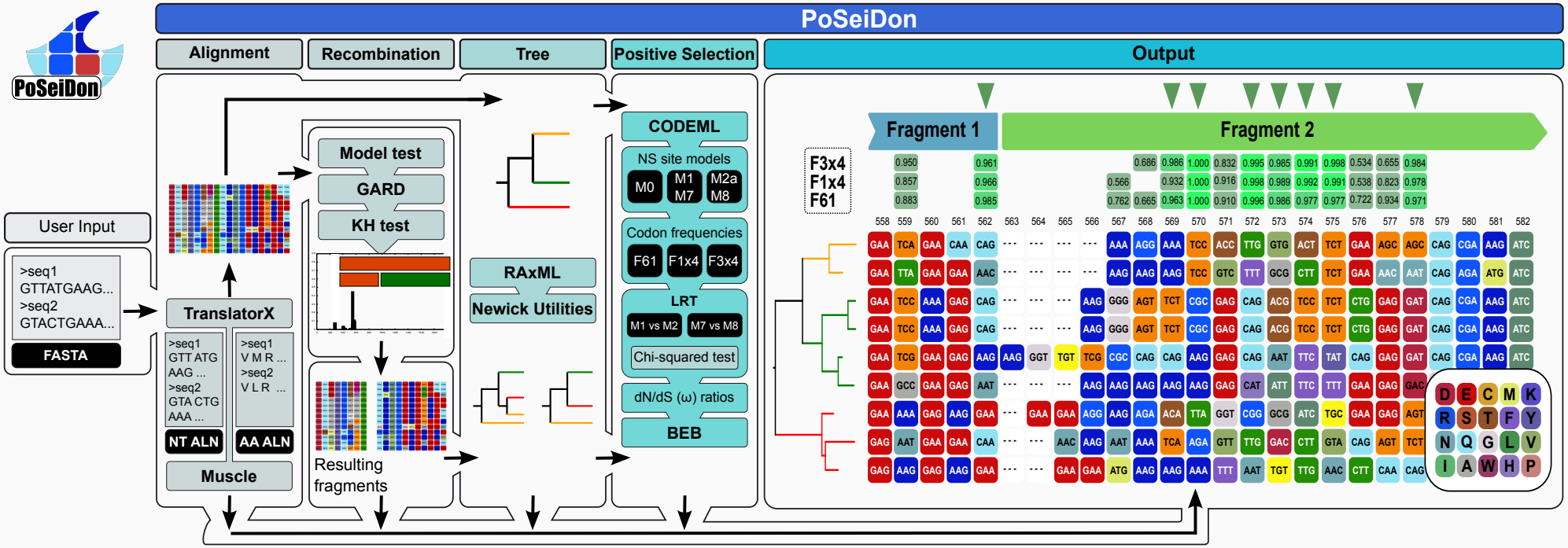

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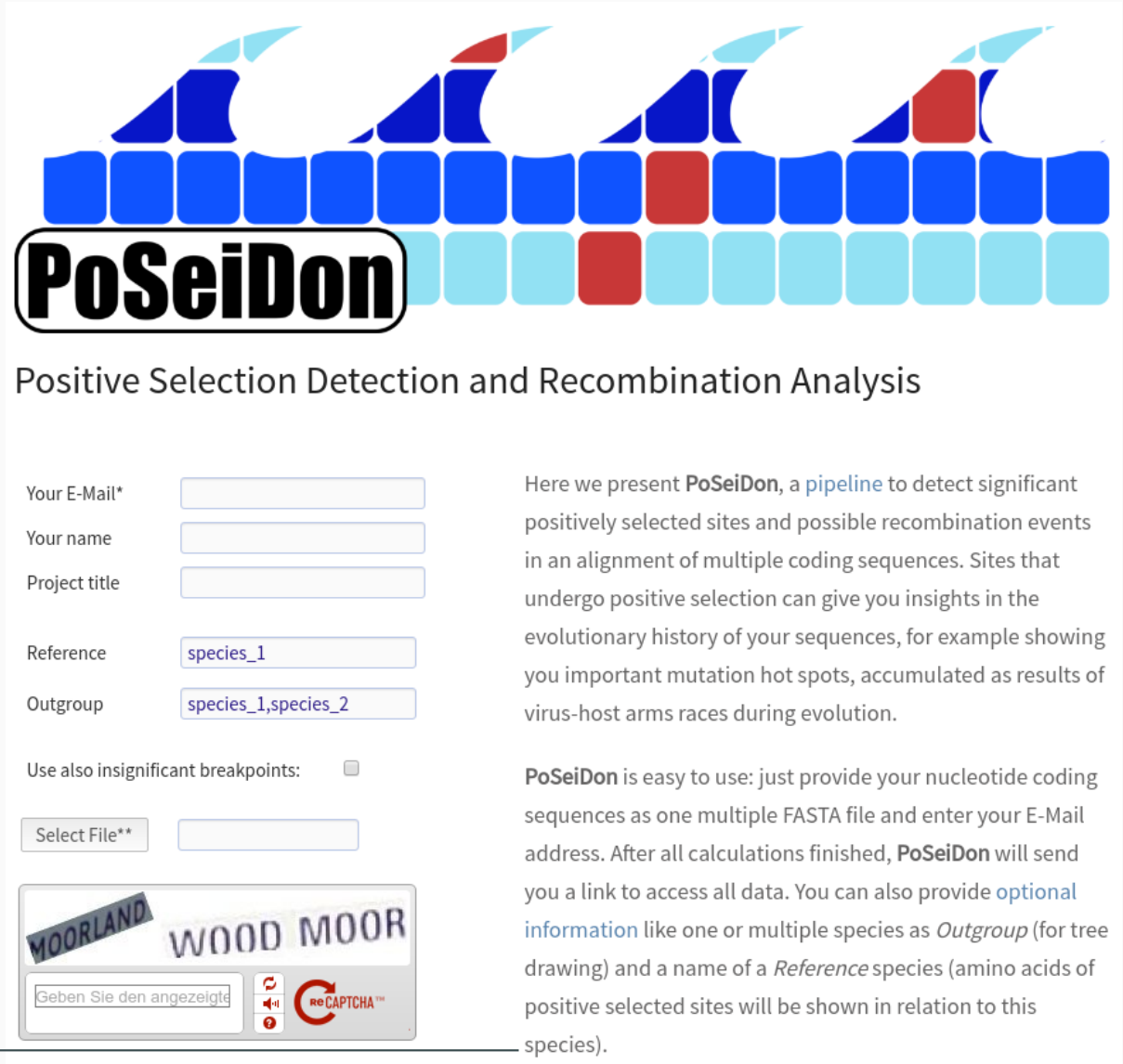
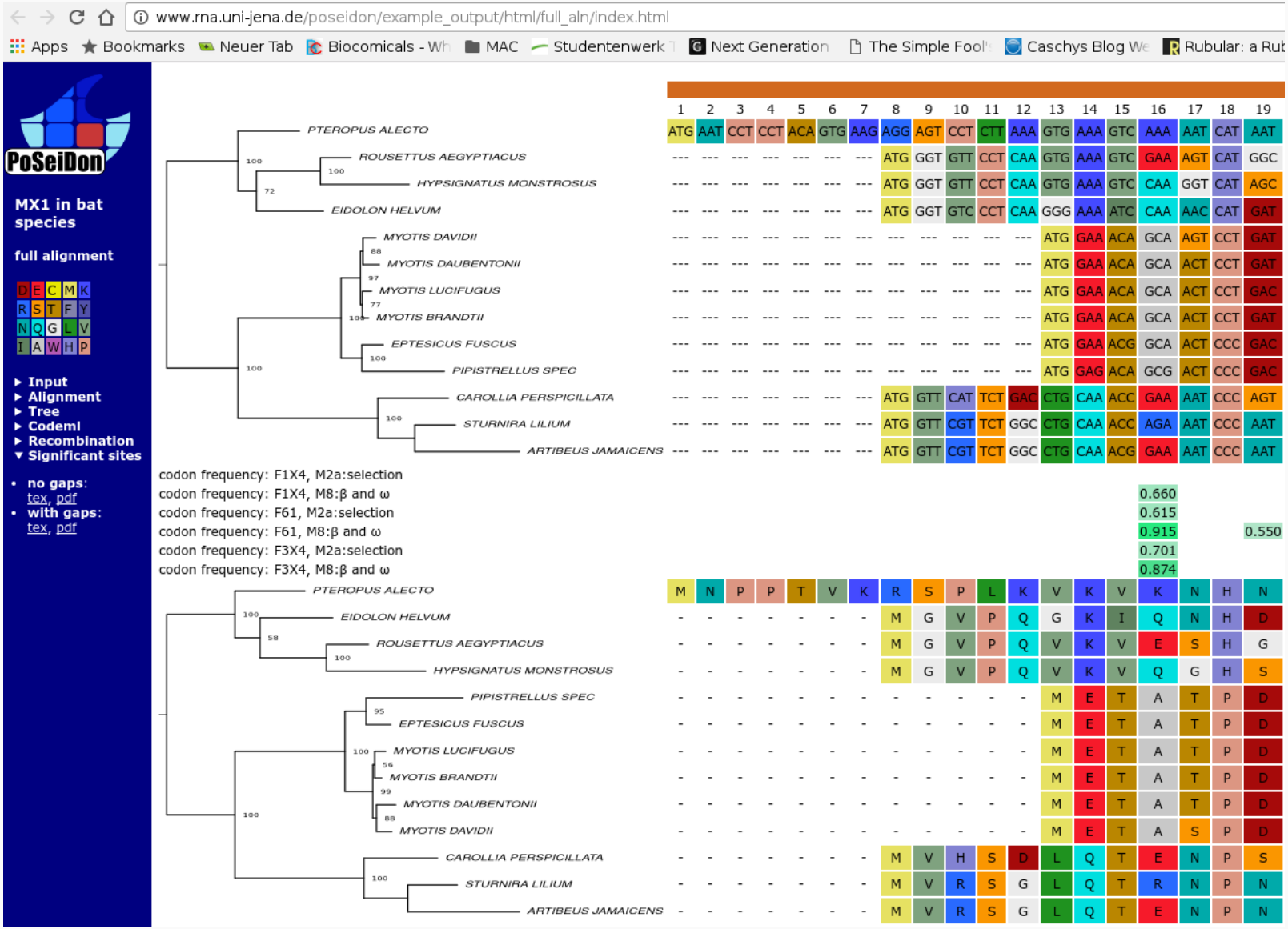
The Interface



`www.rna.uni-jena.de/poseidon`

The Output


www.rna.uni-jena.de/poseidon/example_output/html/full_aln/index.html
Apps
Bookmarks
Neuer Tab
Biocomicals - Wh
MAC
Studentenwerk T
Next Generation
The Simple Fool
Caschys Blog We
Rubular: a Rub
PoSeiDon
MX1 in bat species
full alignment
Input
Alignment
Tree
Codeml
Recombination
Significant sites
no gaps: tex, pdf
with gaps: tex, pdf
PTEROPUS ALECTO
ROUSETTUS AEGYPTIACUS
HYPSIGNATUS MONSTROSUS
EIDOLON HELVUM
MYOTIS DAVIDII
MYOTIS DAUBENTONII
MYOTIS LUCIFUGUS
MYOTIS BRANDTII
EPTESICUS FUSCUS
PIPISTRELLUS SPEC
CAROLLIA PERSPICILLATA
STURNIRA LILIUM
ARTIBEUS JAMAICENS
codon frequency: F1X4, M2a:selection
codon frequency: F1X4, M8:β and ω
codon frequency: F61, M2a:selection
codon frequency: F61, M8:β and ω
codon frequency: F3X4, M2a:selection
codon frequency: F3X4, M8:β and ω
0.660
0.615
0.915
0.550
0.701
0.874

Outlook

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- improve interface
- support `branch-site` models
- upload your own tree/alignment
- distribute source code to run on local machines

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- check and include suggestions of the reviewers 

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Thanks!

Questions?

Backup slides

"Now, here, you see, it takes all the running you can do, to keep in the same place."

– Red Queen to Alice in Lewis Carroll's *"Through the Looking-Glass"*

Run for your Lives!

"Now, here, you see, it takes all the running you can do, to keep in the same place."

Iron Maiden *et al.* "The Number of the Beast (album)." EMI, *Battery Studios*, 39:11, London, England (1982)

Calculating selective pressure, K_a/K_s

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- K_a/K_s – dN/dS – ω κ – Ts/Tv

Example: calculating K_a/K_s

Val			Met			Arg			Thr			
G	T	T	A	T	G	A	A	G	A	C	C	Total

Example: calculating K_a/K_s

		Val			Met			Arg			Thr			
	G	T	T	A	T	G	A	A	G	A	C	C	Total
degeneracy			(4)						(2)			(4)	

Example: calculating K_a/K_s

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	G	T	T	A	T	G	A	A	G	A	C	C	Total
degeneracy			(4)						(2)			(4)	
# non-syn sites	1	1	0	1	1	1	1	1	$\frac{2}{3}$	1	1	0	$9\frac{2}{3}$

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	G	T	T	A	T	G	A	A	G	A	C	C	Total
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# syn sites	0	0	1	0	0	0	0	0	$\frac{1}{3}$	0	0	1	$2\frac{1}{3}$

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	G	T	T	A	T	G	A	A	G	A	C	C	Total
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- nucleotide sites give $9\frac{2}{3}$ non-synonymous sites and $2\frac{1}{3}$ synonymous sites in this peptide

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	G	T	T	A	T	G	A	A	G	A	C	C	Total
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Val			**Leu**			Arg			Thr			
G	T	**A**	**C**	T	G	A	A	**A**	A	C	C	Total

Example: calculating K_a/K_s

	Val			Met			Arg			Thr			
	G	T	T	A	T	G	A	A	G	A	C	C	Total
degeneracy			(4)						(2)			(4)	
# non-syn sites	1	1	0	1	1	1	1	1	$\frac{2}{3}$	1	1	0	$9\frac{2}{3}$
# syn sites	0	0	1	0	0	0	0	0	$\frac{1}{3}$	0	0	1	$2\frac{1}{3}$

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	Val			**Leu**			Arg			Thr			
	G	T	**A**	**C**	T	G	A	A	**A**	A	C	C	Total
# substitutions													
# non-syn	0	0	0	1	0	0	0	0	0	0	0	0	1

Example: calculating K_a/K_s

	Val			Met			Arg			Thr			
	G	T	T	A	T	G	A	A	G	A	C	C	Total
degeneracy			(4)						(2)			(4)	
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	Val			**Leu**			Arg			Thr			
	G	T	**A**	**C**	T	G	A	A	**A**	A	C	C	Total
# substitutions													
# non-syn	0	0	0	1	0	0	0	0	0	0	0	0	1
# syn	0	0	1	0	0	0	0	0	1	0	0	0	2

Example: calculating K_a/K_s

Now,

$$K_a = \frac{\#nonsyn\_substitutions}{\#nonsyn\_sites} = \frac{1}{9\frac{2}{3}} = 0.103$$

and

$$K_s = \frac{\#syn\_substitutions}{\#syn\_sites} = \frac{2}{2\frac{1}{3}} = 0.857$$

Thus,

$$\frac{K_a}{K_s} = \frac{dN}{dS} = \omega = \frac{0.103}{0.857} = 0.12$$

CodeML: **Output**

- *CodonFreq=F3x4* (estimation of codon frequency distribution)
- *NSsites=M2a* (positive selection)

Model	NSsites	p	Parameters
M0 (one ratio)	0	1	ω
M1a (neutral)	1	2	p_0 ($p_1 = 1 - p_0$), $\omega_0 < 1$, $\omega_1 = 1$
M2a (selection)	2	4	p_0, p_1 ($p_2 = 1 - p_0 - p_1$), $\omega_0 < 1$, $\omega_1 = 1$, $\omega_2 > 1$
M3 (discrete)	3	5	p_0, p_1 ($p_2 = 1 - p_0 - p_1$) ω_0, ω_1, ω_2
M7 (beta)	7	2	p, q
M8 (beta&ω)	8	4	p_0 ($p_1 = 1 - p_0$), p, q, $\omega_s > 1$

NOTE.—The site models are implemented using the control variable NSsites in CODEML, and p is the number of free parameters in the ω distribution.

$\Longrightarrow$ [codeml.variable.mlc]