

Supplementary Table S4. Results of likelihood-based analysis of coevolution among protein residues within the COI protein. In part A, the total number of pairs are shown for analyzing coevolution with respect to volume, polarity, and hydrophobicity within the set of 23 unique snake sites, as well as with the results for polarity among all sites. The fraction of sites that demonstrated significant evidence of coevolutionary replacements at the $p < 0.05$ level are given for all analyses, along with the fraction of these “significant” pairs that are expected to be truly coevolving based on the number of comparisons made (i.e., $1 -$ the false discovery rate). In part B, highly significant ($p < 0.01$) unique site pairs are shown (based on simulations of the null log likelihood ratio distribution, which were quite close to expectations from the Chi Square distribution). Site numbers in (B) are based on the cow CO reference.

A.

	Volume	Polarity	Hydrophobicity	Polar-All
Site Pairs	126	232	147	3407
Coevolving Pairs (5% cutoff)	88.9%	65.5%	90.5%	59.8%
Coevolving Pair Fraction	94.38%	92.37%	94.47%	91.65%

B.

Polarity			Hydrophobicity		
Site 1	Site 2	$2\Delta\ln L$	Site 1	Site 2	$2\Delta\ln L$
286	447	17.103252	286	447	20.033842
258	286	15.344366	231	443	15.524782
258	447	15.343738	258	286	15.348934
231	443	13.402264	258	447	15.348934
267	447	12.67101	267	286	14.816056
267	286	12.670488	267	447	14.816056
258	267	11.461646	26	231	12.456162
258	299	11.423728	26	443	12.456162
231	281	10.837166	258	299	11.958086
281	443	10.837164	258	267	11.434084
272	281	10.206224	231	281	11.067008
272	443	10.197028	281	443	10.814424
231	272	10.197026	256	353	10.753326
205	231	9.548508	301	353	10.753326
205	443	9.548508	256	301	10.75308
35	299	9.483356	194	353	10.741258
194	256	9.45481	194	256	10.741256
256	301	9.45481	194	301	10.741256
256	353	9.45481	174	281	10.542516
194	301	9.454804	272	443	10.19837
194	353	9.454804	231	272	10.194886
301	353	9.454804	272	281	9.984506
174	231	9.418532	174	231	9.81607
174	443	9.418532	174	443	9.81607
266	301	9.333612	205	231	9.550284
266	353	9.333612	205	443	9.550284
194	266	9.333606	205	281	8.971526
256	266	9.33351	299	353	8.880646

174	281	9.222674	299	301	8.880642
37	256	9.156168	194	299	8.880224
37	194	9.156166	256	299	8.87743
37	301	9.156166	174	272	8.274962
37	353	9.156166	194	267	8.017124
205	281	8.959538	256	267	8.015986
194	299	8.823206	267	353	8.01271
299	301	8.823198	267	301	8.012708
299	353	8.823198	26	281	7.665456
256	299	8.823088	231	353	7.278846
26	256	8.554376	194	231	7.278812
26	194	8.554372	194	443	7.278812
26	301	8.554372	353	443	7.278812
26	353	8.554372	231	256	7.278
35	205	8.212686	231	301	7.278
267	301	8.011872	256	443	7.27794
267	353	8.011872	301	443	7.27794
194	267	8.01187	174	205	7.132574
256	267	8.01187	26	272	7.076318
37	266	7.438014	108	286	7.017936
54	194	7.28251	108	447	7.017936
54	301	7.28251	26	174	6.750424
54	353	7.28251	205	272	6.732824
54	256	7.282434			
54	108	7.195216			
266	299	7.106348			
174	272	7.02517			
37	299	6.939808			
108	286	6.73709			
108	447	6.73709			
194	231	6.71859			
194	443	6.71859			
301	443	6.71859			
353	443	6.71859			
231	301	6.718578			
231	353	6.718578			
256	443	6.71853			
231	256	6.718508			
