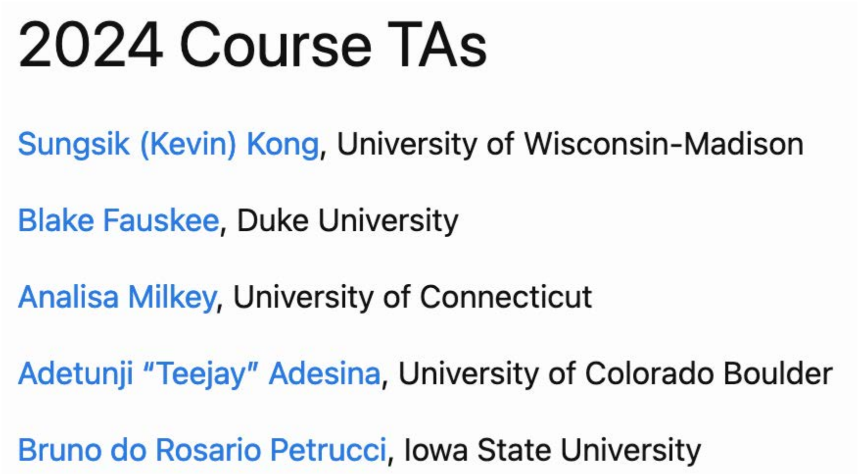
Marine Biological Laboratory

THE UNIVERSITY OF CHICAGO

Workshop on Molecular Evolution

Capstone seminar



2024 Course TAs

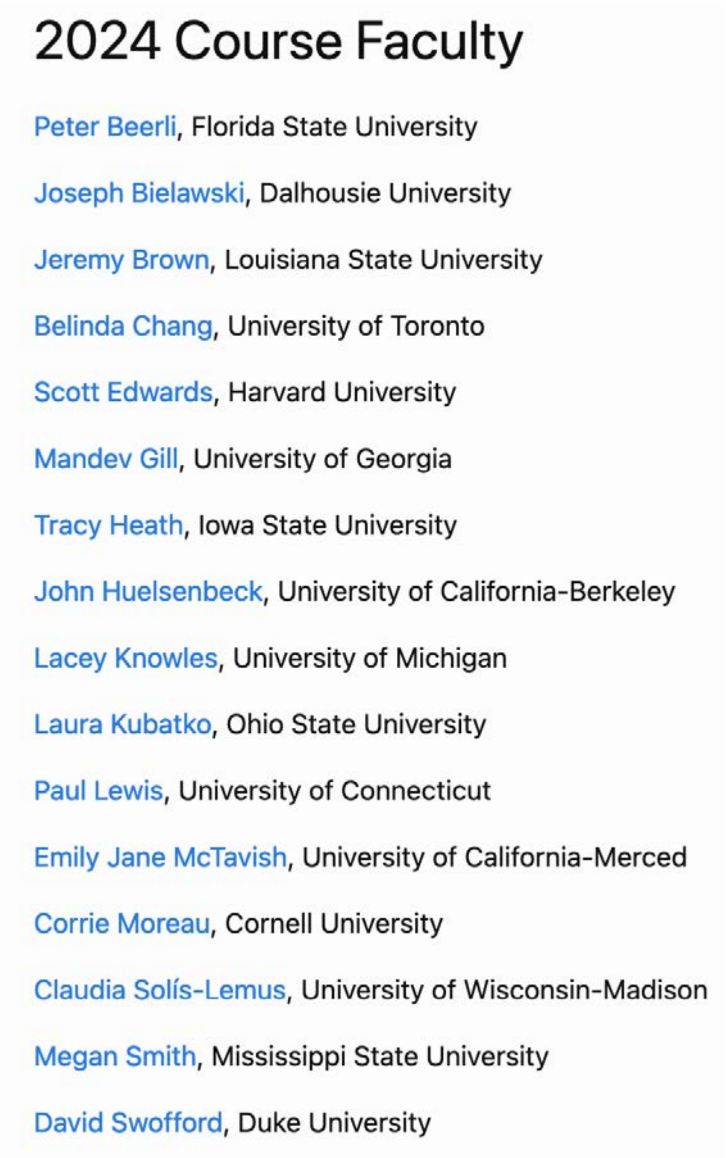
Sungsik (Kevin) Kong, University of Wisconsin-Madison

Blake Fauskee, Duke University

Analisa Milkey, University of Connecticut

Adetunji “Teejay” Adesina, University of Colorado Boulder

Bruno do Rosario Petrucci, Iowa State University



2024 Course Faculty

Peter Beerli, Florida State University

Joseph Bielawski, Dalhousie University

Jeremy Brown, Louisiana State University

Belinda Chang, University of Toronto

Scott Edwards, Harvard University

Mandev Gill, University of Georgia

Tracy Heath, Iowa State University

John Huelsenbeck, University of California-Berkeley

Lacey Knowles, University of Michigan

Laura Kubatko, Ohio State University

Paul Lewis, University of Connecticut

Emily Jane McTavish, University of California-Merced

Corrie Moreau, Cornell University

Claudia Solís-Lemus, University of Wisconsin-Madison

Megan Smith, Mississippi State University

David Swofford, Duke University

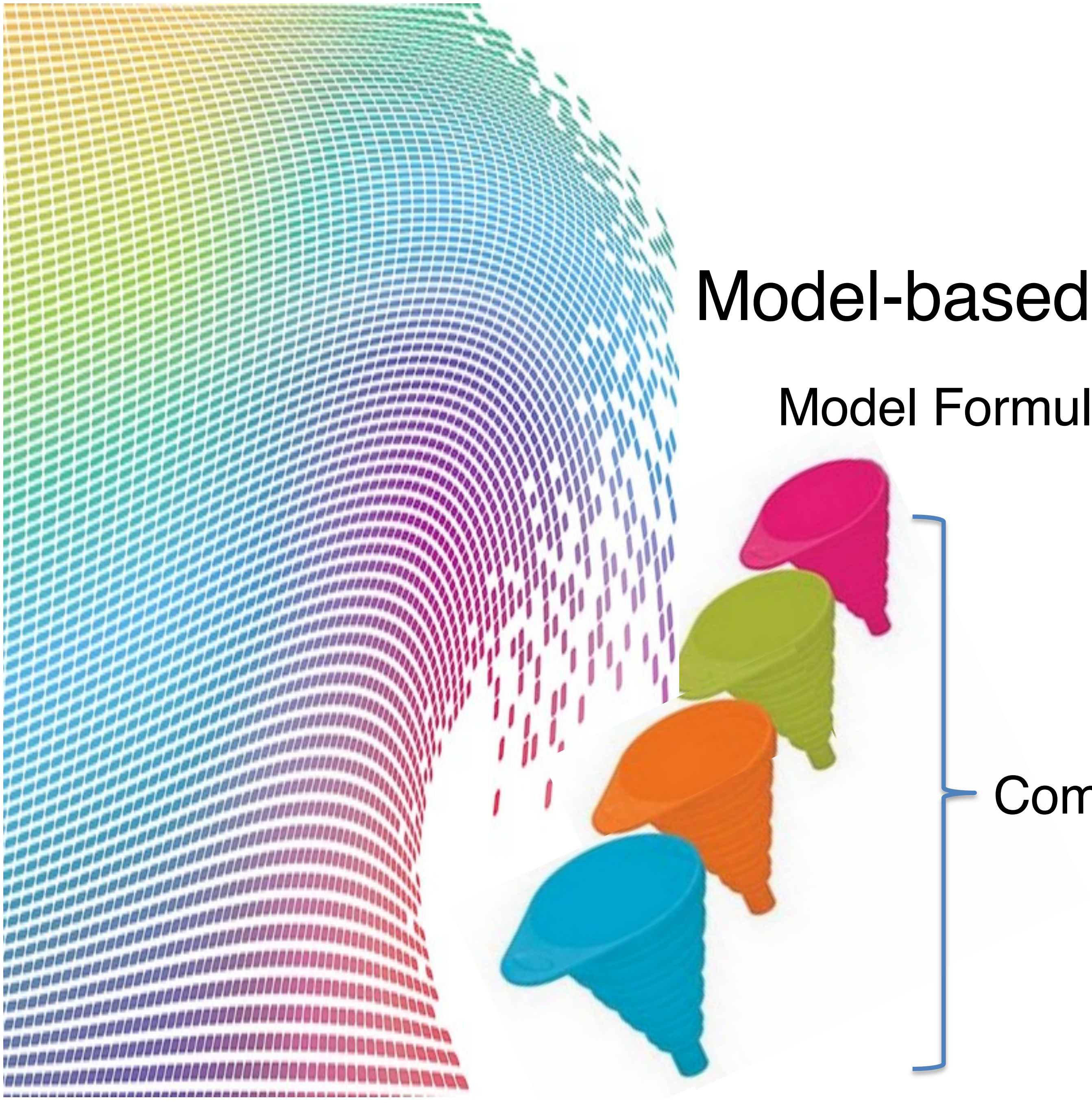
Evolutionary applications of genomic data

L. Lacey Knowles

Dept. of Ecology and Evolutionary Biology
University of Michigan

Illustration credit: John Megahan

Genomic data



Model-based analyses

Model Formulation

Competing models

Evolutionary applications of genomic data:

- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Inferring species boundaries (aka species delimitation)
- Demographic inference

- All models are flawed..., but they are important because models are how we communicate our knowledge to a statistical apparatus

Evolutionary applications of genomic data

what I’ll emphasize:

- Decisions/choices we make about model formulation
- Recognizing the subjectivity of model formulation itself when making inferences
- Decisions when applying to empirical data (e.g., all the data, subset of data, what subset of data)

Evolutionary applications of model-based analyses:

(i) Inferring species boundaries (aka species delimitation)

(ii) Phylogenetic inference (and beyond the species tree)

(iii) Biogeographic study

(iv) Phylogeography

(v) Adaptive evolution

Evolutionary applications of model-based analyses:

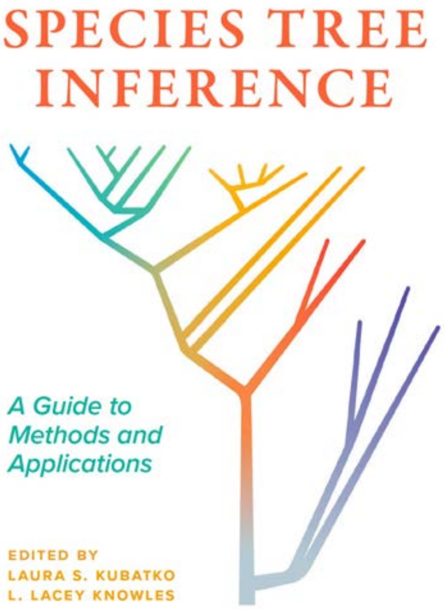
(i) Inferring species boundaries (aka species delimitation)

(ii) Phylogenetic inference (and beyond the species tree)

(iii) Biogeographic study

(iv) Phylogeography

(v) Adaptive evolution



Laura S. Kubatko and
L. Lacey Knowles
Species Tree Inference

30% off
with code P321 at
press.princeton.edu

Model-based approaches for phylogeographic inference

Discussion points:

- Why models are important

- Generic versus informed models

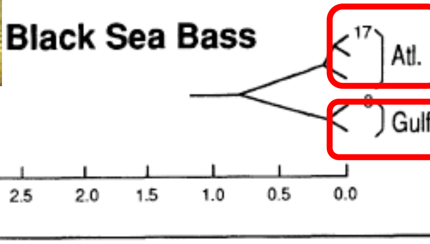
- Species-specific expectations of genetic variation
(e.g.. trait-based hypotheses, spatially explicit coalescent models, etc.)

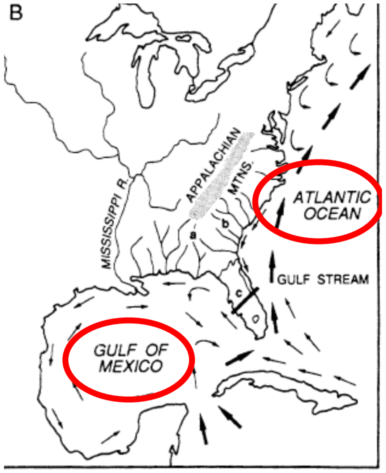
- Concordance versus discord among species in communities
(i.e.. lessons from comparative phylogeography)

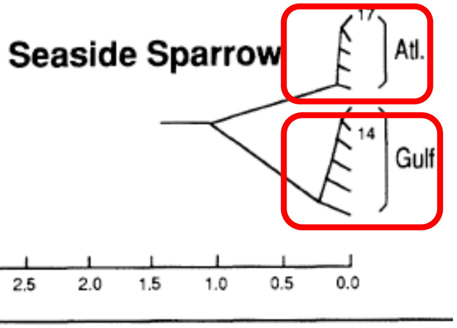
Why the transition from describing patterns of genetic variation to understanding process requires model-based approach

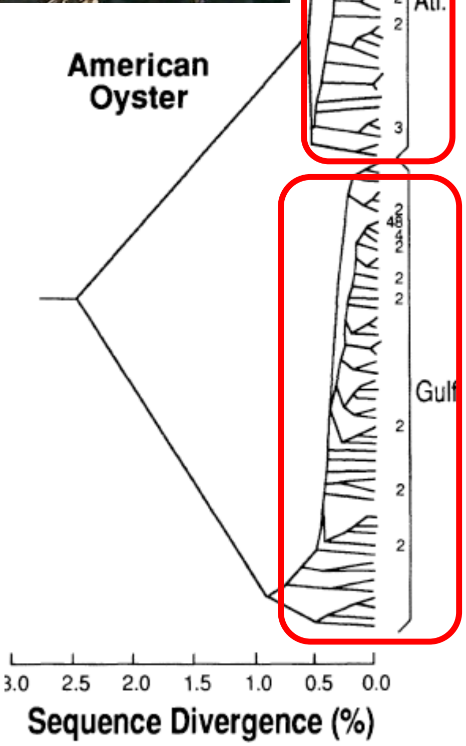
Classics in phylogeography

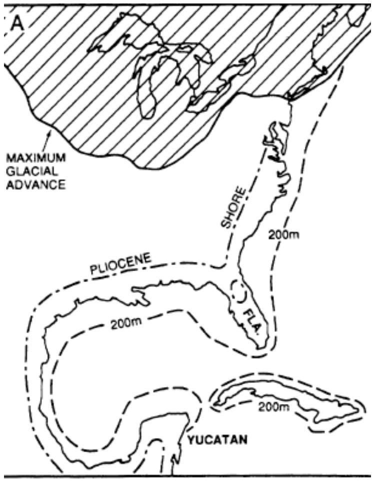
Concordance reflects a common vicariant history of population separation

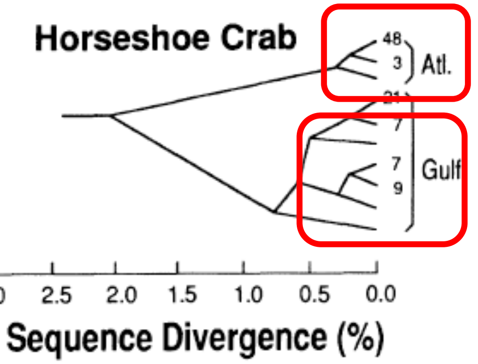








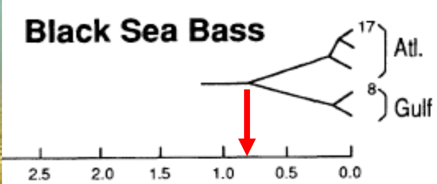


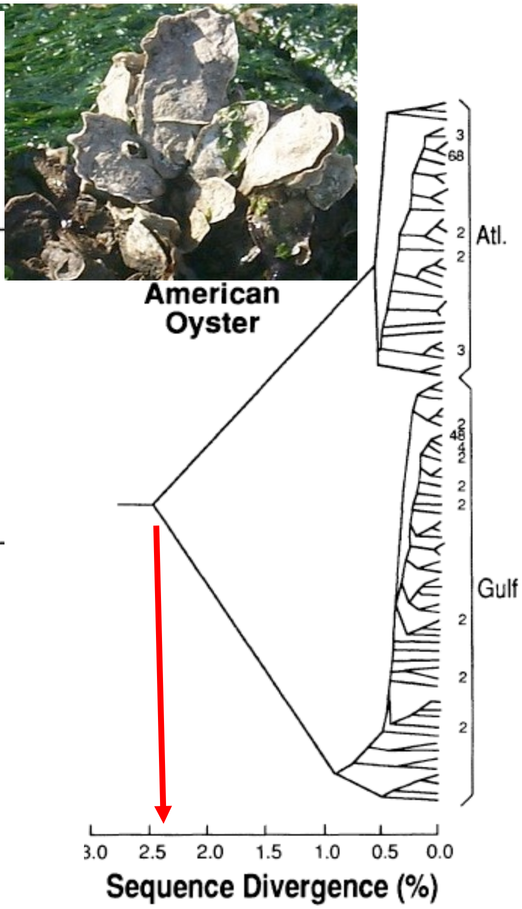


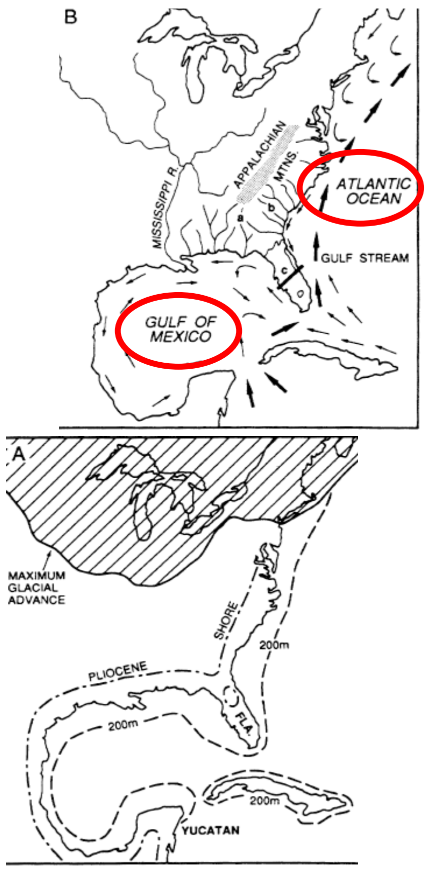
Avise 1992

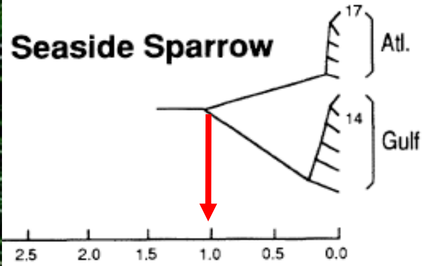
The data may be consistent with a shared response to a specific geologic event, despite differing gene tree depths among taxa? Or maybe not?

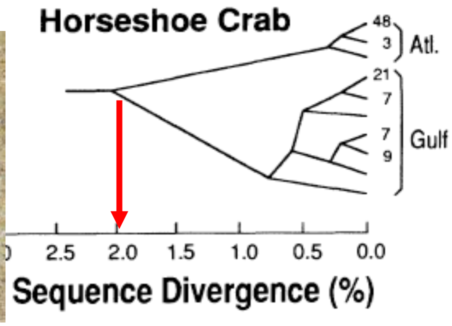
By looking only at the gene trees,
it isn't clear how the differences in gene tree depths
should be interpreted!





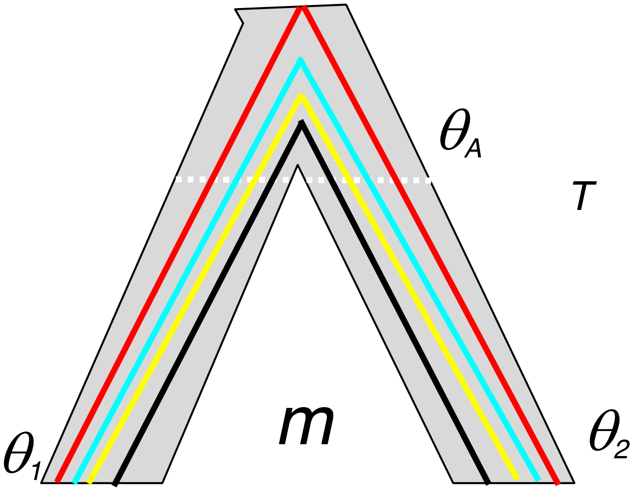






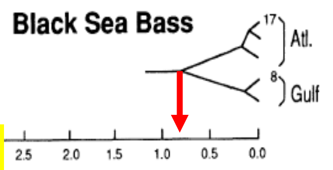
To test for shared vicariant history of the coastal community:

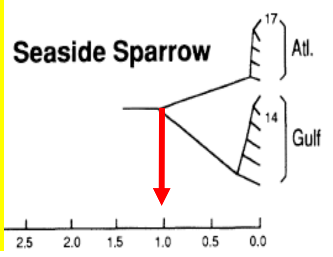
Assess statistically how much of a difference in the depths of the gene trees would still be consistent with the same geologic event based on the timing of divergence

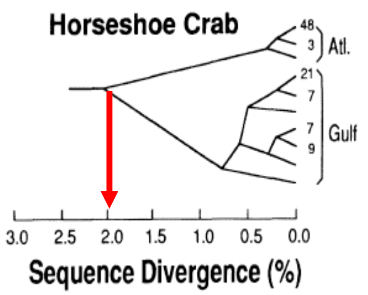


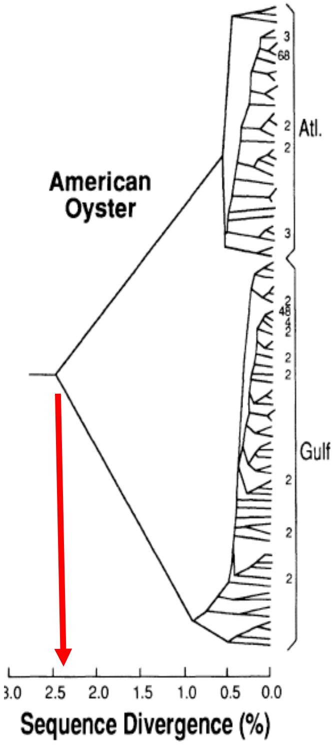
Present

Expectation of T is based on the geologic event (i.e., sea level change) – that is, prediction based on information that is independent of the genetic data









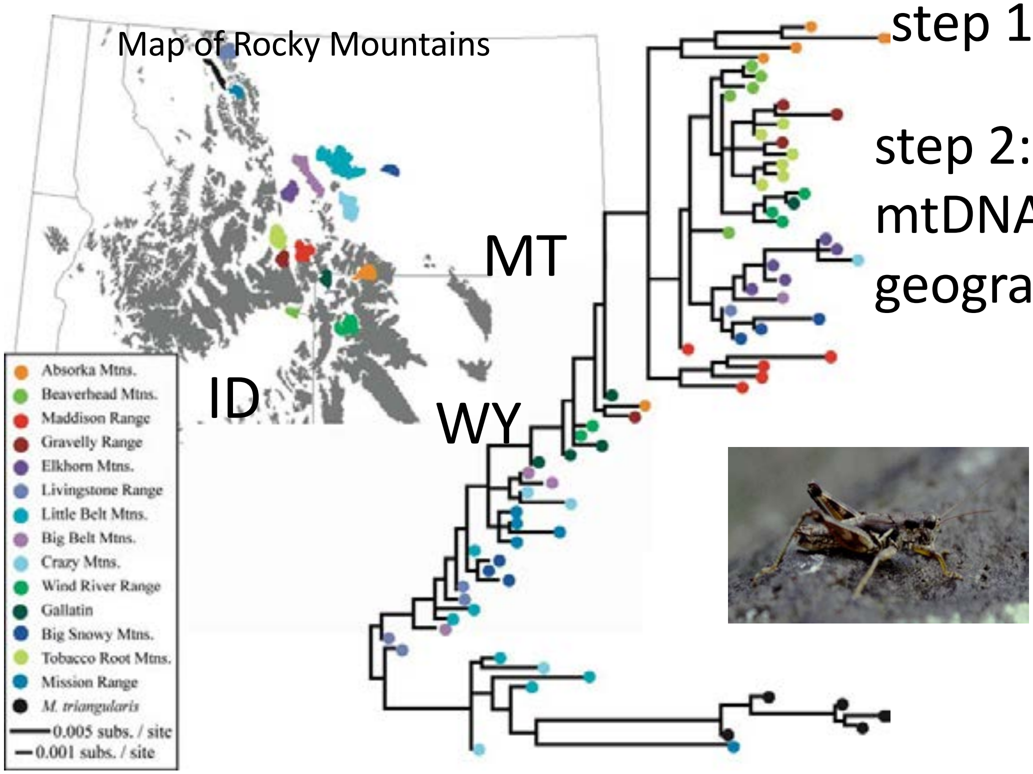
In the past, the central focus was on the 'phylo' component

PHYLOgeography

Use of gene trees predominated and genetic variation across populations described by:

step 1: reconstruct a gene tree

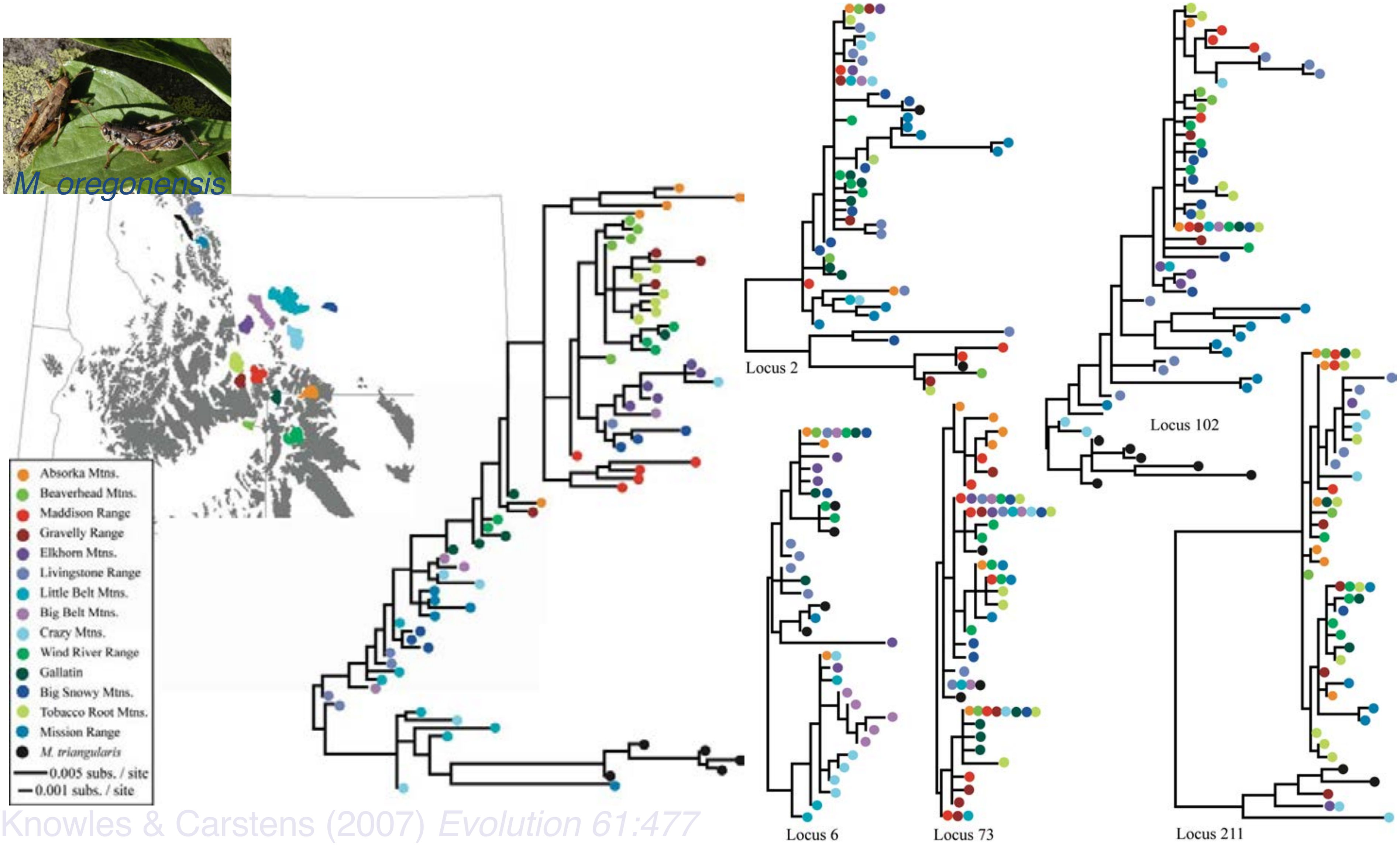
step 2: compare the relationships among mtDNA sequences/haplotypes to the geographic distribution of haplotypes



grasshopper haplotypes across populations (color coded by the mountain top where individual was collected)

But different loci have different gene trees

Phylogenetic relationships among populations (i.e., what's the underlying geographic history of divergence)?

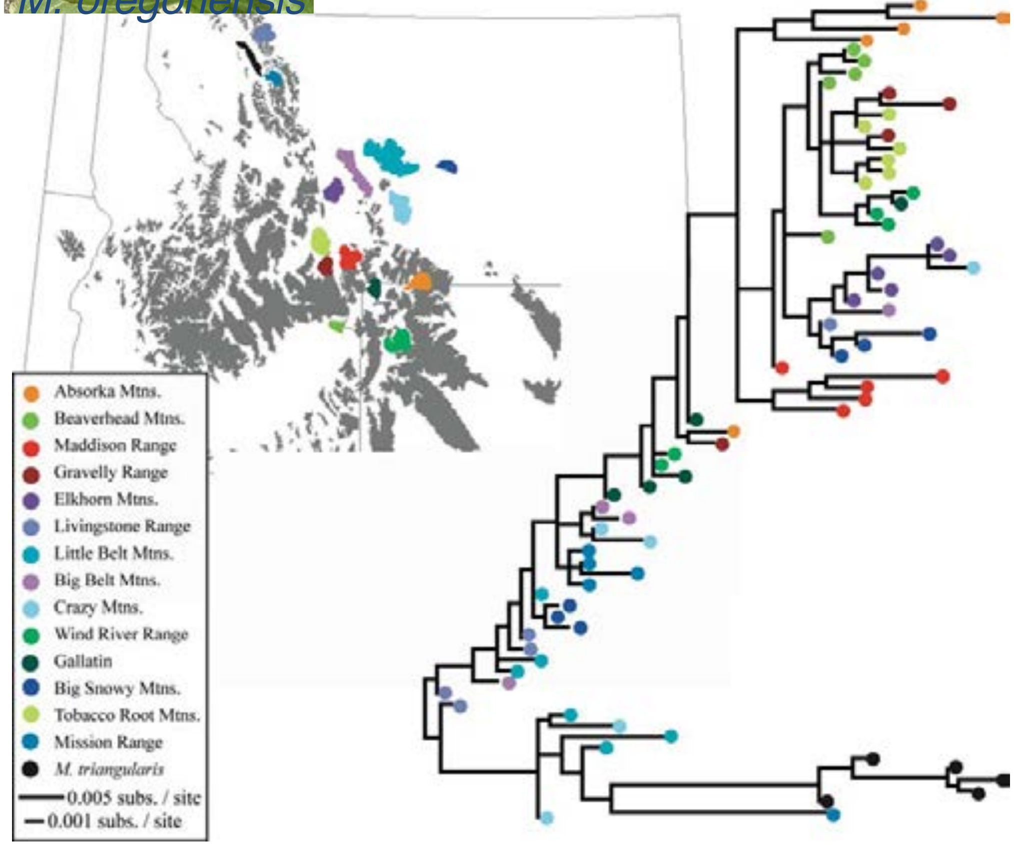


Knowles & Carstens (2007) *Evolution 61:477*

Different processes can produce similar genetic patterns

Recent isolation or migration?

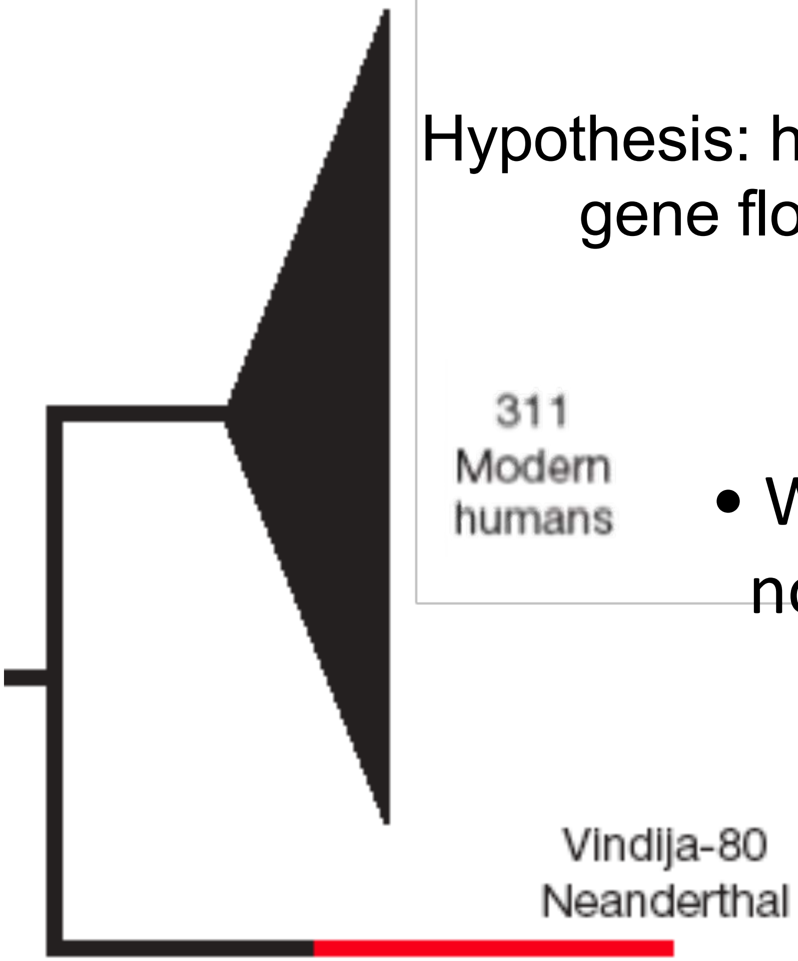
$F_{ST} = 0.15$



Knowles & Carstens (2007) *Evolution 61:477*

Interbreeding between Neanderthals and humans?

Hypothesis: humans replaced Neanderthals without gene flow between the separate species



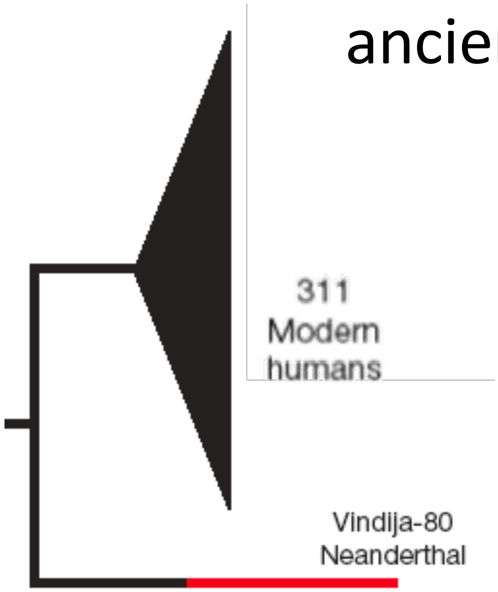
- What are two bits of evidence for no gene flow based on this tree?

Problem with interpreting gene tree as evidence of "divergence with no gene flow"

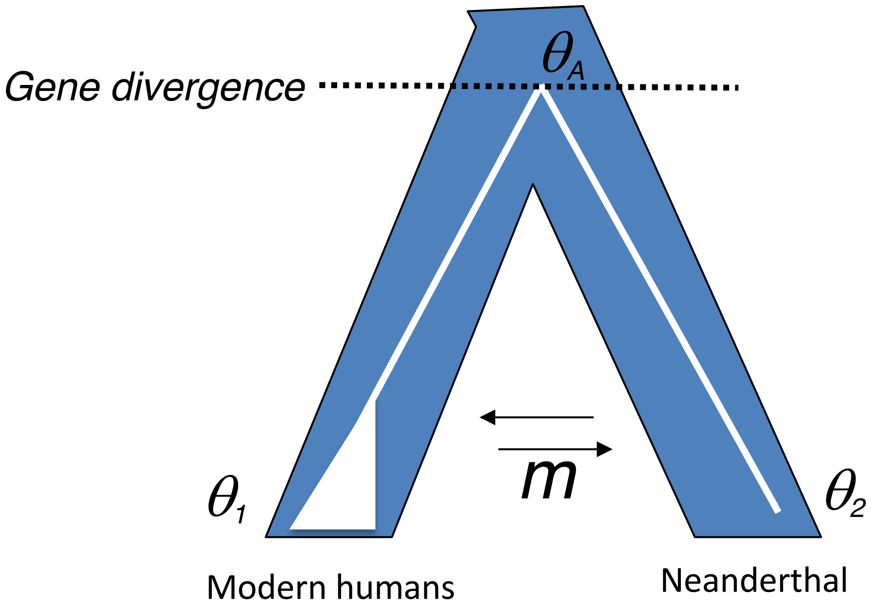
Nordberg

Interbreeding between Neanderthals and humans?

- Model based test of the hypothesis: what's the probability that this gene tree is compatible with ancient gene flow between humans and Neanderthal



(Bayesian program IM)

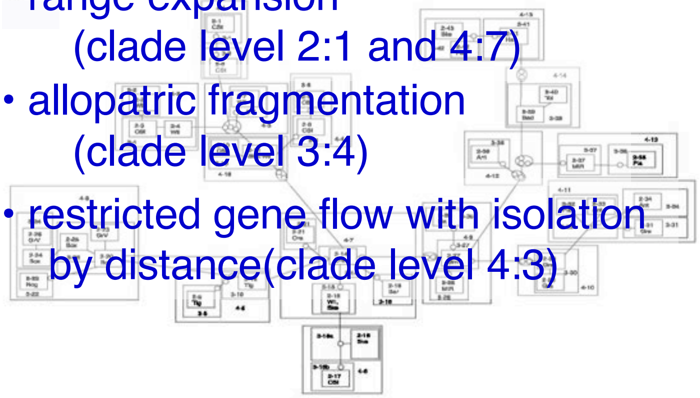


Result: yes, tree is compatible; does this mean there was gene flow?

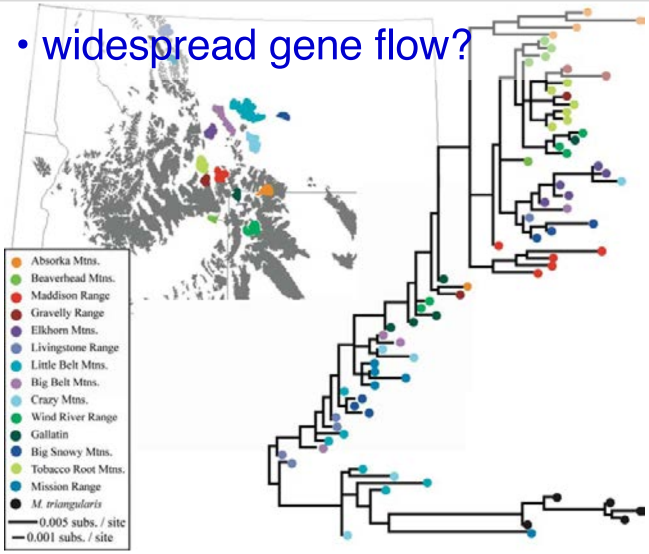
- Not necessarily because with single gene not a lot of power to evaluate the hypothesis

Nordberg

Equating a gene tree (or network) with a species' history is not appropriate for making inferences about evolutionary processes



- range expansion
  (clade level 2:1 and 4:7)
- allopatric fragmentation
  (clade level 3:4)
- restricted gene flow with isolation
  by distance(clade level 4:3)



- widespread gene flow?

Without a model:

- inferred processes may (*or may not*) be accurate because different processes can produce a similar pattern in genetic data and gene trees may differ across loci

- no measure of the uncertainty/support surrounding hypotheses or evaluating competing hypotheses

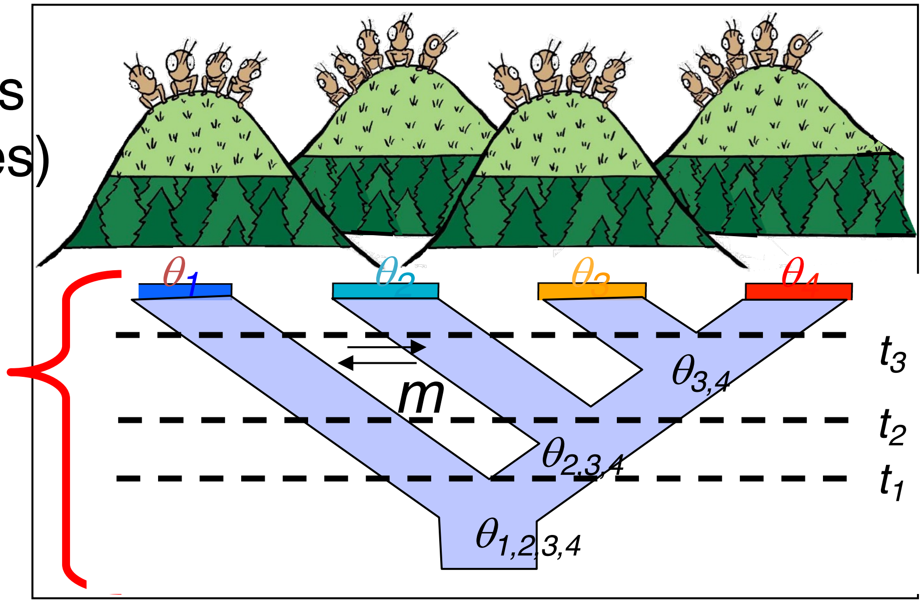
- no framework for incorporate additional data (e.g., geologic or ecological information)

- inherent lack of power when individual loci analyzed separately, and discordance among loci is uninterpretable

Understanding historical process necessitates model-based approaches

- accommodate and make full use of multilocus data (individual gene trees differ so trying to interpret their patterns would lead you to many different stories)

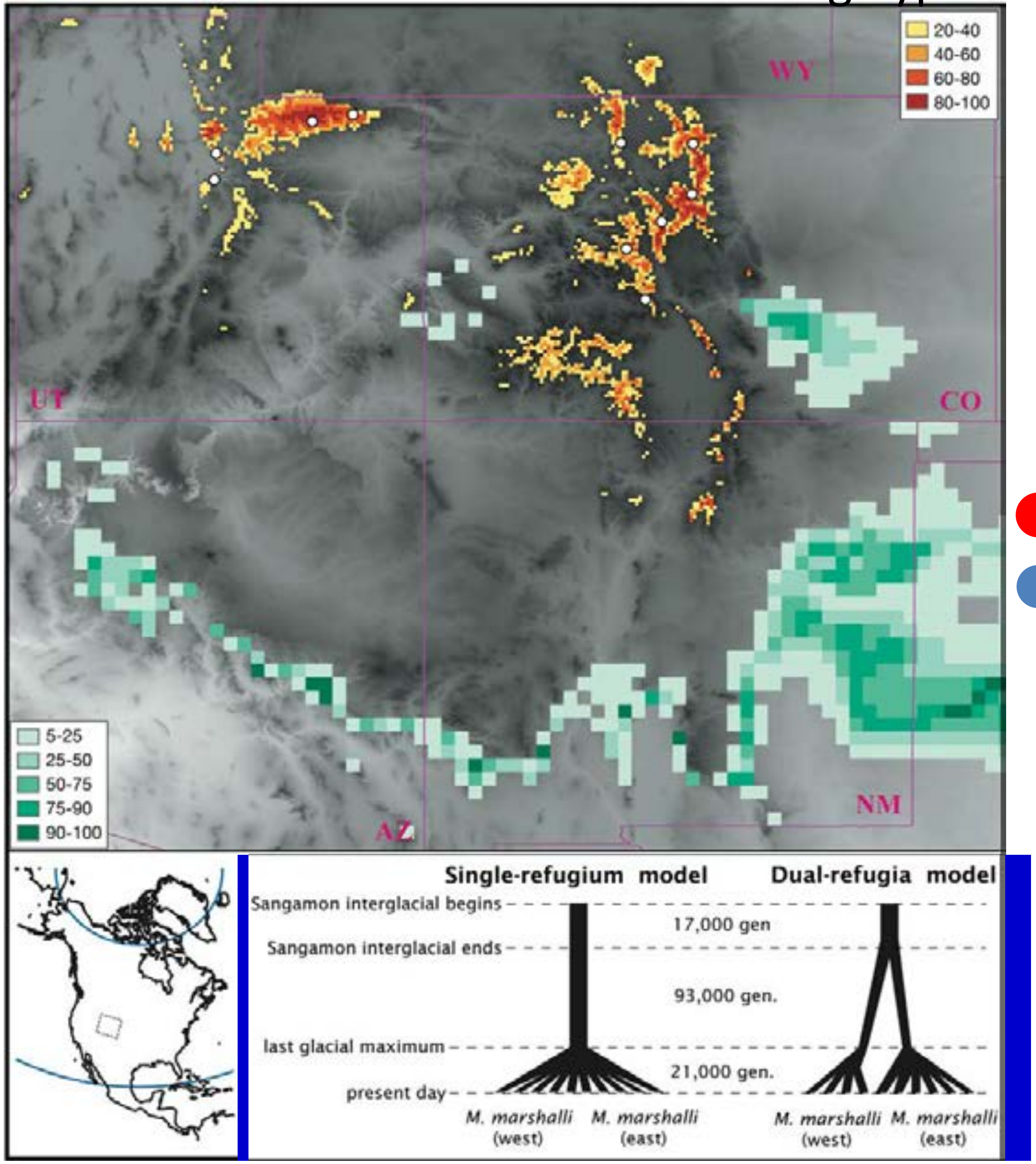
Explicit model of a species' history



- estimate evolutionary parameters (e.g., population size, migration rates, divergence times, or demographic changes like expansions or bottlenecks, the geographic coordinates of the ancestral population)

- test alternative hypotheses/models (e.g., distinguish between a hierarchical vicariant divergence model versus a stepping-stone colonization model, or isolation by distance)

- Incorporate additional non-genetic sources information to inform our choice of models for testing hypotheses



Coupled genetic and ecological-niche models to test hypotheses about ancestral refuges

🔴 Projections of current distribution

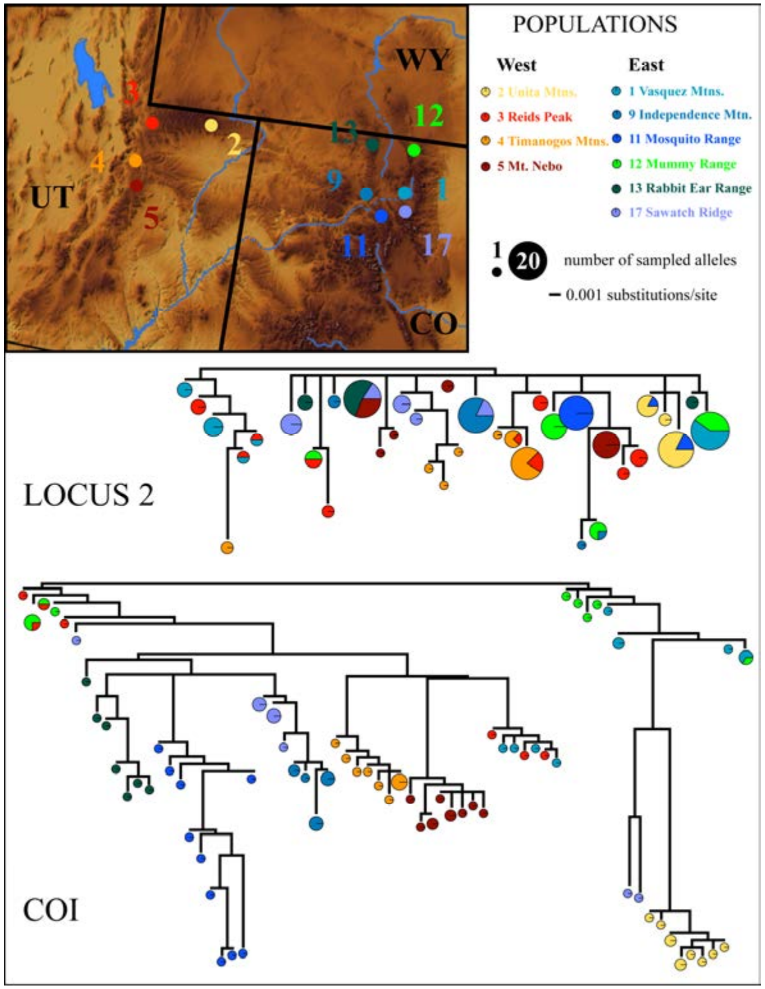
🔵 Projections of past distribution 21,000 years ago

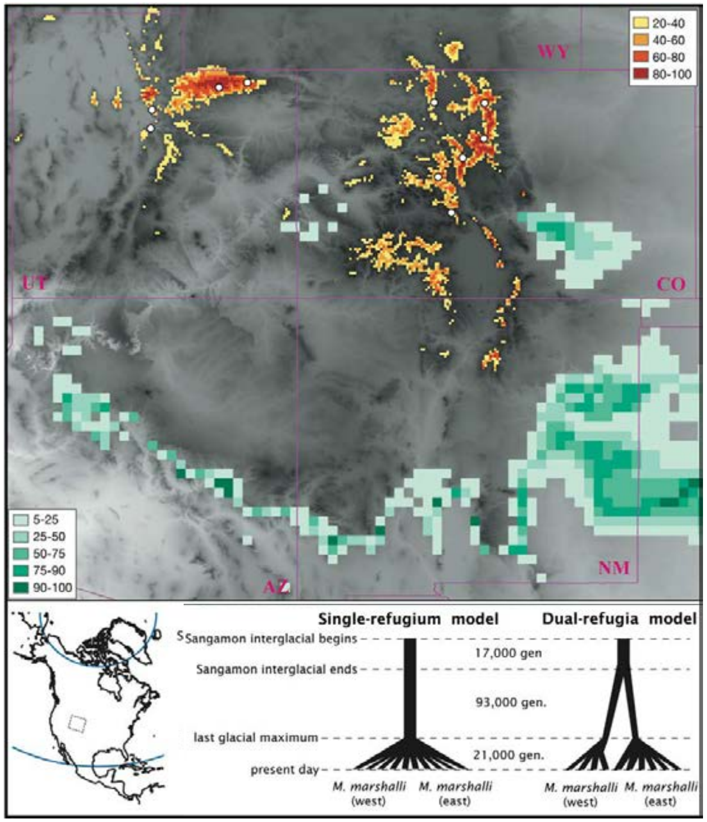
(based on 19 bioclimatic variables; analyzed with MAXENT)

Knowles et al. 2007 Current Biology 17:1-7.

Coupled genetic and ecological-niche model:

With sequence data from multiple loci, we could reject the fragmentation of a single refugial population, suggesting divergence among multiple refugia promoted divergence.





Knowles et al. 2007 Current Biology 17:1-7.

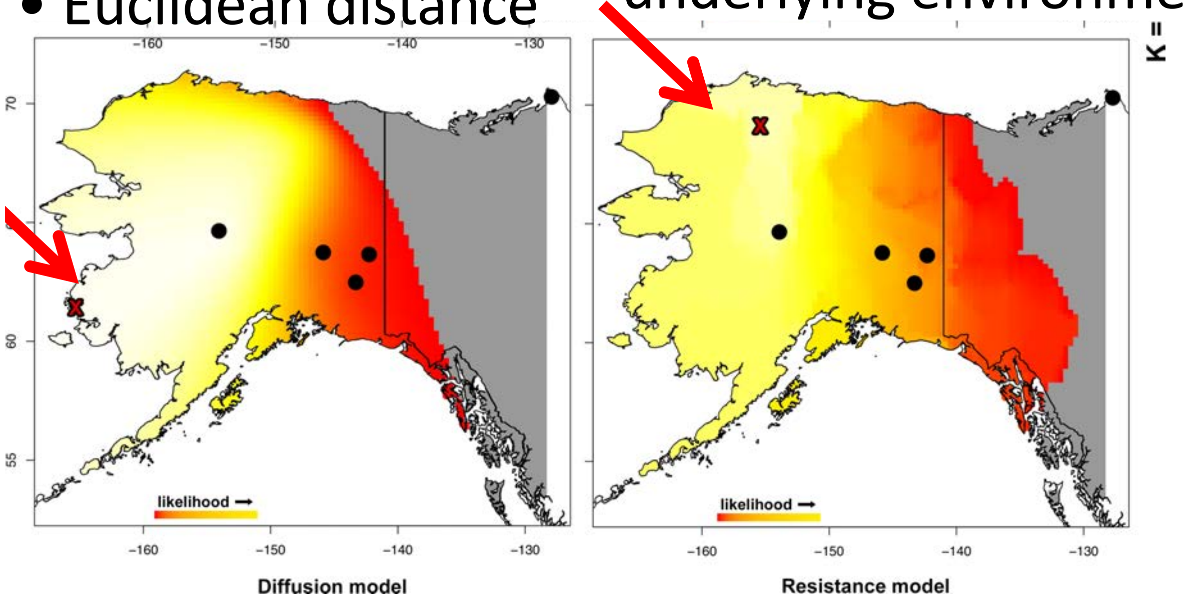
There are many different reasons why it is desirable to combine genetic data with other types of information (e.g., geographic or distributional data, ecological information, etc)

Why is it desirable to combine genetic data with other types of information?

Capture biologically reality!

- resistance distance (based on underlying environmental setting)

- Euclidean distance



- Direction and location of ancestral source of expanding population differs between Euclidean and resistance distance (He et al. 2017)

Likelihood surface of location of source population during expansion (He et al. 2017) based on allele frequency gradients, represented by Ψ-statistics (Peter & Slatkin 2013)

He et al. 2017. Inferring the geographic origin of a range expansion: latitudinal and longitudinal coordinates inferred from genomic data in an ABC framework with the program X-ORIGIN. *Mol. Ecol.* 26:6908-6920. DOI: 10.1111/mec.14380

Use genetic data to corroborate inferences based on other data types

ENMs do not provide precise location of Pleistocene refuge for hickory trees

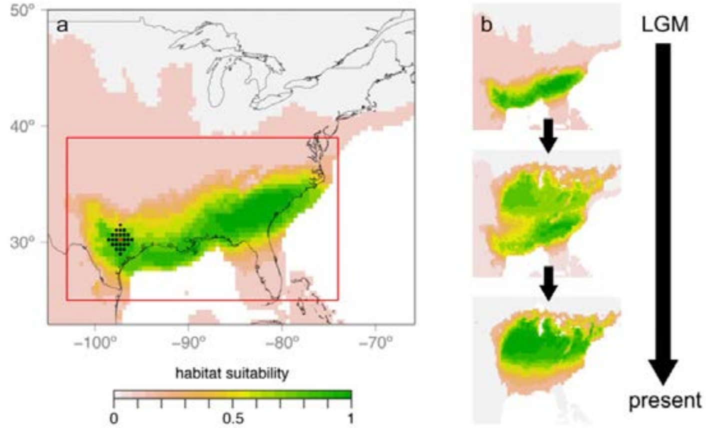
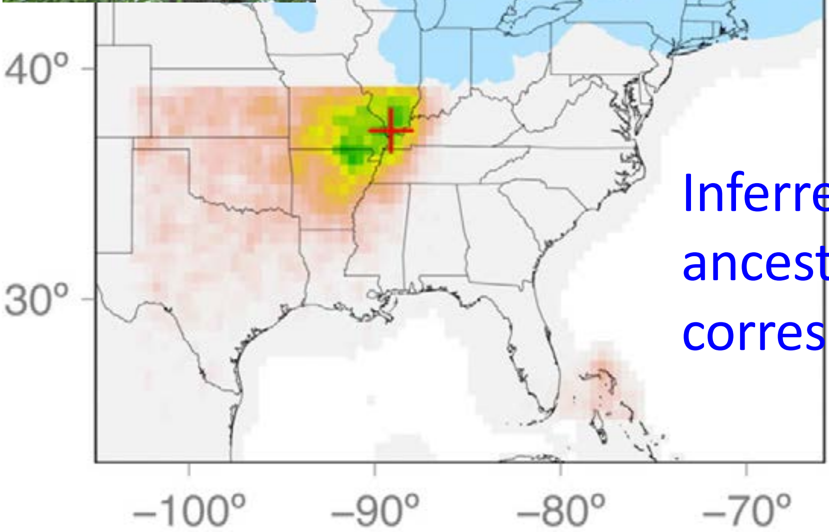


Fig. 1. Schematic overview of demographic simulations. (*A*) Simulations were initiated in the LGM landscape (shown here for *C. cordiformis*) from a central deme (see red dot as an example) plus an area extending three additional demes (black dots) in all directions. Different geographic sources of



Inferred likelihood of geographic coordinates of ancestral refugia population – this location corresponds to a macrofossil of the hickory species

Fig. 2. Estimated expansion origins (Ω; red cross) in *C. cordiformis* (*A*) and *C. ovata* (*B*). The shading of pixels depicts a probability surface (kernel density) showing the likelihood that each pixel served as the expansion origin relative to the pixel with the highest likelihood (i.e., Ω). Glaciated regions are shown in blue. The results presented in *A* and *B* are based on retention of four and three PC axes of variation in genetic summary statistics, respectively. Results based on retaining additional PC axes are presented in *SI Appendix*, Figs. S2 and S3.

Bemmels JB, Knowles LL, Dick CW (2019) Genomic evidence of survival near ice sheet margins for some, but not all, North American trees. *PNAS* 116:8431-8436.

Statistical inference in phylogeography:

Need to define a model

To see how variation in the parameters (e.g., mutation rates, migration rates, selection coefficients) leads to specific patterns of genetic variation (i.e., patterns of variation among DNA sequences, among SNPs, etc.)

How do we decide upon a model*:

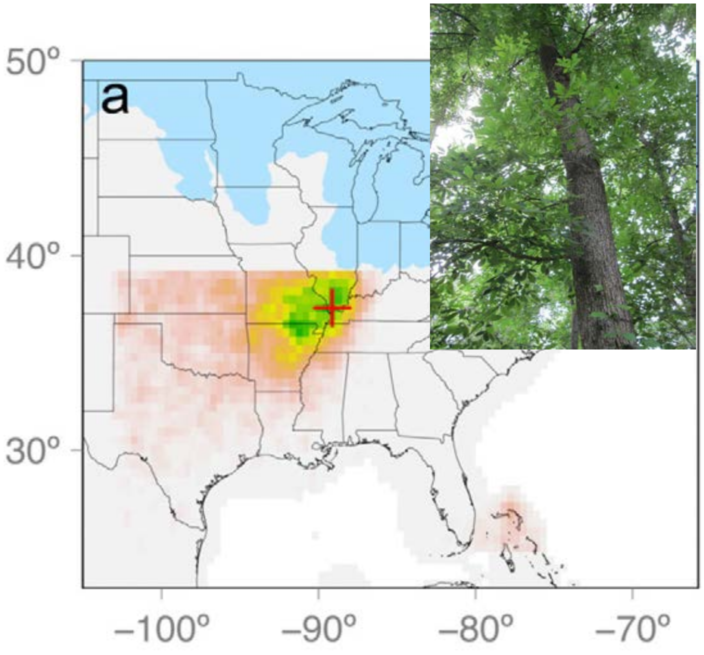
- informed from information independent of the genetic data itself
  - that is, a specific biological narrative motivates the model

- models informed by genetic data

- generic models

* All models are simplifications, and vary in their relative degree of abstraction

Expansion model used because of known displacement of hickory trees from current distribution by glacial ice sheet.



Bemmels et al. 2019 PNAS 116:8431-8436

Inferred geographic coordinates of source of expansion, where the geographic coordinate is a parameter in the model (inferred using ABC; see *He et al.* 2017. Inferring the geographic origin of a range expansion: latitudinal and longitudinal coordinates inferred from genomic data in an ABC framework with the program X-ORIGIN. *Mol. Ecol.* 26:6908-6920. DOI: 10.1111/mec.14380

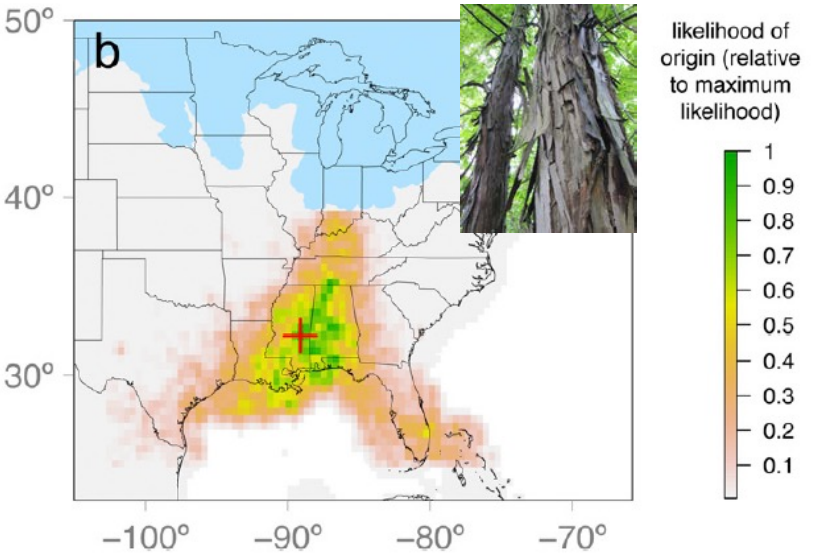
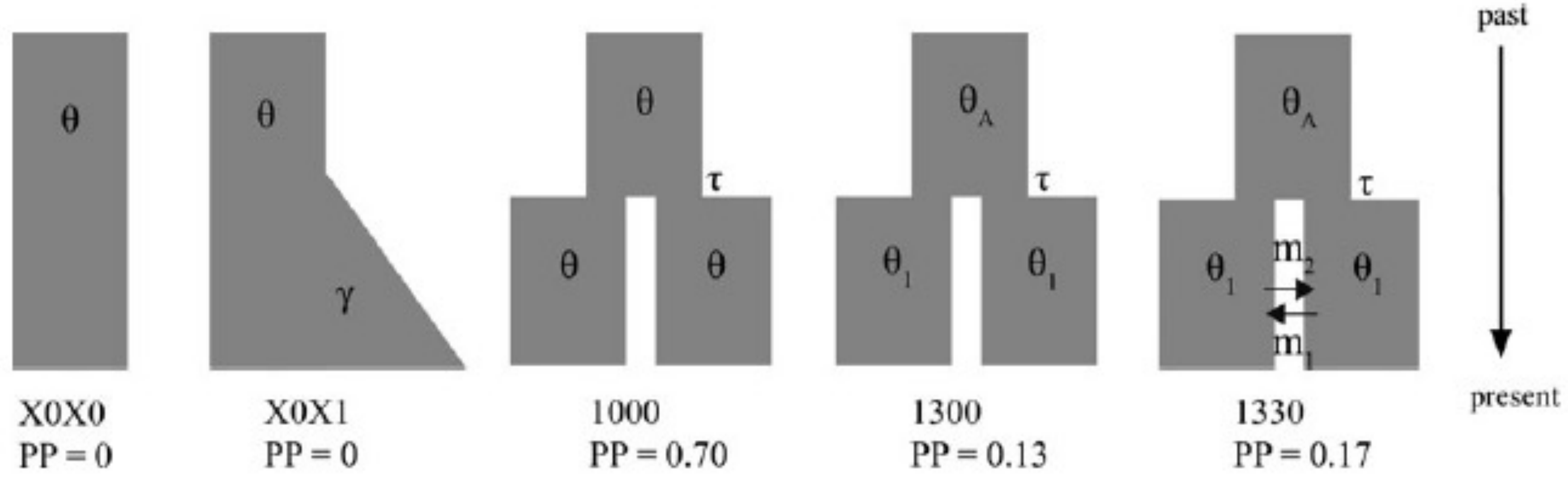


Fig. 2. Estimated expansion origins (Ω; red cross) in *C. cordiformis* (*A*) and *C. ovata* (*B*). The shading of pixels depicts a probability surface (kernel density) showing the likelihood that each pixel served as the expansion origin relative to the pixel with the highest likelihood (i.e., Ω). Glaciated regions are shown in blue. The results presented in *A* and *B* are based on retention of four and three PC axes of variation in genetic summary statistics, respectively. Results based on retaining additional PC axes are presented in *SI Appendix*, Figs. S2 and S3.

Generic models in phylogeography

Tests of 142 objectively identified models (e.g., program like PHRAPL)



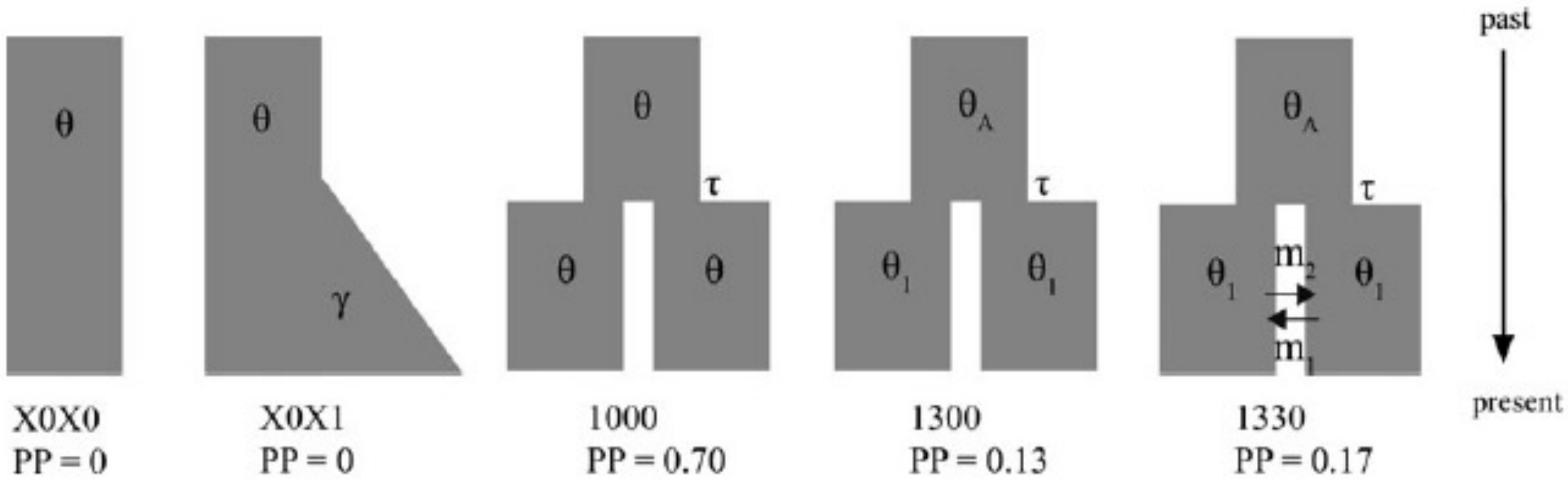
Pelletier & Carstens (2014 Mol. Ecol.)

- PHRAPL can create hundreds of possible histories that have a mixture of gene flow, population subdivision, and/or population size differences and compare these models using AIC (O'Meara)

Model choice in phylogeography: generic versus informed

- generic models

Tests of 142 objectively identified models

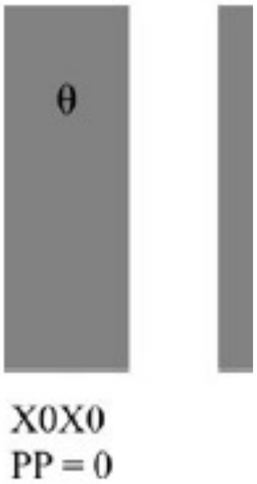


Pelletier & Carstens (2014 Mol. Ecol.)

Statistical procedures themselves may seem to provide a legitimacy to modeling approach – the advocacy of objective models in phylogeography

Model choice d

Tests of 142 c



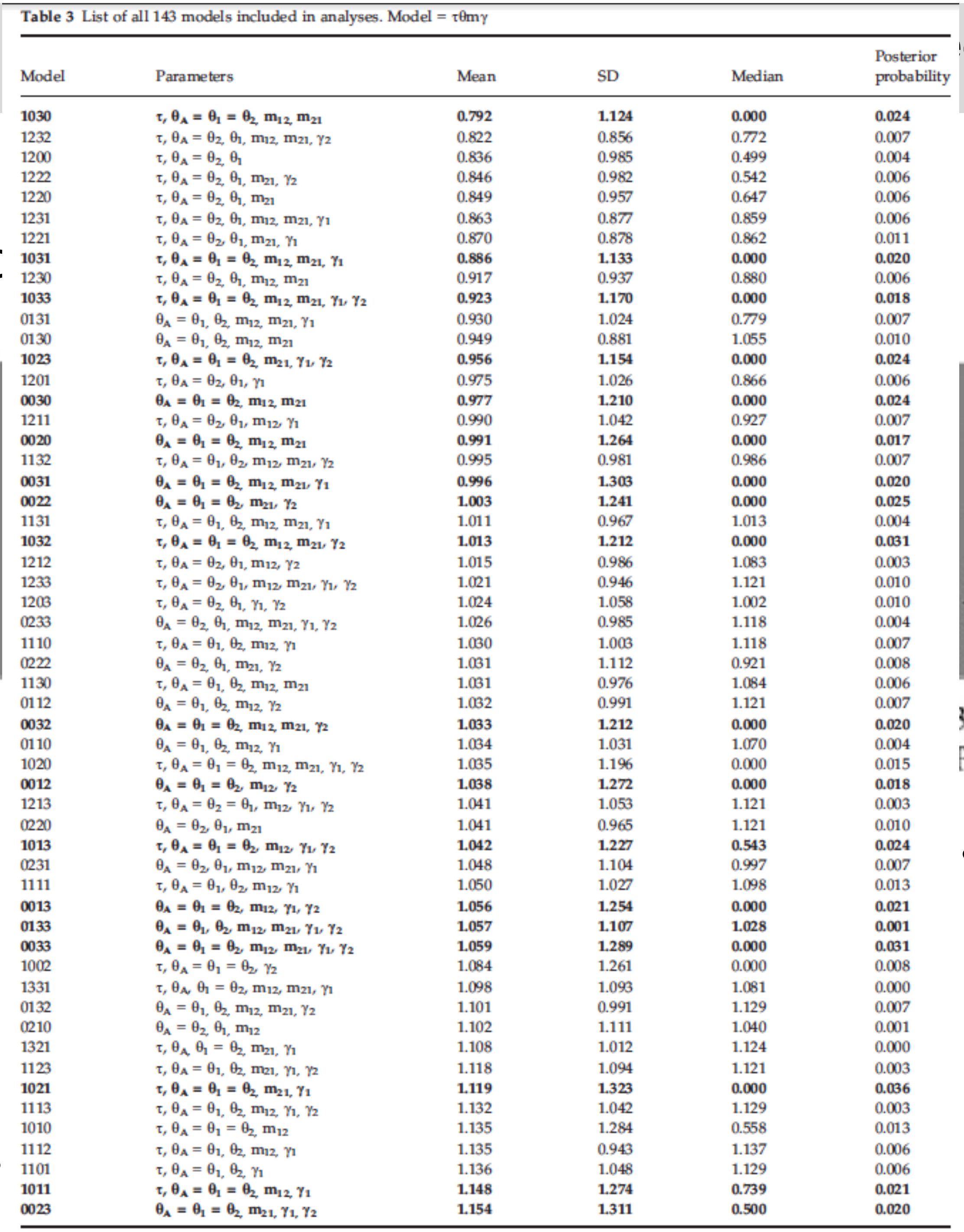
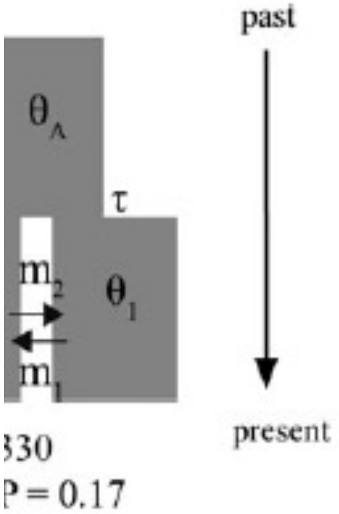


Table 3 List of all 143 models included in analyses. Model = τθmγ

Model	Parameters	Mean	SD	Median	Posterior probability
1030	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, m_{21}$**	**0.792**	**1.124**	**0.000**	**0.024**
1232	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_2$	0.822	0.856	0.772	0.007
1200	$\tau, \theta_A = \theta_2, \theta_1$	0.836	0.985	0.499	0.004
1222	$\tau, \theta_A = \theta_2, \theta_1, m_{21}, \gamma_2$	0.846	0.982	0.542	0.006
1220	$\tau, \theta_A = \theta_2, \theta_1, m_{21}$	0.849	0.957	0.647	0.006
1231	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_1$	0.863	0.877	0.859	0.006
1221	$\tau, \theta_A = \theta_2, \theta_1, m_{21}, \gamma_1$	0.870	0.878	0.862	0.011
1031	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1$**	**0.886**	**1.133**	**0.000**	**0.020**
1230	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, m_{21}$	0.917	0.937	0.880	0.006
1033	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$**	**0.923**	**1.170**	**0.000**	**0.018**
0131	$\theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1$	0.930	1.024	0.779	0.007
0130	$\theta_A = \theta_1, \theta_2, m_{12}, m_{21}$	0.949	0.881	1.055	0.010
1023	**$\tau, \theta_A = \theta_1 = \theta_2, m_{21}, \gamma_1, \gamma_2$**	**0.956**	**1.154**	**0.000**	**0.024**
1201	$\tau, \theta_A = \theta_2, \theta_1, \gamma_1$	0.975	1.026	0.866	0.006
0030	**$\theta_A = \theta_1 = \theta_2, m_{12}, m_{21}$**	**0.977**	**1.210**	**0.000**	**0.024**
1211	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, \gamma_1$	0.990	1.042	0.927	0.007
0020	**$\theta_A = \theta_1 = \theta_2, m_{12}, m_{21}$**	**0.991**	**1.264**	**0.000**	**0.017**
1132	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_2$	0.995	0.981	0.986	0.007
0031	**$\theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1$**	**0.996**	**1.303**	**0.000**	**0.020**
0022	**$\theta_A = \theta_1 = \theta_2, m_{21}, \gamma_2$**	**1.003**	**1.241**	**0.000**	**0.025**
1131	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1$	1.011	0.967	1.013	0.004
1032	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_2$**	**1.013**	**1.212**	**0.000**	**0.031**
1212	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, \gamma_2$	1.015	0.986	1.083	0.003
1233	$\tau, \theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.021	0.946	1.121	0.010
1203	$\tau, \theta_A = \theta_2, \theta_1, \gamma_1, \gamma_2$	1.024	1.058	1.002	0.010
0233	$\theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.026	0.985	1.118	0.004
1110	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, \gamma_1$	1.030	1.003	1.118	0.007
0222	$\theta_A = \theta_2, \theta_1, m_{21}, \gamma_2$	1.031	1.112	0.921	0.008
1130	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, m_{21}$	1.031	0.976	1.084	0.006
0112	$\theta_A = \theta_1, \theta_2, m_{12}, \gamma_2$	1.032	0.991	1.121	0.007
0032	**$\theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_2$**	**1.033**	**1.212**	**0.000**	**0.020**
0110	$\theta_A = \theta_1, \theta_2, m_{12}, \gamma_1$	1.034	1.031	1.070	0.004
1020	$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.035	1.196	0.000	0.015
0012	**$\theta_A = \theta_1 = \theta_2, m_{12}, \gamma_2$**	**1.038**	**1.272**	**0.000**	**0.018**
1213	$\tau, \theta_A = \theta_2 = \theta_1, m_{12}, \gamma_1, \gamma_2$	1.041	1.053	1.121	0.003
0220	$\theta_A = \theta_2, \theta_1, m_{21}$	1.041	0.965	1.121	0.010
1013	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, \gamma_1, \gamma_2$**	**1.042**	**1.227**	**0.543**	**0.024**
0231	$\theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_1$	1.048	1.104	0.997	0.007
1111	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, \gamma_1$	1.050	1.027	1.098	0.013
0013	**$\theta_A = \theta_1 = \theta_2, m_{12}, \gamma_1, \gamma_2$**	**1.056**	**1.254**	**0.000**	**0.021**
0133	**$\theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$**	**1.057**	**1.107**	**1.028**	**0.001**
0033	**$\theta_A = \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$**	**1.059**	**1.289**	**0.000**	**0.031**
1002	$\tau, \theta_A = \theta_1 = \theta_2, \gamma_2$	1.084	1.261	0.000	0.008
1331	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1$	1.098	1.093	1.081	0.000
0132	$\theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_2$	1.101	0.991	1.129	0.007
0210	$\theta_A = \theta_2, \theta_1, m_{12}$	1.102	1.111	1.040	0.001
1321	$\tau, \theta_A, \theta_1 = \theta_2, m_{21}, \gamma_1$	1.108	1.012	1.124	0.000
1123	$\tau, \theta_A = \theta_1, \theta_2, m_{21}, \gamma_1, \gamma_2$	1.118	1.094	1.121	0.003
1021	**$\tau, \theta_A = \theta_1 = \theta_2, m_{21}, \gamma_1$**	**1.119**	**1.323**	**0.000**	**0.036**
1113	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, \gamma_1, \gamma_2$	1.132	1.042	1.129	0.003
1010	$\tau, \theta_A = \theta_1 = \theta_2, m_{12}$	1.135	1.284	0.558	0.013
1112	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, \gamma_1$	1.135	0.943	1.137	0.006
1101	$\tau, \theta_A = \theta_1, \theta_2, \gamma_1$	1.136	1.048	1.129	0.006
1011	**$\tau, \theta_A = \theta_1 = \theta_2, m_{12}, \gamma_1$**	**1.148**	**1.274**	**0.739**	**0.021**
0023	**$\theta_A = \theta_1 = \theta_2, m_{21}, \gamma_1, \gamma_2$**	**1.154**	**1.311**	**0.500**	**0.020**

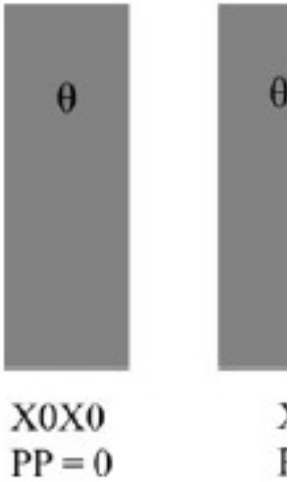


& Carstens (2014 Mol. Ecol.)

- generic models

Model choice i l

Tests of 142 ob



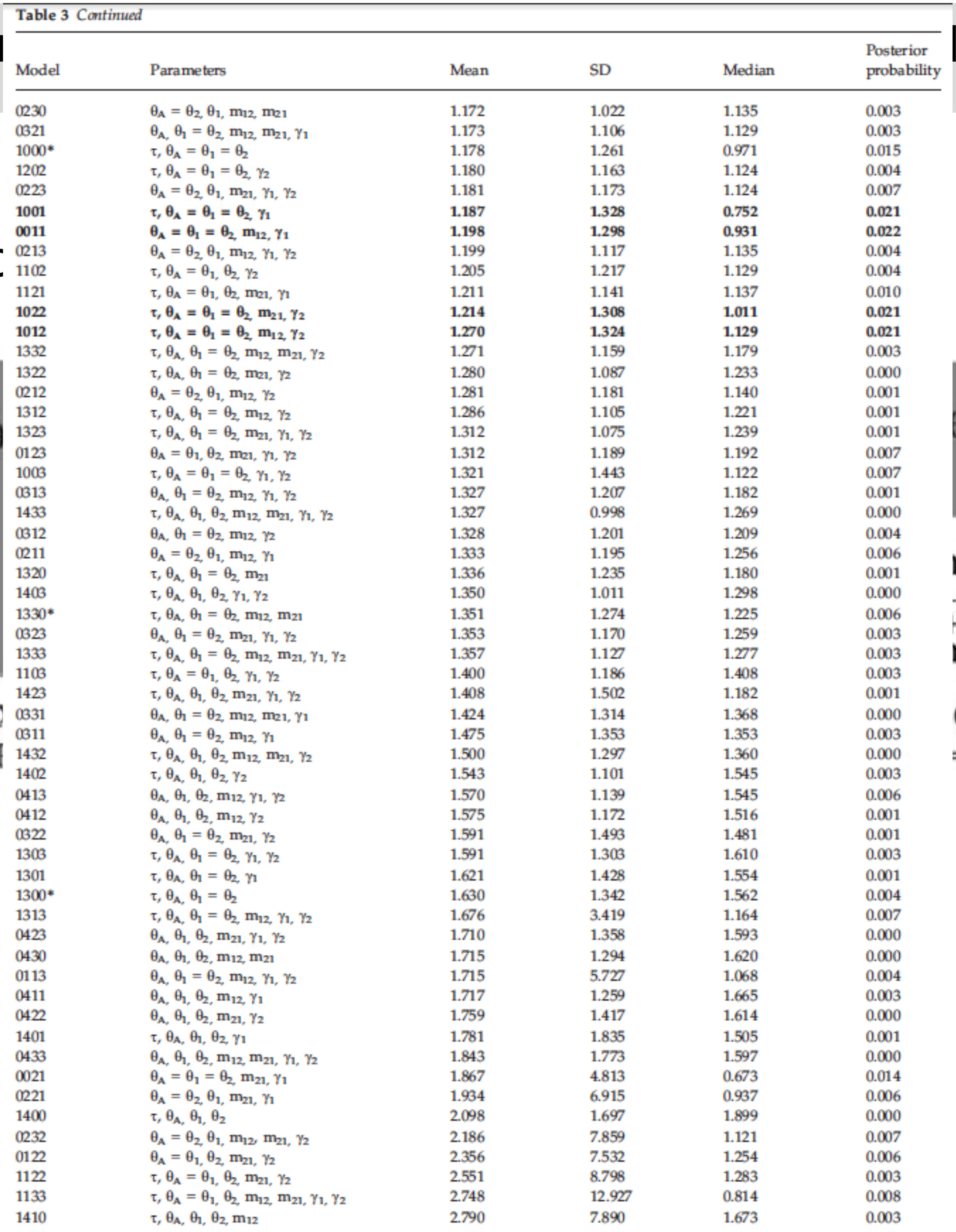
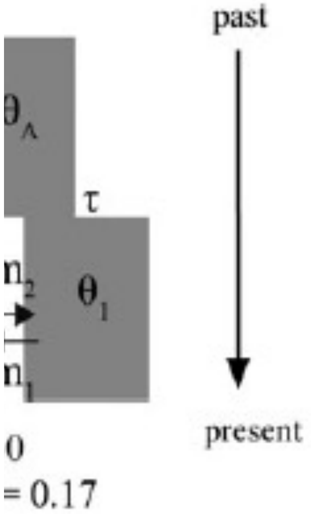


Table 3 *Continued*

Model	Parameters	Mean	SD	Median	Posterior probability
0230	$\theta_A = \theta_2, \theta_1, m_{12}, m_{21}$	1.172	1.022	1.135	0.003
0321	$\theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1$	1.173	1.106	1.129	0.003
1000*	$\tau, \theta_A = \theta_1 = \theta_2$	1.178	1.261	0.971	0.015
1202	$\tau, \theta_A = \theta_1 = \theta_2, \gamma_2$	1.180	1.163	1.124	0.004
0223	$\theta_A = \theta_2, \theta_1, m_{21}, \gamma_1, \gamma_2$	1.181	1.173	1.124	0.007
1001	$\boldsymbol{\tau, \theta_A = \theta_1 = \theta_2, \gamma_1}$	**1.187**	**1.328**	**0.752**	**0.021**
0011	$\boldsymbol{\theta_A = \theta_1 = \theta_2, m_{12}, \gamma_1}$	**1.198**	**1.298**	**0.931**	**0.022**
0213	$\theta_A = \theta_2, \theta_1, m_{12}, \gamma_1, \gamma_2$	1.199	1.117	1.135	0.004
1102	$\tau, \theta_A = \theta_1, \theta_2, \gamma_2$	1.205	1.217	1.129	0.004
1121	$\tau, \theta_A = \theta_1, \theta_2, m_{21}, \gamma_1$	1.211	1.141	1.137	0.010
1022	$\boldsymbol{\tau, \theta_A = \theta_1 = \theta_2, m_{21}, \gamma_2}$	**1.214**	**1.308**	**1.011**	**0.021**
1012	$\boldsymbol{\tau, \theta_A = \theta_1 = \theta_2, m_{12}, \gamma_2}$	**1.270**	**1.324**	**1.129**	**0.021**
1332	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_2$	1.271	1.159	1.179	0.003
1322	$\tau, \theta_A, \theta_1 = \theta_2, m_{21}, \gamma_2$	1.280	1.087	1.233	0.000
0212	$\theta_A = \theta_2, \theta_1, m_{12}, \gamma_2$	1.281	1.181	1.140	0.001
1312	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, \gamma_2$	1.286	1.105	1.221	0.001
1323	$\tau, \theta_A, \theta_1 = \theta_2, m_{21}, \gamma_1, \gamma_2$	1.312	1.075	1.239	0.001
0123	$\theta_A = \theta_1, \theta_2, m_{21}, \gamma_1, \gamma_2$	1.312	1.189	1.192	0.007
1003	$\tau, \theta_A = \theta_1 = \theta_2, \gamma_1, \gamma_2$	1.321	1.443	1.122	0.007
0313	$\theta_A, \theta_1 = \theta_2, m_{12}, \gamma_1, \gamma_2$	1.327	1.207	1.182	0.001
1433	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.327	0.998	1.269	0.000
0312	$\theta_A, \theta_1 = \theta_2, m_{12}, \gamma_2$	1.328	1.201	1.209	0.004
0211	$\theta_A = \theta_2, \theta_1, m_{12}, \gamma_1$	1.333	1.195	1.256	0.006
1320	$\tau, \theta_A, \theta_1 = \theta_2, m_{21}$	1.336	1.235	1.180	0.001
1403	$\tau, \theta_A, \theta_1, \theta_2, \gamma_1, \gamma_2$	1.350	1.011	1.298	0.000
1330*	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, m_{21}$	1.351	1.274	1.225	0.006
0323	$\theta_A, \theta_1 = \theta_2, m_{21}, \gamma_1, \gamma_2$	1.353	1.170	1.259	0.003
1333	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.357	1.127	1.277	0.003
1103	$\tau, \theta_A = \theta_1, \theta_2, \gamma_1, \gamma_2$	1.400	1.186	1.408	0.003
1423	$\tau, \theta_A, \theta_1, \theta_2, m_{21}, \gamma_1, \gamma_2$	1.408	1.502	1.182	0.001
0331	$\theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_1$	1.424	1.314	1.368	0.000
0311	$\theta_A, \theta_1 = \theta_2, m_{12}, \gamma_1$	1.475	1.353	1.353	0.003
1432	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_2$	1.500	1.297	1.360	0.000
1402	$\tau, \theta_A, \theta_1, \theta_2, \gamma_2$	1.543	1.101	1.545	0.003
0413	$\theta_A, \theta_1, \theta_2, m_{12}, \gamma_1, \gamma_2$	1.570	1.139	1.545	0.006
0412	$\theta_A, \theta_1, \theta_2, m_{12}, \gamma_2$	1.575	1.172	1.516	0.001
0322	$\theta_A, \theta_1 = \theta_2, m_{21}, \gamma_2$	1.591	1.493	1.481	0.001
1303	$\tau, \theta_A, \theta_1 = \theta_2, \gamma_1, \gamma_2$	1.591	1.303	1.610	0.003
1301	$\tau, \theta_A, \theta_1 = \theta_2, \gamma_1$	1.621	1.428	1.554	0.001
1300*	$\tau, \theta_A, \theta_1 = \theta_2$	1.630	1.342	1.562	0.004
1313	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, \gamma_1, \gamma_2$	1.676	3.419	1.164	0.007
0423	$\theta_A, \theta_1, \theta_2, m_{21}, \gamma_1, \gamma_2$	1.710	1.358	1.593	0.000
0430	$\theta_A, \theta_1, \theta_2, m_{12}, m_{21}$	1.715	1.294	1.620	0.000
0113	$\theta_A, \theta_1 = \theta_2, m_{12}, \gamma_1, \gamma_2$	1.715	5.727	1.068	0.004
0411	$\theta_A, \theta_1, \theta_2, m_{12}, \gamma_1$	1.717	1.259	1.665	0.003
0422	$\theta_A, \theta_1, \theta_2, m_{21}, \gamma_2$	1.759	1.417	1.614	0.000
1401	$\tau, \theta_A, \theta_1, \theta_2, \gamma_1$	1.781	1.835	1.505	0.001
0433	$\theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	1.843	1.773	1.597	0.000
0021	$\theta_A = \theta_1 = \theta_2, m_{21}, \gamma_1$	1.867	4.813	0.673	0.014
0221	$\theta_A = \theta_2, \theta_1, m_{21}, \gamma_1$	1.934	6.915	0.937	0.006
1400	$\tau, \theta_A, \theta_1, \theta_2$	2.098	1.697	1.899	0.000
0232	$\theta_A = \theta_2, \theta_1, m_{12}, m_{21}, \gamma_2$	2.186	7.859	1.121	0.007
0122	$\theta_A = \theta_1, \theta_2, m_{21}, \gamma_2$	2.356	7.532	1.254	0.006
1122	$\tau, \theta_A = \theta_1, \theta_2, m_{21}, \gamma_2$	2.551	8.798	1.283	0.003
1133	$\tau, \theta_A = \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	2.748	12.927	0.814	0.008
1410	$\tau, \theta_A, \theta_1, \theta_2, m_{12}$	2.790	7.890	1.673	0.003



Carstens (2014 Mol. Ecol.)

- generic models

Model choice in phylogeography: generic versus informed

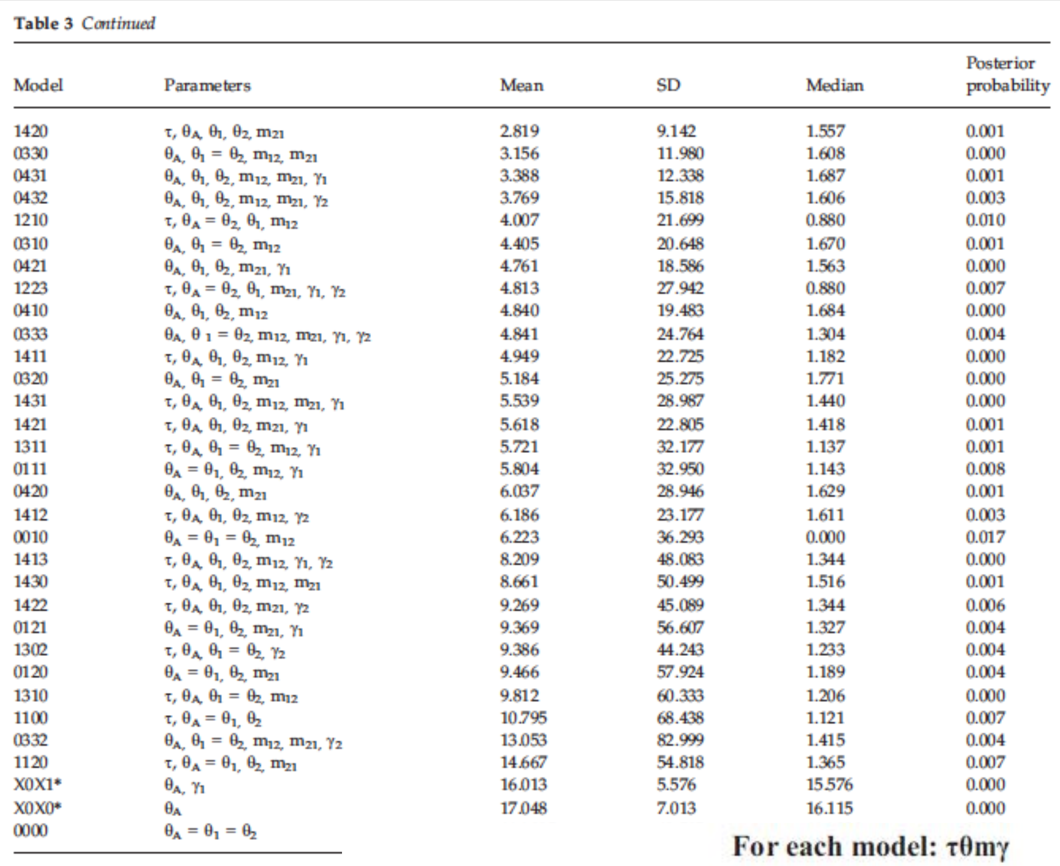
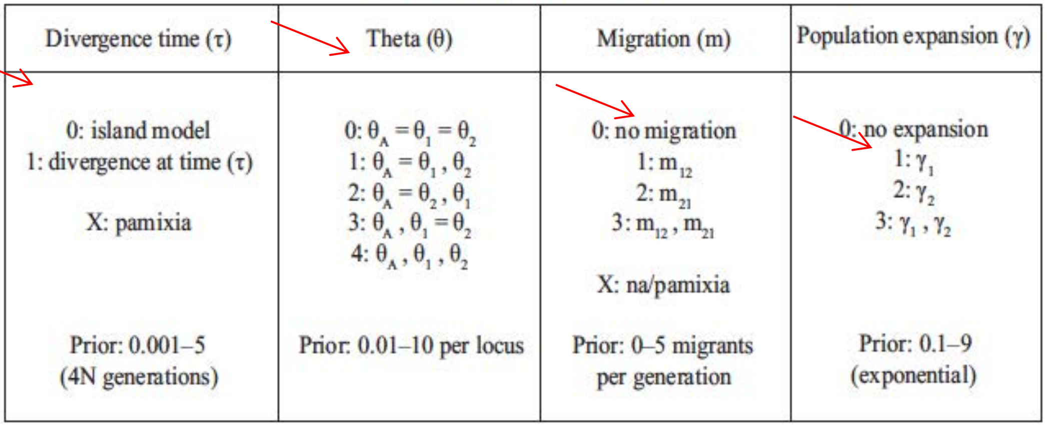


Table 3 *Continued*

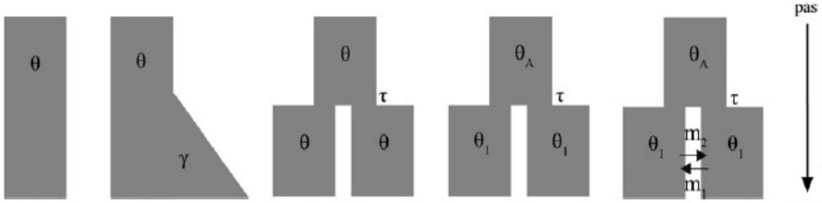
Model	Parameters	Mean	SD	Median	Posterior probability
1420	$\tau, \theta_A, \theta_1, \theta_2, m_{21}$	2.819	9.142	1.557	0.001
0330	$\theta_A, \theta_1 = \theta_2, m_{12}, m_{21}$	3.156	11.980	1.608	0.000
0431	$\theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1$	3.388	12.338	1.687	0.001
0432	$\theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_2$	3.769	15.818	1.606	0.003
1210	$\tau, \theta_A = \theta_2, \theta_1, m_{12}$	4.007	21.699	0.880	0.010
0310	$\theta_A, \theta_1 = \theta_2, m_{12}$	4.405	20.648	1.670	0.001
0421	$\theta_A, \theta_1, \theta_2, m_{21}, \gamma_1$	4.761	18.586	1.563	0.000
1223	$\tau, \theta_A = \theta_2, \theta_1, m_{21}, \gamma_1, \gamma_2$	4.813	27.942	0.880	0.007
0410	$\theta_A, \theta_1, \theta_2, m_{12}$	4.840	19.483	1.684	0.000
0333	$\theta_A, \theta\ 1 = \theta_2, m_{12}, m_{21}, \gamma_1, \gamma_2$	4.841	24.764	1.304	0.004
1411	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, \gamma_1$	4.949	22.725	1.182	0.000
0320	$\theta_A, \theta_1 = \theta_2, m_{21}$	5.184	25.275	1.771	0.000
1431	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, m_{21}, \gamma_1$	5.539	28.987	1.440	0.000
1421	$\tau, \theta_A, \theta_1, \theta_2, m_{21}, \gamma_1$	5.618	22.805	1.418	0.001
1311	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}, \gamma_1$	5.721	32.177	1.137	0.001
0111	$\theta_A = \theta_1, \theta_2, m_{12}, \gamma_1$	5.804	32.950	1.143	0.008
0420	$\theta_A, \theta_1, \theta_2, m_{21}$	6.037	28.946	1.629	0.001
1412	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, \gamma_2$	6.186	23.177	1.611	0.003
0010	$\theta_A = \theta_1 = \theta_2, m_{12}$	6.223	36.293	0.000	0.017
1413	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, \gamma_1, \gamma_2$	8.209	48.083	1.344	0.000
1430	$\tau, \theta_A, \theta_1, \theta_2, m_{12}, m_{21}$	8.661	50.499	1.516	0.001
1422	$\tau, \theta_A, \theta_1, \theta_2, m_{21}, \gamma_2$	9.269	45.089	1.344	0.006
0121	$\theta_A = \theta_1, \theta_2, m_{21}, \gamma_1$	9.369	56.607	1.327	0.004
1302	$\tau, \theta_A, \theta_1 = \theta_2, \gamma_2$	9.386	44.243	1.233	0.004
0120	$\theta_A = \theta_1, \theta_2, m_{21}$	9.466	57.924	1.189	0.004
1310	$\tau, \theta_A, \theta_1 = \theta_2, m_{12}$	9.812	60.333	1.206	0.000
1100	$\tau, \theta_A = \theta_1, \theta_2$	10.795	68.438	1.121	0.007
0332	$\theta_A, \theta_1 = \theta_2, m_{12}, m_{21}, \gamma_2$	13.053	82.999	1.415	0.004
1120	$\tau, \theta_A = \theta_1, \theta_2, m_{21}$	14.667	54.818	1.365	0.007
X0X1*	θ_A, γ_1	16.013	5.576	15.576	0.000
X0X0*	θ_A	17.048	7.013	16.115	0.000
0000	$\theta_A = \theta_1 = \theta_2$				

For each model: τθmγ

The answer is model 1023!



Divergence time (τ)	Theta (θ)	Migration (m)	Population expansion (γ)
0: island model 1: divergence at time (τ) X: pamixia	0: $\theta_A = \theta_1 = \theta_2$ 1: $\theta_A = \theta_1, \theta_2$ 2: $\theta_A = \theta_2, \theta_1$ 3: $\theta_A, \theta_1 = \theta_2$ 4: $\theta_A, \theta_1, \theta_2$	0: no migration 1: m_{12} 2: m_{21} 3: m_{12}, m_{21} X: na/pamixia	0: no expansion 1: γ_1 2: γ_2 3: γ_1, γ_2
Prior: 0.001–5 (4N generations)	Prior: 0.01–10 per locus	Prior: 0–5 migrants per generation	Prior: 0.1–9 (exponential)



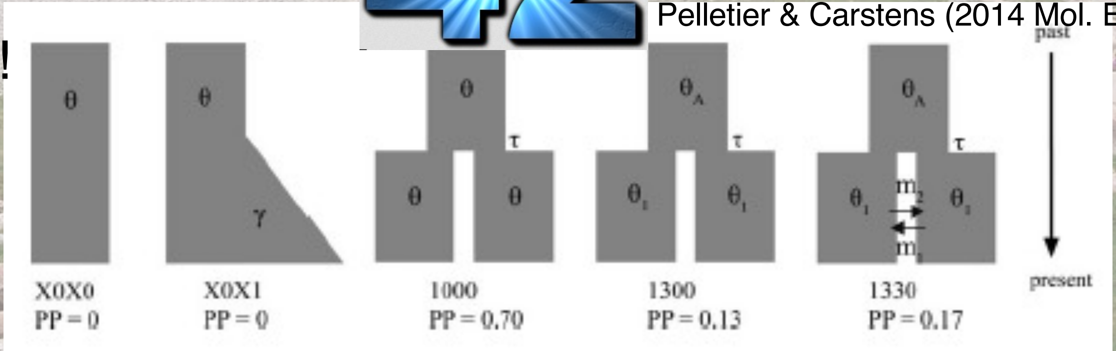
Biological insights depend on the questions we (the scientist) ask!

- Should we expect (or want) or computer programs to define the questions we ask!?!

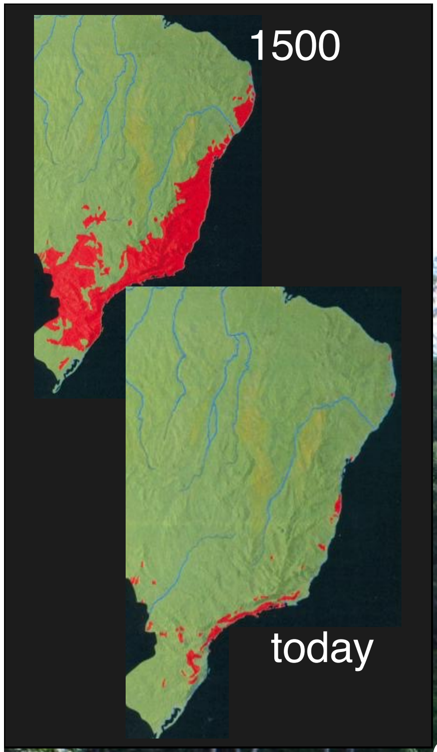
The answer is: 42

The answer is model 1023!

Pelletier & Carstens (2014 Mol. Ecol.)



- Model formulation is a way of communicating our expert knowledge to statistical apparatus to test hypotheses



Model-based approach:

Forecasting spatial patterns of diversity in poorly explored, highly threatened ecosystems

Model-based approach:

Directly model historical processes through a combination of ecological-niche models under paleoclimates and genetic analyses, discovered a central region in the Brazilian Atlantic forest that served as a biodiversity refuge during climatic extremes.

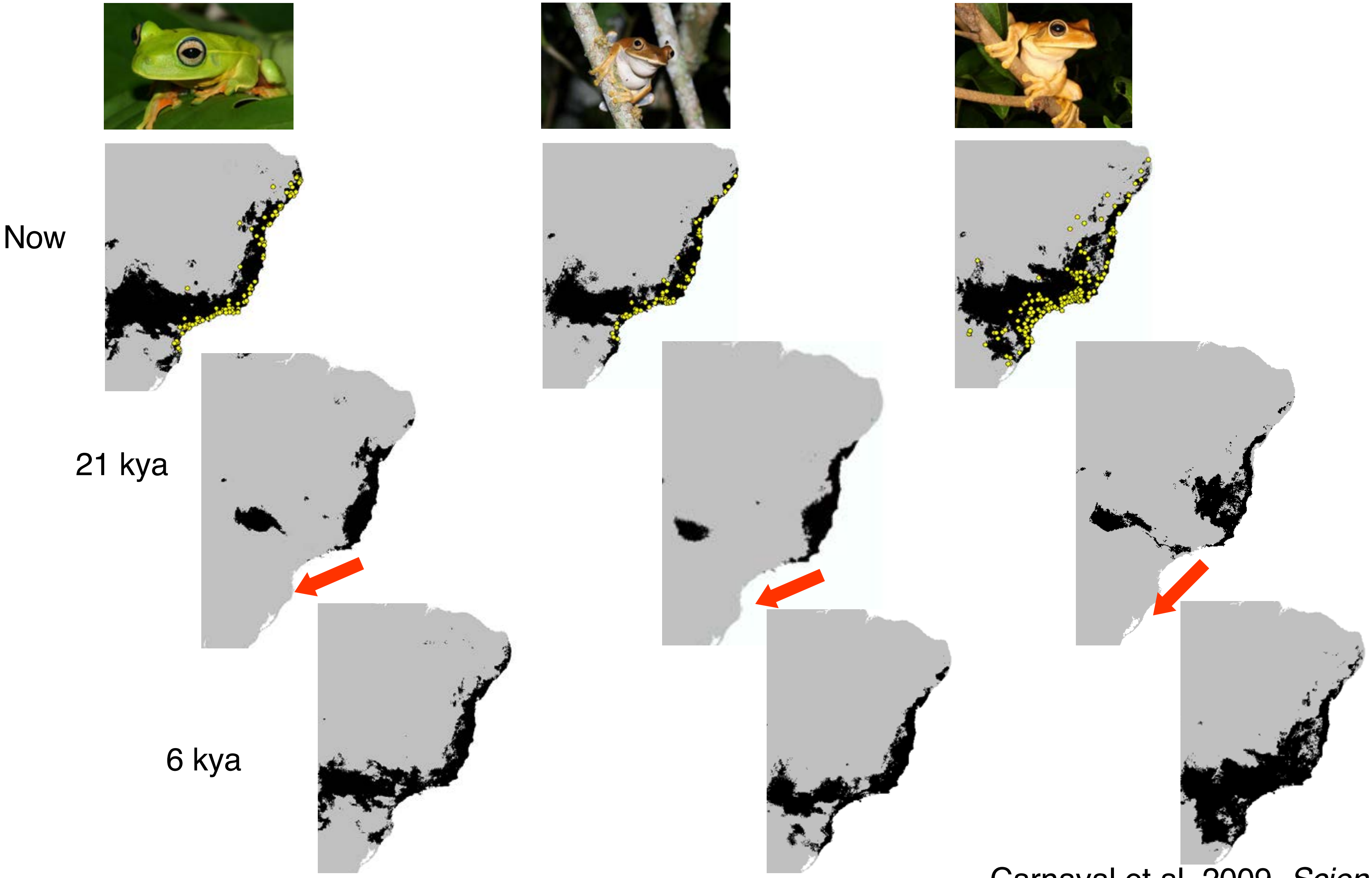
Hypsiboas albomarginatus

H. semilineatus

H. faber

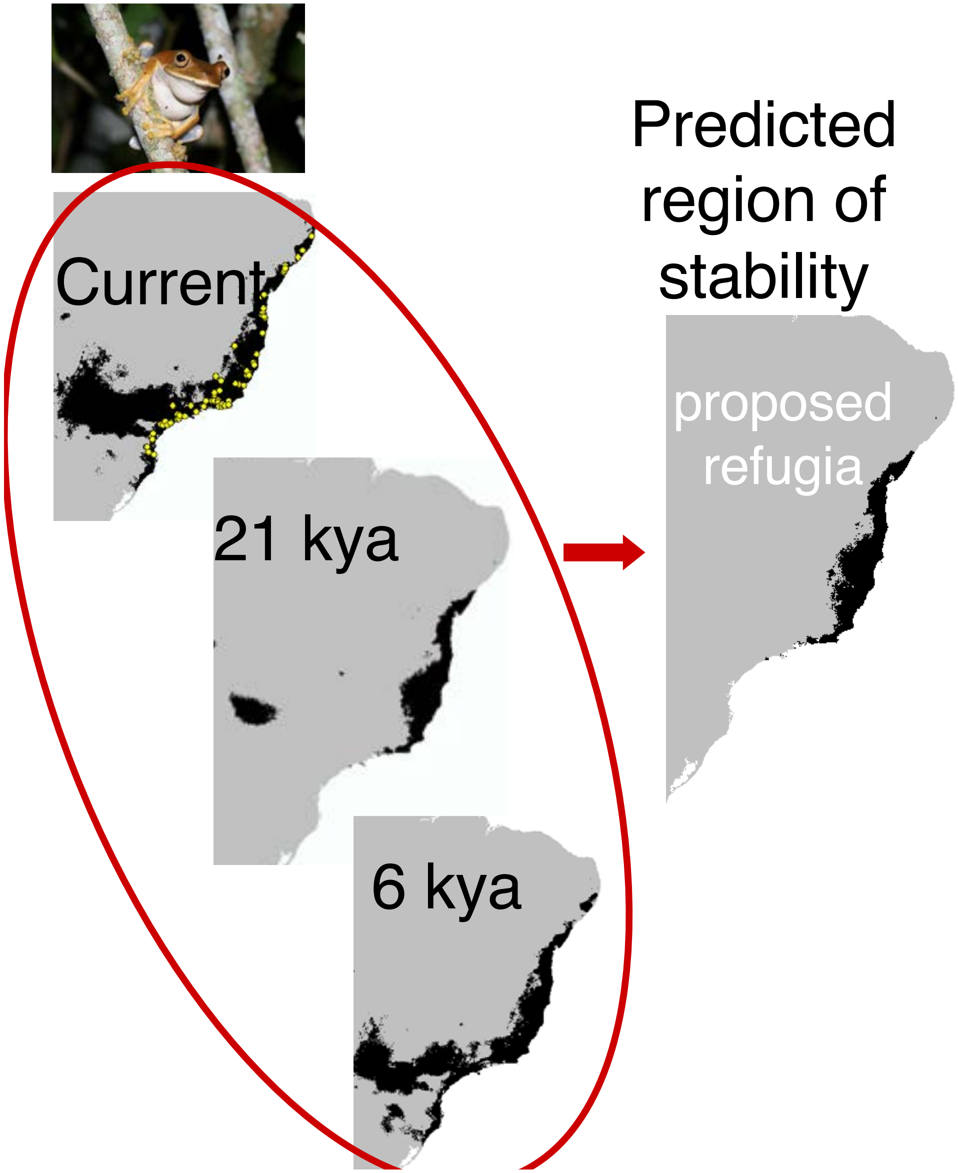
Carnaval et al. 2009. *Science*

Model species distributions under current conditions and climatic extremes (based on climatic niches with MAXENT)



Carnaval et al. 2009. *Science*

Model species distributions under current conditions and climatic extremes (based on climatic niches with MAXENT)

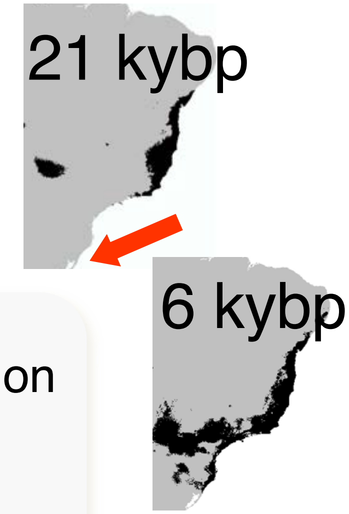


Maps of stable and unstable areas raise specific hypotheses about regional differences in persistence and hence diversity, which lead to phylogeographic predictions that can be tested with molecular data

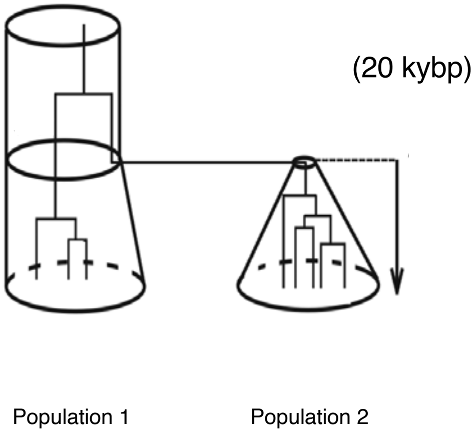
Carnaval et al. 2009. *Science*

Different demographic scenarios motivated by stable/unstable areas:

Results support community responses for both models using hierarchical Approximate Bayesian Computation:

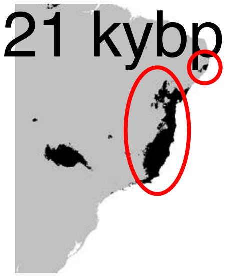


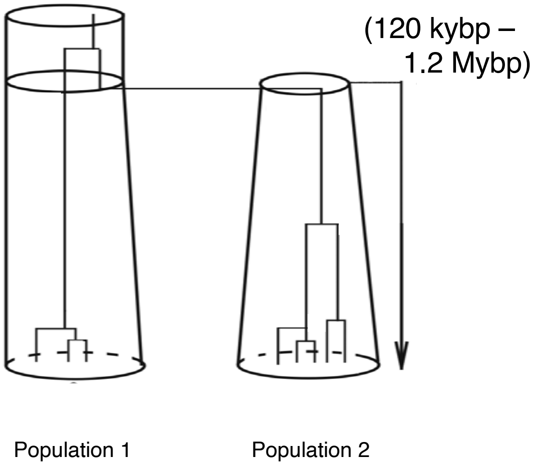
recent colonization



(i) simultaneous, multi-species colonization of unstable areas from adjacent refugial populations since the LGM

long-term persistence





(ii) assemblage-scale, long-term persistence of populations in isolated refugial areas (i.e., temporally stable regions)

Carnaval et al. 2009. *Science*

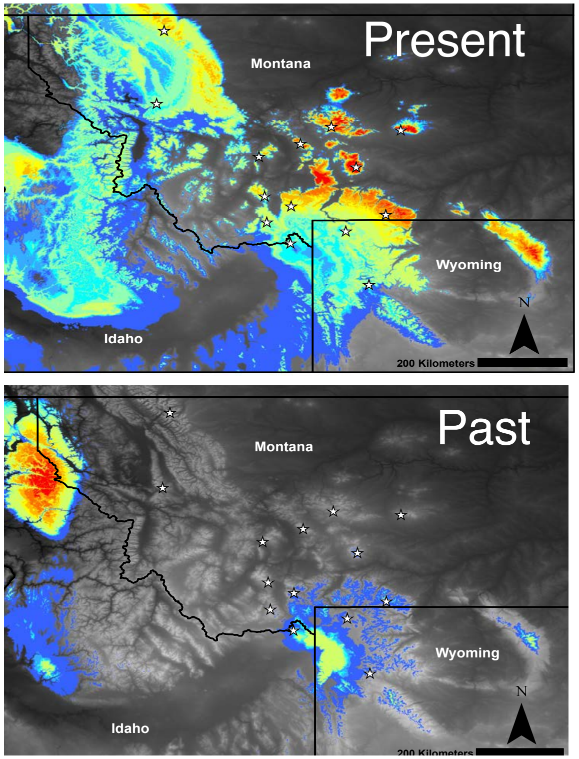
* All models are simplifications, but they vary in their relative degree of abstraction

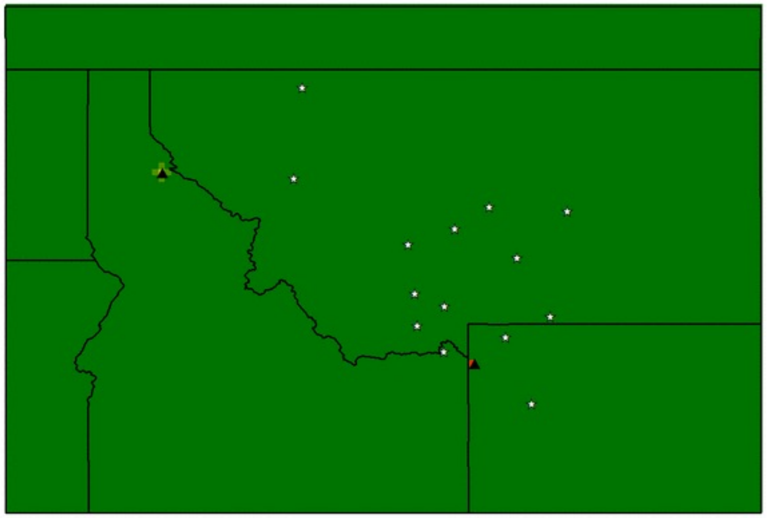
Different ways to model population expansion:

(i) Model as population size change with no spatial aspect of expansion (e.g., Brazilian Atlantic forest areas of instability associated with recent expansion)

(ii) Model expansion process across landscape explicitly

ENM based on paleoclimatic data 6kya





iDDC: Generate species-specific expectations for patterns of genetic variation

He, Edwards & Knowles, Evolution 2013

integrative
Distributional
Demographic
Coalescent
modeling

Distributional model
(i.e., ecological niche model) with
predictions on probability of occurrence
across the landscape

Demographic model
informed by habitat
suitabilities

Spatially-explicit coalescent
simulations based on
demographic model

Tests of hypotheses/models
using ABC

Habitat suitability scores

40	20	10	5
100	60	20	10
100	100	40	40
80	80	60	60

K(m)

400 (40)	200 (20)	100 (10)	50 (5)
1000 (100)	600 (60)	200 (20)	100 (10)
1000 (100)	1000 (100)	400 (40)	400 (40)
800 (80)	800 (80)	600 (60)	600 (60)

Carrying capacity: k_i

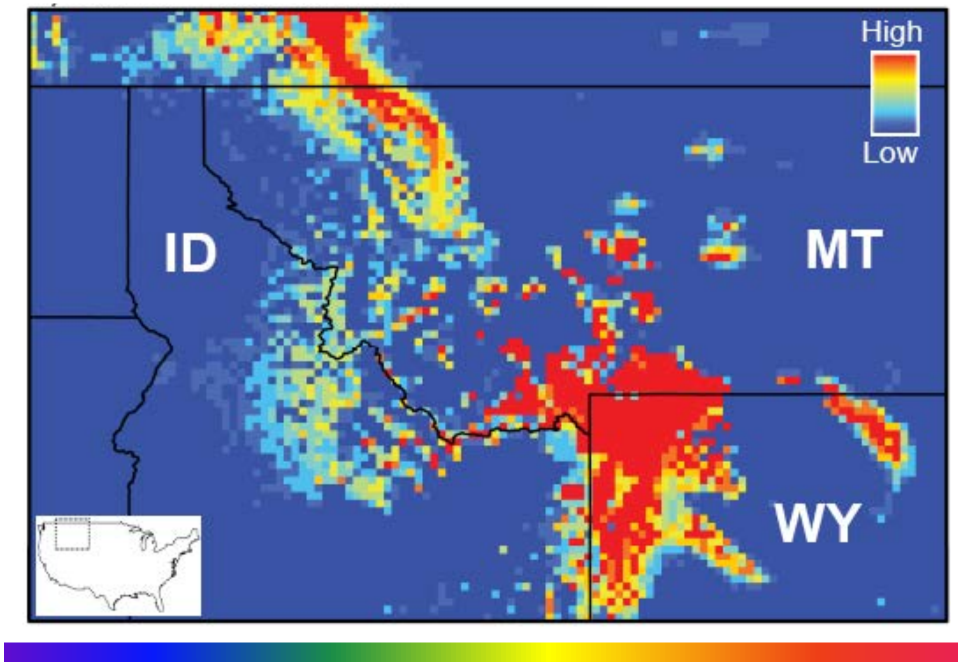
Gene coalescence across the landscape

SPLATCHE2

also Knowles & Serrano Mol. Ecol., 2010

iDDC: integrative Distributional, Demographic, Coalescent modeling

SPECIES-SPECIFIC
Spatially explicit
quantitative information
about probabilities of
occurrence based on
habitat suitability



low habitat suitability

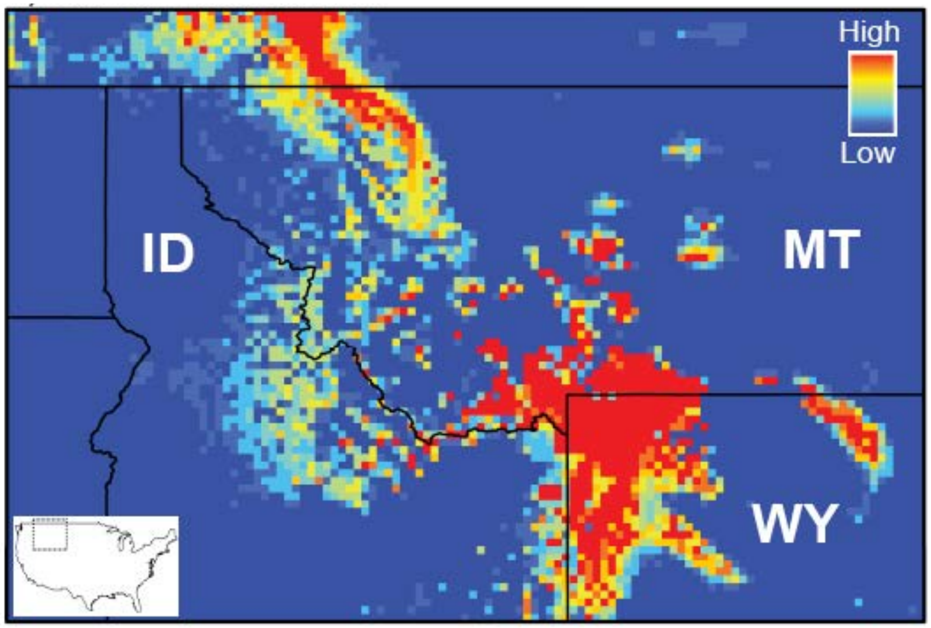
high habitat suitability

Habitat suitability scores

40	20	10	5
100	60	20	10
100	100	40	40
80	80	60	60

iDDC: integrative Distributional, Demographic, Coalescent modeling

Spatially explicit
probabilities of occurrence based on
habitat suitability



⇩

SPECIES-SPECIFIC Spatially explicit demographic model

- carrying capacity: *k*
- migration rate: m
- logistic growth rate: r

low habitat suitability

high habitat suitability

K(m)

400 (40)	200 (20)	100 (10)	50 (5)
1000 (100)	600 (60)	200 (20)	100 (10)
1000 (100)	1000 (100)	400 (40)	400 (40)
800 (80)	800 (80)	600 (60)	600 (60)

low *K*

high *K*

low *m*

High *m*

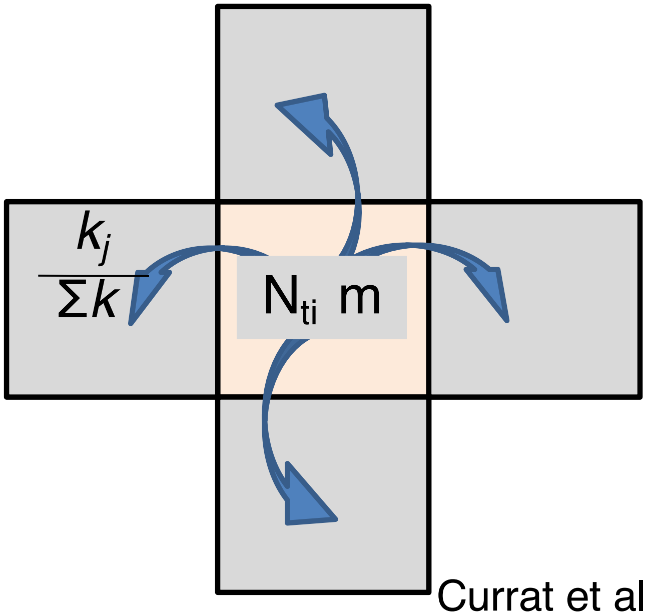
e.g.: SPECIES-SPECIFIC Demographic model:

At each generation:
-the population density, N_{ti}, of each deme is logistically regulated
-followed by a migration step
-the population densities and number of immigrants (N_{ti} and m) are stored and used during the genetic simulations

- carrying capacity: k_i

- # of emigrants leaving deme i: N_{ti} m

- # of immigrants entering deme j: $\frac{k_j}{\Sigma k}$



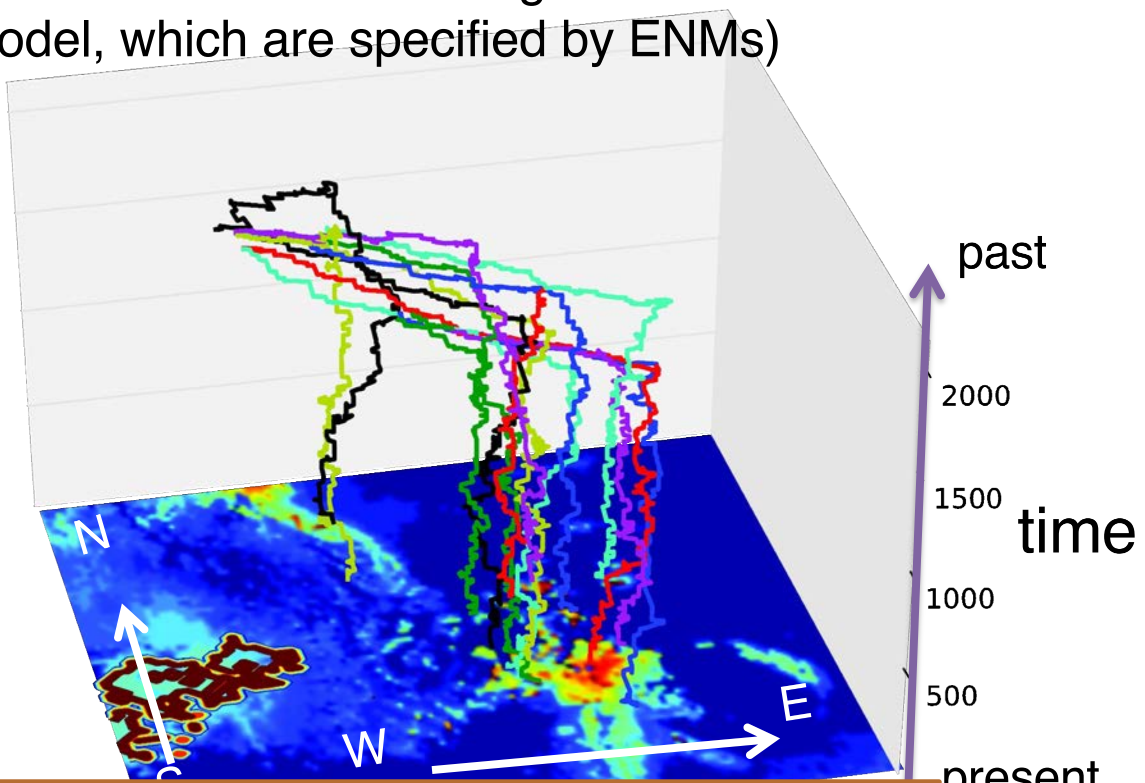
Currat et al. 2004

iDDC: integrative Distributional, Demographic, Coalescent modeling

•spatially-explicit genealogies to generate genetic patterns

-at each generation (looking backwards in time), genes have probability of:

(i) staying in the same deme,
(ii) move to a different deme, or
(iii) coalesce with another gene lineage
(depending upon the population densities and migration rates from the demographic model, which are specified by ENMs)



Suggested software: Quesztal package (Becheler and Knowles 2022)

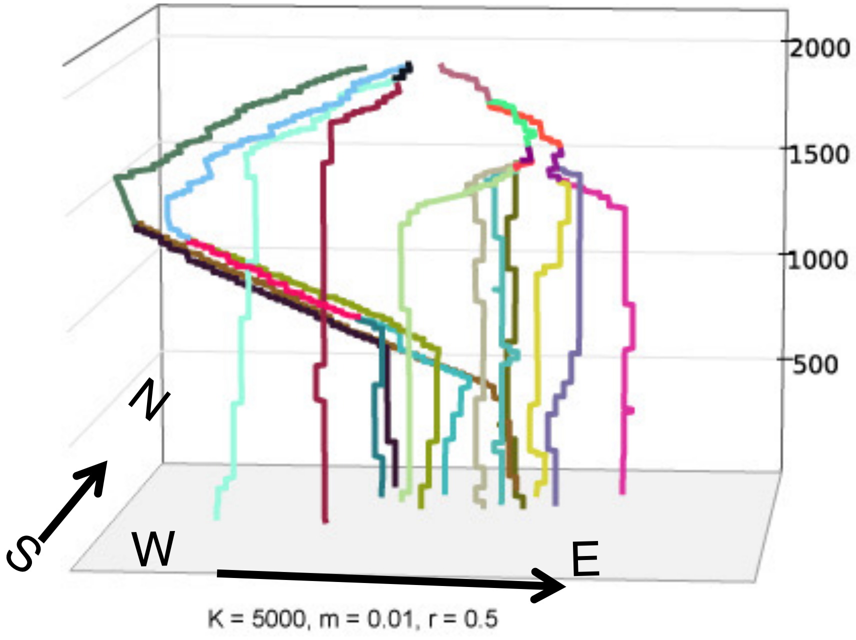
Under different demographic parameters (e.g., different *k* and *m*), same set of sampled populations would have different coalescent histories

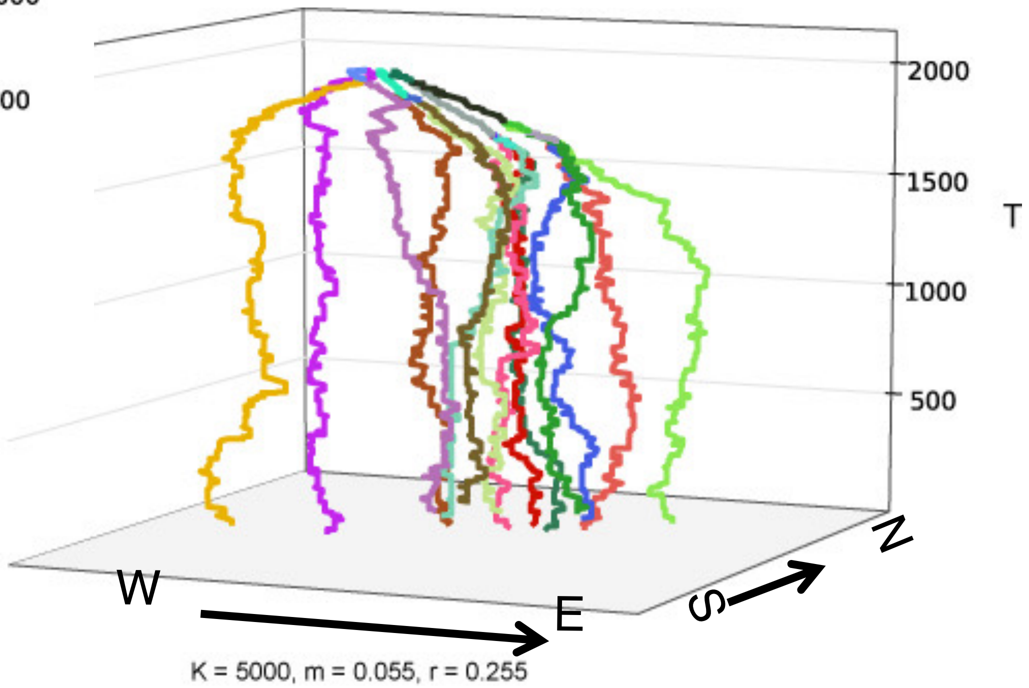
because of different probabilities to:

(i) stay in the same deme,

(ii) move to a different deme, or

(iii) coalesce with another gene lineage

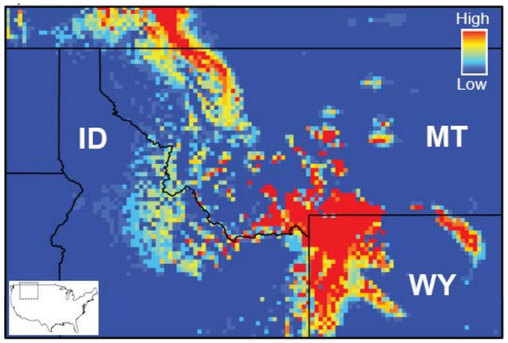




(iv) Mutations accumulate along the branches of the genealogy according to a Poisson process with rate *μt*

- Simulate predicted patterns of genetic variation for set of parameters under the model

Species-distribution model (SDM) generates predictions on probability of occurrence across the landscape



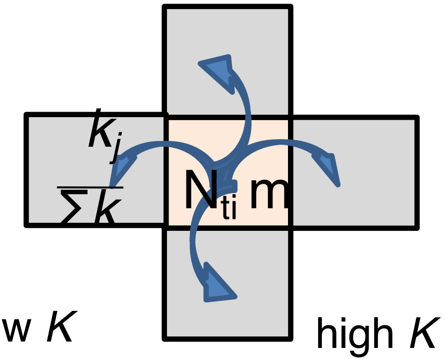
low habitat suitability

high habitat suitability

Habitat suitability scores

40	20	10	5
100	60	20	10
100	100	40	40
80	80	60	60

Spatially explicit demographic model (localized population densities, migration and growth rates)



low *K*

high *K*

low *m* and *r*

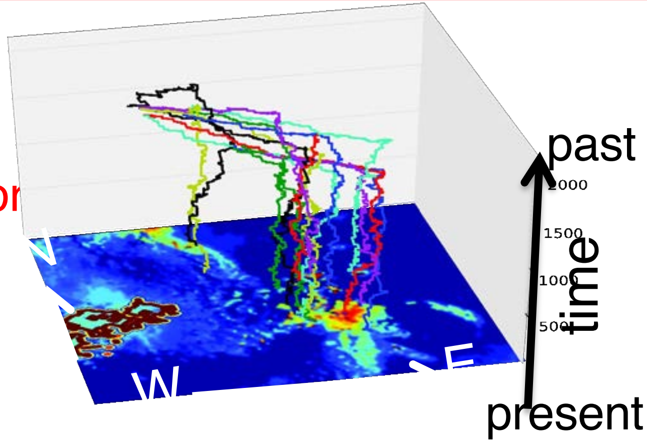
High *m* and *r*

K(m)

400 (40)	200 (20)	100 (10)	50 (5)
1000 (100)	600 (60)	200 (20)	100 (10)
1000 (100)	1000 (100)	400 (40)	400 (40)
800 (80)	800 (80)	600 (60)	600 (60)

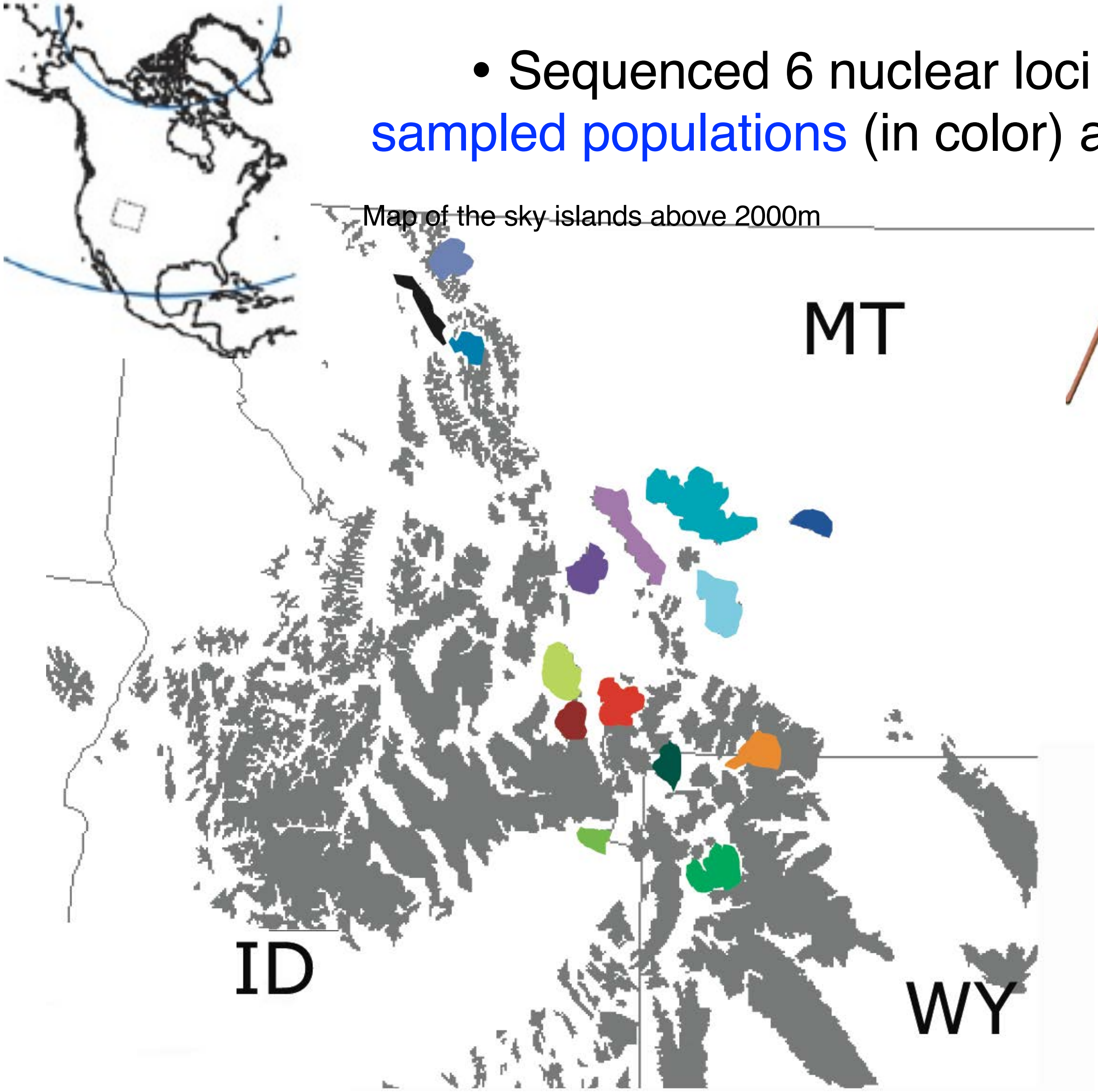
Carrying capacity: k_i

Spatially explicit coalescent model to generate predicted patterns of genetic variation for the empirically sampled population localities

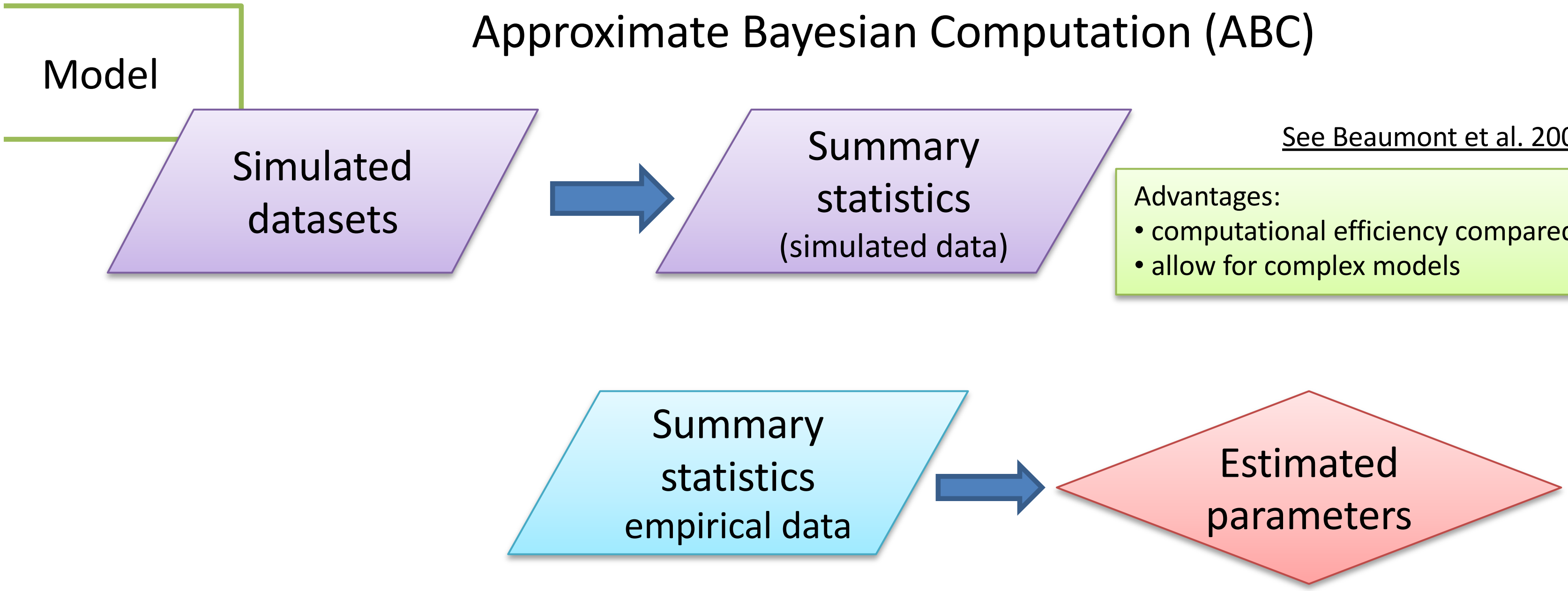


Gene coalescence across the landscape

- Sequenced 6 nuclear loci in 114 individuals of sampled populations (in color) across the species range



iDDC : Model Selection & Parameter Estimation using Approximate Bayesian Computation (ABC)



Model

Simulated datasets

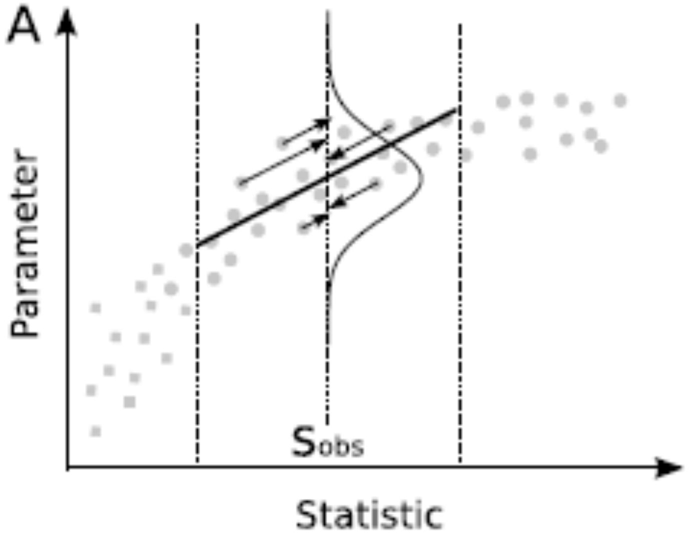
Summary statistics (simulated data)

Summary statistics empirical data

Estimated parameters

See Beaumont et al. 2002

Advantages:
- computational efficiency compared to ML methods
- allow for complex models



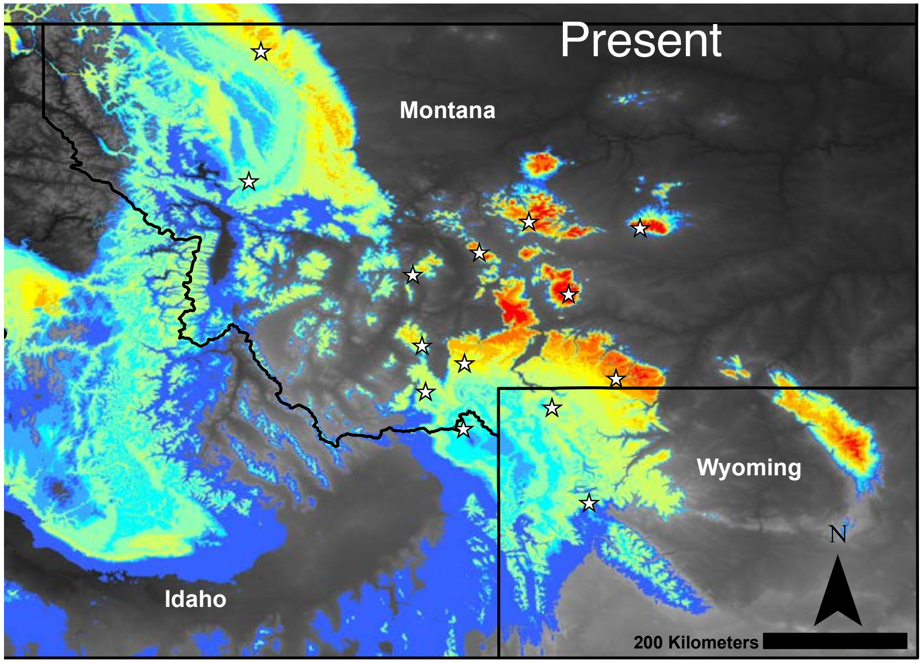
We can identify sets of parameters for specific models that produce simulated data that matches the empirical data.

Suggested software: abctoolbox (Wegmann et al. 2010)

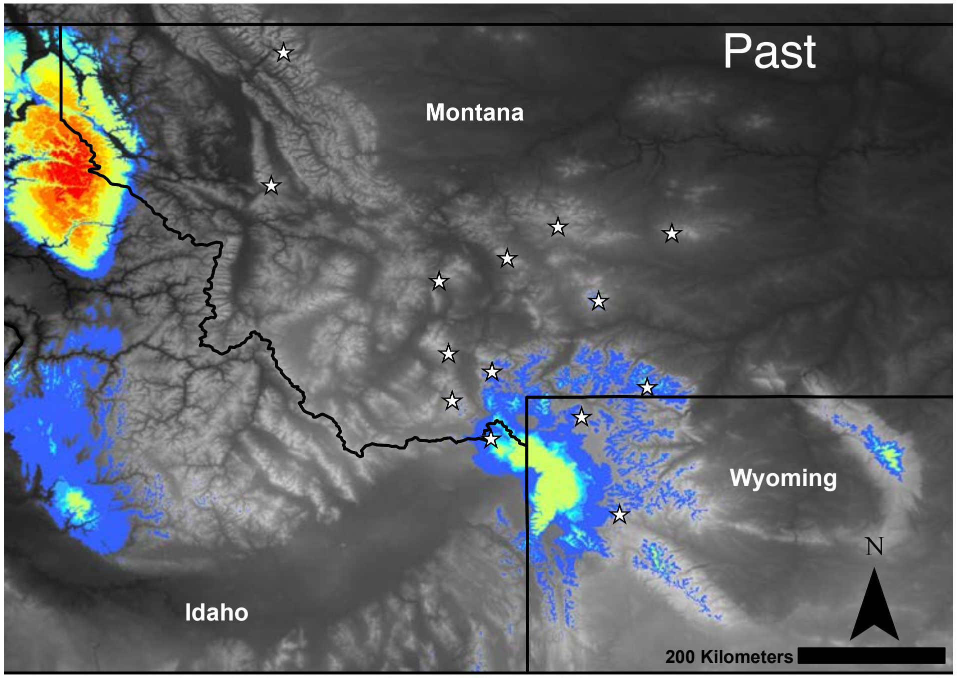
What geographic configuration of sky island populations promotes species divergence?

Population connectivity determined by contemporary sky island distribution versus Colonization of present sky island distribution from glacial refugia

19 bioclimatic variables used in modeling distributions



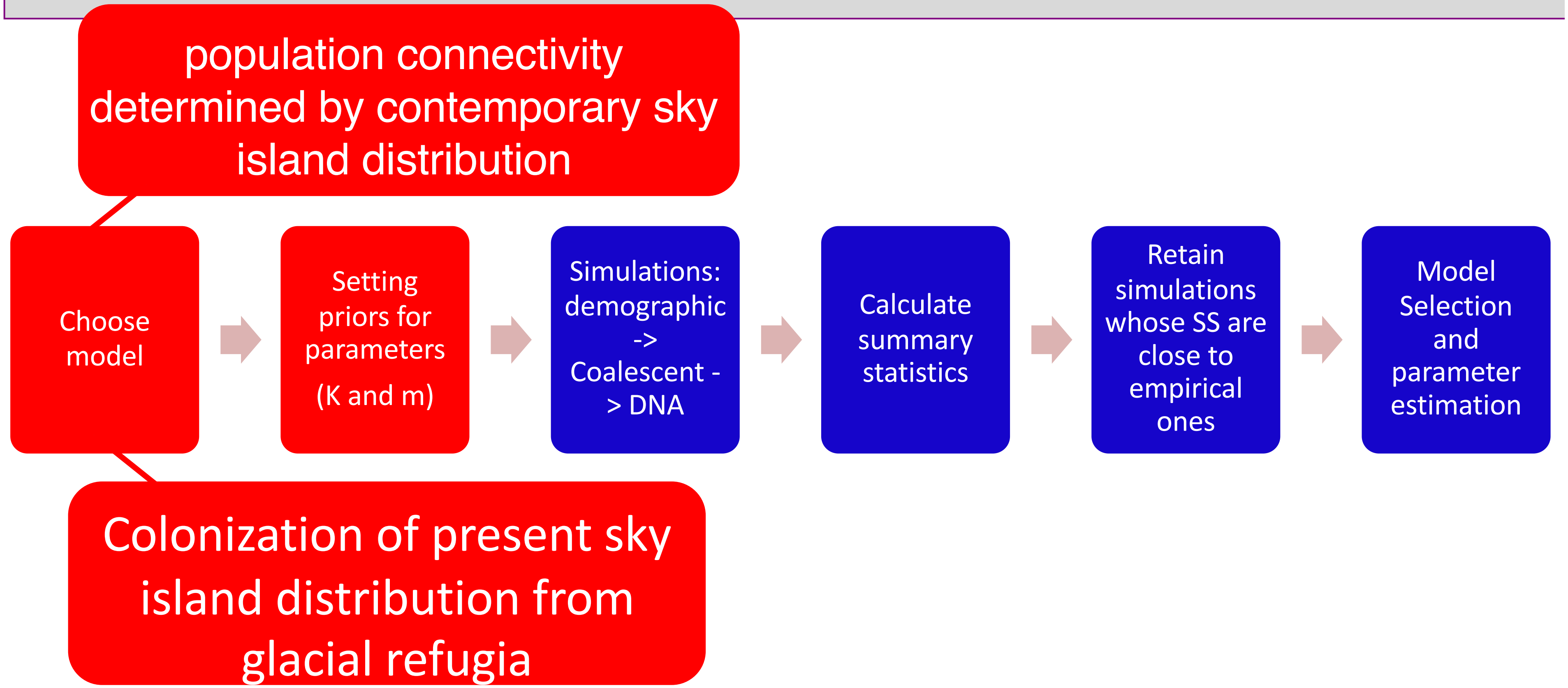
ENM based on current environmental data



ENM based on paleoclimatic data 6kya

- grasshoppers are flightless habitat specialists restricted to montane meadows

iDDC tests of drivers of divergence



population connectivity determined by contemporary sky island distribution

Choose model

Setting priors for parameters (K and m)

Simulations: demographic -> Coalescent -> DNA

Calculate summary statistics

Retain simulations whose SS are close to empirical ones

Model Selection and parameter estimation

Colonization of present sky island distribution from glacial refugia

6 anonymous nuclear loci from 114 individuals sampled across the range of *M. oregonensis*

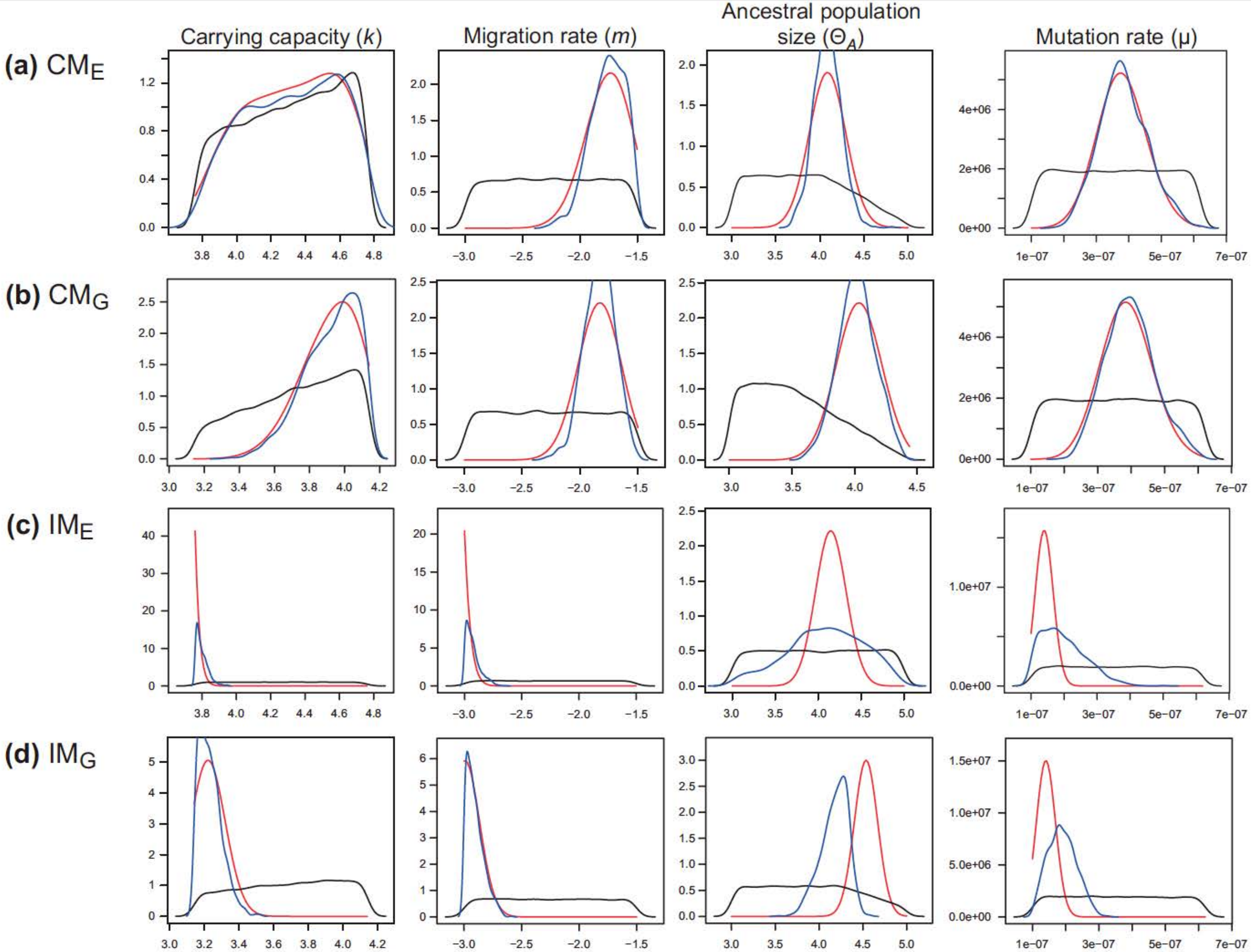
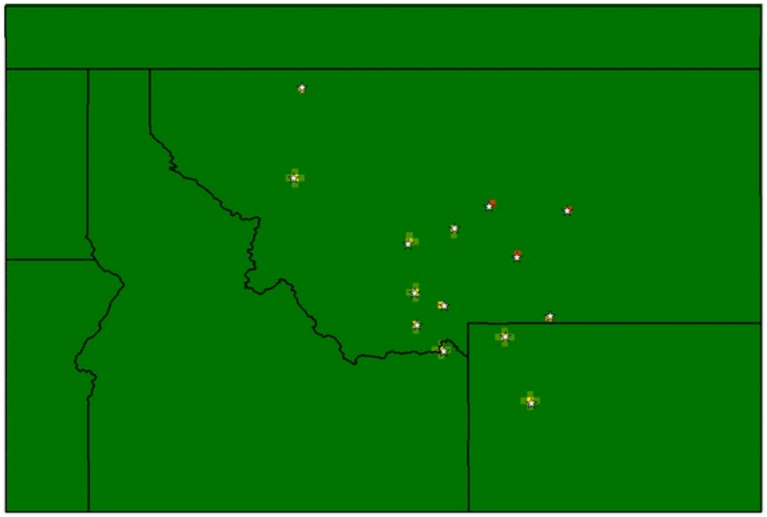
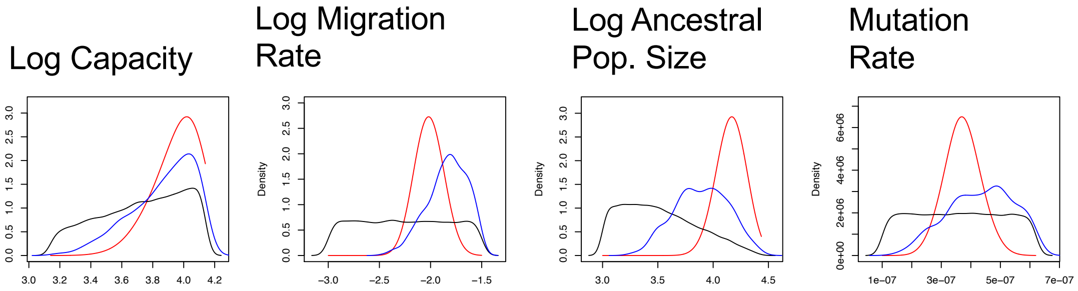


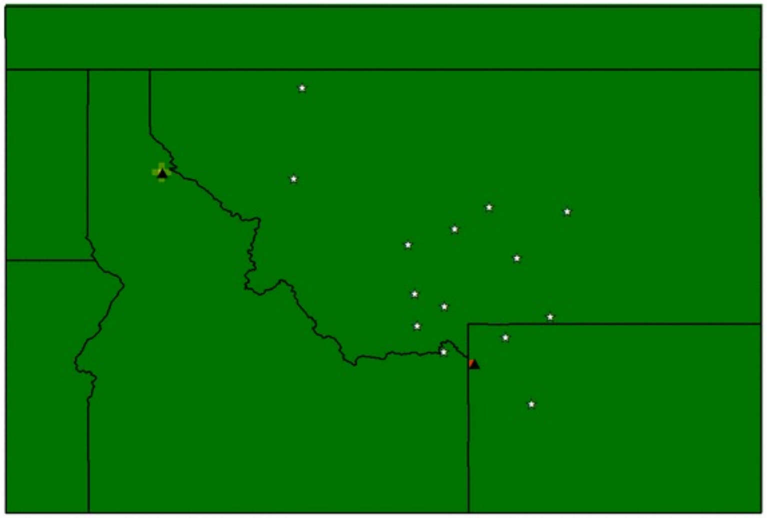
Figure 4. Posterior distribution (red line) of parameter estimates (i.e. carrying capacity, *k*, migration rate, *m*, ancestral population size θ_A, and mutation rate, μ) for each of the two colonization models, (a) CM_E and (b) CM_G, and the two sky island isolation models, (c) IM_E and (d) IM_G, where the subscripts E and G refer to connectivity patterns determined by either environmental heterogeneity or geographic distance, respectively. Results are based on a GLM regression adjustment of the 5000 closet simulations to each model. The distribution of the retained simulations (blue line) and the prior (black line) demonstrate the improvement that the GLM procedure had on parameter estimates and that the data contained information relevant to estimating the parameters.





Model tests based on comparing marginal likelihoods:

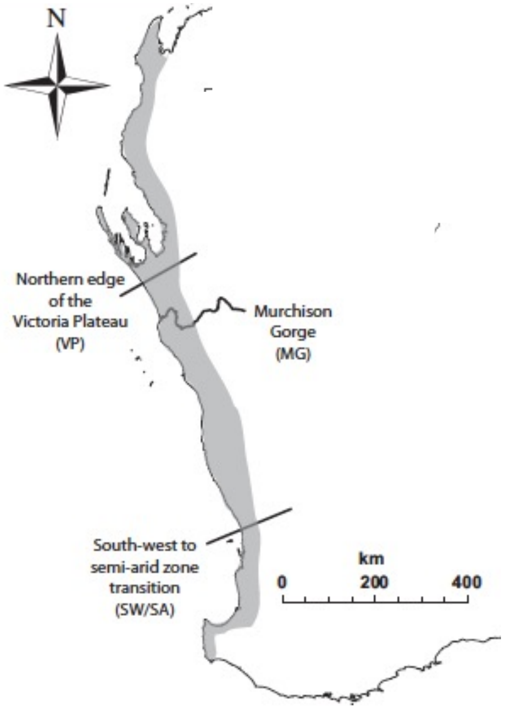
(i) population connectivity determined by contemporary sky island distribution



Patterns of genetic variation reflect: (ii) a colonization history from glacial refugia to present sky island distribution

Knowles LL, *Massatti R* (2017) Distributional shifts – not geographic isolation – as a probable driver of montane species divergence. *Ecography* 40:1475-1485.

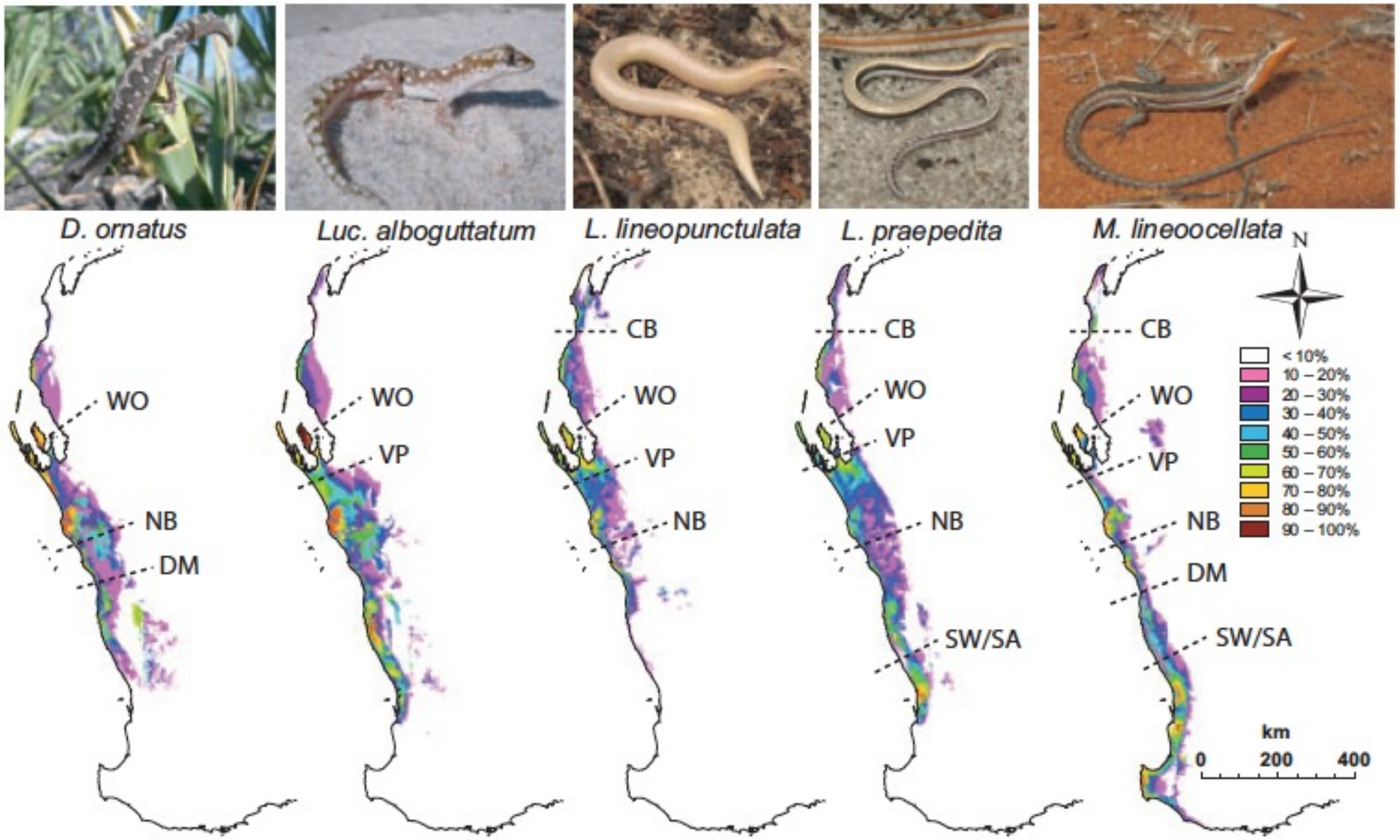
Explicit modeling of movement across landscape in phylogeography models



N
Northern edge of the Victoria Plateau (VP)
Murchison Gorge (MG)
South-west to semi-arid zone transition (SW/SA)
km
0
200
400

Linear distribution of populations along SW coast suggests isolation-by-distance may be important in structuring patterns of genetic variation

Edwards, Keogh, Knowles (2012) *Mol. Ecol.*



But species vary in their specialization to sand-dunes, suggesting habitat differences across space may be important in structuring patterns of genetic variation

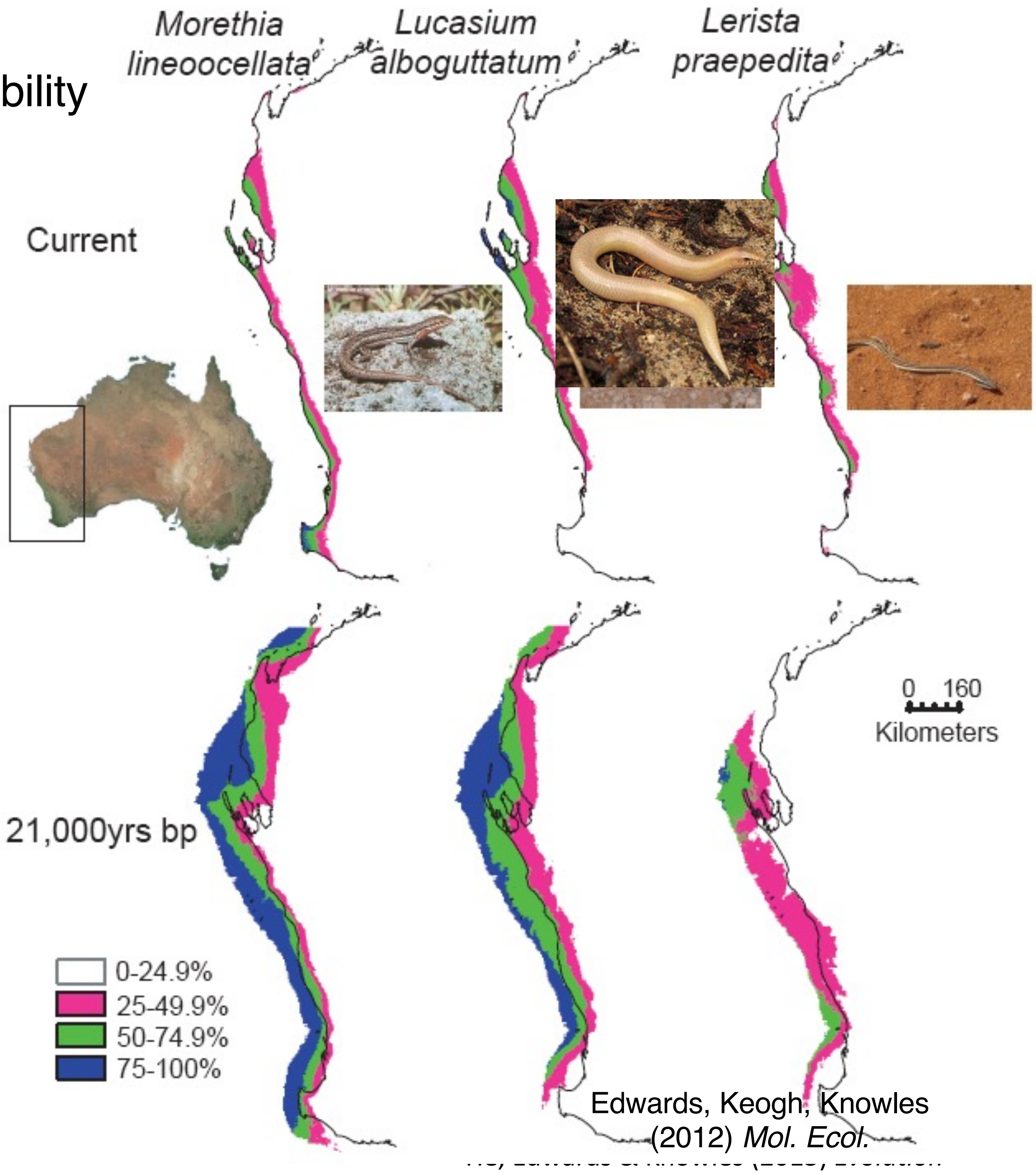
Edwards, Keogh, Knowles (2012) *Mol. Ecol.*

Climatic conditions have changed over time

Current distribution (contemporary climatic data)

Habitat suitability

□ 0-24.
🟥 25-49
🟩 50-74
🟦 75-10

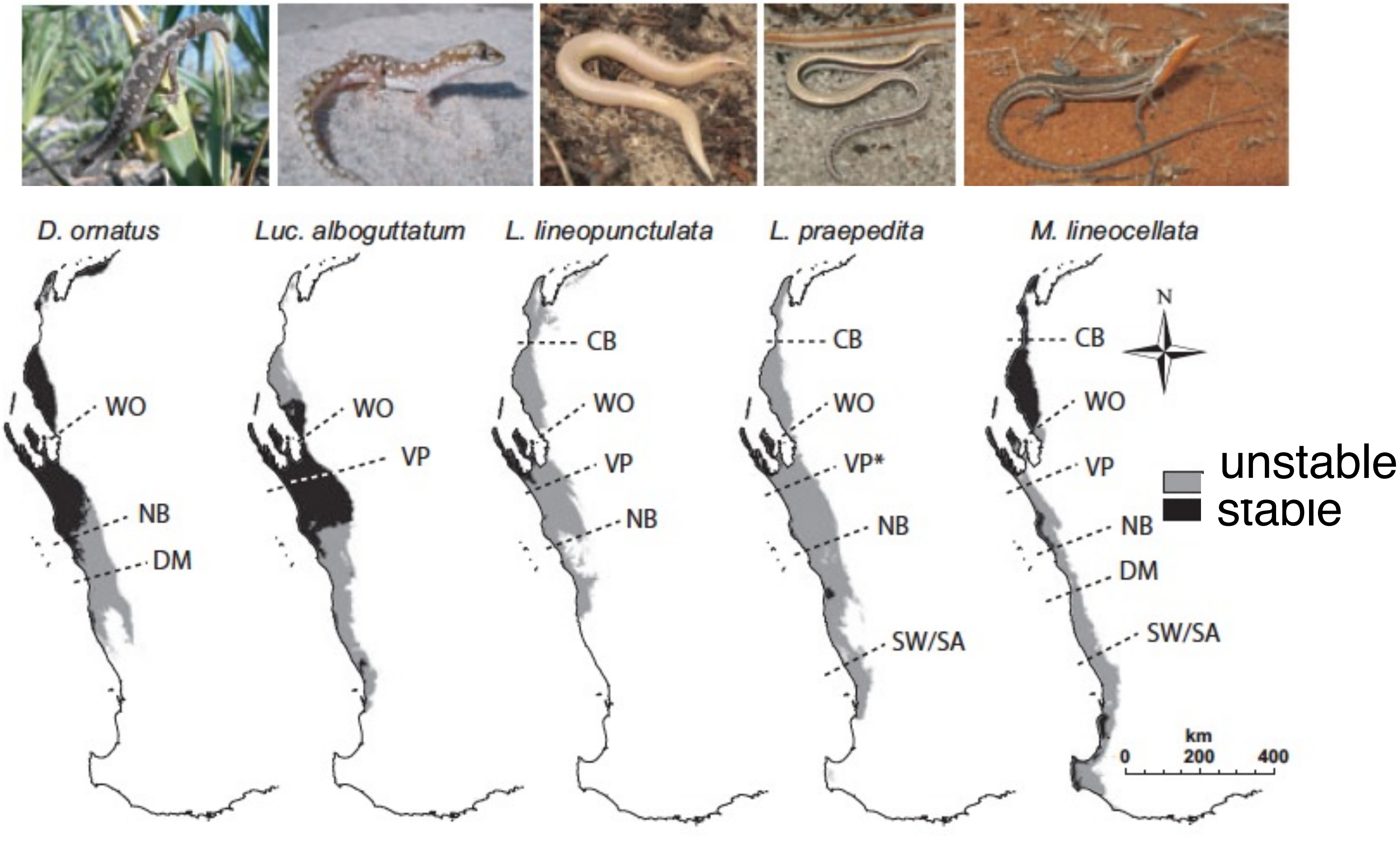


Past distribution (based on paleoclimatic data 21,000 yrs bp)

(based on ecological-niche models, ENMs, with MAXENT)

Edwards, Keogh, Knowles (2012) *Mol. Ecol.*

ts), Edwards & Knowles (2013) *Evolution*



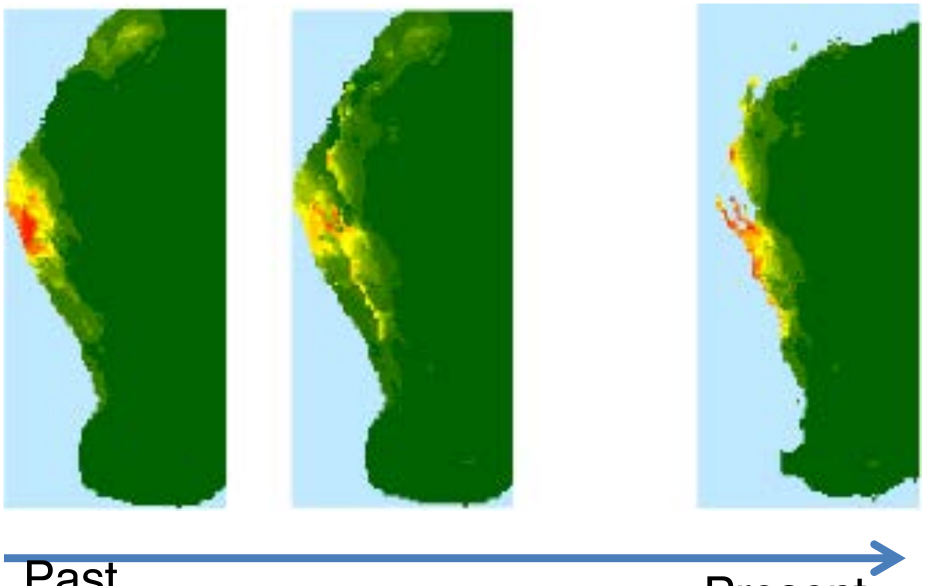
Climate-induced distributional shifts may structure genetic variation, given differences in stability of habitat over time

Edwards et al. (2012) *Mol. Ecol.*

Transforming hypotheses into testable phylogeographic models:

Incorporate history of shifts in species distribution in explicit spatial framework

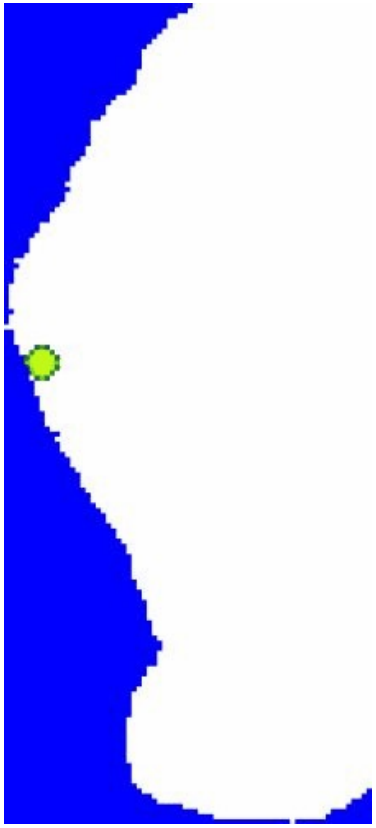
Colonization by dynamic niche



Past

Present

Dynamic ENM



- Start from LGM refugia
- Colonize with changing layers of ENM

Spatially explicit coalescent model to capture movement across space

integrative
Distributional
Demographic
Coalescent
modeling

iDDC:

Distributional model
(i.e., ecological niche model)

⇩

Demographic model

⇩

Coalescent model

Hypotheses

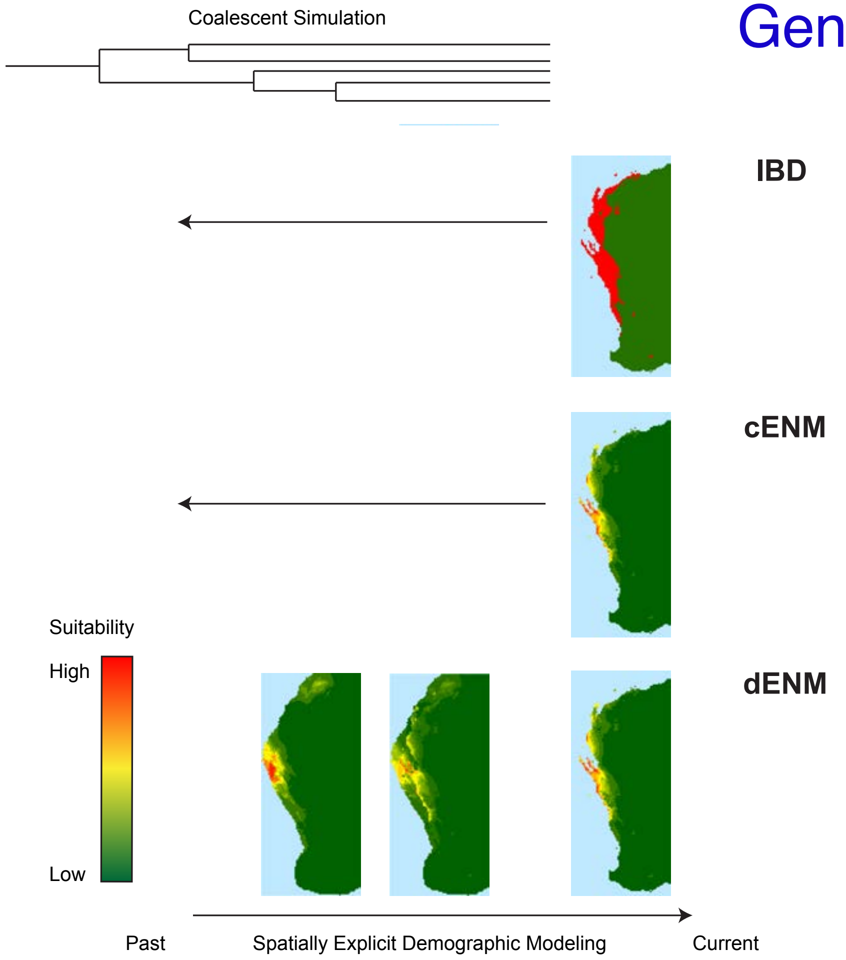
- geographic isolation alone (IBD)

- population connectivity determined by current landscape, as measured from ENM
- population connectivity determined by distributional shifts associated with climate change, as modeled by current and paleoclimatic data

24 anonymous nuclear loci from 89 individuals sampled across the range of *Lerista* (shown by dots)

He, Edwards & Knowles (2013) *Evolution*

iDDC modeling:



low *K*
high *K*
low *m*
high *m*

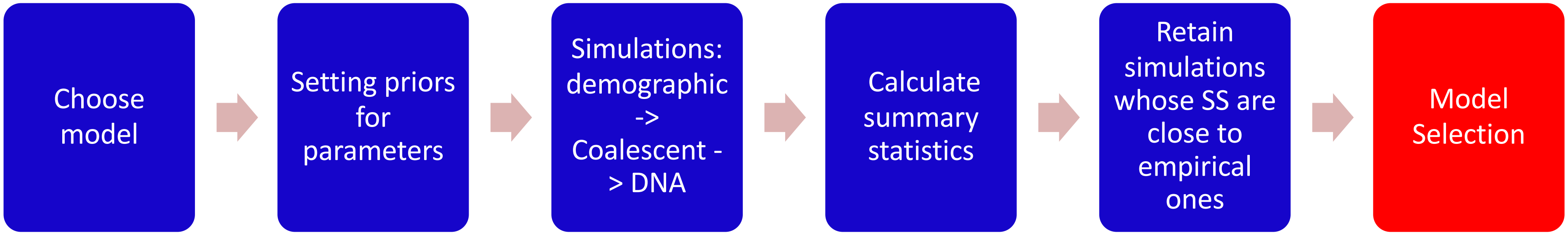
Generate lots of simulated data sets under each model (IBD, cENM, dENM).

We can identify sets of parameters for specific models that produce simulated data that matches the empirical data.

Model Selection using Approximate Bayesian Computation (ABC)

He, Edwards & Knowles (2013) *Evolution*

Tests of hypotheses/models using ABC



Choose model

Setting priors for parameters

Simulations: demographic -> Coalescent -> DNA

Calculate summary statistics

Retain simulations whose SS are close to empirical ones

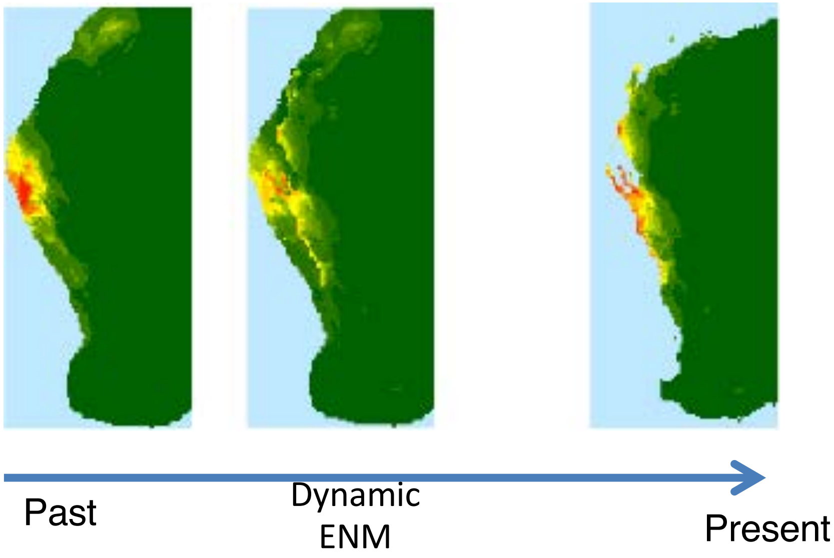
Model Selection

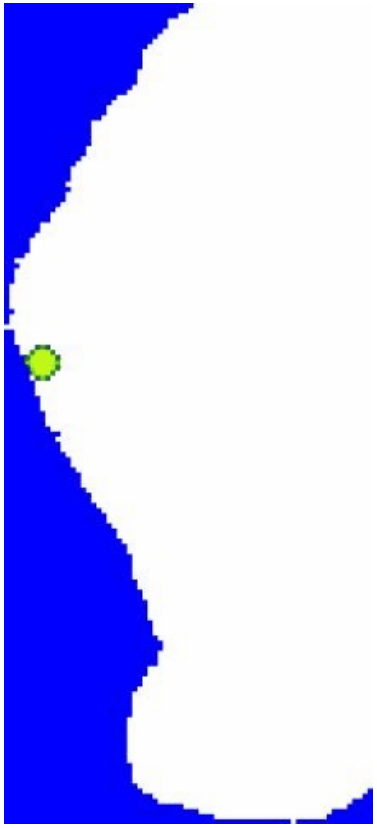
Comparison of Bayes factor showed that

Colonization by dynamic ENM

>> Isolation by contemporary ENM

> Isolation by distance





- Start from LGM refugia
- Colonize with changing layers of ENM

He, Edwards & Knowles (2013) *Evolution*

Advantages of iDDC:

- Flexible (expand to multiple species)
- Complex history
- Test of different historical processes
- Model verifications for ABC, e.g.:

- Is the model capable of generating the observed data: the likelihood of the empirical data can be compared with the likelihoods of other retained simulations (a *p* -value of 0 means all the simulations had a higher likelihood than the observed data)

- Compute the coefficient of variation of each parameter explained by each PLSs of the summary statistics as an indicator for the power of the estimation

- Accuracy of parameter estimation in the most supported model evaluate using 1000 PODs generated from prior distributions of the parameters

Challenges:

- iDDC is computationally intensive

Evolutionary applications of genomic data

what I’ll emphasize:

- Decisions/choices we make about model formulation

- Recognizing the subjectivity of model formulation itself when making inferences

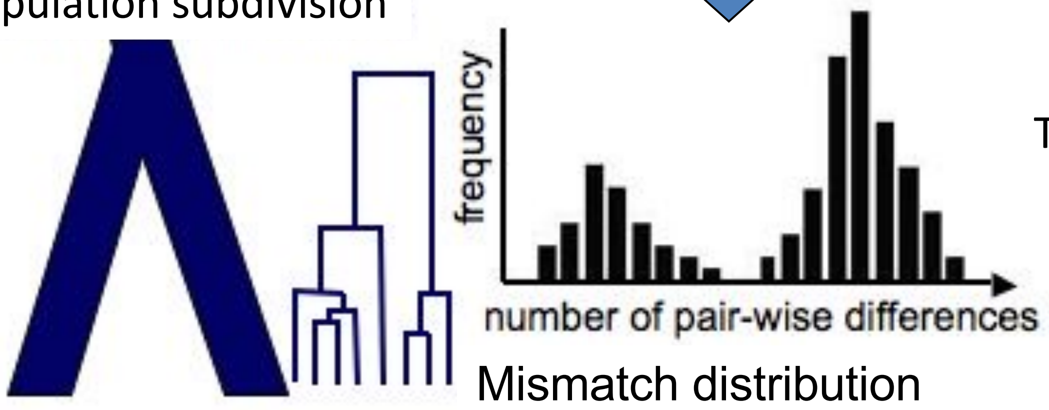
- Decisions when applying to empirical data (e.g., all the data, subset of data, what subset of data)

    - Decide how to extract information from genetic data

Summary statistics of genetic variation will have different values depending upon the biogeographic and demographic processes generating the genetic data

Summaries of genetic variation

Population subdivision

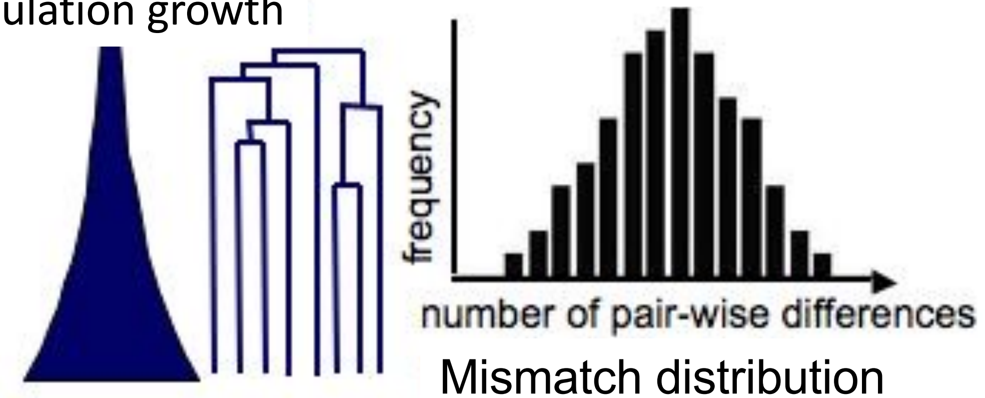


Mismatch distribution
(Rogers & Harpending 1992)

Tajima's D > 0

θ, pi

Population growth



Mismatch distribution
(Rogers & Harpending 1992)

Tajima's D < 0

θ, pi

Decisions about how to extract information from genetic data

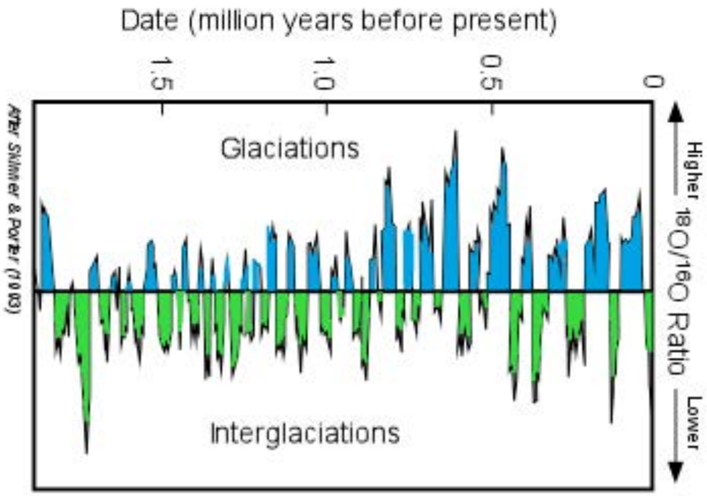
⇒ use of summary statistic (sacrifices information content for simplification and ease)

- observed quantities are compared to expectations

⇒ calculate full likelihood of the sequence data (computationally demanding, and may not work for complex models, but makes full use of the data)

Understanding the effects of rapid climate change on species diversity:

Did the frequent and repeated shifts in species distribution in response to the Pleistocene glacial cycles promote or inhibit divergence?



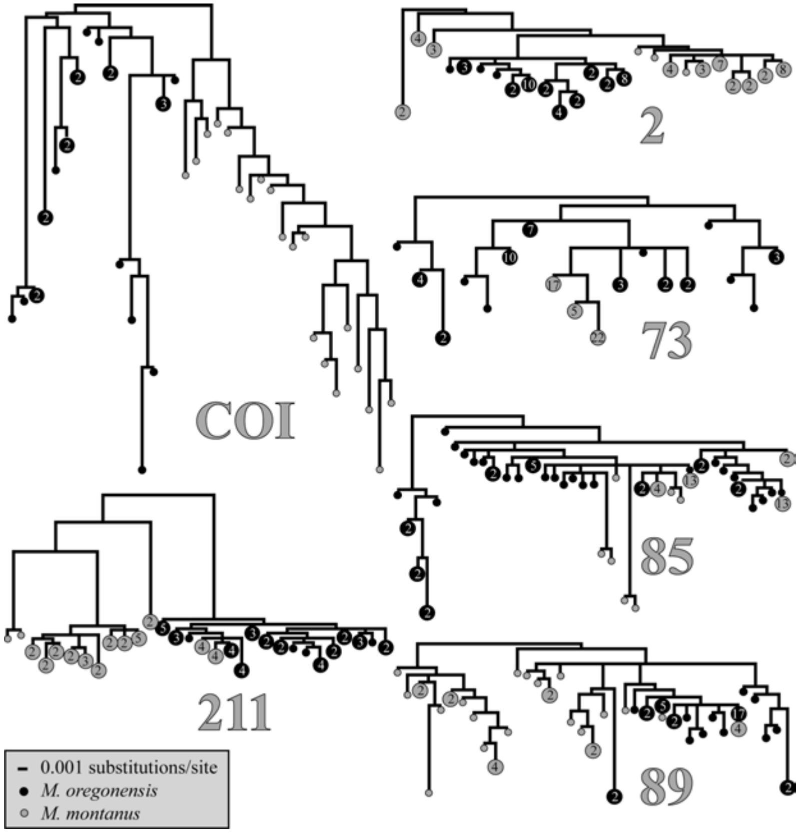
After Skinner & Porter (1983)

What is the timing of divergence?

- Pleistocene versus pre-Pleistocene?
- Glacial versus inter-glacial?

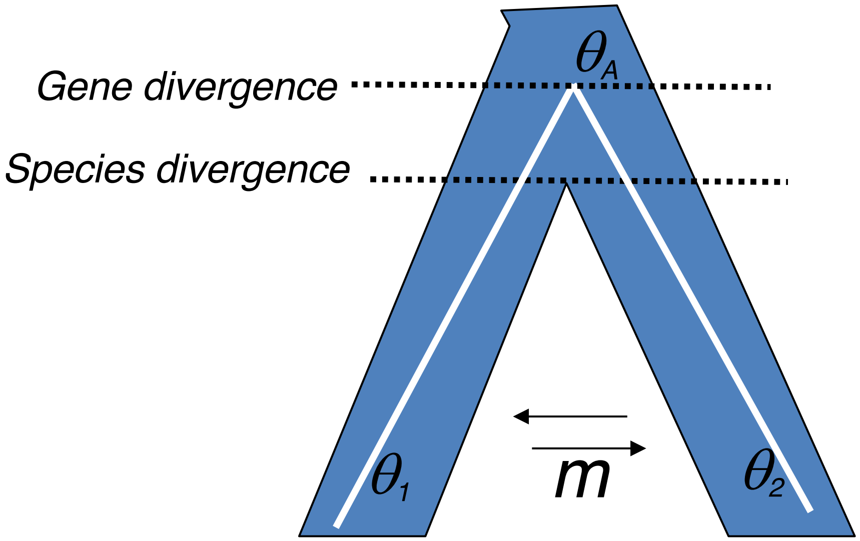
Carstens & Knowles 2007, Mol. Ecol. 16:619-27.

- Use multilocus data and a coalescent framework to estimate the timing of divergence



23 *M. montanus* 36 *M. oregonensis*

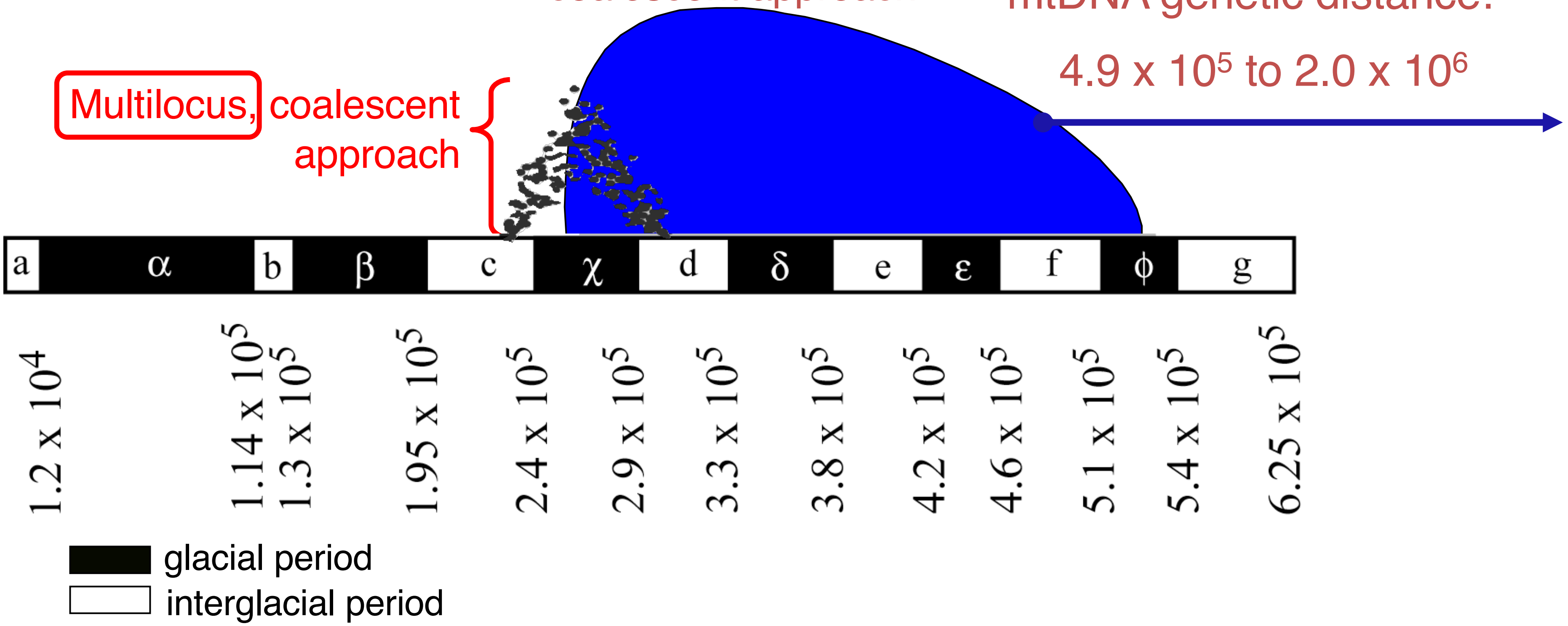
(Bayesian program IM)



Timing of divergence?

Carstens & Knowles 2007, Mol. Ecol. 16:619-27.

Precise estimate of T suggests species diverged during a glacial period



Single locus, coalescent approach

Multilocus, coalescent approach

estimate from average mtDNA genetic distance:

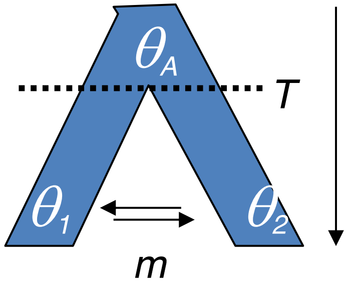
4.9×10^5 to 2.0×10^6

*same mutation rate used in the different approaches

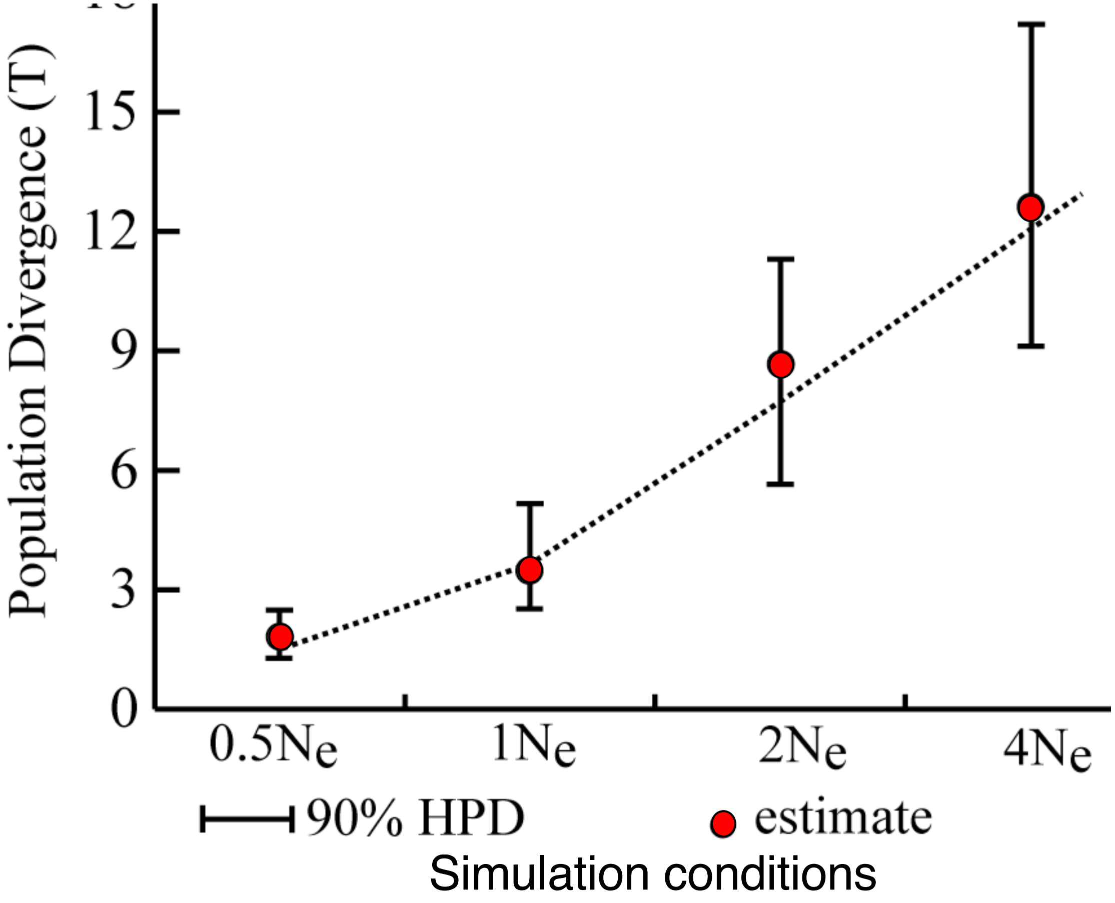
Carstens & Knowles 2007, Mol. Ecol. 16:619-27.

Verified the accuracy of the speciation model given the data (only 6 loci)

(estimates may be compromised when the complexity of the model exceeds the information content of the genetic data)



- Simulate genetic data under models of evolution matching the empirical grasshopper data and ask whether the inferred divergence time matches the divergence time used to simulate the data



Carstens & Knowles 2007, Mol. Ecol. 16:619-27.

How do we decide upon a model*:

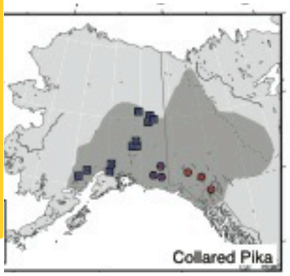
- informed from information independent of the genetic data itself
  - that is, a specific biological narrative motivates the model

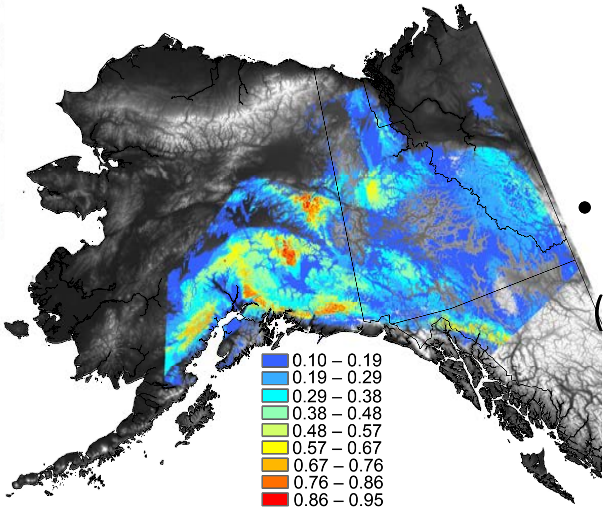
- models informed by the genetic data (…but be careful not to use same data twice)

- arbitrary/generic models

* All models are simplifications, and vary in the degree of their relative degree of abstraction

Informing model based on preliminary tests based on genetic data

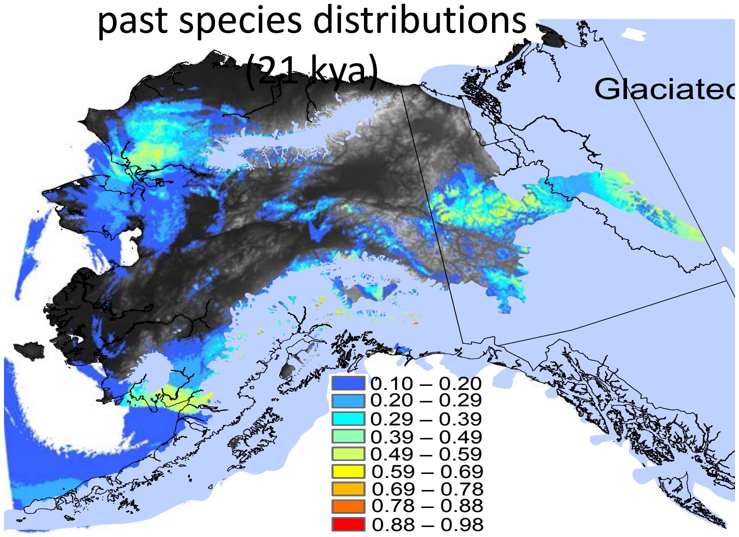




- Projected distribution from MAXENT based on contemporary bioclimatic variables (e.g., max and minimum temperatures and precipitation, etc)

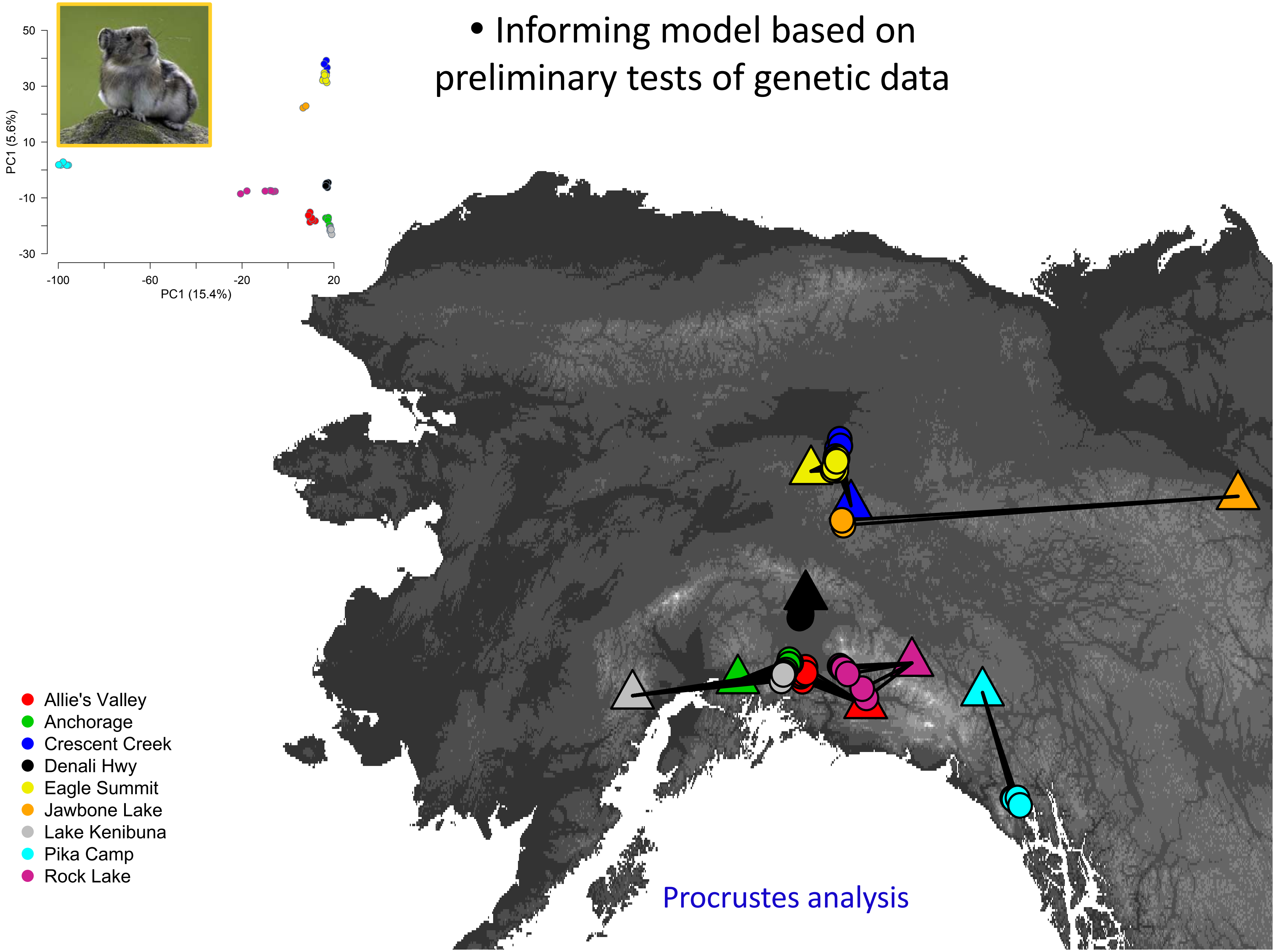
Sometimes ENMs not sufficient to define model

- Paleoclimatic data used to model past species distributions (21 kya)



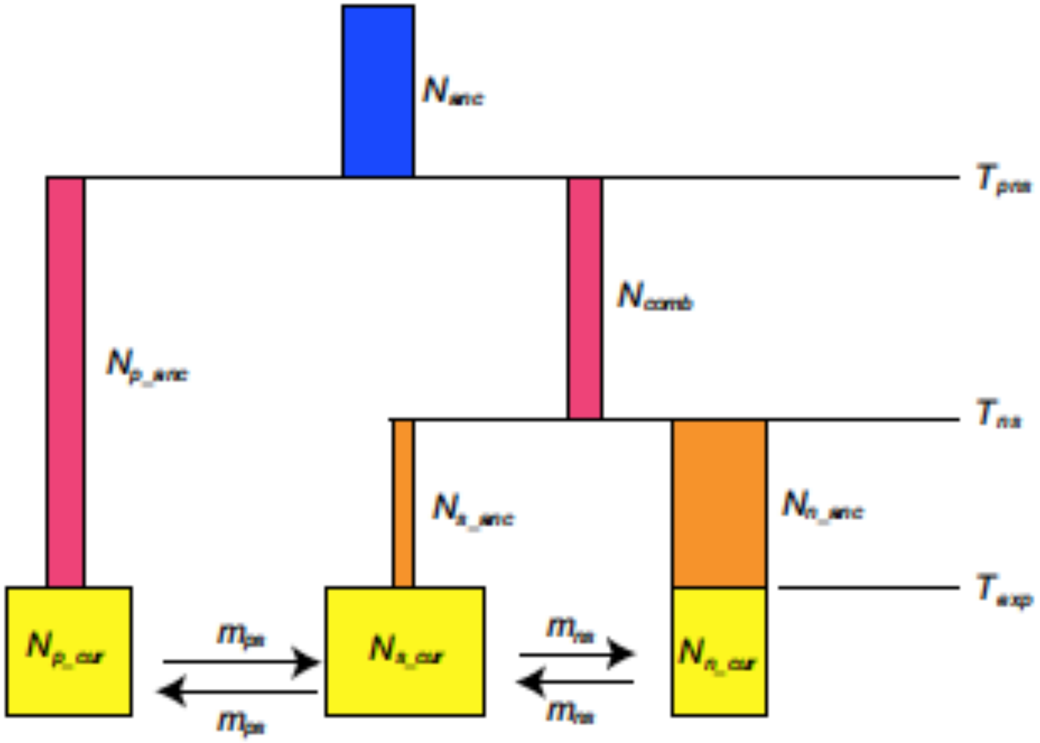
Lanier et al. (2015) *Mol. Ecol.* 24:3688-3705

- Informing model based on preliminary tests of genetic data



Procrustes analysis

To better understand the historical demographic trends for pika populations, we estimated divergence time, gene flow and population size changes among different populations using the site-frequency spectrum (SFS) using FastSimCoal.



10,892 variable SNPs

Fig. 2 Hypothesized demographic history of pika populations used in FASTSIMCOAL2 analyses. Pika ancestors diverged (Tpns generations ago) into ancestral populations of Pika Camp (Np_anc) and the other populations (Nns). Later, the divergence into southern (Ns_anc) and northern refugia (Nn_anc) occurred, and populations experienced recent expansions and exchanged migrants. The estimates of these parameters are listed in Table 4.

Lanier et al. (2015) *Mol. Ecol.* 24:3688-3705

- Our results indicate that contemporary factors alone (i.e., current habitat continuity and glacial corridors) are not sufficient to explain connectivity among populations of Collared Pikas across their range

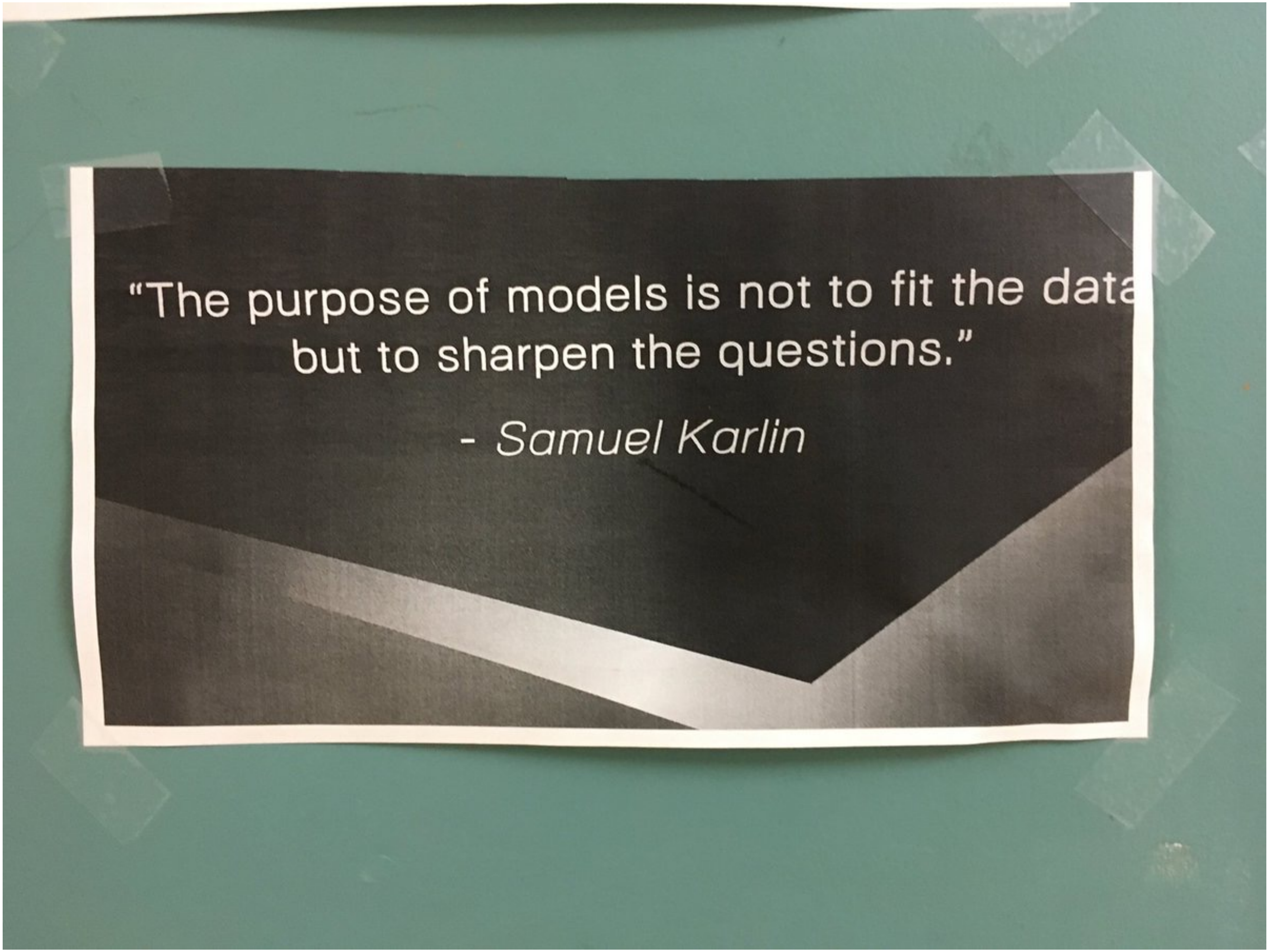
- Instead, the results provide strong support for the predominance of three divergent lineages, likely separated in different Pleistocene refugia, with population expansion among lineages predating the Last Glacial Maximum

Lanier HC, Massatti R, He Q, Olson LE, Knowles LL (2015) Colonization from divergent ancestors: glaciation signatures on contemporary patterns of genetic variation in Collared Pikas (Ochotona collaris). Mol. Ecol. 24:3688-3705.

How do we know if we used the “right” model?

In practice we can never completely model the evolutionary processes, all we can hope for is that we have captured the important features.

(i.e., YOUR knowledge about a biological system is key!)



“The purpose of models is not to fit the data but to sharpen the questions.”

- *Samuel Karlin*

Evolutionary applications of genomic data

- Accounting for species-specific traits
- Spatially explicit coalescent models
- Comparative analyses of genetic variation across species

Evolutionary applications of genomic data

- Accounting for species-specific traits
- Spatially explicit coalescent models
- Comparative analyses of genetic variation across species

Evolutionary applications of genomic data

What I'll emphasize:

- Decisions/choices we make about model formulation

- Recognizing the subjectivity of model formulation itself when making inferences

- Decisions when applying to empirical data

(e.g., all the data, subset of data, what subset of data)

Does microhabitat differences affect species responses to climate change?

- start with descriptive analysis to explore hypotheses

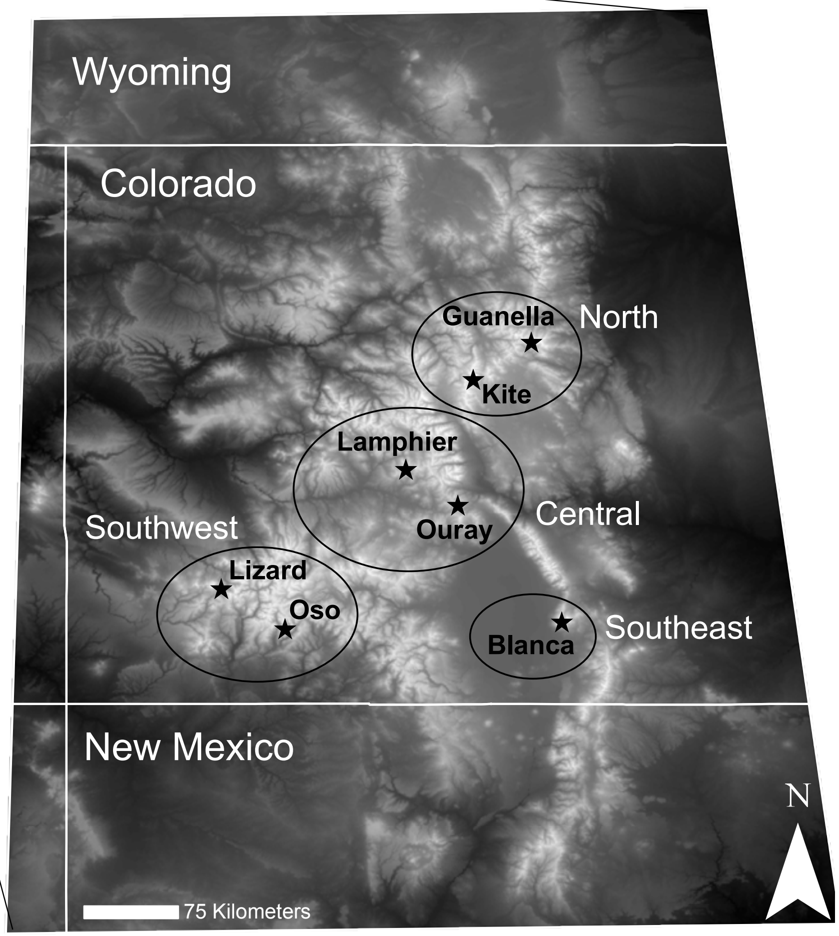
- follow-up with spatially explicit models to test hypotheses about why patterns of genetic variation differ among species (i.e., generate species-specific patterns of genetic variation)

Sky island community responses to climate change similarly (based on patterns of genetic differentiation)

Carex chalciolepis

Carex nova

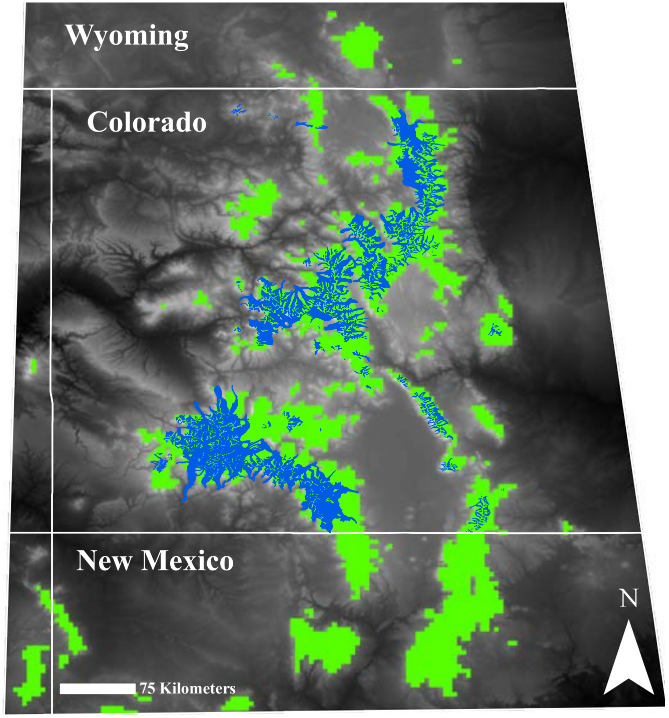
Massatti & Knowles
(2014 Evolution)



Sky island communities: responses to climate change

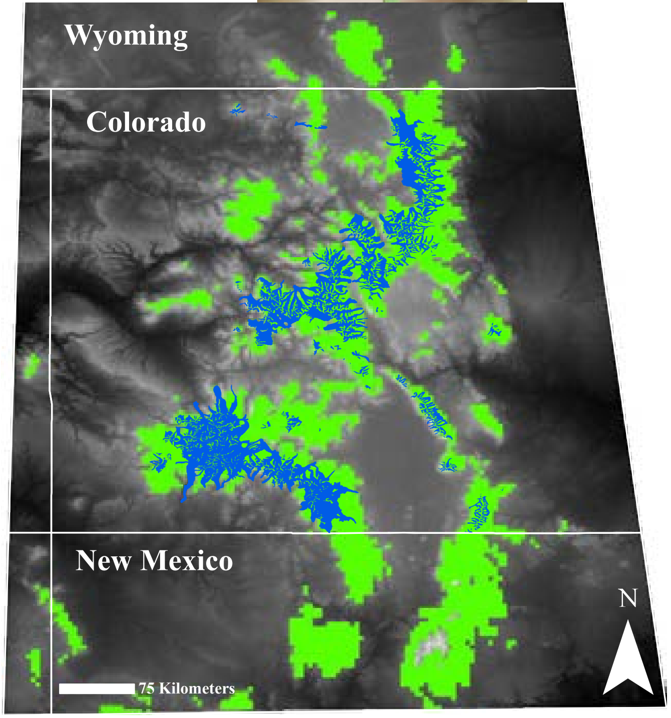
- co-distributed, abundant taxa with similar natural histories and dispersal abilities

Carex chalciolepis



- so similar that ENMs project very similar past distributions

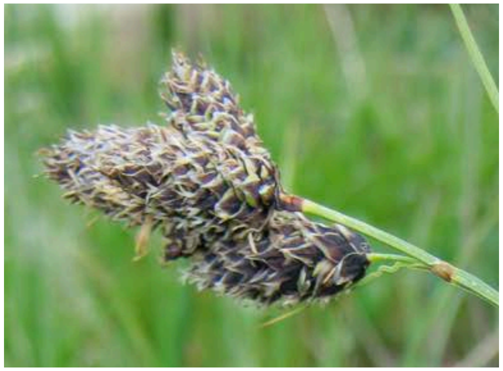
C. nova



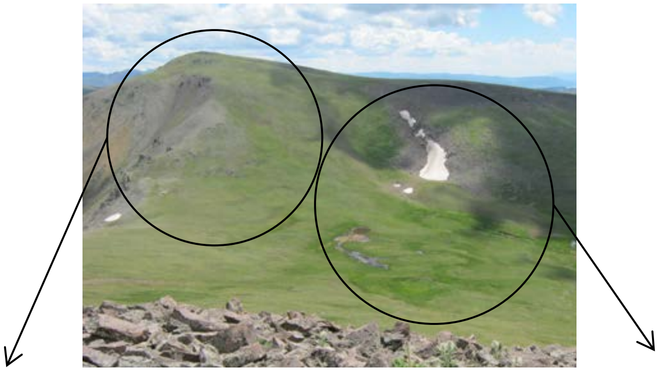
• taxa differ in microhabitats

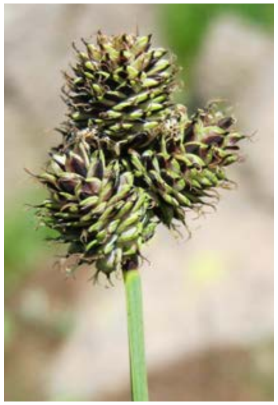
inhabits slopes and ridges

restricted to wetlands



Carex chalciolepis

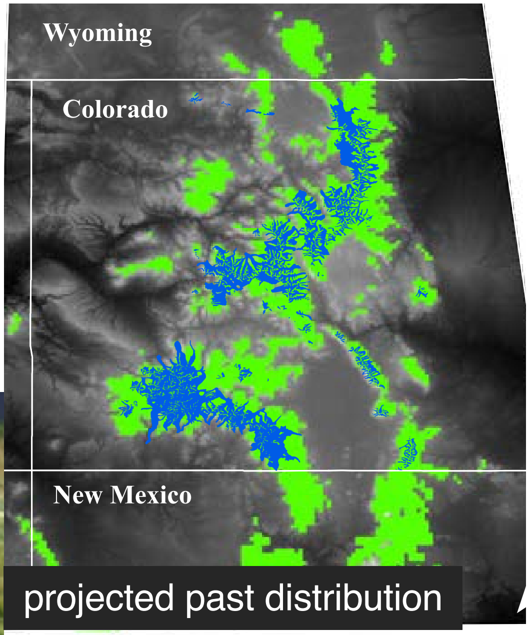




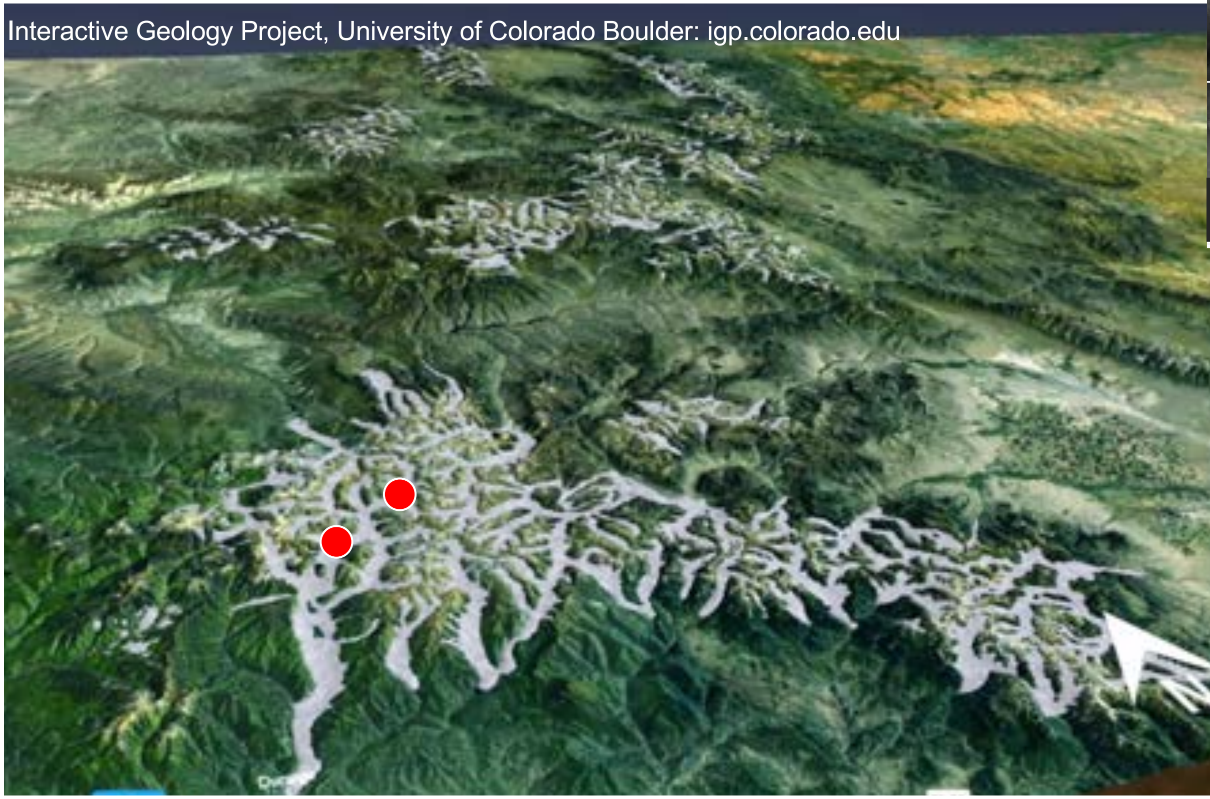
Carex nova

Given that ecological niche models (ENMs) are similar between species (both present and during LGM)…

why would we predict discord in patterns of genetic variation between the plant species?



projected past distribution

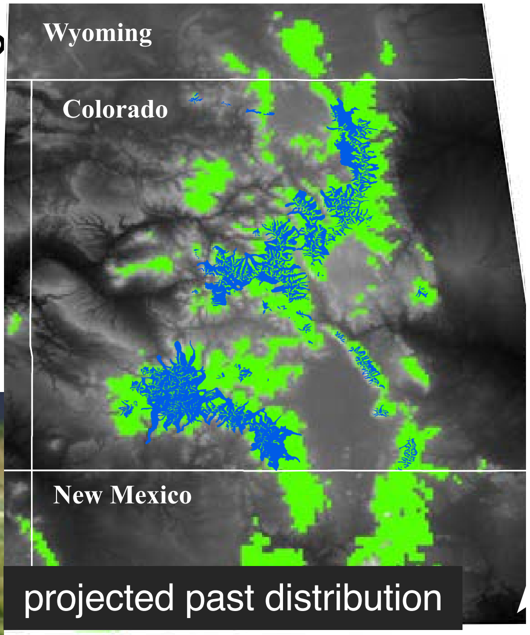


Interactive Geology Project, University of Colorado Boulder: igp.colorado.edu

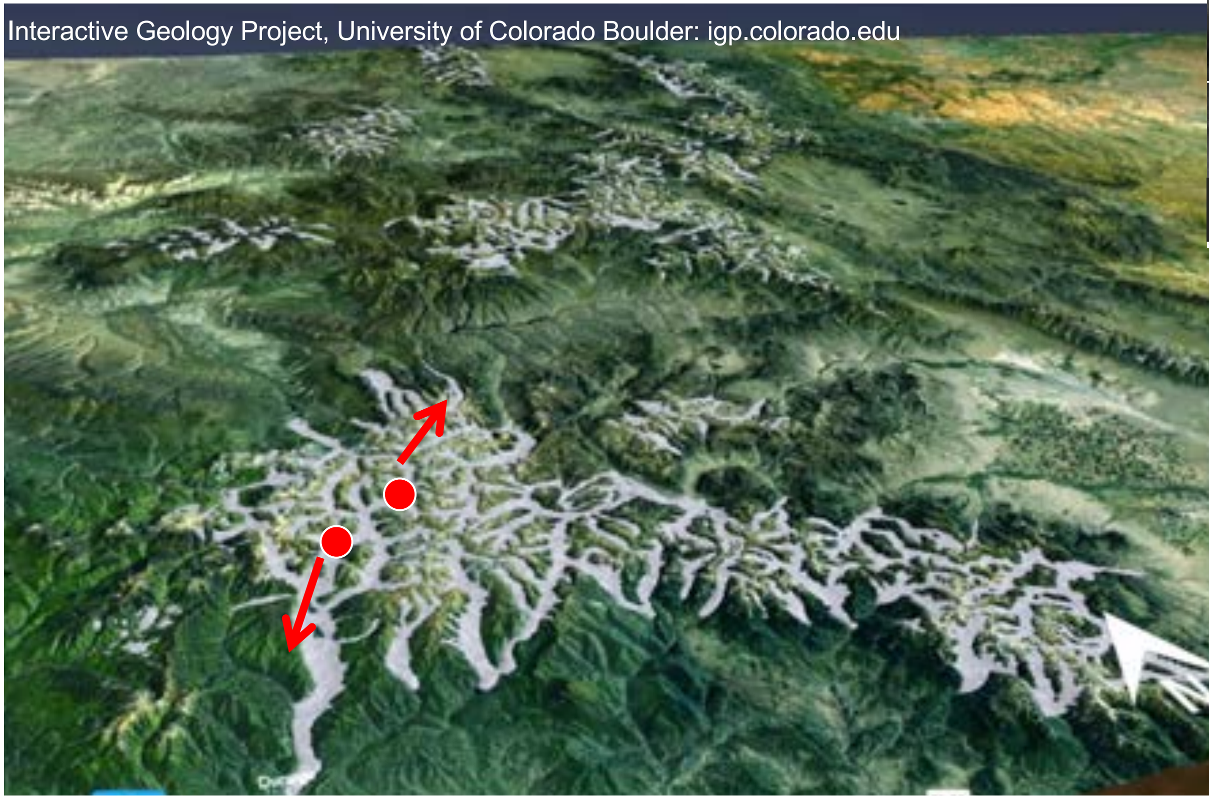
If microhabitat matters…

- glaciers in drainages would have displaced populations of wetland specialist

Why should microhabitat matter for sky island inhabitants?



projected past distribution


Interactive Geology Project, University of Colorado Boulder: igp.colorado.edu

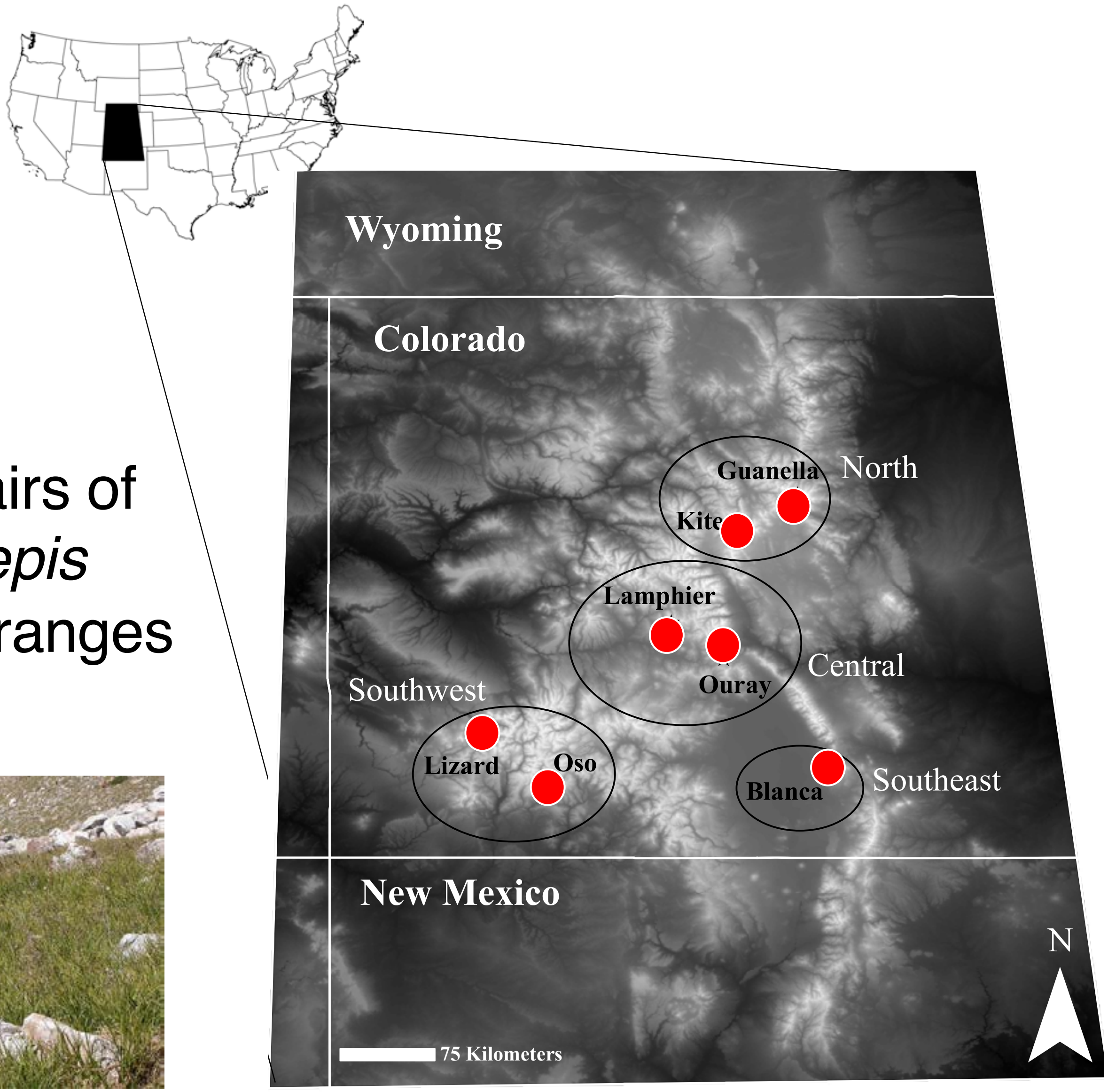
If microhabitat matters…

- distances separating populations may have been considerable greater in the past – *but only in the wetland specialist*

1. Sky island communities: microhabitat differences and responses to climate change

- SNPs from over 22,000 loci (RADseq)

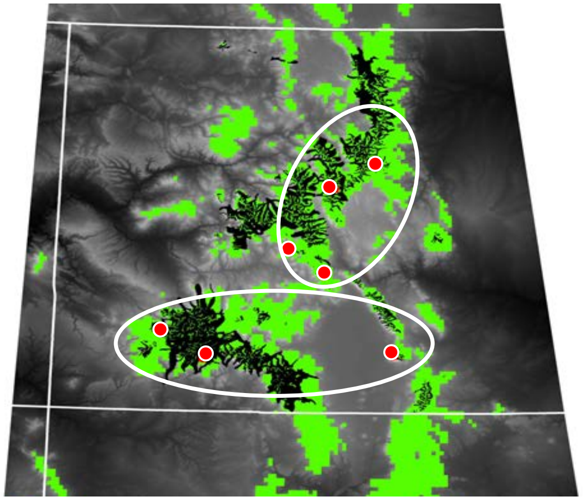
- sampled population pairs of *C. nova* and *C. chalciolepis* from different mountain ranges



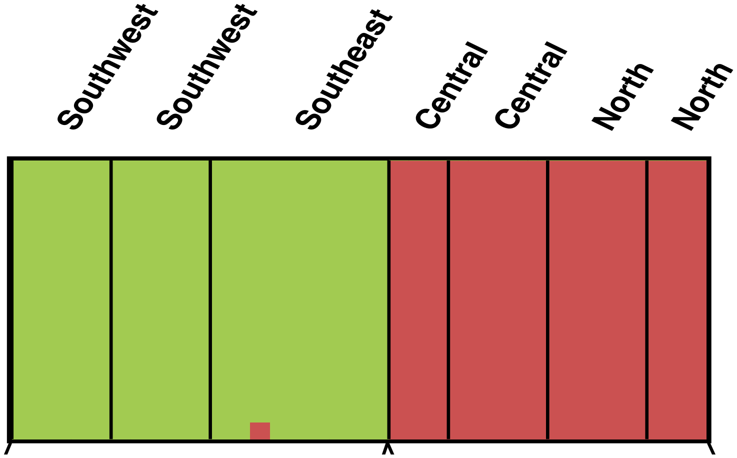
Massatti and Knowles, Evolution (in press)

restricted to wetlands

C. nova



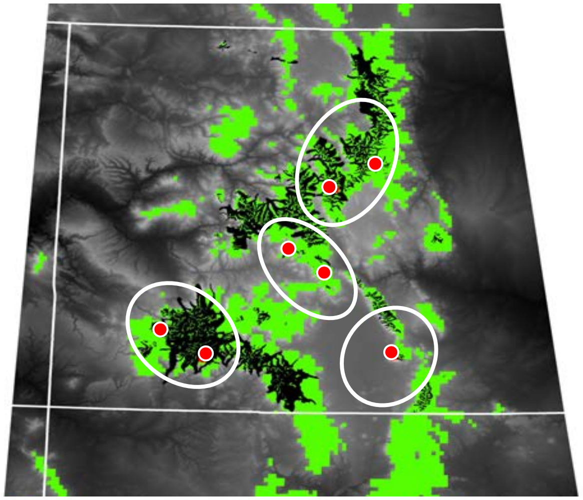
projected past distribution



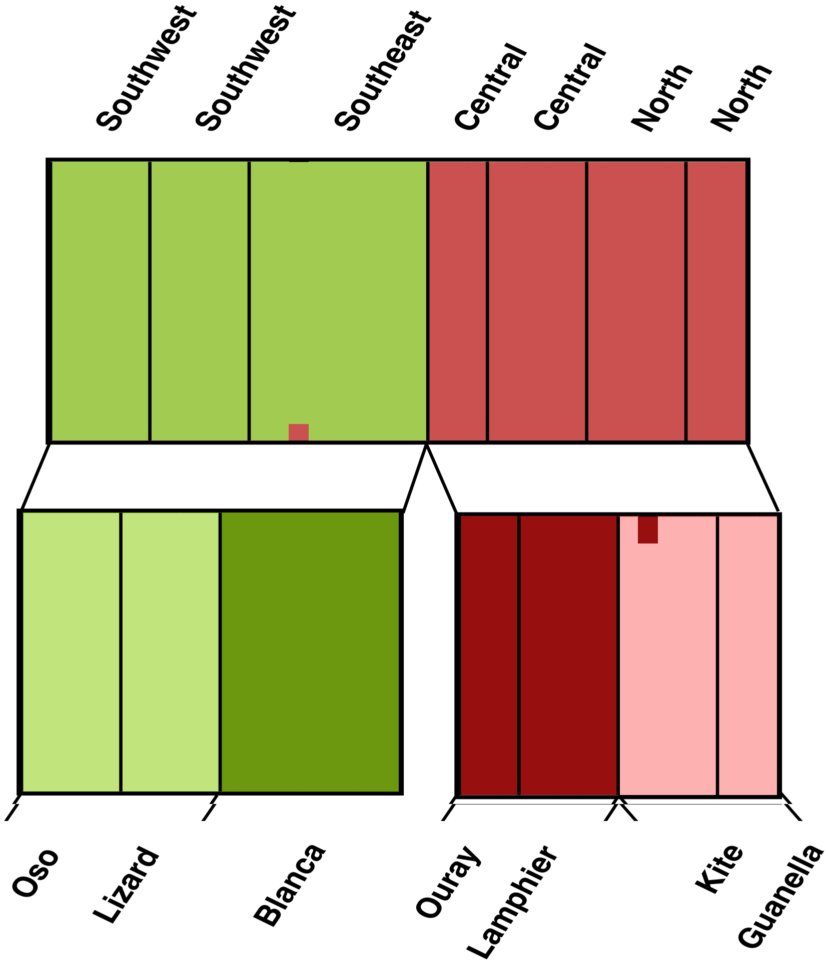
- Structure analysis of SNPs from over 22,000 loci

C. nova

restricted to wetlands



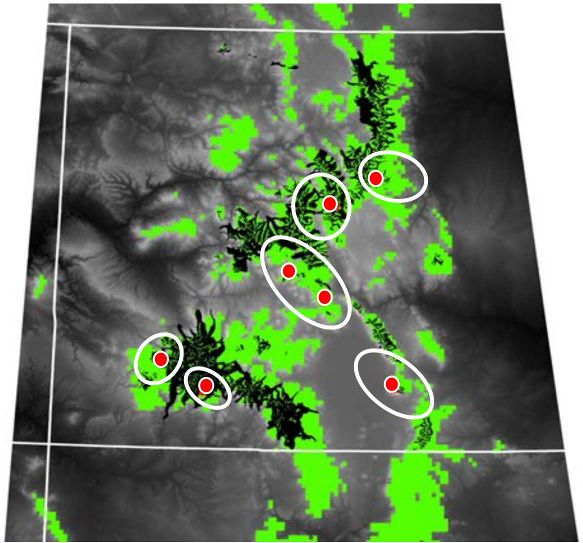
projected past distribution



- Structure analysis of SNPs from over 22,000 loci

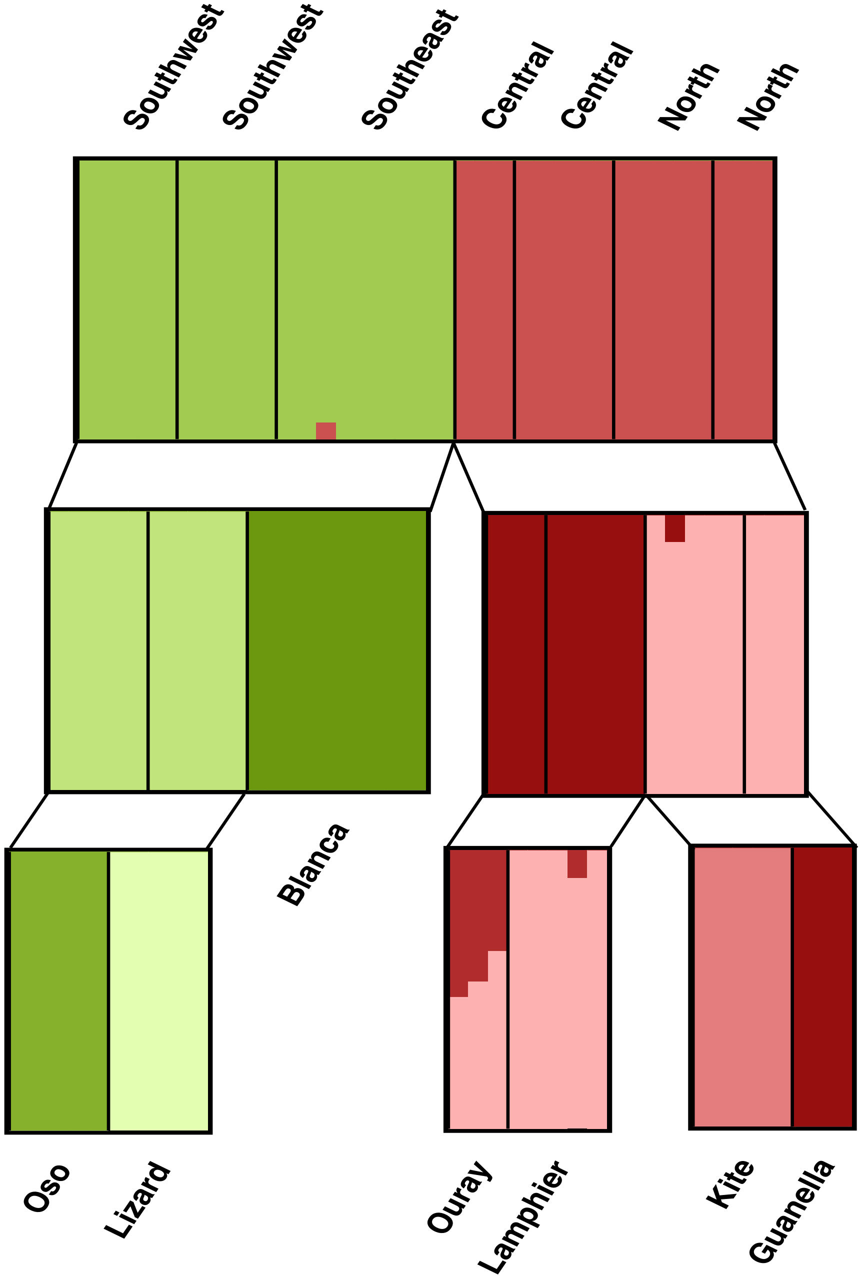
C. nova

restricted to wetlands



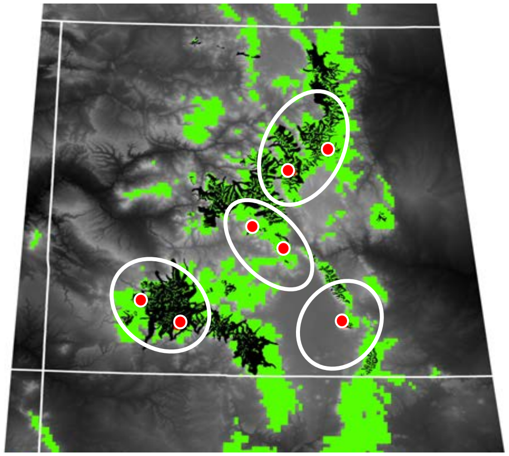
projected past distribution

Massatti and Knowles, Evolution (in press)



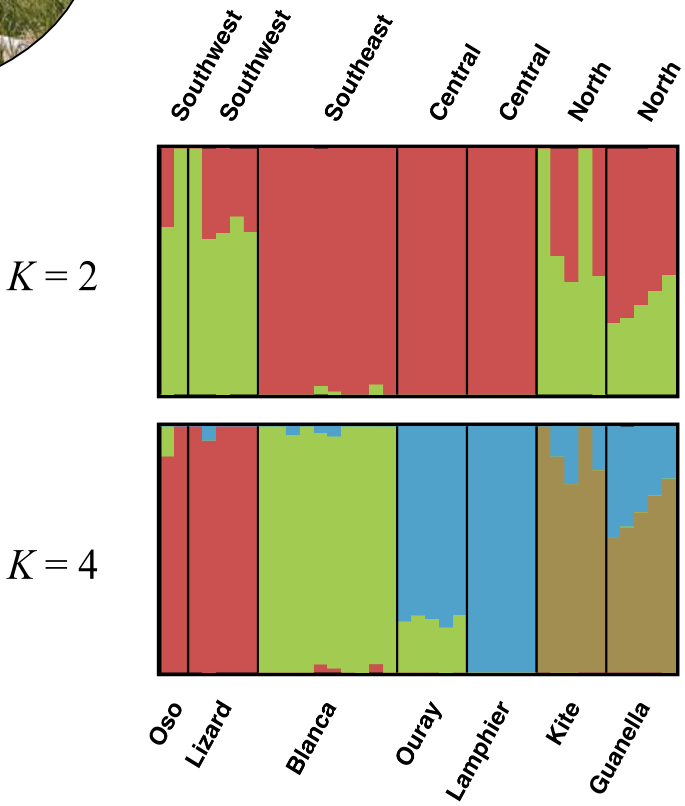
- STRUCTURE analysis of SNPs from over 22,000 loci

inhabits slopes and ridges

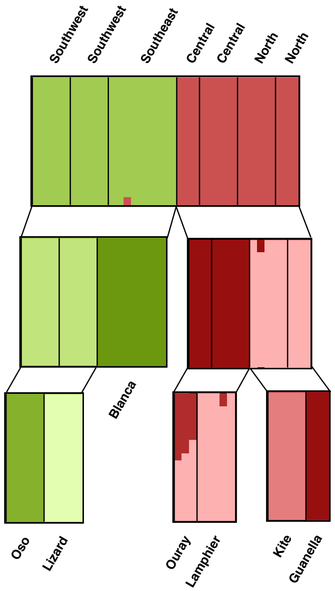


projected past distribution

C. chalciolepis

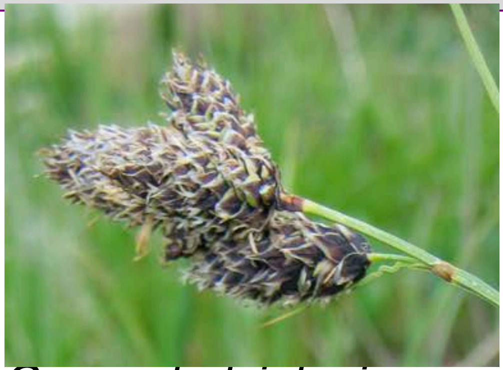


C. nova



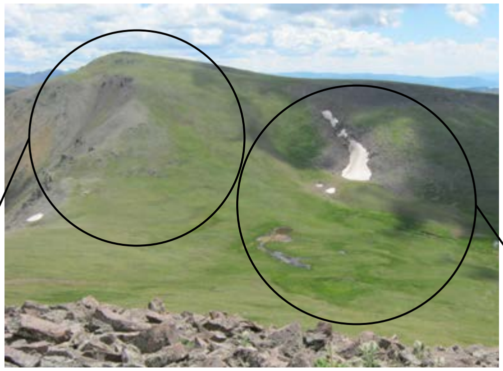
Massatti and Knowles, Evolution (in press)

Genomic patterns support predictions of an interaction between microhabitat affinity and climate change (glaciers are barrier for movement of wetland specialists only)



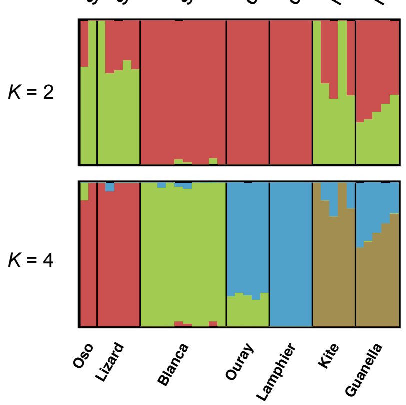
Carex chalciolepis

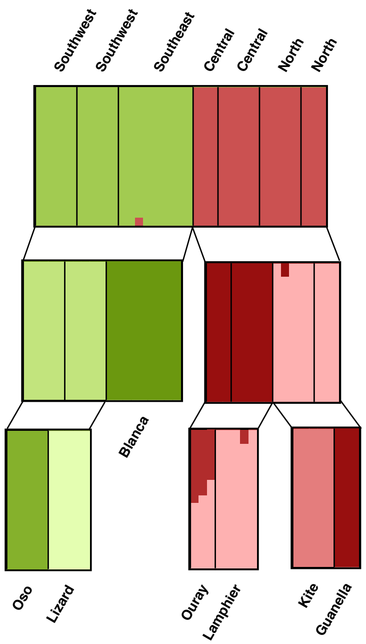
dry ridges



Carex nova

wetland specialists



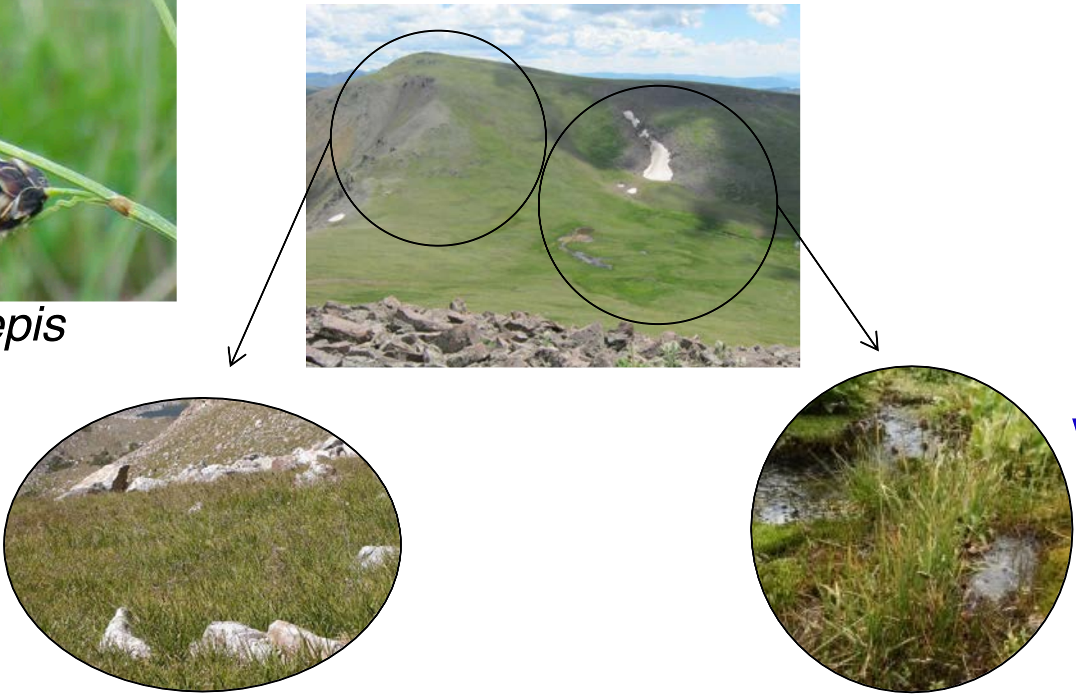


Genomic patterns support prediction of an interaction between microhabitat affinity and climate change

Massatti & Knowles (2014) *Evolution*

Carex chalciolepis

dry ridges



Carex nova

wetland specialists

Test if observed discordant phylogeographic structure could be caused by differences in microhabitat affinity ….

- generate species-specific expectations for patterns of genetic variation

(i.e., glaciers are barrier for movement of wetland specialists only)

iDDC: Generate species-specific expectations for patterns of genetic variation

He, Edwards & Knowles, Evolution 2013

integrative
Distributional
Demographic
Coalescent
modeling

Distributional model
(i.e., ecological niche model) with
predictions on probability of occurrence
across the landscape

⇩

Demographic model
informed by habitat
suitailities

⇩

Spatially-explicit coalescent
simulations based on
demographic model

⇩

Tests of hypotheses/models
using ABC

Habitat suitability scores

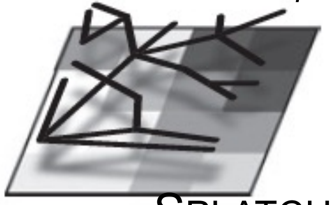
40	20	10	5
100	60	20	10
100	100	40	40
80	80	60	60

K(m)

400 (40)	200 (20)	100 (10)	50 (5)
1000 (100)	600 (60)	200 (20)	100 (10)
1000 (100)	1000 (100)	400 (40)	400 (40)
800 (80)	800 (80)	600 (60)	600 (60)

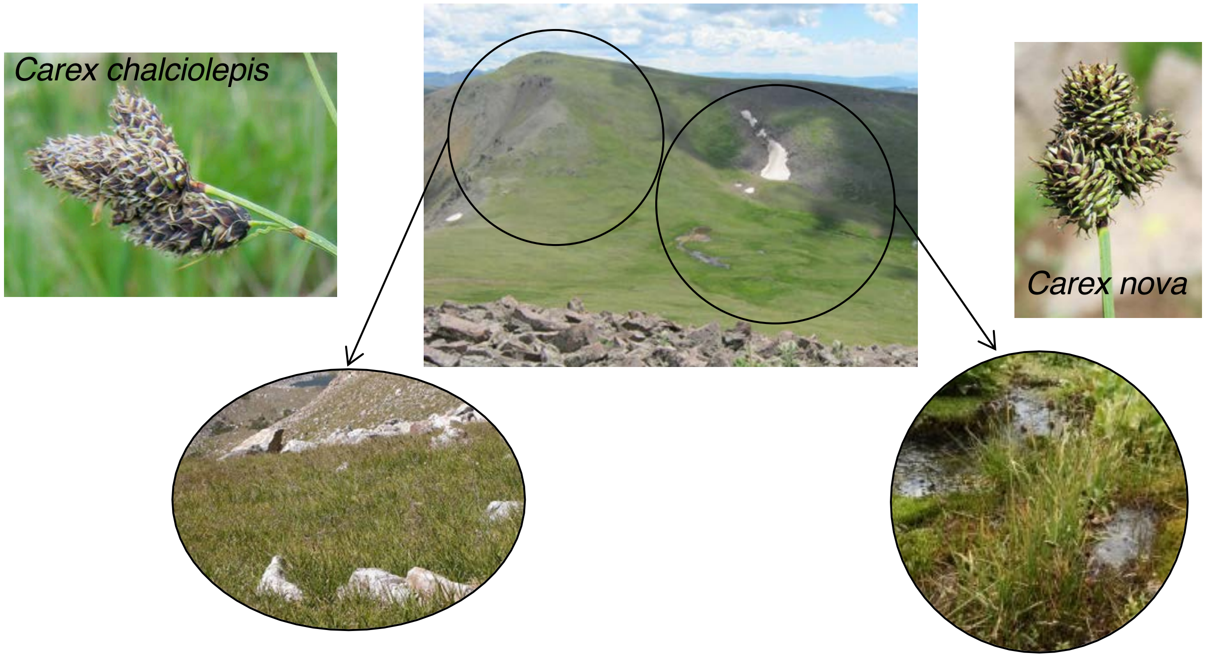
Carrying capacity: k_i

Gene coalescence across the landscape



SPLATCHE2

iDDC: Generate species-specific expectations for patterns of genetic variation



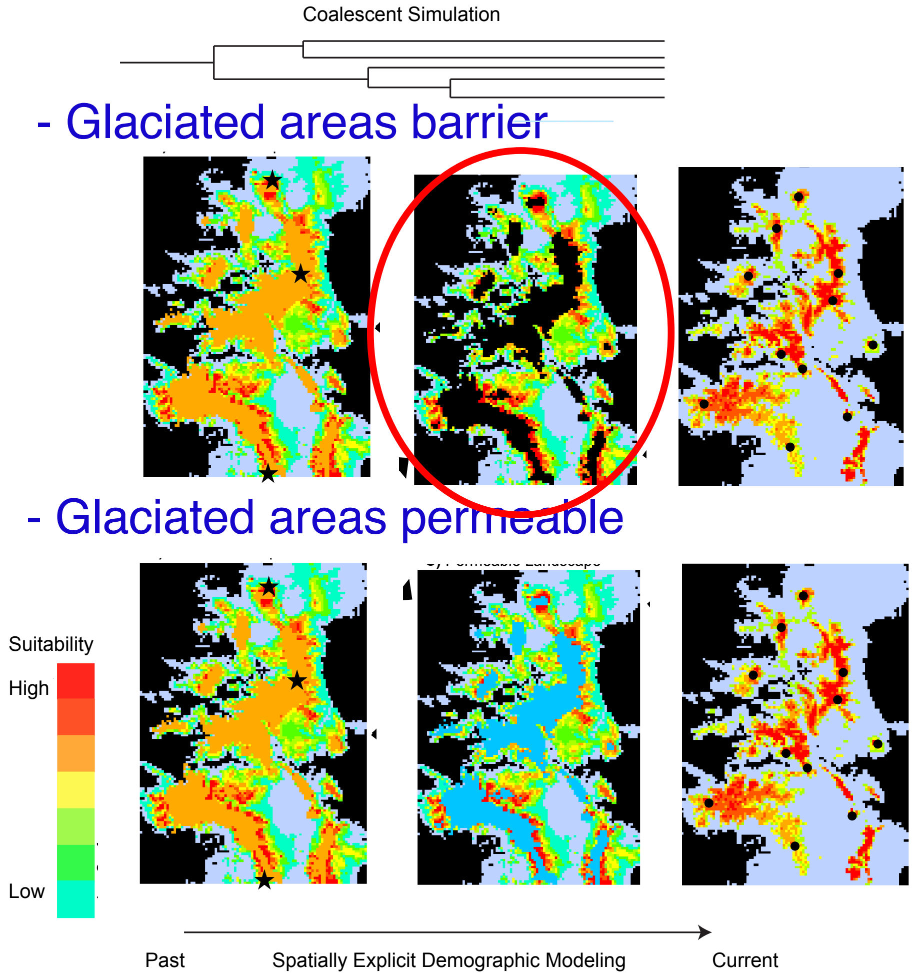
H: species-specific responses to climate change

- Glaciated areas act as barriers, but only in wetland specialist

So genetic discord between species is not dismissed as reflecting idiosyncratic nature of history; genetic discord predicted from taxon-specific traits!

iDDC modeling:

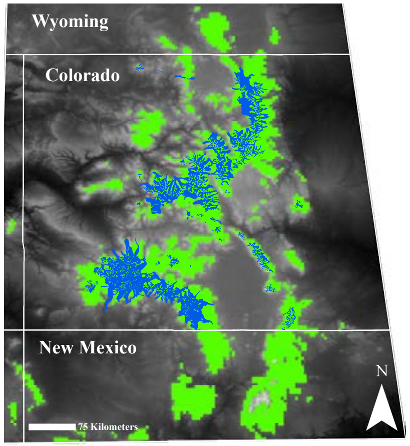
- Glaciated areas barrier
- Glaciated areas permeable



high *K* low *K*

high *m* low *m*

Glaciers shown in blue



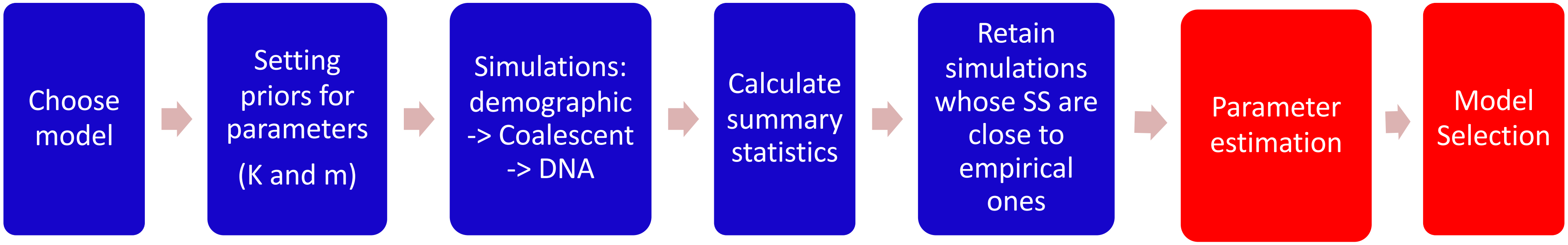
Generate lots of simulated data sets under each model

We identify sets of parameters for the models that produce simulated data that match the empirical data.

Model Selection using Approximate Bayesian Computation (ABC)

Massatti & Knowles (2016) Mol. Ecol.

Tests of hypotheses/models using ABC



Choose model

Setting priors for parameters (K and m)

Simulations: demographic -> Coalescent -> DNA

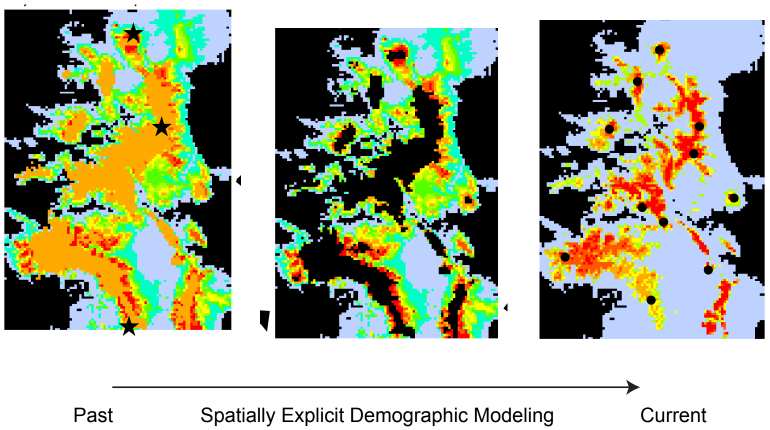
Calculate summary statistics

Retain simulations whose SS are close to empirical ones

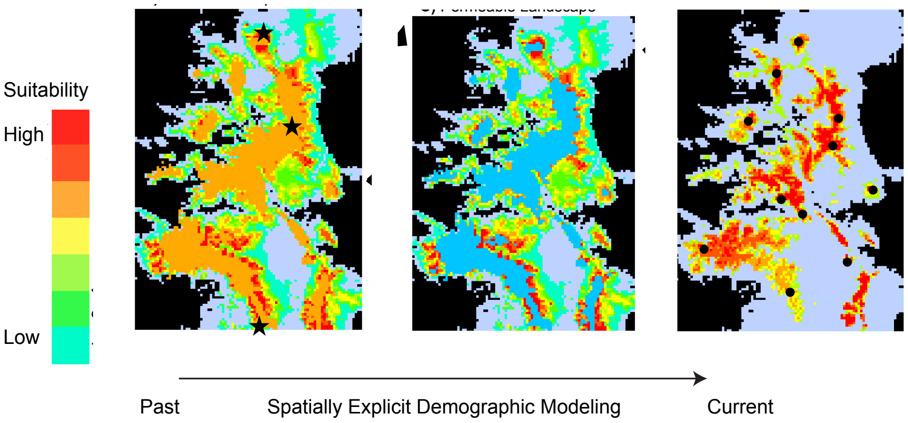
Parameter estimation

Model Selection

Model: Glaciated areas barrier

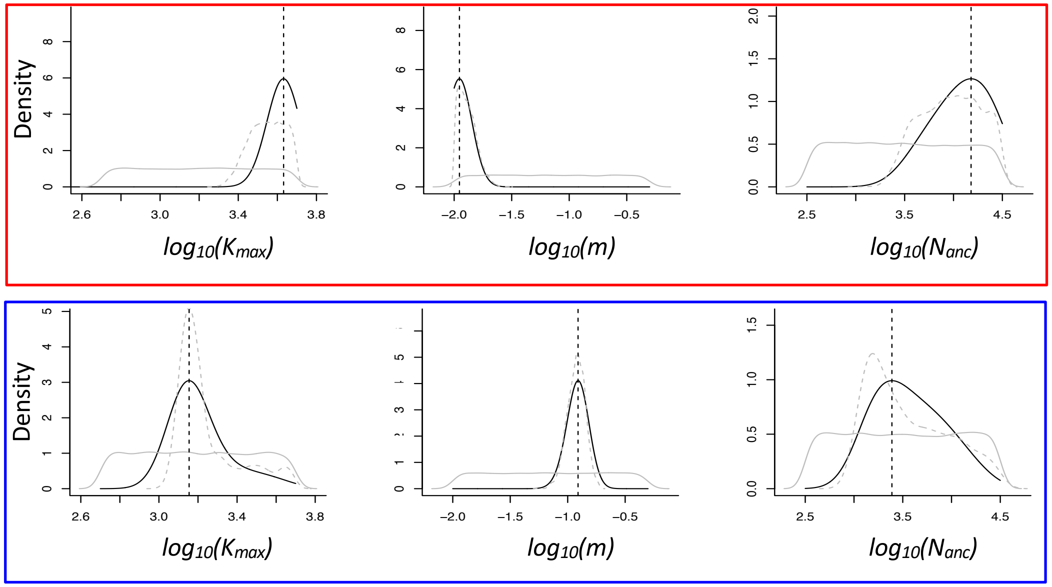


Model: Glaciated areas permeable



high *K*
low *K*
high *m*
low *m*

5000 simulations closest to empirical data retained for parameter estimation



Marginal densities:

	Barrier Model	Permeable Model
Carex chalciolepis Bayes factor ~3	4.87×10^{-5} (0.65)	1.38×10^{-4} (0.97)
Carex nova Bayes factor ~23	1.29×10^{-4} (0.84)	5.68×10^{-6} (0.08)

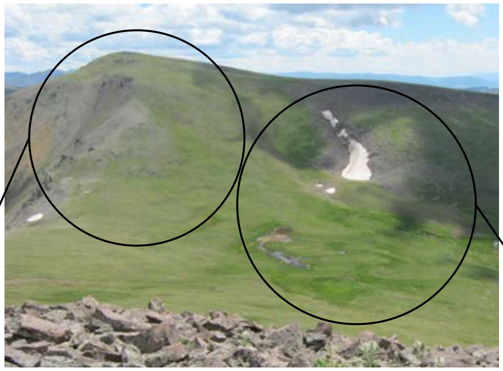
Is the most probable model capable of generating the observed data ?

(compare the L of retained simulated data sets to the L for the empirical data: *"P-value")*

Massatti & Knowles (2016) Mol. Ecol.

Refined hypotheses based on taxon-specific traits in comparative phylogeography

- statistical tests of discordant phylogeographic structure that is predicted from differences in taxon-specific traits



Massatti & Knowles LL (2014) Microhabitat differences impact phylogeographic concordance of co-distributed species: genomic evidence in montane sedges (Carex L.) from the Rocky Mountains. Evolution 68:2833-2846.

- Glaciated areas act as barriers, but only in wetland specialist

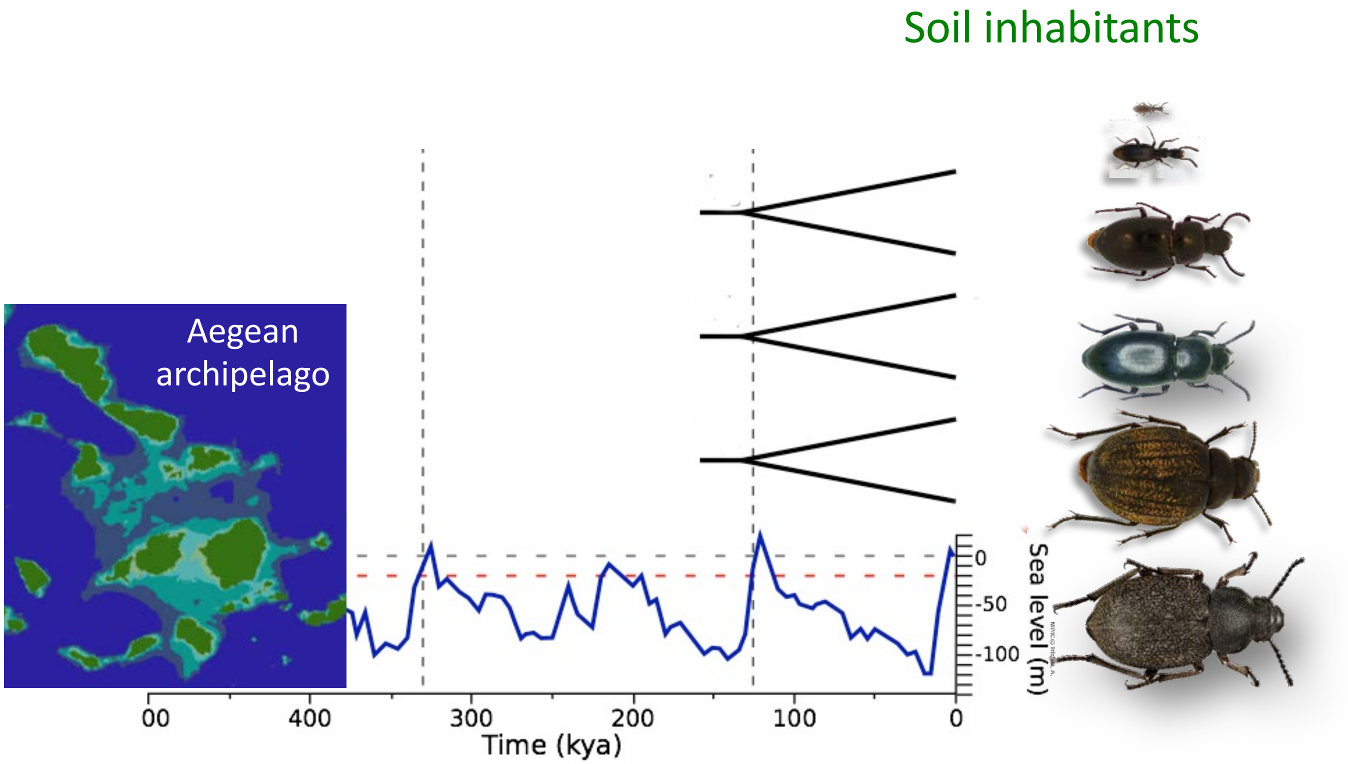
Communities may be characterized by species-specific responses to climate change

Inference based on samples from communities

- How we use similarity of the association between genes and geography across species to test evolutionary hypotheses

- Importance of considering refined-hypotheses based on taxon-specific traits

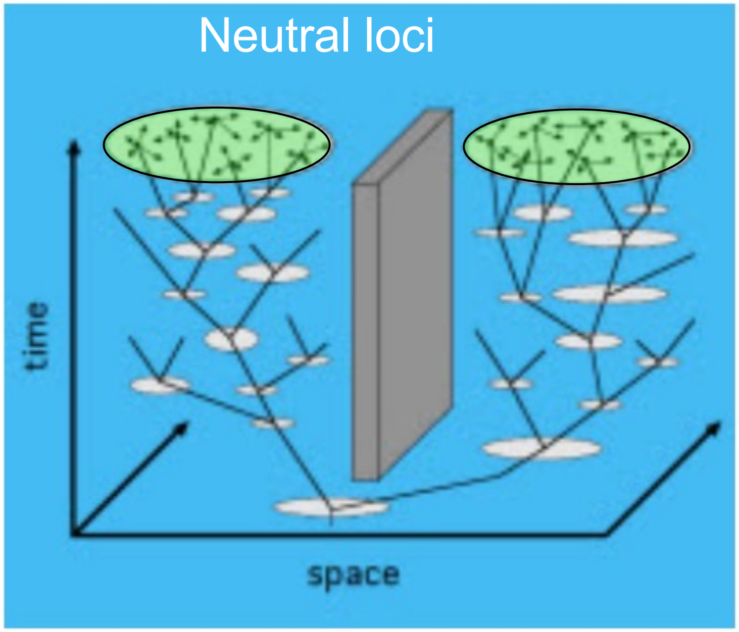
Refined hypotheses based on taxon-specific traits in comparative phylogeography

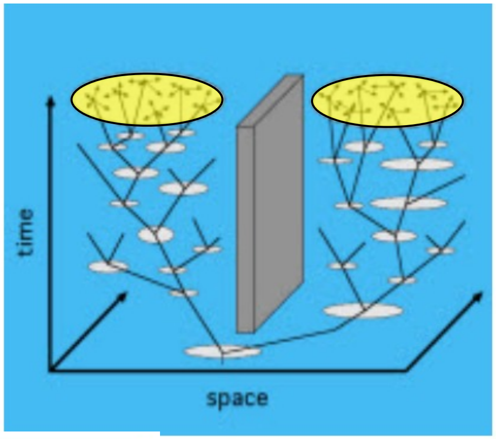


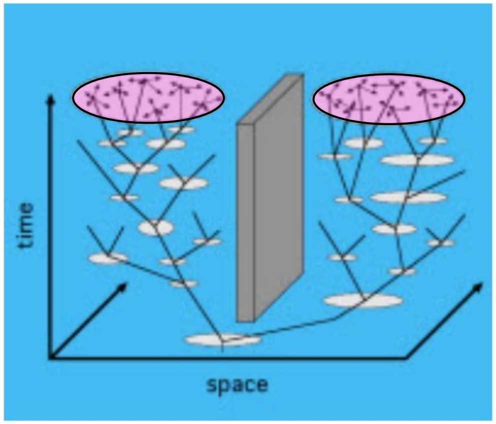
- key to avoid misleading inference

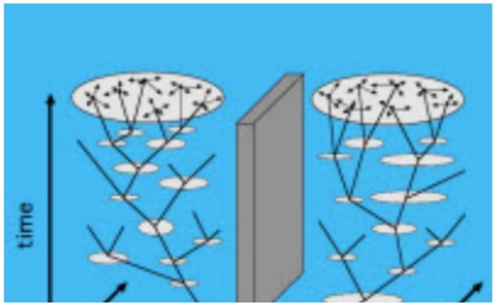
- bias toward tests of the effects of abiotic factors if rely on similarity in genetic structure across taxa for hypothesis testing

Genes and Geography Across Species

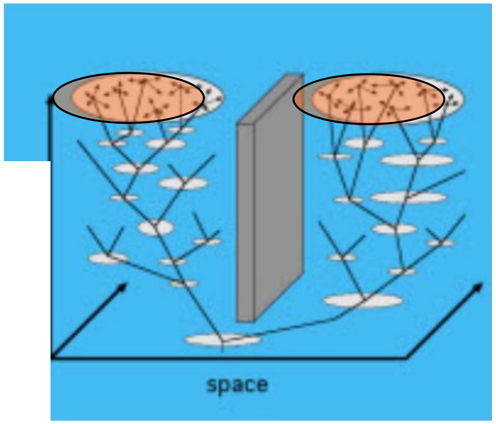




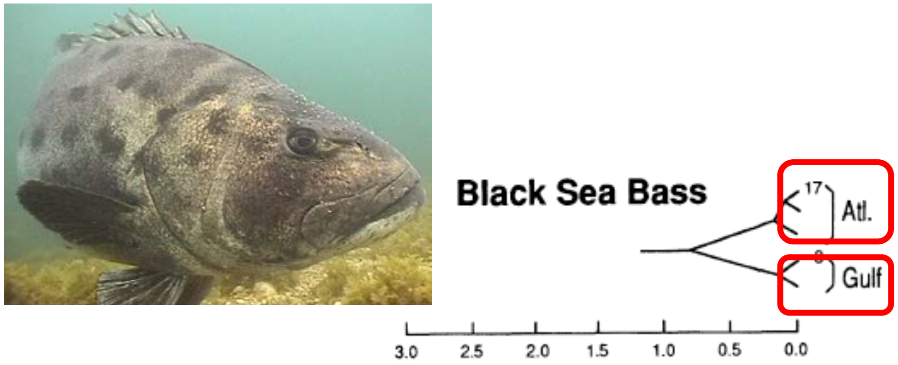


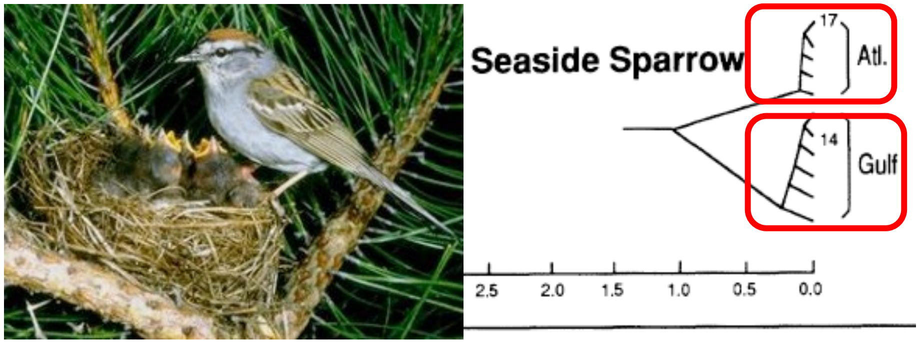


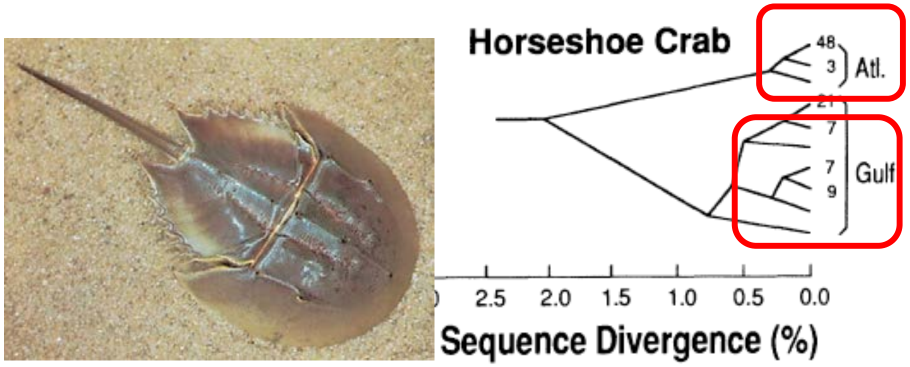
similarity of the association between genes and geography across species – CONCORDANCE – is typically used to test evolutionary hypotheses

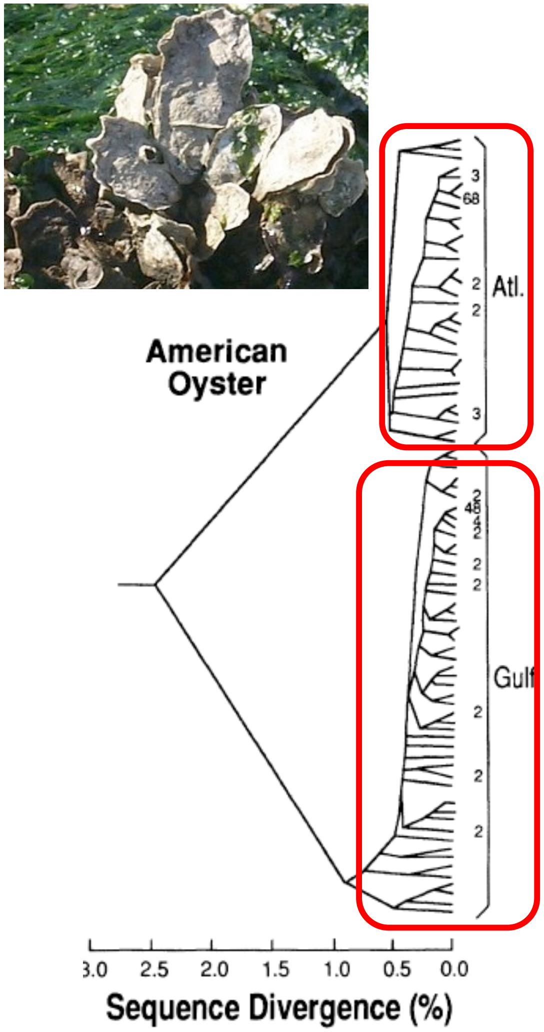


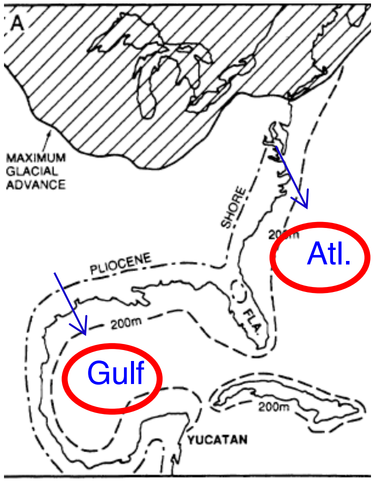
Concordance used in descriptive studies





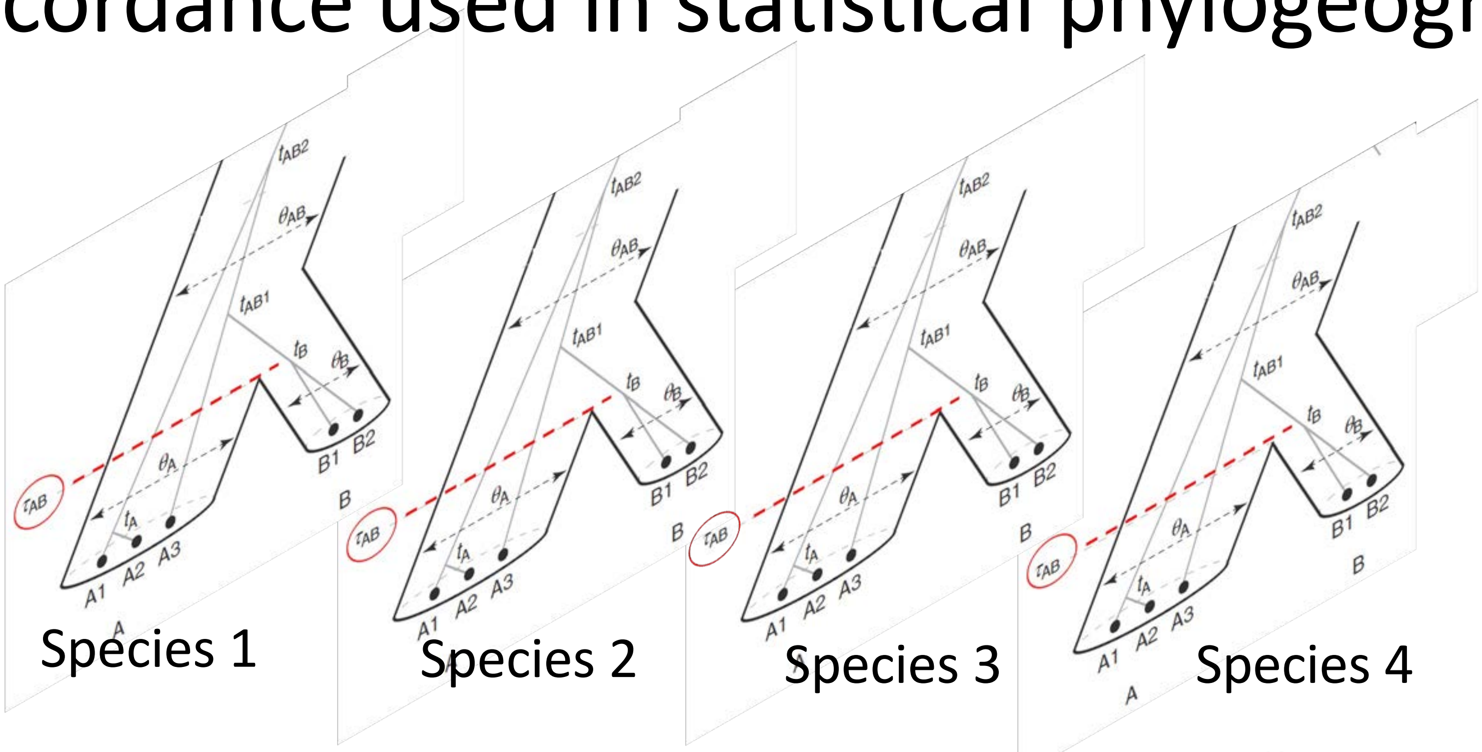






Avise 1992

Concordance used in statistical phylogeography



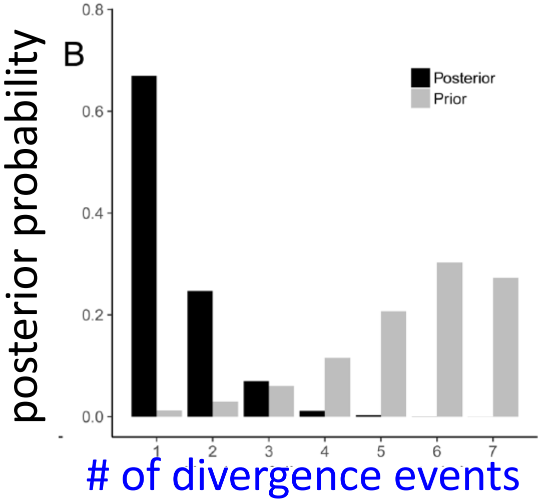
Species 1

Species 2

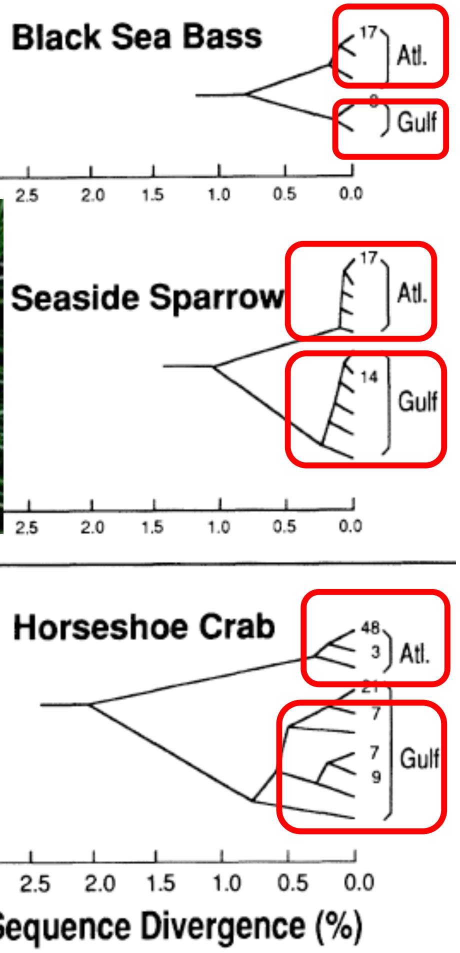
Species 3

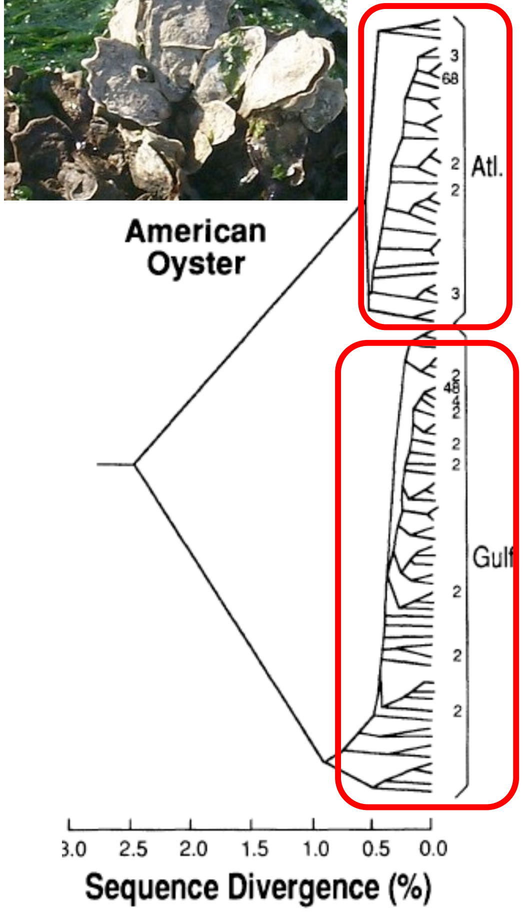
Species 4

Statistically evaluate a parameterized model of co-divergence among species using hierarchical Approximate Bayesian Computation (hABC)

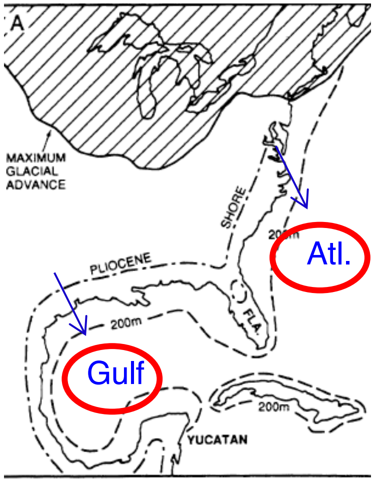


Concordance to test hypotheses





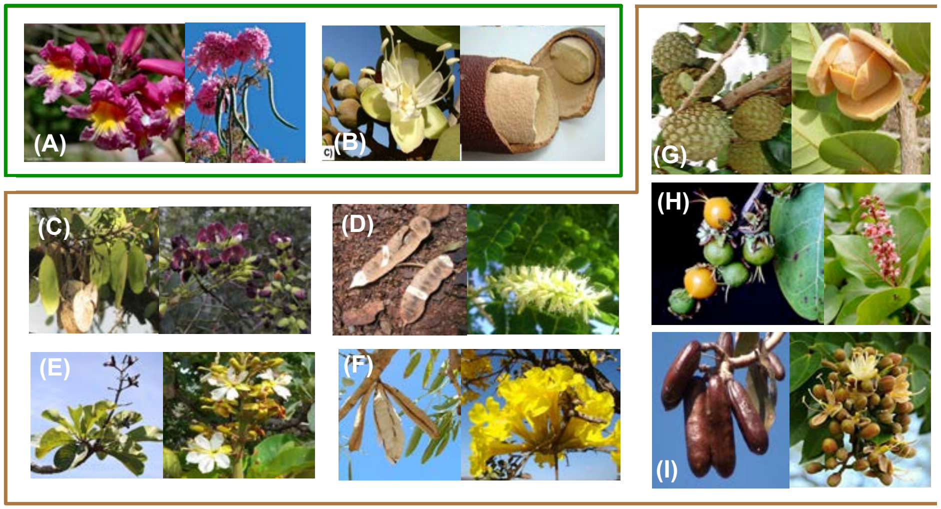
Biogeographic barrier

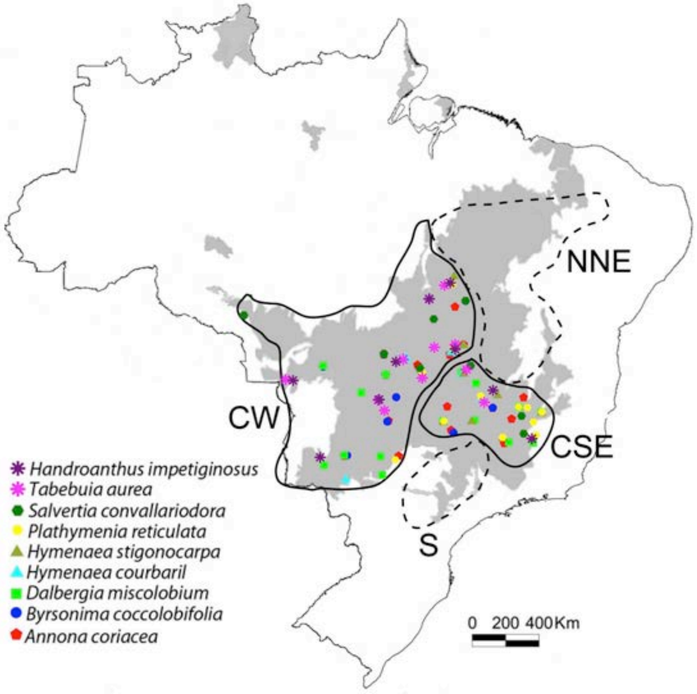


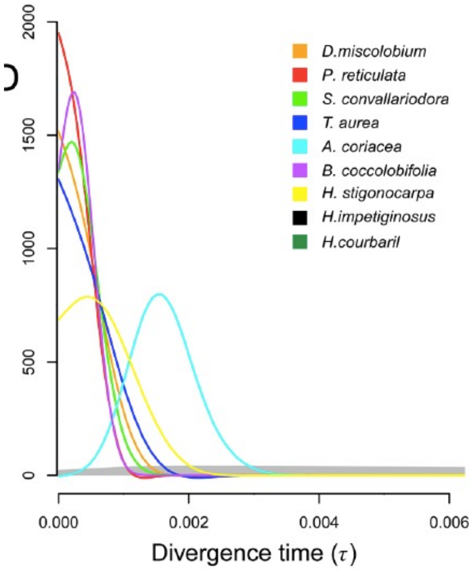
Avise 1992

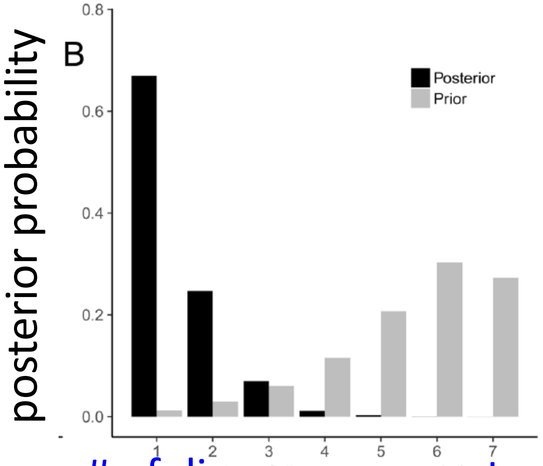
Concordance to test hypotheses using hABC

Estimate degree of co-divergence among species to evaluate hypothesized barrier associated with floristic provinces in Cerrado







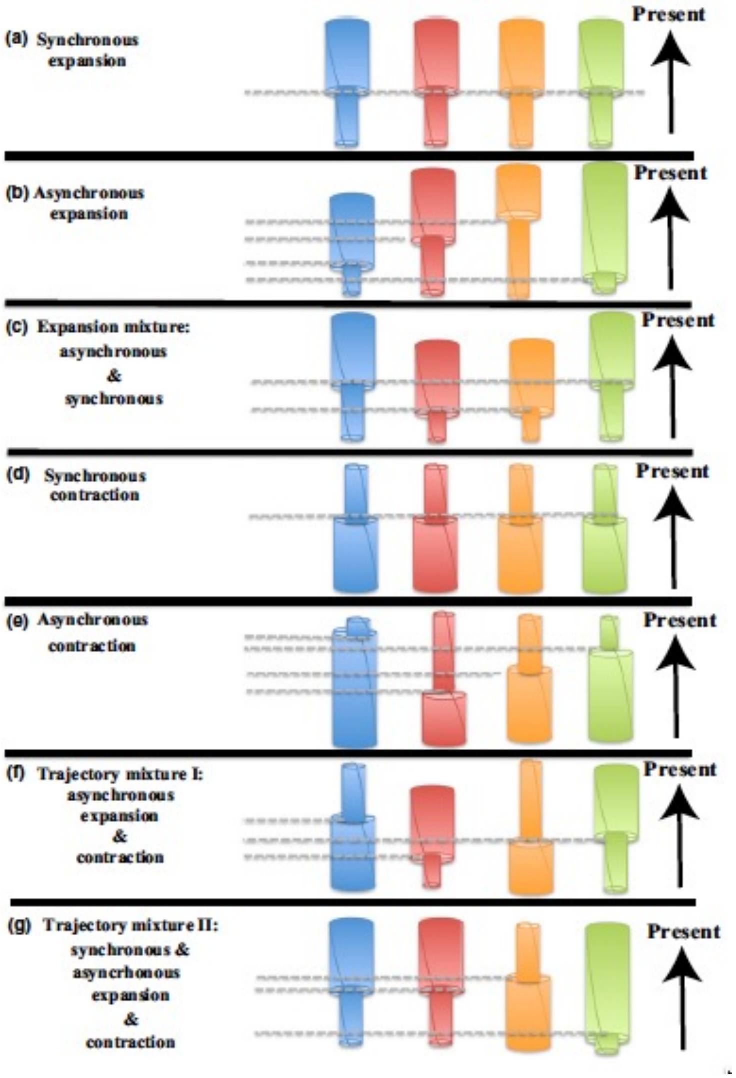


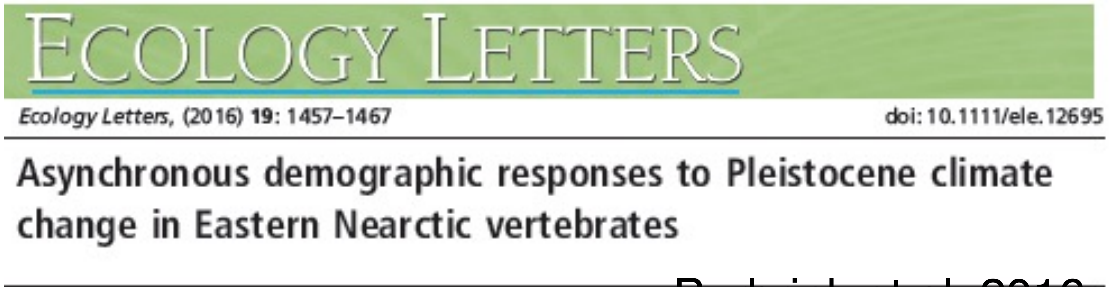
# of divergence events

concordance is a hyper-parameter in model that is estimated from genetic data across multiple species

.Resende et al. (in prep)

Concordance to test hypotheses of co-expansion


(a) Synchronous expansion
Present
(b) Asynchronous expansion
Present
(c) Expansion mixture: asynchronous & synchronous
Present
(d) Synchronous contraction
Present
(e) Asynchronous contraction
Present
(f) Trajectory mixture I: asynchronous expansion & contraction
Present
(g) Trajectory mixture II: synchronous & asyncrhonous expansion & contraction
Present


ECOLOGY LETTERS

Ecology Letters, (2016) **19**: 1457–1467 doi: 10.1111/ele.12695

Asynchronous demographic responses to Pleistocene climate change in Eastern Nearctic vertebrates

Burbrink et al. 2016

Genes and Geography across species

~~Biotic component?~~

CONCORDANCE

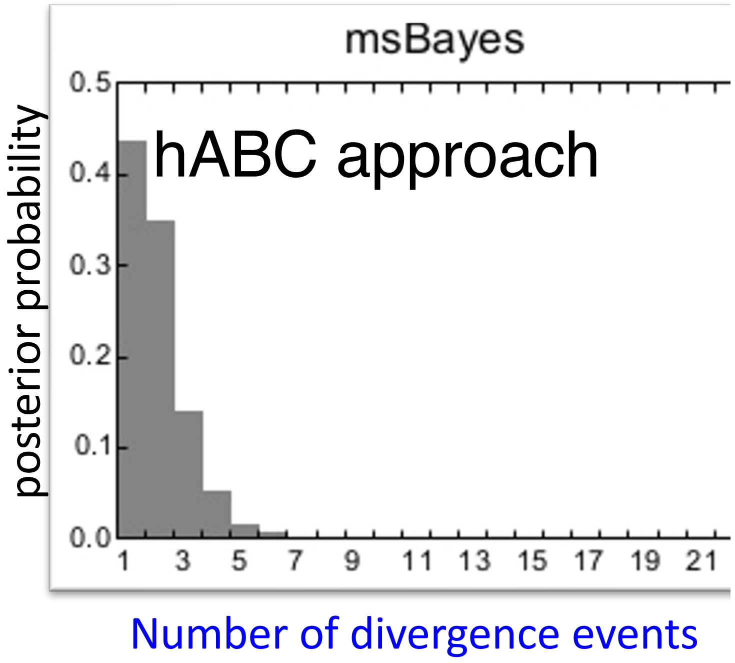
for testing hypotheses
about evolutionary history

- potential for misleading inference by not considering both biotic and abiotic components

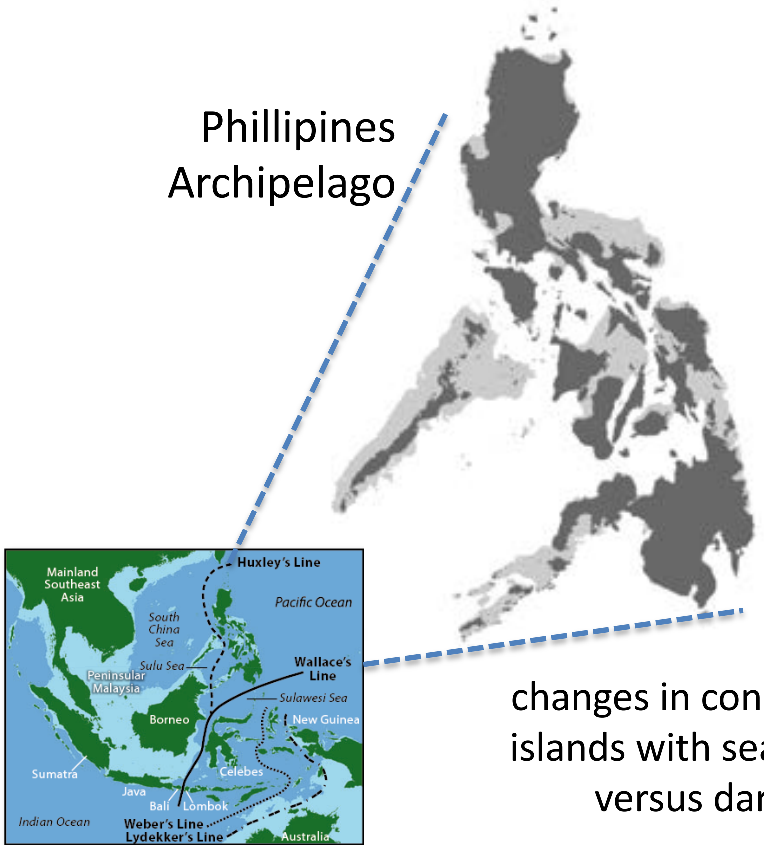
Concordance criteria for hypothesis testing

Hypothesis of simultaneous divergence to test whether sea-level oscillations during the Pleistocene caused diversification

Oaks et al. (2012) *Evolution*



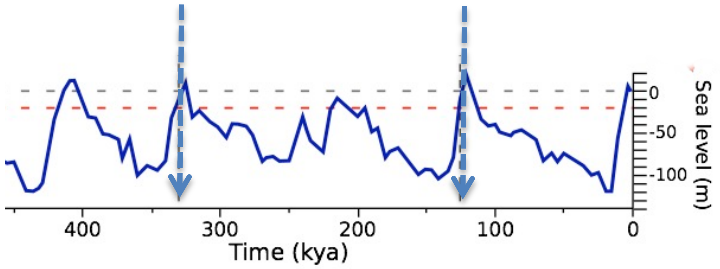
hABC approach



Phillipines Archipelago

- Inferred the distribution of divergence times among 22 pairs of co-distributed vertebrate taxa

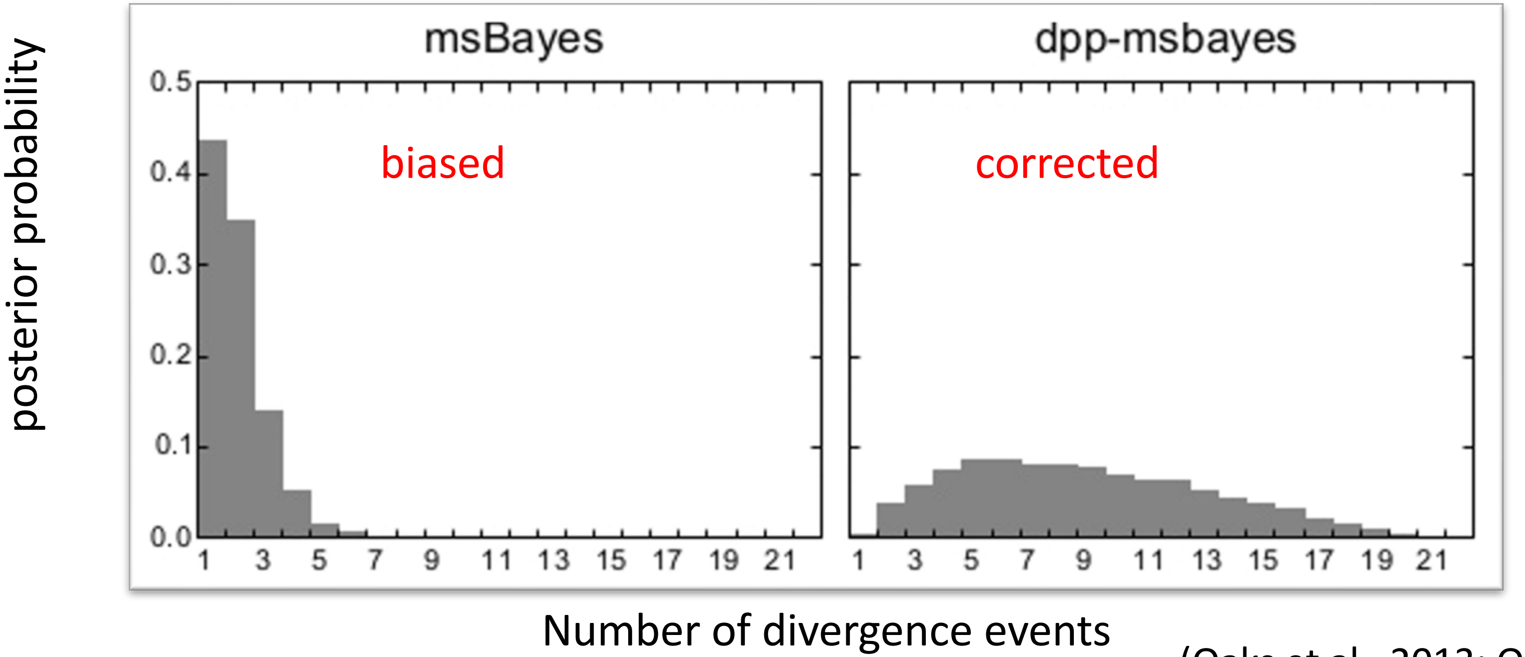
changes in connectivity/isolation of islands with sea-level changes (light versus dark grey outlines)



Concordance criteria for hypothesis testing

Hypothesis of simultaneous divergence to test whether sea-level oscillations during the Pleistocene caused diversification

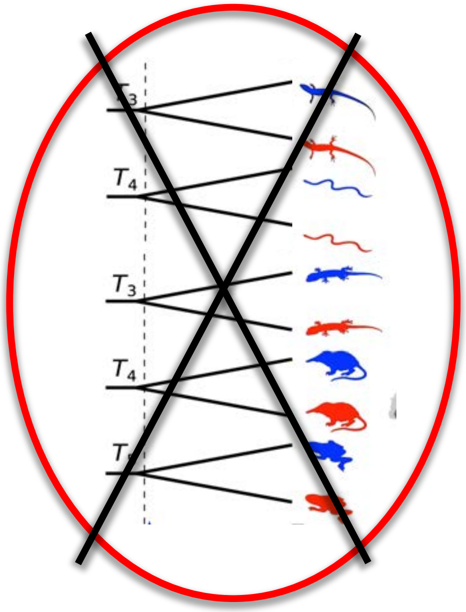
Performed a suite of simulation-based power analyses



(Oaks et al., 2013; Oaks, 2014)

Should this be interpreted as a rejection of the “species pump” model of diversification in which sea-level changes drive divergence?

Hypothesis of phylogeographic concordance Is TOO generic



Hypothesis of simultaneous divergence to test whether sea-level oscillations during the Pleistocene caused diversification

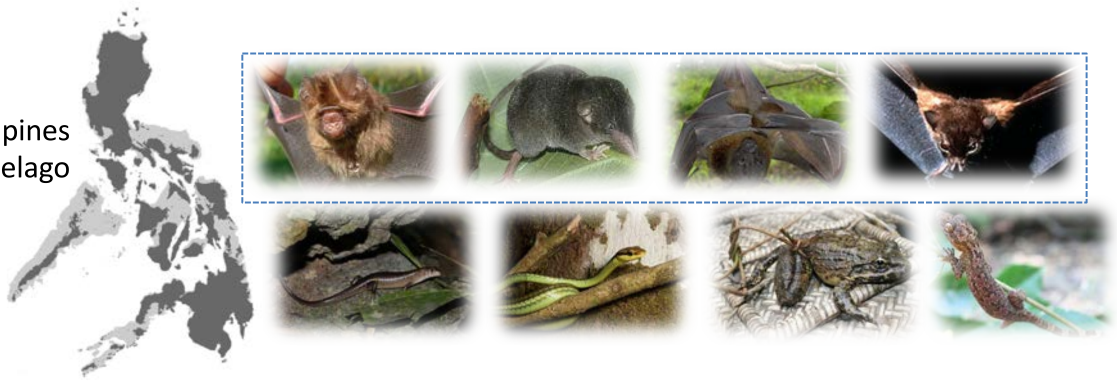
(Oaks et al., 2013; Oaks, 2014)

Concordance is arguably too generic of a hypothesis across these disparate taxa to test the "species pump" model of divergence.

~~Generic~~ Refined hypothesis of phylogeographic concordance

- a study design that considers taxon attributes

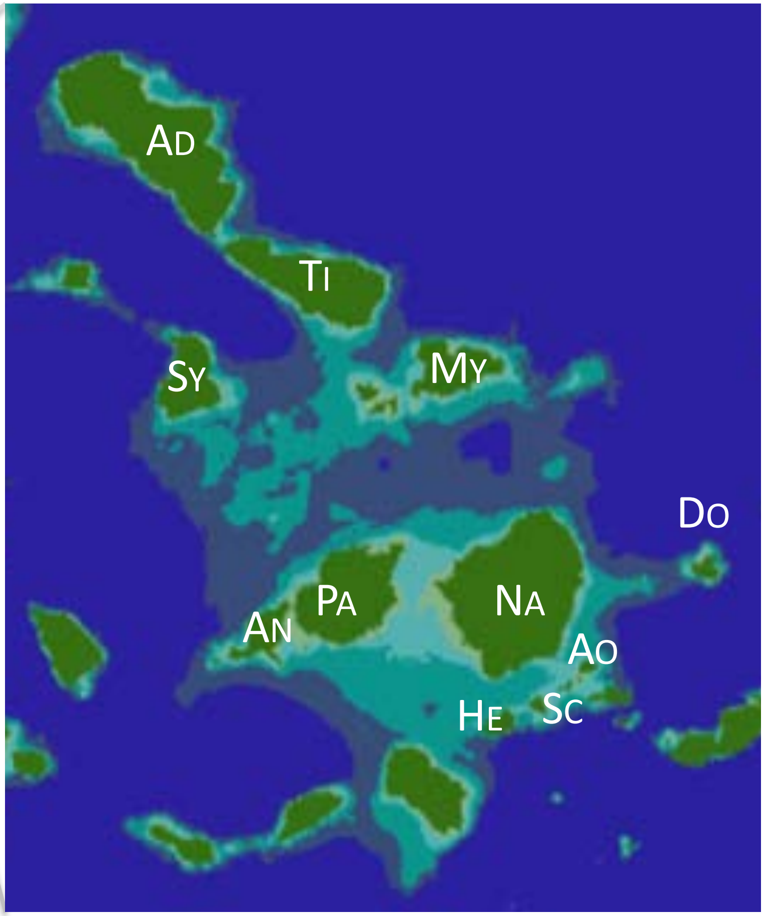
Hypothesis of simultaneous divergence to test whether sea-level oscillations during the Pleistocene caused diversification



Refined models of phylogeographic concordance to test the "species pump" model

Aegean archipelago

🟩 Current dry land
🟩 120 m isobath

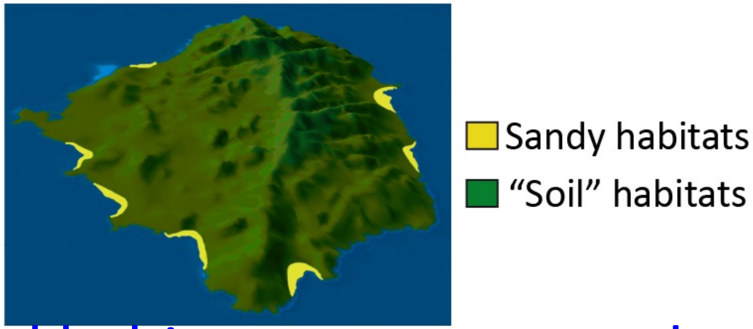


🟩	current dry land	🟦	-60 to -90 m
🟩	0 to -30 m	🟦	-90 to -120 m
🟩	-30 to -60 m	🟦	below -120 m

13 species of darkling beetles (Coleoptera: Tenebrionidae)

Papadopoulou & Knowles(2015) *Mol. Ecol.*

- taxa differ in their soil associations



Ephemerality of sand habitats may supersede effects of sea-level connections!

Soil – stable habitat

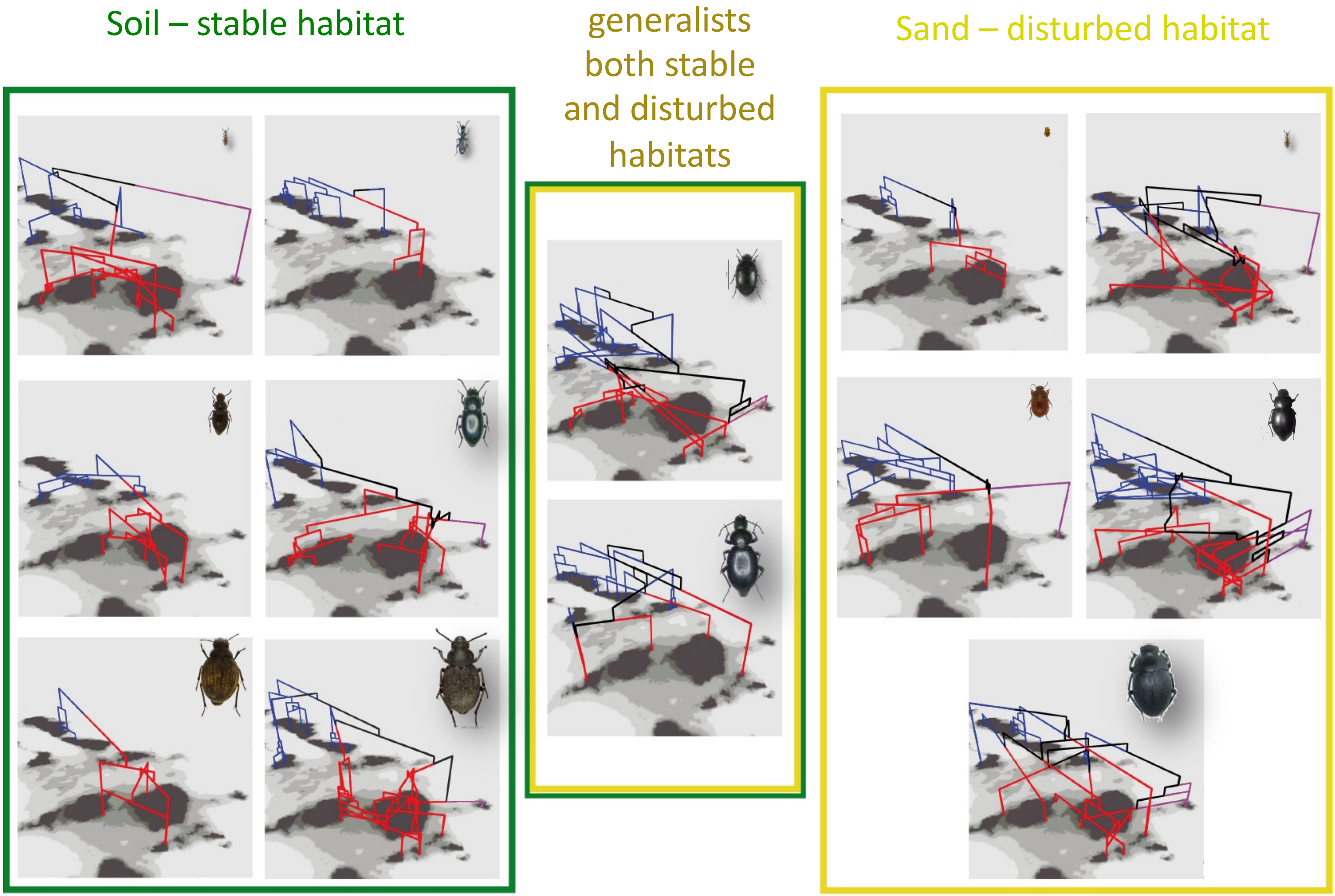
Sand – disturbed habitat

Generalists on both soil & sand

- uniform trophic ecology & inherent dispersal abilities

Papadopoulou & Knowles(2015) *Mol. Ecol.*

Different degrees of structure of mtDNA gene trees suggestive of differences in habitat stability



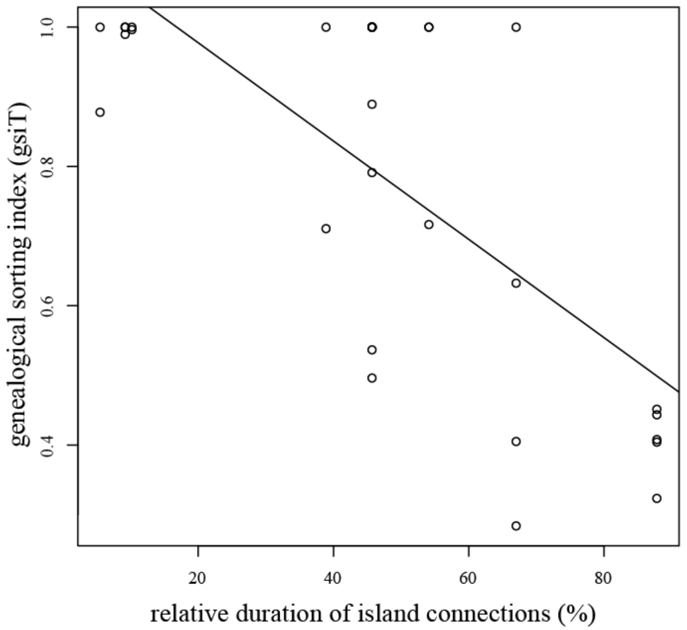
Soil – stable habitat

generalists both stable and disturbed habitats

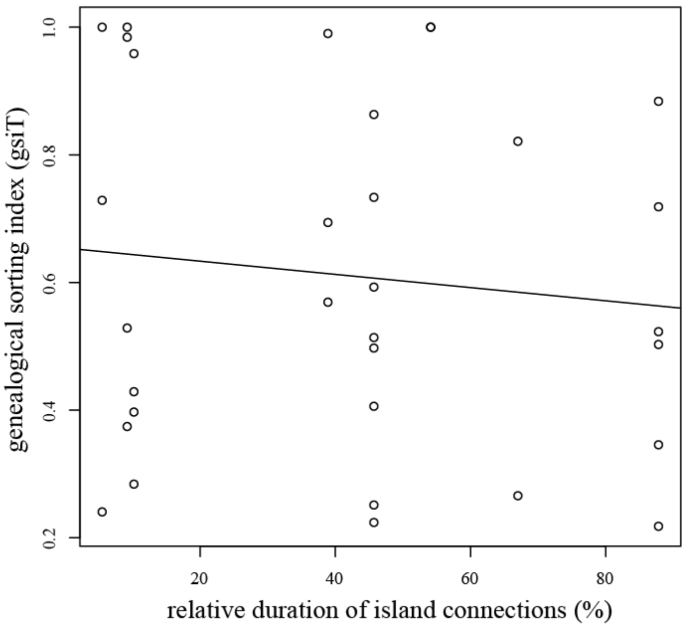
Sand – disturbed habitat

🟦 Northern Islands bathymetrically separated by 95m trench from 🟥 Southern islands

Degree of lineage sorting correlated with duration of island connections?



Soil – stable habitat: R^2_{adj}=0.48, p<<0.001



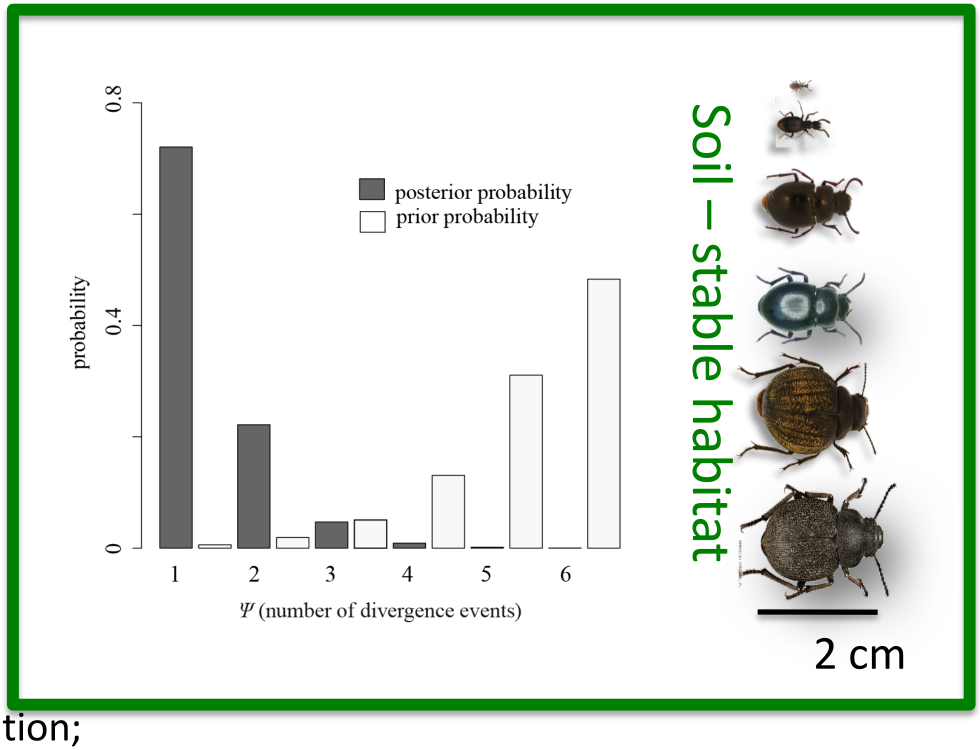
Sand – disturbed habitat: R^2_{adj}=0.01, p=0.54

Model comparisons in subsequent analyses also identified the relative duration of island connection in combination with habitat type as the best predictors of genealogical sorting (in contrast to other explanatory variables such as body size or island size) based on AICs

Papadopoulou & Knowles (2015) *Mol. Ecol*. 24: 4252-4268

Refined hypothesis for tests of concordance that focus on stable-habitat taxa

Test of simultaneous divergence



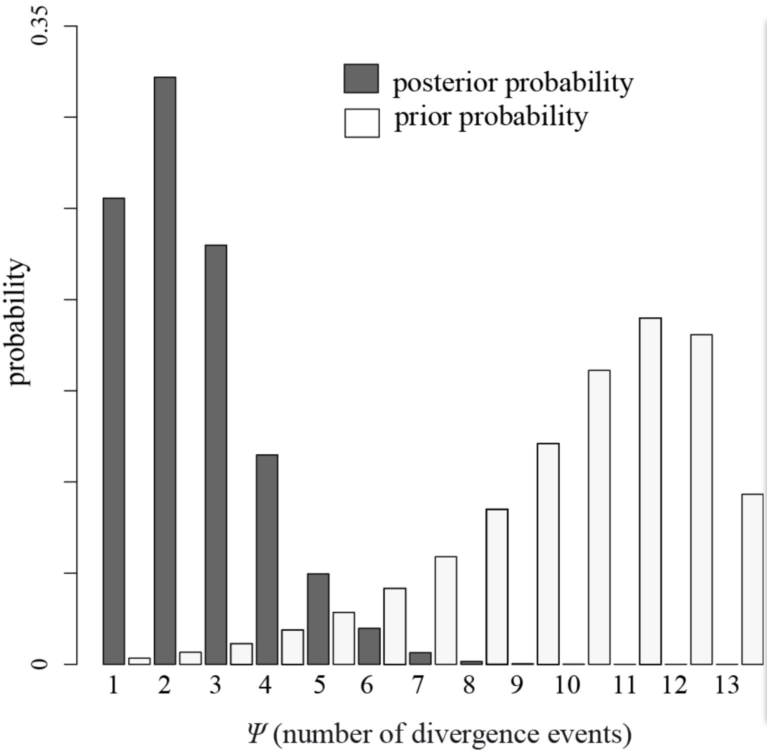
hABC: hierarchical Approximate Bayesian Computation;
Implemented in dpp-msbayes (Oaks, 2014)

By focusing on ecologically equivalent taxa, test of concordance supported the species pump model of divergence

Papadopoulou & Knowles (2015) *Mol. Ecol*. 24: 4252-4268

Generic hypotheses of global phylogeographic concordance

No evidence for simultaneous divergence

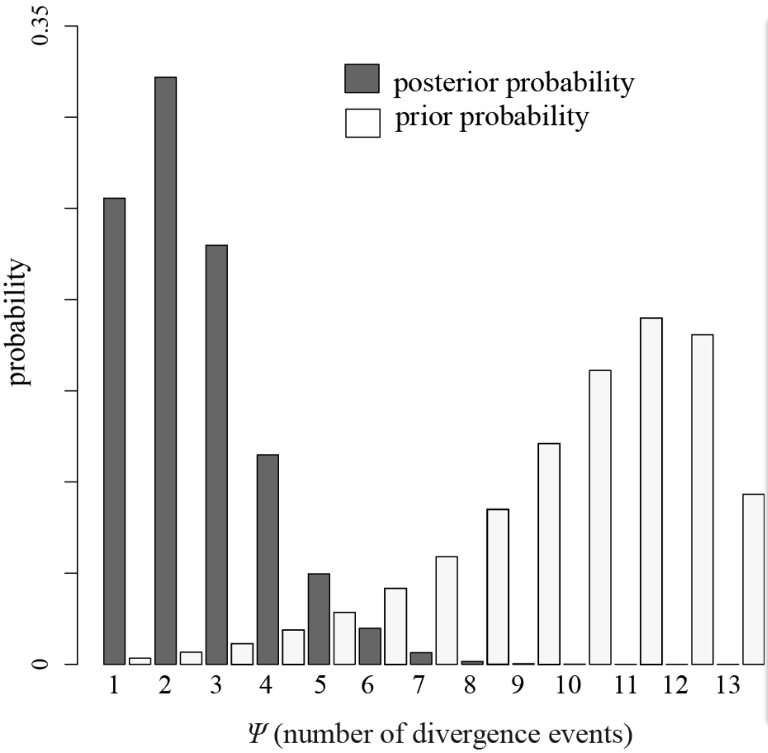


hABC implemented in
dpp-msbayes (Oaks, 2014)

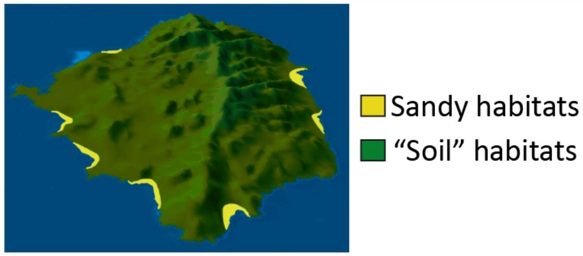
Papadopoulou & Knowles (2015) *Mol. Ecol*. 24: 4252-4268

Generic hypotheses of global phylogeographic concordance

No evidence for simultaneous divergence



Ephemerality of sand habitats!

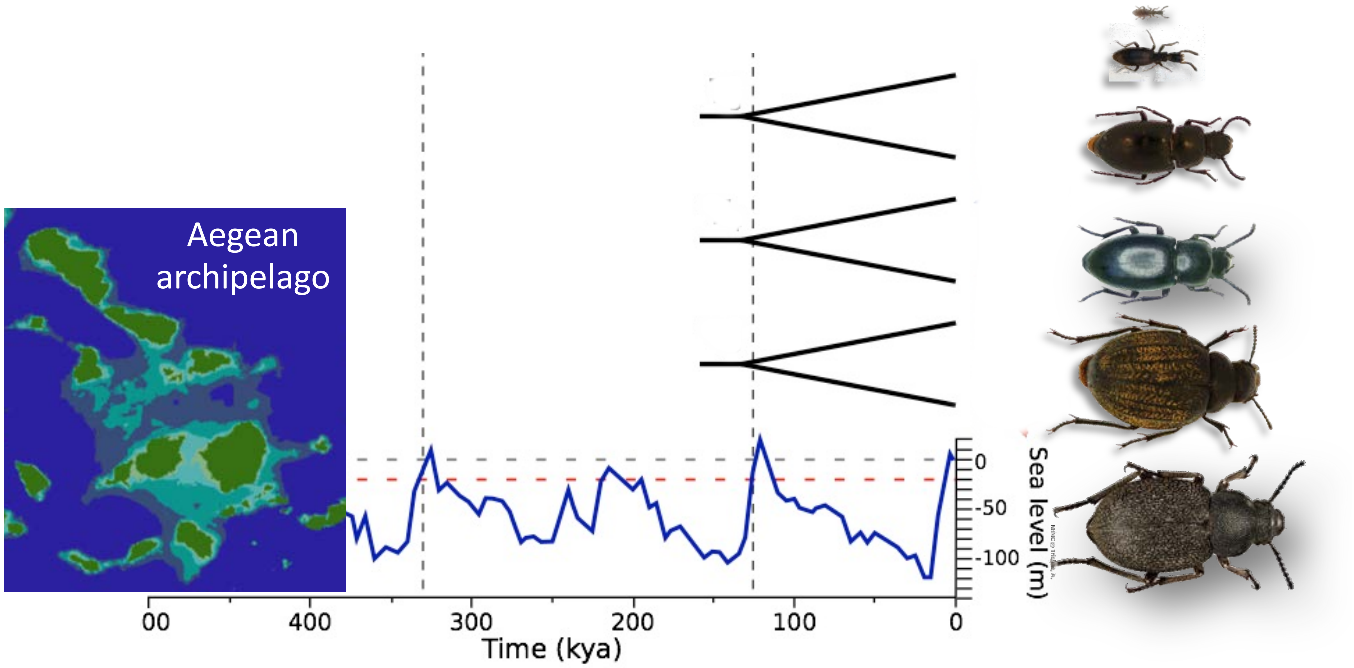


~~Lack of global concordance~~ → ~~rejection of species pump model of~~ divergence ???

Papadopoulou & Knowles (2015) *Mol. Ecol*. 24: 4252-4268

Refined hypotheses based on taxon-specific traits in comparative phylogeography

Soil– stable habitat

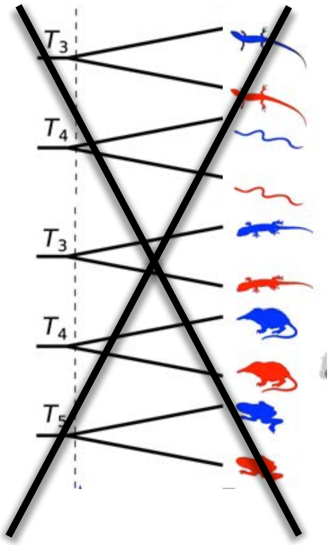


- refinement of the expectation for concordance is needed for concordance itself to be a meaningful metric

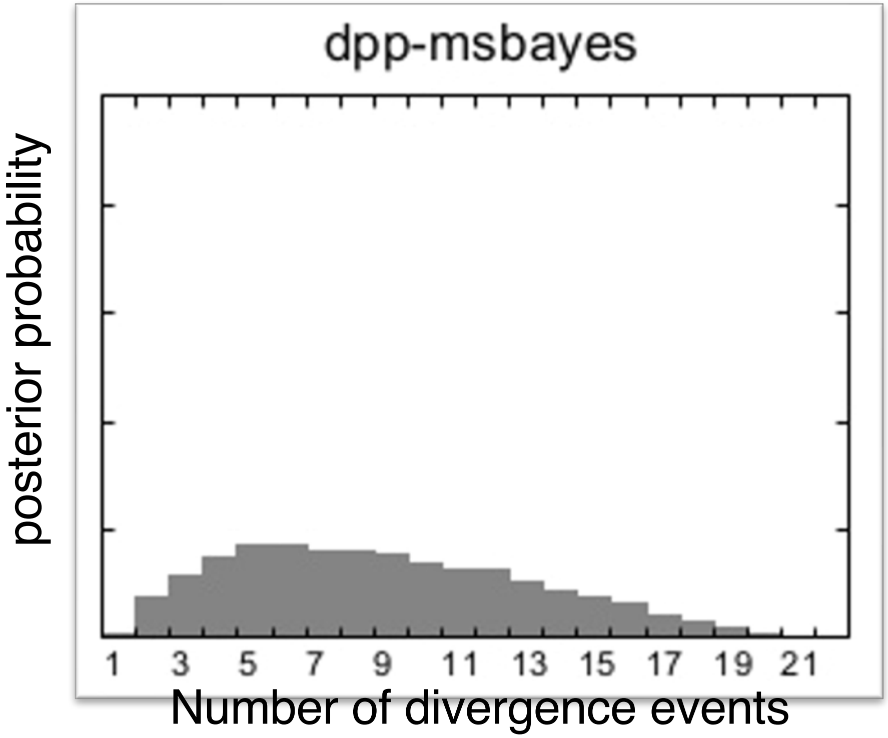
- reduced predictive power of generic hypotheses – their rejection leads to inconclusive statements that do not offer particularly meaningful insights

Papadopoulou & Knowles (2016) *PNAS*

- comparative phylogeographic methods are designed to quantify congruence, rather than gain insights from discordant patterns



- indirectly encourages users to emphasize idiosyncratic aspects of history!



- ad hoc interpretations of discordance

- NEED development/application of methods for statistical evaluation of phylogeographic discord as an expectation

Papadopoulou & Knowles (2016) *PNAS*

Refined hypotheses based on taxon-specific traits in comparative phylogeography

- Model formulation is a way of communicating our expert knowledge to statistical apparatus to test hypotheses

Biological insights:

(i) hypotheses that capture processes structuring genetic variation, and
(ii) model-based approaches to evaluate statistical support for alternative hypotheses

Does microhabitat affect responses to climate change

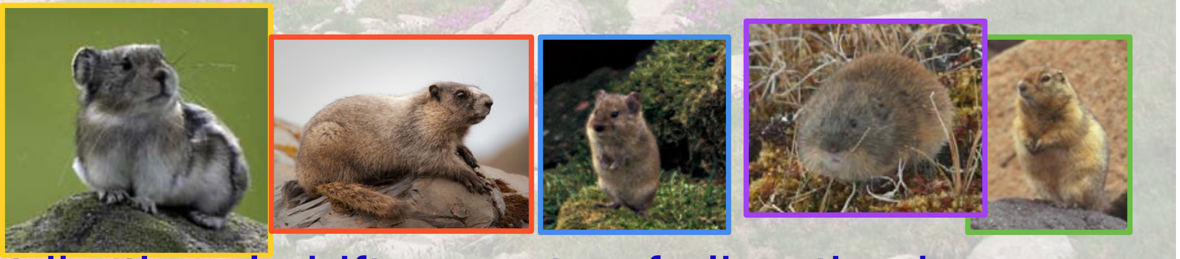
Massatti & Knowles (2014, 2016)
Evolution, Mol. Ecol.

Role of habitat stability in structuring genetic variation

He et al (2013) *Evolution*

Present versus past distributions as drivers of divergence

Knowles & Massatti (2017) *Ecography*



Extent of distributional shifts or rate of climatic change as determinants of concordant patterns of genetic structure

Knowles et al. (2016) *J. Biogeogr.*
He et al. (2017) *Mol Ecol.*

Biological insights:

(i) hypotheses that capture processes structuring genetic variation, and

(ii) model-based approaches to evaluate statistical support for alternative hypotheses

Does microhabitat affect responses to climate change

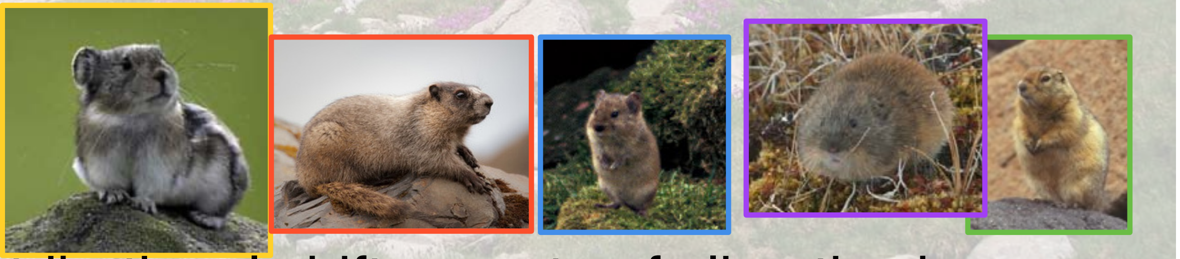
Massatti & Knowles (2014, 2016)
Evolution, Mol. Ecol.

Role of habitat stability in structuring genetic variation

He et al (2013) *Evolution*

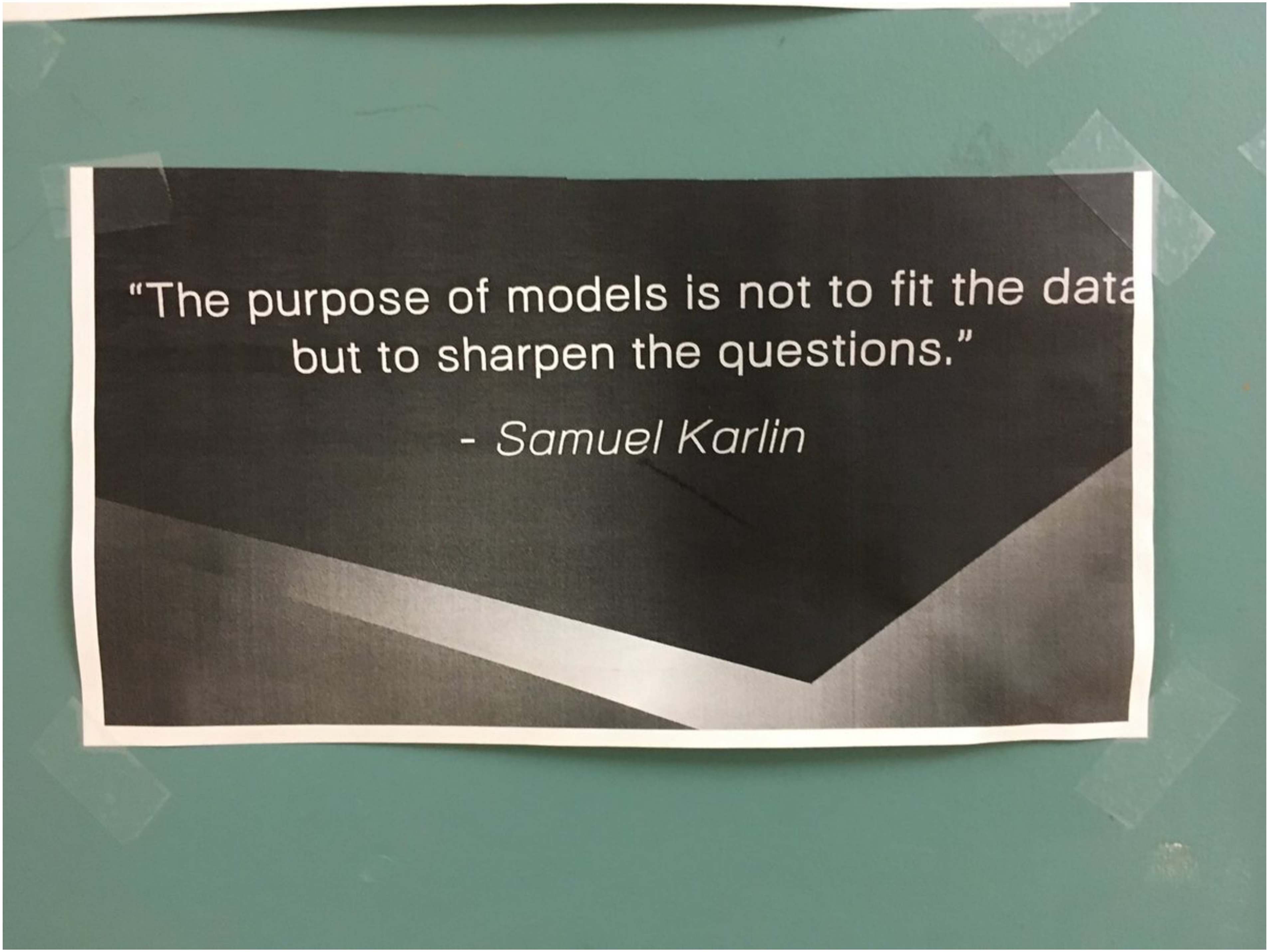
Present versus past distributions as drivers of divergence

Knowles & Massatti (2017) *Ecography*



Extent of distributional shifts or rate of climatic change as determinants of concordant patterns of genetic structure

Knowles et al. (2016) *J. Biogeogr.*
He et al. (2017) *Mol Ecol.*



"The purpose of models is not to fit the data but to sharpen the questions."

- *Samuel Karlin*

Evolutionary applications of model-based analyses:

(i) Inferring species boundaries (aka species delimitation)

(ii) Phylogenetic inference (and beyond the species tree)

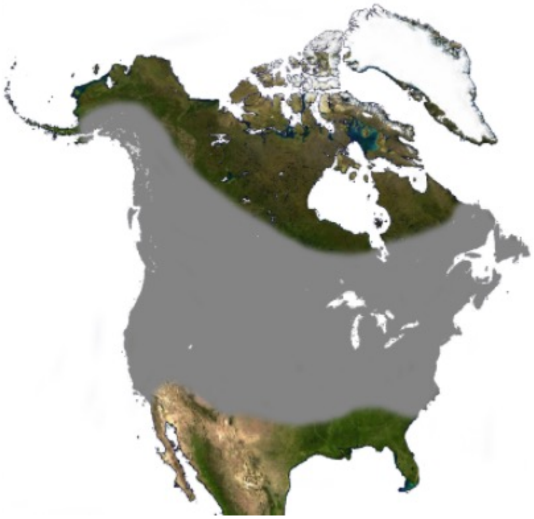
(iii) Biogeographic study

(iv) Phylogeography

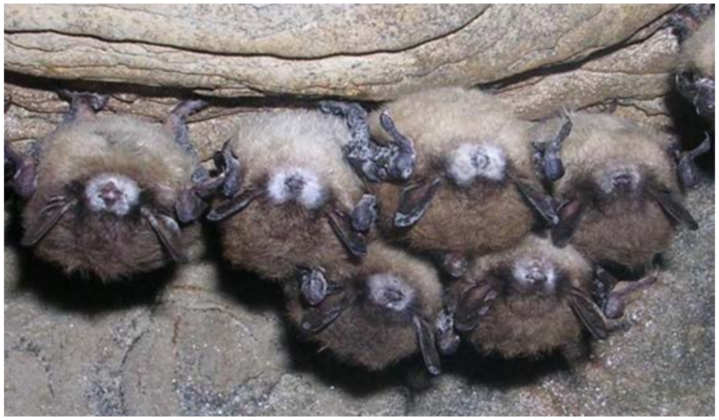
(v) Adaptive evolution

Myotis lucifugus

Little brown bats are widespread in North America and were the most abundant species in the eastern US prior to white nose syndrome (WNS), which is caused by introduced fungal pathogen

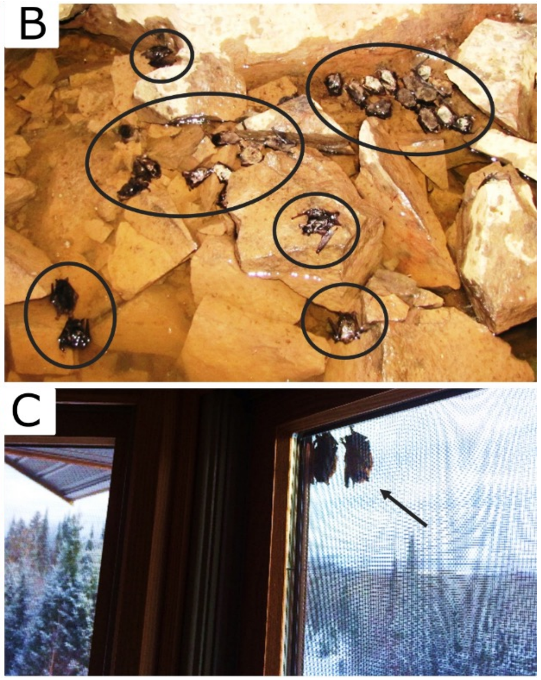


Little brown bats decimated by white nose syndrome (WNS)



Population declines > 90% since introduction of fungal pathogen that causes WNS

Dead bats in underground hibernation sites (shown here on the floor of a mine)



Others leave hibernating sites prematurely, like these dead bats on the outer screen of a house < 1 km from a hibernation site (note the snowy landscape).

Myotis lucifugus

Survival of the species may ultimately depend upon its capacity for adaptive change

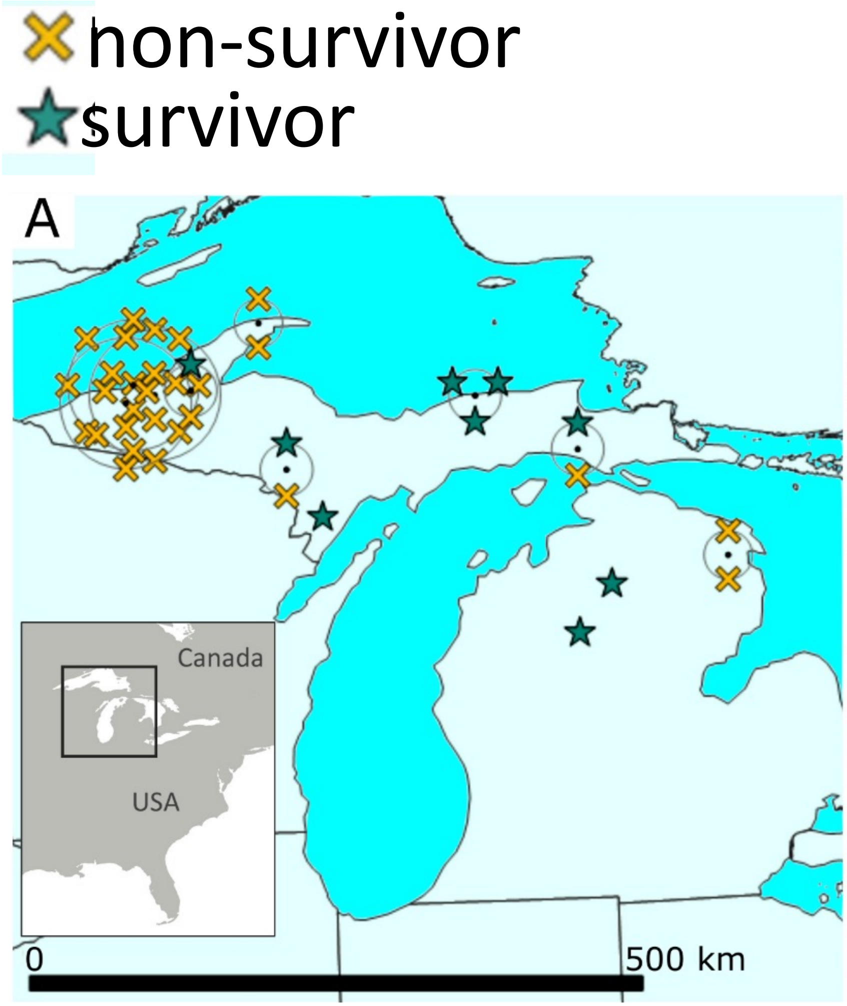
- Compare the genetic makeup of wild survivors and non-survivors of WNS to tests for adaptive change

Giorgia G. Auteri

UNIVERSITY OF MICHIGAN

Auteri GG, Knowles LL (2020) Decimated little brown bat population show potential for adaptive change. *Scientific Reports.* 10:3023. doi.org/10.1038/s41598-020-59797-4

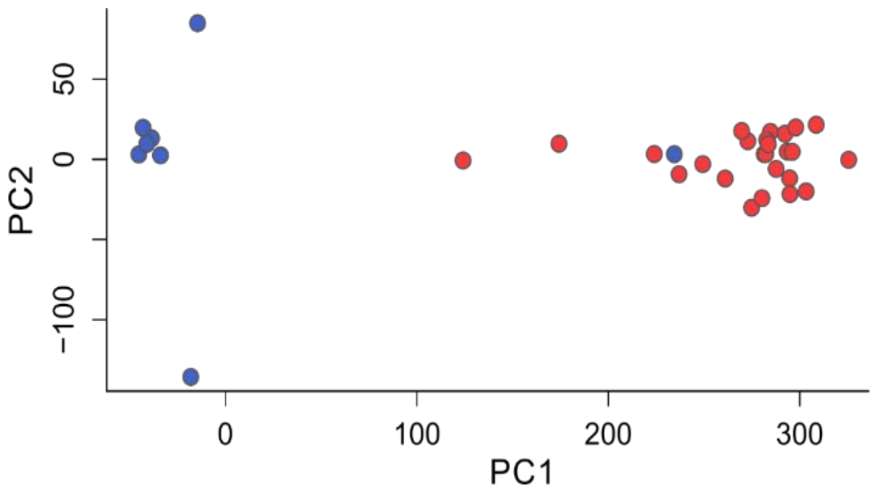
Studied geographically isolated population of little brown bats



WNS arrived in 2014

- RADseq: 14,345 loci , 19,797 SNPs

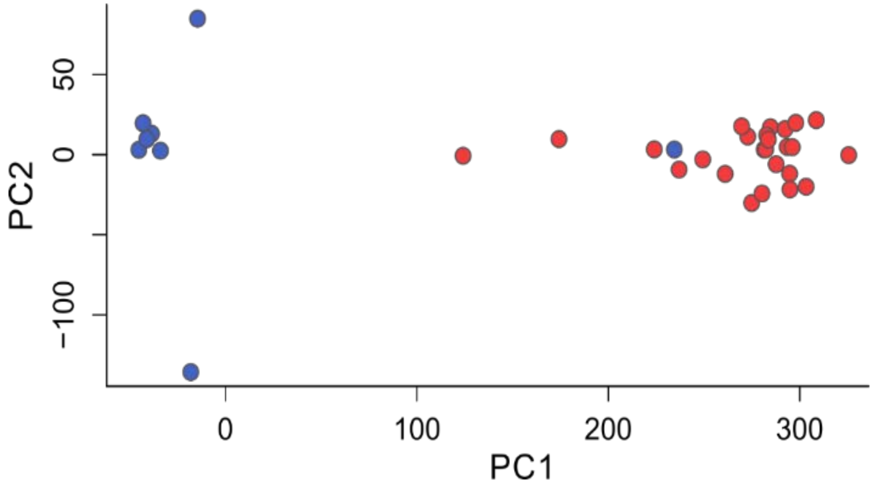
Evidence of strong genetic drift caused by the massive population losses in little brown bats.



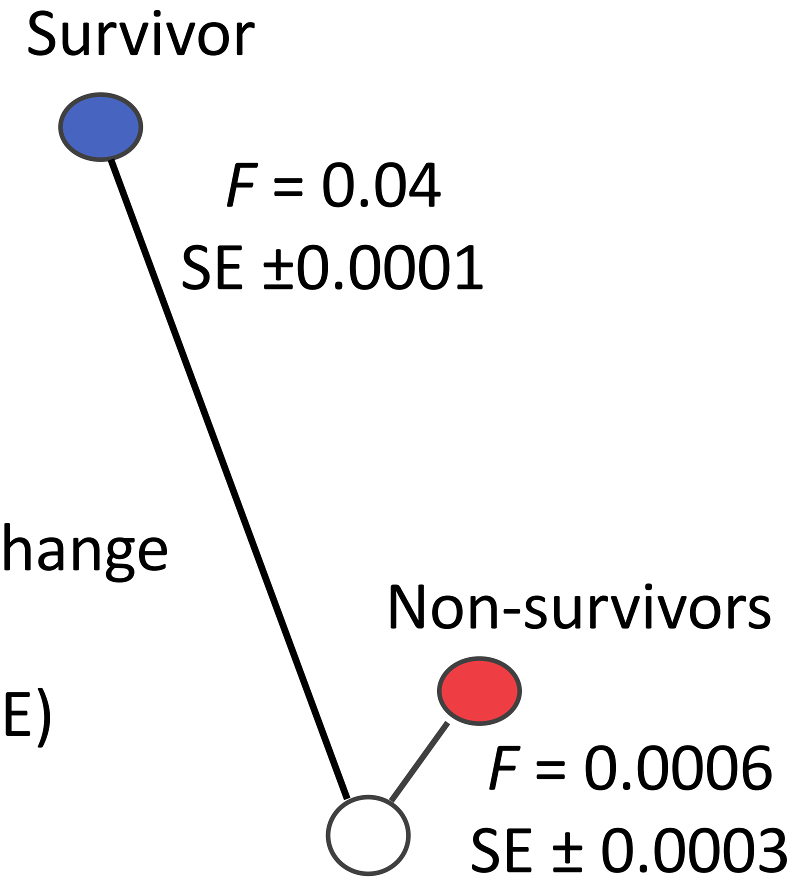
PCA of survivors of WNS (in blue) with non-survivors (in red) projected onto the PC axes

- 14,345 SNPs and 33 individuals

Evidence of strong genetic drift caused by the massive population losses in little brown bats.



Quantified rate of evolutionary change
from inferred ancestor
(using F-model in STRUCTURE)



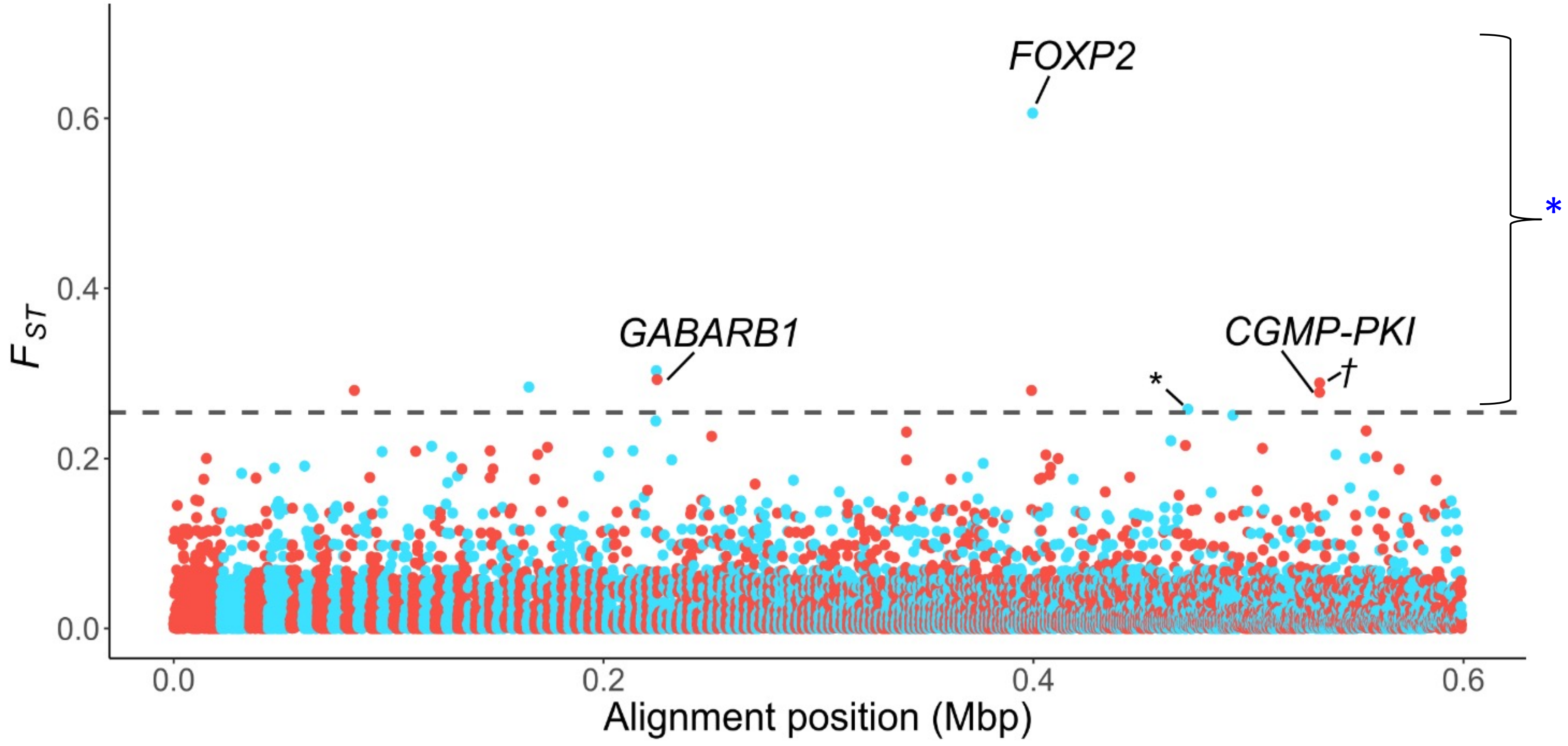
Survivor

F = 0.04
SE ±0.0001

Non-survivors

F = 0.0006
SE ± 0.0003

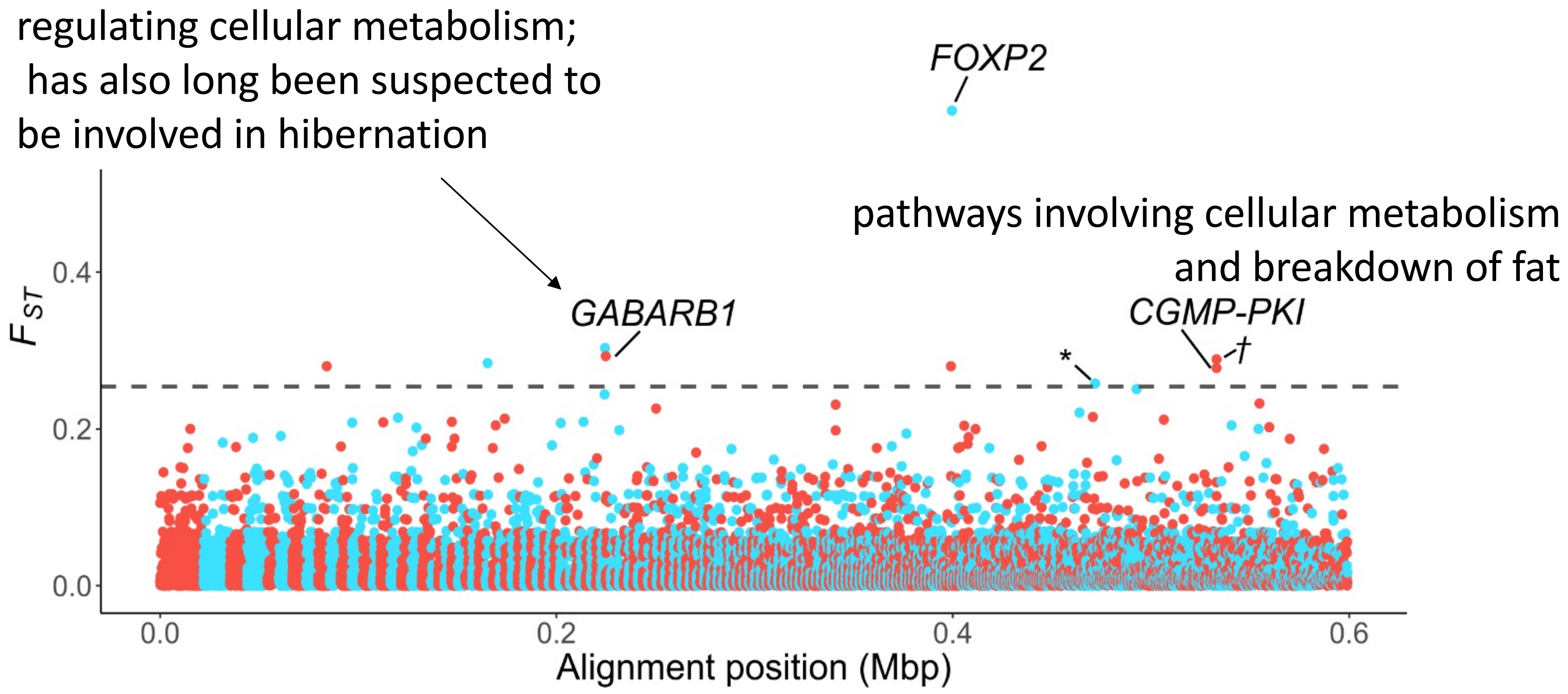
To identify genetic changes among individuals that might have contributed to their survival of WNS, as opposed to changes due to strong genetic drift, used an F_{ST}-outlier approach



- alternating red and blue mark different genomic scaffolds

*signature of selection can be detected by levels of genetic differentiation at a gene that exceeds background levels across the genome

Links between metabolic demands and survival



regulating cellular metabolism;
has also long been suspected to
be involved in hibernation

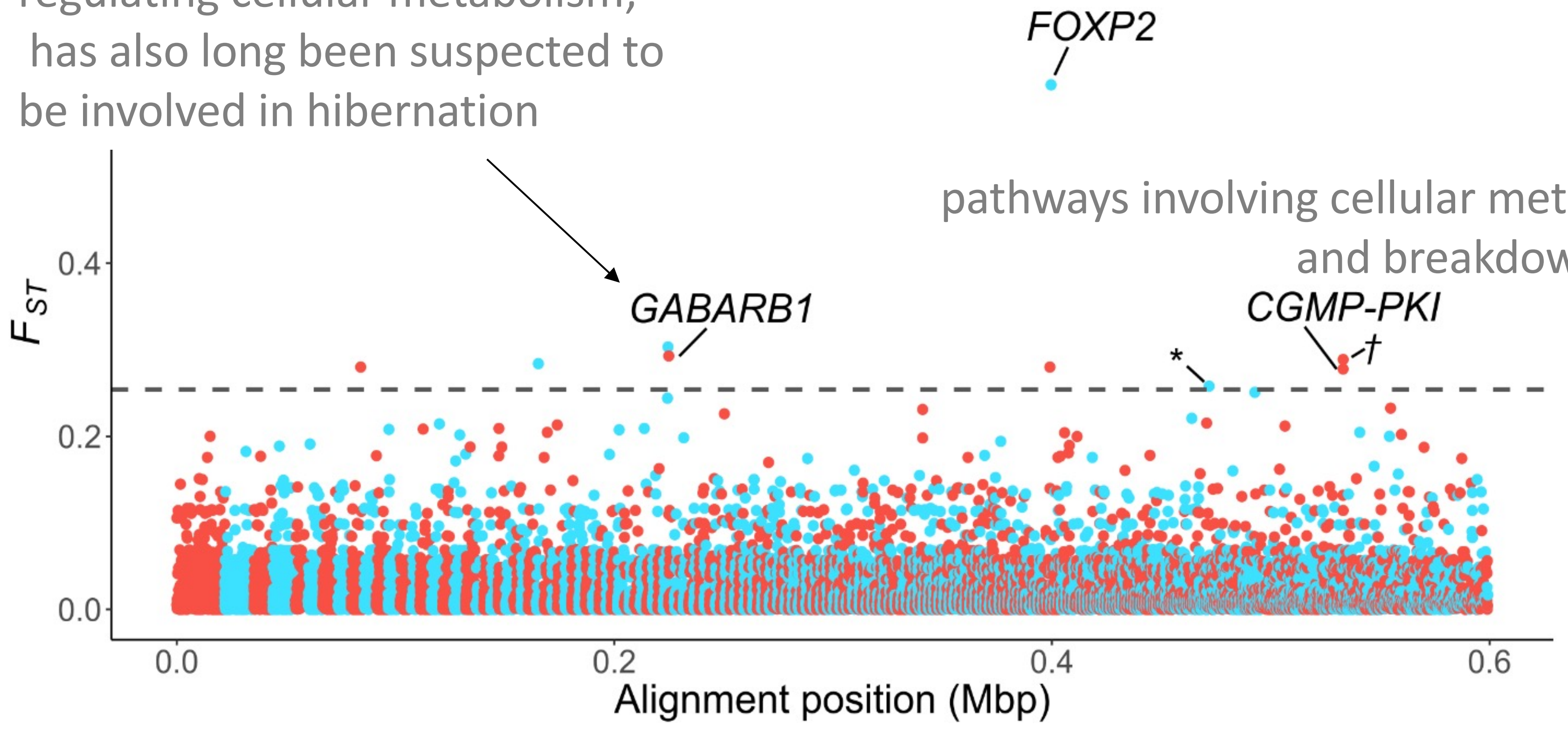
pathways involving cellular metabolism
and breakdown of fat

Physiological functions that make immediate sense in an adaptive context—deaths from the WNS fungus are a result of too frequent arousals from hibernation that causes starvation.

Links between metabolic demands and survival

associated with vocalizations, and echolocation in bats

regulating cellular metabolism; has also long been suspected to be involved in hibernation



pathways involving cellular metabolism and breakdown of fat

Variation in calls is closely associated with type of prey and the habitat bats must navigate, potentially adaptive shifts might result from selective pressures related to proficient hunting or prey preferences

Too soon to claim that the species will be “saved” via an evolutionary rescue effect.

© Steve Byland

Evidence of potentially adaptive evolution in the survivors of little brown bats is particularly notable on several fronts:

Too soon to claim that the species will be "saved" via an evolutionary rescue effect.

© Steve Byland

Evidence of potentially adaptive evolution in the survivors of little brown bats is particularly notable on several fronts:

- We detected selectively driven divergence, despite strong genetic drift caused by the massive population losses in little brown bats.

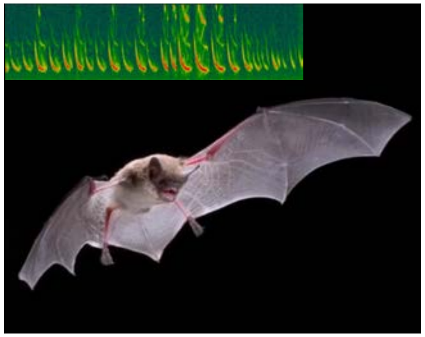
Too soon to claim that the species will be “saved” via an evolutionary rescue effect.

Evidence of potentially adaptive evolution in the survivors of little brown bats is particularly notable on several fronts:

© Steve Byland

- We detected selectively driven divergence, despite strong genetic drift caused by the massive population losses in little brown bats.

- These evolutionary changes were detected in less than three generations since exposure to WNS



Too soon to claim that the species will be "saved" via an evolutionary rescue effect.

Evidence of potentially adaptive evolution in the survivors of little brown bats is particularly notable on several fronts:

© Steve Byland

- We detected selectively driven divergence, despite strong genetic drift caused by the massive population losses in little brown bats.
- These evolutionary changes were detected in less than three generations since exposure to WNS
- Putatively selected loci and their potential adaptive functions point to multifaceted nature of selection (i.e., genes linked to physiological and behavioral traits, whose roles vary across habitats of highly seasonal environments)

Evolutionary applications of model-based analyses:

(i) Inferring species boundaries (aka species delimitation)

(ii) Phylogenetic inference (and beyond the species tree)

(iii) Biogeographic study

(iv) Phylogeography

(v) Adaptive evolution

Species delimitation
(discovery)

Learning goals:

- Describe applications of the multispecies coalescent (MSC) to species delimitation
- Explain the merit/limitations of the multispecies coalescent (MSC) to delimitation
- Describe (i) how over-estimation of species numbers might occur with applications based on the MSC (ii) what determines the degree of overestimation
- Explain the relevance of the speciation process to delimitation approaches

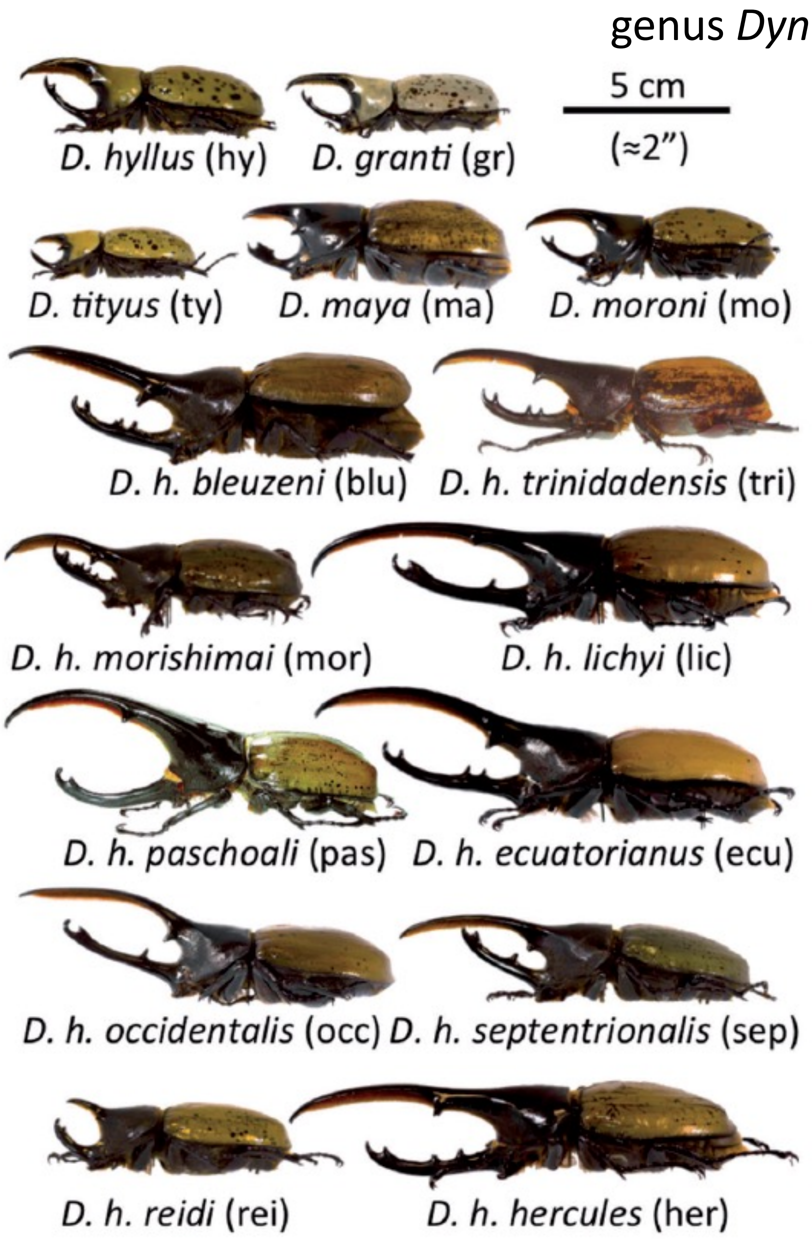
Hypotheses about species boundaries

Model-based inference of species boundaries

Statistical evaluation of a hypothesized species delimitation model

5 species

1 species

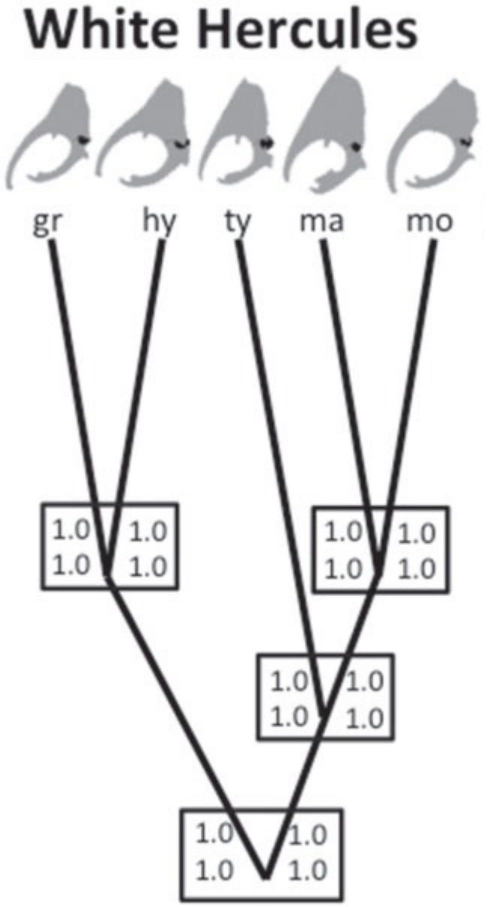


Huang & Knowles (2016) *Syst. Biol.*

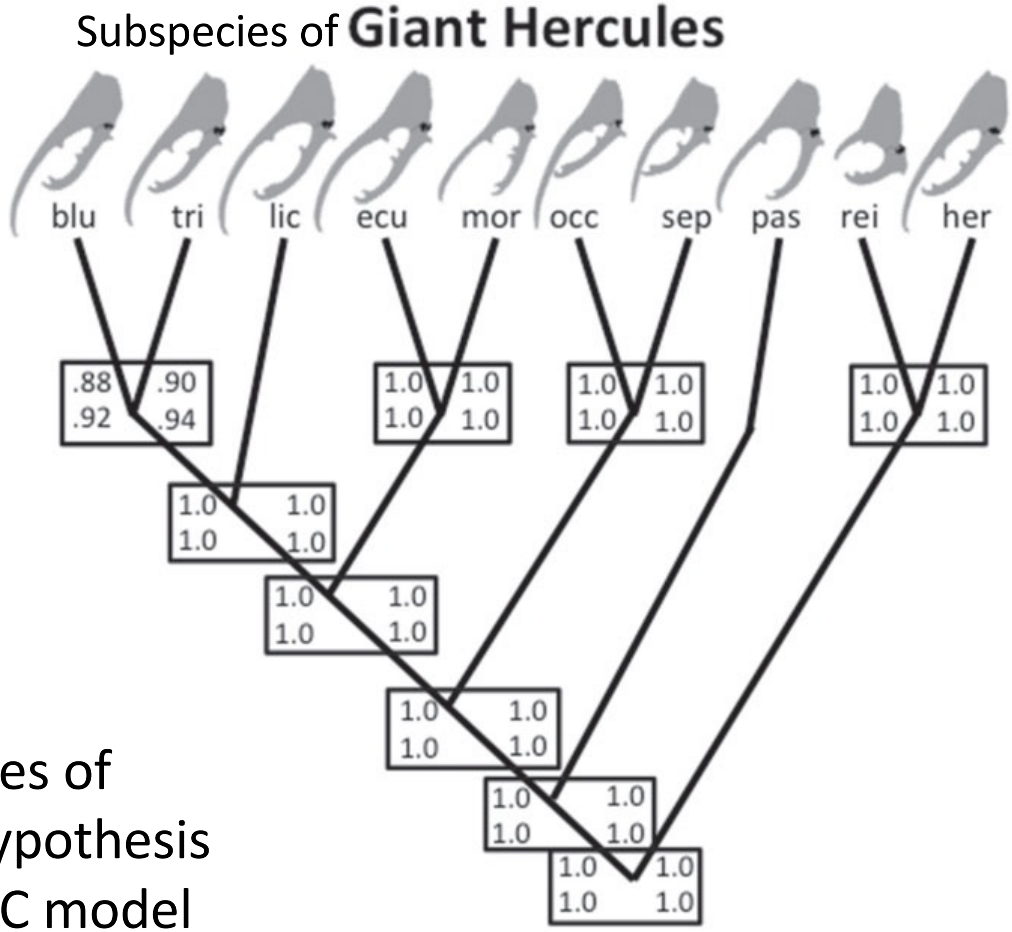
Model-based inference of species boundaries

5 recognized species
In North America

1 recognized species
In South America



Subspecies of



Probabilities of
delimitation hypothesis
under the MSC model

genus *Dynastes*

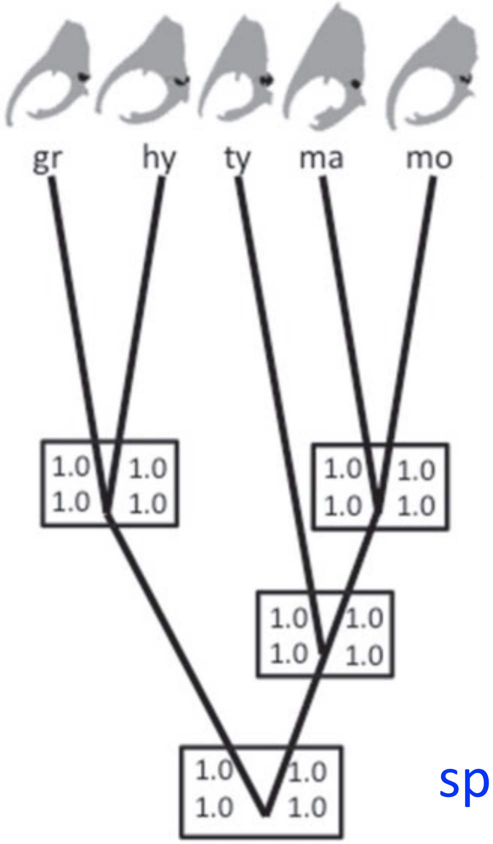
Huang & Knowles (2016) *Syst. Biol.*

Model-based inference of species boundaries

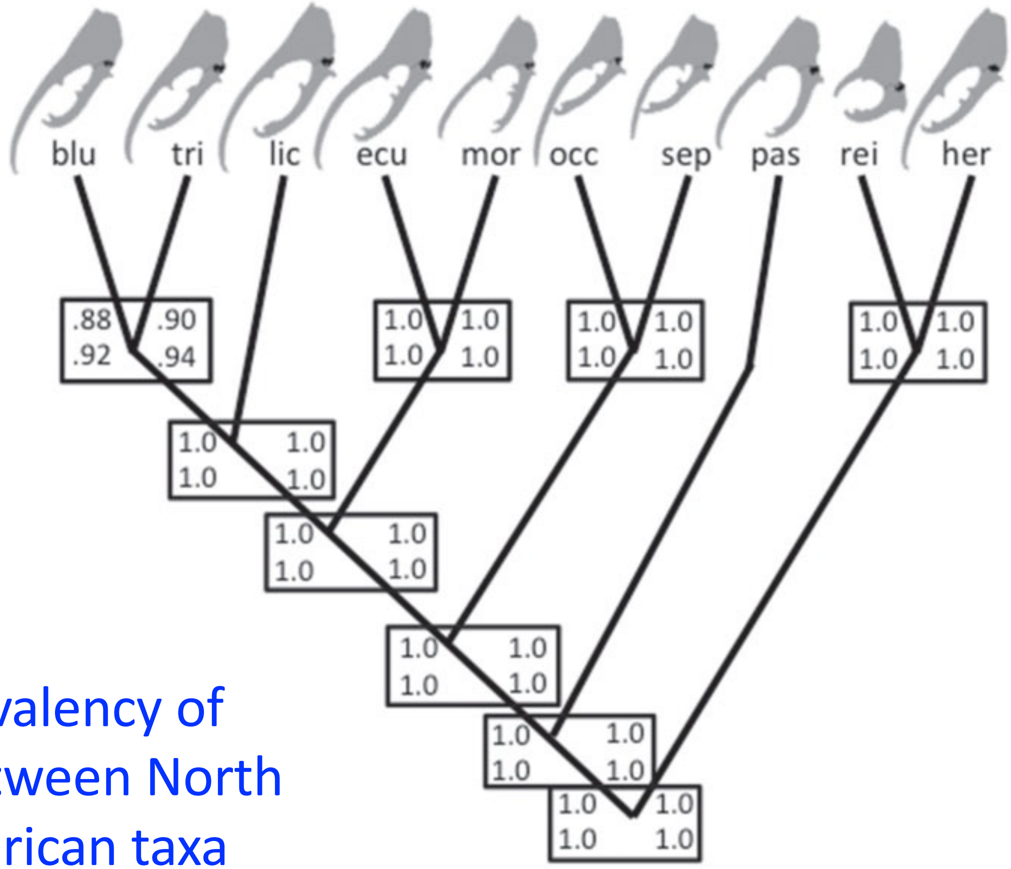
5 recognized species
In North America

1 recognized species
In South America

White Hercules



10 inferred species of **Giant Hercules**



Statistical equivalency of species status between North and South American taxa

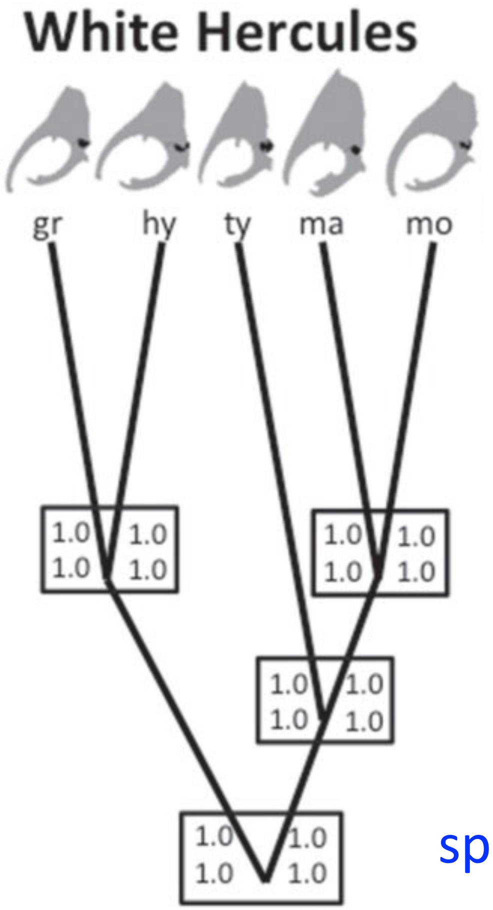
genus *Dynastes*

Huang & Knowles (2016) *Syst. Biol.*

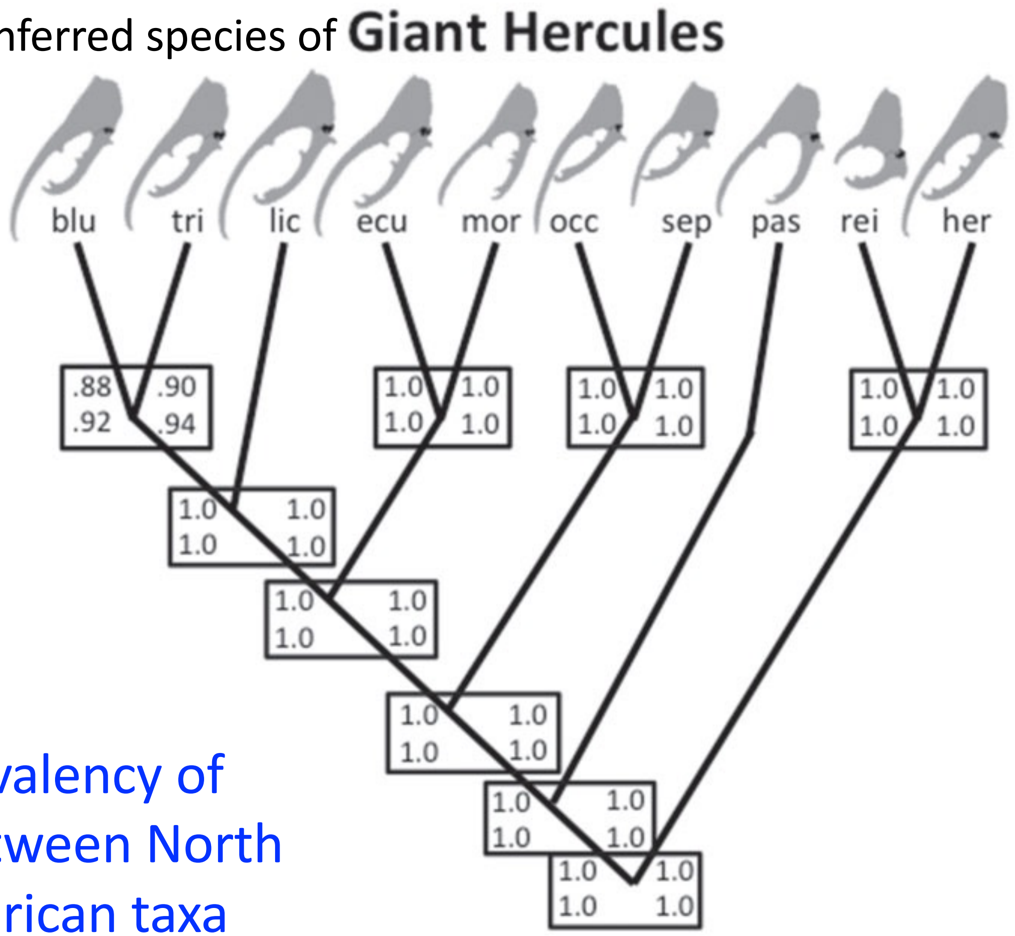
Model-based inference of species boundaries

5 recognized species
In North America

1 recognized species
In South America



10 inferred species of



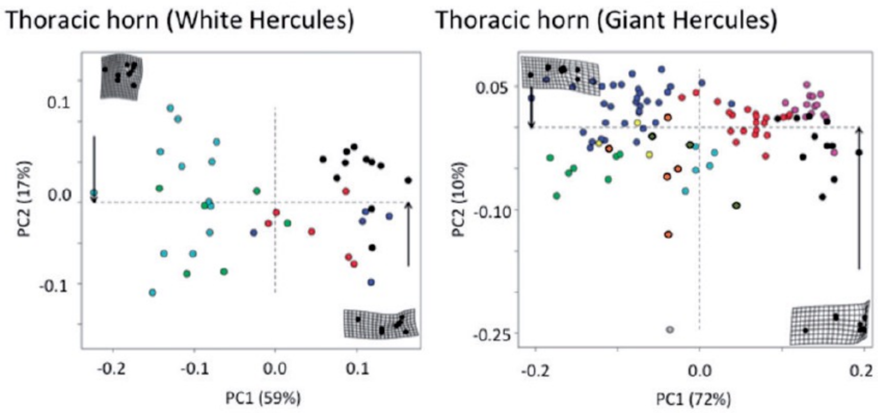
Statistical equivalency of species status between North and South American taxa

genus *Dynastes*

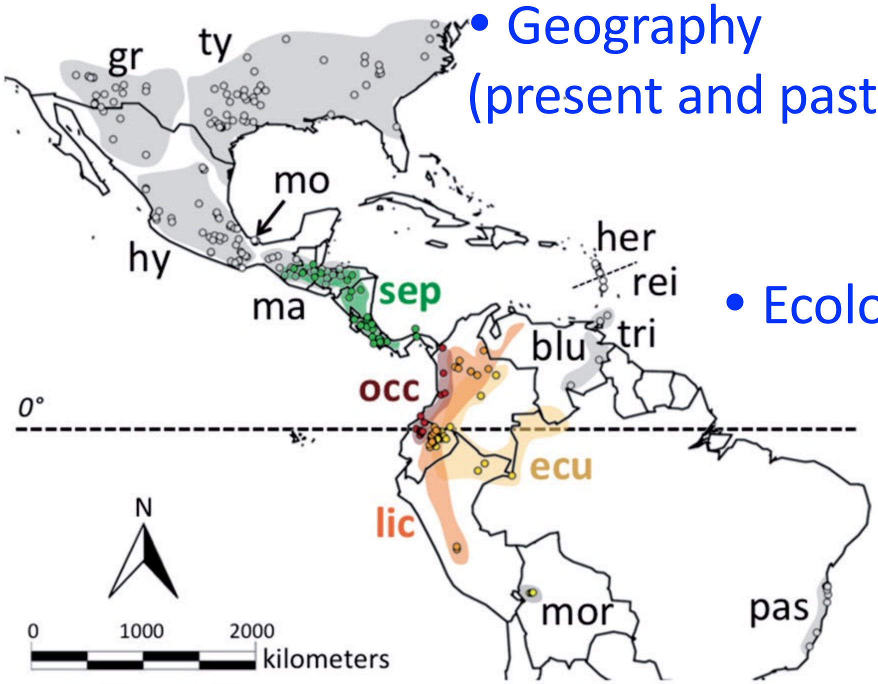
Huang & Knowles (2016) *Syst. Biol.*

Integration across data types to corroborate delimited taxa

- Quantification of phenotype

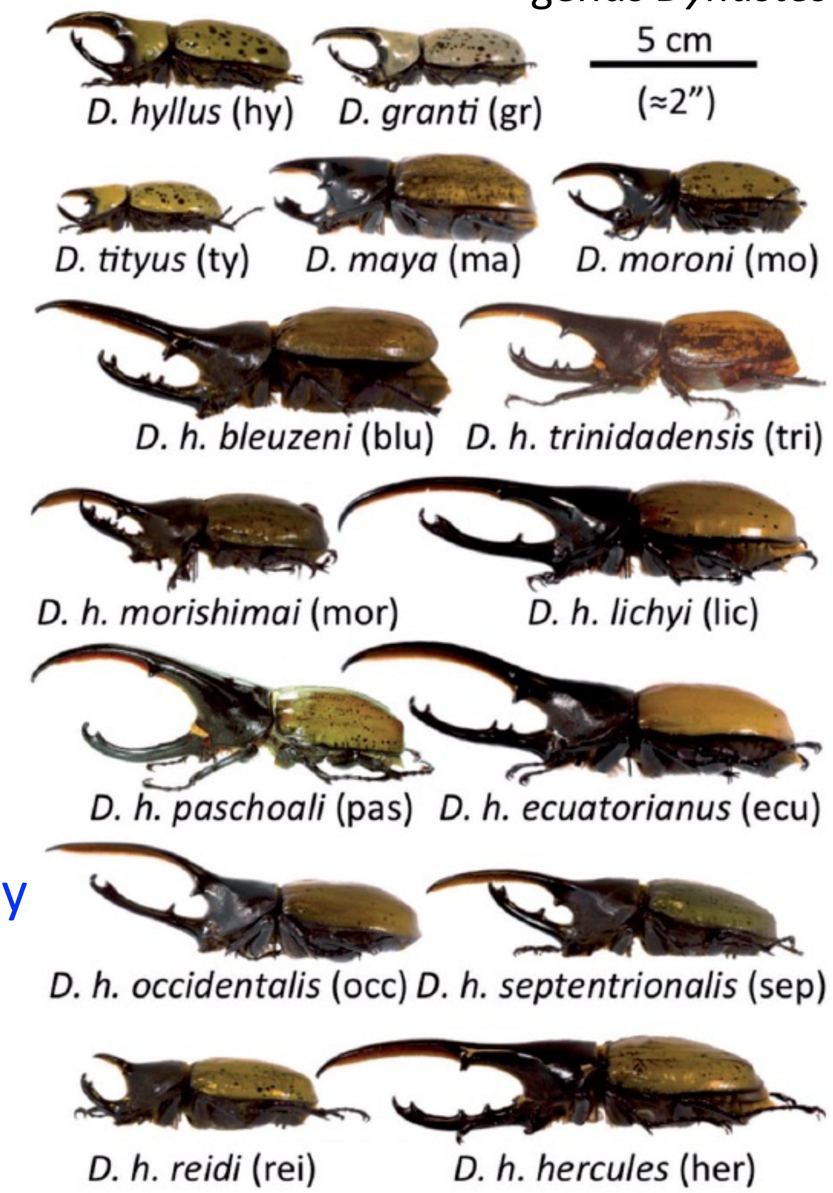


- Geography (present and past)



- Ecology

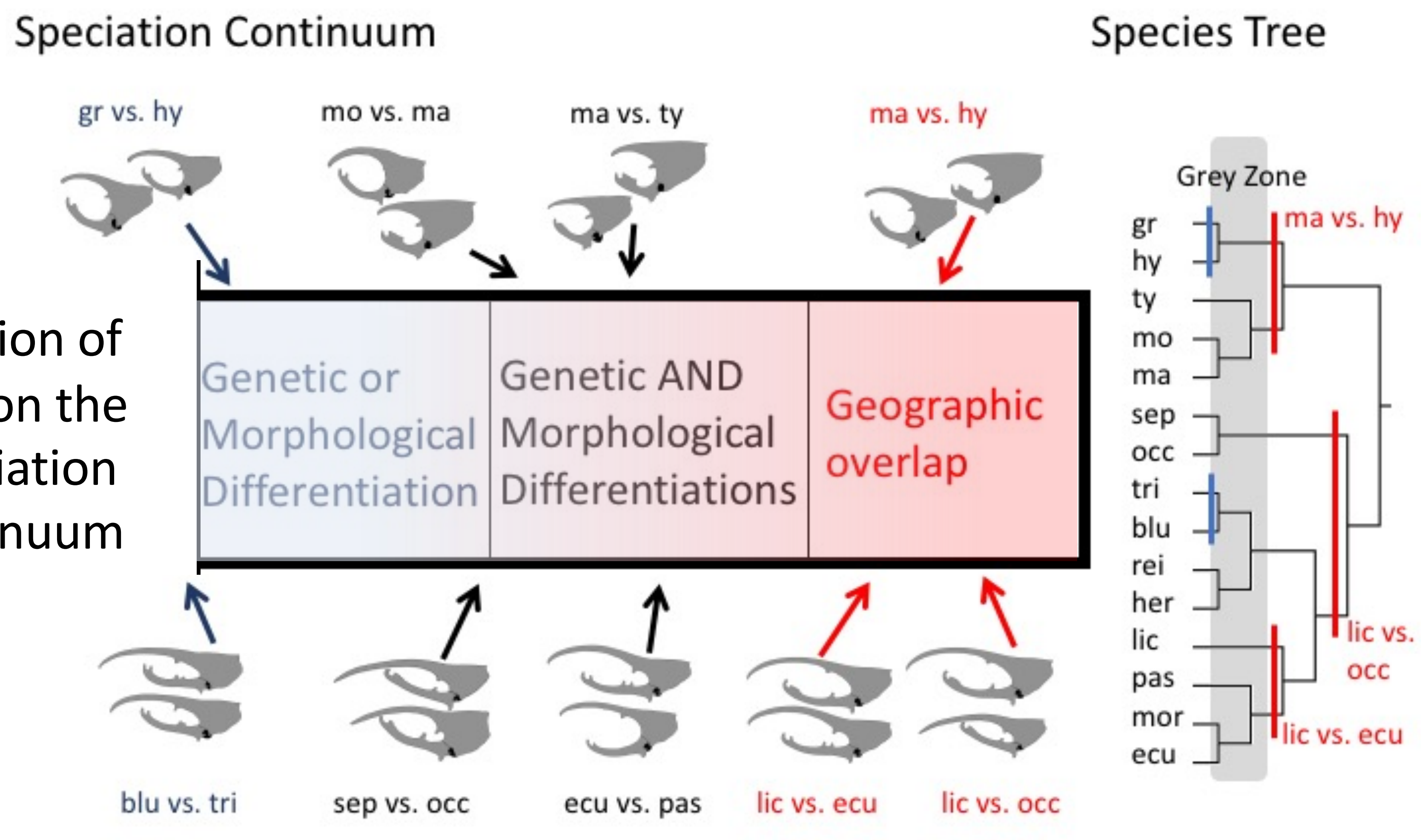
genus *Dynastes*



Huang & Knowles (2016) *Syst. Biol.*

Integrative data also provides insights into the divergence process

Position of taxa on the speciation continuum



Huang & Knowles (2016) *Syst. Biol.*

Transformative potential of model-based analyses:

- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation based on genetic data alone
- Demographic inference

....models are how we communicate
our knowledge to a statistical apparatus

Transformative potential of model-based analyses:

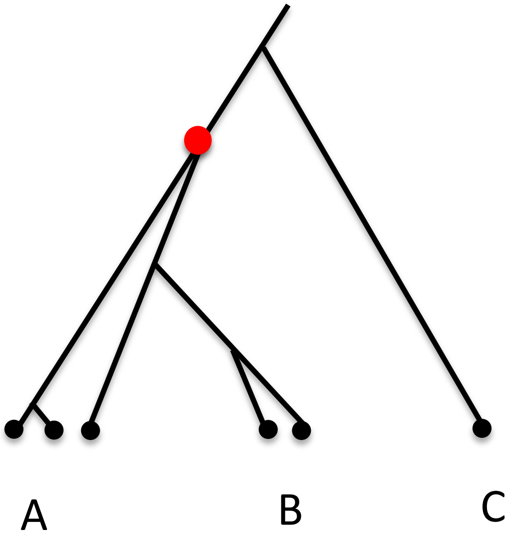
- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation based on genetic data alone
- Demographic inference

- All models are flawed..., some are more or less useful

....models are how we communicate
our knowledge to a statistical apparatus

Transformative potential of model-based analyses:

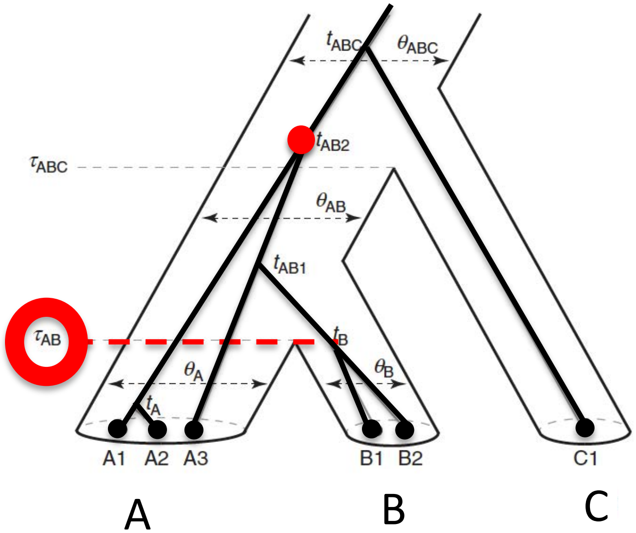
- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation
- Demographic inference (e.g., estimate divergence between population A and B)



Model of gene lineage divergence under an assumption of a molecular clock

Transformative potential of model-based analyses:

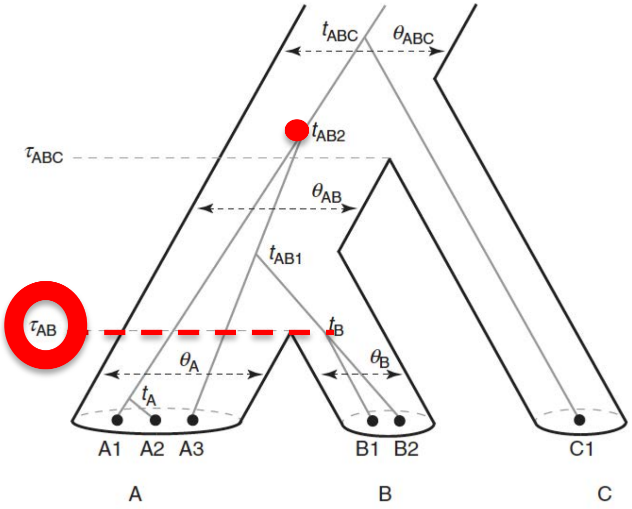
- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation
- Demographic inference (e.g., estimate divergence between population A and B)



Coalescent model of
gene lineage sorting process

Transformative potential of model-based analyses:

- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation
- Demographic inference (e.g., time of divergence)

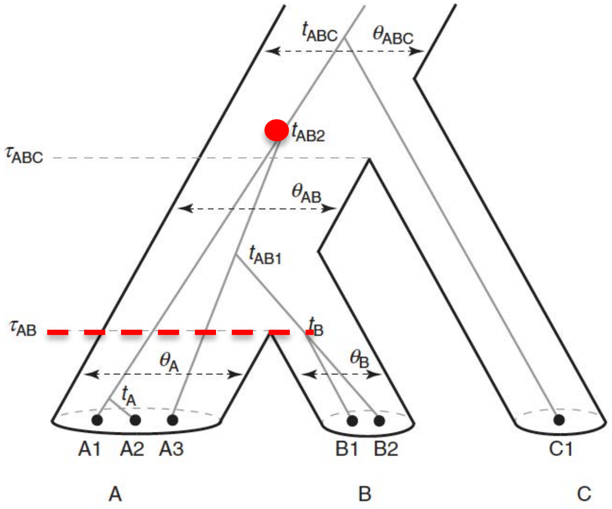


- All models are flawed..., some are more or less useful

....depending upon how effectively they represent our expert knowledge of evolution

Transformative potential of model-based analyses:

- Codon substitution and analysis of natural selection
- Adaptive molecular evolution
- Divergence time estimation and biogeographic analysis
- Phylogenetic inference
- Species delimitation
- Demographic inference (e.g., time of divergence)

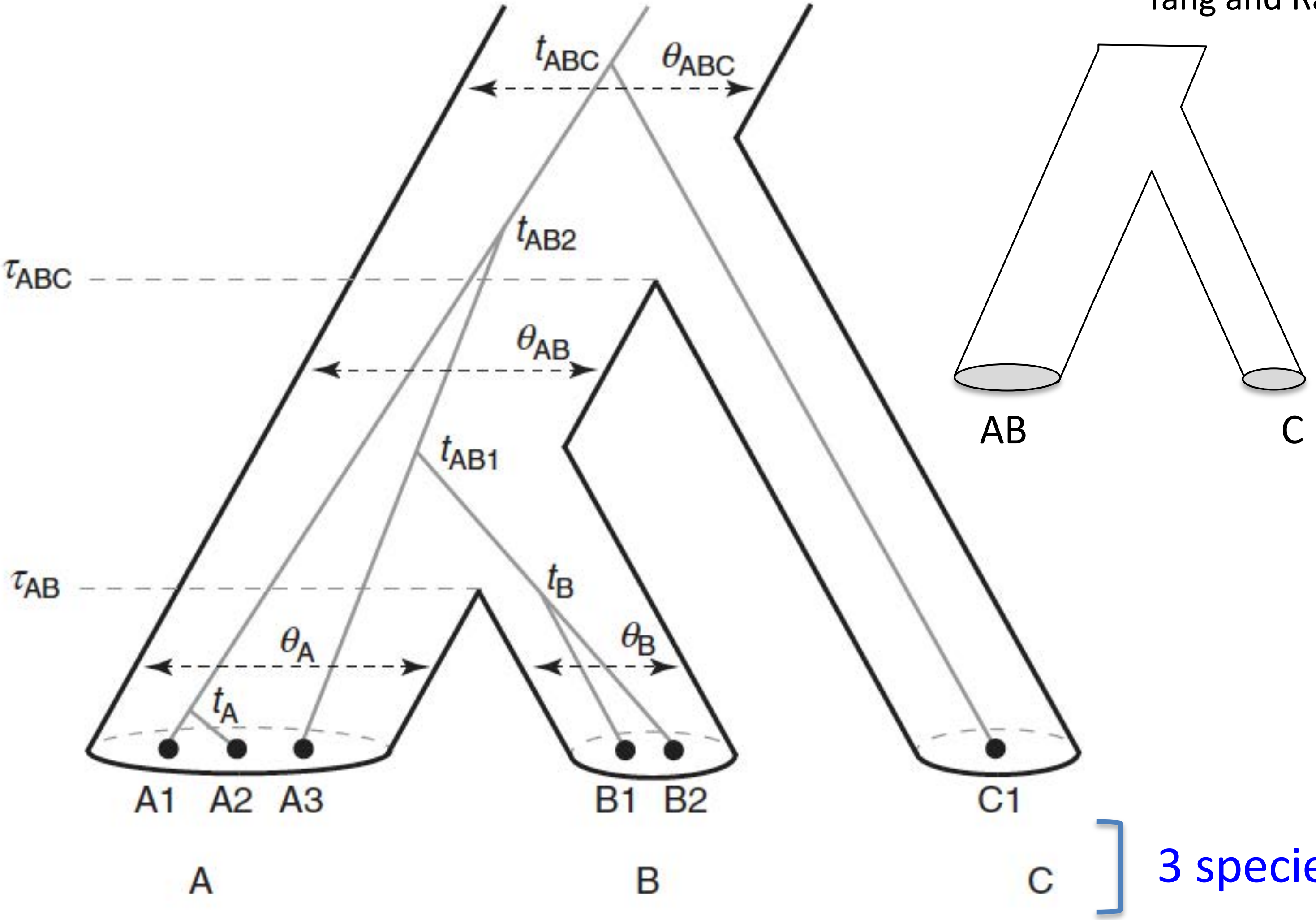


- All models are flawed..., some are more or less useful

....depending upon how effectively they represent our expert knowledge of evolution

Multispecies coalescent (MSC) model used to evaluate different species delimitation hypotheses

Yang and Rannala (2010) *PNAS*

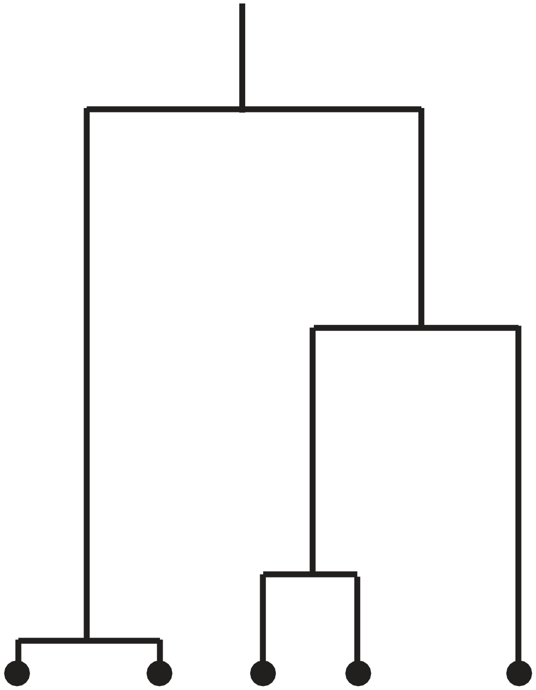


2 species

3 species

Different species delimitation hypotheses are formulated as competing statistical models and inferred from genetic data through Bayesian model selection (i.e., through calculation of posterior probabilities of a model), as in the popular program bpp

Delimitation with the Coalescent

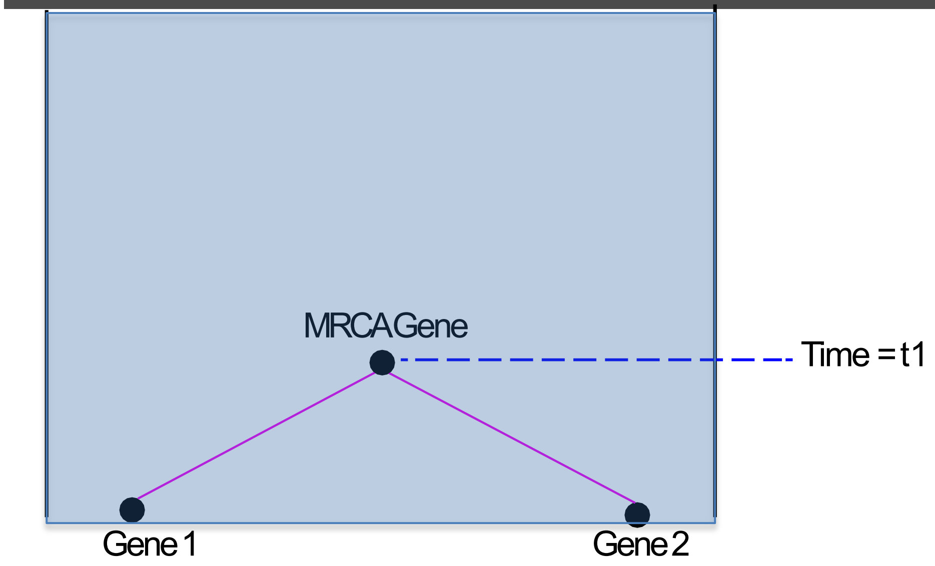


- Have a gene tree

Coalescent Theory Applications in a Nutshell

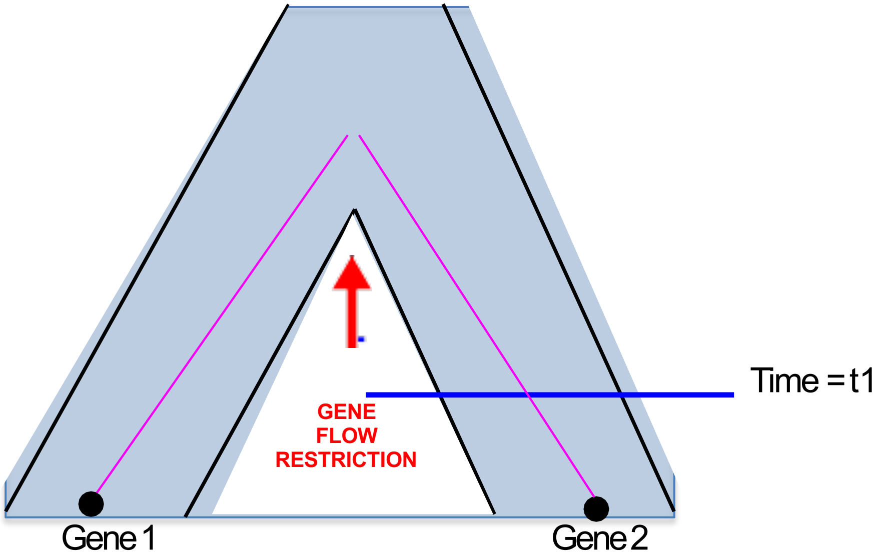
- Makes predictions about the *waiting time* between coalescence events based on population size and sample size.
- “coalescence events” (backward-time) = = “divergence events” (forward-time)
- Predictions are based on assumptions of particular properties of the population that the genes (or individuals having those genes) are evolving.
- Deviances in observed waiting times from that predicted can be used to make inferences about deviances in actual population properties from assumed Wright-Fisher panmictic population

How Does Structuring Change the Coalescent Times?



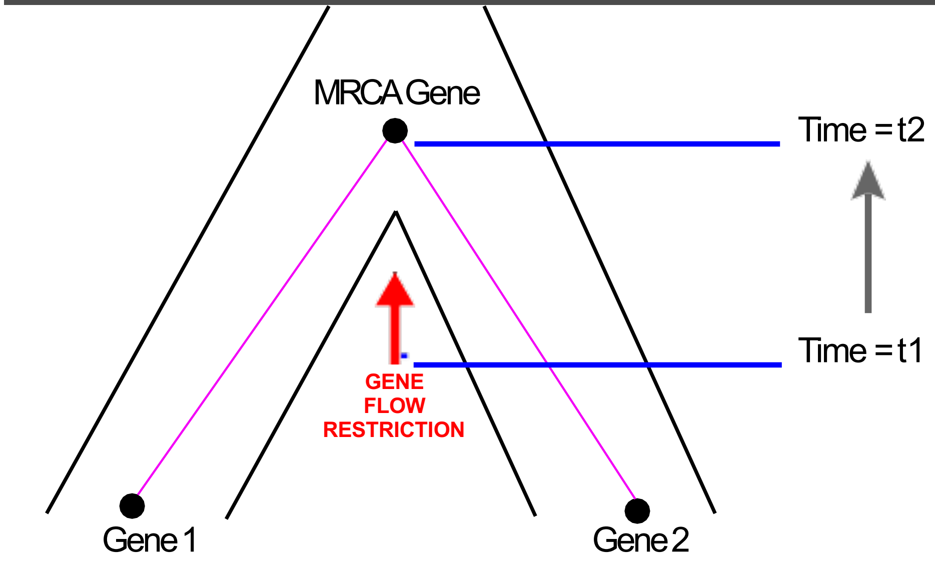
- Recall that the coalescent makes predictions about the timings to coalescence for genes sampled at random from a panmictic population.

How Does Structuring Change the Coalescent Times?



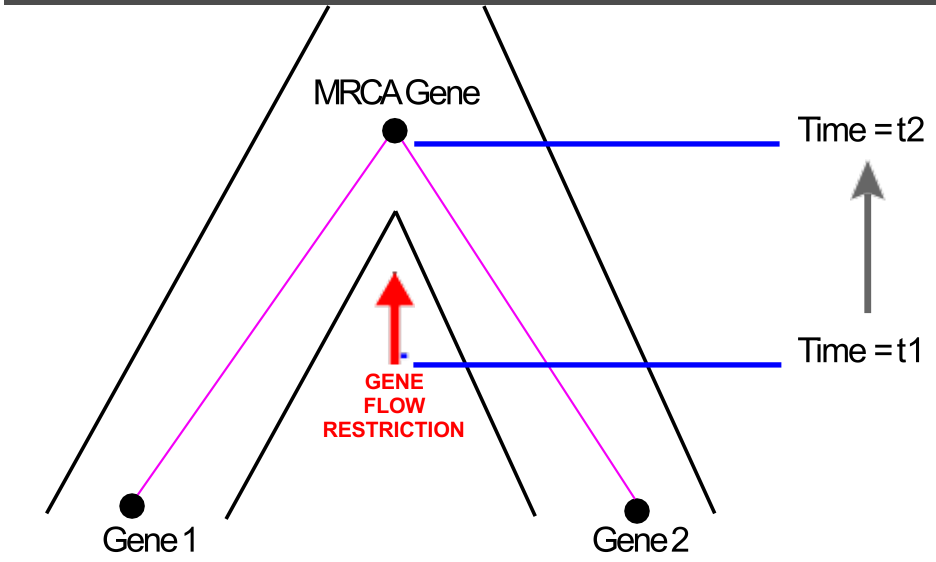
- Recall that the coalescent makes predictions about the timings to coalescence for genes sampled at random from a panmictic population.
- What happens if there are restrictions to panmixia?

How Does Structuring Change the Coalescent Times?



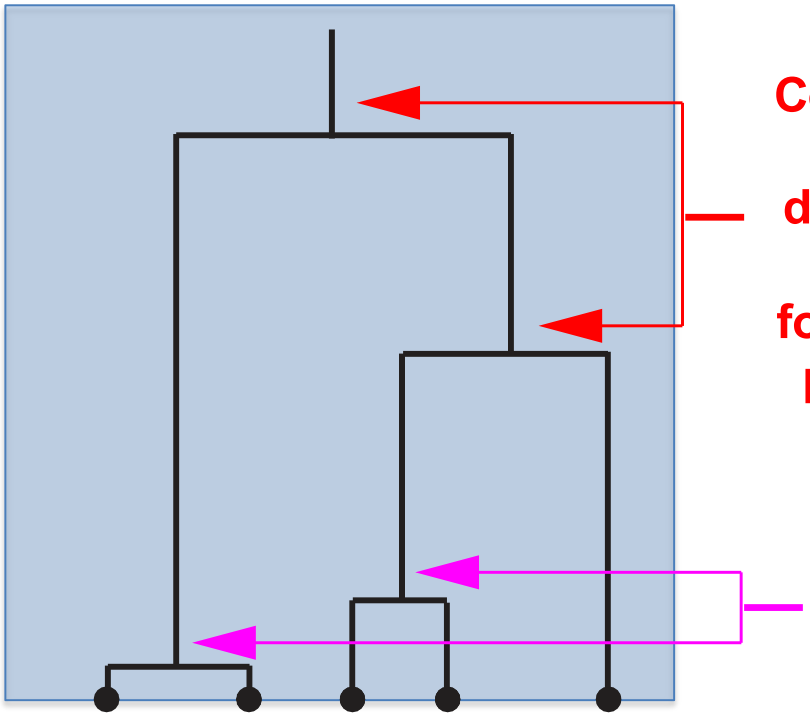
- Recall that the coalescent makes predictions about the timings to coalescence for genes sampled at random from a panmictic population.
- What happens if there are restrictions to panmixia?
- Then the timings to coalescent get *extended*

How Does Structuring Change the Coalescent Times?



- Recall that the coalescent makes predictions about the timings to coalescence for genes sampled at random from a panmictic population.
- What happens if there are restrictions to panmixia?
- Then the timings to coalescent get *extended*
- This is the basis of the multispecies coalescent, MSC

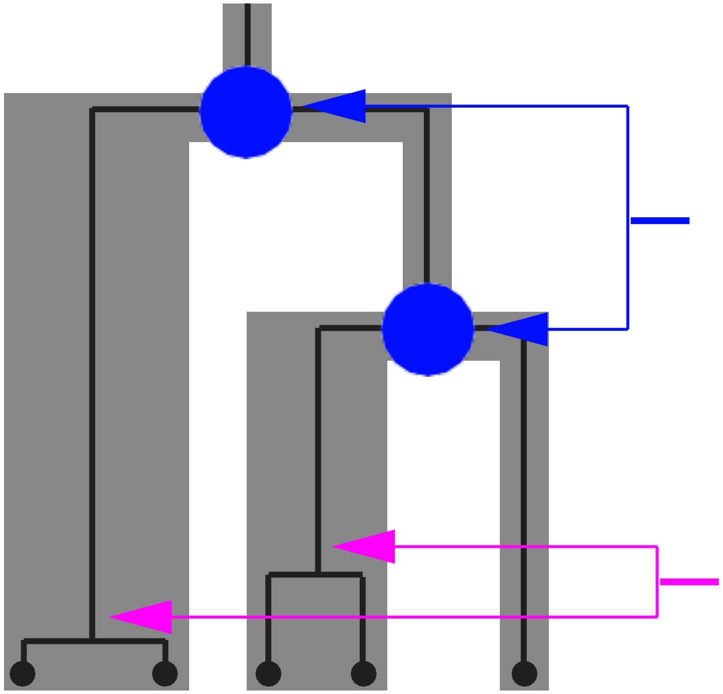
Delimiting Units with the MSC



Coalescence times deeper than predicted for panmictic population

Coalescence times as predicted for panmictic population

Delimiting Units with the MSC

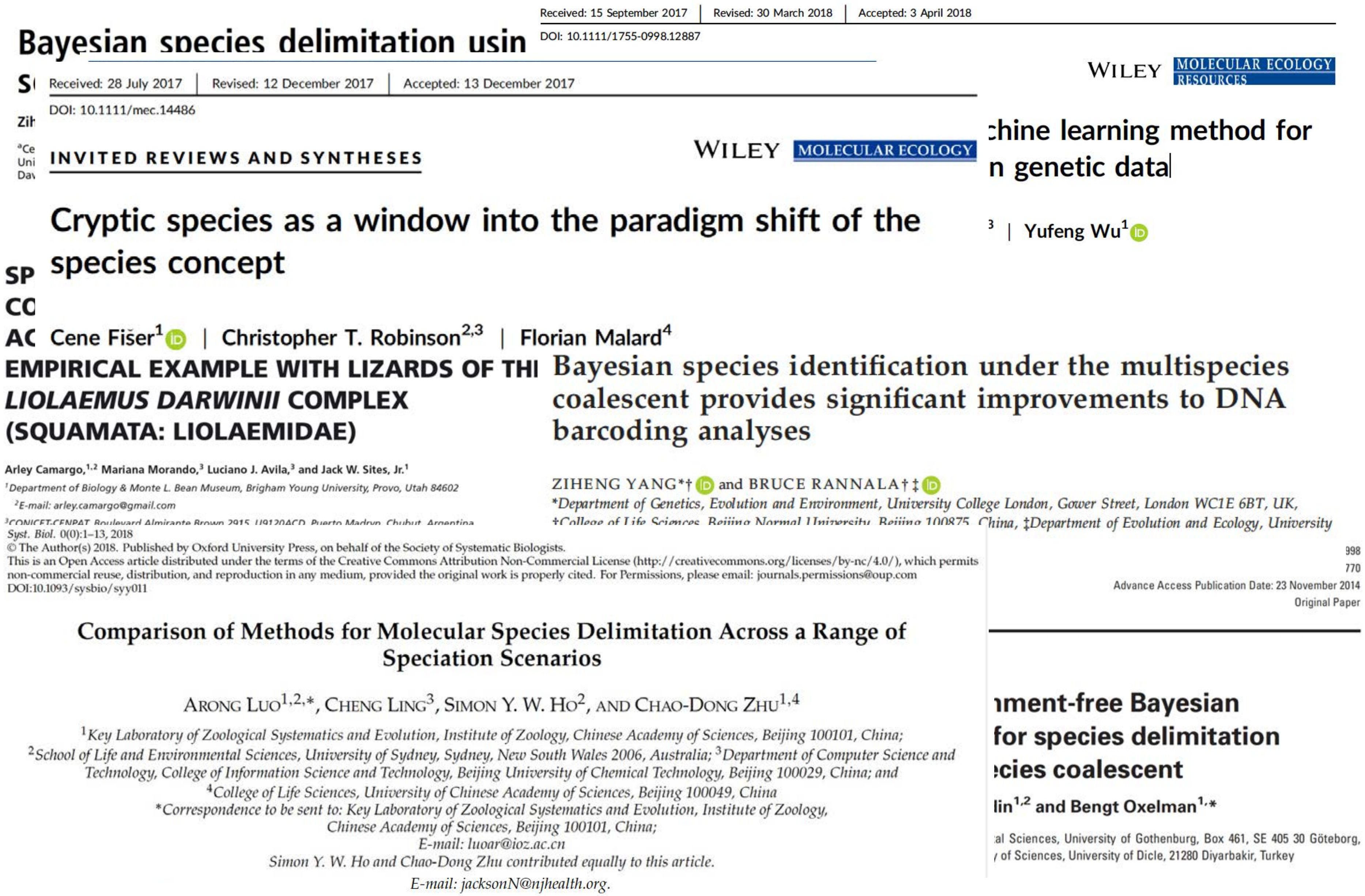


Detected restrictions in gene flow

Coalescence times as predicted for panmictic population

- the MSC models the extensions in timings of coalescent events as disruptions of Wright-Fisher panmixia.
- It fits a “containing tree” to these disruptions (i.e., 3 species in this example)

Explosion of applications using the MSC for delimitation



Received: 15 September 2017 | Revised: 30 March 2018 | Accepted: 3 April 2018

DOI: 10.1111/1755-0998.12887

WILEY MOLECULAR ECOLOGY RESOURCES

chine learning method for
n genetic data

3 | Yufeng Wu1

Bayesian species delimitation usin

S

Zih

aCe
Uni
Dav

Received: 28 July 2017 | Revised: 12 December 2017 | Accepted: 13 December 2017

DOI: 10.1111/mec.14486

WILEY MOLECULAR ECOLOGY

INVITED REVIEWS AND SYNTHESES

Cryptic species as a window into the paradigm shift of the species concept

Cene Fišer1 | Christopher T. Robinson2,3 | Florian Malard4

SP
CO
AC
EMPIRICAL EXAMPLE WITH LIZARDS OF THI
LIOLAEMUS DARWINII COMPLEX
(SQUAMATA: LIOLAEMIDAE)

Arley Camargo,1,2 Mariana Morando,3 Luciano J. Avila,3 and Jack W. Sites, Jr.1

1*Department of Biology & Monte L. Bean Museum, Brigham Young University, Provo, Utah 84602*

2*E-mail: arley.camargo@gmail.com*

3*CONICET-CENPAT, Boulevard Almirante Brown 2915, U9120ACD, Puerto Madryn, Chubut, Argentina*

Bayesian species identification under the multispecies coalescent provides significant improvements to DNA barcoding analyses

ZIHENG YANG*† and BRUCE RANNALA†‡

**Department of Genetics, Evolution and Environment, University College London, Gower Street, London WC1E 6BT, UK,*
†College of Life Sciences, Beijing Normal University, Beijing 100875, China, ‡Department of Evolution and Ecology, University

Syst. Biol. 0(0):1–13, 2018

© The Author(s) 2018. Published by Oxford University Press, on behalf of the Society of Systematic Biologists.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial reuse, distribution, and reproduction in any medium, provided the original work is properly cited. For Permissions, please email: journals.permissions@oup.com
DOI:10.1093/sysbio/syy011

Comparison of Methods for Molecular Species Delimitation Across a Range of Speciation Scenarios

ARONG LUO1,2,*, CHENG LING3, SIMON Y. W. HO2, AND CHAO-DONG ZHU1,4

1*Key Laboratory of Zoological Systematics and Evolution, Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China;*
2*School of Life and Environmental Sciences, University of Sydney, Sydney, New South Wales 2006, Australia;* 3*Department of Computer Science and Technology, College of Information Science and Technology, Beijing University of Chemical Technology, Beijing 100029, China; and*
4*College of Life Sciences, University of Chinese Academy of Sciences, Beijing 100049, China*
**Correspondence to be sent to: Key Laboratory of Zoological Systematics and Evolution, Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China;*
E-mail: luoar@ioz.ac.cn
Simon Y. W. Ho and Chao-Dong Zhu contributed equally to this article.
E-mail: jacksonN@njhealth.org.

998
770
Advance Access Publication Date: 23 November 2014
Original Paper

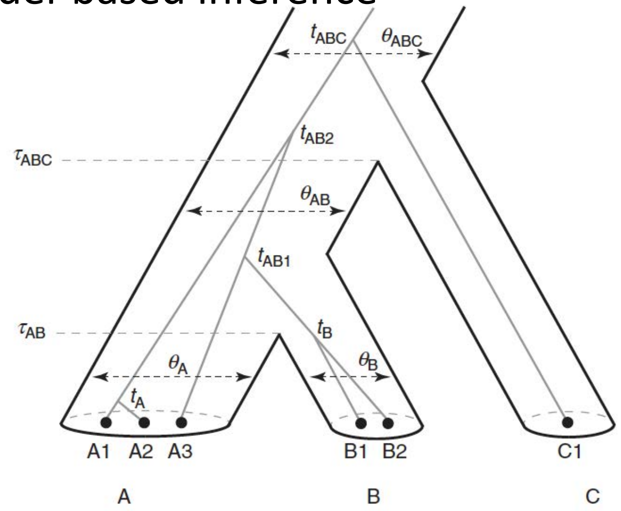
ıment-free Bayesian
for species delimitation
ecies coalescent

lin1,2 and Bengt Oxelman1,*

al Sciences, University of Gothenburg, Box 461, SE 405 30 Göteborg,
y of Sciences, University of Dicle, 21280 Diyarbakir, Turkey

Pros of species delimitation under MSC

Model-based inference



- Can delimit species before reciprocal monophyly of alleles or fixed differences

Knowles & Carstens (2007) *Syst. Biol.*

- Still detects lineages under low gene flow

Zhang et al. (2011) *Syst. Biol.*

- Accuracy of species delimitation to sampling can be evaluated (i.e., will more data change status)

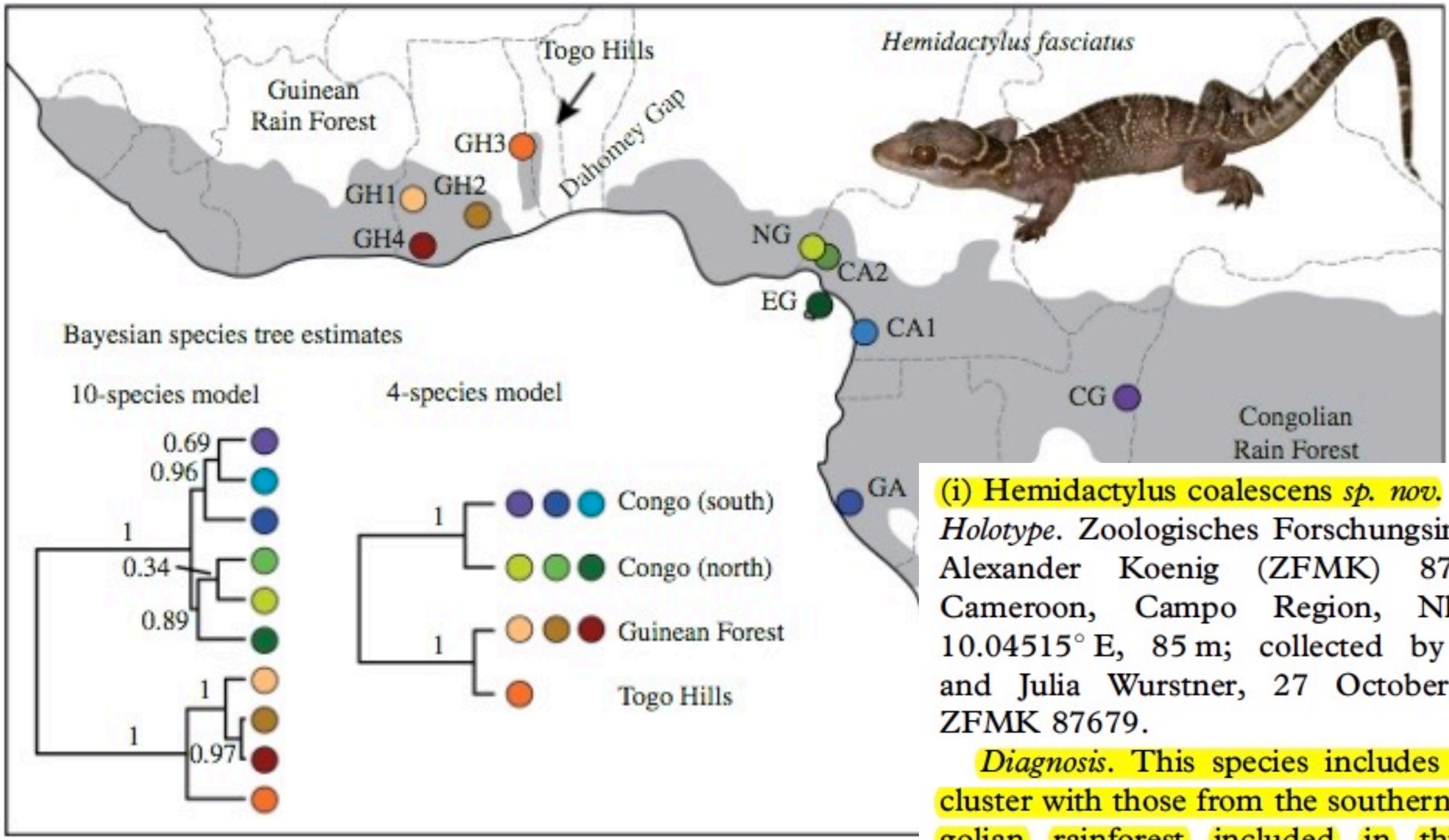
- De facto standardization for objectively delimiting taxa (i.e., data treated equally among all living things and avoid subjectiveness of what characters to measure)

Fujita et al. (2012) *TREE*

- Can take into account uncertainty in gene trees

Yang & Rannala 2010

Model-based inference: probability of different hypotheses about species boundaries based on genetic data alone!



Leache & Fujita (2010) *Proc. R. Soc. B.*

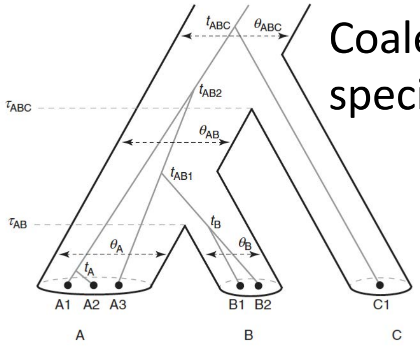
(i) Hemidactylus coalescens *sp. nov.*

Holotype. Zoologisches Forschungsinstitut und Museum Alexander Koenig (ZFMK) 87680, adult male; Cameroon, Campo Region, Nkoelon, 2.3972° N, 10.04515° E, 85 m; collected by Michael F. Barej and Julia Wurstner, 27 October 2007. Paratype = ZFMK 87679.

Diagnosis. This species includes all populations that cluster with those from the southern portion of the Congolian rainforest included in this study (southern Cameroon, Gabon and Congo), with strong support in the Bayesian species delimitation model.

Etymology. This species is named after the coalescent process used to delimit the species.

Data-informed summary suggests problems…..



Coalescent-based species delimitation

Most newly discovered species go undescribed.

- Less than 30% of researchers applying MSC models made taxonomic recommendations!
- Less than 25% of researchers applying MSC models actually use results to describe new species!

Carstens et al. 2013

💔 the multispecies coalescent for delimiting species

- All models are flawed...

some are more or less useful.

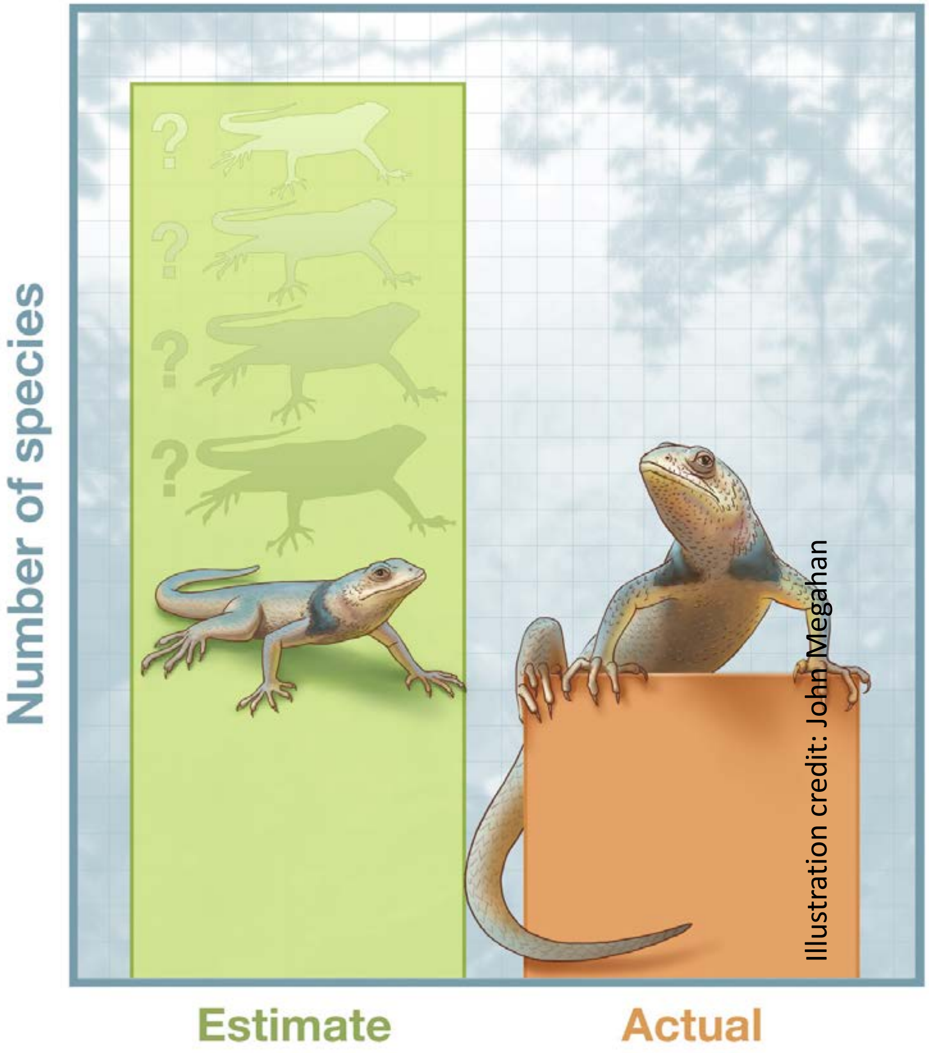
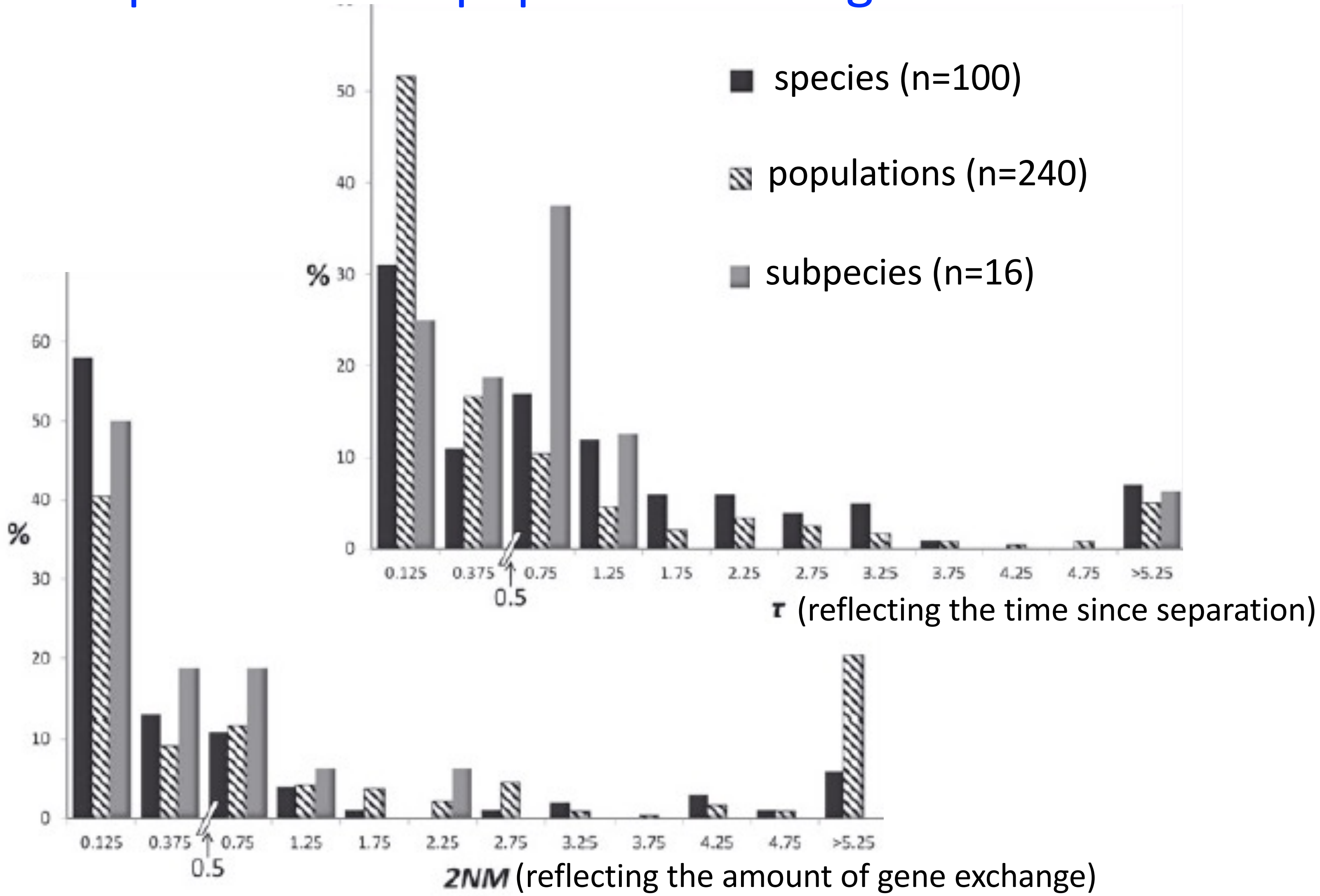


Illustration credit: John Megahan

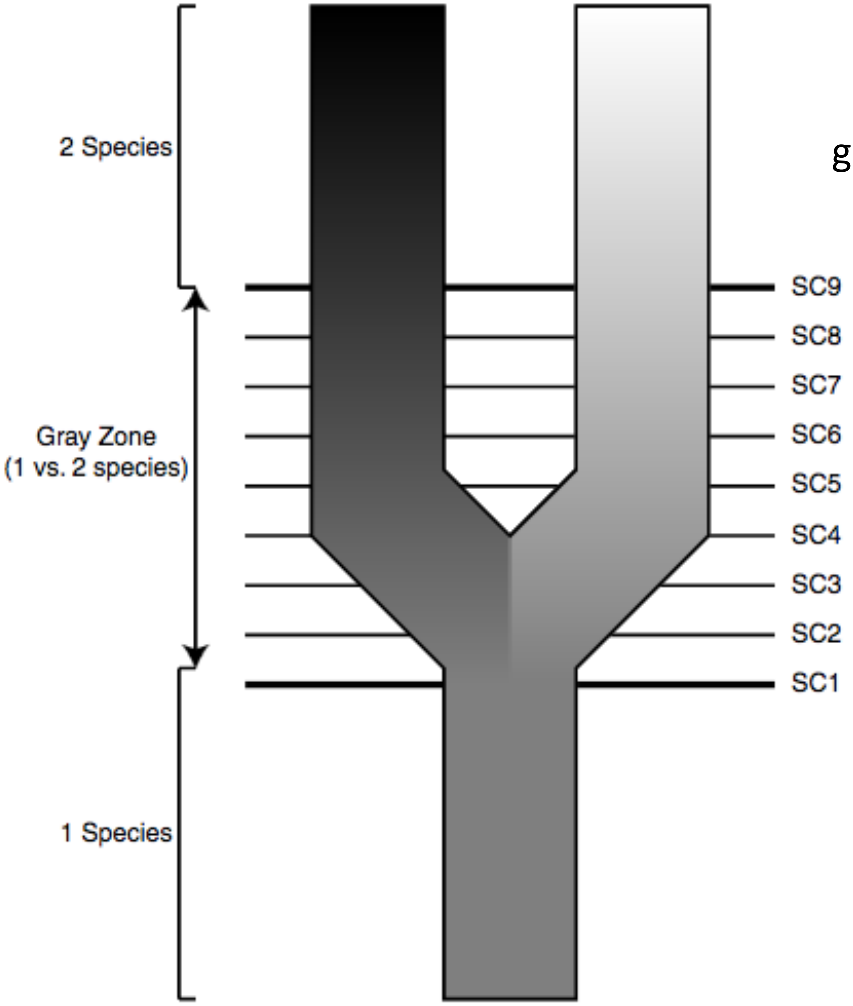
Sukumaran & Knowles (2017) *PNAS*

No genetic distinction that separates species versus population divergence



Pinho and Hey(2010) *Evolution*

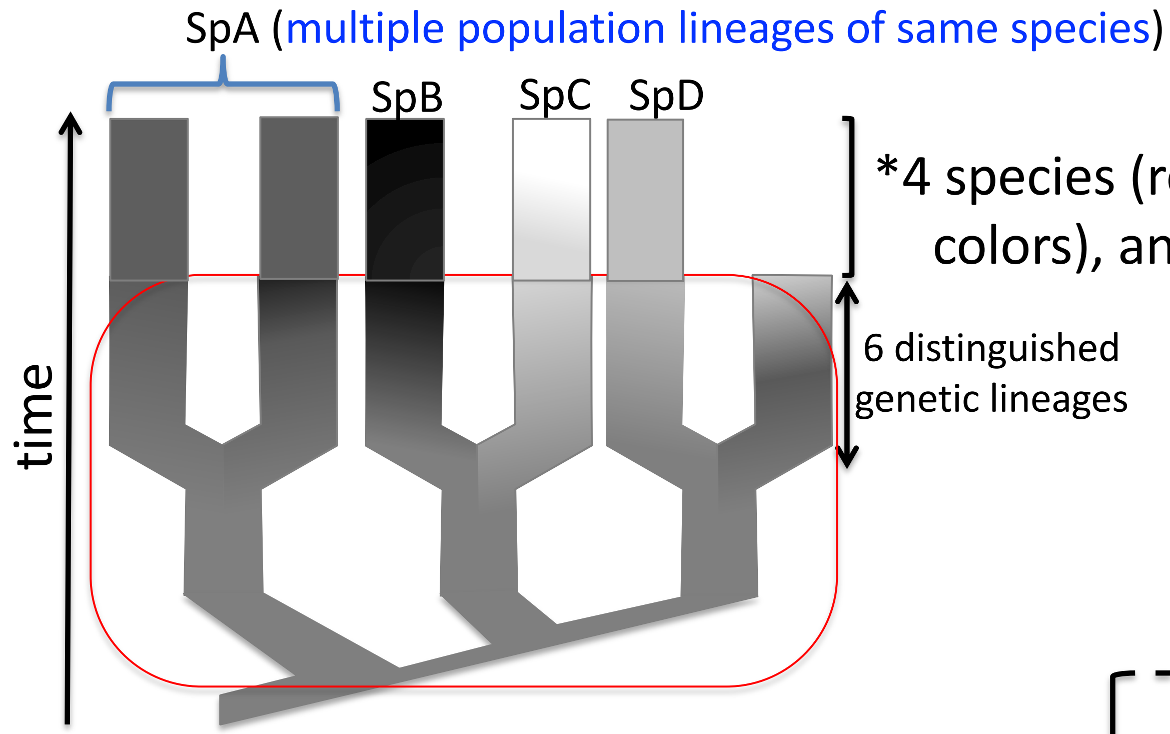
Eventually all species concepts agree…so no big deal right?!?



general lineage concept

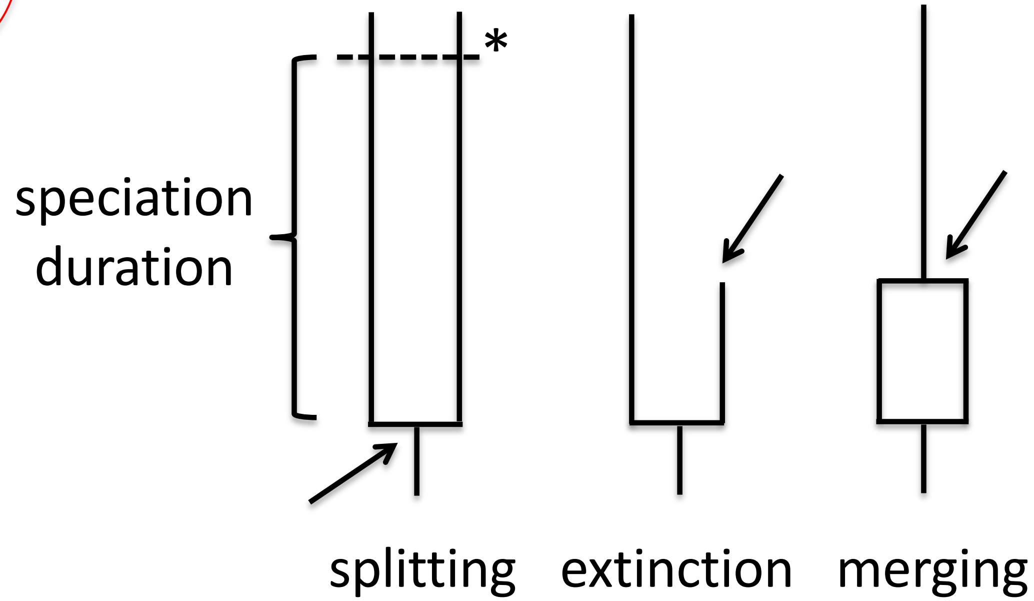
de Querroz 2005, 2007

* Not all lineages become species!
And multiple population lineages of the same species!



*4 species (represented by different colors), and protracted process

6 distinguished genetic lineages



The MSC dominates the field…

How bad is the confounding of population verus species divergence?

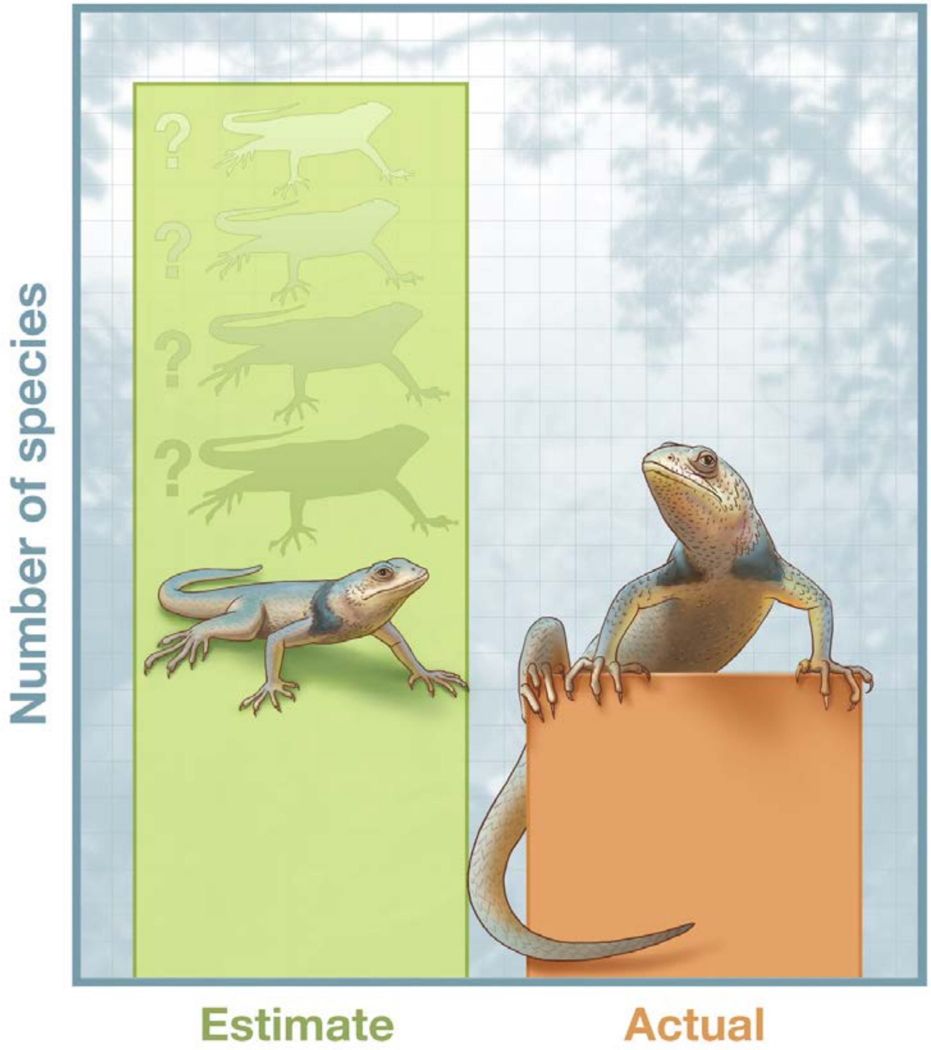
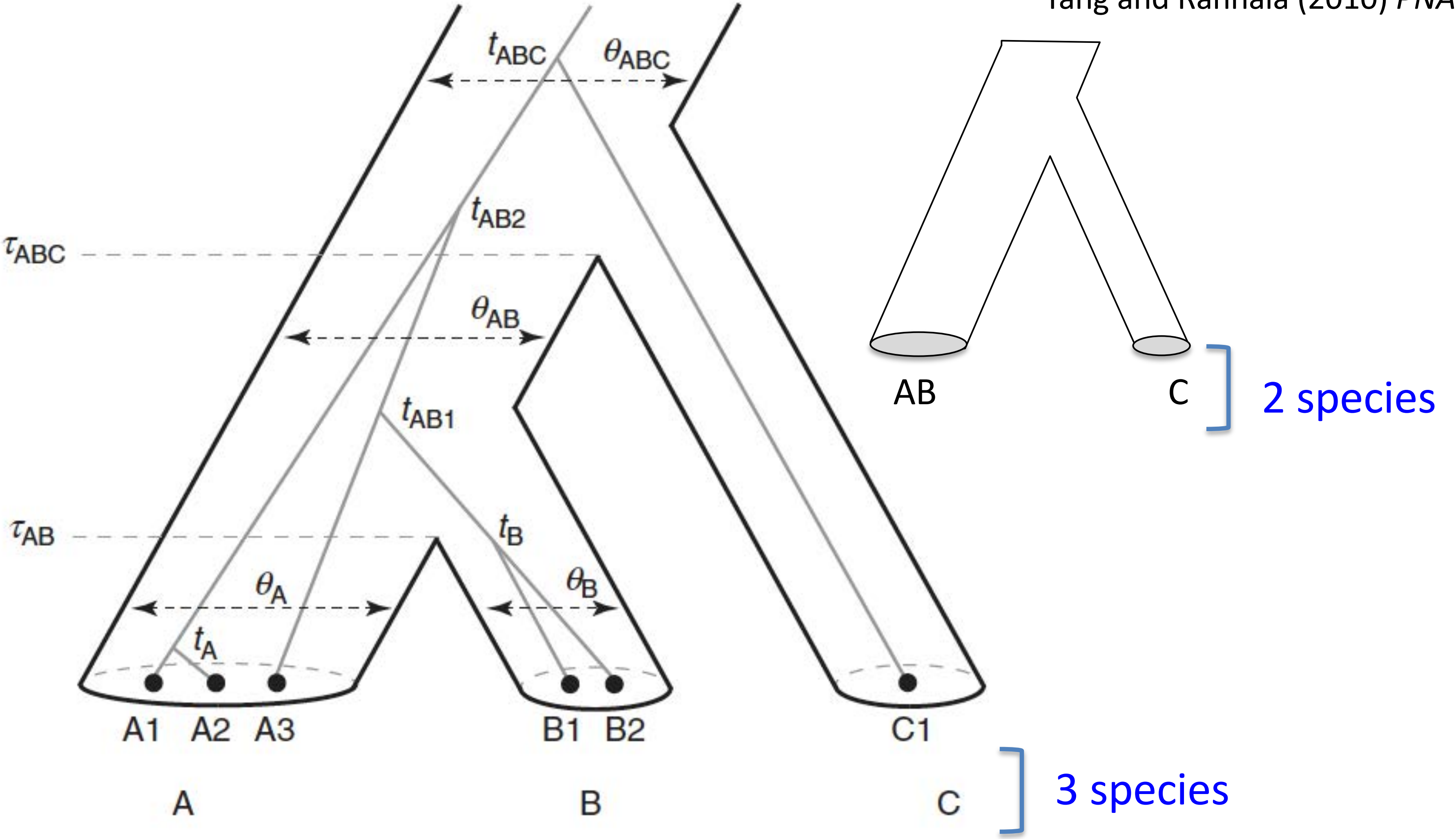


Illustration credit: John Megahan

Sukumaran & Knowles (2017) *PNAS*

Multispecies coalescent (MSC) model used to evaluate different species delimitation hypotheses

Yang and Rannala (2010) *PNAS*



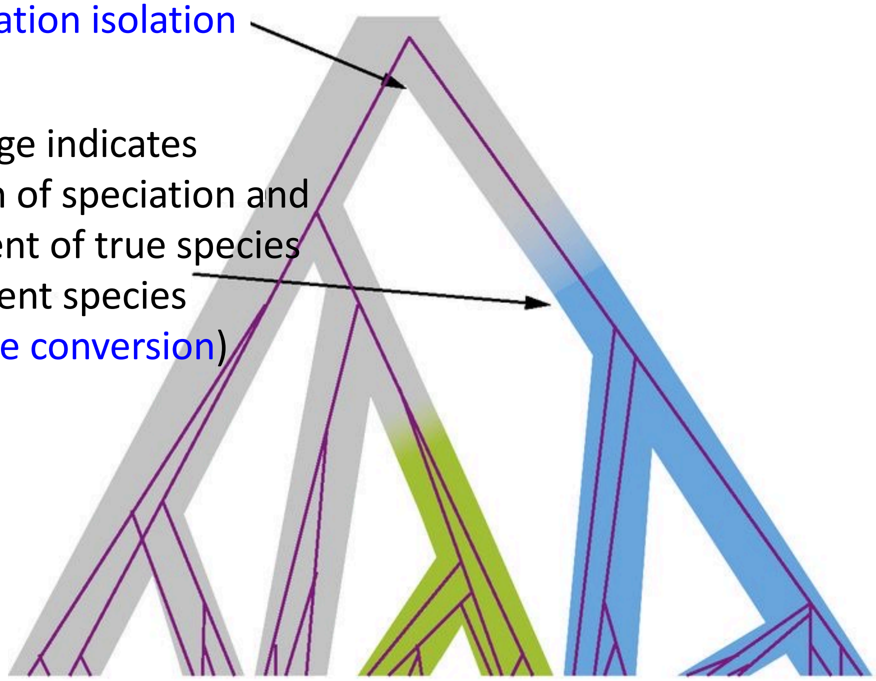
Different species delimitation hypotheses are formulated as competing models and inferred from genetic data through Bayesian model selection (i.e., through calculation of posterior probabilities of a model), as in the popular program bpp

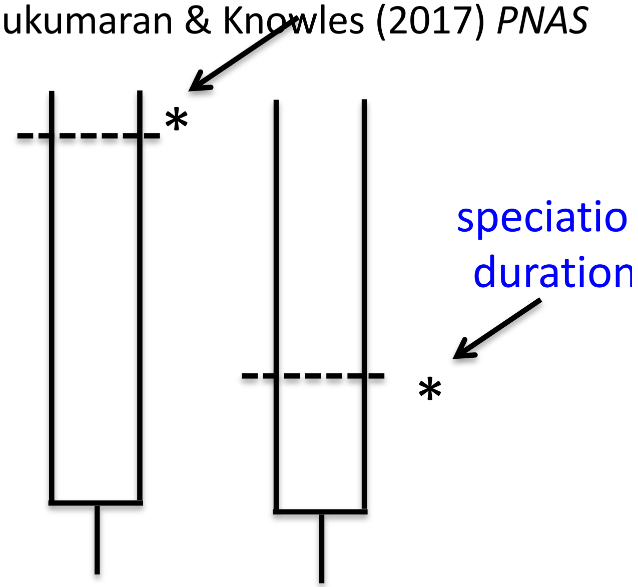
Simulate data to account for differences in speciation duration (i.e., speciation is not instantaneous)

Sukumaran & Knowles (2017) *PNAS*

Splitting events such as this are initiation of speciation through, e.g., population isolation

Color change indicates completion of speciation and development of true species from incipient species (i.e., lineage conversion)

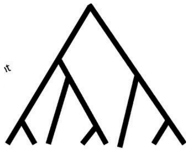




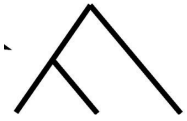
speciatio duration

splitting

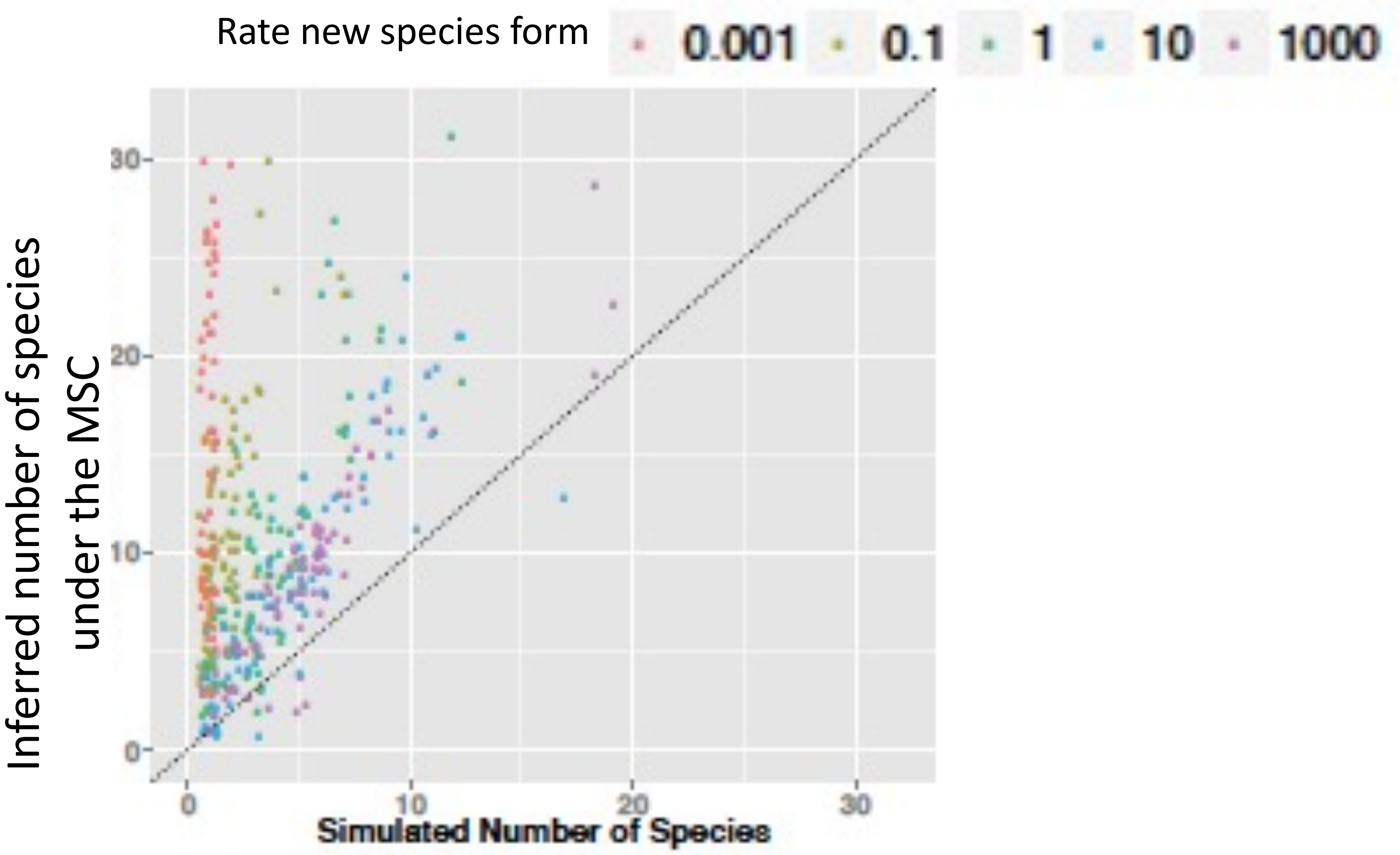
Does the MSC accurately delimit species?



Model with 8 vs 3 species

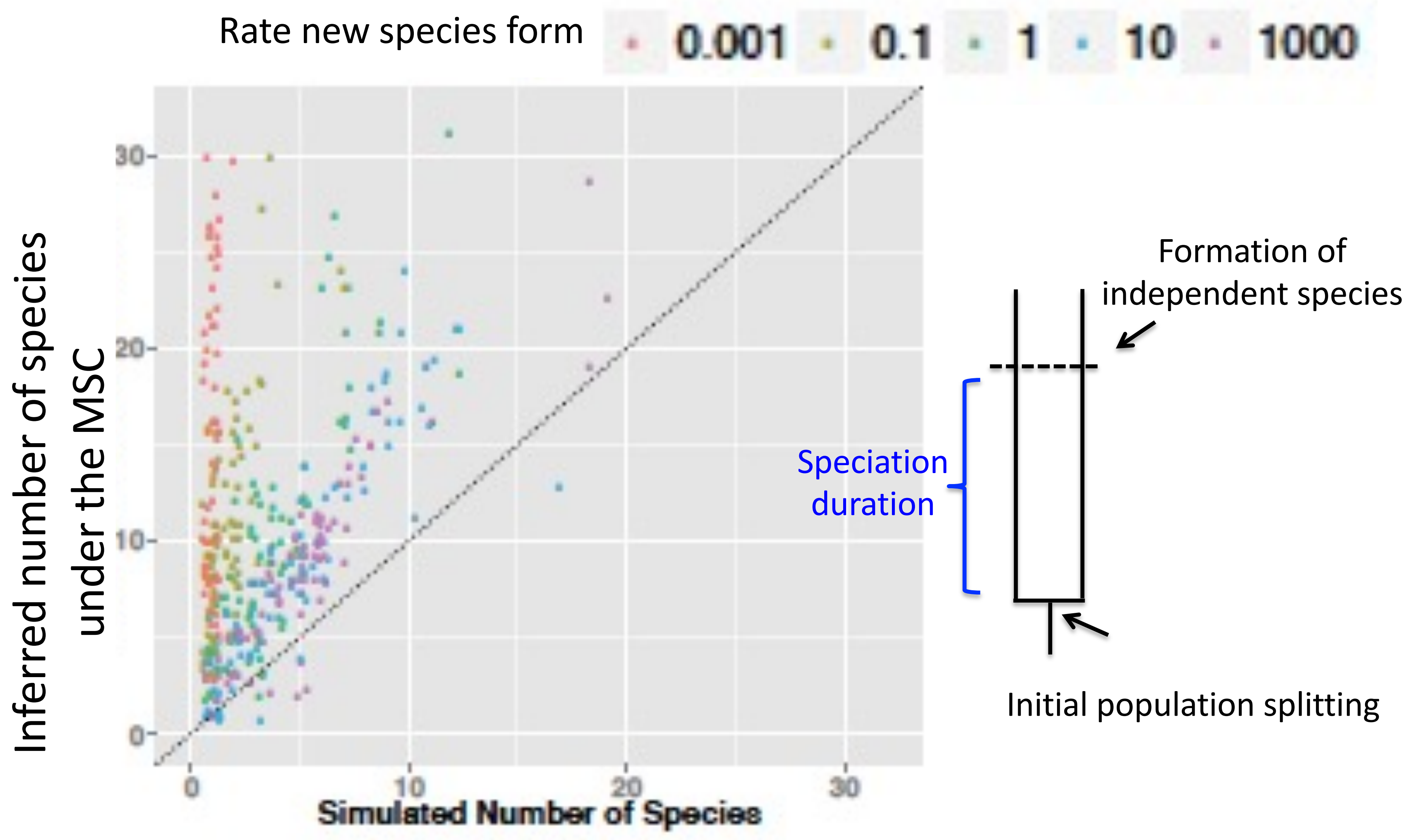


Degree of overestimation of species richness under the MSC



Sukumaran & Knowles (2017) *PNAS*

Degree of overestimation of species richness under the MSC depends on the speciation duration



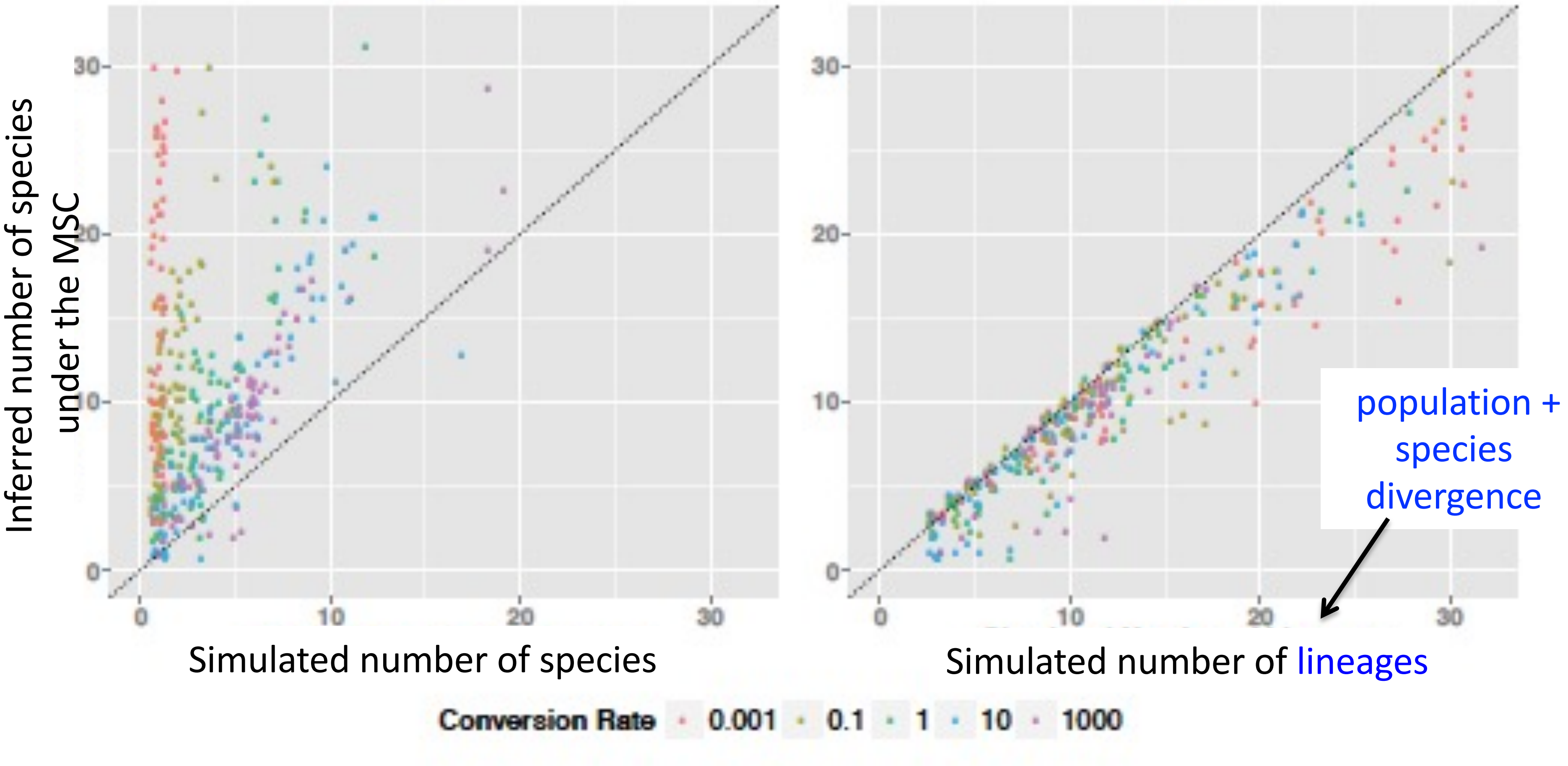
Formation of independent species

Speciation duration

Initial population splitting

Sukumaran & Knowles (2017) *PNAS*

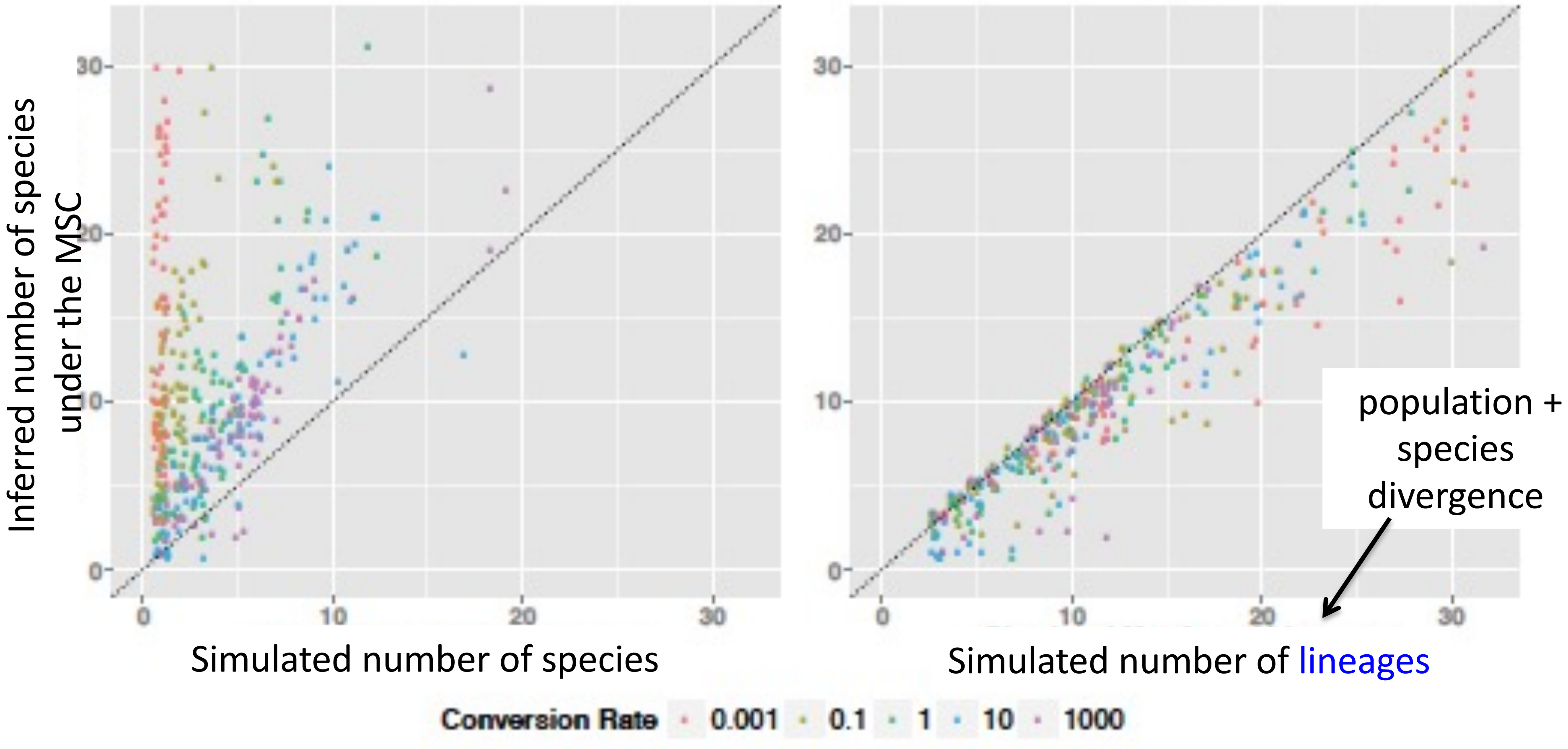
MSC powerful model for detecting genetic structure



population + species divergence

Sukumaran & Knowles (2017) *PNAS*

MSC powerful model for detecting genetic structure



population + species divergence

HOWEVER, the MSC is not capable of distinguishing genetic structure due to population versus species divergence

Sukumaran & Knowles (2017) *PNAS*

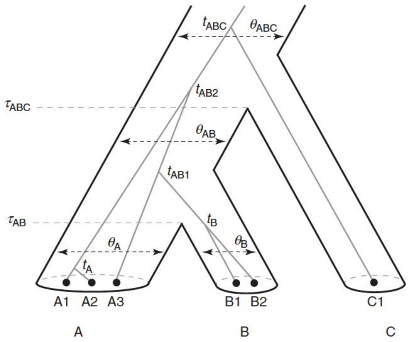
Problems with species delimitation under the MSC

- MSC detects structure – not species

Sukumaran & Knowles (2017) *PNAS*

(different statistical delimitation methods all based on the MSC, which also means seeking consensus across methods is not a good way to fail)

See Rannala (2015) Current Zoology 61, 846-853



- “Robustness” to lineage detection with low levels of gene flow is not the same as accurate species delimitation

- Sensitivity to sampling (e.g., sparse geographic coverage over-splits species)

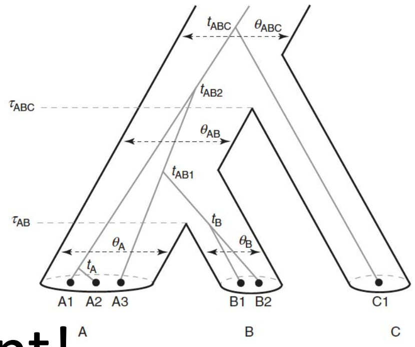
Chambers & Hillis (2020) *Syst. Biol.*

- MSC is not a de facto standardization for delimiting taxa: degree of over estimation varies depending on speciation process

Sukumaran & Knowles (2017) *PNAS*

Accurate species delimitation cannot be achieved with current models based on MSC

Delimitation under the MSC:
genetic structure = species



- Don’t run MSC and add a caveat – what’s the point!

- STOP reporting about all this “cryptic” diversity

Model-based delimitation:

- Erroneous species boundaries are inferred from current model-based genetic approaches

Delimitation under the MSC:

- genetic structure = species

- Relying on heuristics to interpret results from current genetic methods (e.g., bpp) is not the answer; does not validate the MSC for species delimitation

Ad hoc heuristics to interpret results from MSC-based models for delimitation

- Genealogical sorting index*: $2\tau/\theta$

(i.e., population divergence time relative to the population size)

Cummings et al. (2008) Evolution 62-9: 2411–2422

- use population divergence parameters (e.g., distantly related species, lots of migration)*

*Jackson et al. (2018) Syst. Biol.

*Leache et al. (2018) Syst. Biol.

These heuristics do not validate the MSC for species delimitation

Using diverse sources of data for inferring species boundaries has a long systematic tradition, but not with model-based inference.

Joint analysis of morphology and genetic data!

Solis-Lemus C, Knowles LL, Ané C (2014) Bayesian species delimitation combining multiple genes and traits in a unified framework. Evolution 69:492-507.

Hypotheses about species boundaries

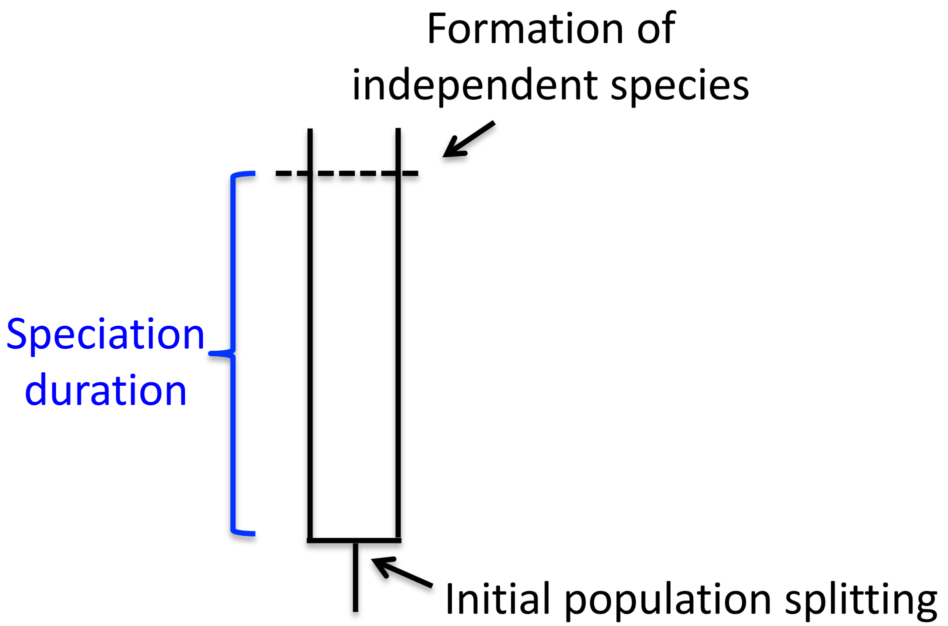
PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Incorporating the speciation process into species delimitation

Jeet Sukumaran[1]*, Mark T. Holder[2], L. Lacey Knowles[3]

- We model the formation of new population lineages and their subsequent development into independent species modeled as separate processes



Formation of independent species

Speciation duration

Initial population splitting

PLOS Computational Biology | https://doi.org/10.1371/journal.pcbi.1008924 May 13, 2021

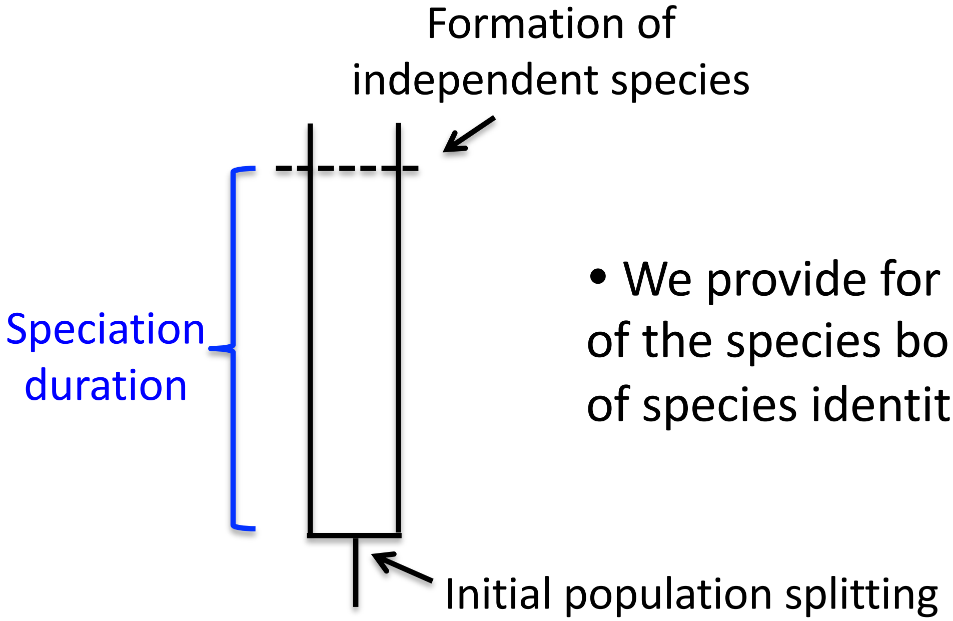
PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Incorporating the speciation process into species delimitation

Jeet Sukumaran[1]*, Mark T. Holder[2], L. Lacey Knowles[3]

- We model the formation of new population lineages and their subsequent development into independent species modeled as separate processes



Formation of independent species

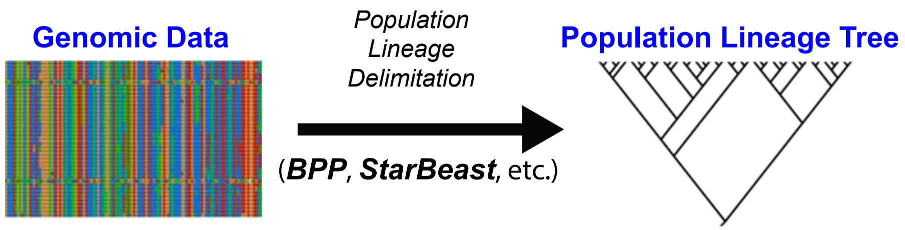
Speciation duration

Initial population splitting

- We provide for a way to incorporate current understanding of the species boundaries in the system through specification of species identities for a subset of population lineages

PLOS Computational Biology | https://doi.org/10.1371/journal.pcbi.1008924 May 13, 2021

DELINEATE: a species delimitation method which makes probabilistic statements about whether or not distinct lineages are members of the same species



Genomic Data

Population Lineage Delimitation

(***BPP***, ***StarBeast***, etc.)

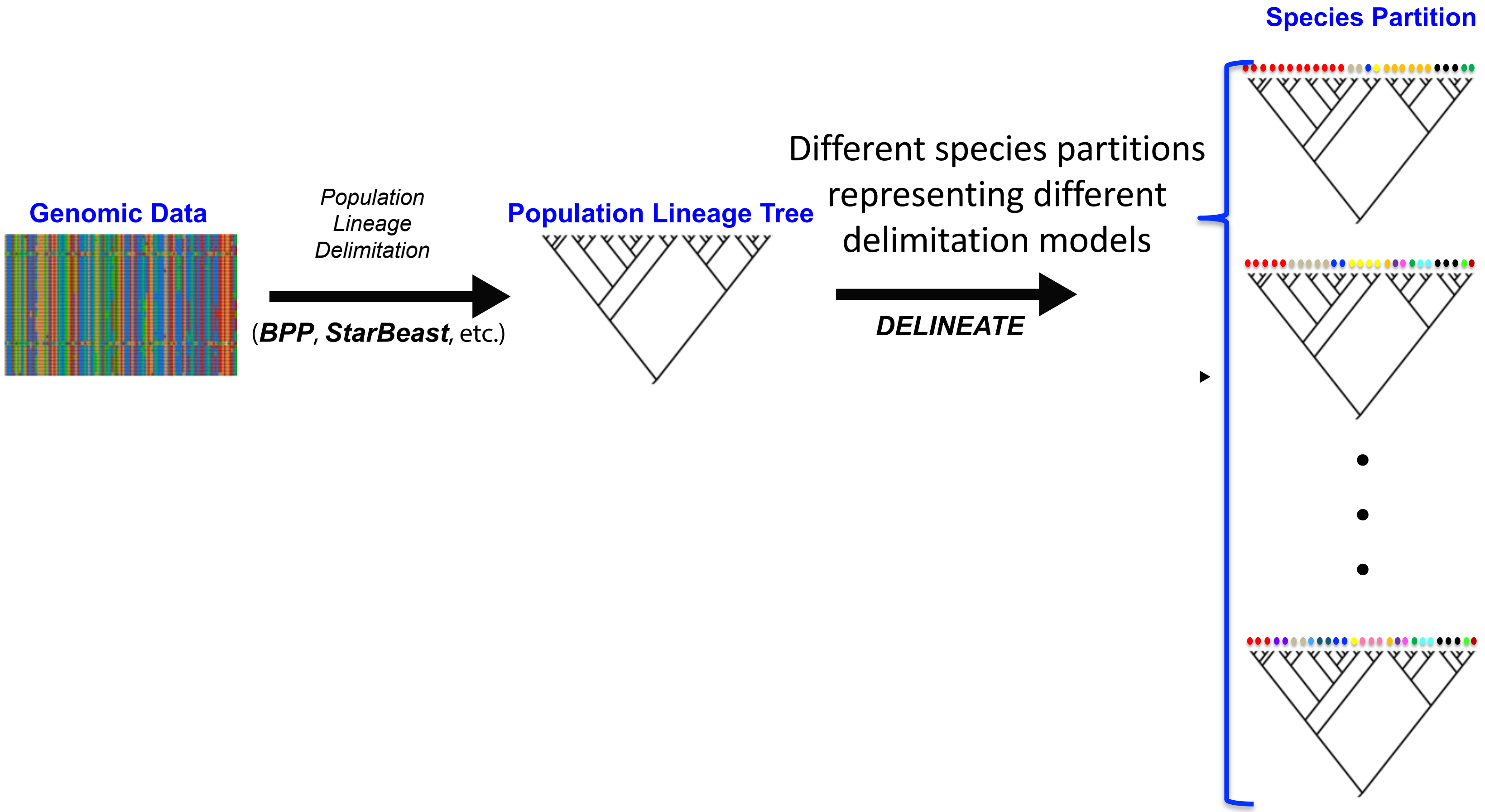
Population Lineage Tree

- Lineages are Wright-Fisher populations within which the neutral coalescent process dominates

- Boundaries between lineages are structure imposed by ancestral population splitting or isolation

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

DELINEATE



Genomic Data

Population Lineage Delimitation

(***BPP***, ***StarBeast***, etc.)

Population Lineage Tree

Different species partitions representing different delimitation models

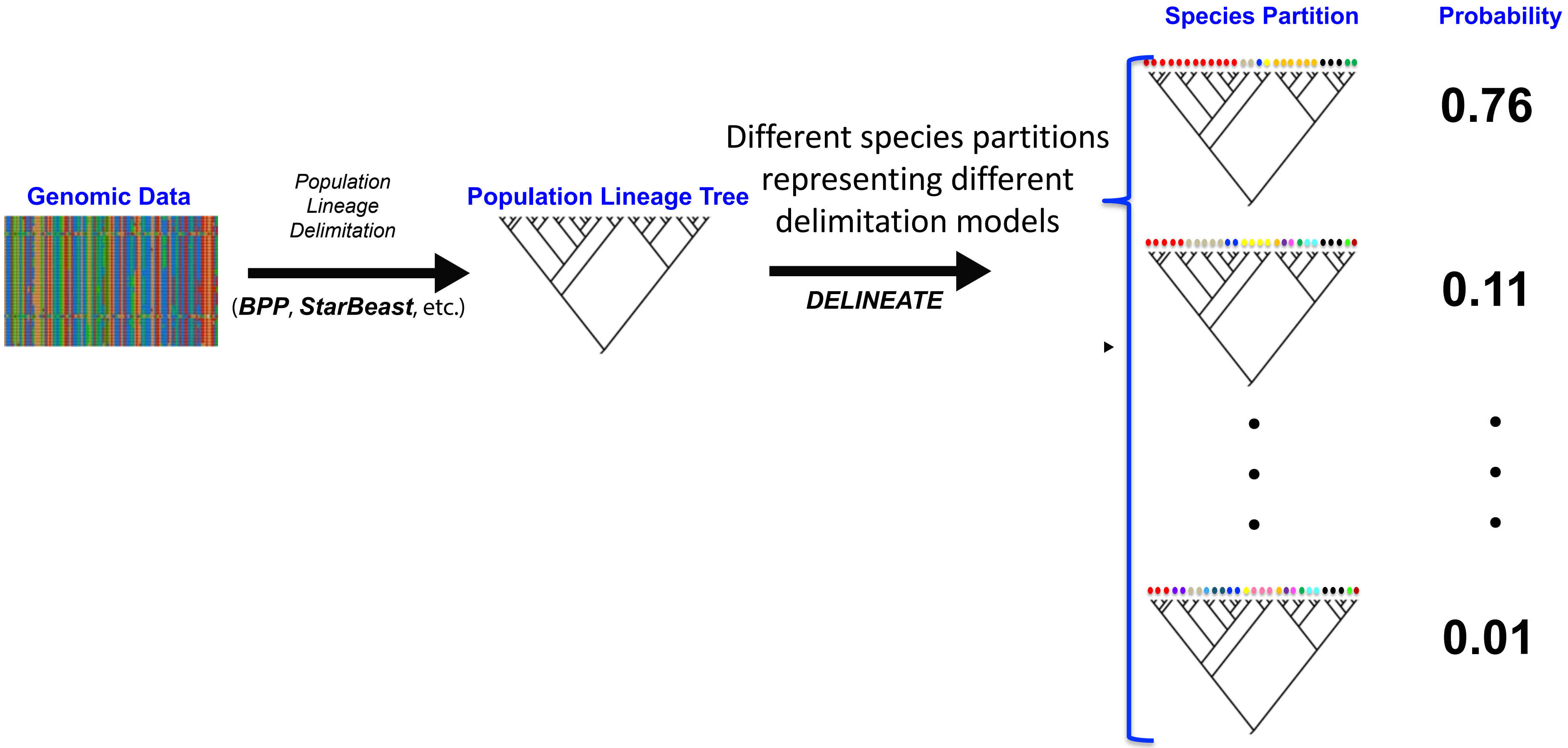
DELINEATE

Species Partition

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

DELINEATE

- probabilities of different *partitions* are calculated conditional on the lineage tree and the speciation dynamic parameters that capture the tempo of speciation



Genomic Data

Population Lineage Delimitation

(***BPP***, ***StarBeast***, etc.)

Population Lineage Tree

Different species partitions representing different delimitation models

DELINEATE

Species Partition

Probability

0.76

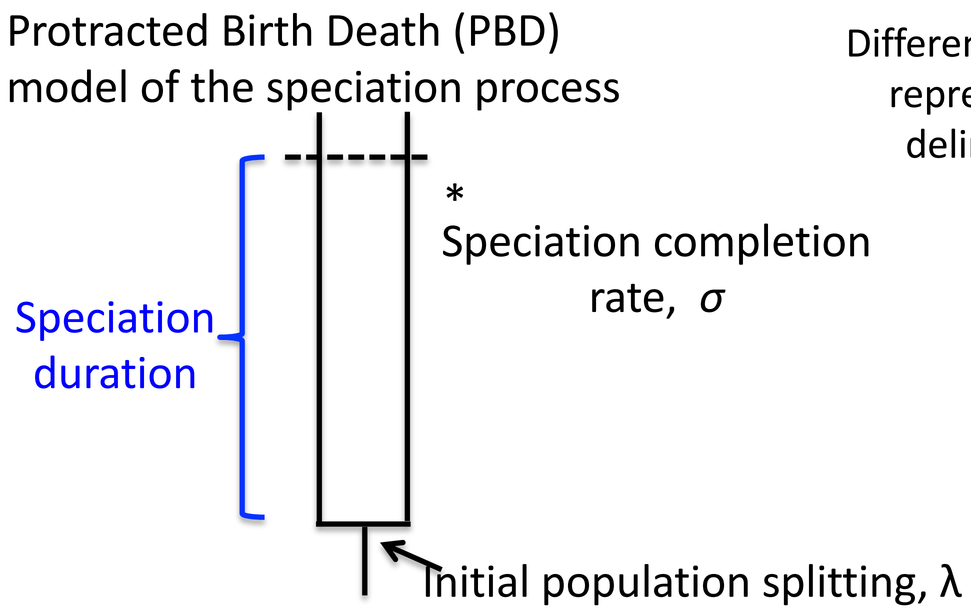
0.11

0.01

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

DELINEATE

- probabilities of different *partitions* are calculated conditional on the lineage tree and the speciation dynamic parameters that capture the tempo of speciation



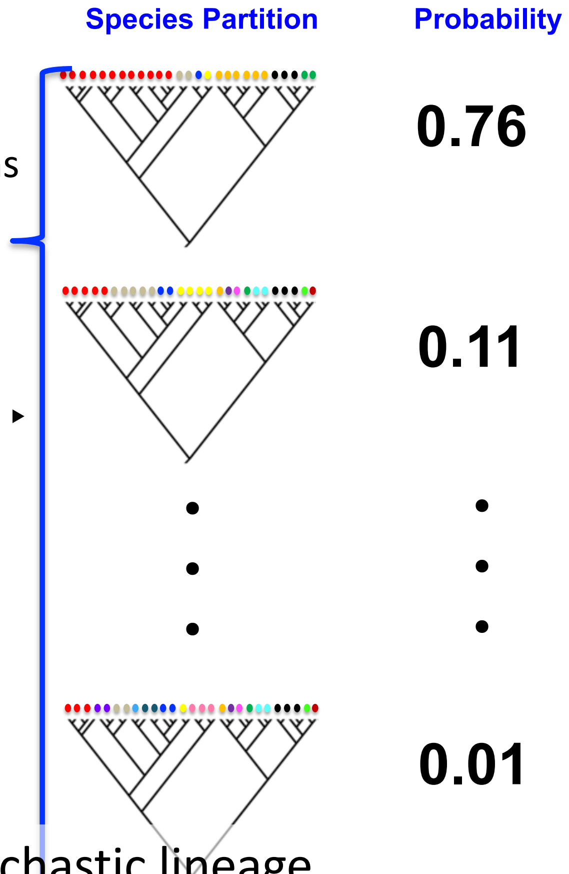
Protracted Birth Death (PBD) model of the speciation process

Speciation duration

* Speciation completion rate, σ

Initial population splitting, λ

Different species partitions representing different delimitation models



Species Partition	Probability
	0.76
	0.11
• • •	• • •
	0.01

* This process, as modeled in DELINEATE, is initiated by a stochastic lineage splitting process that extends over a duration of time that is determined stochastically by a speciation completion rate parameter

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

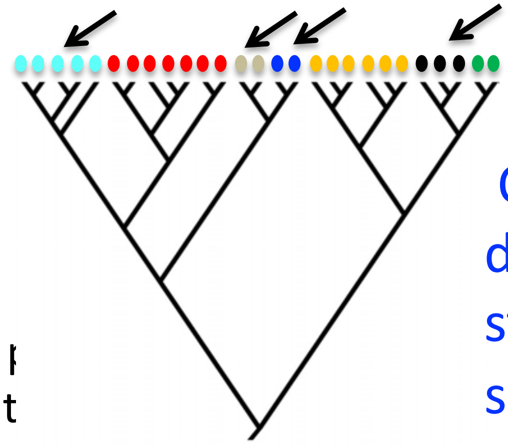
PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Incorporating the speciation process into species delimitation

Jeet Sukumaran[1]*, Mark T. Holder[2], L. Lacey Knowles[3]

- We retain the rational of a comparative context in our computational framework: specification of species identities of a subset of population lineages that are well studied



Collect sequences of lineages from well described species in addition to those less studied, which are the focus of inference of species boundaries

Each

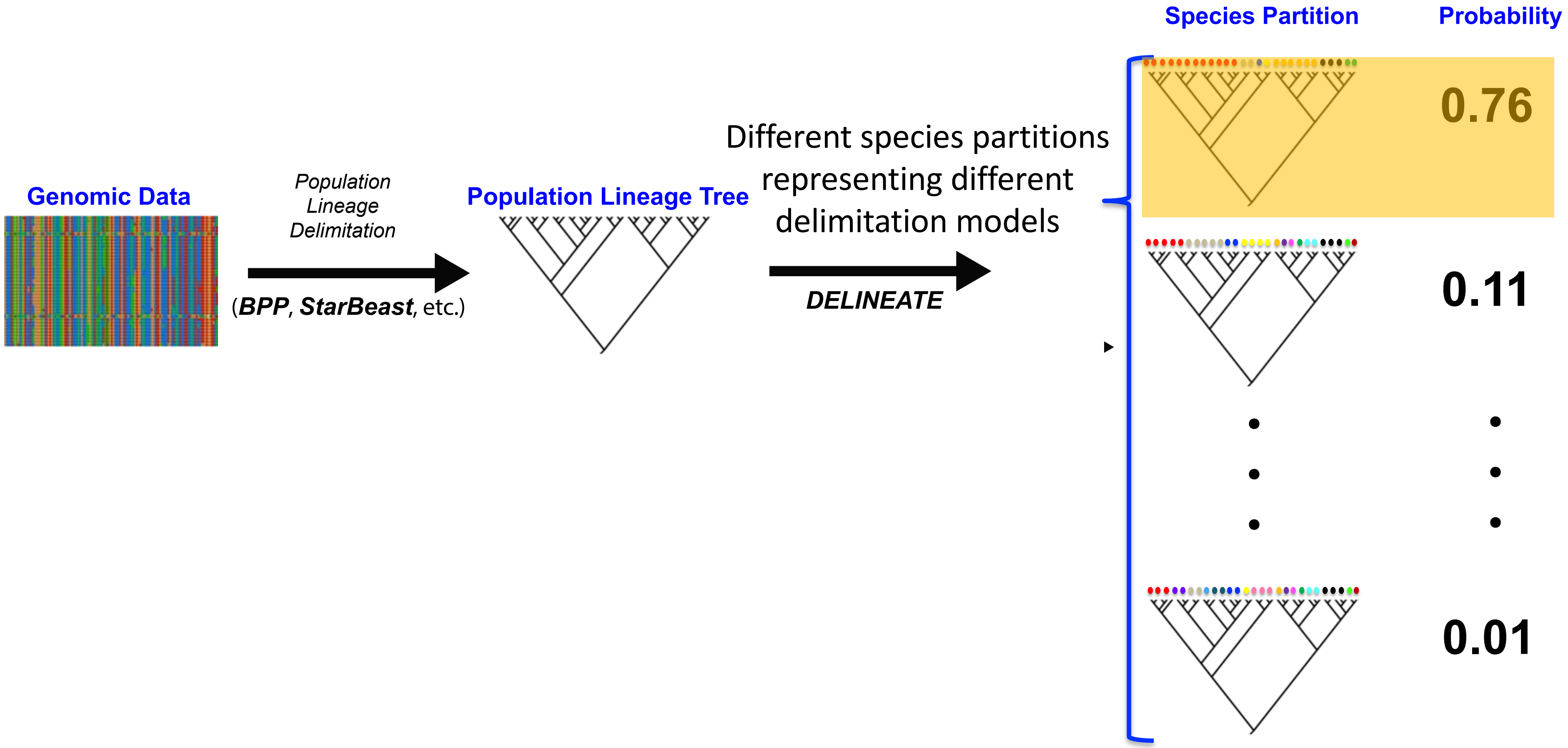
represent

species delimitation

PLOS Computational Biology | https://doi.org/10.1371/journal.pcbi.1008924 May 13, 2021

DELINEATE

- Preferred partition with highest probability



Species Partition

Probability

Genomic Data

Population Lineage Delimitation

(***BPP***, ***StarBeast***, etc.)

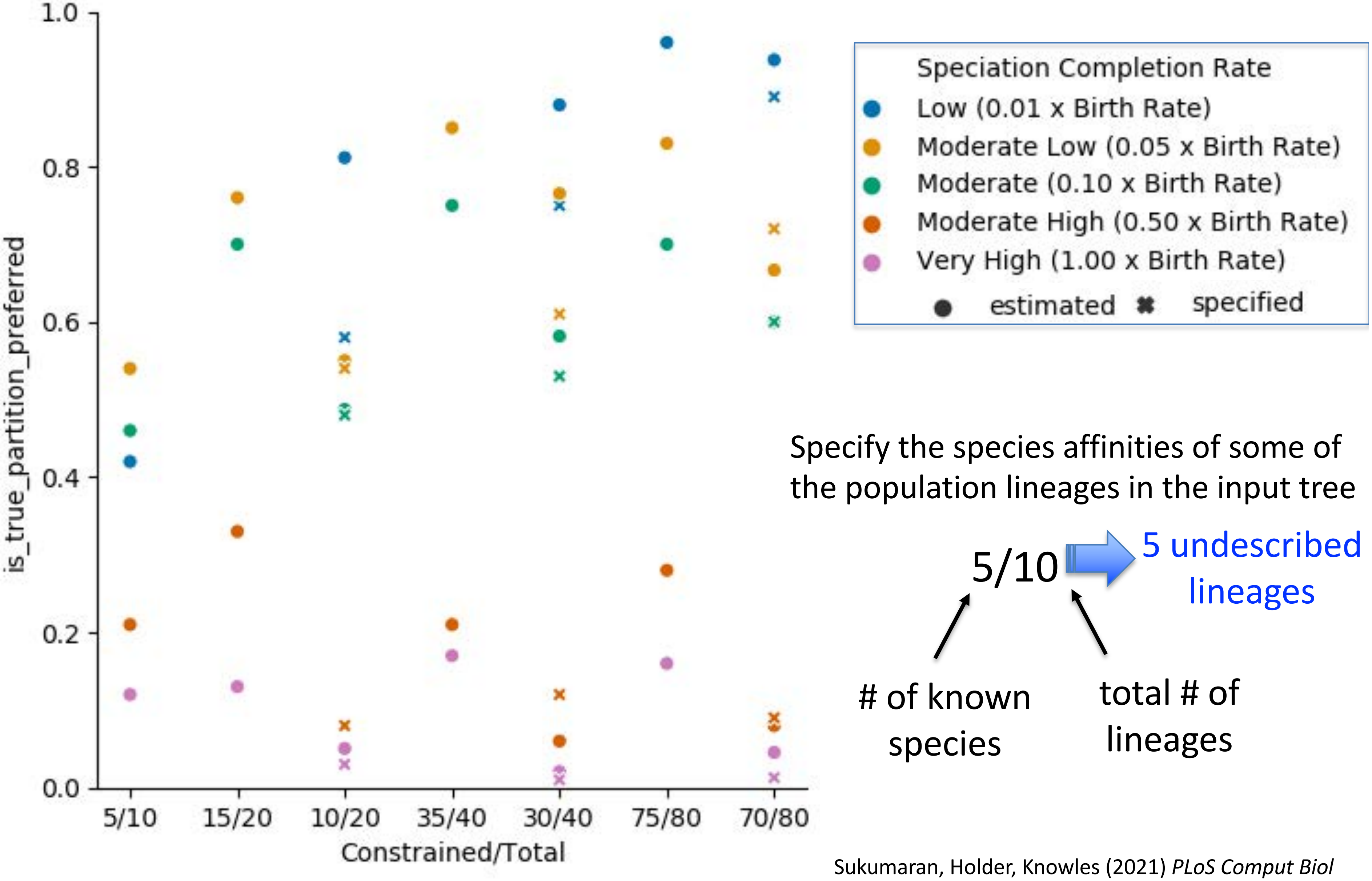
Population Lineage Tree

Different species partitions representing different delimitation models

DELINEATE

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

Accuracy: recovery of true species partition for different sized trees with different numbers of undescribed lineages



Specify the species affinities of some of the population lineages in the input tree

5/10 → 5 undescribed lineages

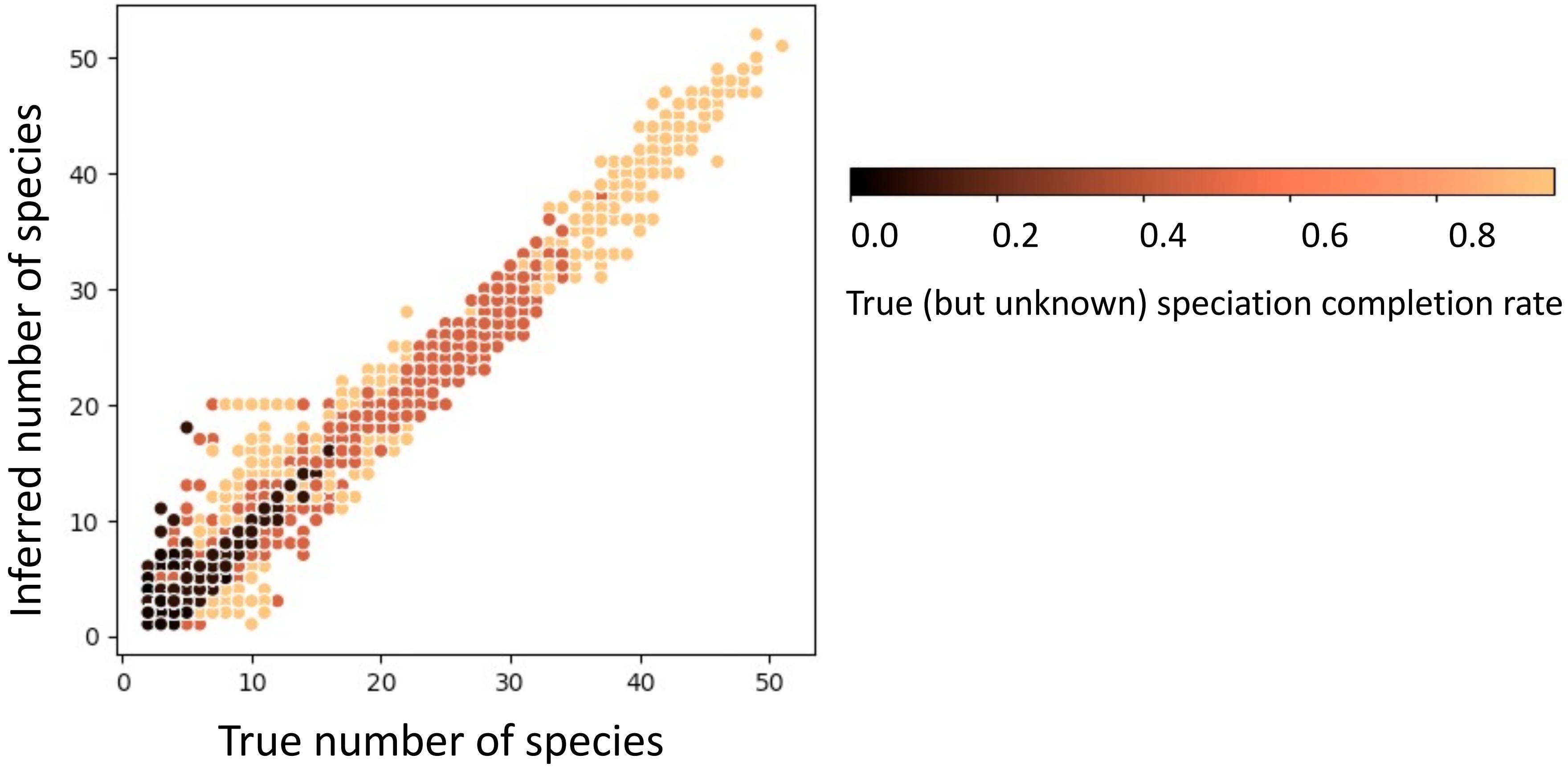
# of known species

total # of lineages

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

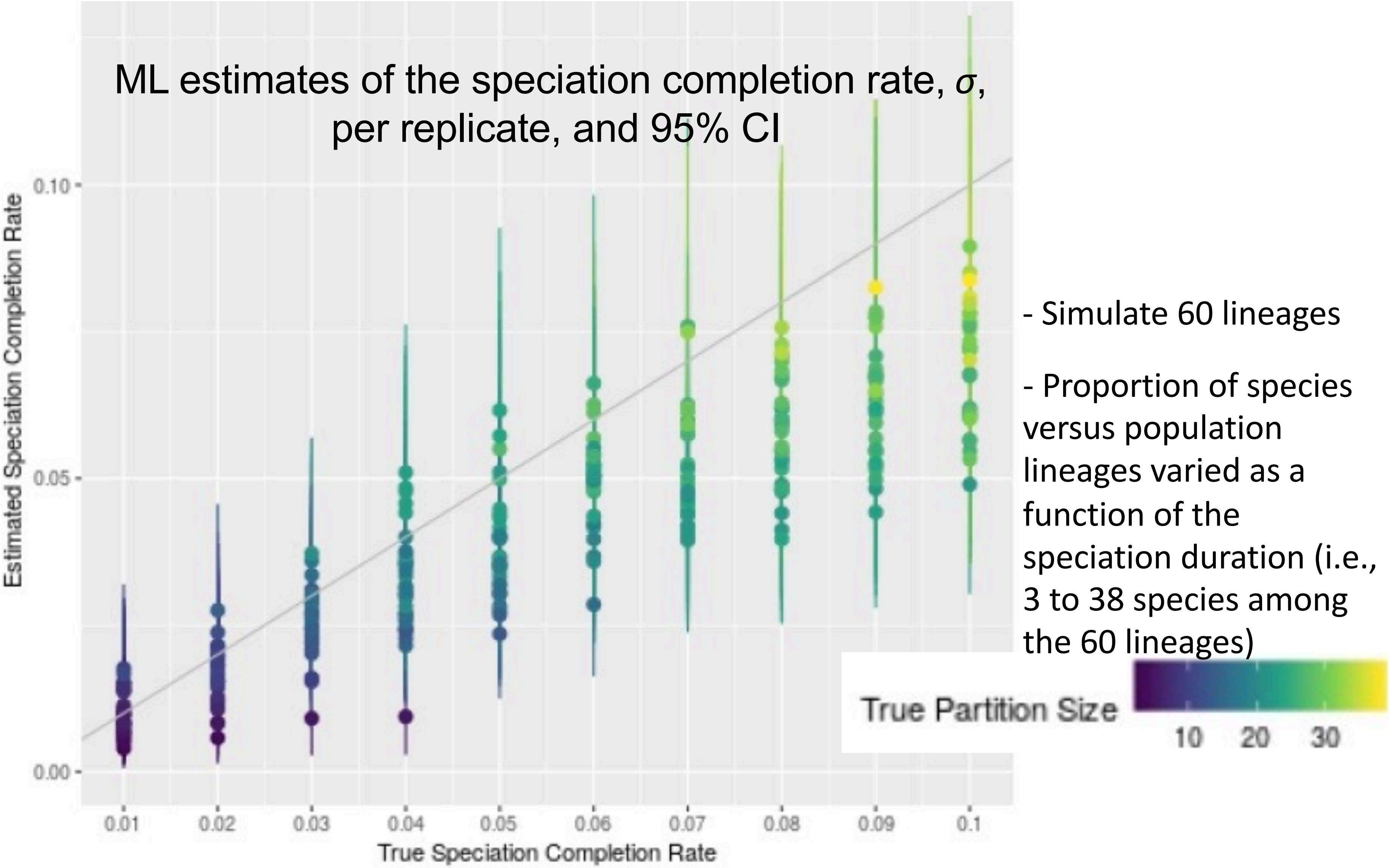
Other implementations/applications of DELINEATE

Quantification of biodiversity with a model of an extended speciation process



Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

Can estimate the speciation completion rate, *σ,* if input data contains at least one con-specific statement and one hetero-specific statement



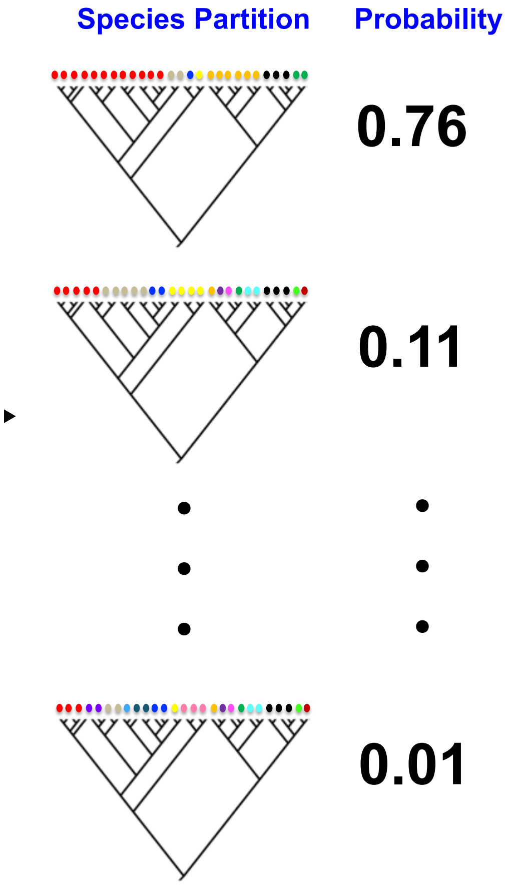
ML estimates of the speciation completion rate, *σ*, per replicate, and 95% CI

- Simulate 60 lineages

- Proportion of species versus population lineages varied as a function of the speciation duration (i.e., 3 to 38 species among the 60 lineages)

Other implementations/applications of DELINEATE

- Integrate across partitions to determine if target populations are new species or belong to previously described species

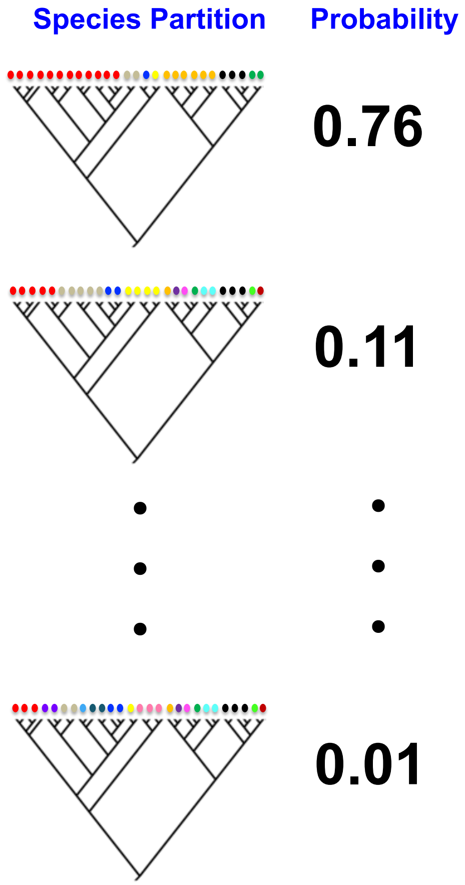


Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

Other implementations/applications of DELINEATE

- Integrate across partitions to determine if target populations are new species or belong to previously described species

- Conduct delimitation without having to specify affinities for subsets of taxa if apply estimate of speciation completion rate from other independent data (e.g., related clades) in which similar speciation dynamics can be assumed



Species Partition Probability

0.76

0.11

0.01

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

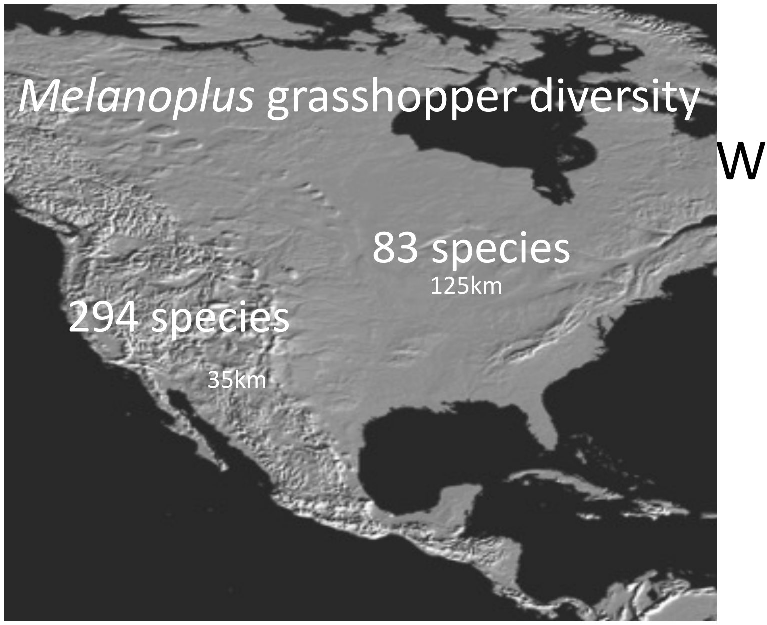
DELINEATE: a new class of delimitation models that incorporate the speciation process

- address the proliferation of artifactual species that results as within-species population lineages, detected due to restrictions in gene flow, are mis-identified as distinct species (as under the MSC)

- can assign probabilistically lineages of unknown affinities to pre-existing or new species

- we are able to learn not only about species boundaries, but also about the tempo of the speciation process itself

DELINEATE: the process of population splitting and species conversion are decoupled



We can ask whether the higher diversity reflects:

- higher rates of population isolation (perhaps due to landscape complexity or dynamic geographies), or

- higher rates of development of speciation isolating mechanisms

- Big Data: Between and within species genetic structure; specifically, target capture of 15,000 loci developed from RADseq across 30,000 individuals across the ranges of 352 species

DELINEATE: a new class of delimitation models that incorporate the speciation process

- addresses the proliferation of artifactual species that results as within-species population lineages, detected due to restrictions in gene flow, are identified as distinct species

- can assign probabilistically lineages of unknown affinities to pre-existing or new species

- we are able to learn not only about species boundaries, but also about the tempo of the speciation process itself

- By explicitly accounting for restrictions in gene flow not only between, but also within species, we also address the limits of genetic data for delimiting species.

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

Limitations of genetic data alone for species delimitation

- Without any information about species affinities for a subset of taxa, or about speciation dynamics, accurate delimitation is not possible

Sukumaran, Holder, Knowles (2021) *PLoS Comput Biol*

Limitations of DELINEATE

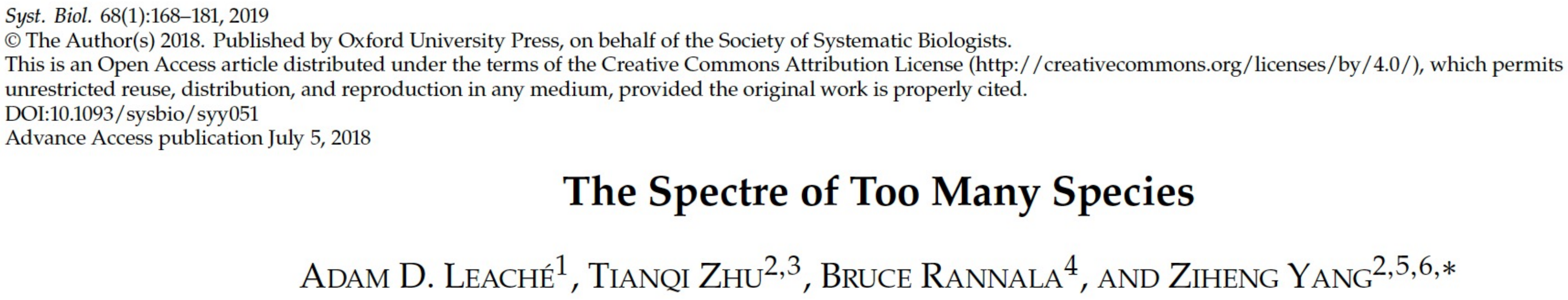
- Without any information about species affinities for a subset of taxa, or about speciation dynamics, accurate delimitation is not possible

That is, without incorporating independent information from other data sources, genetic data alone is not sufficient for accurate delimitation of species.

Software: *DELINEATE* https://github.com/jeetsukumaran/delineate

- Phylogenetic modeling approach that delineates species versus population lineages under a protracted speciation model

Skeptical of statements that claim otherwise:

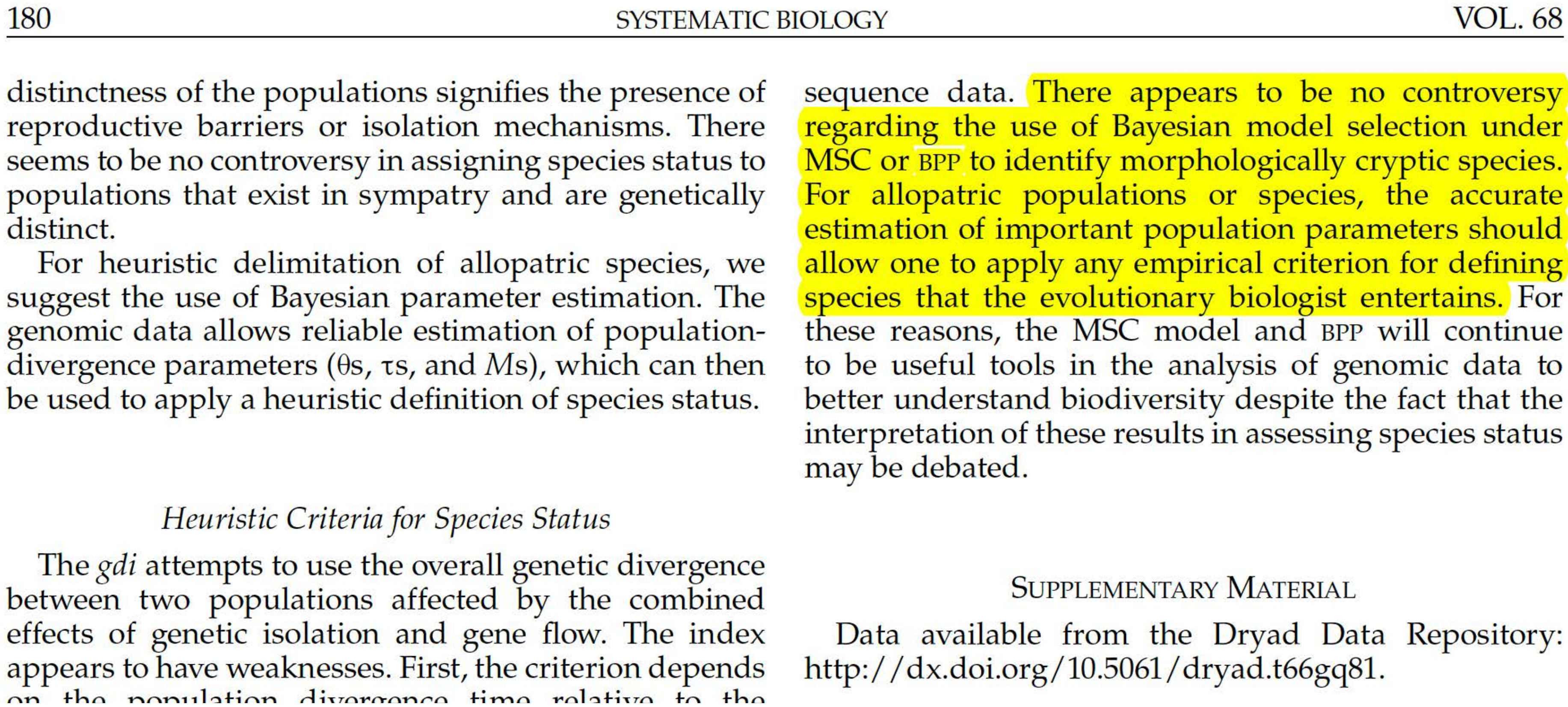


Syst. Biol. 68(1):168–181, 2019

DOI:10.1093/sysbio/syy051
Advance Access publication July 5, 2018

The Spectre of Too Many Species

Adam D. Leaché[1], Tianqi Zhu[2,3], Bruce Rannala[4], and Ziheng Yang[2,5,6,*]



distinctness of the populations signifies the presence of reproductive barriers or isolation mechanisms. There seems to be no controversy in assigning species status to populations that exist in sympatry and are genetically distinct.

For heuristic delimitation of allopatric species, we suggest the use of Bayesian parameter estimation. The genomic data allows reliable estimation of population-divergence parameters (θs, τs, and Ms), which can then be used to apply a heuristic definition of species status.

Heuristic Criteria for Species Status

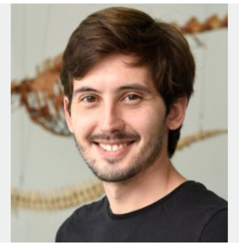
The *gdi* attempts to use the overall genetic divergence between two populations affected by the combined effects of genetic isolation and gene flow. The index appears to have weaknesses. First, the criterion depends on the population divergence time relative to the

sequence data. There appears to be no controversy regarding the use of Bayesian model selection under MSC or BPP to identify morphologically cryptic species. For allopatric populations or species, the accurate estimation of important population parameters should allow one to apply any empirical criterion for defining species that the evolutionary biologist entertains. For these reasons, the MSC model and BPP will continue to be useful tools in the analysis of genomic data to better understand biodiversity despite the fact that the interpretation of these results in assessing species status may be debated.

Supplementary Material

Data available from the Dryad Data Repository: http://dx.doi.org/10.5061/dryad.t66gq81.

Examine the robustness of the MSC by considering the geography of genetic divergence



Arnaud Becheler

https://becheler.github.io/pages/applications.html

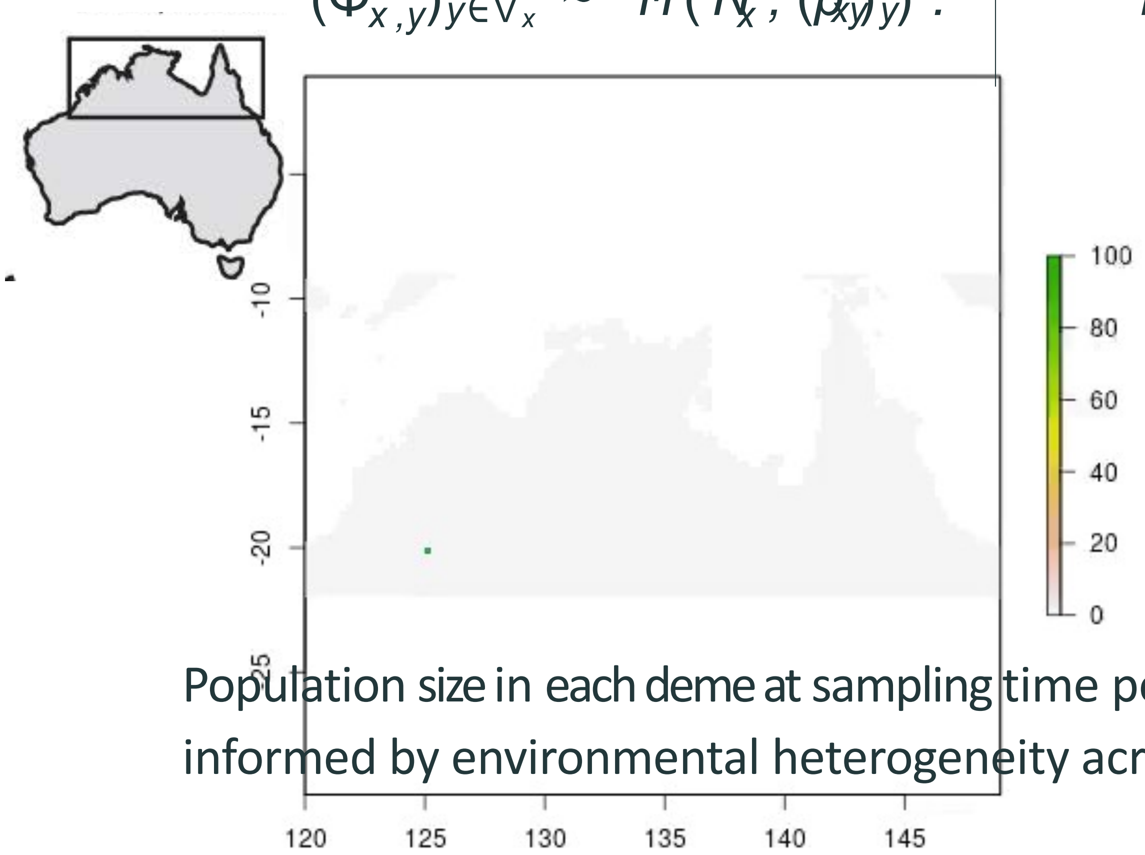
QUEZTAL: biologically informed demographic model over evolutionary time scales

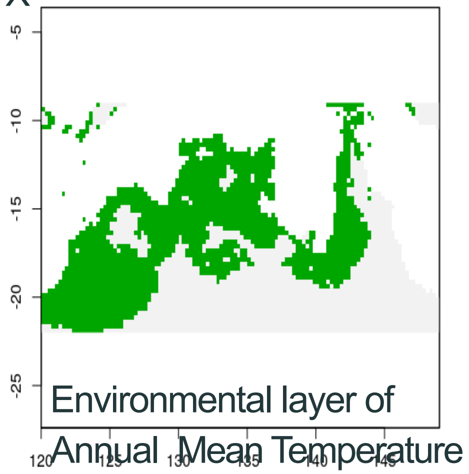
Flux de propagules Φ :

$$(\Phi^t_{x,y})_{y\in V_x} \sim M(\tilde{N}^t_x, (p_{xy})_y) \; .$$

Taille de population *N* :

$$N_j^{t+1} = \underset{i\in X}{} \; \Phi^t_{i,j}$$





Environmental layer of Annual Mean Temperature is higher than 26.4 C°

Population size in each deme at sampling time per generation informed by environmental heterogeneity across landscape

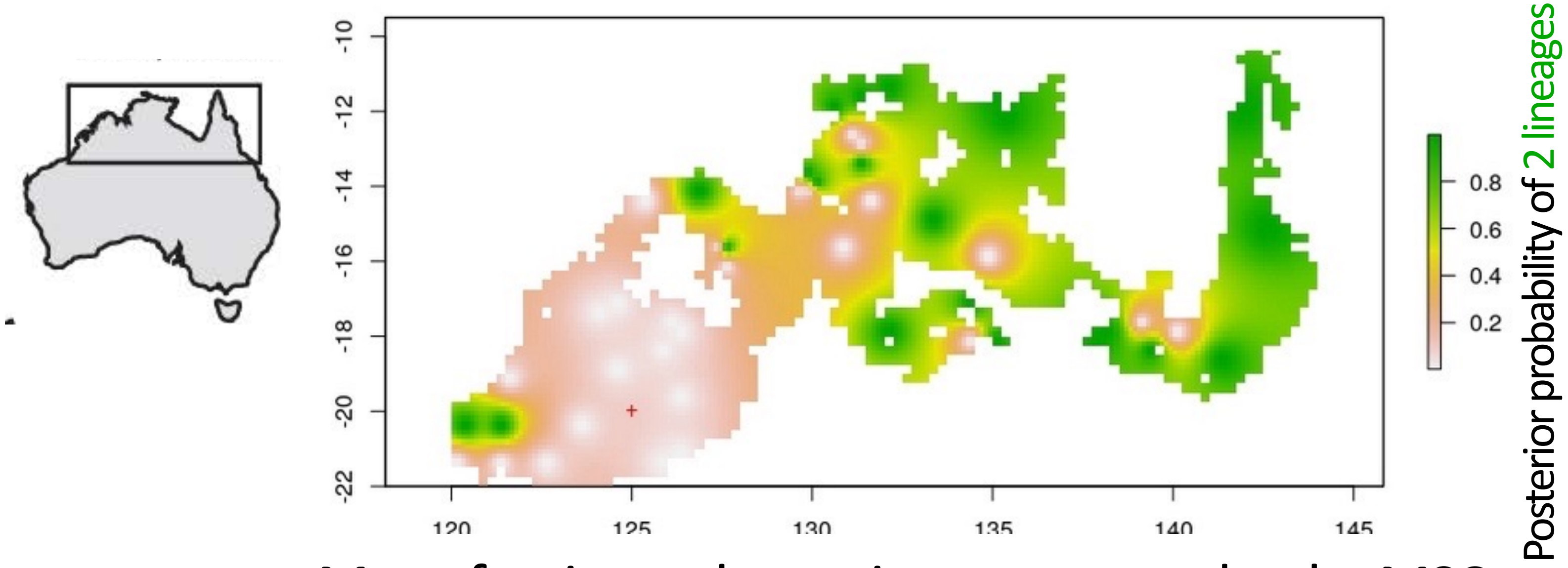
Becheler & Knowles (in prep)

Geographic predictions of genetic structure

associated with IBD, IBE, barriers, and stochastic population extinction

- Inform sampling strategy to avoid misinterpretations about genetic divergence

Robustness of the MSC



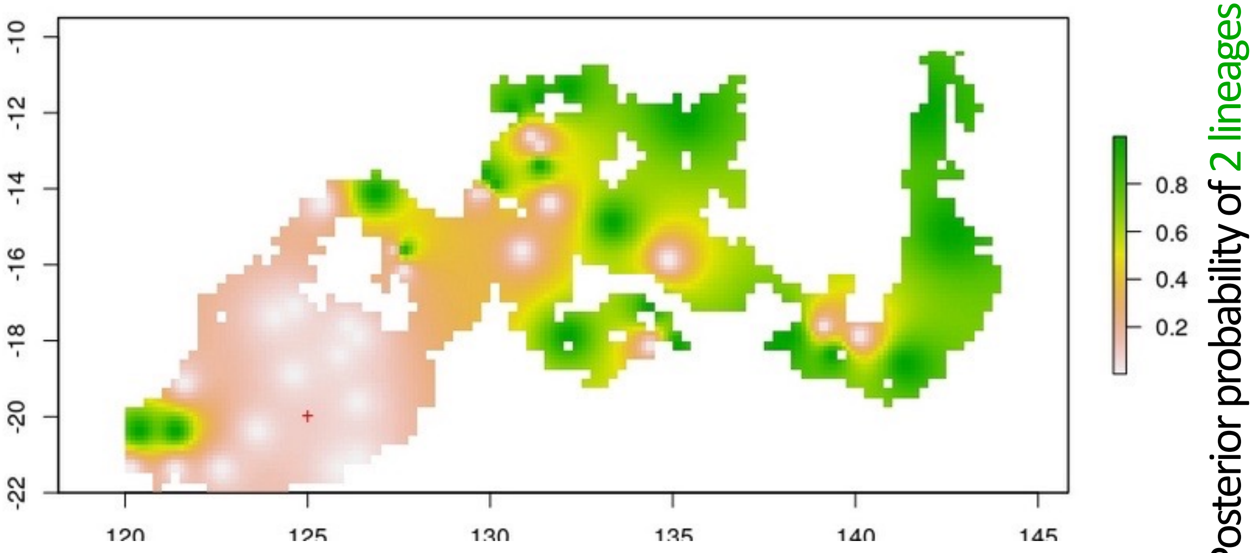
Map of estimated genetic structure under the MSC

(implemented in bpp where genetic divergence between sampled locations across the map to coordinate at x)

Geographic predictions of genetic structure

associated with IBD, IBE, barriers, and stochastic population extinction

Robustness of the MSC



Map of estimated genetic structure under the MSC

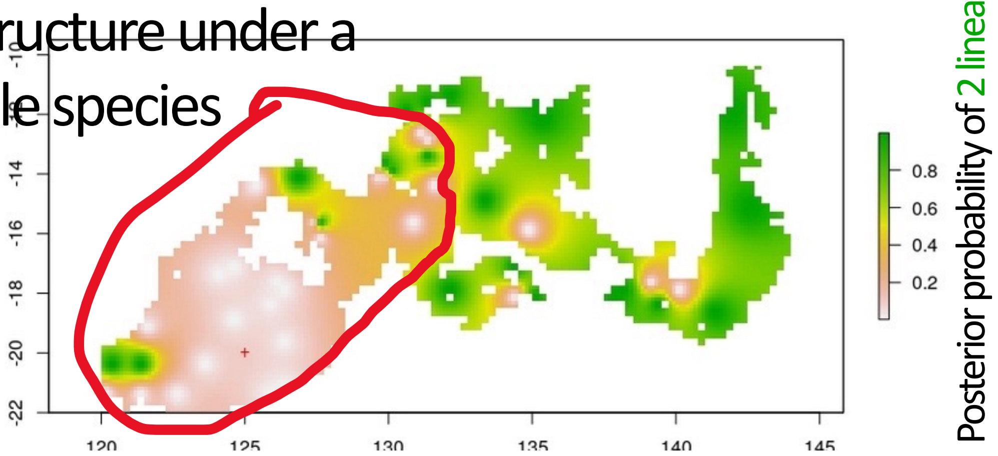
(implemented in bpp where genetic divergence between sampled locations across the map to coordinate at x)

- Avoid overestimation of species diversity by conflating genetic structure within species with genetic divergence between species

Geographic predictions of genetic structure

associated with IBD, IBE, barriers, and stochastic population extinction

model doesn’t predict genetic structure under a single species



REJECT model of no speciation

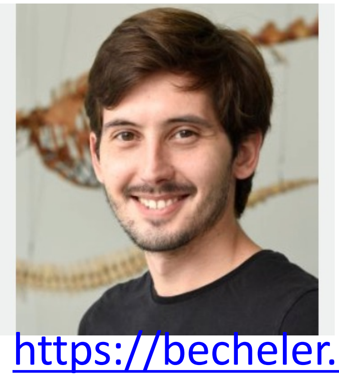
- Identify genetic structure that support hypothesis of speciation

Thank you!

former Postdoctoral fellows:

Jeet Sukumaran
San Diego State Univ.

https://github.com/jeetsukumaran/delineate



Arnaud Becheler
University of Michigan

https://becheler.github.io/pages/applications.html

Anna Papadopoulou

Mark Holder
Univ. of Kansas

Former UM
Ph. D. students:

Giorgia G. Auteri

Qixin He

Rob Massatti

support NSF & the UM

knowlesl@umich.edu