Análise Estatística de Simuladores
Lecture 6: Approximate Bayesian computation (ABC)

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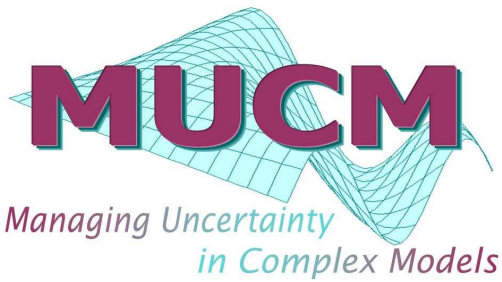


The University of Nottingham

Mini-course lecture notes

All the slides from the course will be made available at
`www.professores.uff.br/lbastos`

or from

`www.maths.nottingham.ac.uk/personal/pmzrdw`

Please email us with questions, comments, suggestions for improvements etc!

Contents

This lecture is all about a Monte Carlo method of calibration known as ABC (approximate Bayesian computation).

1. Stochastic modelling
2. ABC algorithm
3. Approximate MCMC
4. Dating primate divergence times

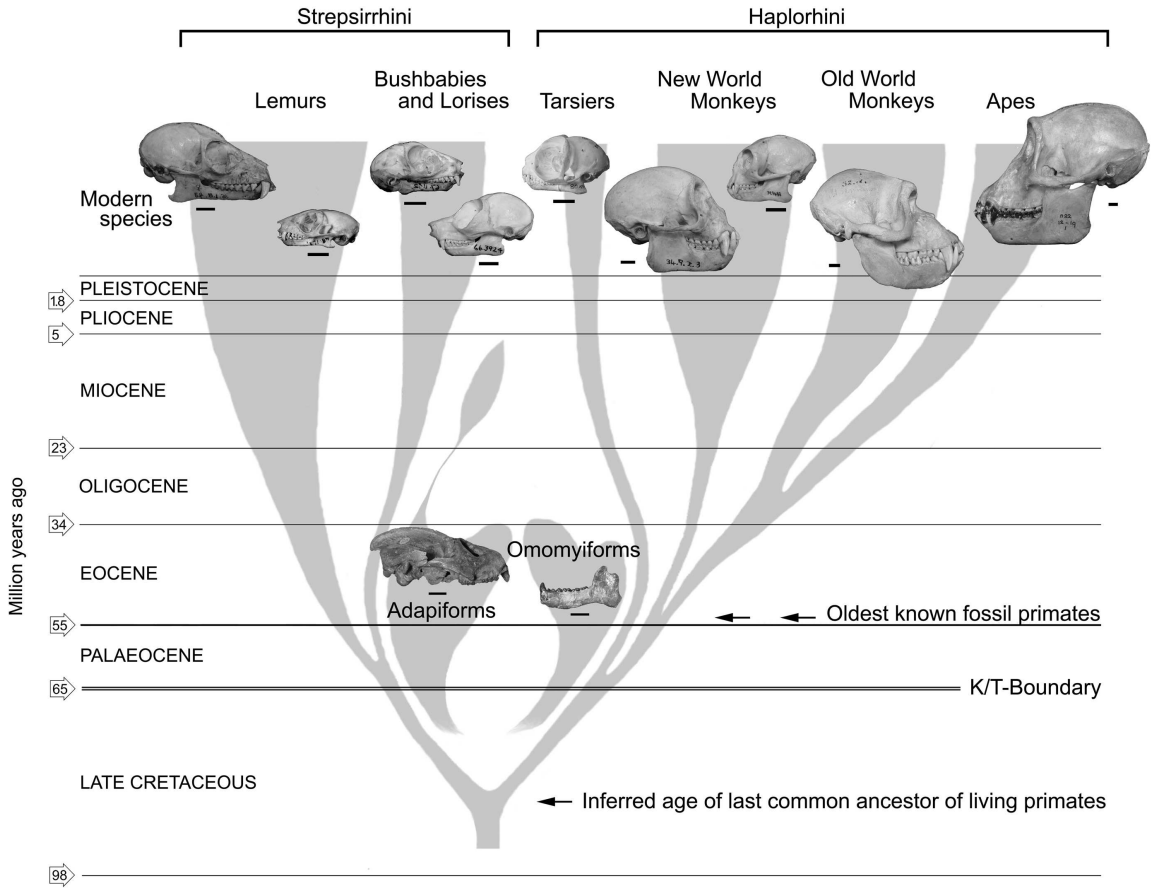
Stochastic modelling

Fitting to data

For forwards models we specify parameters θ and i.c.s and the model generates output X. Usually, we are interested in the inverse-problem, i.e., observe data $\mathcal{D}$, want to estimate parameter values.

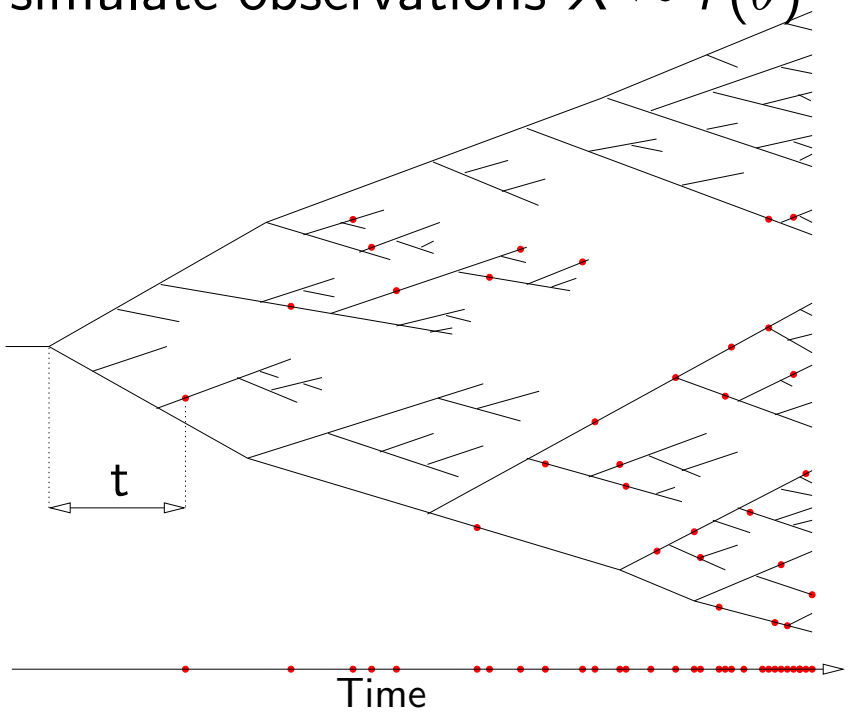
Different terminology:

- Calibration
- Data assimilation
- Parameter estimation
- Inverse-problem
- Bayesian inference



We now switch attention to stochastic computer models. Two types of statistical model:

- Prescribed models - likelihood function is specified $\pi(X|\theta)$
- Implicit models - mechanism to simulate observations $X \sim f(\theta)$



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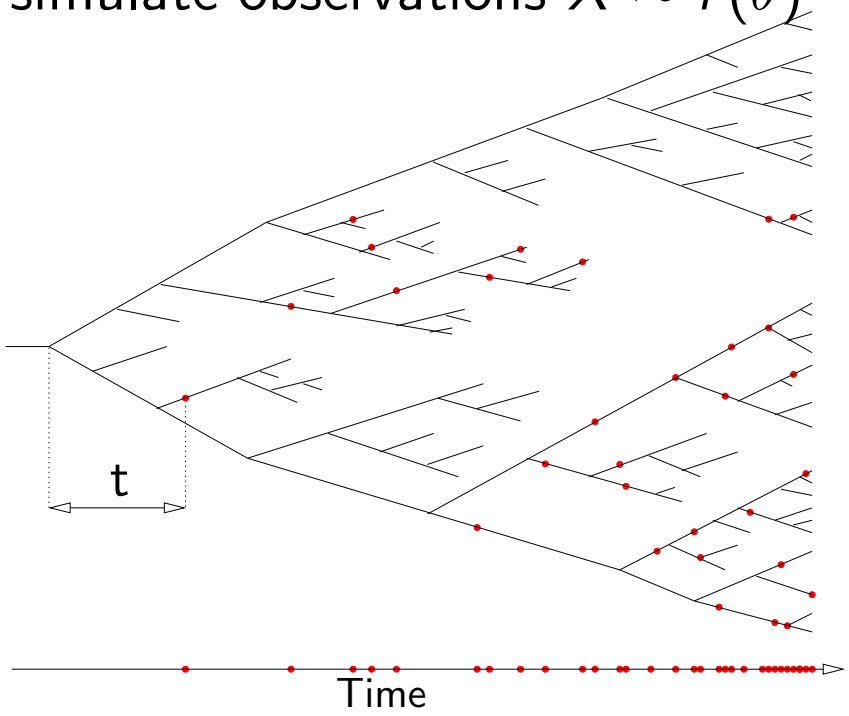
- Implicit models - mechanism to simulate observations $X \sim f(\theta)$

Implicit models give scientists more freedom to build complex models, and the increase in computer power has made their use more practicable.

Implicit models are popular in many disciplines, eg ecology, epidemiology, population biology, genetics.



Bayesian Inference

Aim to sample from the posterior distribution:

$$\pi(\theta|\mathcal{D}) \propto \frac{\text{prior} \times \text{likelihood}}{\text{evidence}} = \frac{\pi(\theta)\pi(\mathcal{D}|\theta)}{\pi(\mathcal{D})}.$$

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- The basic idea behind Monte Carlo methods is that instead of analytically calculating quantities of interest using the density $\pi(\theta)$, we instead sample from it and use the samples to approximate.
- For example, suppose we wish to find

$$\mathbb{E}f(\Theta) = \int f(\theta)\pi(\theta)\mathrm{d}\theta$$

If we can generate iid samples $\theta_1, \ldots, \theta_N \sim \pi(\theta)$ then we can use the Monte Carlo approximation

$$\mathbb{E}f(\Theta) \approx \frac{1}{N}\sum_{i=1}^{N} f(\theta_i)$$

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  - $\pi(\mathcal{D}|\theta)$ not even known up to a normalizing constant - completely intractable distribution.
  - completely intractable distributions can occur when you have highly dependent data arising from an underlying tree or graphical structure.
    - Population Genetics
    - Epidemiology
    - Evolutionary Biology

Approximate Bayesian Computation

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ABC methods are becoming popular in the biological sciences.

- Genetics - Siegmund *et al.* (DNA methylation in cancer cells); Foll *et al.* (using polymorphism markers to infer pop structure)
- Epidemiology - Blum and Tran (Cuban HIV-AIDS); Tanaka *et al.* (Tuberculosis)
- Population biology - Ratmann *et al.* (protein networks); Cornuet *et al.* (population history).

Likelihood-Free Inference

Rejection Algorithm

- Draw θ from prior $\pi(\cdot)$
- Accept θ with probability $\pi(\mathcal{D} \mid \theta)$

Accepted θ are independent draws from the posterior distribution, $\pi(\theta \mid \mathcal{D})$.

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Accepted θ are independent draws from the posterior distribution, $\pi(\theta \mid \mathcal{D})$.
If the likelihood, $\mathbb{P}(\mathcal{D}|\theta)$, is unknown:

'Mechanical' Rejection Algorithm

- Draw θ from $\pi(\cdot)$
- Simulate $X \sim f(\theta)$
- Accept θ if $\mathcal{D} = X$

Theorem: The rejection algorithm samples from the posterior

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$$\text{Then} \qquad \mathbb{P}(I = 1|\theta) = \pi(\mathcal{D}|\theta)$$

$$\text{So} \qquad \mathbb{P}(I = 1) = \int \mathbb{P}(I = 1|\theta)\pi(\theta)\mathrm{d}\theta$$

$$= \int \pi(\mathcal{D}|\theta)\pi(\theta)\mathrm{d}\theta$$

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$$= \int \pi(\mathcal{D}|\theta)\pi(\theta)\mathrm{d}\theta$$

$$\text{Hence} \qquad \pi(\theta|I = 1) = \frac{\mathbb{P}(I = 1|\theta)\pi(\theta)}{\mathbb{P}(I = 1)}$$

$$= \frac{\pi(\mathcal{D}|\theta)\pi(\theta)}{\int \pi(\mathcal{D}|\theta)\pi(\theta)\mathrm{d}\theta} = \pi(\theta|\mathcal{D})$$

Acceptance rate

The acceptance rate is $\mathbb{P}(\mathcal{D})$: the number of runs to get n observations is negative binomial, with mean $\frac{n}{\mathbb{P}(\mathcal{D})}$

This opens the opportunity for calculating Bayes factors comparing two different models, η_1 and η_2.

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Estimate $\mathbb{P}_{\eta 1}(\mathcal{D})$ by the acceptance rate when using η_1 etc. See Xavier Didelot's work for more details.

Approximate Bayesian Computation I

If $\mathbb{P}(\mathcal{D})$ is small, we will rarely accept any θ. Instead, there is an approximate version:

Approximate Rejection Algorithm

- Draw θ from $\pi(\theta)$
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This generates observations from $\pi(\theta \mid \rho(\mathcal{D}, X) < \delta)$:

- As $\delta \to \infty$, we get observations from the prior, $\pi(\theta)$.
- If $\delta = 0$, we generate observations from $\pi(\theta \mid \mathcal{D})$.

δ reflects the tension between computability and accuracy.

Approximate Bayesian Computation II

If the data are too high dimensional we never observe simulations that are 'close' to the field data.
Reduce the dimension using summary statistics, $S(\mathcal{D})$.

Approximate Rejection Algorithm With Summaries

- Draw θ from $\pi(\theta)$
- Simulate $X \sim \eta(\theta)$
- Accept θ if $\rho(S(\mathcal{D}), S(X)) < \delta$

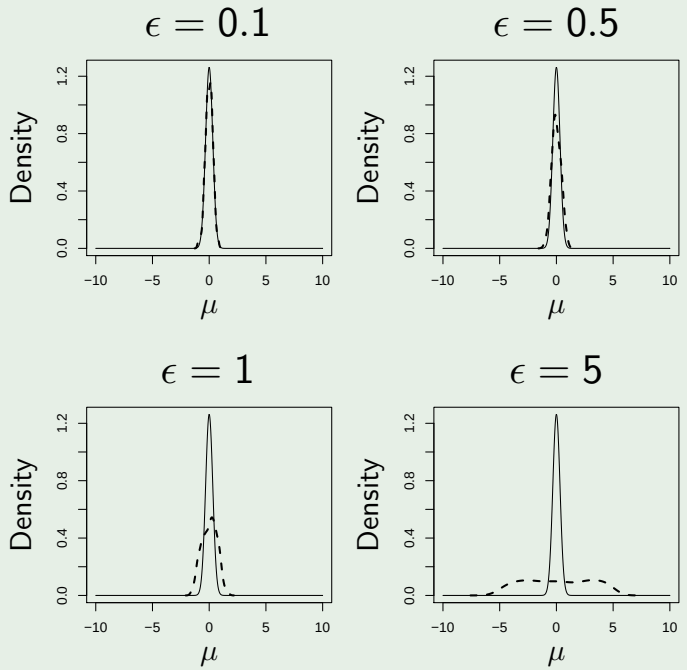
If S is sufficient this is equivalent to the previous algorithm (see Paul Fearnhead and Dennis Prangle's work for more details).

There are many other extensions: approximate MCMC, approximate SMC, approximate particle-MCMC, etc.

Example (Gaussian Distribution)

Suppose $X_i \sim N(\mu, \sigma^2)$, with σ^2 known, and give μ an improper flat prior distribution, $\pi(\mu) = 1$ for $\mu \in \mathbb{R}$.

1000 samples



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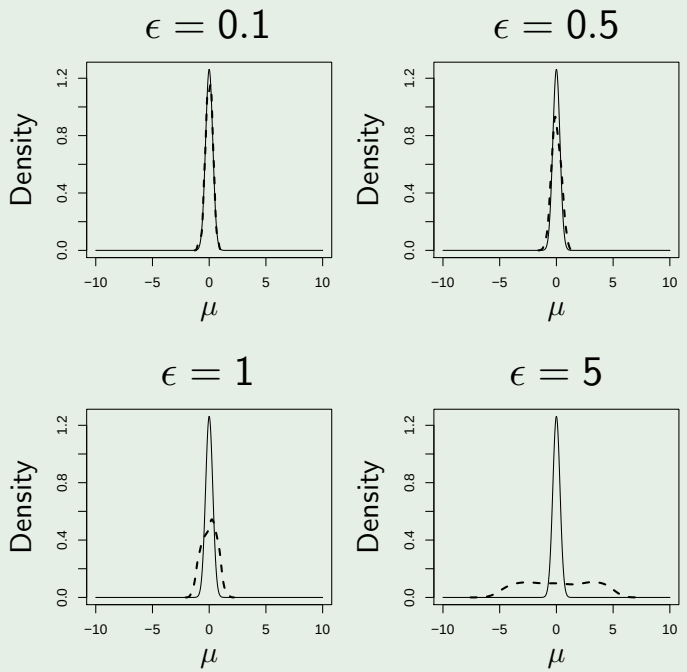

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- Simulate $X_i \sim N(\mu, \sigma^2)$
- Accept μ if $|\bar{x}| < \epsilon$.

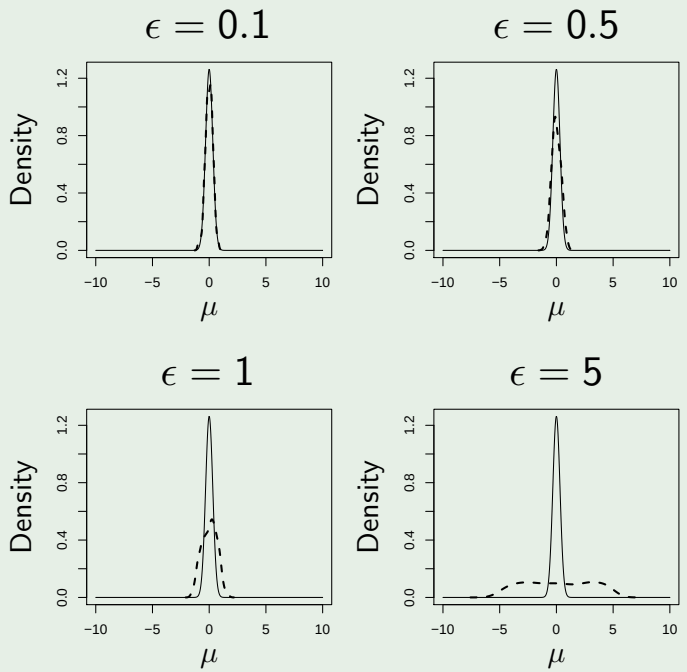
Then $\pi(\mu \mid |\bar{x}| \leq \epsilon) =$

$$\frac{\Phi\left(\frac{\epsilon-\mu}{\sqrt{\sigma^2/n}}\right) - \Phi\left(\frac{-\epsilon-\mu}{\sqrt{\sigma^2/n}}\right)}{2\epsilon}$$

and

$$\mathbb{V}ar(\mu \mid |\bar{x}| \leq \epsilon) = \mathbb{V}ar(\mu \mid \bar{x} = 0) + \frac{\epsilon^2}{3}$$

1000 samples



Markov chain Monte Carlo (MCMC)

Metropolis-Hastings Algorithm

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Suppose we wish to simulate from a (possibly multivariate) distribution $\pi(x)$. We need to find a transition kernel $Q(x, y)$ such that

- Simulation of a Markov chain $\{X_1, X_2, \ldots\}$ with transition kernel Q is straightforward.
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The Metropolis-Hastings algorithm tells us how to build transition kernels such that the Markov chain converges to the distribution $\pi(x)$.

Metropolis-Hastings Algorithm - II

Metropolis-Hastings Algorithm

1. Choose a starting location $X_0 = x_0$.
2. Suppose at time t, we have $X_t = x$. Propose a candidate value y from proposal distribution $q(x, y)$.
3. Calculate the 'Metropolis-Hastings acceptance probability' $\alpha(x, y)$ given by

$$\alpha(x, y) = \min\left(1, \frac{\pi(y)q(y, x)}{\pi(x)q(x, y)}\right)$$

4. Accept the move with probability $\alpha(x, y)$. If the move is rejected, stay at x. That is, we set

$$X_{t+1} = \begin{cases} y & \text{with probability } \alpha(x, y) \\ x & \text{with probability } 1 - \alpha(x, y) \end{cases}$$

Approximate MCMC for Bayesian inference

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Metropolis-Hastings(MCMC) Algorithm

- Suppose we are currently at θ. Propose θ' from density $q(\theta, \theta')$.
- Calculate

$$h(\theta, \theta') = \min\left(1, \frac{\pi(\theta')\pi(D|\theta')q(\theta', \theta)}{\pi(\theta)\pi(D|\theta)q(\theta, \theta')}\right).$$

- Accept the move to θ' with probability $h(\theta, \theta')$, else stay at θ.

This will simulate a Markov chain $\{\theta_1, \theta_2, \ldots\}$ which has stationary distribution $\pi(\theta|\mathcal{D})$.

Approximate MCMC (Marjoram *et al.*)

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However, we are assuming that we have a complex computer model and don't know the likelihood function $\pi(\mathcal{D}|\theta)$.

Instead, we can approximate this ratio using simulation giving us the approximate MCMC algorithm.

Approximate Metropolis-Hastings Algorithm

- Suppose we are currently at θ. Propose θ' from density $q(\theta, \theta')$.
- Simulate X from $f(\theta')$.
- If $\rho(\mathcal{D}, X) \leq \epsilon$, calculate

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$\exists$ approximate sequential Monte Carlo methods (see Sisson *et al.*).

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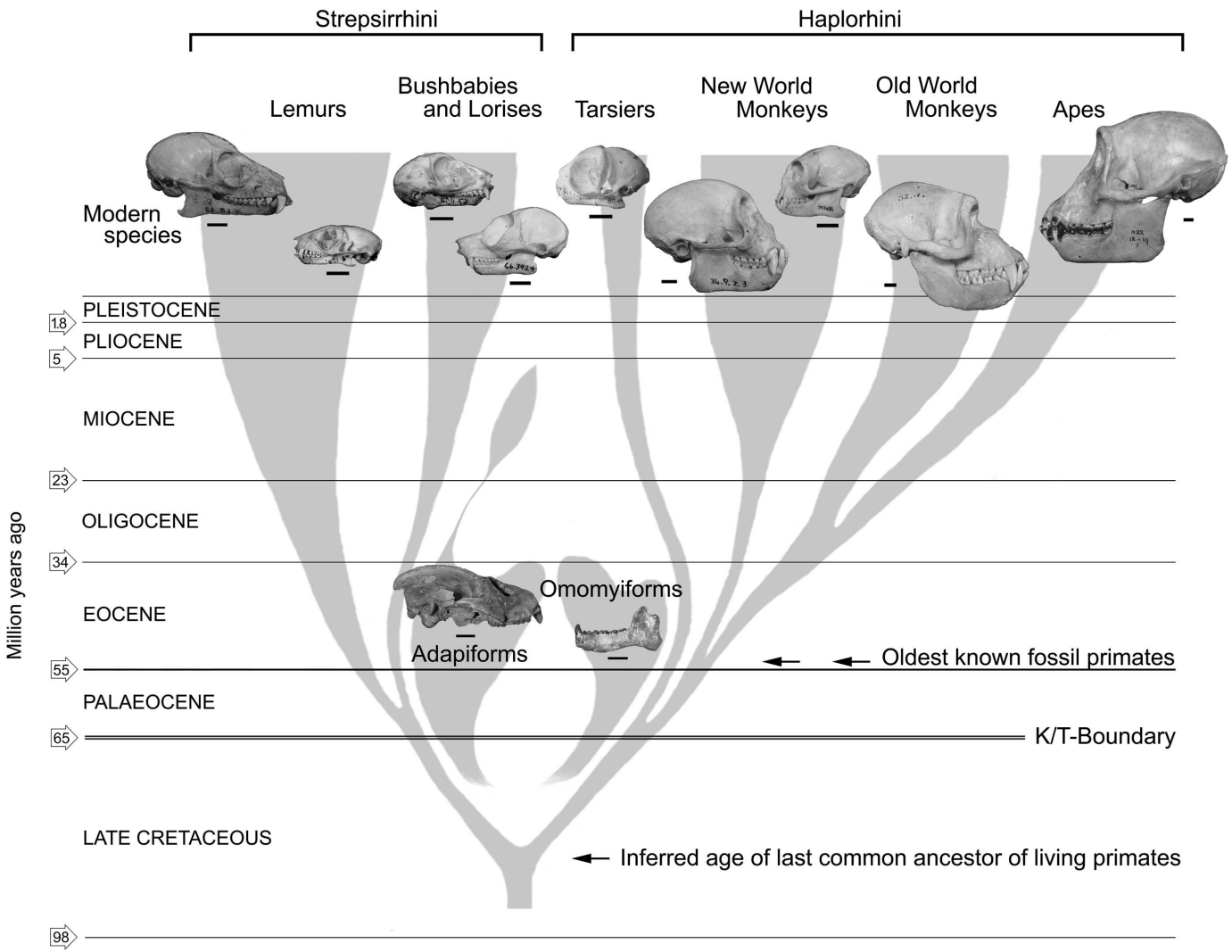
However, despite numerous uses in application papers, there are many unresolved issues with ABC methods

- The methods are approximate with the quality of the approximation unknown in general
  - Wilkinson 2009 partially answers this question.
- Several implementation decisions are required. Choice of
  - metric
  - tolerance
  - summary statistic, etc

Estimating the Primate Divergence

Geologic time



Reconciling molecular and fossil records?

Molecules vs morphology

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  - Fossil evidence can only provide a lower bound on the age.
  - Dates the appearance of morphological differences.
  - Prevailing view: the first appearance of a species in the fossil record is "... accepted as more nearly objective and basic than opinions as to the time when the group really originated", Simpson, 1965.
  - Oldest primate fossil is 55 million years old.

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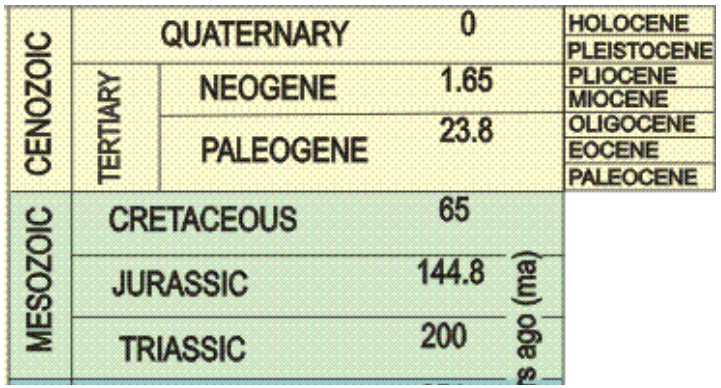
- Did primates evolve to fill an evolutionary niche?



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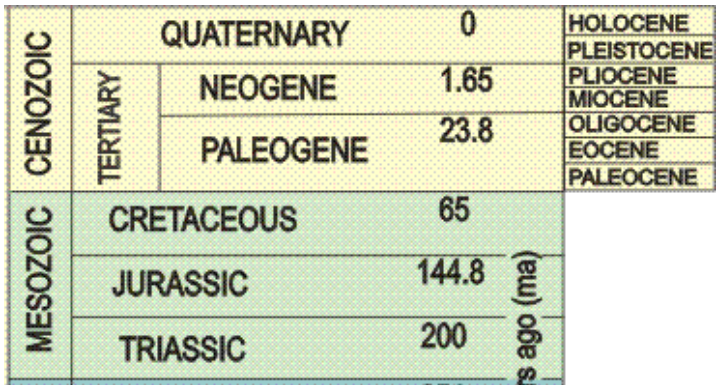

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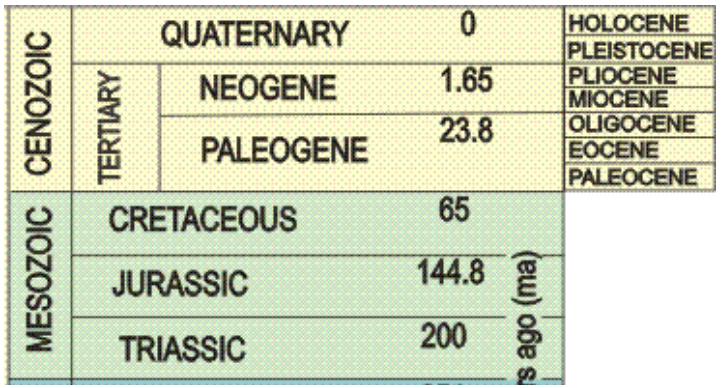

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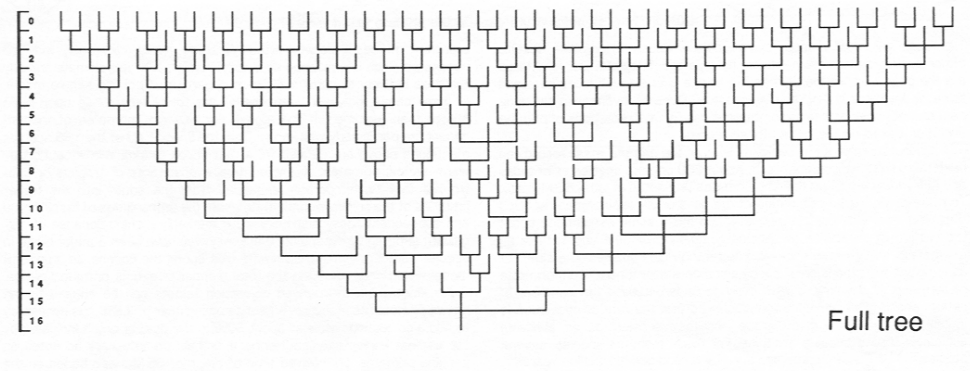
- Did primates evolve to fill an evolutionary niche?
  - Timing of primate evolution relative to evolution of angiosperms and large fruit bearing plants.
  - Divergence time has consequences for theories about the dispersion of primates to the new world.

Why is this difficult?

Non-repeatable event



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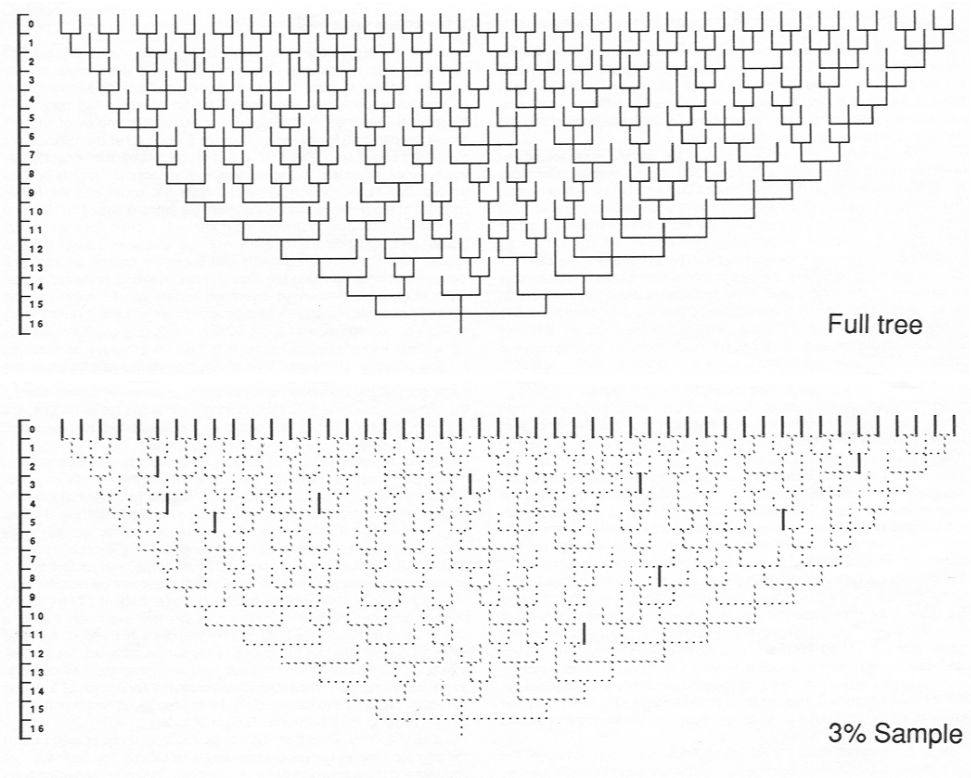

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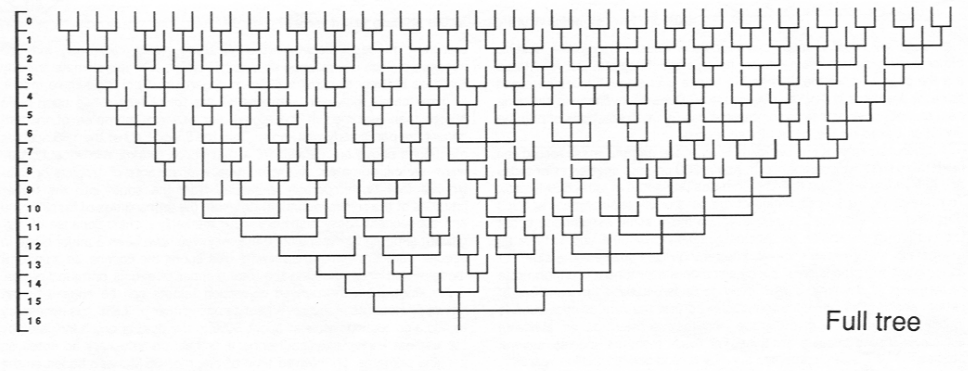
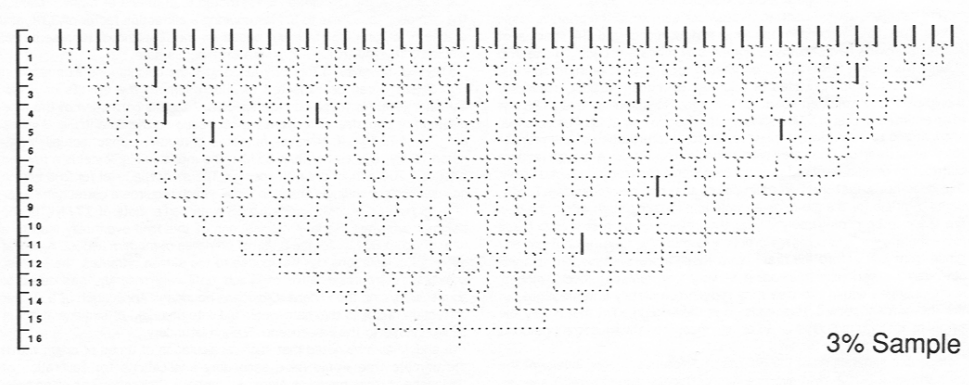
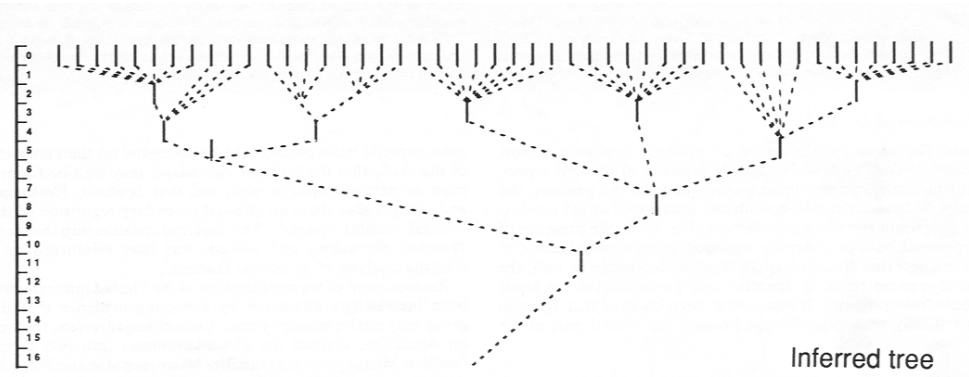






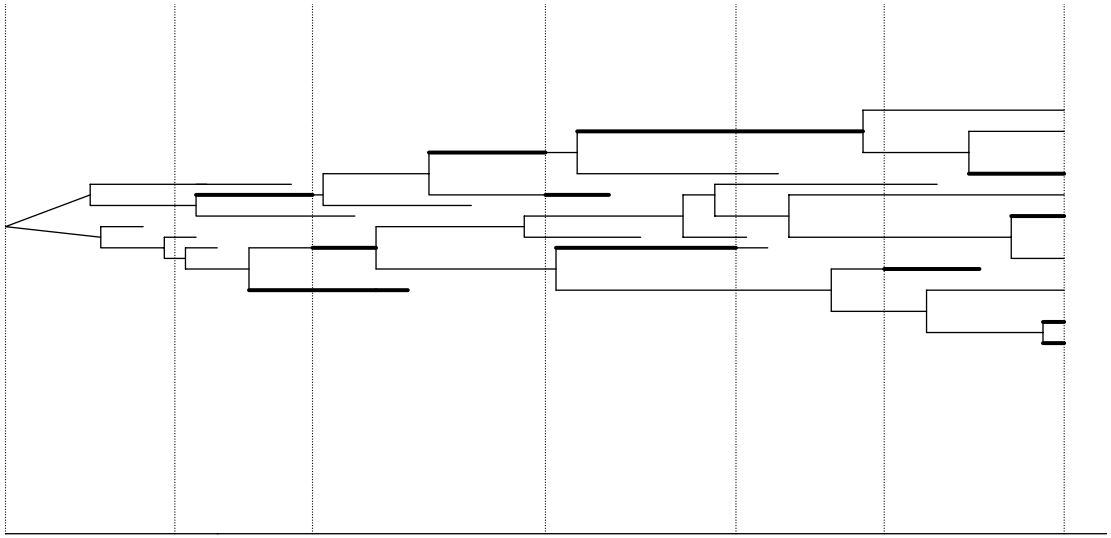
Data

Robert Martin and Christophe Soligo

Epoch	k	Time at base of Interval k	Primate fossil counts (D_k)	Anthropoid fossil counts (S_k)
Late-Pleistocene	1	0.15	22	22
Middle-Pleistocene	2	0.9	28	28
Early-Pleistocene	3	1.8	30	30
Late-Pliocene	4	3.6	43	40
Early-Pliocene	5	5.3	12	11
Late-Miocene	6	11.2	38	34
Middle-Miocene	7	16.4	46	43
Early-Miocene	8	23.8	34	28
Late-Oligocene	9	28.5	3	2
Early-Oligocene	10	33.7	22	6
Late-Eocene	11	37.0	30	2
Middle-Eocene	12	49.0	119	0
Early-Eocene	13	54.8	65	
Pre-Eocene	14		0	

- The oldest primate fossil is 54.8 million years old.
- The oldest anthropoid fossil is 37 million years old.

Speciation



Used an inhomogeneous binary Markov branching process to model evolution:

- Assume each species lives for a random period of time $\sigma \sim \text{Exponential}(\lambda)$
- Specify the offspring distribution; if a species dies at time t replace it by L_t new species where $\mathbb{P}(L_t = 0) = p_0(t), \mathbb{P}(L_t = 2) = p_2(t)$.

Offspring distribution

If a species dies at time t replace it by L_t new species where $\mathbb{P}(L_t = 0) = p_0(t), \mathbb{P}(L_t = 2) = p_2(t)$.

- Determine the offspring probabilities by fixing the expected population growth $\mathbb{E}(Z(t)) = f(t; \boldsymbol{\lambda})$ and using the fact that

$$\mathbb{E}(Z(t) = n | Z(0) = 2) = 2 \exp\left(\lambda \int_0^t (m(u) - 1) du\right)$$

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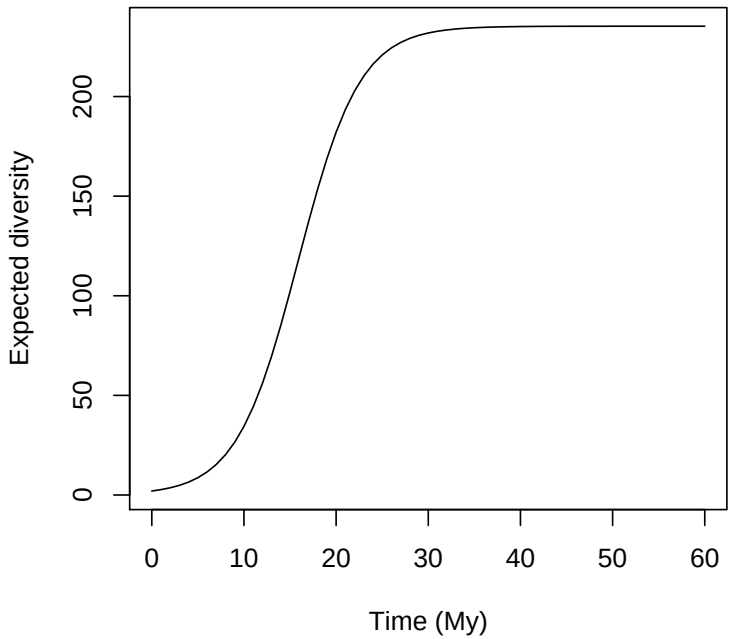
For example, assume logistic growth and set

$$\mathbb{E}Z(t) = \frac{2}{\gamma + (1 - \gamma)\exp(-\rho t)}$$

Treat γ and ρ as unknown parameters and infer them in the subsequent analysis.



Fossil Find Model

Recall that time is split into geologic epochs. We have two different models for the number of fossils found in each epoch $\{D_i\}$, given an evolutionary tree $\mathcal{T}$.

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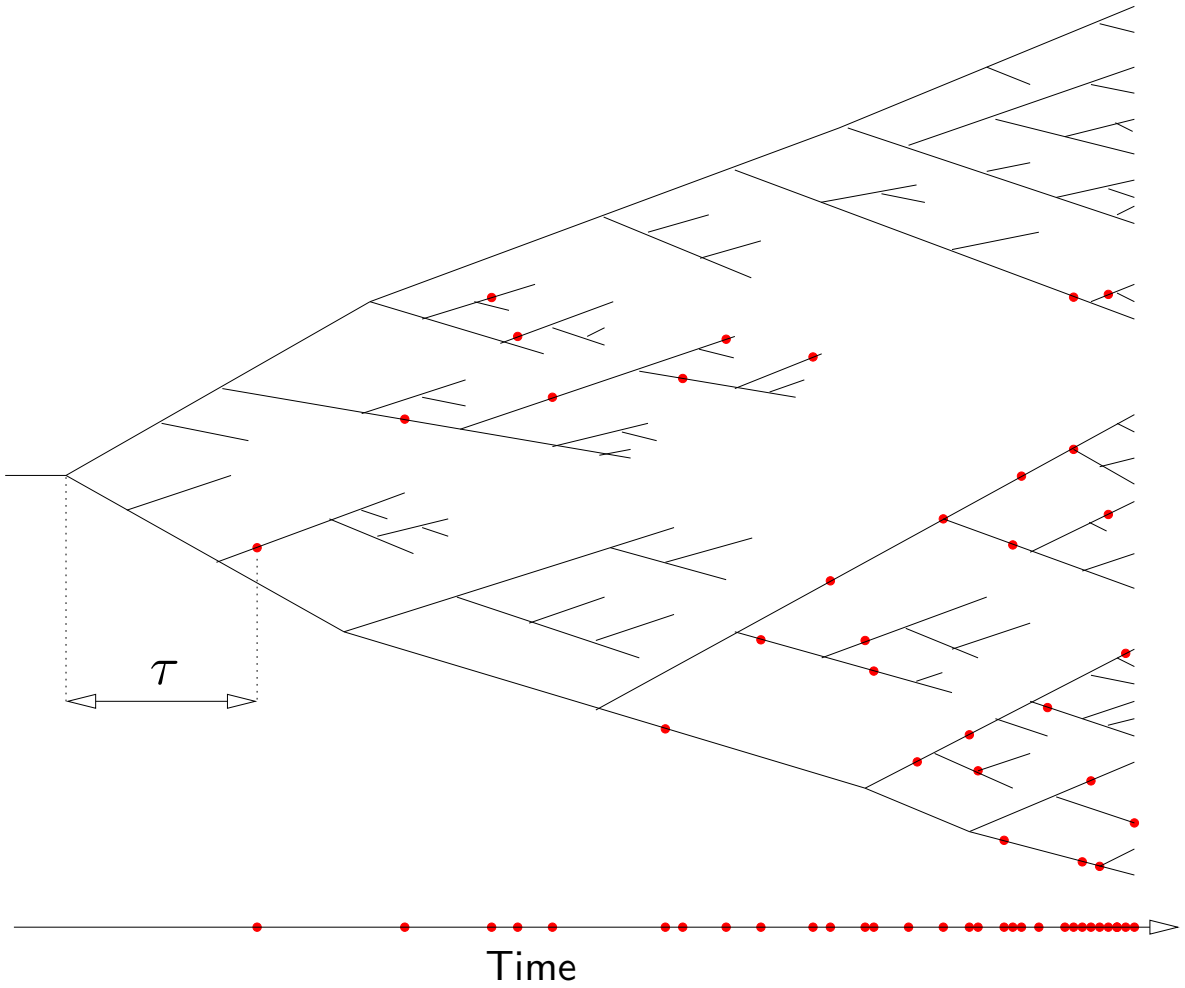
NOTE: Sampling rates vary for each epoch - accounts for variable sampling, e.g., pull of the recent

Specify the divergence time

Assume

- the primates diverged $54.8 + \tau$ million years ago.



Prior Distributions

We give all parameters prior distributions:

- Temporal gaps between the oldest fossil and the root of the primate and anthropoid trees $\tau \sim U[0, 100]$ and $\tau^* \sim U[0, 100]$.
- Expected life duration of each species $1/\lambda \sim U[2, 3]$
- Growth parameters $\gamma \sim [0.005, 0.015]$ and $\rho \sim U[0, 0.5]$.
- Sampling fractions $\alpha_i \sim U[0, 1]$ (or sampling rates $\beta_i \sim \Gamma(a, b)$).

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The likelihood function $\mathbb{P}(\mathcal{D}|\theta)$ is intractable.

$\Downarrow$

MCMC, IS, etc, not possible!
So we use ABC instead.

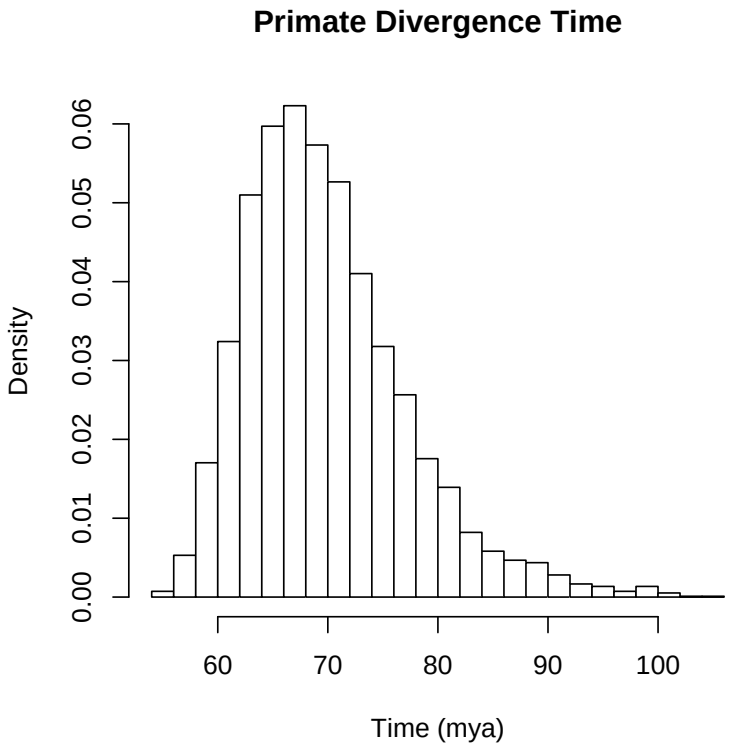
ABC choices

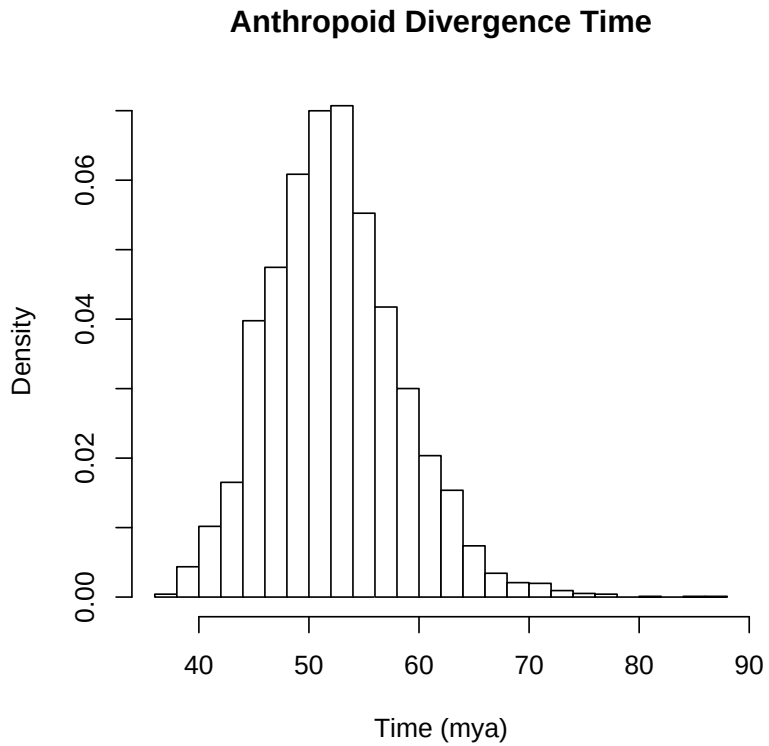
- Metric

$$\rho(\mathcal{D}, \mathcal{D}') = \sum_{i=1}^{14} \left| \frac{D_i}{D_+} - \frac{D'_i}{D'_+} \right| + \left| \frac{D'_+}{D_+} - 1 \right| + \left| \frac{N'_0}{N_0} - 1 \right|$$

- Tolerance: use the smallest feasible value $\delta = 0.1$
- No summaries here

Results





Modelling the K-T crash causes shorter tails in the posterior distribution of the divergence times.

Uncertainty in the data

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On top of this, there is uncertainty regarding

- whether a bone fragment represents a new species, e.g., homo florensis (the hobbit man), or a microcephalic human, etc?
- whether two bone fragments represent the same species
- which epoch the species should be assigned to.
- ....

None of these potential sources of errors are accounted for in the model.

Uncertainty in the model

Modelling inevitably involves numerous subjective assumptions. Some of these we judge to be less important.

- Binary trees
- Splitting rather than budding
- Memoryless age distribution
- Etc.

Other assumptions are potentially more influential, particularly where features have been ignored.

- Early Eocene warming (the Paleocene-Eocene Thermal Maximum)
- Warming in the mid-miocene
- Small mass-extinction events in the Cenozoic

We assumed logistic growth for the diversity, ignoring these smaller fluctuations which are likely to be important for the preservation of fossils in well sampled regions.

Choice of metric

We know that the data from some epochs is more reliable:

- Presumably classification and dating errors are more likely in well sampled epochs - any fossil that is possibly a Cretaceous primate is likely to be well studied.
- Similarly, large D_i presumably have a more variable error than small values of D_i.

Similarly, we know the computer model prediction is more unreliable in some epochs.

- We ignored warm periods in the Eocene and Miocene. During these times primates are believed to have moved away from the tropics, perhaps allowing for more speciation (due to additional space and resources).
- The majority of primate fossils come from the UK, US, France and China, despite our belief that primates originated in the Africa and the observation that nearly all extant species live in tropical or subtropical regions.

Choice of metric

Our analysis used a metric which contained the total variation distance between the two sets of proportions

$$\rho(\mathcal{D}, \mathcal{D}') = \sum_{i=1}^{14} \left| \frac{D_i}{D_+} - \frac{D'_i}{D'_+} \right| + \left| \frac{D'_+}{D_+} - 1 \right| + \left| \frac{N'_0}{N_0} - 1 \right|$$

We can rewrite the variation distance part as

$$\sum_{i=1}^{14} \left| \frac{D_i}{D_+} - \frac{D'_i}{D'_+} \right| = \sum \left| \frac{D'_i}{D'_+} \right| \left| \frac{D'_+}{D_+} \frac{D_i}{D'_i} - 1 \right|$$

so that the contribution from each epoch is weighted by $\left| D'_i / D'_+ \right|$.

Unfortunately, we can see that $\frac{D'_+}{D_+}$ occurs in every weight, which is undesirable.

Also, each term is given equal weight, hence assuming an equal level of accuracy.

An improved metric

In theory, we can account for all these issues by using the generalised ABC algorithm. We could use an acceptance probability of the form

$$\pi_\epsilon(\mathcal{D}') = \pi(N_0'|N_0) \prod_{i=1}^{14} \pi_i(D_i'|D_i)$$

where $\pi_i(D_i'|D_i)$ is the density of the error on D_i.
In practice, this is a difficult exercise in elicitation in order to specify the errors, and to convolve all the different sources of error.

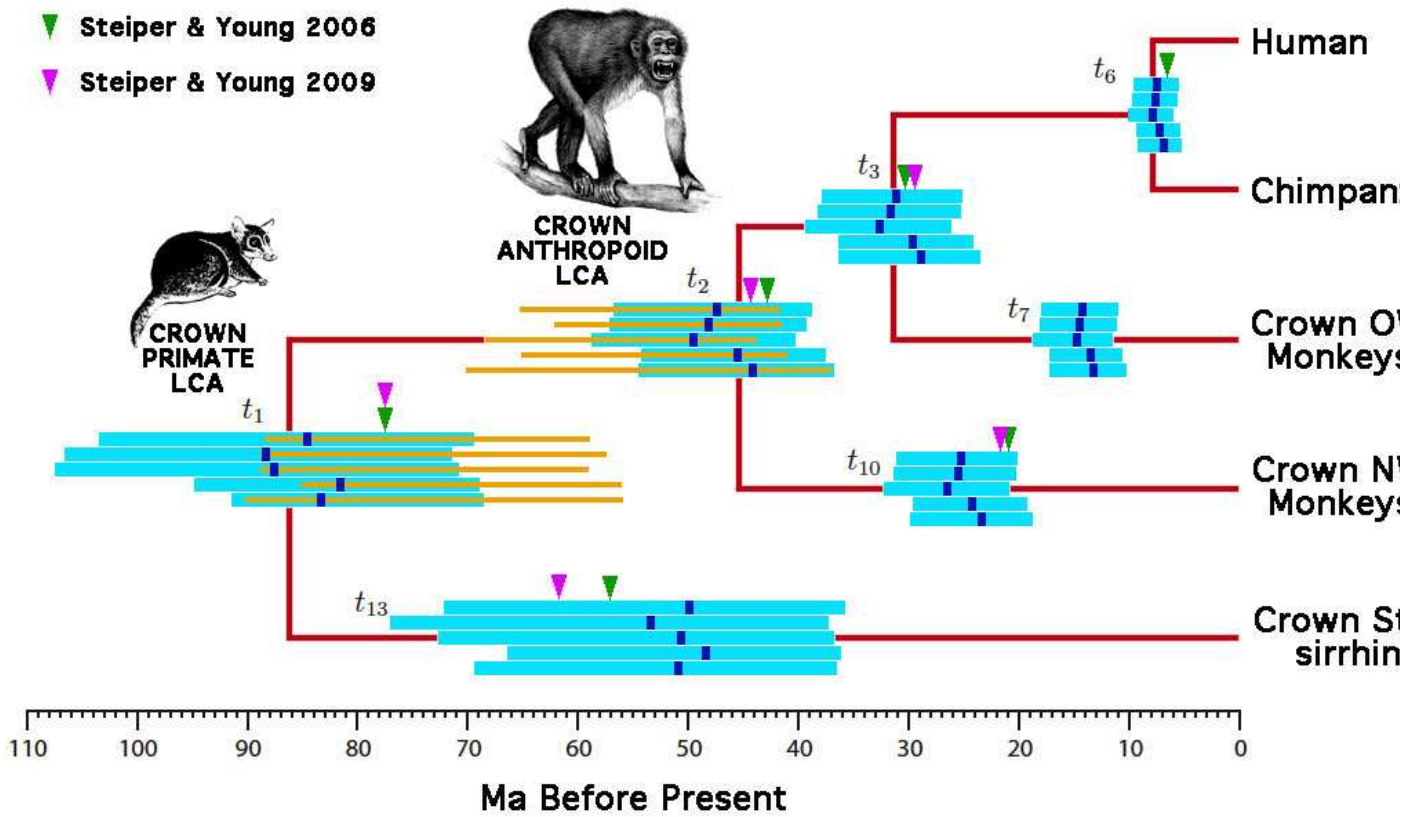
It is also a difficult computational challenge. Two ideas that help:

- We can use the fact that we know the distribution of D_i given N_i, to help break down the problem (e.g. we could accept the tree with probability $\prod \pi(D_i|N_i)$).
- Sequential particle methods can be used (plain SMC, not ABC-SMC).

Results of joint analysis

Wilkinson, Steiper, etal 2010

We can combine fossil divergence time estimates with genetic evidence to estimate the shape of the primate phylogeny



Extension results

Using just the fossil record, we find

- 95% CI for primate divergence time is $[83.4, 54.8]$ Mya.
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Combining these estimate with dna evidence we find

- 95% CI for primate divergence time is $[106.8, 69.2]$ Mya
- 95% CI for anthropoid divergence time is $[56.4, 38.8]$ Mya.
- the human-chimp divergence occured $[9.6, 5.7]$ Mya.

Summary

Approximate Bayesian computation (ABC) algorithms provide a likelihood-free approach to inference.

- ABC methods directly approximate the posterior distribution, whereas we use emulators to approximate the simulator.
- ABC methods are trivial to apply and can be used on any cheap stochastic model
- Care must be taken to ensure that a sensible tolerance and metric are used.

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Thank you for listening!

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- MUCM toolkit, available at `http://mucm.aston.ac.uk/MUCM/MUCMToolkit/`