

# **Brownian motion models, multiple characters, and phylogenies**

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NIMBioS Evol Quant Gen tutorial

# What will approximate change of quantitative characters?

- ... when it occurs by genetic drift of pre-existing alleles?
- ... when it also occurs by mutation to new alleles?
- ... when variable selection affects the alleles at each locus?
- ... when selection is on the fitness based on the whole phenotype?

# Edwards and Cavalli-Sforza's approximation



Luca Cavalli-Sforza (and Edwards), 1963



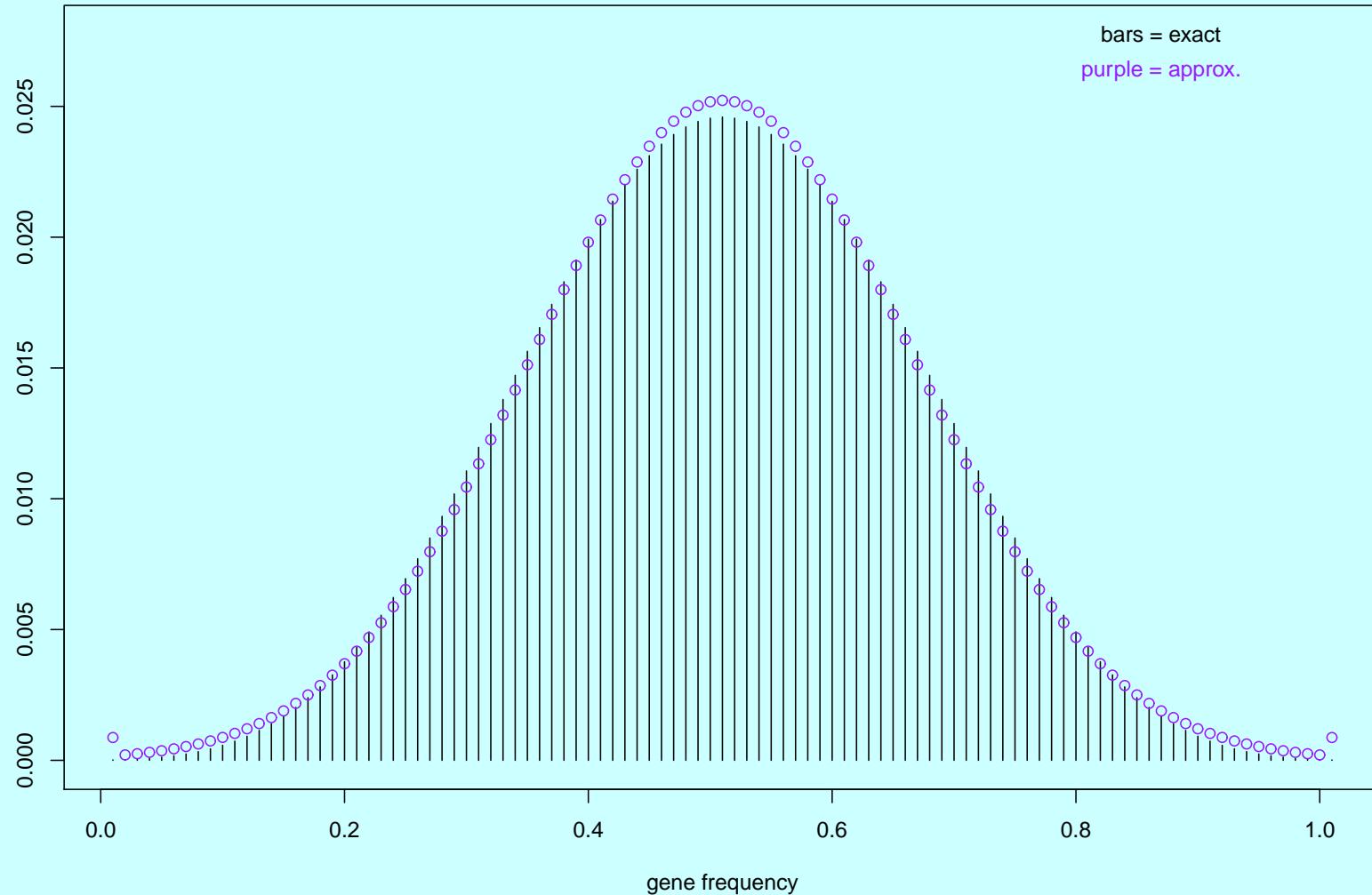
Anthony Edwards, 1970

The expectation of gene frequency change in one generation (under pure genetic drift without mutation) is zero. The variance is the binomial variance

$$E[(\Delta p)^2] = \frac{p(1-p)}{2N_e}$$

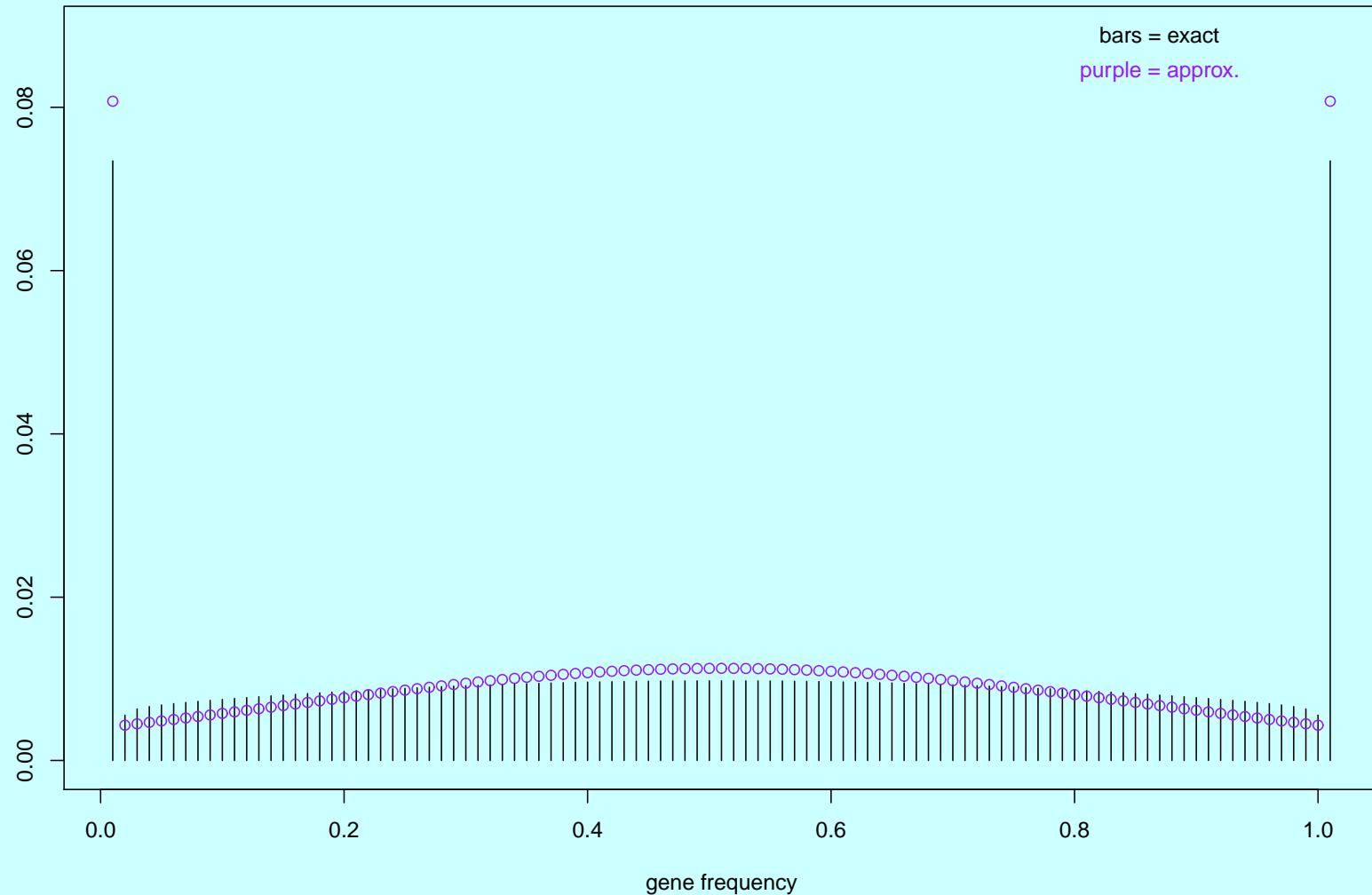
That variance is not constant: it varies with  $p$  (in a parabola), but maybe we can roughly approximate it by dealing with the case where all populations have roughly similar gene frequencies, so the variances are nearly the same. Maybe. Roughly.

# How good is this?



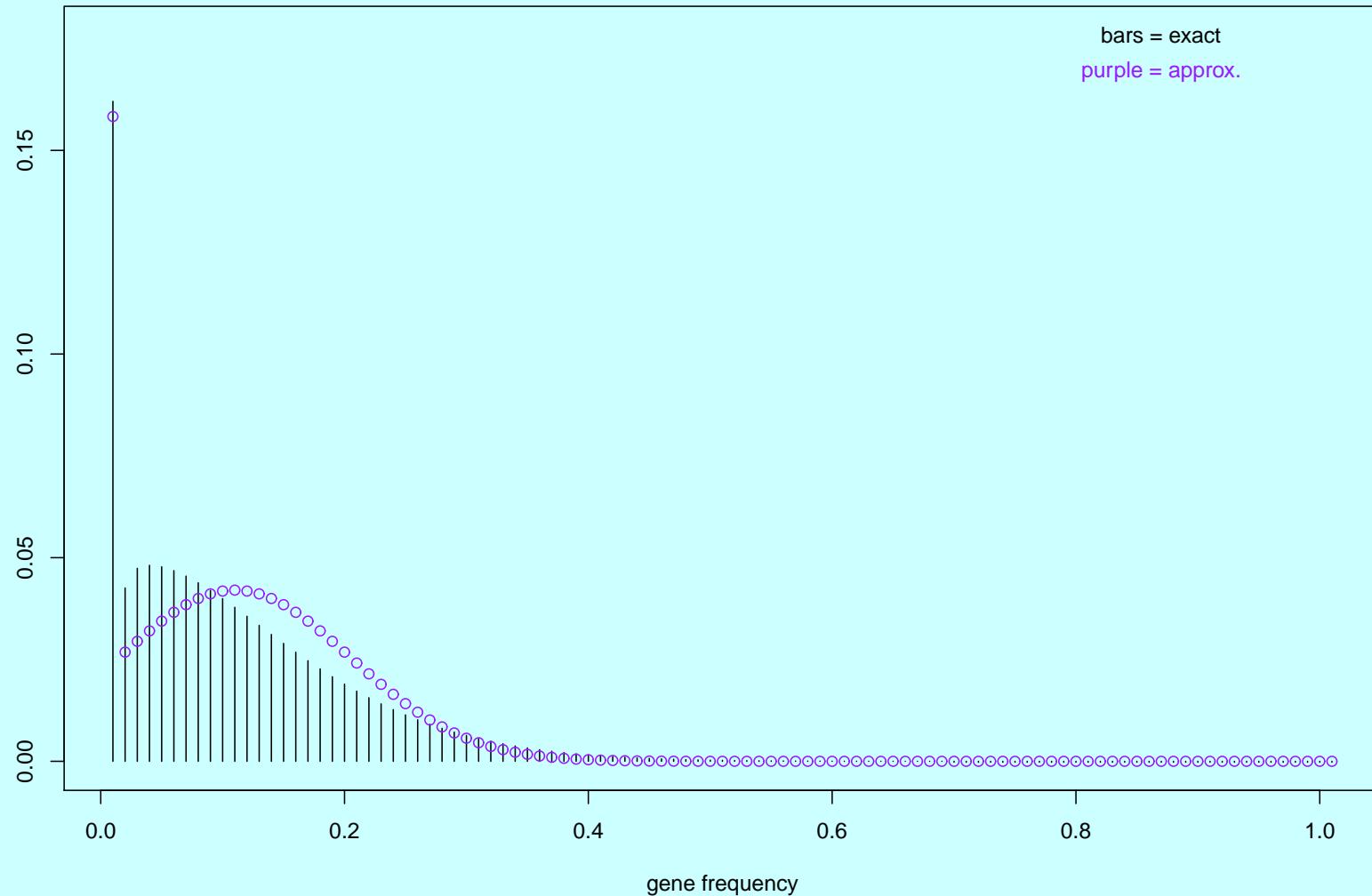
Starting with  $p = 0.5$ , after 10 generations in a population of size 50.

# How good is this?



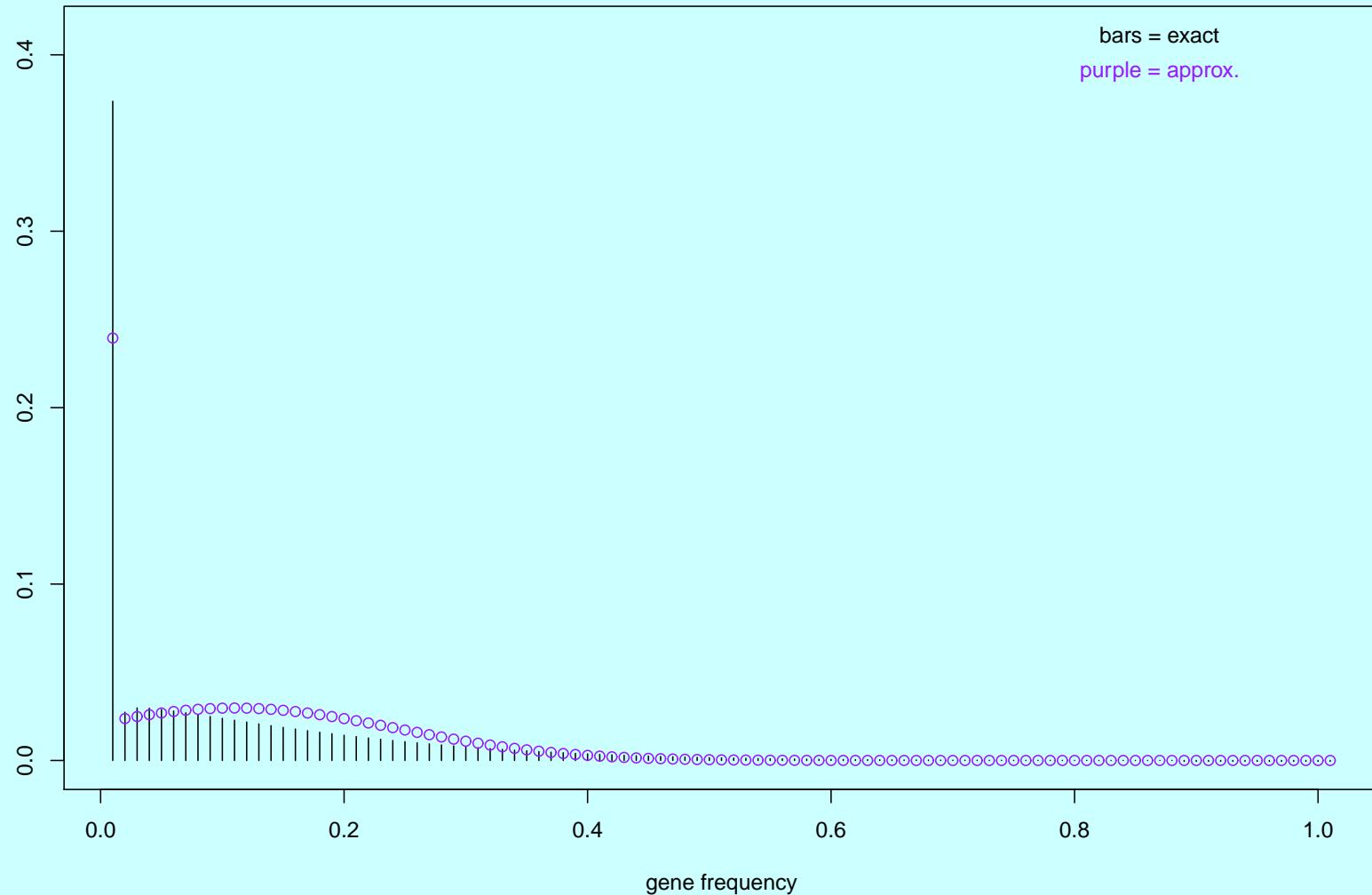
Starting with  $p = 0.5$ , after 50 generations in a population of size 50.

# How good is this?



Starting with  $p = 0.1$ , after 10 generations in a population of size 50.

# How good is this?



Starting with  $p = 0.1$ , after 20 generations in a population of size 50.

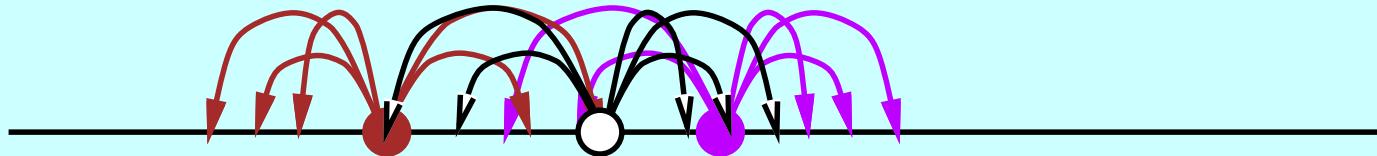
## What about a quantitative character?

If a quantitative character is a sum of contributions from a number of loci, then if the individual locus gene frequencies have their change approximated by Brownian Motion, the linear combination will also change by Brownian motion. This works for multiple alleles.

- if there is any dominance, there will be some nonlinearity and the approximation will be less good.
- Epistasis can cause even more trouble.

First discussed by me (Felsenstein, 1973).

## But, if there are mutations making incremental changes ..



... as we saw with the discussion of quantitative characters, if a relatively constant genetic variance is maintained, and mutations have additive effects, then genetic drift will cause the mean to change in a random walk close to Brownian Motion.

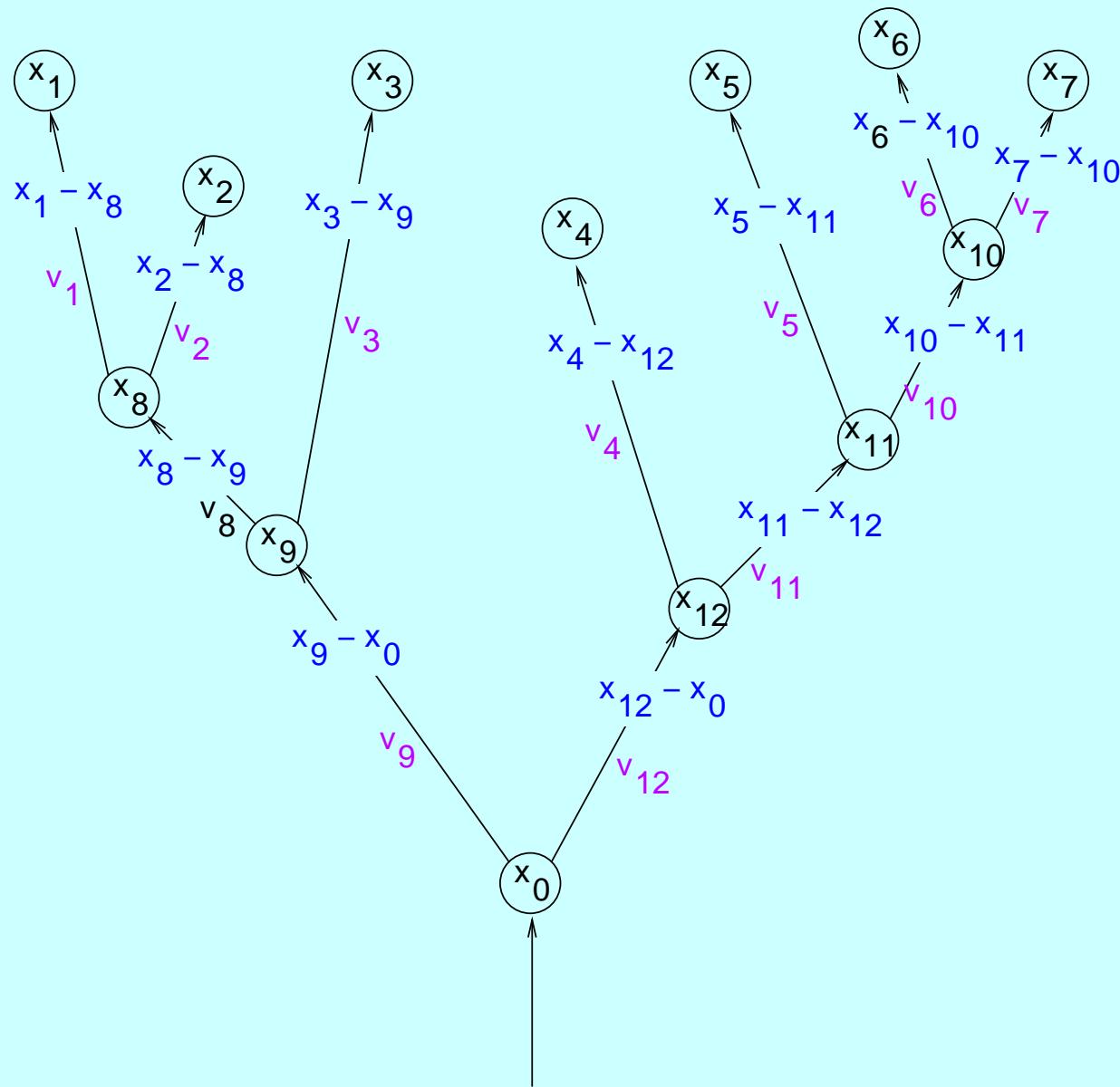
*However*, if one approaches some limit where most mutations oppose movement to it, and there are no mutations allowing you to go past that limit, this approximation will be poor.

## Brownian motion is mathematically tractable

You can easily compute transition probabilities from one value to another, since the net change after “time”  $t$  is normal, with mean zero and variance  $\sigma^2 t$ , and changes in successive time intervals are independent.

When two lineages share a period of common ancestry, the resulting tip species have phenotypes that covary, the covariance being the variance expected during their shared ancestry.

# Brownian motion along a tree



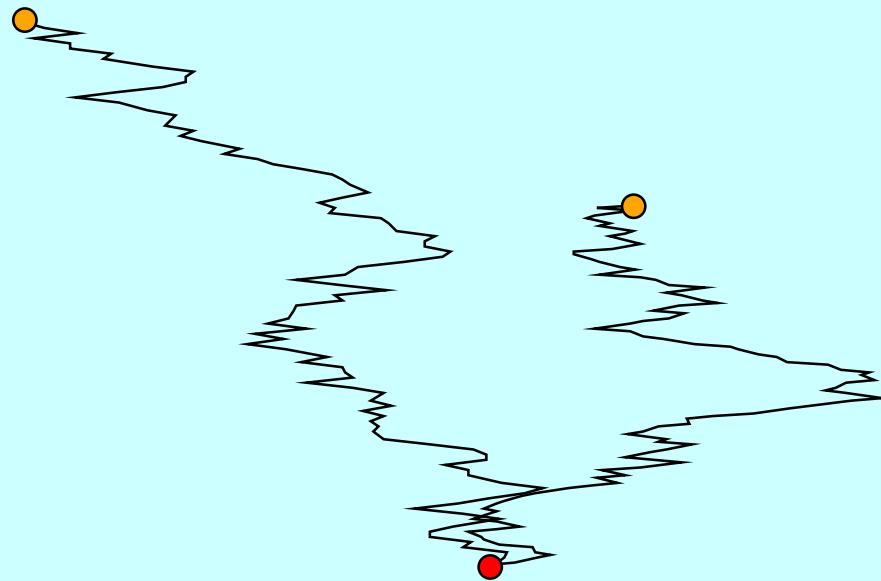
## Covariances of species on the tree

$$\begin{bmatrix} v_1 + v_8 + v_9 & v_8 + v_9 & v_9 & 0 & 0 & 0 & 0 \\ v_8 + v_9 & v_2 + v_8 + v_9 & v_9 & 0 & 0 & 0 & 0 \\ v_9 & v_9 & v_3 + v_9 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & v_4 + v_{12} & v_{12} & v_{12} & v_{12} \\ 0 & 0 & 0 & v_{12} & v_5 + v_{11} + v_{12} & v_{11} + v_{12} & v_{11} + v_{12} \\ 0 & 0 & 0 & v_{12} & v_{11} + v_{12} & v_6 + v_{10} + v_{11} + v_{12} & v_{10} + v_{11} + v_{12} \\ 0 & 0 & 0 & v_{12} & v_{11} + v_{12} & v_{10} + v_{11} + v_{12} & v_7 + v_{10} + v_{11} + v_{12} \end{bmatrix}$$

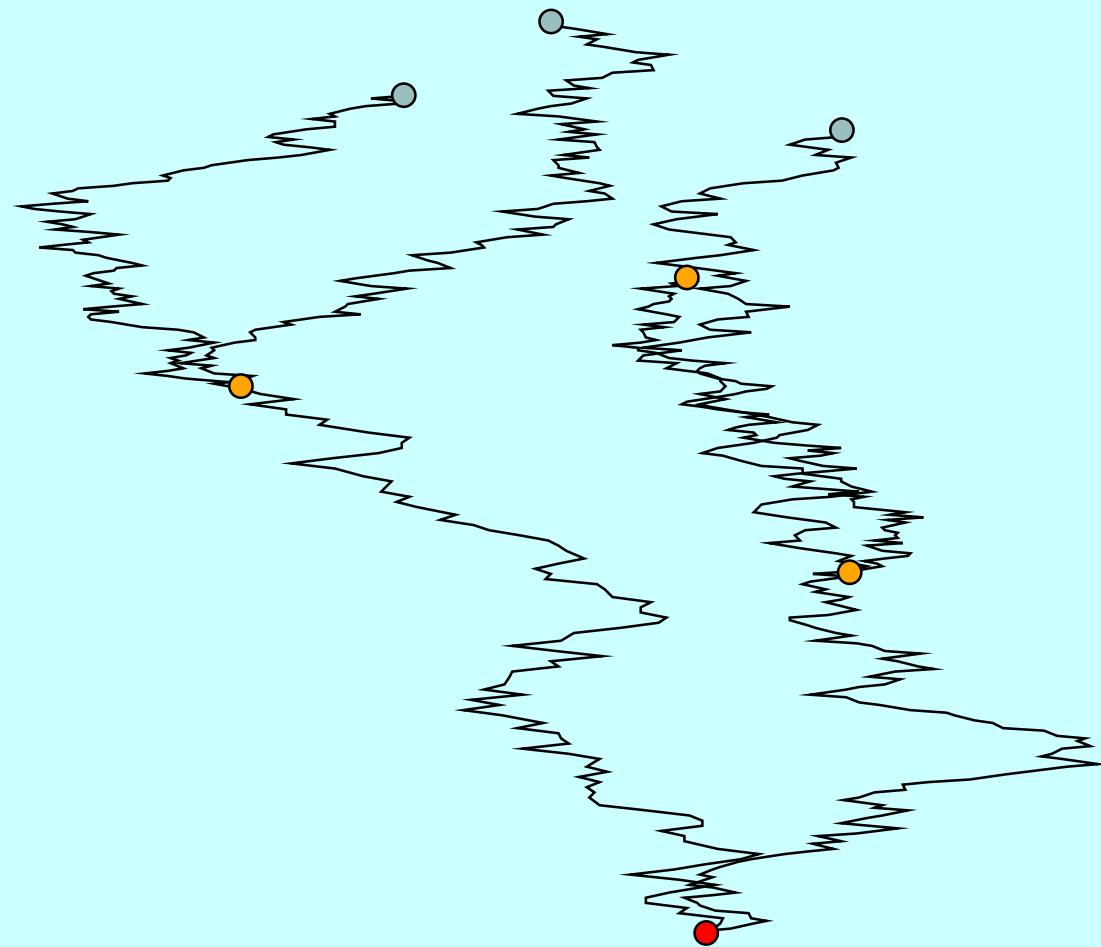
# An outcome of Brownian motion on a 5-species tree



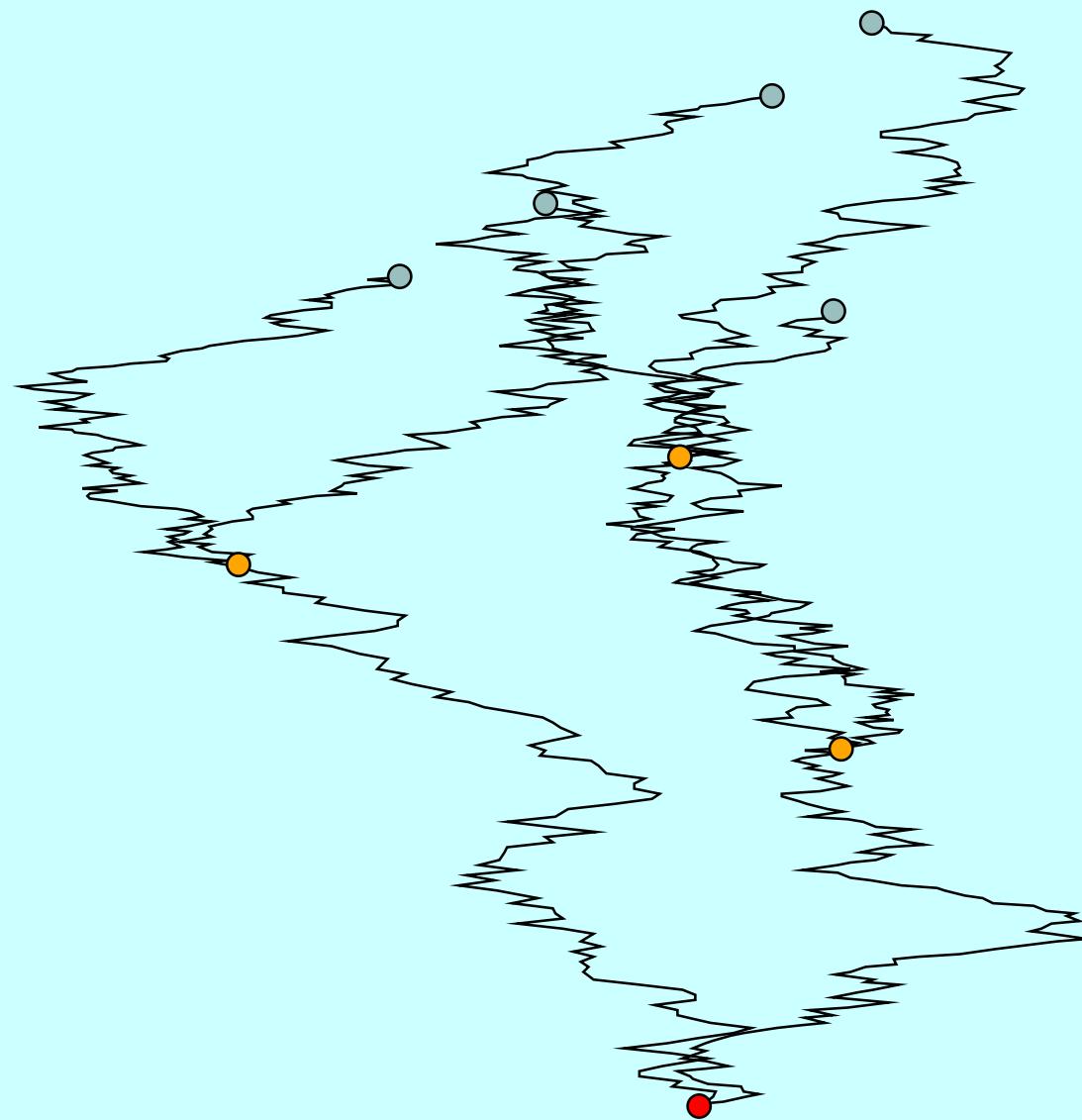
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## “Pruning” a tree in the Brownian motion case

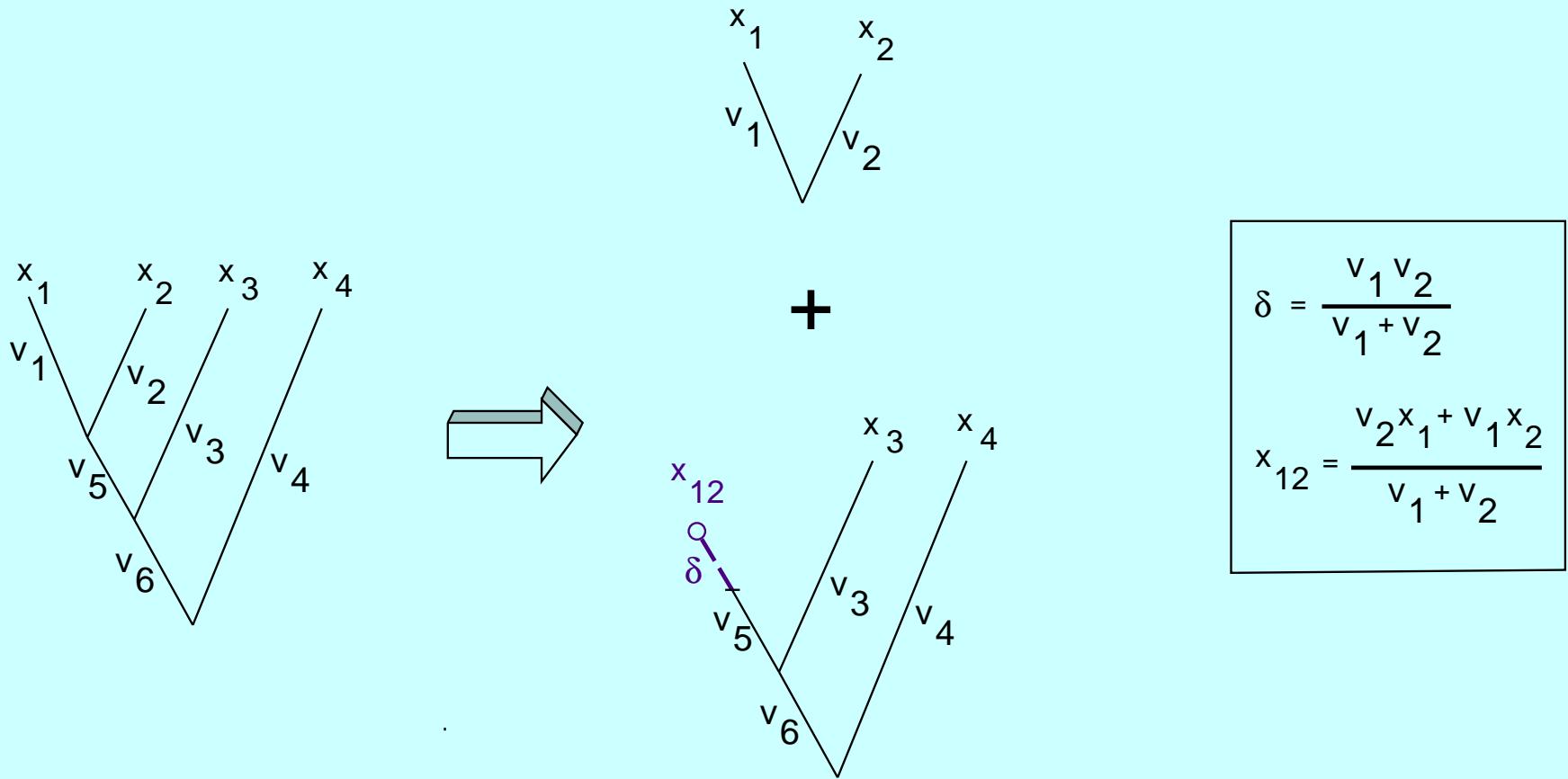
One can take two neighboring tips, and consider their difference  $x_1 - x_2$  as well as a weighted average  $ax_1 + (1 - a)x_2$ . Using weights  $a : 1 - a = 1/v_1 : 1/v_2$ , the weighted average is independent of the difference, and the difference is also independent of the rest of the tree.

In fact, this weighted average behaves like a tip: Its covariances with the other species are the same as those of  $x_1$  and  $x_2$ . It acts just as if the tree were pruned, cutting off species 1 and 2, leaving a single species whose variance is a bit bigger.

$$\text{Var}[ax_1 + (1 - a)x_2] = v_8 + v_9 + \frac{v_1 v_2}{v_1 + v_2}$$

so in effect, a small extra amount of branch length is added.

## “Pruning” a tree in the Brownian motion case



(True in the sense that the log-likelihoods – which are a bit different than the usual likelihoods – add up, since the likelihoods multiply).

## With selection ... life is harder (REVIEW)

There is the “Breeder’s Equation” of Wright and Fisher (1920’s)

$$\Delta z = h^2 S$$



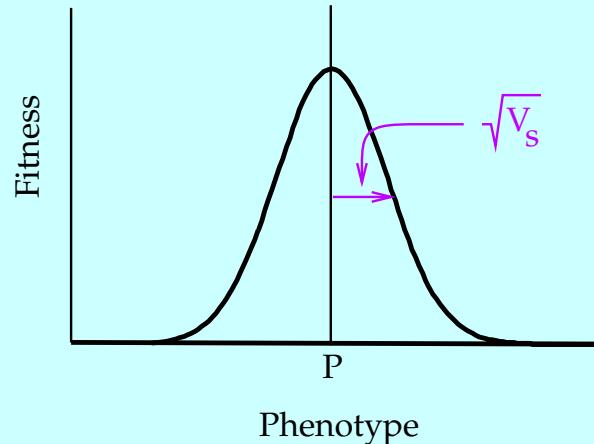
and Russ Lande’s (1976) recasting of that in terms of slopes of mean fitness surfaces:

$$S = V_P \frac{d \log (\bar{w})}{d \bar{x}}$$

$$\Delta z = (V_A/V_P) V_P \frac{d \log (\bar{w})}{d \bar{x}} = V_A \frac{d \log (\bar{w})}{d \bar{x}}$$

Note – it’s heritability times the slope of log of *mean* fitness with respect to *mean* phenotype. There is an exact multivariate analog of this equation.

## Selection towards an optimum (REVIEW)



If fitness as a function of phenotype is:

$$w(x) = \exp \left[ -\frac{(x - p)^2}{2V_s} \right]$$

Then after some completing of squares and integrating, the change of mean phenotype “chases” the optimum:

$$m' - m = \frac{V_A}{V_s + V_P} (p - m)$$

(There is an exact matrix analog of this for multiple characters).

# Sources of evolutionary correlation among characters

Variation (and covariation) in change of characters occurs for two reasons:

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Change of phenotypic means is a result of genetic covariances and selective covariances, where the former affects both response to selection and wandering due to genetic drift.

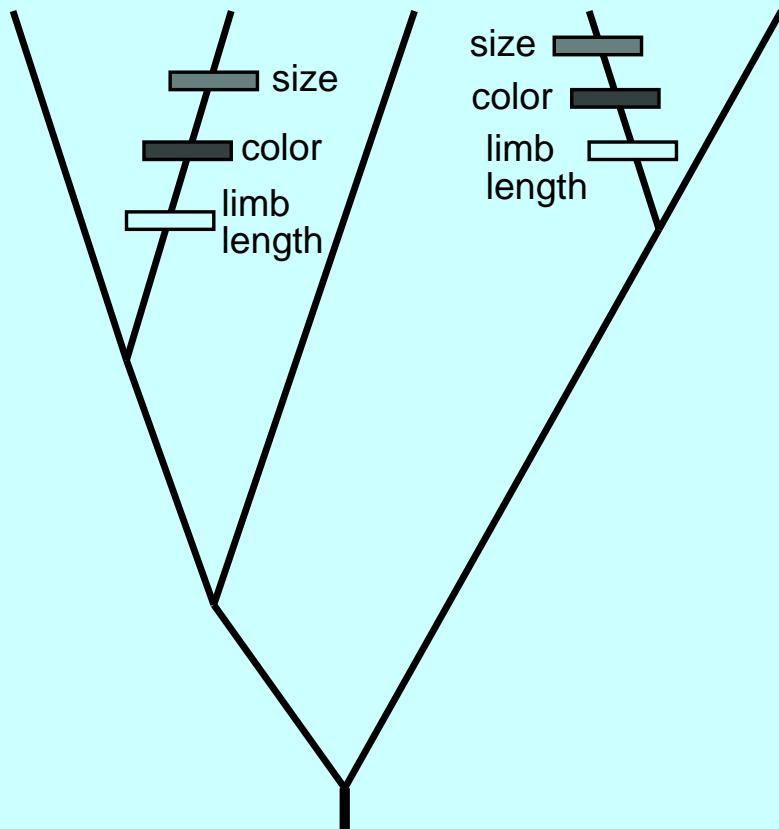
# A simple example of selective covariance

covariation due not to genetic correlation  
but to covariation of the selection pressure

These are Bergmann's, Allen's and Glogler's Rules  
They are presumably not the result of genetic correlations  
but result from patterns of selection

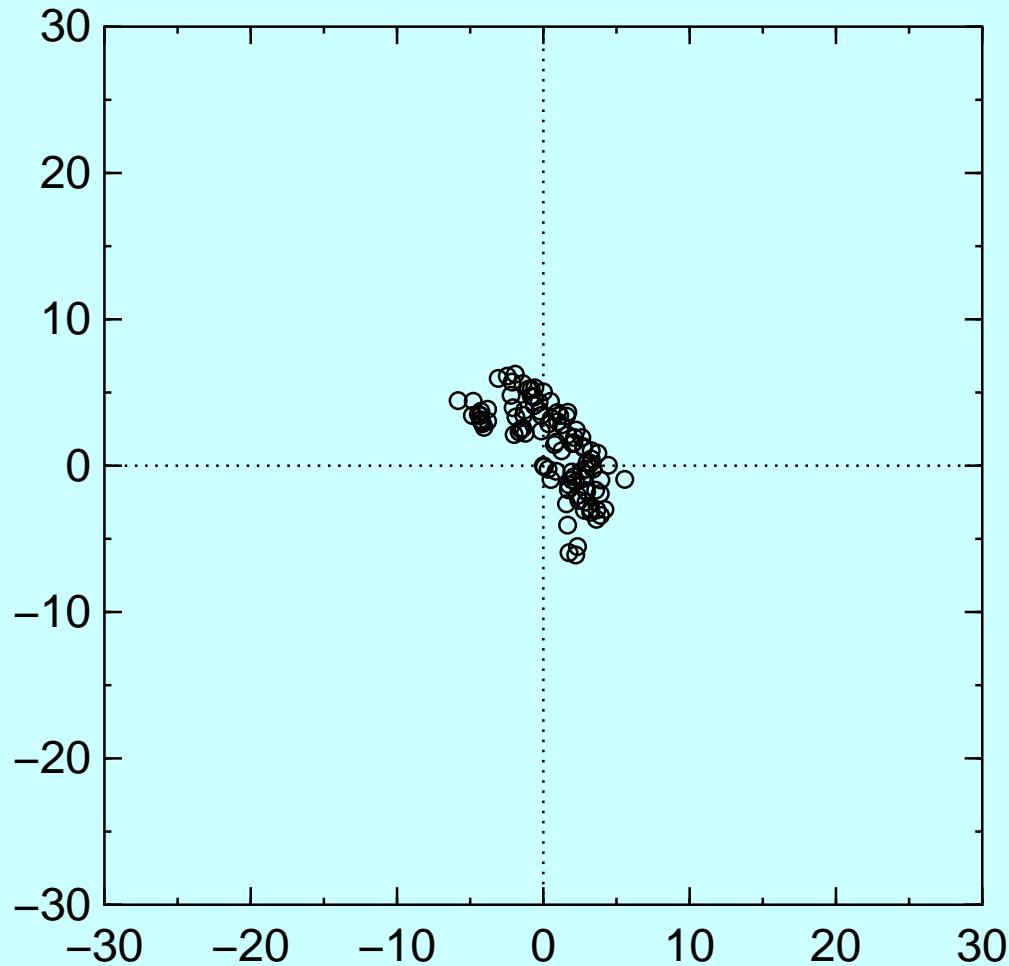
a simple example:

(temperate) (arctic) (temperate) (arctic) (temperate)



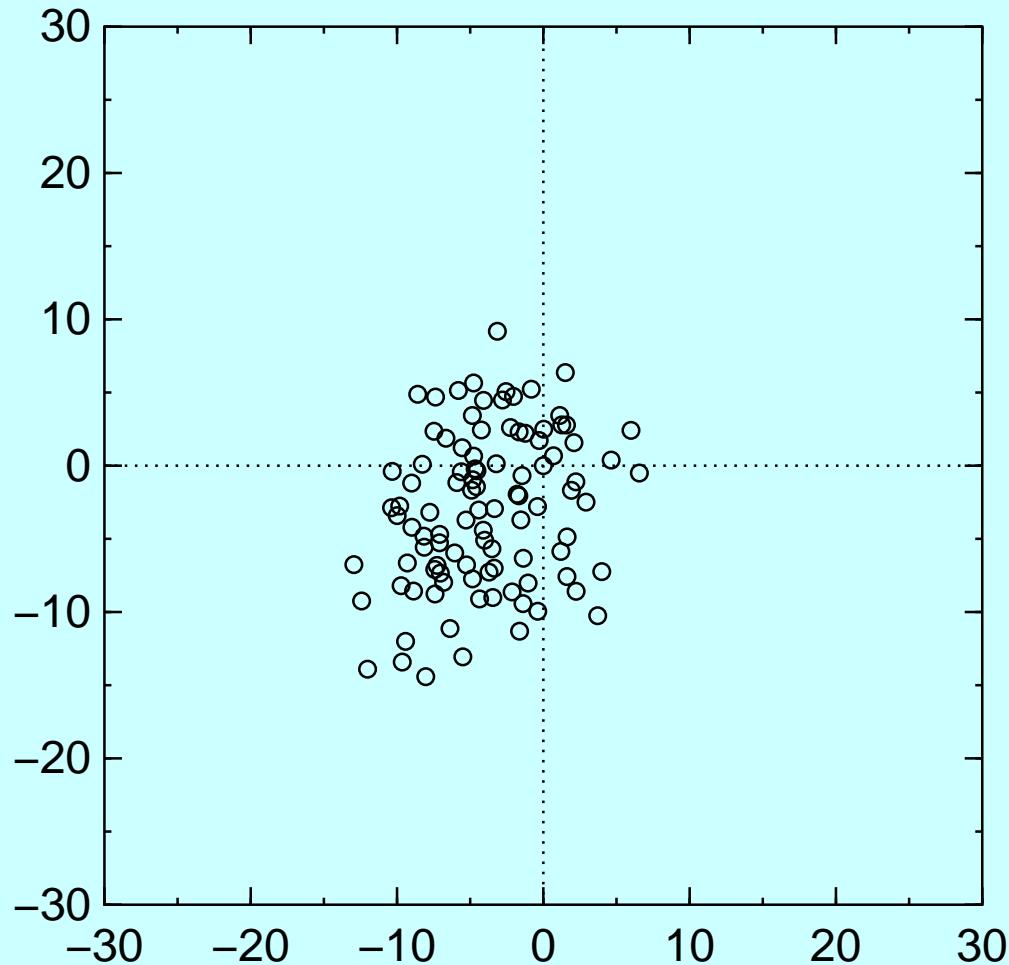
G. L. Stebbins. 1950. *Variation and evolution in plants*. Columbia Univ. Press, New York.  
page 121

## Chasing a peak, simulated with two characters



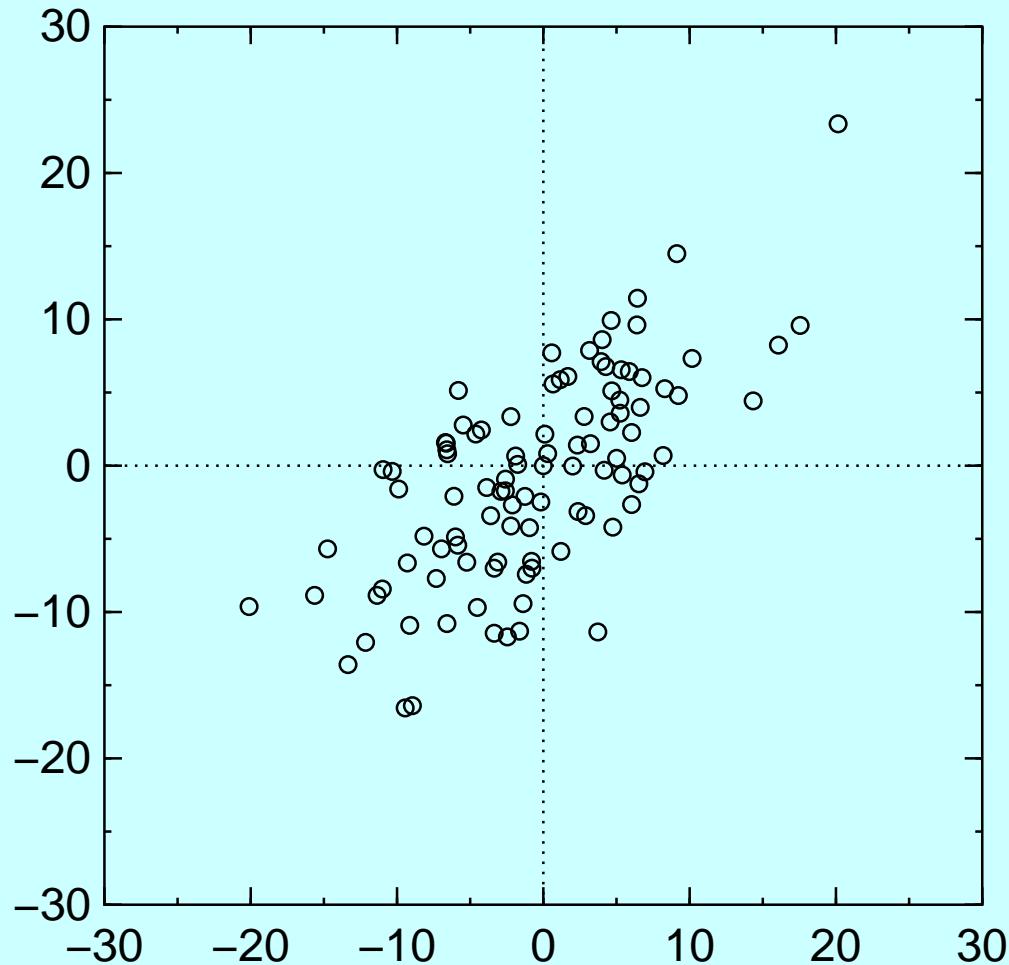
Genetic covariances assumed negative, but the wanderings of the adaptive peaks assumed positively correlated. In the first 100 generations the genetic covariances are most influential.

## Chasing a peak, simulated with two characters



Genetic covariances assumed negative, but the wanderings of the adaptive peaks assumed positively correlated. After a while (every 10th generation up to generation 1000), the wanderings of the peaks start to be influential.

## Chasing a peak, simulated with two characters



Genetic covariances assumed negative, but the wanderings of the adaptive peaks assumed positively correlated. In the long run (every 100th generation up to generation 10,000) the means go mostly where the peaks go.

## A case that has received too little attention

- Suppose characters  $x$  and  $y$  are genetically correlated.
- and  $y$  is under optimum selection, but  $x$  is the one we observe.
- What will we see? In effect, the sum (actually, a weighted average) of an Ornstein-Uhlenbeck process and Brownian Motion.
- So Brownian motion restricted in the short run but not in the long run.
- It will look almost like Ornstein-Uhlenbeck Process with an optimum which wanders by Brownian Motion.

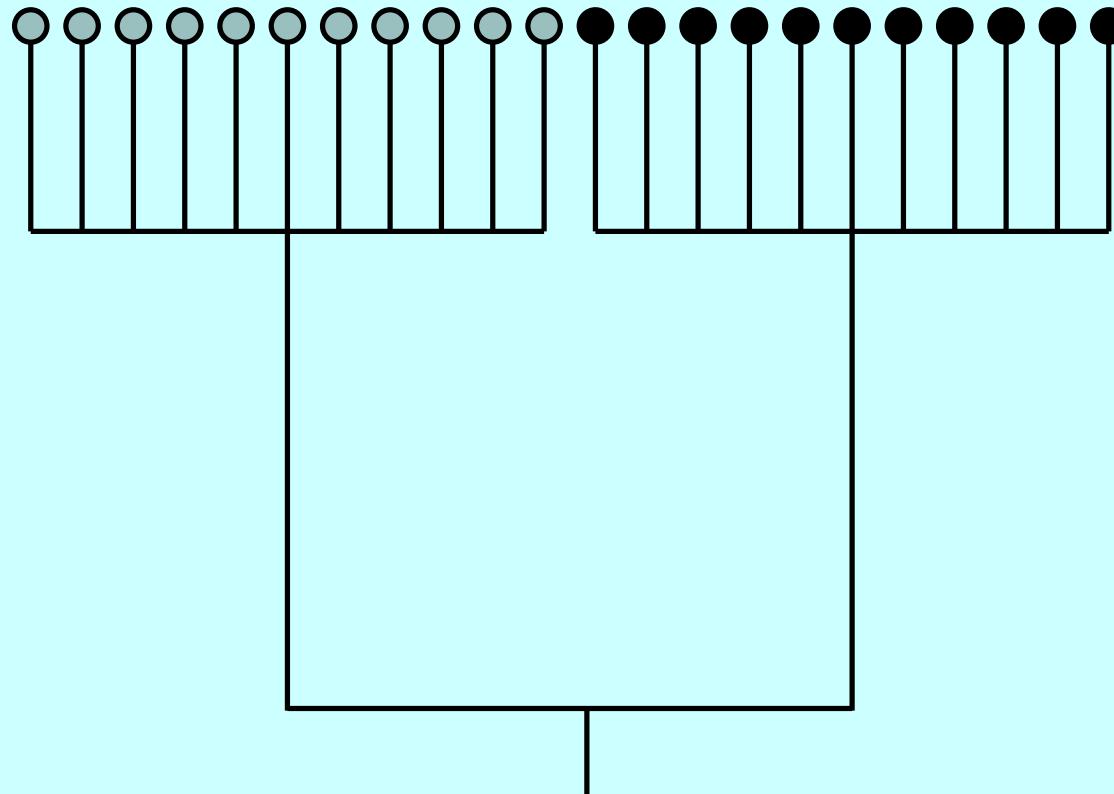
Most models so far do not allow for characters that are observed to covary with those that aren't observed.

# A research program?

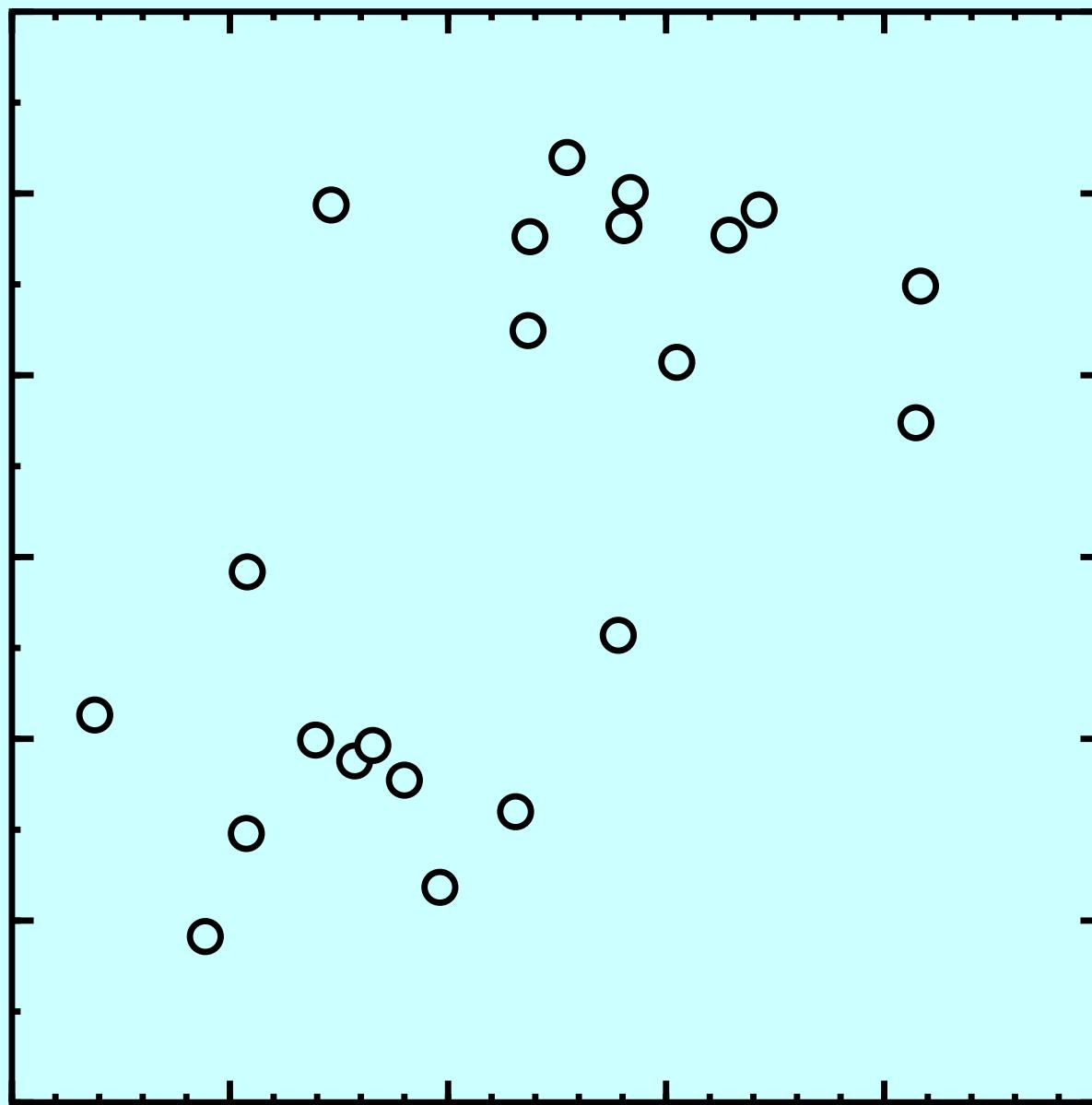
What we could imagine doing is:

- We might hope to infer additive genetic covariances by doing quantitative genetics breeding experiments to infer them from covariances among relatives, perhaps even in multiple species.
- Infer the covariances of the changes along the phylogeny.
- From them, back-calculate the selective covariances.
- The genetic covariances may also be inferrable from differences between nearby tips on the tree if we do not have breeding experiments.
- There is little or no hope of inferring “selective correlations” more directly without a complete understanding of the functional ecology.

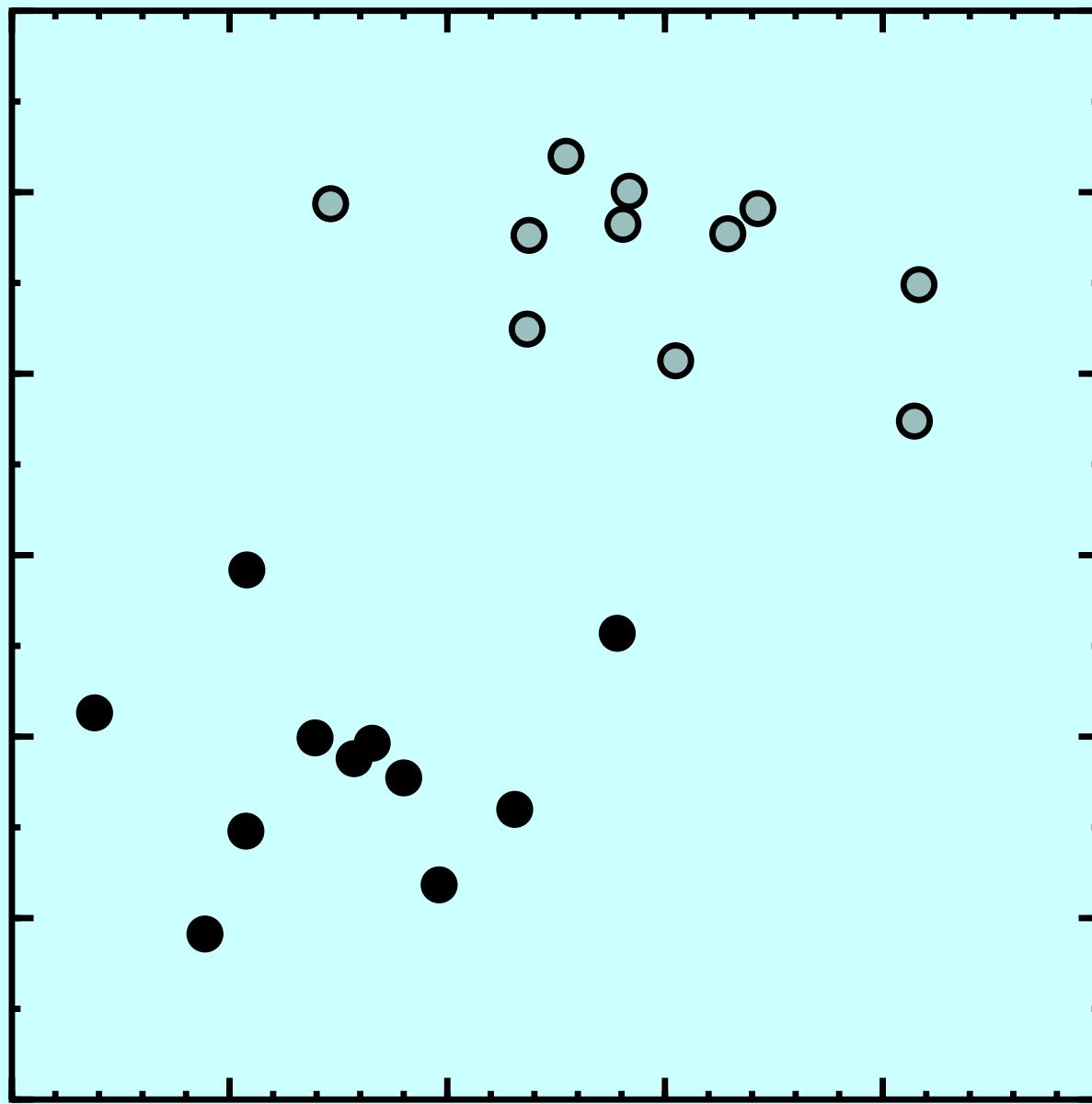
## A simple case to show effects of phylogeny



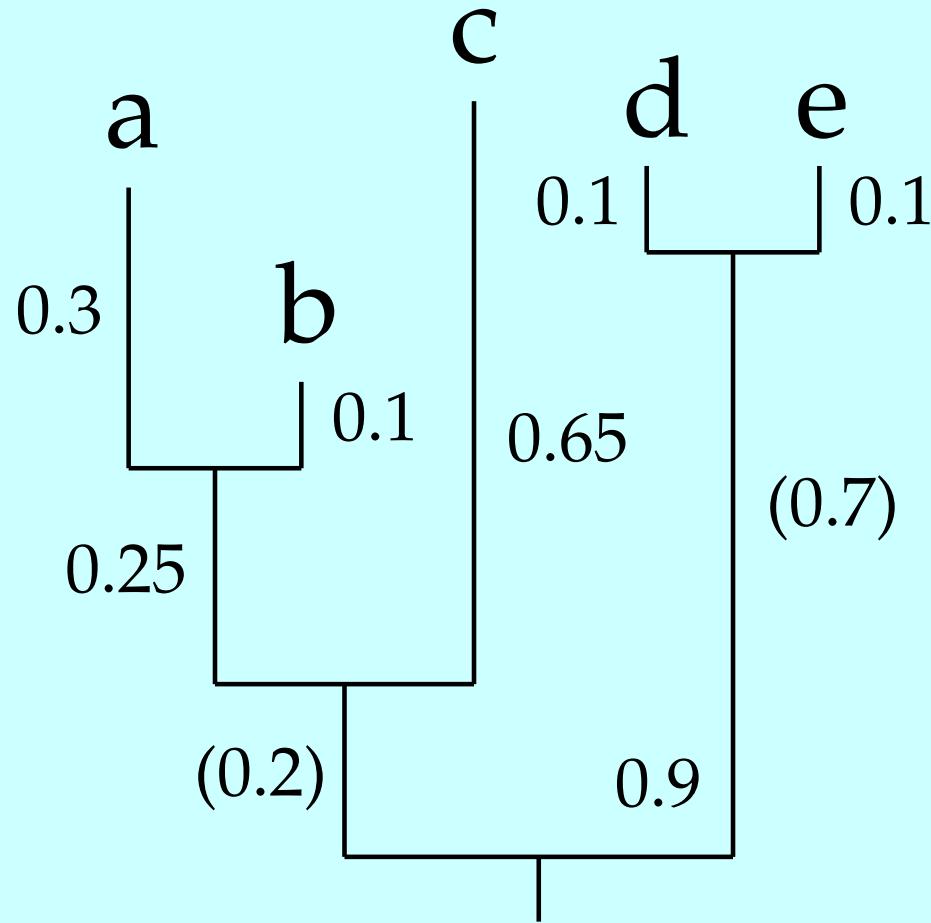
## Two uncorrelated characters evolving on that tree



## Identifying the two clades



## A tree on which we are to observe two characters



## Contrasts on that tree

Contrast

Variance  
proportional  
to

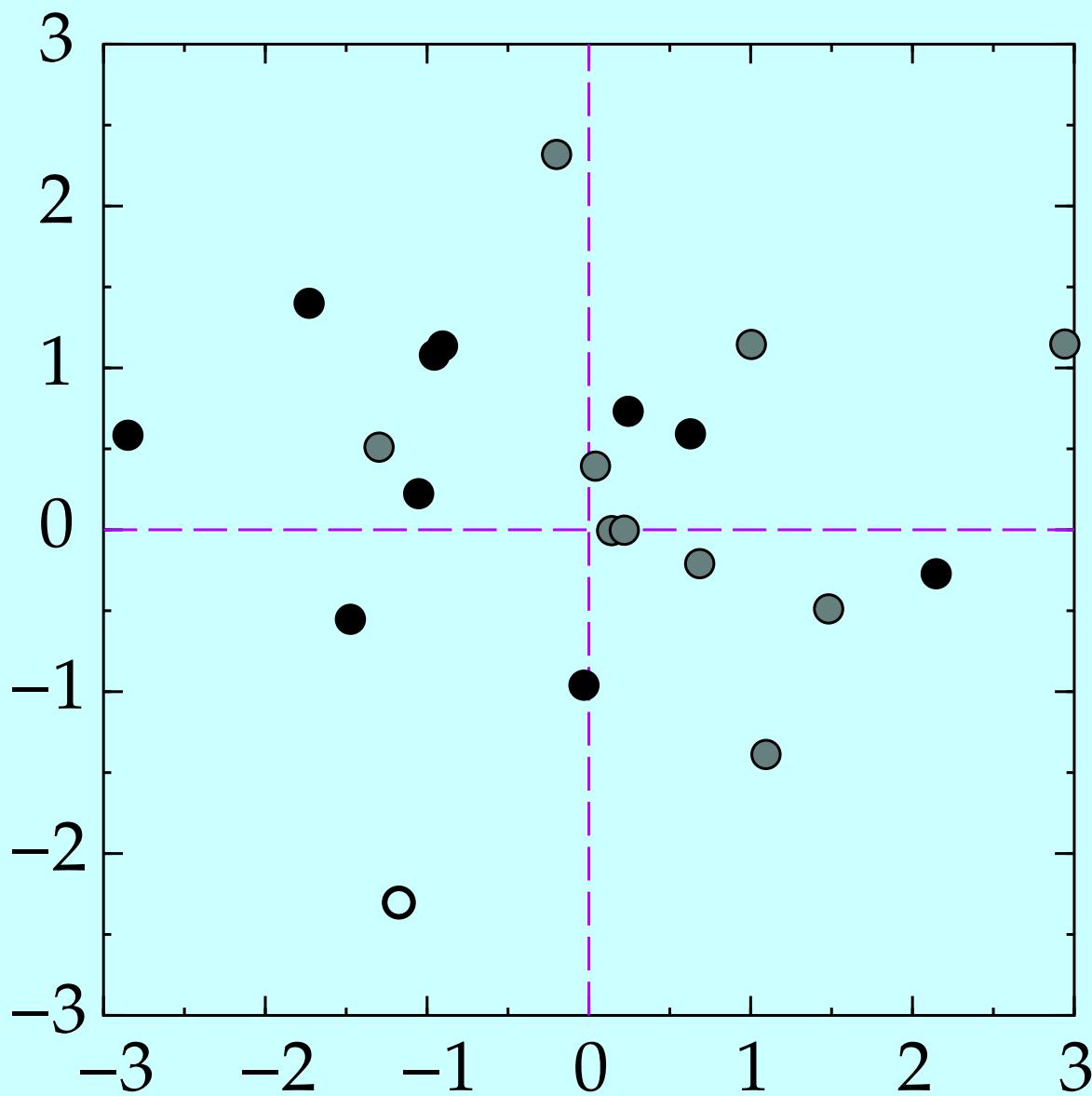
$$y_1 = x_a - x_b \quad 0.4$$

$$y_2 = \frac{1}{4} x_a + \frac{3}{4} x_b - x_c \quad 0.975$$

$$y_3 = \quad \quad \quad x_d - x_e \quad 0.2$$

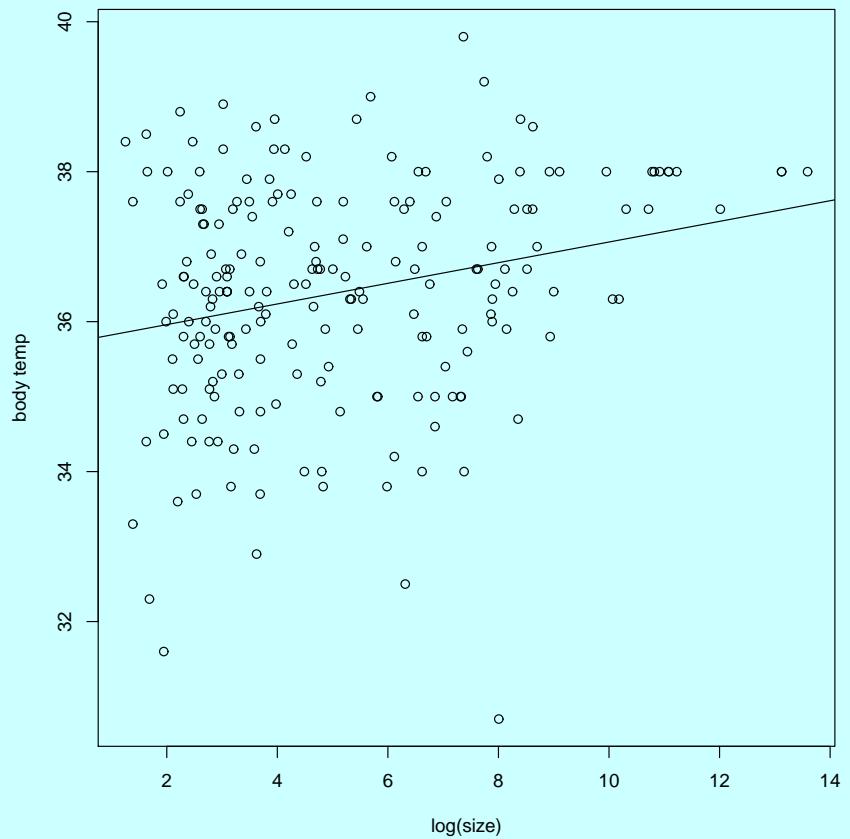
$$y_4 = \frac{1}{6} x_a + \frac{1}{2} x_b + \frac{1}{3} x_c - \frac{1}{2} x_d - \frac{1}{2} x_e \quad 1.11666$$

## Contrasts for the 20-species two-clade example

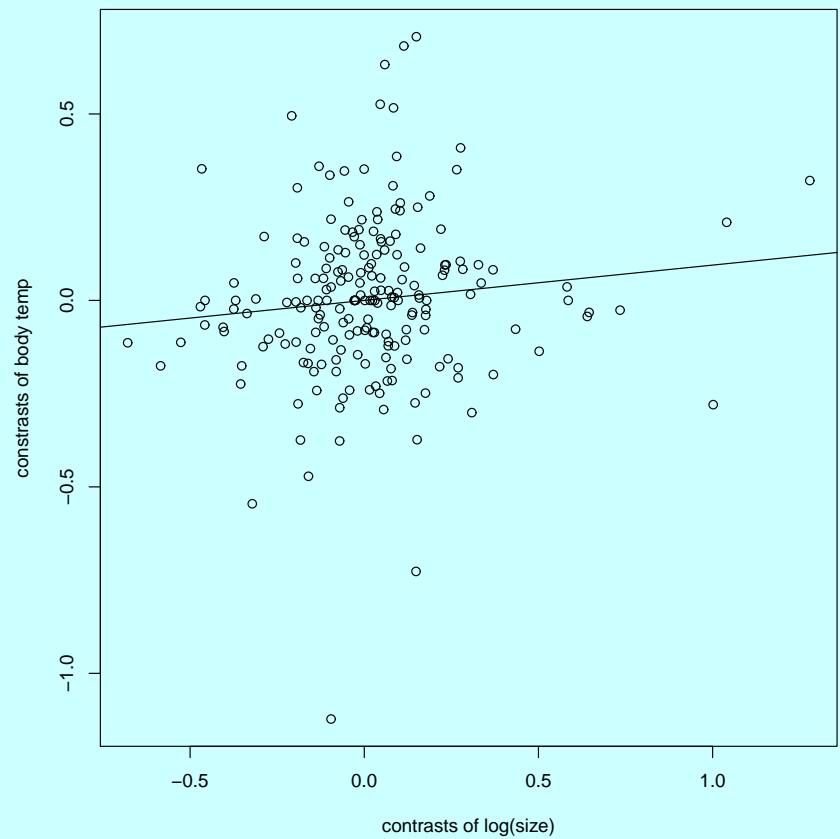


## An example: Riek and Geiser, 2013

Alexander Riek and Fritz Geiser. 2013. Allometry of thermal variables in mammals: consequences of body size and phylogeny. *Biological Reviews* 88 (3): 564-572.



body temperature vs. log(body size)  
( $P$  for slope  $\neq 0$  is 0.000375)



contrasts vs. contrasts  
( $P$  for slope  $\neq 0$  is 0.116)

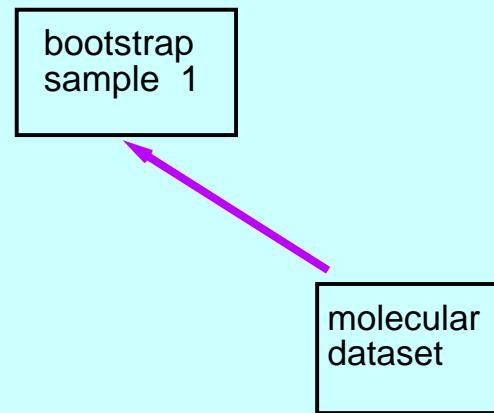
# When the tree is noisy: Propagating bootstrap sampling

morphological  
data

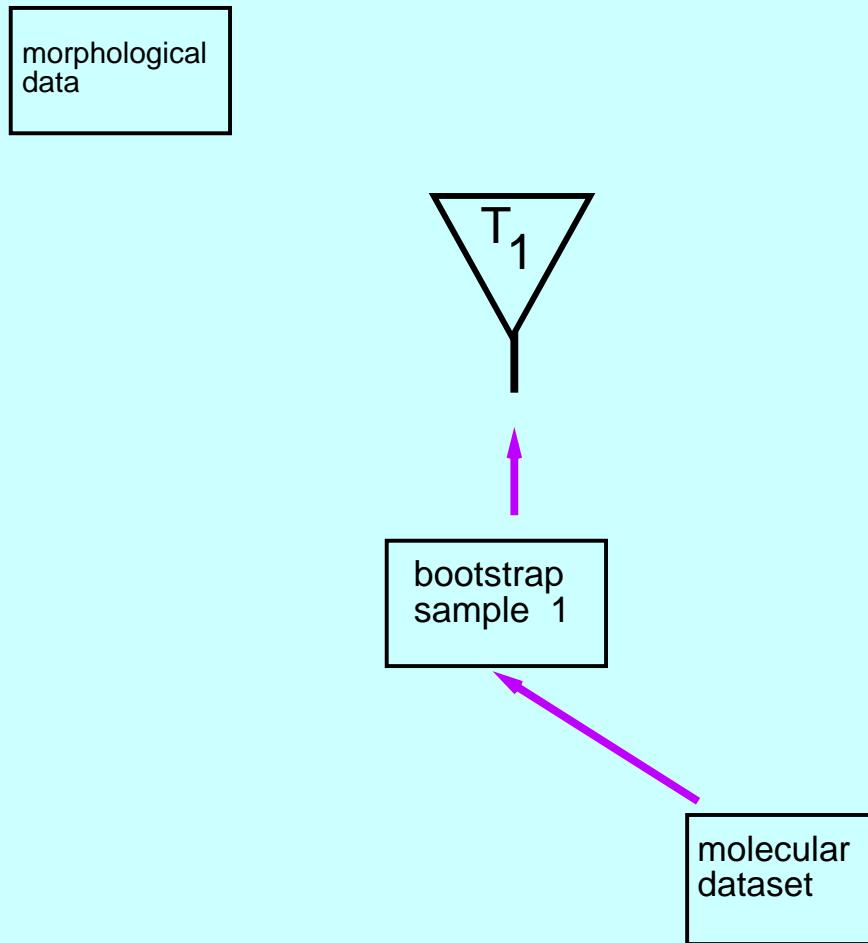
molecular  
dataset

# Propagating bootstrap sampling

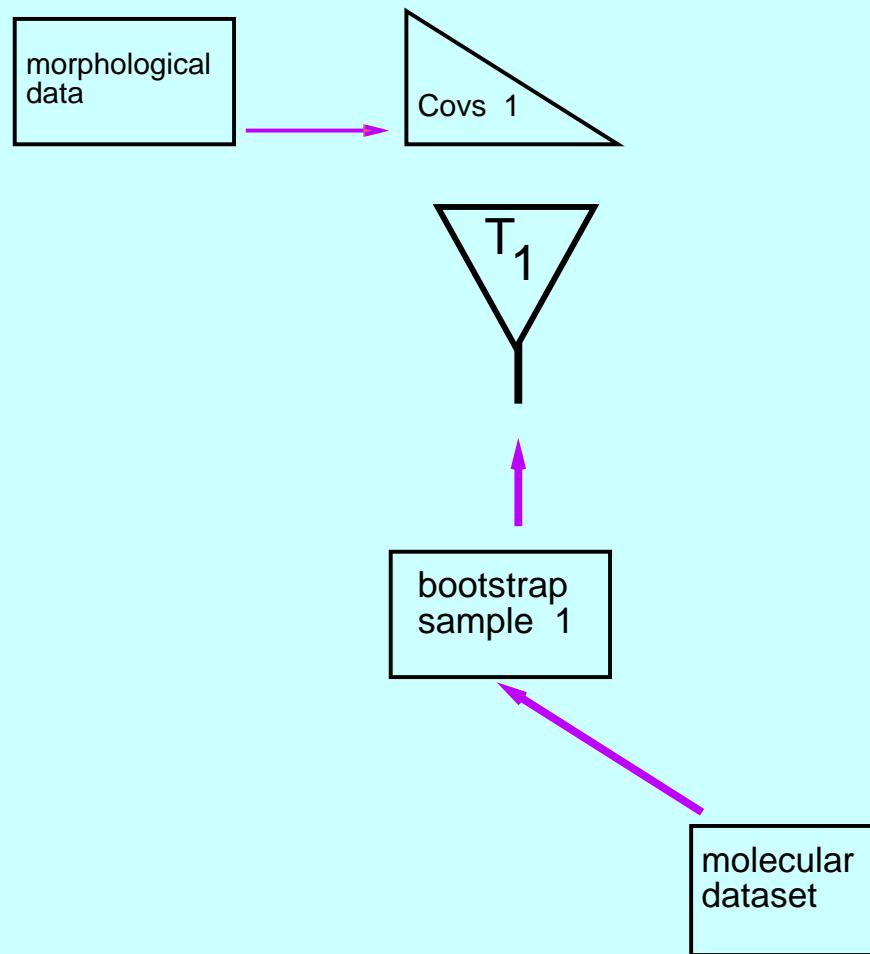
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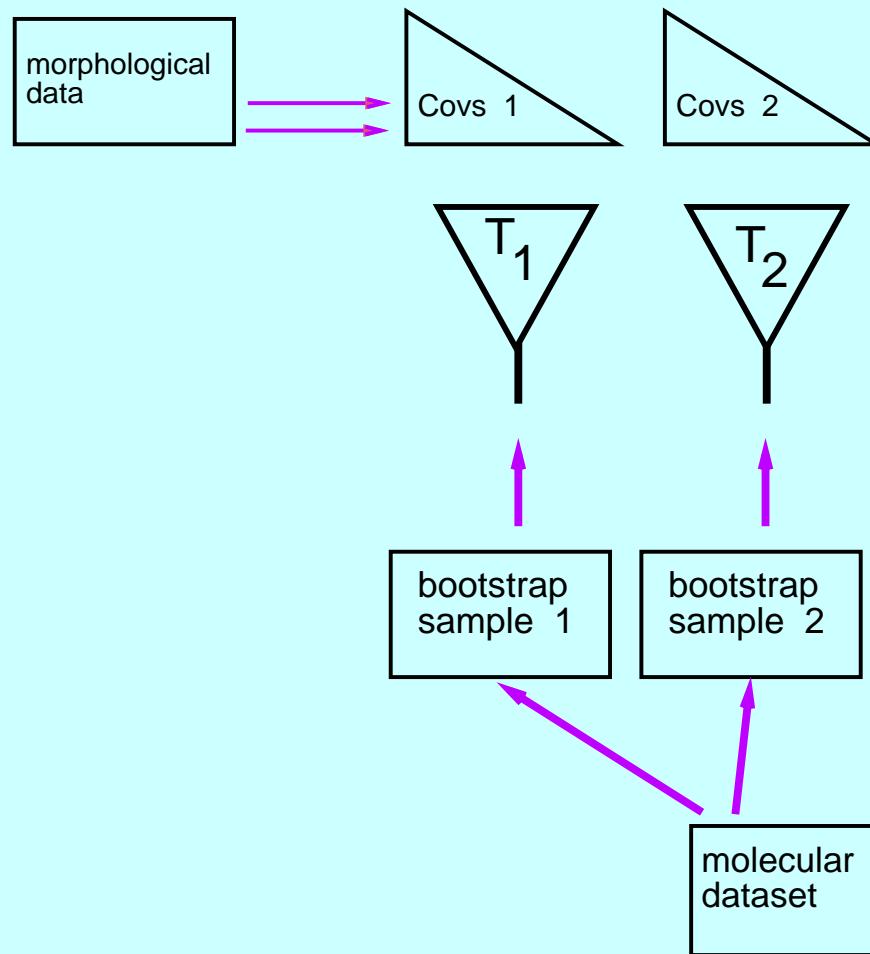
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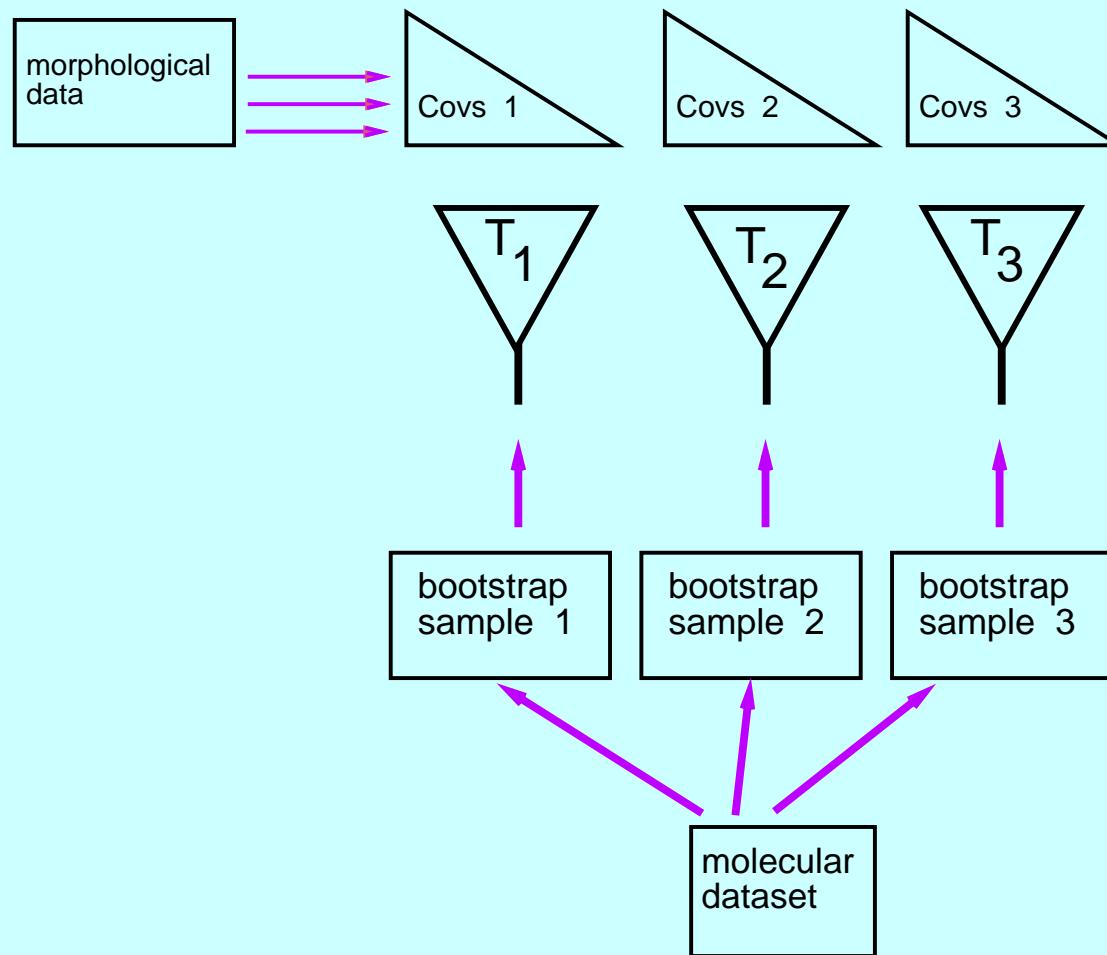
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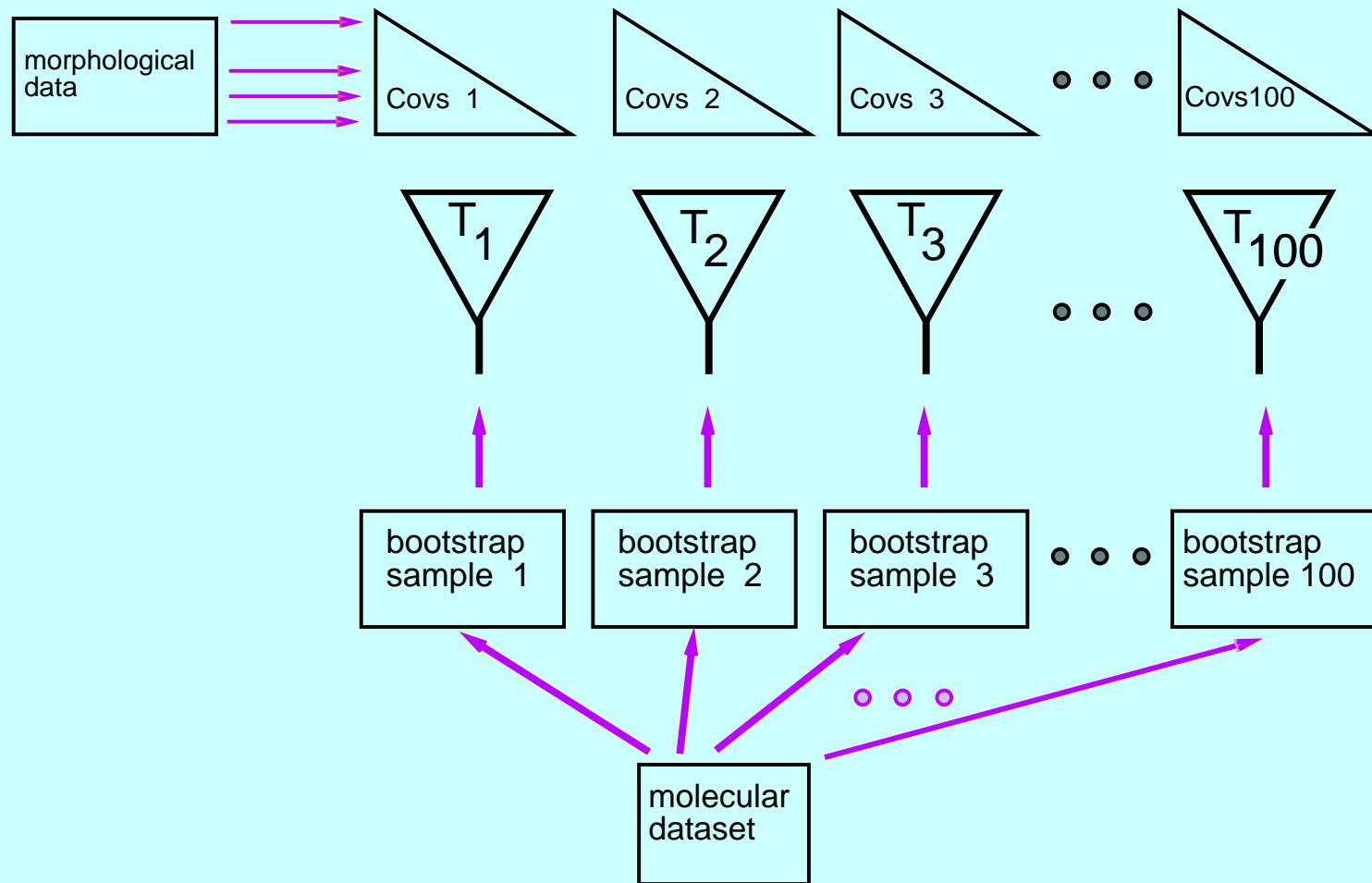
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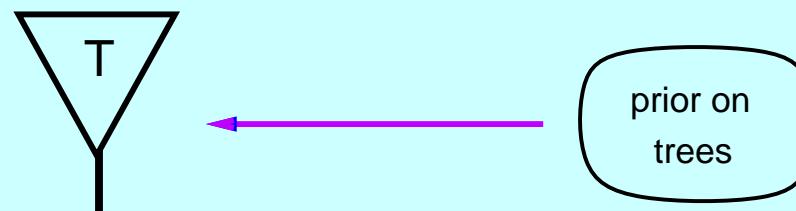
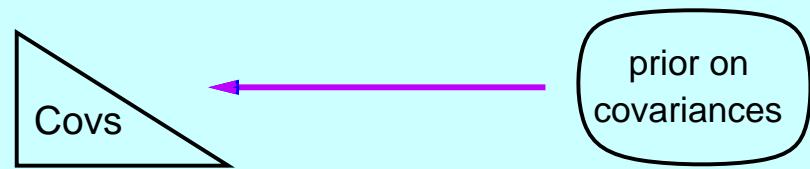
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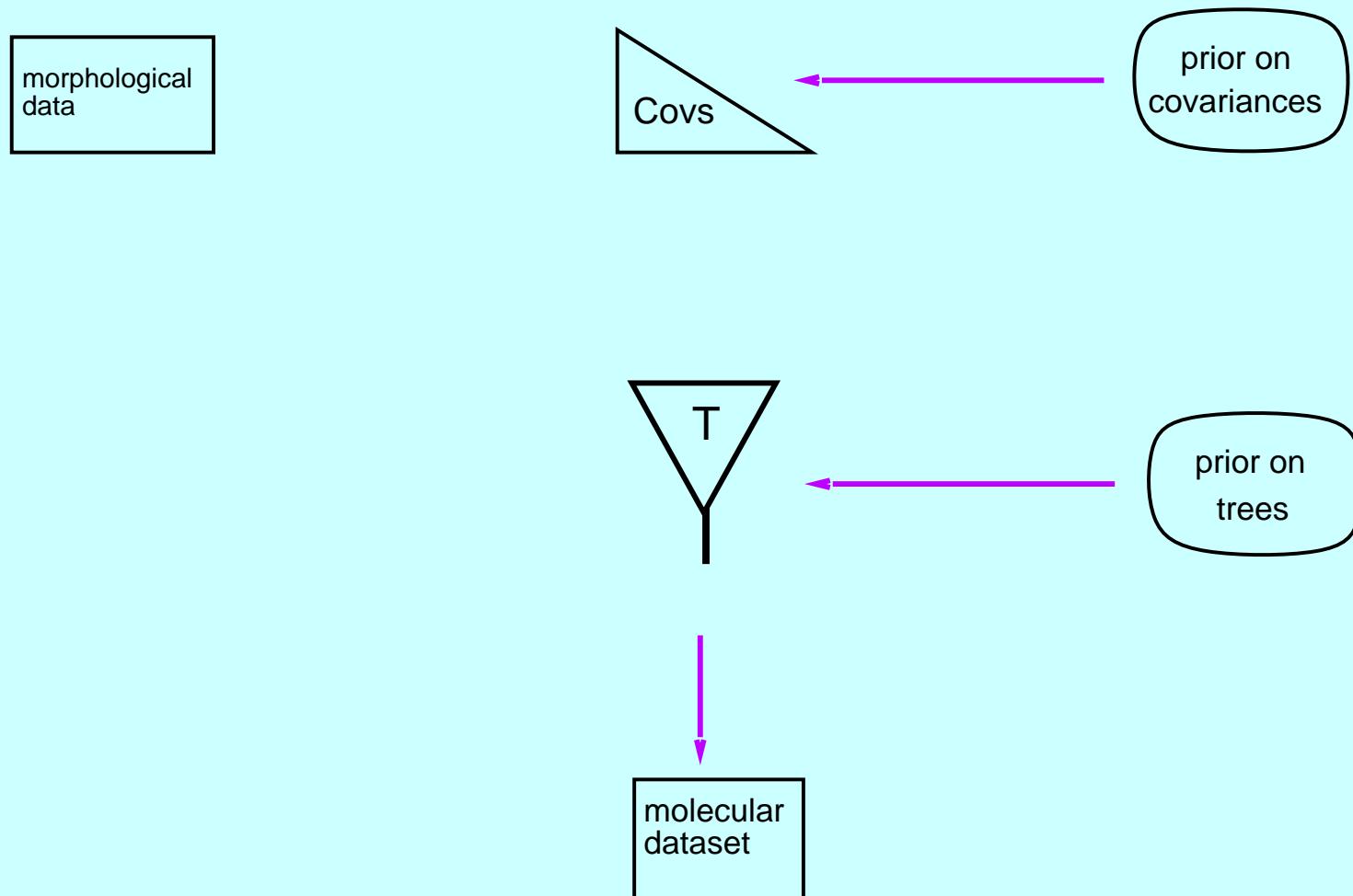
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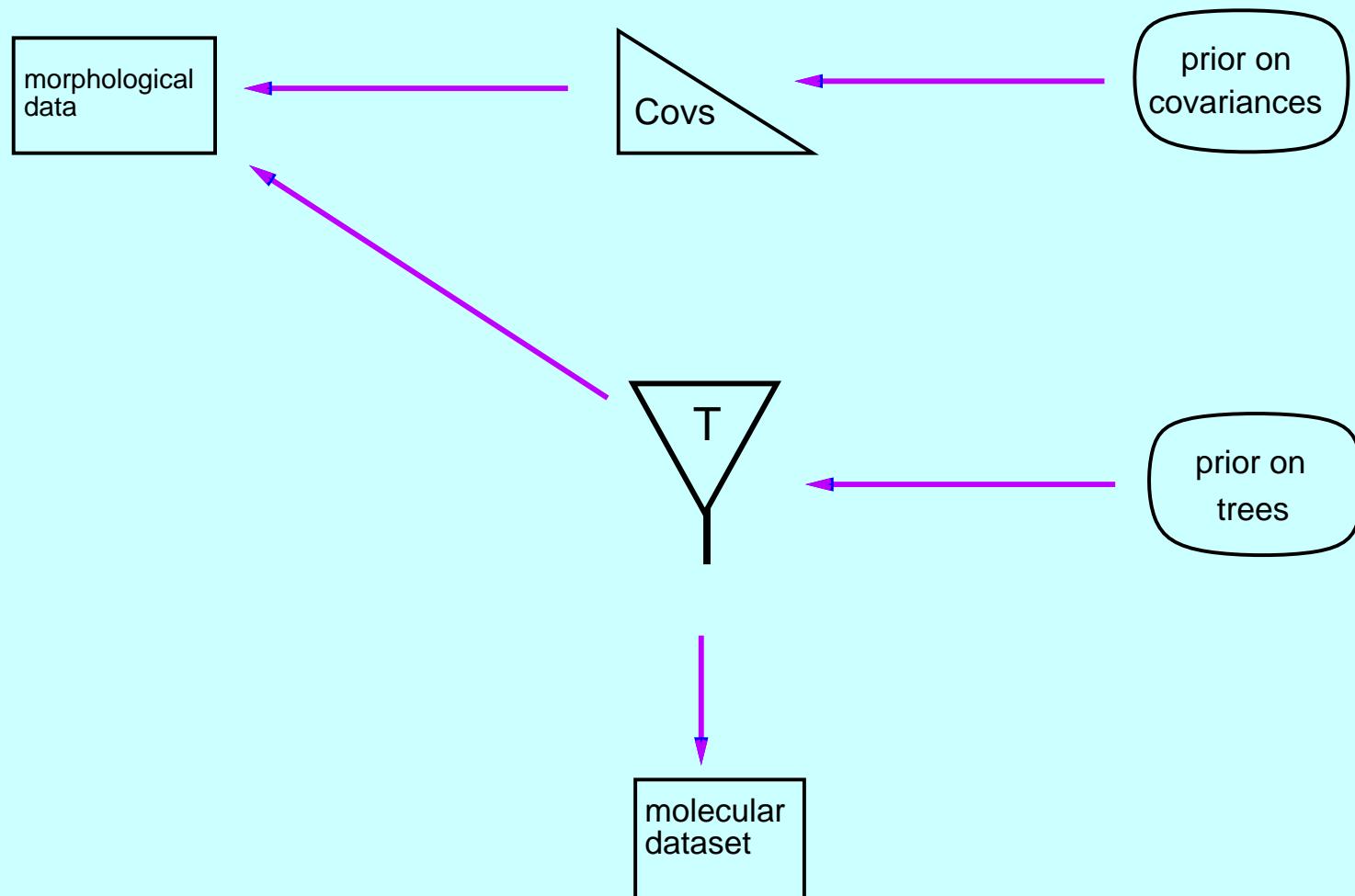
# A Bayesian model



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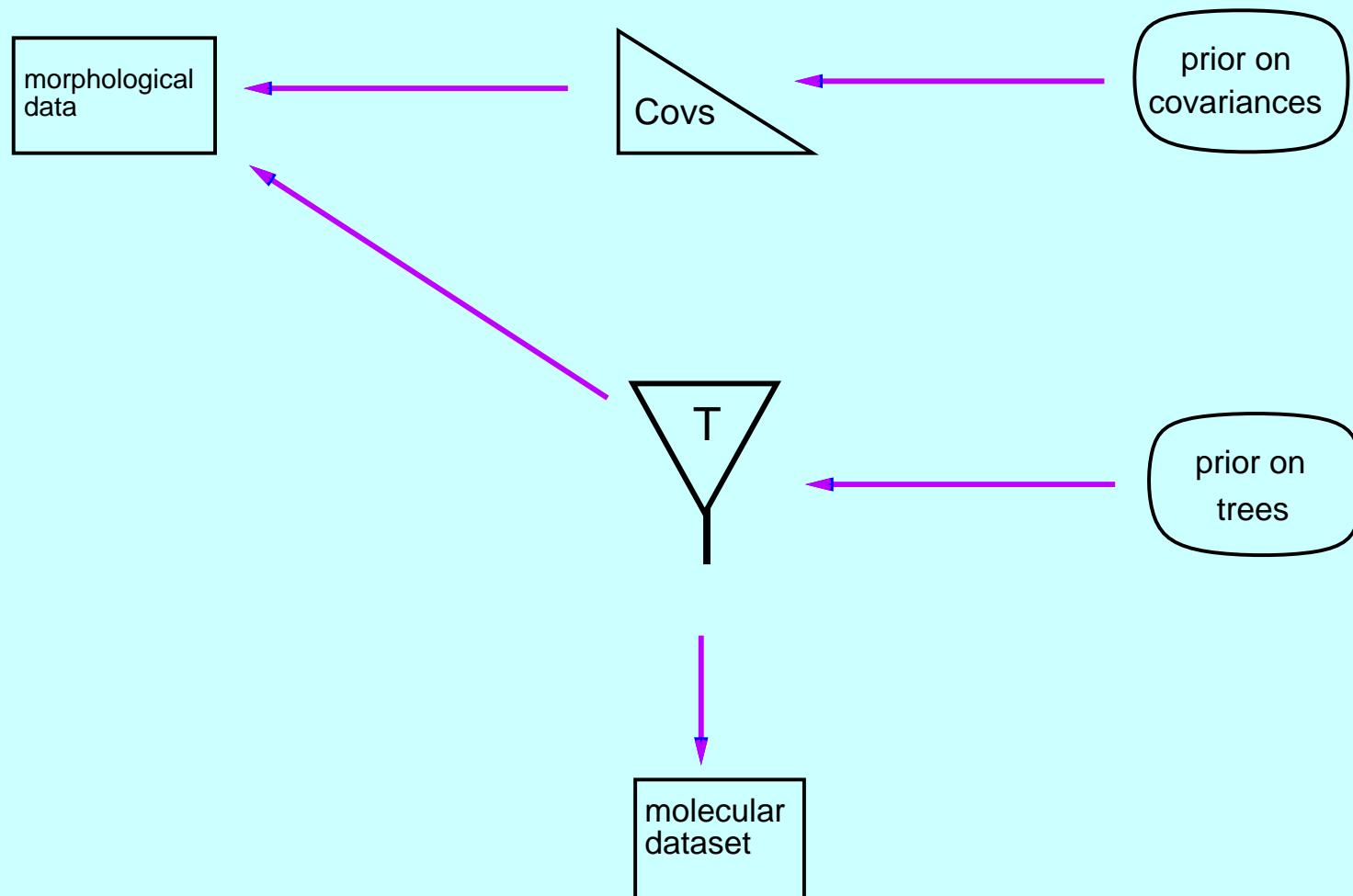


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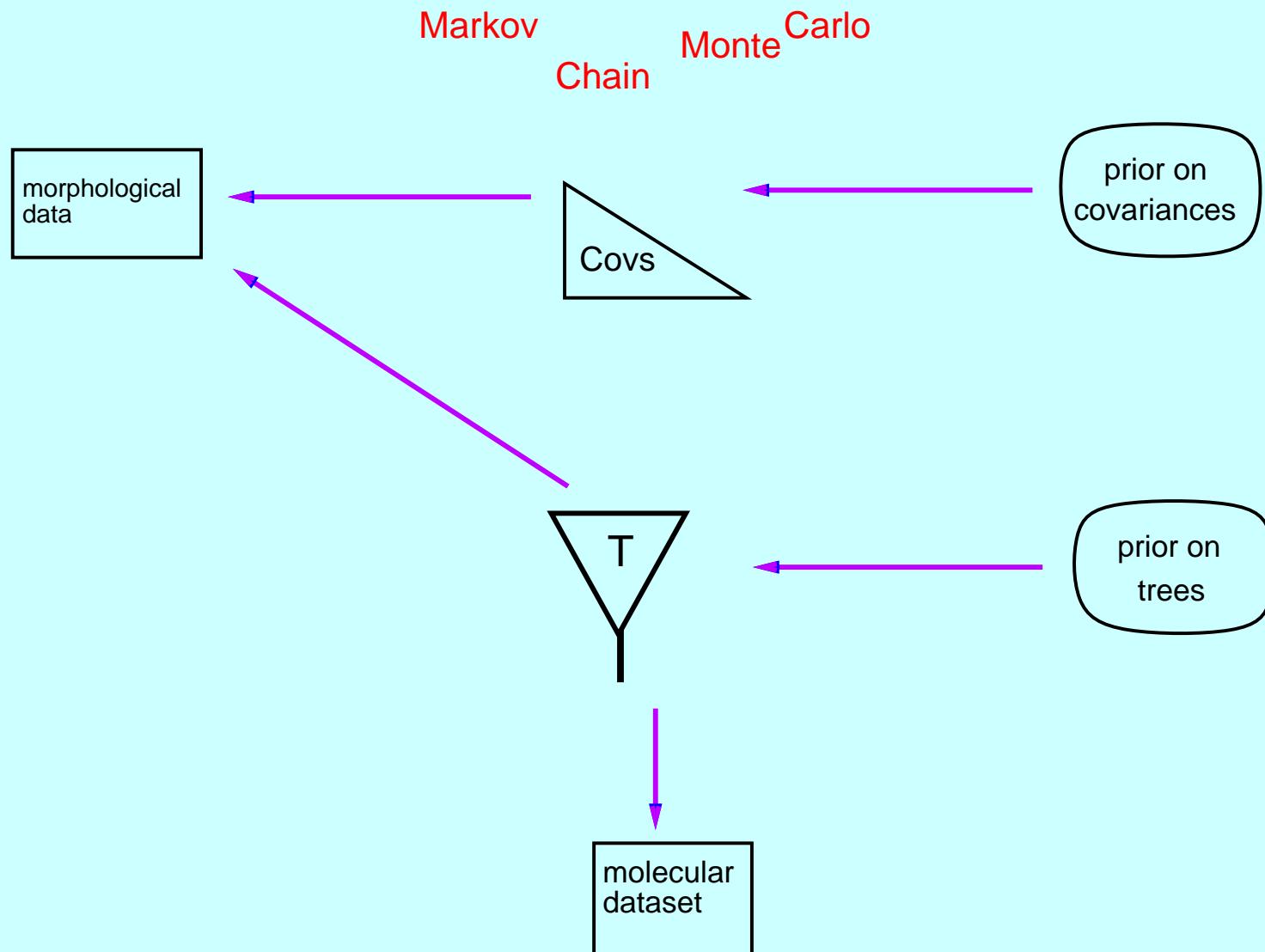


# Bayesian MCMC

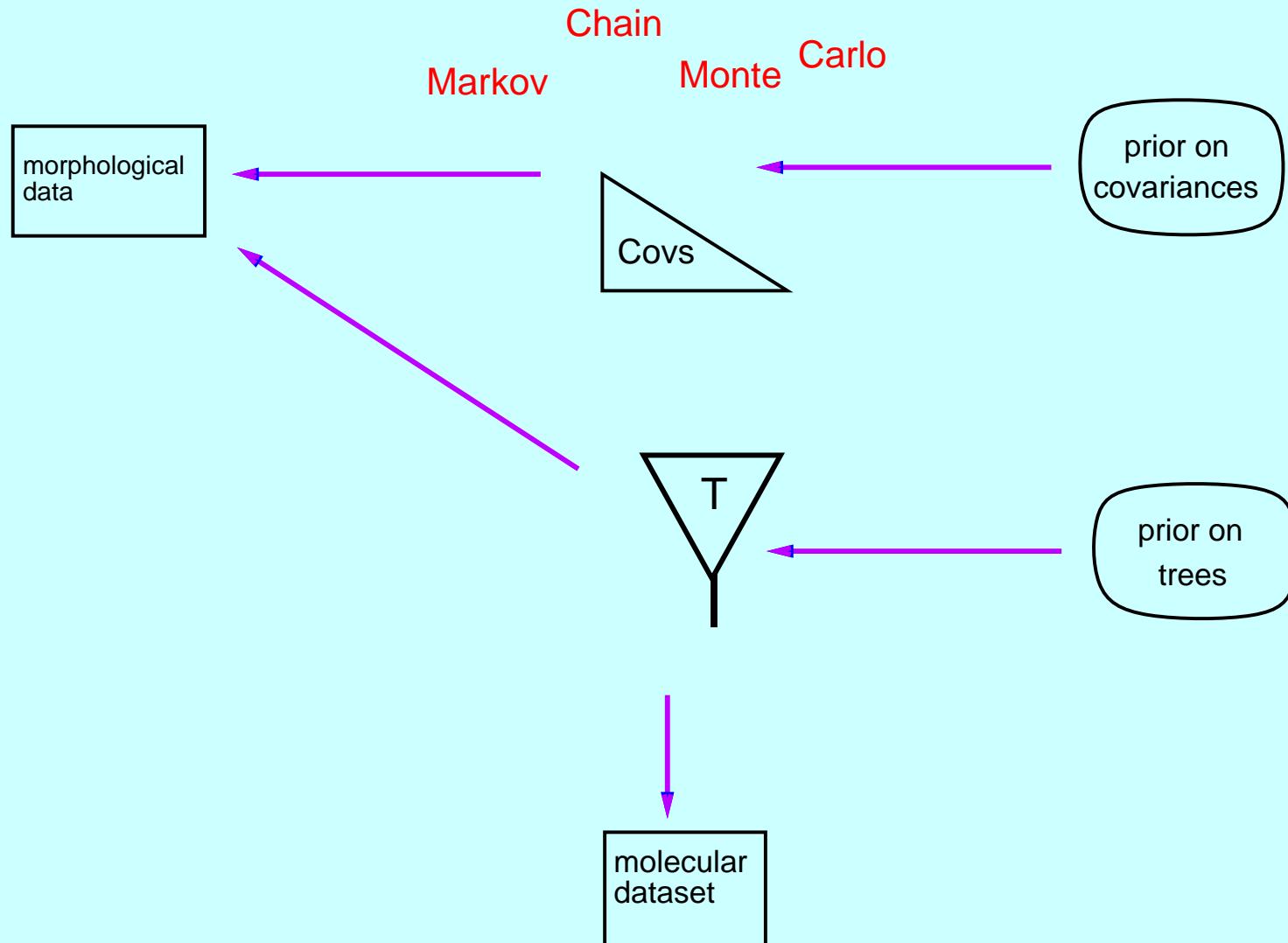
Markov Chain Monte Carlo



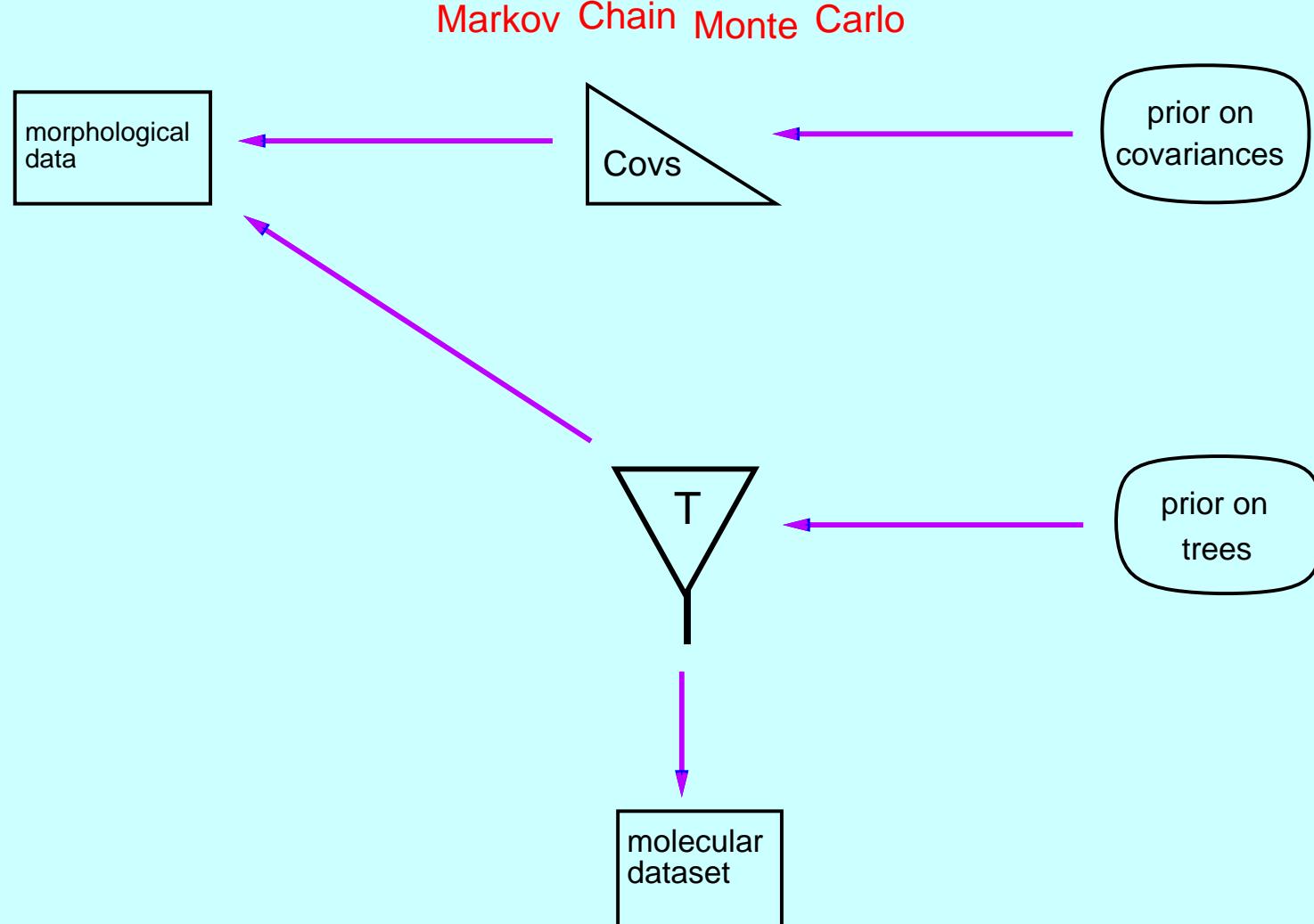
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- Might be able to assume environment does Brownian motion and infer covariances. Less reason to assume environment does Brownian motion than for characters.

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- Expanding to more characters just adds new parameters to estimate

## References for genetic drift

- Feller, W. 1951. Diffusion processes in genetics. pp. 227-246 in *Proceedings of the 2nd Berkeley Symposium on Mathematical Statistics and Probability*, ed. J. Neyman. University of California Press, Berkeley and Los Angeles.  
**[Feller's partial solution of the pure drift process for the Wright-Fisher model (and his famous proof that the process converges to the diffusion process)]**
- Kimura, M. 1955a. Solution of a process of random genetic drift with a continuous model. *Proceedings of the National Academy of Sciences* **41**: 144-150. **[Exact solution in Gegenbaur polynomials for two-allele pure genetic drift in a diffusion process approximation]**
- Kimura, M. 1955b. Random drift in a multi-allelic locus. *Evolution* **9**: 419-435.  
**[The same, for three alleles]**

## References for the Brownian Motion approximation

- Edwards, A.W. F. and L. L. Cavalli-Sforza. 1964. Reconstruction of evolutionary trees. pp. 67–76 in *Phenetic and Phylogenetic Classification*, ed. V. H. Heywood and J. McNeill. Systematics Association Publ. No. 6, London.  
**[The first paper on numerical approaches to phylogeny reconstruction; uses parsimony and proposes likelihood for gene frequency trees]**
- Edwards, A.W. F. 1970. Estimation of the branch points of a branching diffusion process. *Journal of the Royal Statistical Society B* 32: 155–174.  
**[More detailed consideration of the statistical properties of a maximum likelihood approach to gene frequency phylogenies]**
- Felsenstein, J. 1973. Maximum likelihood estimation of evolutionary trees from continuous characters. *American Journal of Human Genetics* 25: 471–492. **[REML approach to gene frequency phylogenies, including the contrasts algorithm for rapid computation of likelihood]**
- Nielsen, R., J. L. Mountain, J. P. Huelsenbeck, and M. Slatkin. 1998. Maximum-likelihood estimation of population divergence times and population phylogeny in models without mutation. *Evolution* 52: 669-677.  
**[Little-noticed but much more exact method that would require MCMC machinery]**

## References on likelihood of Brownian Motion trees

- Thompson, E. A. 1975. *Human Evolutionary Trees*. Cambridge University Press, Cambridge [Thesis monograph on how to infer ML phylogenies from gene frequencies, published because it won a Smith's Prize at Cambridge University]
- Felsenstein, J. 1981. Maximum likelihood estimation of evolutionary trees from continuous characters. *Evolution* 25: 471–492. [Reworks the 1973 paper with more care and some additional algorithmics, including discussion of effect of character covariation]
- Felsenstein, J. 1985. Phylogenies from gene frequencies: A statistical problem. *Systematic Zoology* 34: 300–311. [Shows how gene frequency changes depart from being approximated by Brownian Motion]

## References for multivariate Brownian motion

- Felsenstein, J. 1988. Phylogenies and quantitative characters. *Annual Review of Ecology and Systematics* **19**: 445-471. **[Review with mention of usefulness of threshold model]**
- Felsenstein, J. 2002. Quantitative characters, phylogenies, and morphometrics.pp. 27-44 in *Morphology, Shape, and Phylogenetics*, ed. N. MacLeod. Systematics Association Special Volume Series 64. Taylor and Francis, London. **[Review repeating 1988 material and going into some more detail on the question of threshold models.]**
- Felsenstein, J. 2004. *Inferring Phylogenies*. Sinauer Associates, Sunderland, Massachusetts. **[See particularly Chapters 23–25. Mentions issues with multivariate models, and also sample size issues in contrasts method].**
- Lande, R. 1976. Natural selection and random genetic drift in phenotypic evolution. *Evolution* **30**: 314-334. **[Lande's classic paper on drift versus optimum selection]**
- Lande, R. 1979. The quantitative genetic analysis of multivariate evolution, applied to brain-body size allometry. *Evolution* **33**: 402-416. **[Lande on covarying characters]**

## References

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