Tests of Positive Selection based on the Comparison of Polymorphism and Divergence

Julien Dutheil

dutheil@evolbio.mpg.de

Max Planck Institute for Evolutionary Biology

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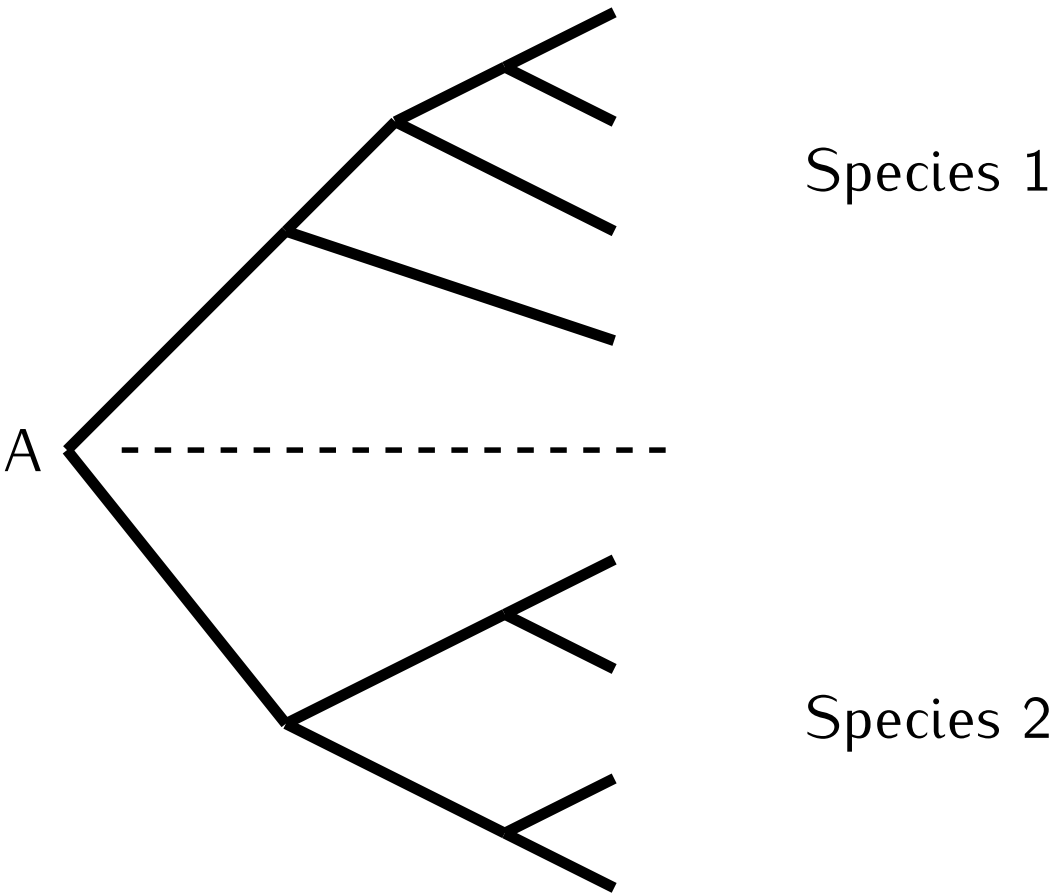
Within vs. between species



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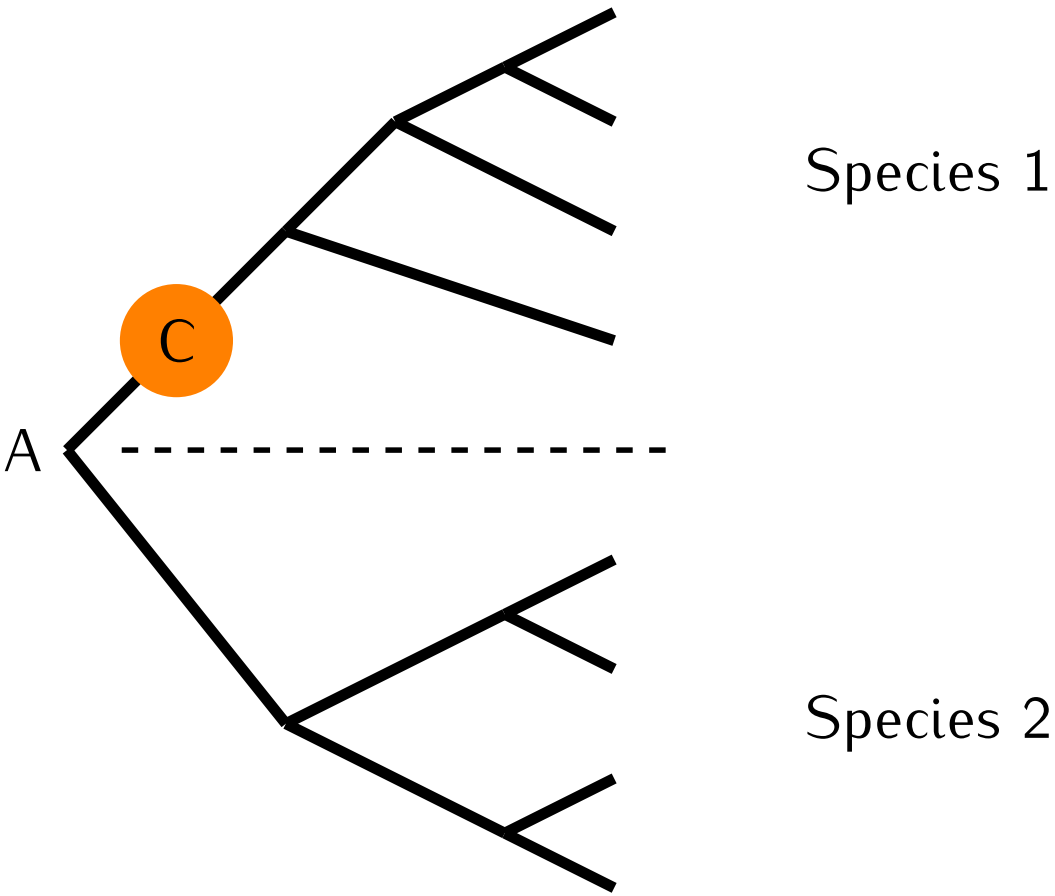

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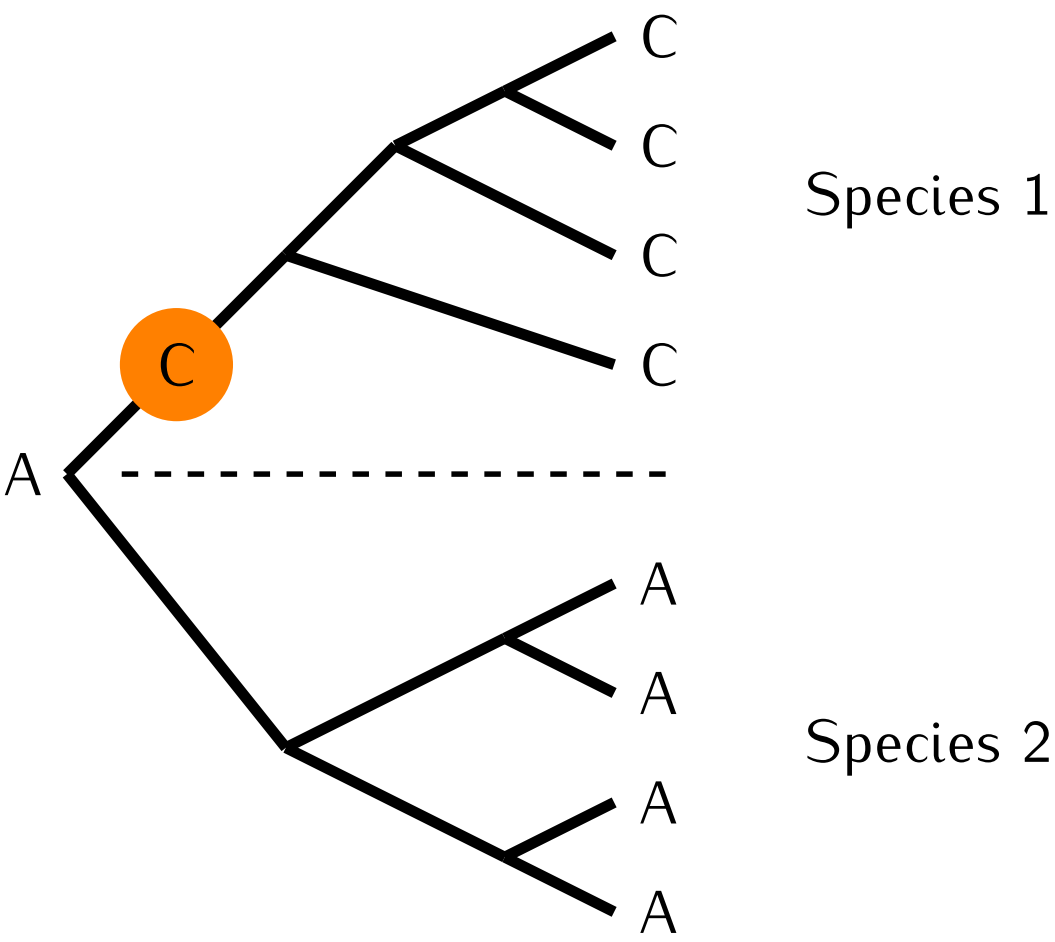

- Mutations on *interspecies branches* lead to fixed differences between species

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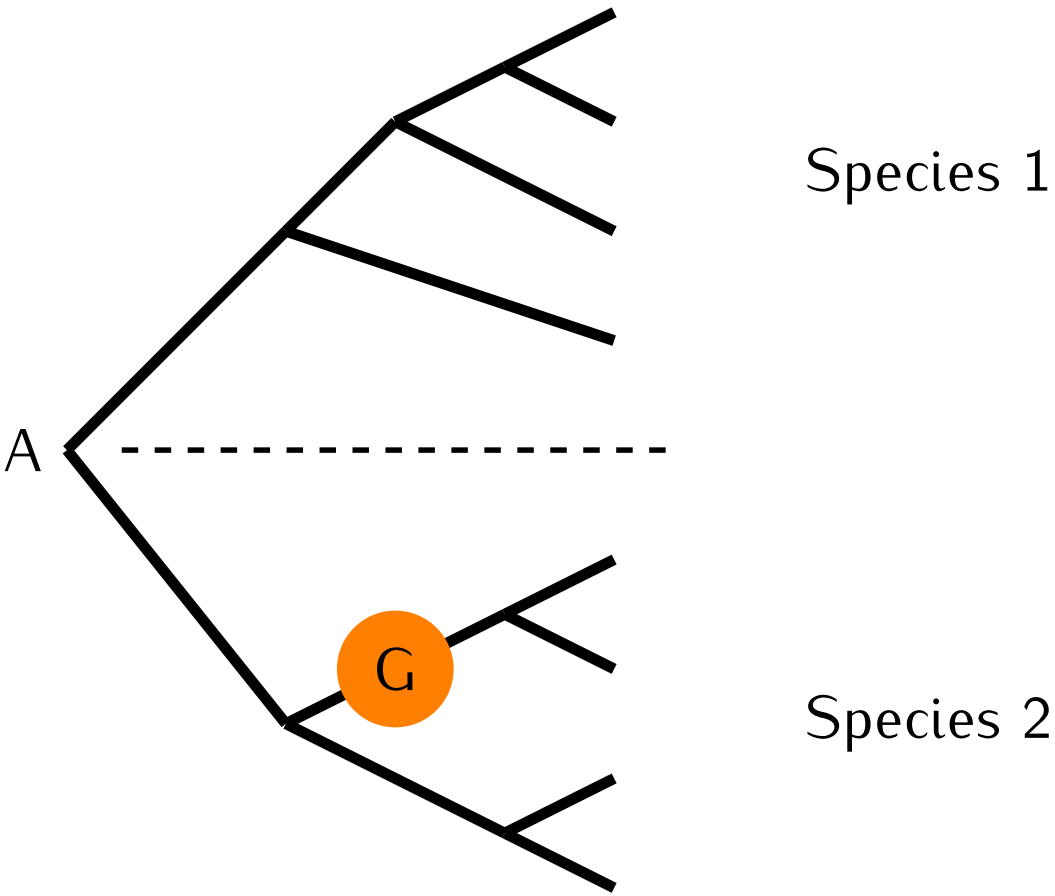

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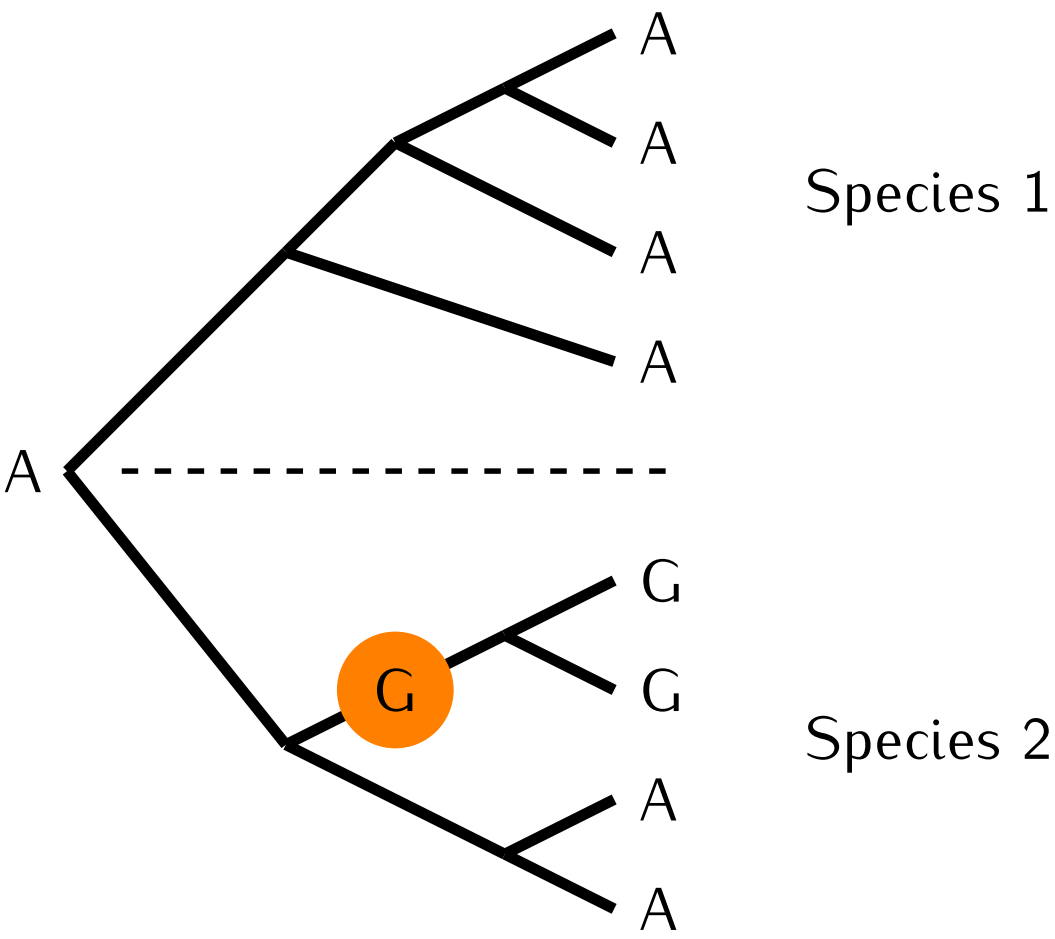

- Mutations on *interspecies branches* lead to fixed differences between species
- Mutations on *intraspecies branches* lead to polymorphism in one species

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1. the ratio of polymorphism vs. divergence is constant between genes
2. the ratio of non-synonymous to synonymous polymorphism equals the ratio of non-synonymous to synonymous divergence

Polymorphism and divergence are two facets of the same process

The HKA test

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- 'Goodness-of-fit' test to assess how consistent distinct regions are with a constant mutation rate
- Assumes free recombination between regions and no recombination within regions

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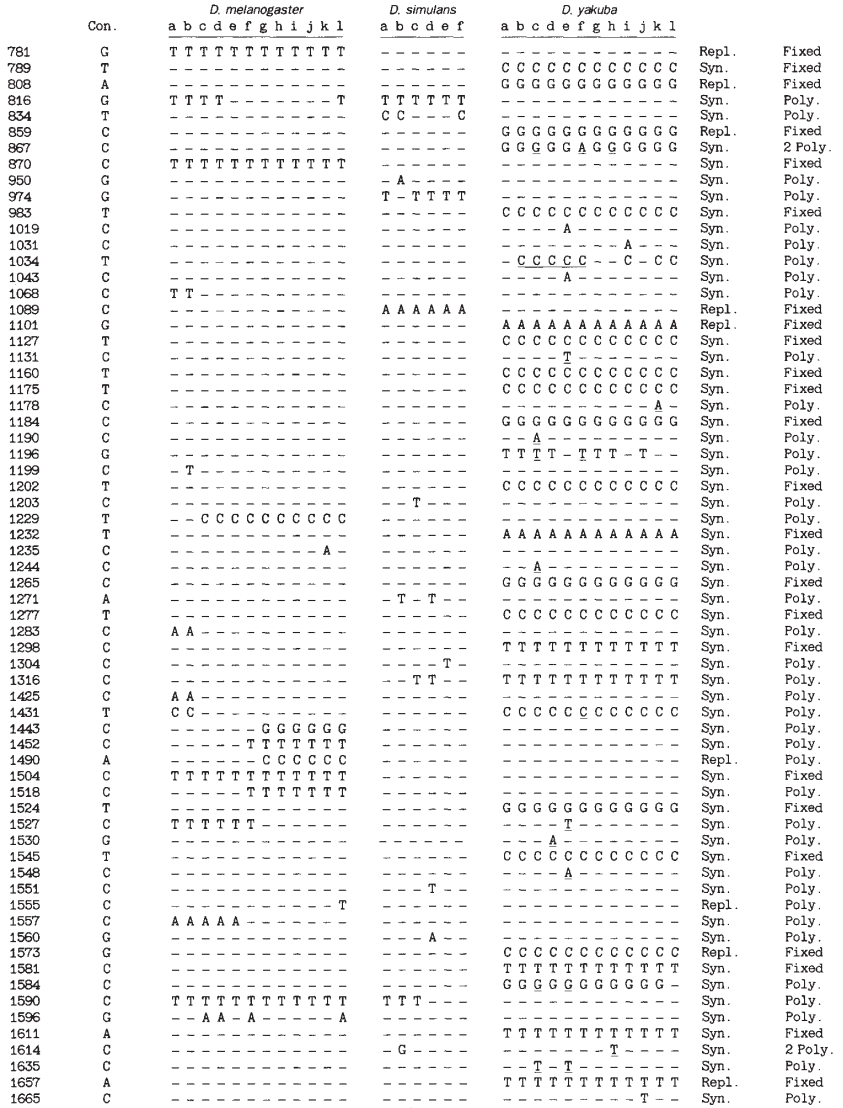

		D. melanogaster	*D. simulans*	*D. yakuba*		
	Con.	a b c d e f g h i j k l	a b c d e f	a b c d e f g h i j k l		
781	G	T T T T T T T T T T T T			Repl.	Fixed
789	T			C C C C C C C C C C C C	Syn.	Fixed
808	A			G G G G G G G G G G G G	Repl.	Fixed
816	G	T T T T T	T T T T T T		Syn.	Poly.
834	T		C C C		Syn.	Poly.
859	C			G G G G G G G G G G G G	Repl.	Fixed
867	C			G G G G A G G G G G G	Syn.	2 Poly.
870	C	T T T T T T T T T T T T			Syn.	Fixed
950	G		A		Syn.	Poly.
974	G		T T T T T		Syn.	Poly.
983	T			C C C C C C C C C C C C	Syn.	Fixed
1019	C			A	Syn.	Poly.
1031	C			A	Syn.	Poly.
1034	T			C C C C C C C C	Syn.	Poly.
1043	C			A	Syn.	Poly.
1068	C	T T			Syn.	Poly.
1089	C		A A A A A A		Repl.	Fixed
1101	G			A A A A A A A A A A A A	Repl.	Fixed
1127	T			C C C C C C C C C C C C	Syn.	Fixed
1131	C			T	Syn.	Poly.
1160	T			C C C C C C C C C C C C	Syn.	Fixed
1175	T			C C C C C C C C C C C C	Syn.	Fixed
1178	C			A	Syn.	Poly.
1184	C			G G G G G G G G G G G G	Syn.	Fixed
1190	C			A	Syn.	Poly.
1196	G			T T T T T T T T T	Syn.	Poly.
1199	C	T			Syn.	Poly.
1202	T			C C C C C C C C C C C C	Syn.	Fixed
1203	C		T		Syn.	Poly.
1229	T	C C C C C C C C C C C			Syn.	Poly.
1232	T			A A A A A A A A A A A A	Syn.	Fixed
1235	C	A			Syn.	Poly.
1244	C			A	Syn.	Poly.
1265	C			G G G G G G G G G G G G	Syn.	Fixed
1271	A		T T		Syn.	Poly.
1277	T			C C C C C C C C C C C C	Syn.	Fixed
1283	C	A A			Syn.	Poly.
1298	C			T T T T T T T T T T T T	Syn.	Fixed
1304	C		T		Syn.	Poly.
1316	C		T T	T T T T T T T T T T T	Syn.	Poly.
1425	C	A A			Syn.	Poly.
1431	T	C C		C C C C C C C C C C C C	Syn.	Poly.
1443	C	G G G G G G			Syn.	Poly.
1452	C	T T T T T T T			Syn.	Poly.
1490	A	C C C C C C			Repl.	Poly.
1504	C	T T T T T T T T T T T T			Syn.	Fixed
1518	C	T T T T T T T			Syn.	Poly.
1524	T			G G G G G G G G G G G G	Syn.	Fixed
1527	C	T T T T T T		T	Syn.	Poly.
1530	G			A	Syn.	Poly.
1545	T			C C C C C C C C C C C C	Syn.	Fixed
1548	C			A	Syn.	Poly.
1551	C		T		Syn.	Poly.
1555	C	T			Repl.	Poly.
1557	C	A A A A A			Syn.	Poly.
1560	G		A		Syn.	Poly.
1573	G			C C C C C C C C C C C C	Repl.	Fixed
1581	C			T T T T T T T T T T T	Syn.	Fixed
1584	C			G G G G G G G G G G G	Syn.	Poly.
1590	C	T T T T T T T T T T T T	T T T		Syn.	Poly.
1596	G	A A A			Syn.	Poly.
1611	A			T T T T T T T T T T T	Syn.	Fixed
1614	C		G	T	Syn.	2 Poly.
1635	C			T T	Syn.	Poly.
1657	A			T T T T T T T T T T T	Repl.	Fixed
1665	C			T	Syn.	Poly.

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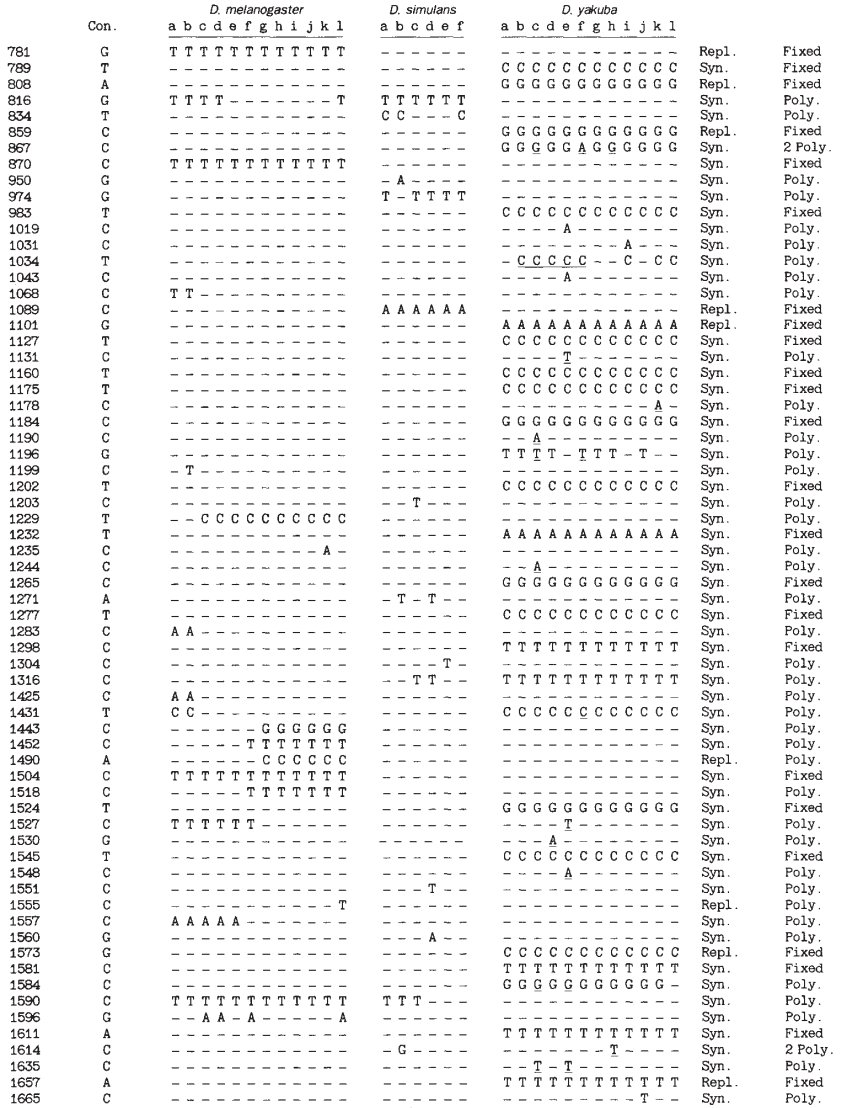
- One coding gene in at least 2 species, with polymorphism data for at least 1 species
- Count synonymous and non-synonymous polymorphisms and fixed differences
- Build a contingency table and perform a G-test

	Fixed	Polym.
Non-syn.	7	2
Synon.	17	42



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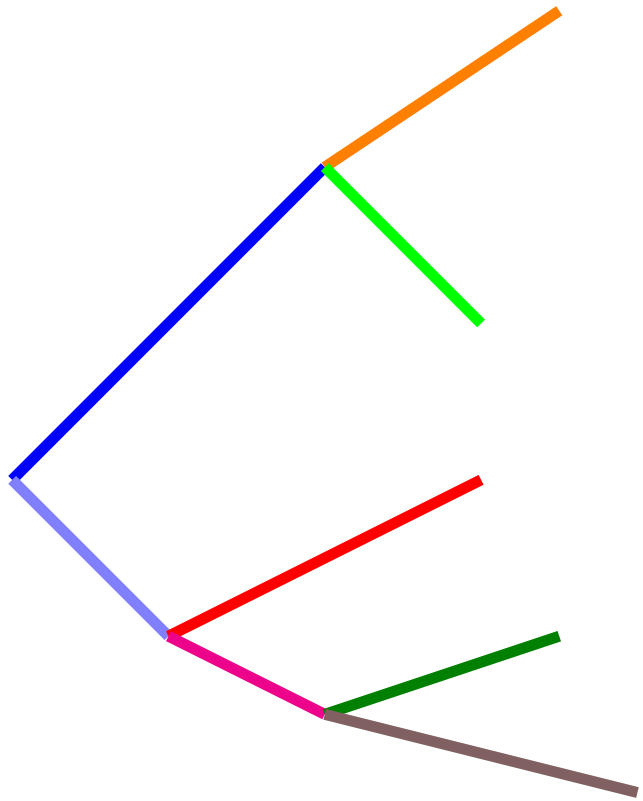

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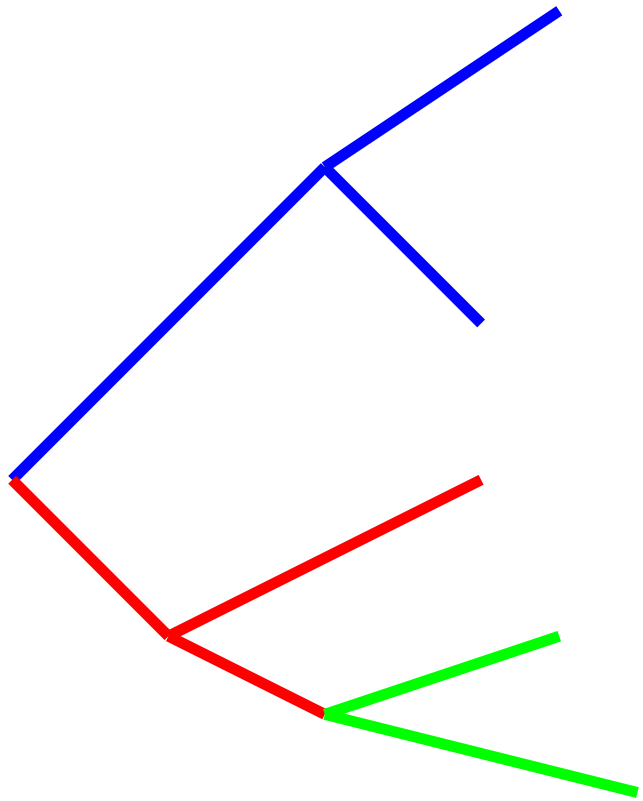
  - Several clades $\Rightarrow$ *clade* model



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  - One per branch $\Rightarrow$ *branch* model
  - Several clades $\Rightarrow$ *clade* model
- Other parameters are constant throughout the tree

Finding the best model

Dutheil et al. (2012)

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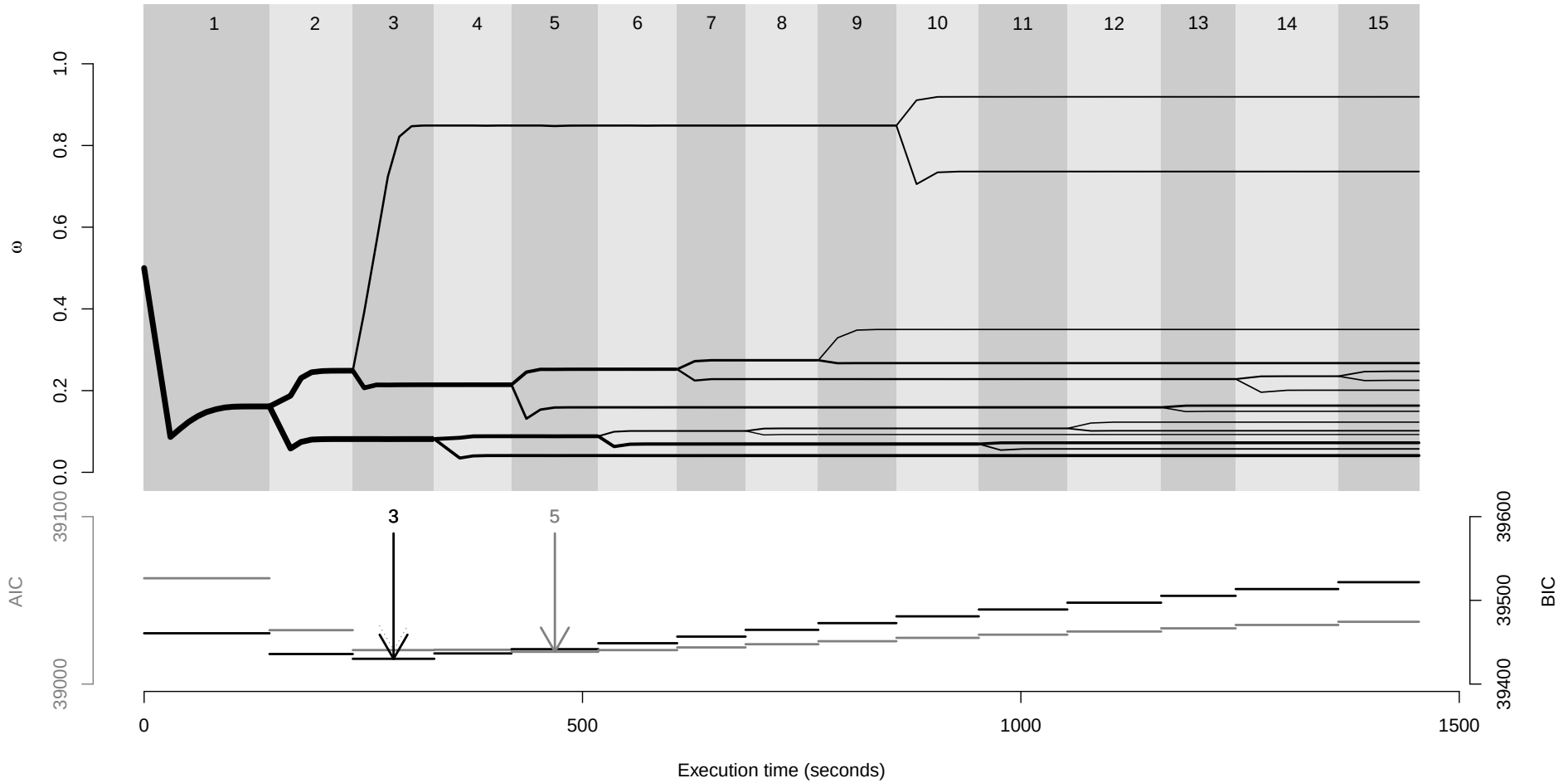

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- Background branches evolve under the M1a model, foreground branches under the M2a model
- Likelihood ratio test to compare with a homogeneous M1a model.