

BAYESIAN DIVERGENCE-TIME ESTIMATION

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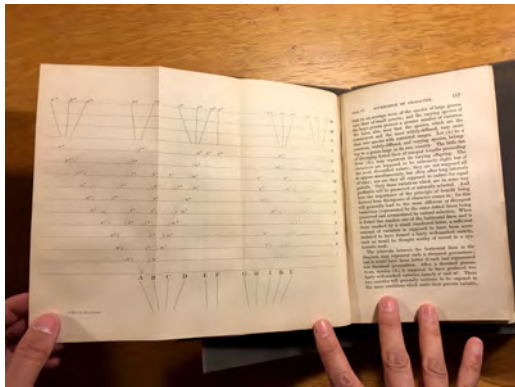


Bayesian Phylogenetics & Macroevolution in RevBayes Workshop
Itasca Biological Station, University of Minnesota
March 26-28, 2019



A TIME-SCALE FOR EVOLUTION

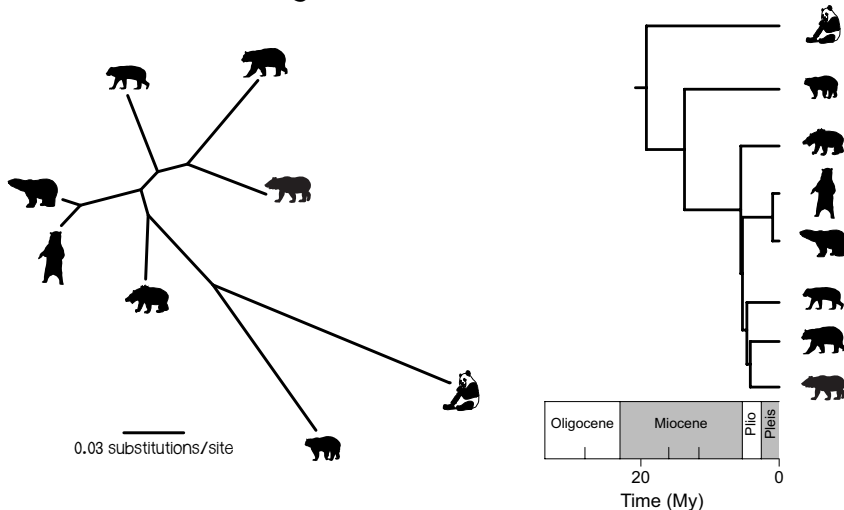
Phylogenies with branch lengths proportional to time provide valuable information about evolutionary history.



1st edition of Darwin's *On the Origin of Species* at Grinnell College (Grinnell, Iowa USA)

A TIME-SCALE FOR EVOLUTION

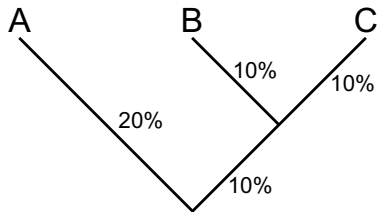
Phylogenies with branch lengths proportional to time provide more information about evolutionary history than unrooted trees with branch lengths in units of substitutions/site.



THE GLOBAL MOLECULAR CLOCK

Assume that the rate of evolutionary change is constant over time

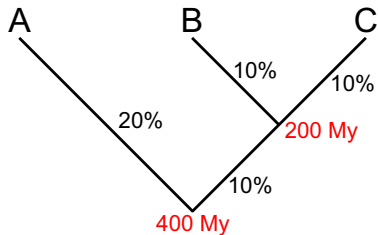
(branch lengths equal percent sequence divergence)



(Based on slides by Jeff Thorne; <http://statgen.ncsu.edu/thorne/compmolevo.html>)

THE GLOBAL MOLECULAR CLOCK

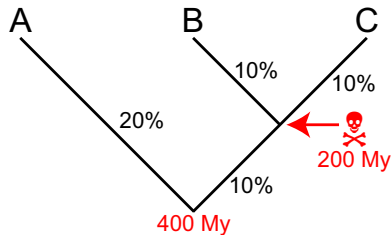
We can date the tree if we know the rate of change is 1% divergence per 10 My



(Based on slides by Jeff Thorne; <http://statgen.ncsu.edu/thorne/compmolevo.html>)

THE GLOBAL MOLECULAR CLOCK

If we found a fossil of the MRCA of **B** and **C**, we can use it to calculate the rate of change & date the root of the tree



(Based on slides by Jeff Thorne; <http://statgen.ncsu.edu/thorne/compmolevo.html>)

REJECTING THE GLOBAL MOLECULAR CLOCK

Rates of evolution vary across lineages and over time

Mutation rate:

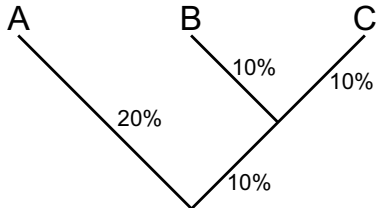
Variation in

- metabolic rate
- generation time
- DNA repair

Fixation rate:

Variation in

- strength and targets of selection
- population sizes

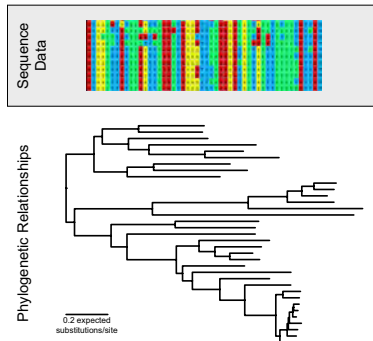


UNCONSTRAINED ANALYSIS

Sequence data provide information about **branch lengths**

In units of **the expected # of substitutions per site**

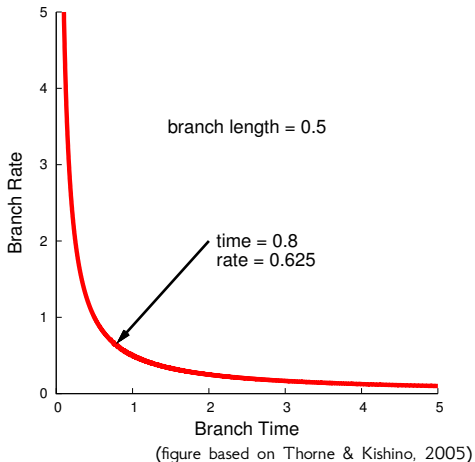
branch length = rate \times time



ESTIMATING RATE & TIME

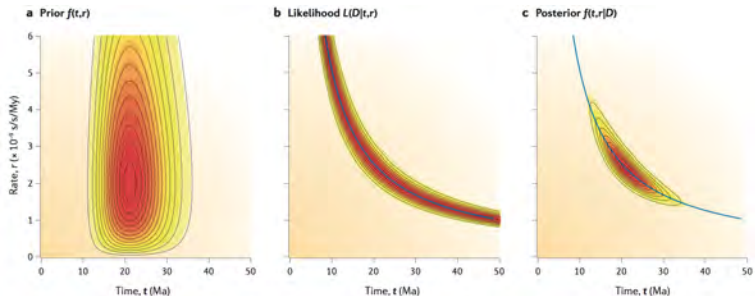
The sequence data provide information about branch length

for any possible rate, there's a time that fits the branch length perfectly



ESTIMATING RATE & TIME

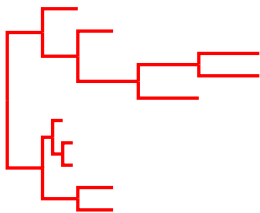
Methods for dating species divergences estimate the **substitution rate** and **time** separately



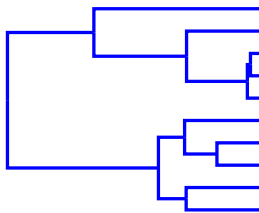
(dos Reis et al. *Nature Reviews Genetics*, 2016)

Tree-time priors for molecular phylogenies are only informative on a **relative** time scale

BAYESIAN DIVERGENCE TIME ESTIMATION



length = rate



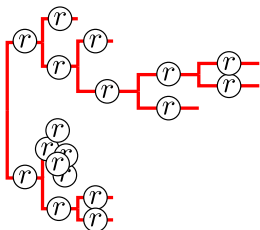
length = time

$$\mathcal{R} = (r_1, r_2, r_3, \dots, r_{2N-2})$$

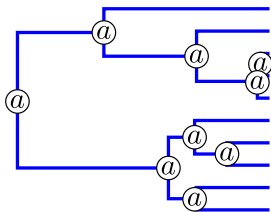
$$\mathcal{A} = (a_1, a_2, a_3, \dots, a_{N-1})$$

$$N = \text{number of tips}$$

BAYESIAN DIVERGENCE TIME ESTIMATION



length = rate



length = time

$$\mathcal{R} = (r_1, r_2, r_3, \dots, r_{2N-2})$$

$$\mathcal{A} = (a_1, a_2, a_3, \dots, a_{N-1})$$

$$N = \text{number of tips}$$

BAYESIAN DIVERGENCE TIME ESTIMATION

Posterior probability

$$f(\mathcal{R}, \mathcal{A}, \theta_{\mathcal{R}}, \theta_{\mathcal{A}}, \theta_s, \mathcal{T} | D)$$

\mathcal{R}	Vector of rates on branches
\mathcal{A}	Vector of internal node ages
$\theta_{\mathcal{R}}, \theta_{\mathcal{A}}, \theta_s$	Model parameters
D	Molecular or morphology data
\mathcal{T}	Tree topology

BAYESIAN DIVERGENCE TIME ESTIMATION

$$f(\mathcal{R}, \mathcal{A}, \theta_{\mathcal{R}}, \theta_{\mathcal{A}}, \theta_s | D) =$$

$$\frac{f(D | \mathcal{R}, \mathcal{A}, \theta_s) f(\mathcal{R} | \theta_{\mathcal{R}}) f(\mathcal{A} | \theta_{\mathcal{A}}) f(\theta_s)}{f(D)}$$

$$f(D | \mathcal{R}, \mathcal{A}, \theta_s)$$

Likelihood

$$f(\mathcal{R} | \theta_{\mathcal{R}})$$

Prior on rates

$$f(\mathcal{A} | \theta_{\mathcal{A}})$$

Prior on node ages

$$f(\theta_s)$$

Prior on substitution parameters

$$f(D)$$

Marginal probability of the data

MODELING RATE VARIATION

Some models describing lineage-specific substitution rate variation:

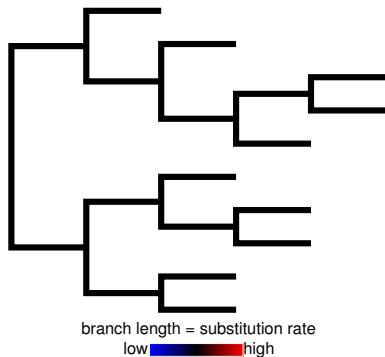
- **Global/strict clock** (Zuckerkandl & Pauling, 1962)
- **Local clocks** (Hasegawa, Kishino & Yano 1989; Kishino & Hasegawa 1990; Yoder & Yang 2000; Yang & Yoder 2003, Drummond and Suchard 2010)
- **Punctuated rate change model** (Huelsenbeck, Larget and Swofford 2000)
- **Autocorrelated rates** (Thorne, Kishino & Painter 1998; Kishino, Thorne & Bruno 2001; Thorne & Kishino 2002; Lepage et al. 2007)
- **Mixture models on branch rates** (Heath, Holder, Huelsenbeck 2012)
- **Uncorrelated/independent rates models** (Drummond et al. 2006; Rannala & Yang 2007; Lepage et al. 2007)

GLOBAL CLOCK

The substitution rate is constant over time

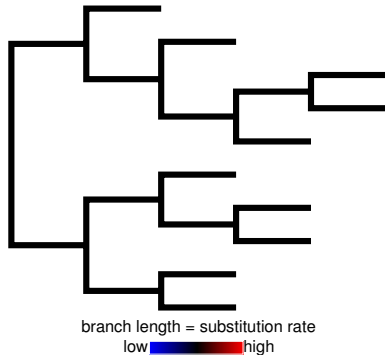
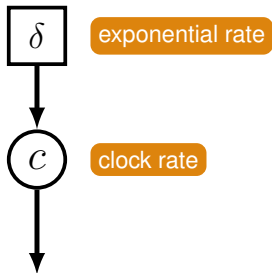
All lineages share the same rate

(Zuckermandl & Pauling, 1962)



GLOBAL CLOCK

$c \sim \text{Exponential}(\delta)$



GLOBAL CLOCK

Draw the graphical model!

$$c \sim \text{Gamma}(\alpha, \beta)$$

α

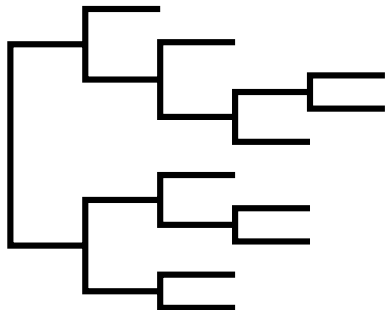
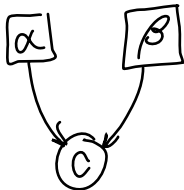
gamma shape


β

gamma scale

c

clock rate



branch length = substitution rate
low  high

RELAXED-CLOCK MODELS

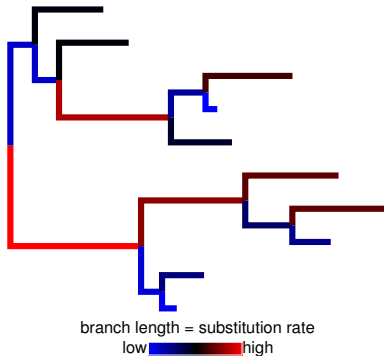
To accommodate variation in substitution rates
'relaxed-clock' models estimate lineage-specific substitution rates

- **Local clocks**
- **Punctuated rate change model**
- **Autocorrelated rates**
- **Mixture models on branch rates**
- **Uncorrelated/independent rates models**

INDEPENDENT/UNCORRELATED RATES

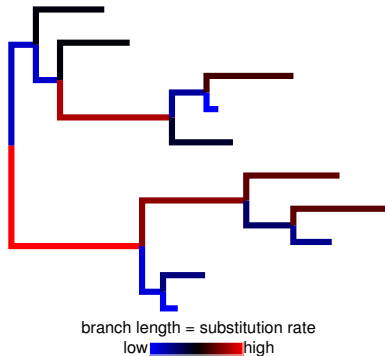
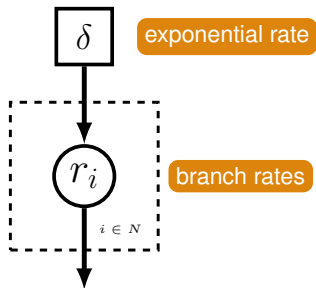
Lineage-specific rates are uncorrelated when the rate assigned to each branch is independently drawn from an underlying distribution

(Drummond et al. 2006; Rannala & Yang 2007; Lepage et al. 2007)



INDEPENDENT/UNCORRELATED RATES

$$r_i \sim \text{Exponential}(\delta)$$

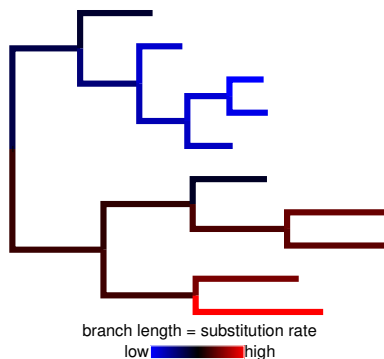


AUTOCORRELATED RATES

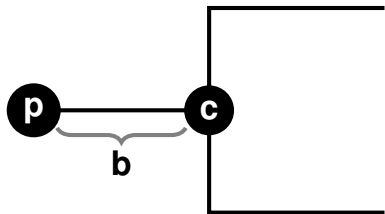
Substitution rates evolve gradually over time – closely related lineages have similar rates

The rate at a node is drawn from a distribution with a mean equal to the parent rate

(Thorne, Kishino, Painter, 1998;
Kishino, Thorne, Bruno, 2001)



AUTOCORRELATED RATES

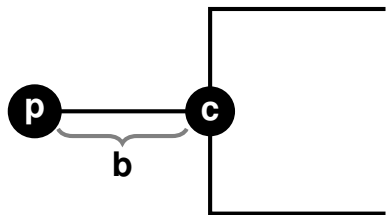


p = parent node

c = child node

b = branch

AUTOCORRELATED RATES



p = parent node

c = child node

b = branch

$$r_c \sim \text{Lognormal}(\mu_c, \sigma_c)$$

$$\sigma_c := \nu t_b$$

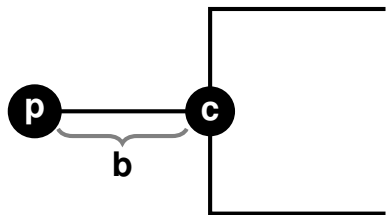
$$\mu_c := \ln(r_p) - \frac{\sigma_c^2}{2}$$

$$r_b := \frac{r_p + r_c}{2}$$

ν = variance parameter

t_b = time duration of branch

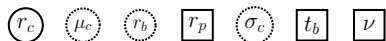
AUTOCORRELATED RATES



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t_b = time duration of branch

AUTOCORRELATED RATES

Draw the graphical model!

see the next slide

Tip: Break the problem up into parts by drawing the model for each equation given. Then, see how you can make connections.

$$r_c \sim \text{Lognormal}(\mu_c, \sigma_c)$$

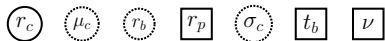
$$\sigma_c := \nu t_b$$

$$\mu_c := \ln(r_p) - \frac{\sigma_c^2}{2}$$

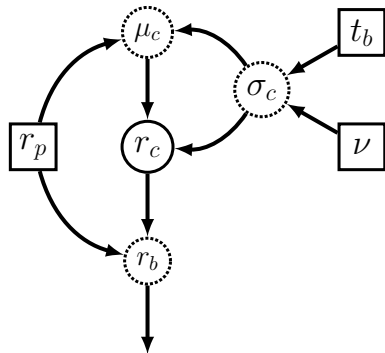
$$r_b := \frac{r_p + r_c}{2}$$

ν = variance parameter

t_b = time duration of branch



AUTOCORRELATED RATES



$$r_c \sim \text{Lognormal}(\mu_c, \sigma_c)$$

$$\sigma_c := \nu t_b$$

$$\mu_c := \ln(r_p) - \frac{\sigma_c^2}{2}$$

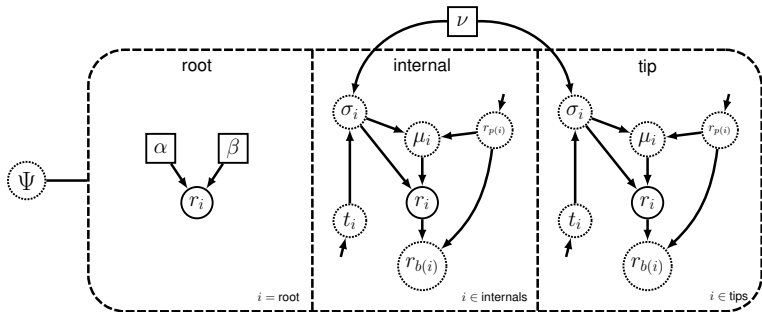
$$r_b := \frac{r_p + r_c}{2}$$

ν = variance parameter

t_b = time duration of branch

AUTOCORRELATED RATES

The rate associated with each node is a stochastic node, drawn from a distribution centered on its parent node



There is a gamma prior distribution on the rate at the root node

MODELING RATE VARIATION

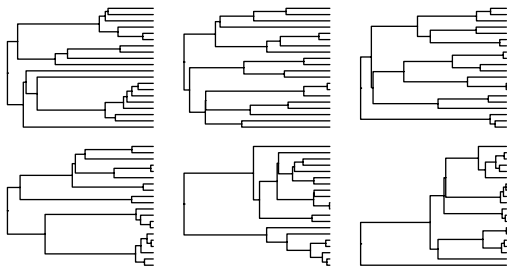
These are only a subset of the available models for branch-rate variation

- **Global/strict clock**
- **Local clocks**
- **Punctuated rate change model**
- **Log-normally distributed autocorrelated rates**
- **Mixture models on branch rates**
- **Uncorrelated/independent rates models**

Considering model selection, uncertainty, & plausibility is **very** important for Bayesian divergence time analysis

PRIORS ON THE TREE AND NODE AGES

Relaxed clock Bayesian analyses require a prior distribution on time trees



Different tree priors make different assumptions about the timing of divergence events and shape of the tree topology

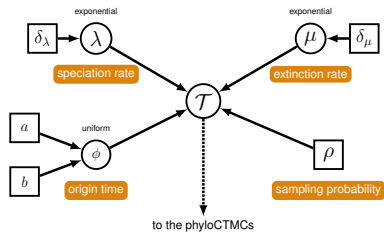
STOCHASTIC BRANCHING PROCESSES

Tree priors based on stochastic models of lineage diversification

Birth-death-sampling

process: at any point in time a lineage can speciate at rate λ or go extinct with a rate of μ

Conditions on a probability of sampling a tip, ρ and the origin time of the process, ϕ



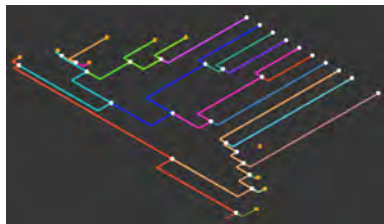
STOCHASTIC BRANCHING PROCESSES

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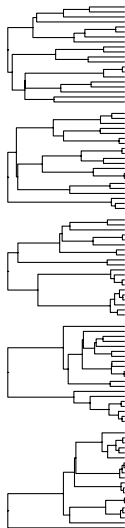
graphical illustration by Will Hurt (computer artist)

STOCHASTIC BRANCHING PROCESSES

Different values of λ and μ lead to different trees

Bayesian inference under these models can be very sensitive to the values of these parameters

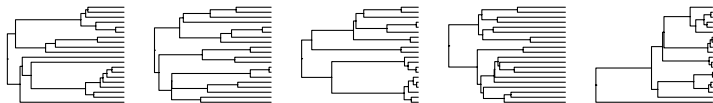
Using hyperpriors on λ and μ (or d and r) accounts for uncertainty in these hyperparameters



PRIORS ON THE TREE AND NODE AGES

Sequence data are only informative on *relative* rates & times

Most tree priors cannot give precise estimates of *absolute* node ages



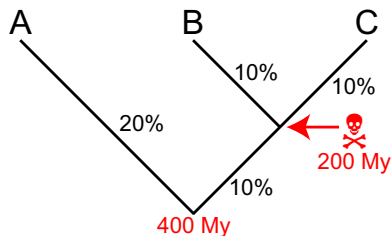
We need additional data (like fossils) to provide absolute time scale

CALIBRATING DIVERGENCE TIMES

Fossils (or other data) are necessary to estimate *absolute* node ages

There is **no information** in the sequence data for absolute time

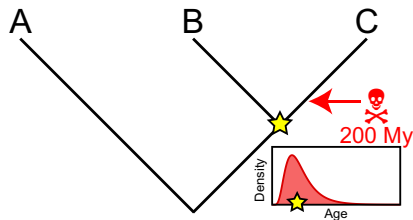
Uncertainty in the placement of fossils



CALIBRATION DENSITIES

Bayesian inference is well suited to accommodating uncertainty in the age of the calibration node

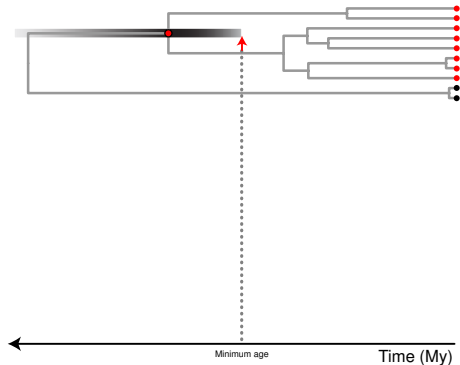
Divergence times are calibrated by placing parametric densities on internal nodes offset by age estimates from the fossil record



FOSSIL CALIBRATION

Age estimates from fossils can provide **minimum** time constraints for internal nodes

Reliable **maximum** bounds are typically unavailable

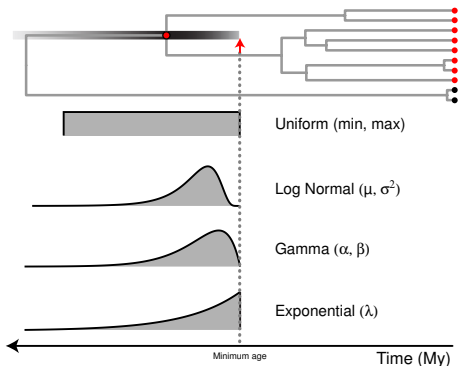


PRIOR DENSITIES ON CALIBRATED NODES

Common practice in Bayesian divergence-time estimation:

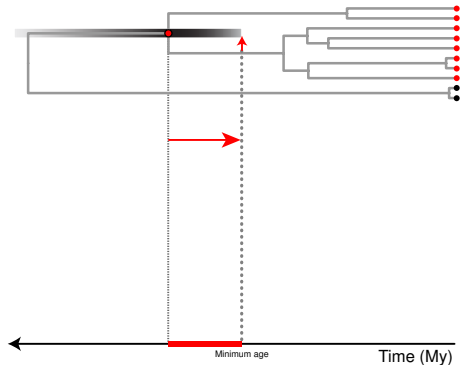
Parametric distributions are typically off-set by the age of the oldest fossil assigned to a clade

These prior densities do not (necessarily) require specification of maximum bounds



PRIOR DENSITIES ON CALIBRATED NODES

Describe the waiting time between the divergence event and the age of the oldest fossil

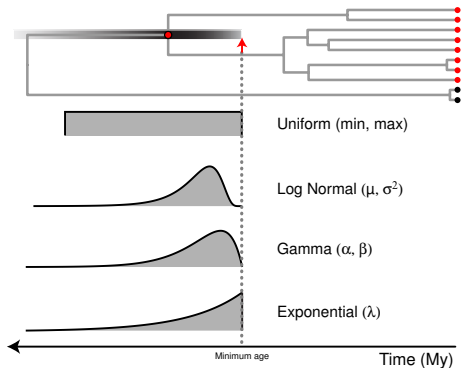


PRIOR DENSITIES ON CALIBRATED NODES

Common practice in Bayesian divergence-time estimation:

Estimates of absolute node ages are driven primarily by the calibration density

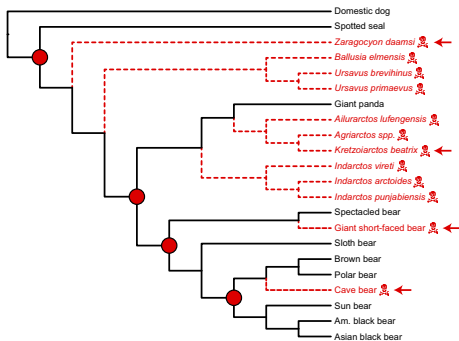
Specifying appropriate densities is a challenge for most molecular biologists



IMPROVING FOSSIL CALIBRATION

We would prefer to eliminate the need for *ad hoc* calibration prior densities

Calibration densities do not account for diversification of fossils



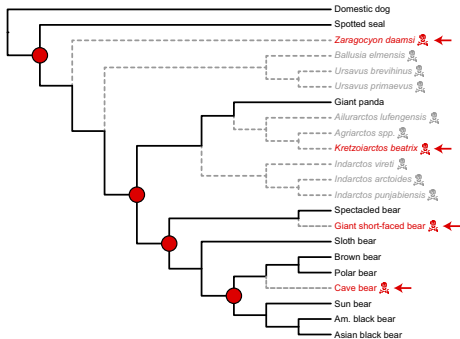
(Krause et al. *BMC Evol. Biol.* 2008; Abella et al. *PLoS ONE* 2012)

IMPROVING FOSSIL CALIBRATION

We want to use all of the available fossils

Example: Bears

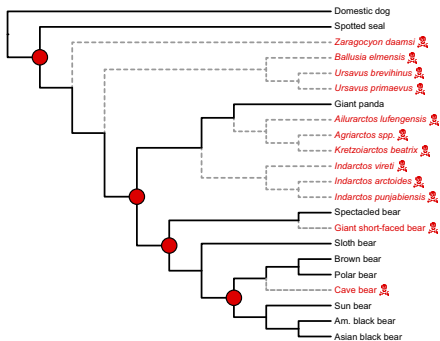
12 fossils are reduced to 4 calibration ages with calibration density methods



(Krause et al. *BMC Evol. Biol.* 2008; Abella et al. *PLoS ONE* 2012)

IMPROVING FOSSIL CALIBRATION

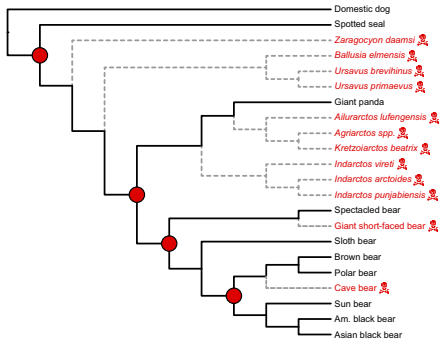
Because fossils are part of the diversification process, we can combine fossil calibration with birth-death models



(Krause et al. *BMC Evol. Biol.* 2008; Abella et al. *PLoS ONE* 2012)

IMPROVING FOSSIL CALIBRATION

This relies on a branching model that accounts for **speciation, extinction, and rates of fossilization, preservation, and recovery**



(Krause et al. *BMC Evol. Biol.* 2008; Abella et al. *PLoS ONE* 2012)

PALEONTOLOGY & NEONTOLOGY

“Except during the interlude of the [Modern] Synthesis, there has been limited communication historically among the disciplines of evolutionary biology, particularly between students of evolutionary history (paleontologists and systematists) and those of molecular, population, and organismal biology. **There has been increasing realization that barriers between these subfields must be overcome if a complete theory of evolution and systematics is to be forged.**”

Reaka-Kudla, M.L. & Colwell, R.: in E.C. Dudley (ed.), *The Unity of Evolutionary Biology: Proceedings of the Fourth International Congress of Systematic & Evolutionary Biology*, Discorides Press, Portland, OR, p. 16.

PALEONTOLOGY & NEONTOLOGY



Biology and Philosophy **19**: 687–720, 2004.

© 2004 Kluwer Academic Publishers. Printed in the Netherlands.

The role of fossils in phylogeny reconstruction: Why is it so difficult to integrate paleobiological and neontological evolutionary biology?

TODD GRANTHAM

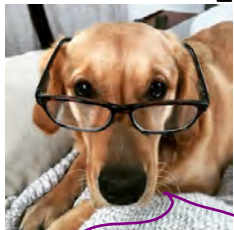
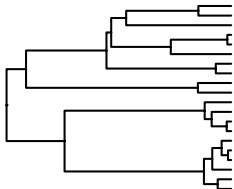
Department of Philosophy, College of Charleston, Charleston, SC 29424, USA
(e-mail: granthamt@cofc.edu)

HIERARCHICAL MODEL REVIEW

Draw the graphical model!

For this tree of 20 species, you assume an uncorrelated rates model, where the substitution rate for each branch is drawn from an exponential distribution.

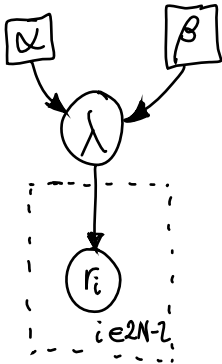
Because you are uncertain about the parameterization of the exponential distribution, you use a gamma distribution as a hyperprior on that parameter with a shape of $\alpha = 5$ and scale of $\beta = 1$.



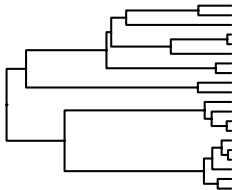
You can do it!

HIERARCHICAL MODEL REVIEW

Draw the graphical model!



$$\begin{aligned} N &= 20 \\ \alpha &= 5 \\ \beta &= 1 \end{aligned}$$



COMBINING FOSSIL & EXTANT DATA

Statistical methods provide a way to integrate paleontological & neontological data

Syst. Biol. 50(6):913–925, 2001

A Likelihood Approach to Estimating Phylogeny from Discrete Morphological Character Data

PAUL O. LEWIS

*Department of Ecology and Evolutionary Biology, The University of Connecticut, Storrs, Connecticut 06269-3043, USA;
E-mail: paul.lewis@uconn.edu*

Syst. Biol. 61(6):973–999, 2012

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DOI:10.1093/sysbio/sys058

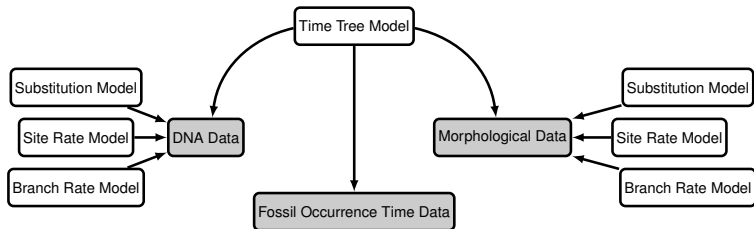
Advance Access publication on June 20, 2012

A Total-Evidence Approach to Dating with Fossils, Applied to the Early Radiation of the Hymenoptera

FREDRIK RONQUIST^{1,*}, SERAINA KLOPFSTEIN¹, LARS VILHELMSSEN², SUSANNE SCHULMEISTER³, DEBRA L. MURRAY⁴, AND ALEXANDR P. RASNITSYN⁵

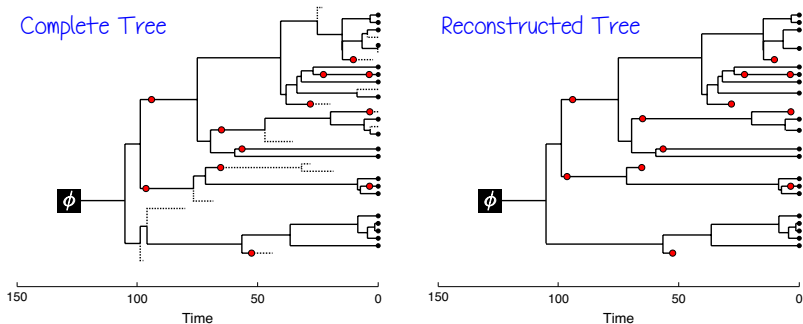
COMBINING FOSSIL & EXTANT DATA

Combine models for sequence evolution, morphological change, & fossil recovery to jointly estimate the tree topology, divergence times, & lineage diversification rates



MODELING THE TREE & OCCURRENCE TIMES

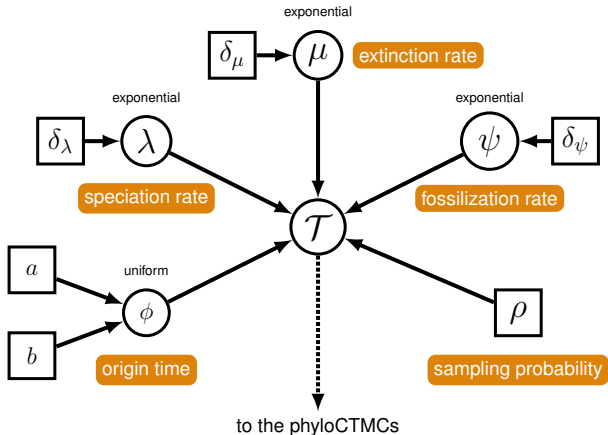
Stadler (2010) introduced a generating model for a serially sampled time tree — this is the *fossilized birth-death process*.



(Stadler. *Journal of Theoretical Biology* 2010)

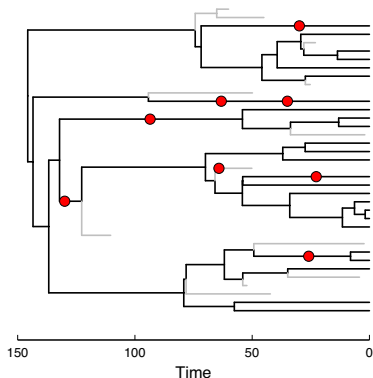
PARAMETERS OF THE FBD

This graph shows the conditional dependence structure of the FBD model, which is a generating process for a sampled, dated time tree and fossil occurrences



THE FOSSILIZED BIRTH-DEATH PROCESS (FBD)

Recovered fossil specimens provide historical observations of the diversification process that generated the tree of extant species



(Heath, Huelsenbeck, Stadler. *PNAS* 2014)

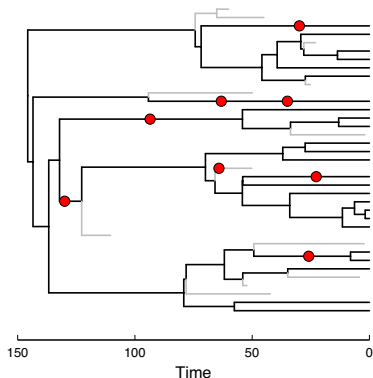
THE FOSSILIZED BIRTH-DEATH PROCESS (FBD)

The probability of the tree and fossil observations under a birth-death model with rate parameters:

λ = speciation

μ = extinction

ψ = fossilization/recovery



(Heath, Huelsenbeck, Stadler. *PNAS* 2014)

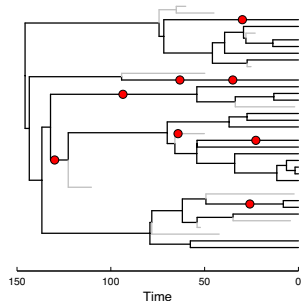
SAMPLED ANCESTORS

Sampled lineages with sampled descendants

Paleobiology, 22(2), 1996, pp. 141–151

On the probability of ancestors in the fossil record

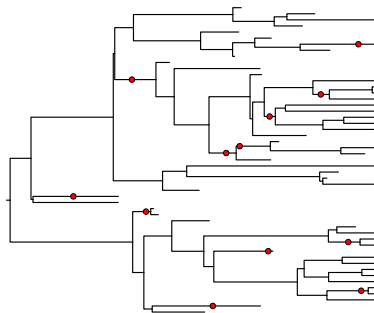
Mike Foote



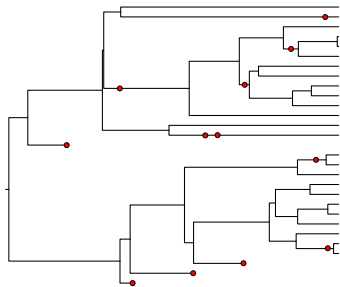
There is a non-zero probability of sampling ancestor-descendant relationships from the fossil record

SAMPLED ANCESTORS

Complete FBD Tree



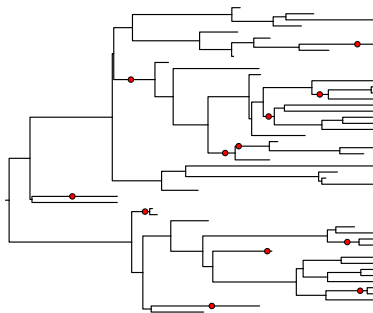
Reconstructed FBD Tree



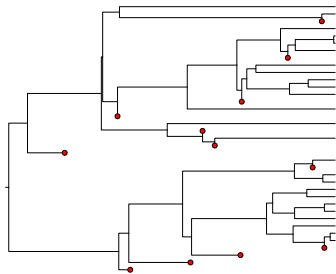
Because fossils & living taxa are assumed to come from a single diversification process, there is a non-zero probability of sampled ancestors

SAMPLED ANCESTORS

Complete FBD Tree



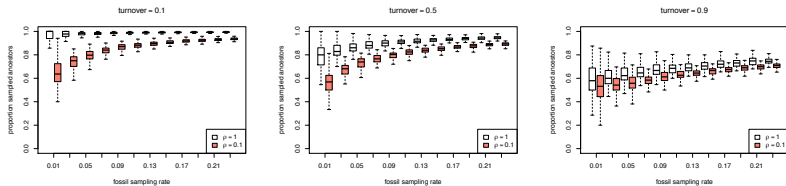
No Sampled Ancestor Tree



If all fossils are forced to be on separate lineages, this induces additional speciation events and will, in turn, influence rate & node-age estimates.

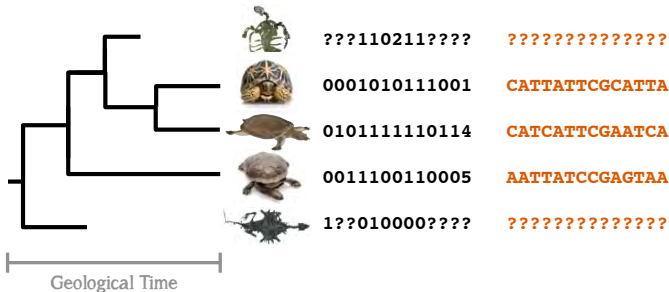
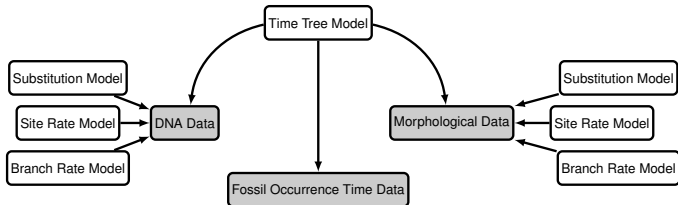
SAMPLED ANCESTORS

The proportion of sampled ancestors depends on the turnover rate, probability of sampling an extant tip, and rate of sampling fossils back in time

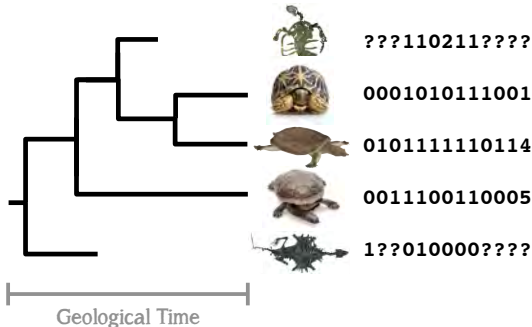


(Pett & Heath, in review)

COMBINING FOSSIL & EXTANT DATA



MODELING MORPHOLOGICAL CHARACTER CHANGE



Syst. Biol. 50(6):913-925, 2001

A Likelihood Approach to Estimating Phylogeny from Discrete Morphological Character Data

PAUL O. LEWIS

*Department of Ecology and Evolutionary Biology, The University of Connecticut, Storrs, Connecticut 06269-3043, USA;
E-mail: paul.lewis@uconn.edu*

MODELING MORPHOLOGICAL CHARACTER CHANGE

The Lewis Mk model

Assumes a character can take k states

Transition rates between states are equal (symmetric)

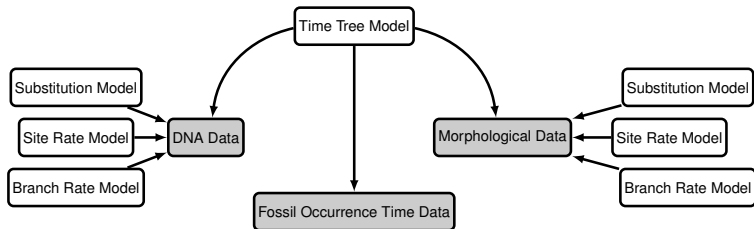
$$Q = \alpha \begin{bmatrix} 1 - k & 1 & \dots & 1 \\ \vdots & 1 - k & \dots & 1 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 1 & \dots & 1 - k \end{bmatrix}$$

T1	0
T2	0
T3	1
T4	2
T5	2
T6	1
T7	1

(Lewis. *Systematic Biology* 2001)

"TOTAL-EVIDENCE" ANALYSIS

Integrating models of molecular and morphological evolution with improved tree priors enables joint inference of the tree topology (extant & extinct) and divergence times



PENGUIN DIVERSITY IN DEEP TIME

How does our understanding of penguin evolution improve when we consider both extant and fossil taxa?

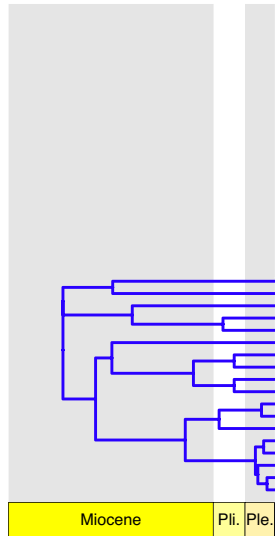


"Penguin Party" by Kate Dzikiewicz

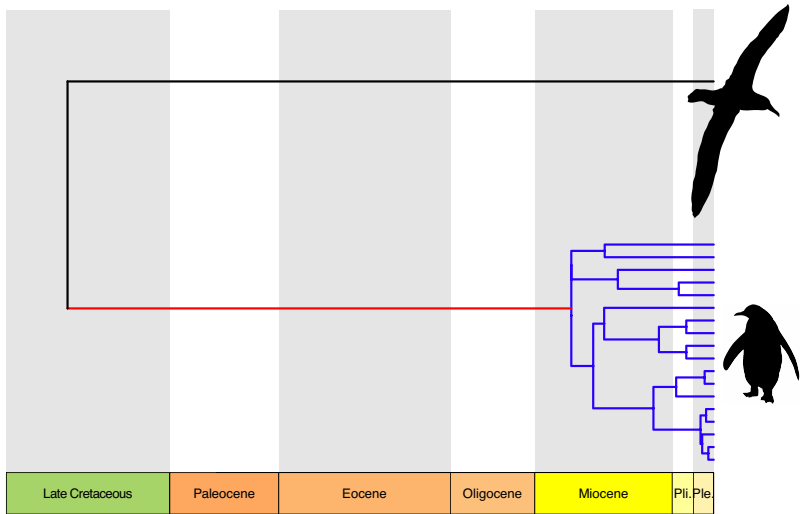


Artistic reconstructions by: Stephanie Abramowicz for Scientific American
Fordyce, R.E. and D.T. Ksepka. The Strangest Bird Scientific American 307, 56 – 61 (2012)

PENGUIN DIVERSITY



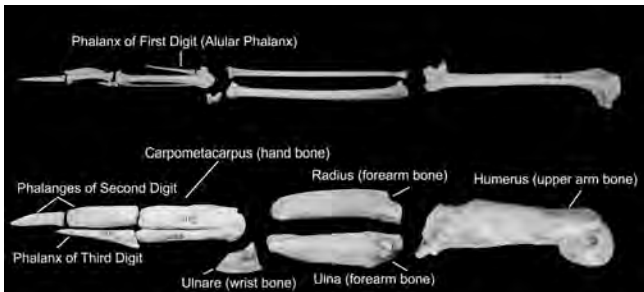
PENGUIN DIVERSITY



(silhouette images from <http://phylopic.org>)

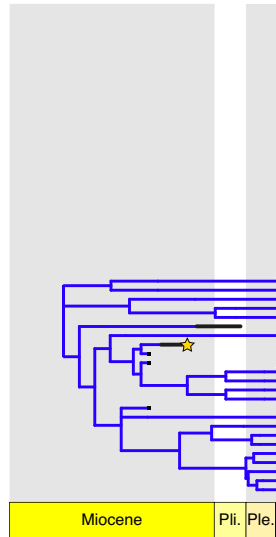
WHAT MAKES A PENGUIN A PENGUIN?

Flattened, solid wing-bones



(image courtesy of D. Ksepka <https://fossilpenguins.wordpress.com>)

FOSSIL PENGUIN DIVERSITY



(*S. urbinai* holotype fossil, 5-7 MYA, image by Martin Chávez)

PENGUINS IN THE OLIGOCENE

Kairuku

- ~1.5 m tall
- slender, with narrow bill
- scapula & pygostyle are more similar to non-penguins
- ~27 Mya



(Ksepka, Fordyce, Ando, & Jones, *J. Vert. Paleo.* 2012)

PENGUINS IN THE PALEOCENE

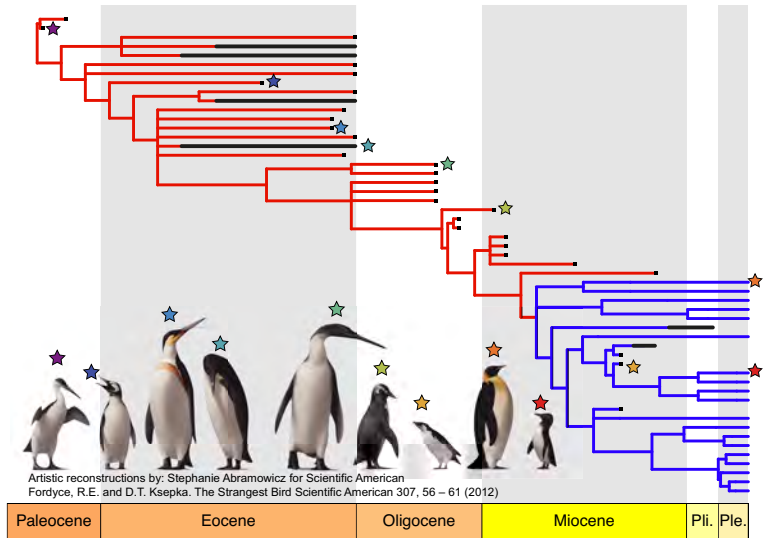
Waimanu

- oldest known penguin species
- intermediate wing morphology
- ~58–61.6 Mya



(Slack et al., *Mol. Biol. Evol.* 2006)

PENGUIN DIVERSITY IN DEEP TIME

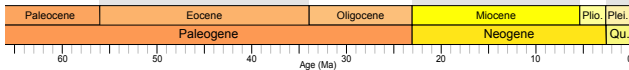


PENGUIN DIVERSITY IN DEEP TIME



19 extant species
36 fossil species

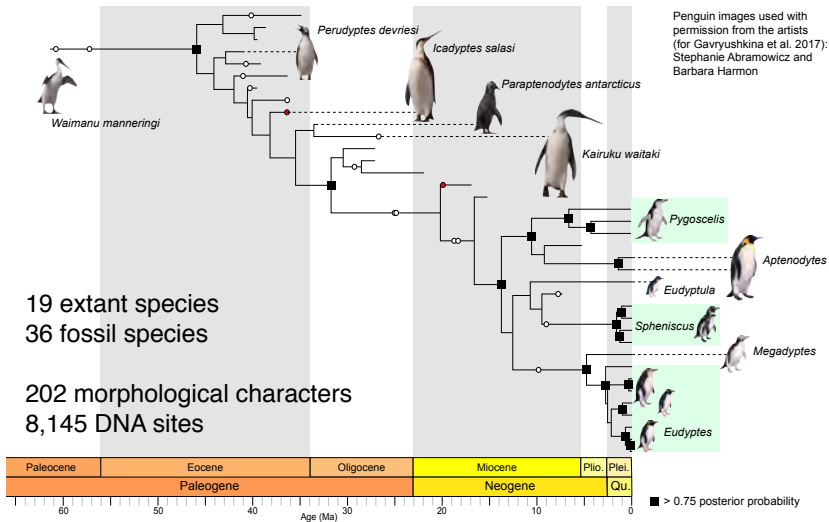
202 morphological characters
8,145 DNA sites



Penguin images used with permission from the artists (for Gavryushkina et al. 2017): Stephanie Abramowicz and Barbara Harmon

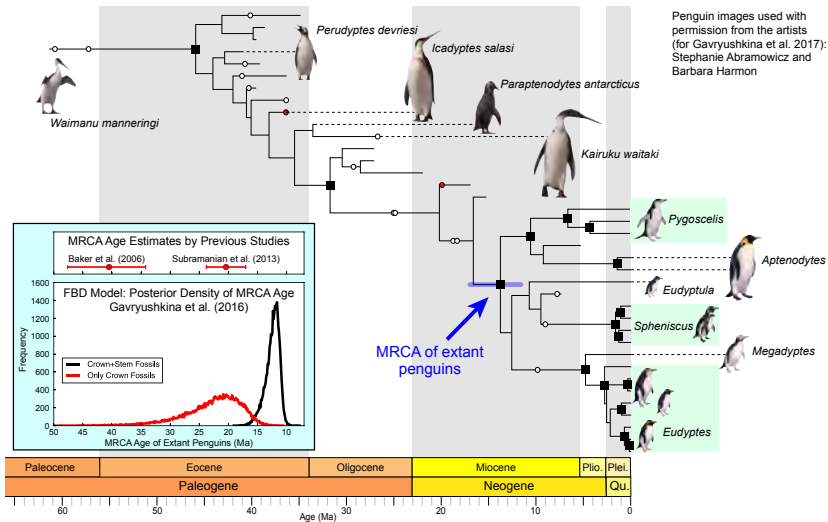
(Gavryushkina, Heath, Ksepka, Welch, Stadler, Drummond. 2017. *Syst. Biol.*)

PENGUIN DIVERSITY IN DEEP TIME



(Gavryushkina, Heath, Ksepka, Welch, Stadler, Drummond. 2017. *Syst. Biol.*)

PENGUIN DIVERSITY IN DEEP TIME

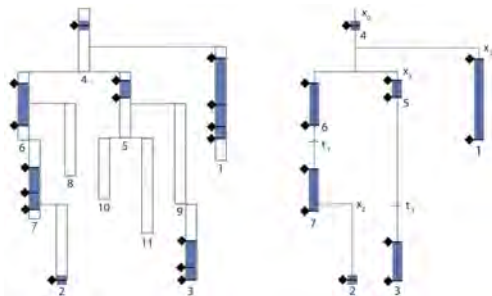


Penguin images used with permission from the artists (for Gavryushkina et al. 2017): Stephanie Abramowicz and Barbara Harmon

(Gavryushkina, Heath, Ksepka, Welch, Stadler, Drummond. 2017. *Syst. Biol.*)

Fossil DATA & PHYLOGENIES

Through collaboration with paleontologists, we are building models to account for the structure of the fossil record and the nature of paleontological data



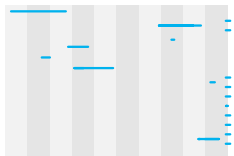
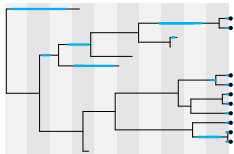
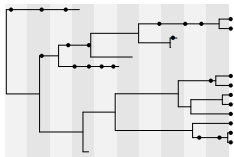
The fossilized birth-death model for the analysis of stratigraphic range data under different speciation modes

Tanja Stadler^{a,b,*}, Alexandra Gavryushkina^{a,b}, Rachel C.M. Warnock^{a,b},
Alexei J. Drummond^c, Tracy A. Heath^d

FOSSIL DATA & PHYLOGENIES

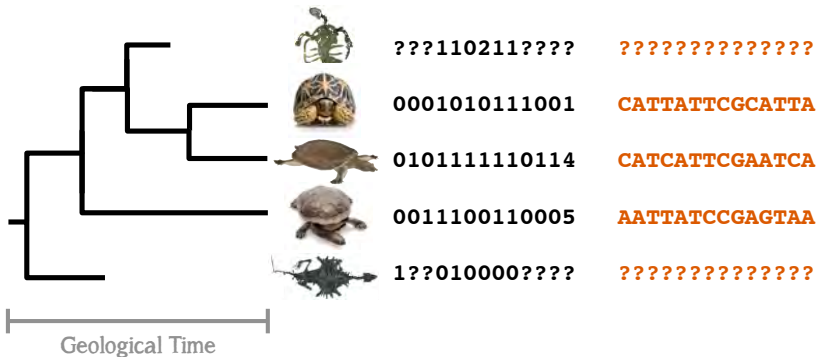
The FBD model can accommodate different kinds of paleontological data

- specimen-level sampling
- when the fossil data are only coded for first and last occurrences (stratigraphic ranges)
- when only stratigraphic range data are available

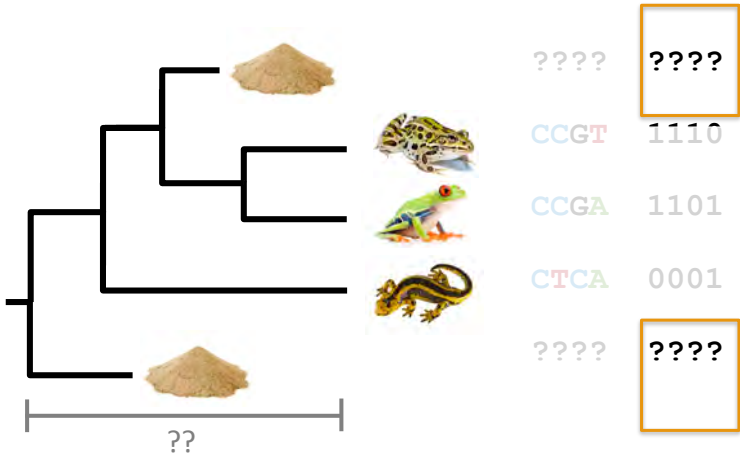


(Stadler et al., *J. Theor. Biol.* 2018)

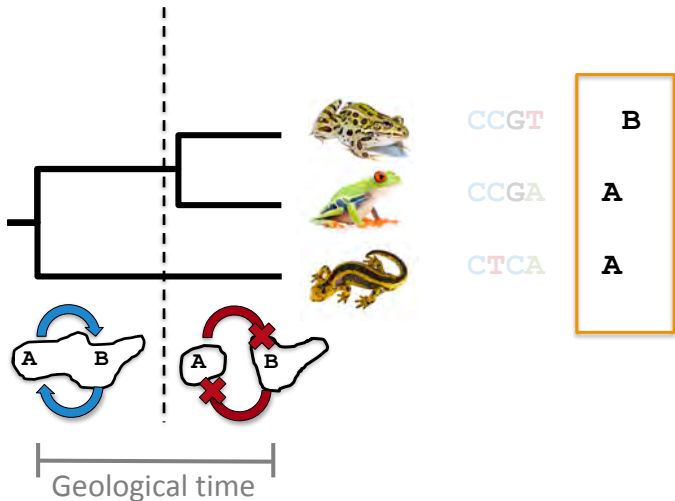
MOLECULES + MORPHOLOGY + FOSSILS



...but I study amphibians...



Molecules + biogeography + paleogeography

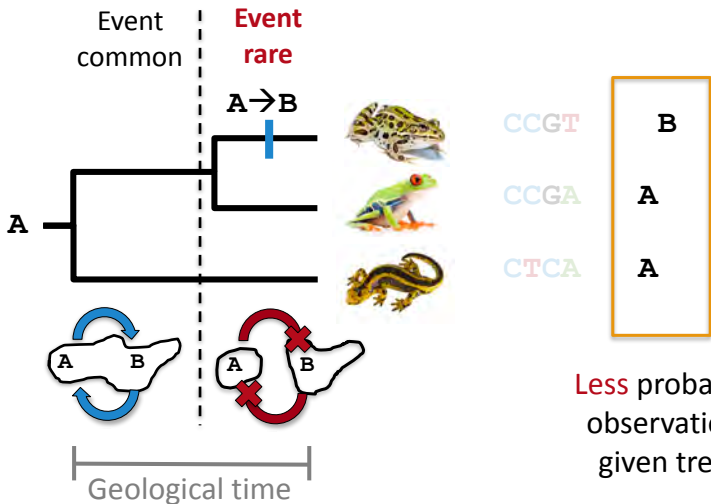


+ Paleogeography

Landis, 2016

(slides courtesy of M. Landis, <http://bit.ly/2aHqB4>)

Events should occur *before* areas split

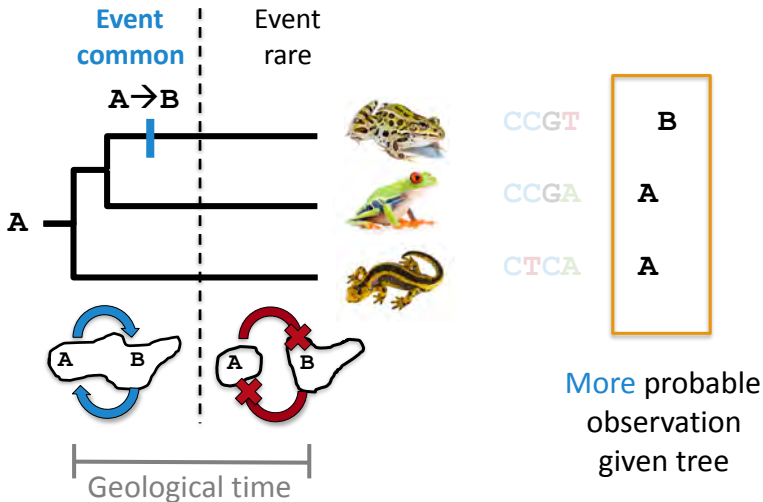


+ Paleogeography

Landis, 2016

(slides courtesy of M. Landis, <http://bit.ly/2aIHqB4>)

Events should occur *before areas split*

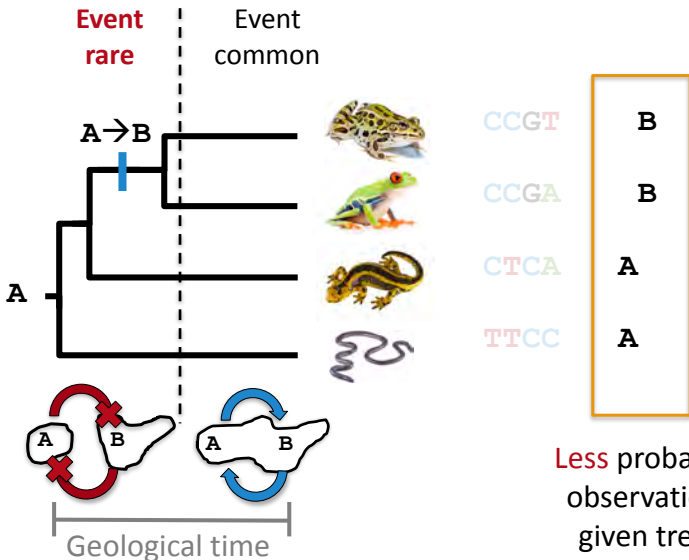


+ Paleogeography

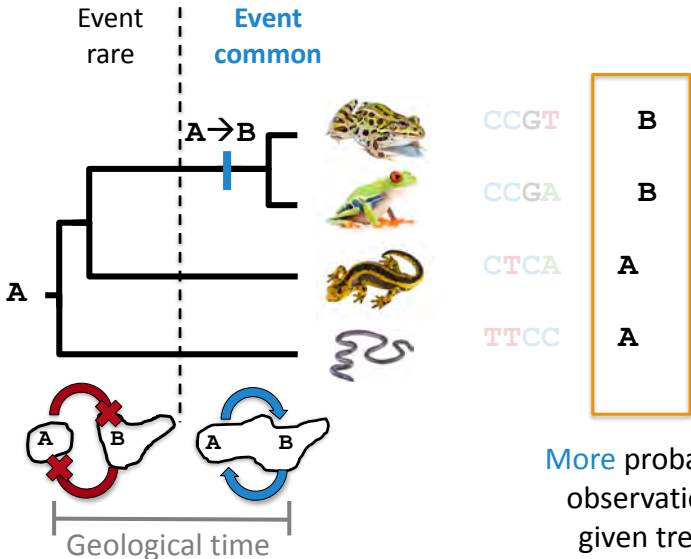
Landis, 2016

(slides courtesy of M. Landis, <http://bit.ly/2aIHqB4>)

Events should occur *after* areas merge



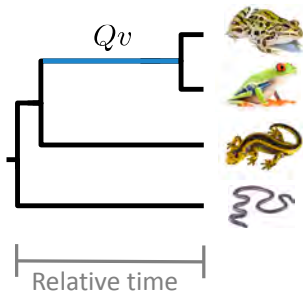
Events should occur *after* areas merge



BIOGEOGRAPHIC DATING

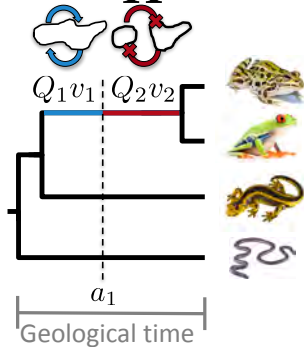
Constant Model

$$P_{ij}(v) = \exp\{Qv\}$$



Epoch Model

$$P_{ij}(\mathbf{v}) = \prod \exp\{Q_k v_k\}$$

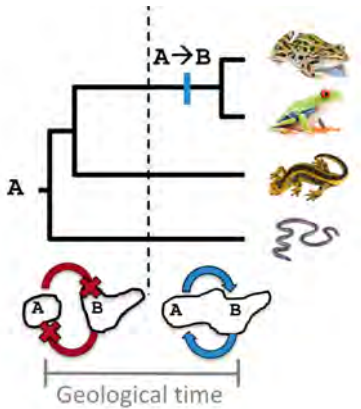


Epoch model Ree et al., 2005
Bielejec et al., 2014

BIOGEOGRAPHIC DATING

Fossil-free calibration

- data: molecular sequences
- data: biogeographic ranges
- empirical paleogeographic model that alters the rates of biogeographic change over time

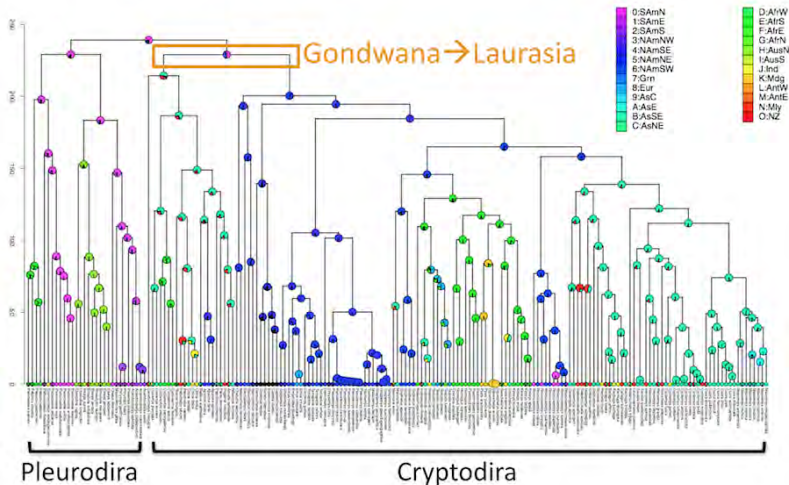


Landis. 2017. "Biogeographic Dating of Speciation Times Using Paleogeographically Informed Processes". *Systematic Biology*

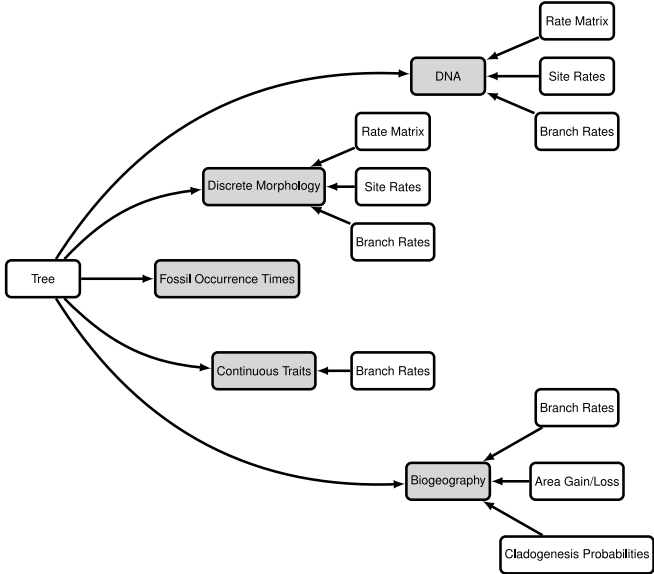
doi: [10.1093/sysbio/syw040](https://doi.org/10.1093/sysbio/syw040).

DATING + ANCESTRAL AREA RECONSTRUCTION

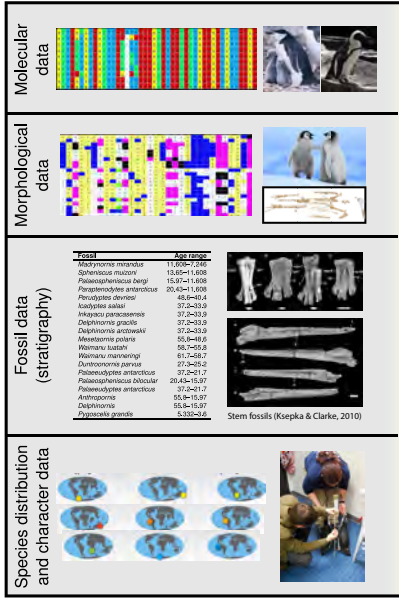
Ancestral area estimates (+G)



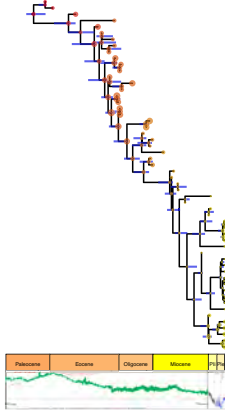
INTEGRATIVE BAYESIAN MODELING



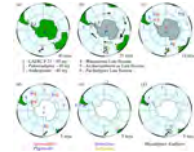
STATISTICAL SYNTHESIS



Statistical Inference



Phylogenetic relationships, divergence dates, and continuous trait reconstruction



Ancestral range reconstruction