Brownian motion models, multiple characters, and phylogenies

Bio 550D: Morphometrics in Biology

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13 October 2016

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?

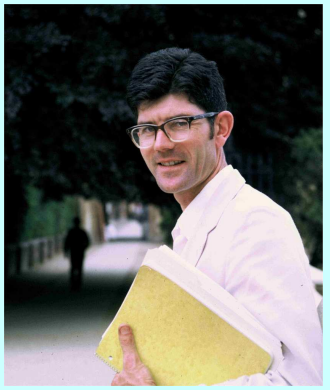
Approximating genetic drift of two alleles

Can we compute transition probabilities for genetic models such as the Wright-Fisher model?

- Can we do this analytically? **No.** (although the right eigenvectors and the eigenvalues are known) the full set of left eigenvalues has never been derived.
- We can take such a model for a given (not-too-big) population size N and compute the transition probability matrix, then either power it up numerically or get its eigenvalues and eigenvectors
- OK, what about the diffusion approximation. Aren't they very close approximations? Yes, they and Kimura (1955a, 1955b) derived transition probabilities for the diffusion process as sums of series in Gegenbaur polynomials. **But** they are difficult to work with.

Edwards and Cavalli-Sforza's approximation

Luca Cavalli-Sforza (and Edwards), 1963



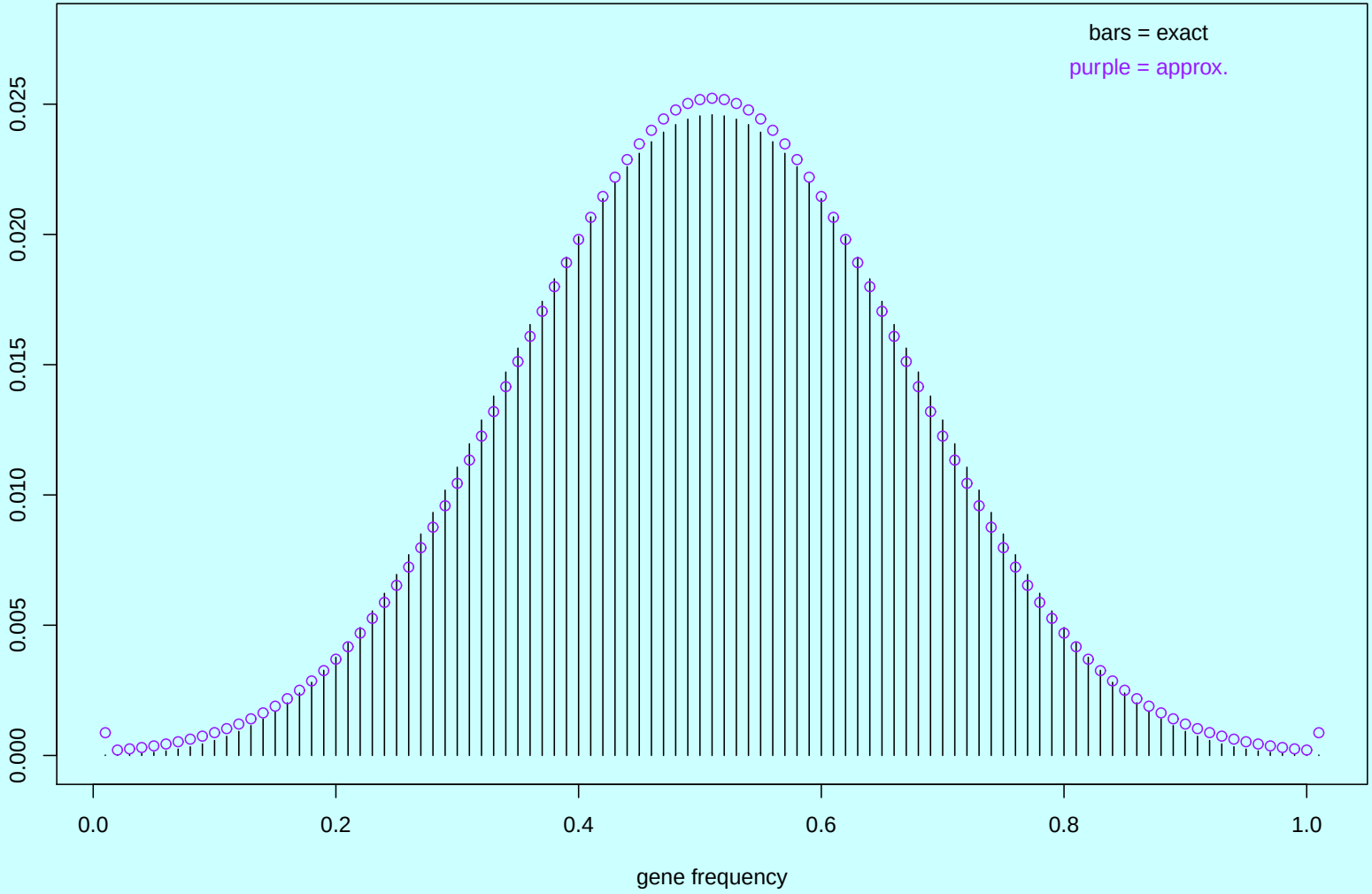
Anthony Edwards, 1970

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

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

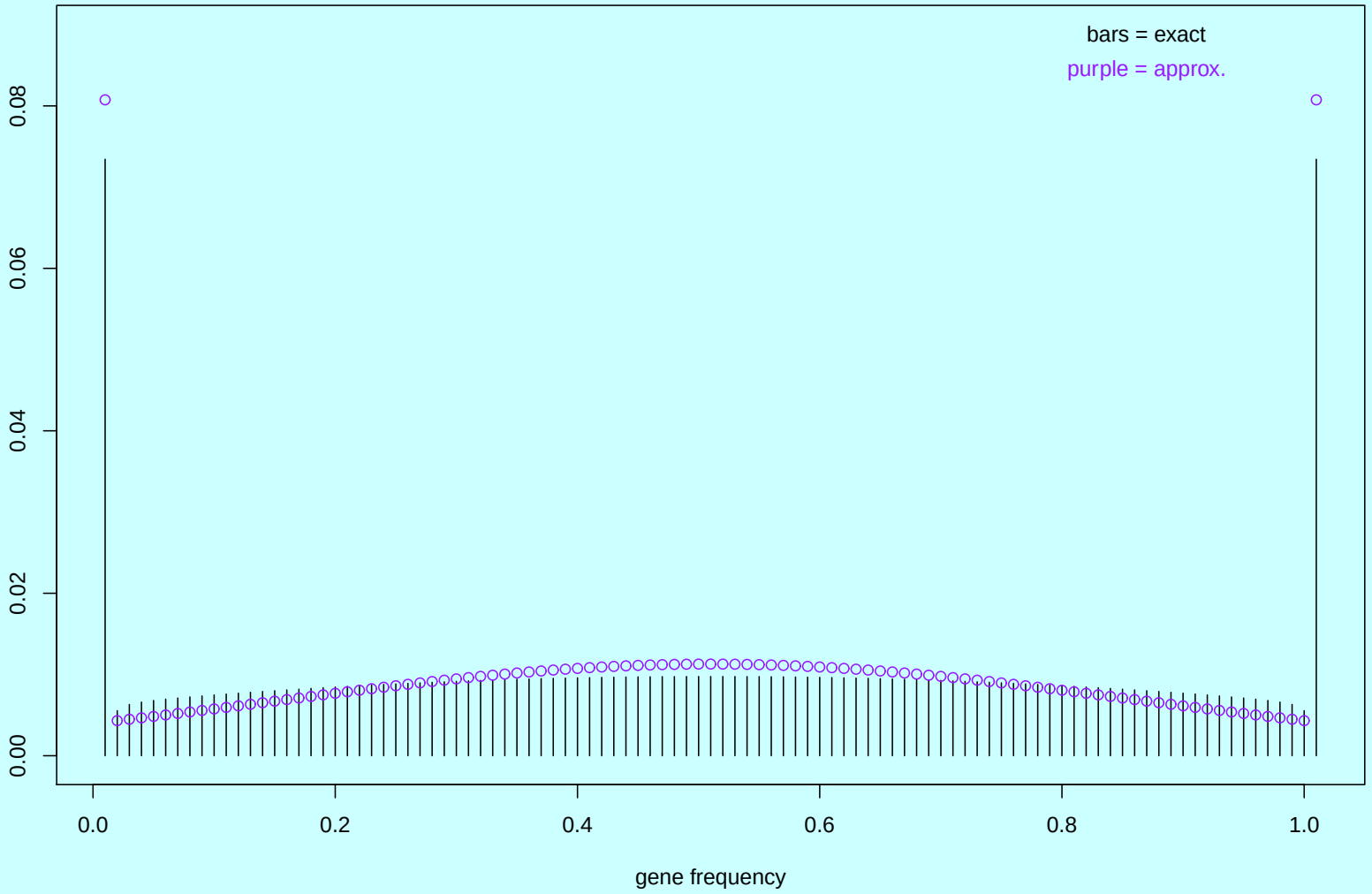
That variance is not constant: it varies with p (in a parabola), but maybe we can roughly approximate it by dealing with the case where all populations have roughly similar gene frequencies, so the variances are nearly the same. Maybe. Roughly.

How good is this?



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

How good is this?



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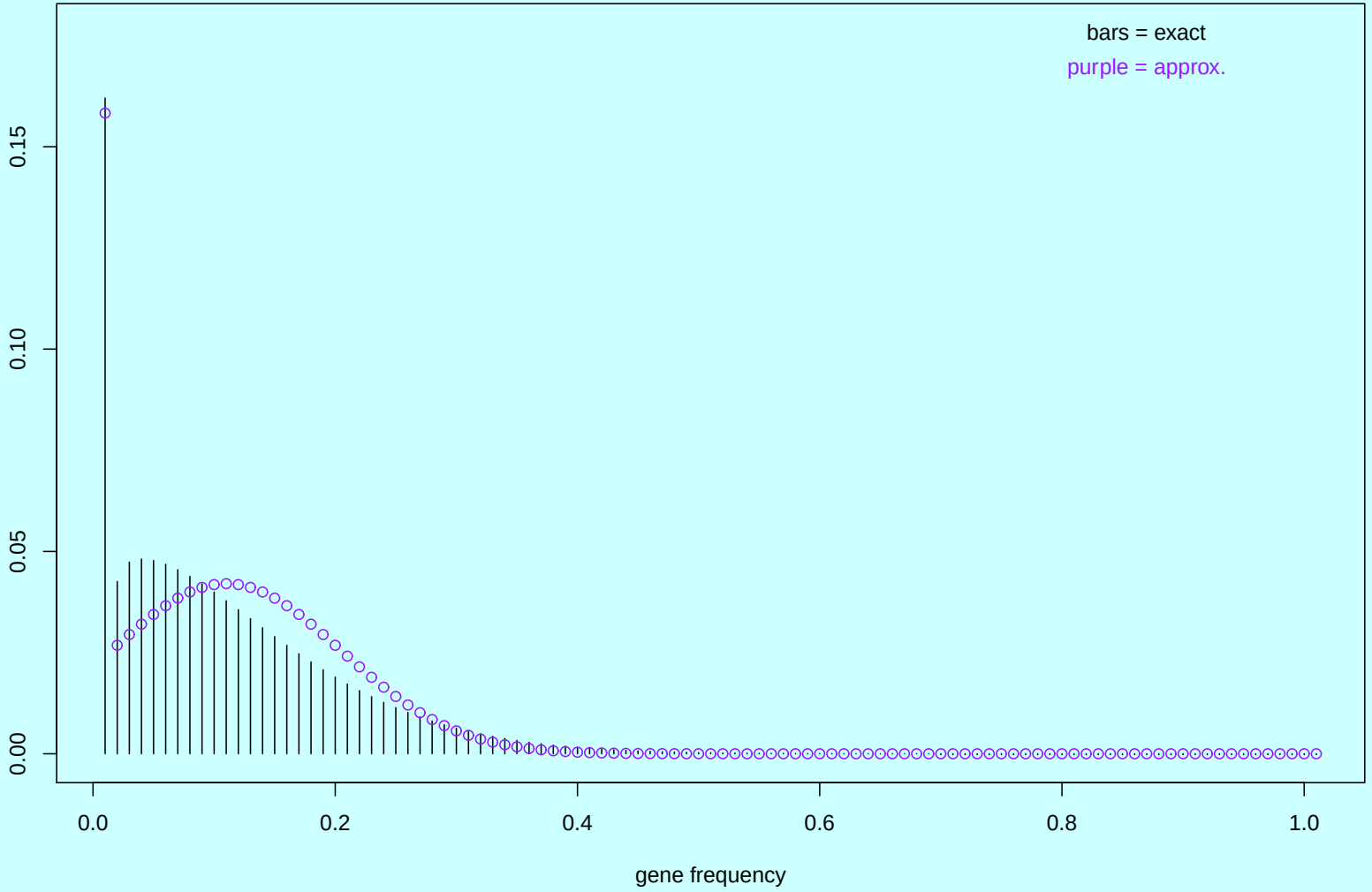
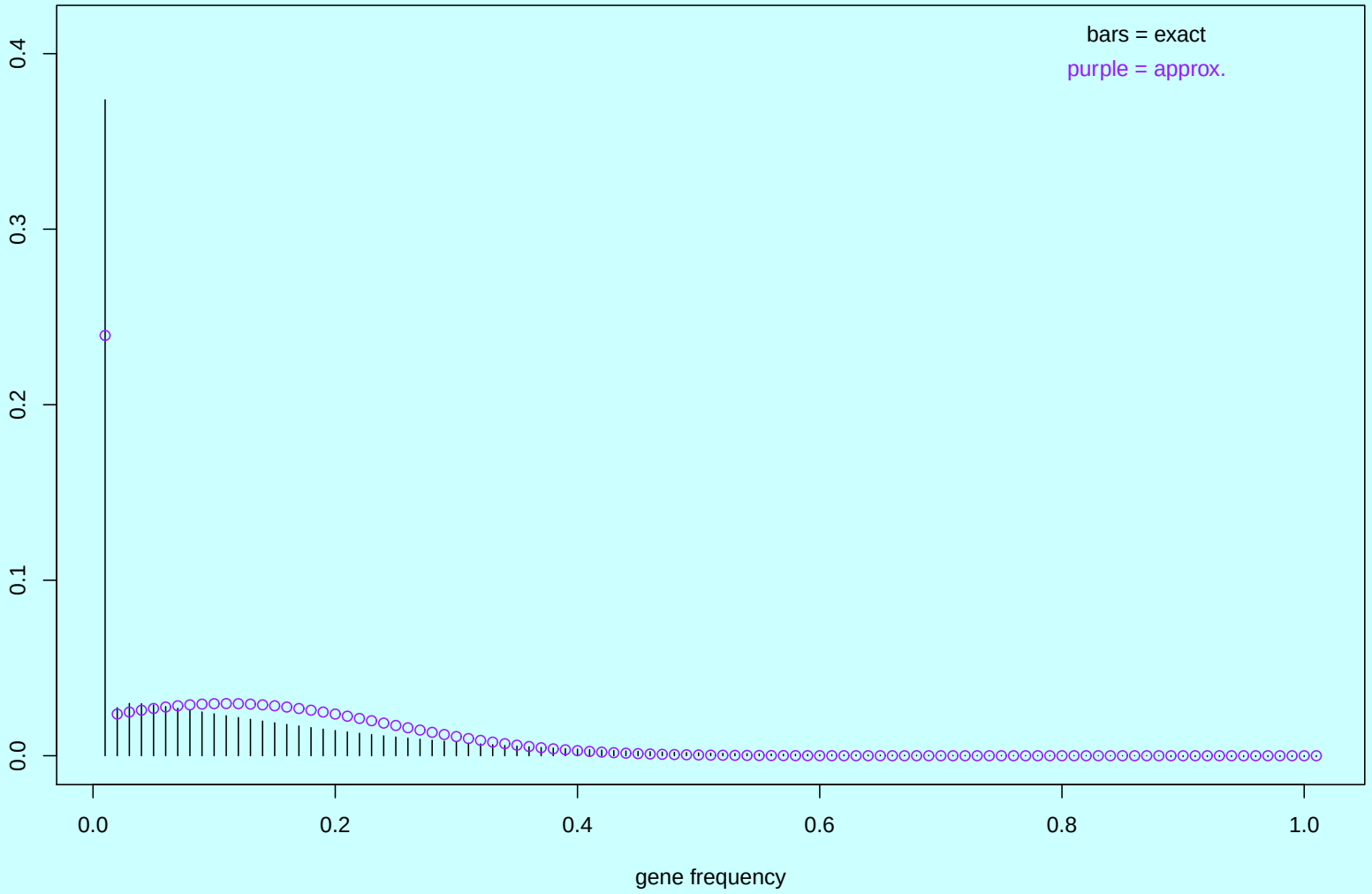


Starting with $p = 0.1$, after 10 generations in a population of size 50.

How good is this?



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

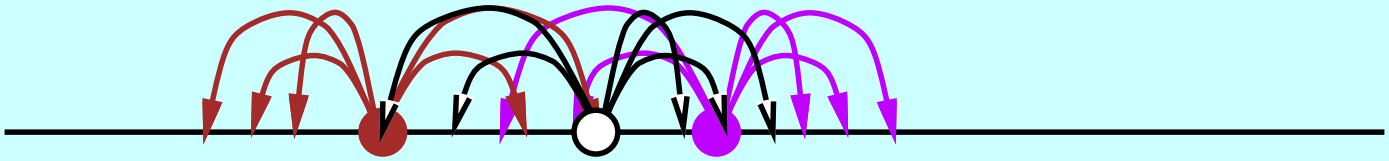
What about a quantitative character?

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.

Covarying character change along a lineage

What is the distribution of changes in multiple characters (say p of them) along a lineage? Simply the appropriate multiple of the infinitesimal rate of change per unit branch length.

If a set of characters $\mathbf{x}$, changes under covarying Brownian motion, in time t (or a pseudo-time branch-length t) the change will be distributed as

$$\mathbf{\Delta x} \sim \mathcal{N}(\mathbf{0}, \mathbf{V}t),$$

(where $\mathbf{V}$ is the covariance matrix of the infinitesimal change of the Brownian Motion).

What causes change in quantitative characters?

For neutral mutation and genetic drift, can show that for a quantitative character with additive genetic variance V_A and population size N the genetic (additive) value of the population mean is:

$$\mathrm{Var}(\Delta\bar{g}) = V_A/N$$

If mutation and drift are at equilibrium:

$$E\left[V_A^{(t+1)}\right] = V_A^{(t)}\left(1 - \frac{1}{2N}\right) + V_M$$

In neutral traits additive genetic variance rules

so that

$$\mathrm{E}\left[\mathrm{V_A}\right] \;=\; 2\mathrm{NV_M}$$

whereby

$$\mathrm{Var}[\Delta\bar{\mathrm{g}}] \;=\; \left(2\mathrm{NV_M}\right)/\mathrm{N} \;=\; 2\mathrm{V_M}$$

an analog of Kimura's result for neutral mutation.

Thus to transform characters to independent Brownian motions of equal evolutionary variance, we could use the additive genetic variance $\mathrm{V_A}$.

With selection ... life is harder

There is the "Breeder's Equation" of Wright and Fisher (1920's)

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

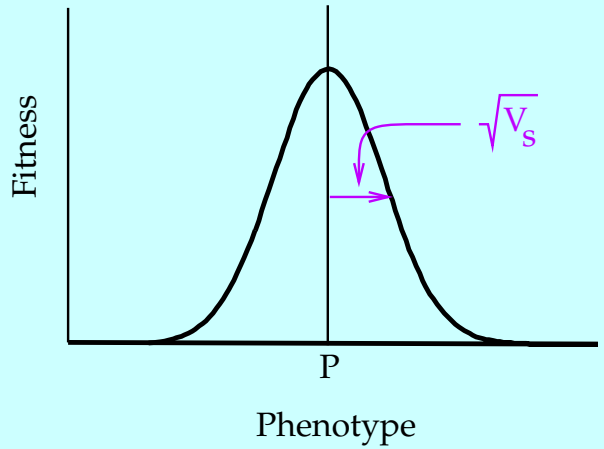
and Russ Lande's (1976) recasting of that in terms of slopes of mean fitness surfaces:

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

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

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



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:

- **Genetic covariances**. (the same loci affect two or more traits)

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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.

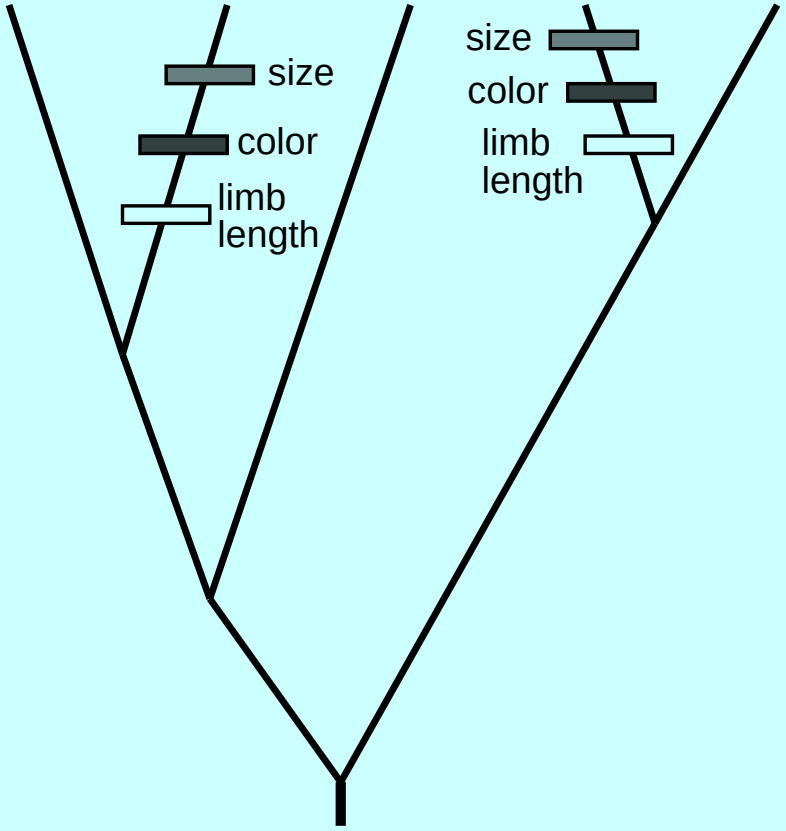
A simple example of selective covariance

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

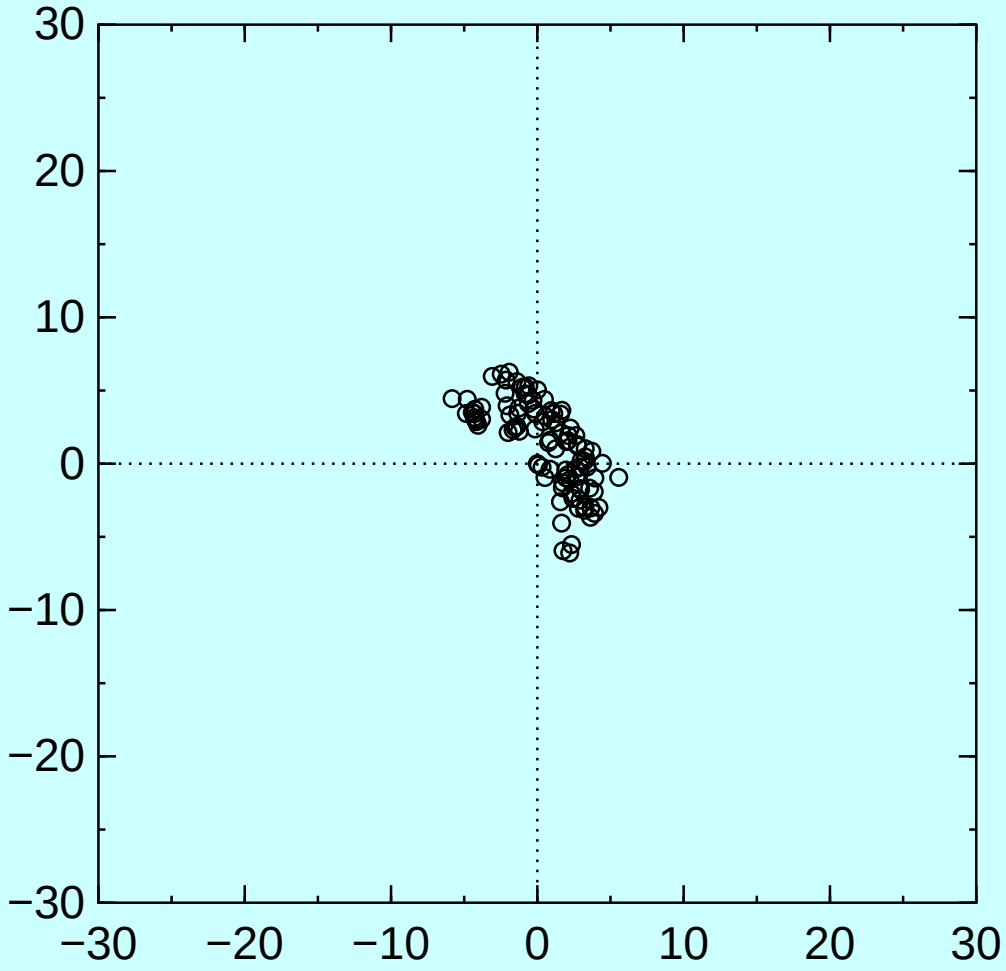
a simple example:

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



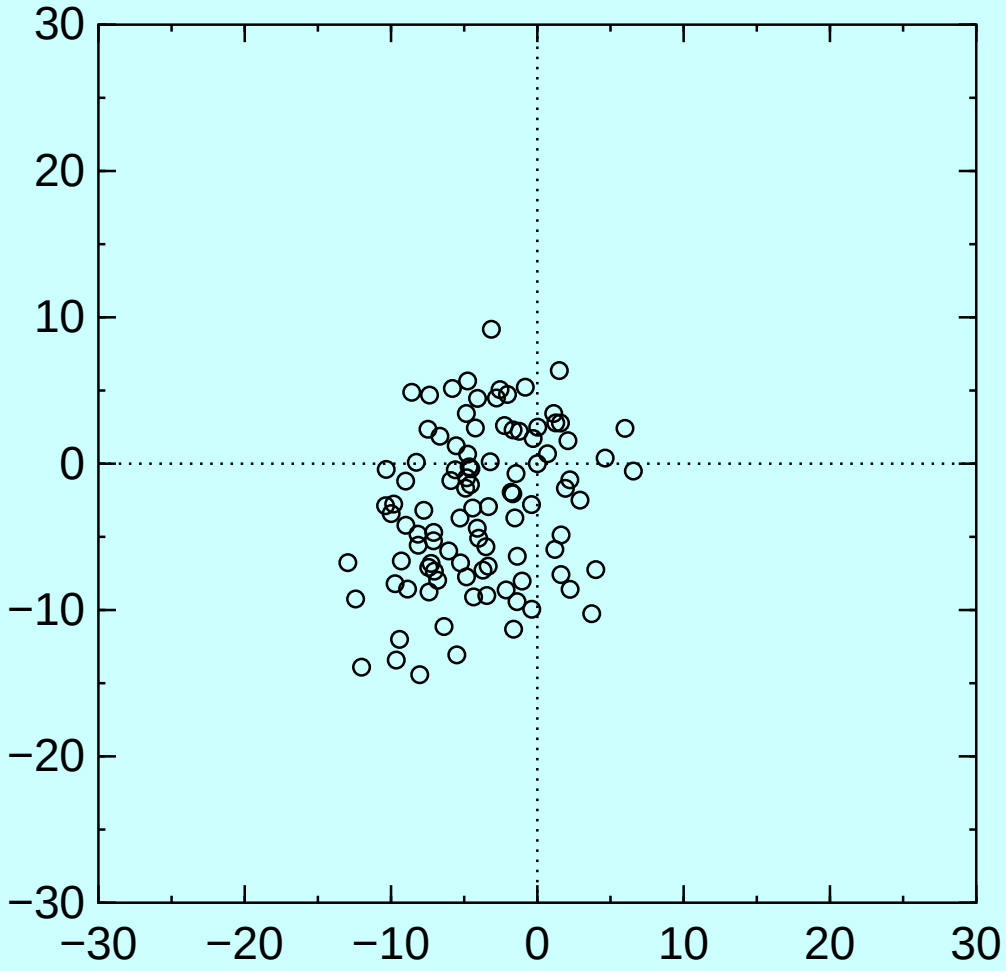
G. L. Stebbins. 1950. *Variation and evolution in plants.* Columbia Univ. Press, New York. page 121

Chasing a peak, simulated with two characters



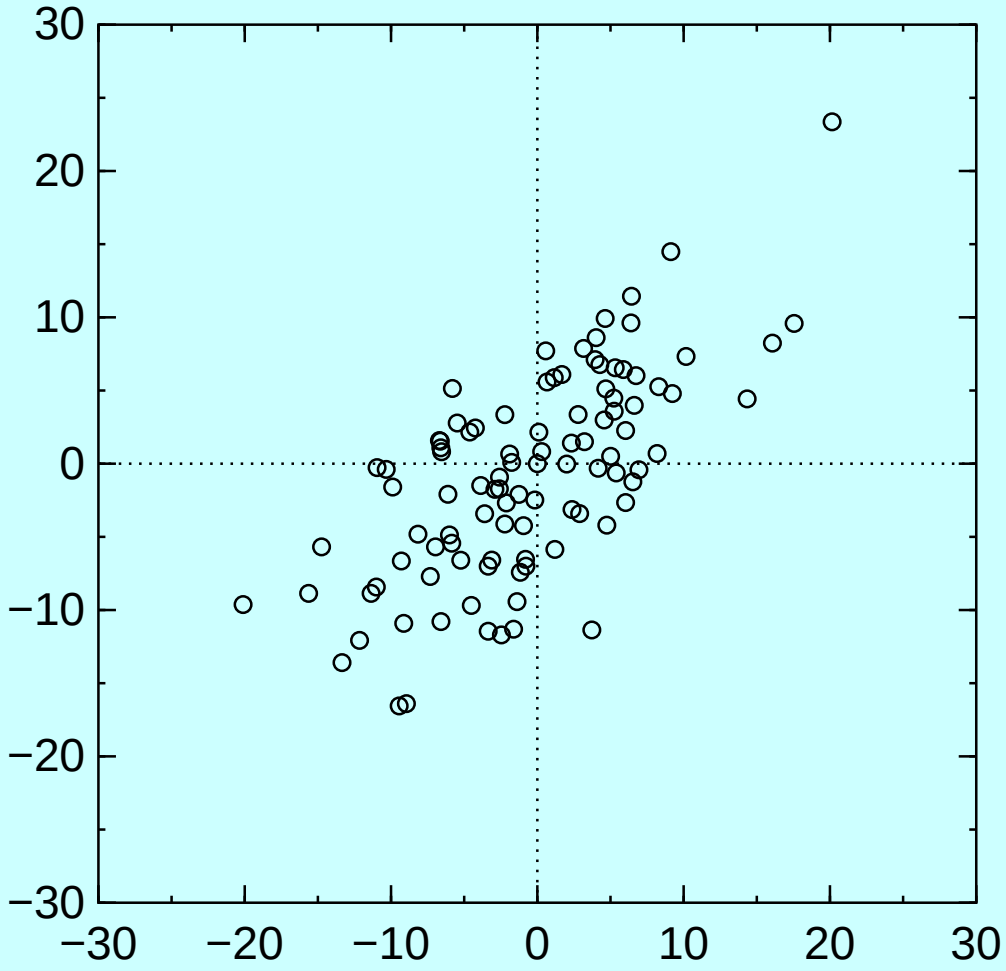
Genetic covariances assumed negative, but the wanderings of the adaptive peaks assumed positively correlated. In the first 100 generations the genetic covariances are most influential.

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.

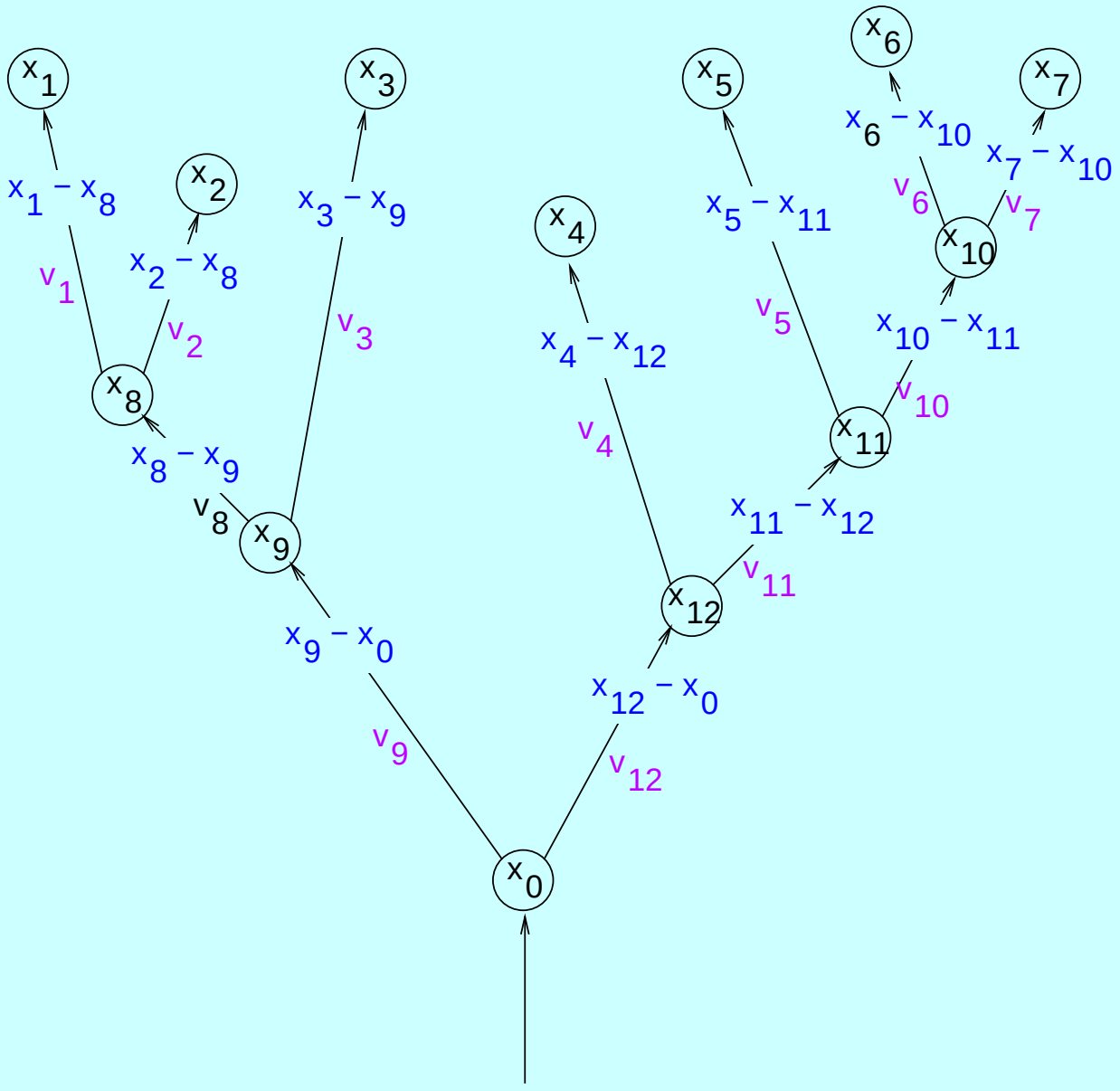
Most models so far do not allow for characters that are observed to covary with those that aren't observed.

A research program?

What we could imagine doing is:

- We might hope to infer additive genetic covariances by doing quantitive 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.

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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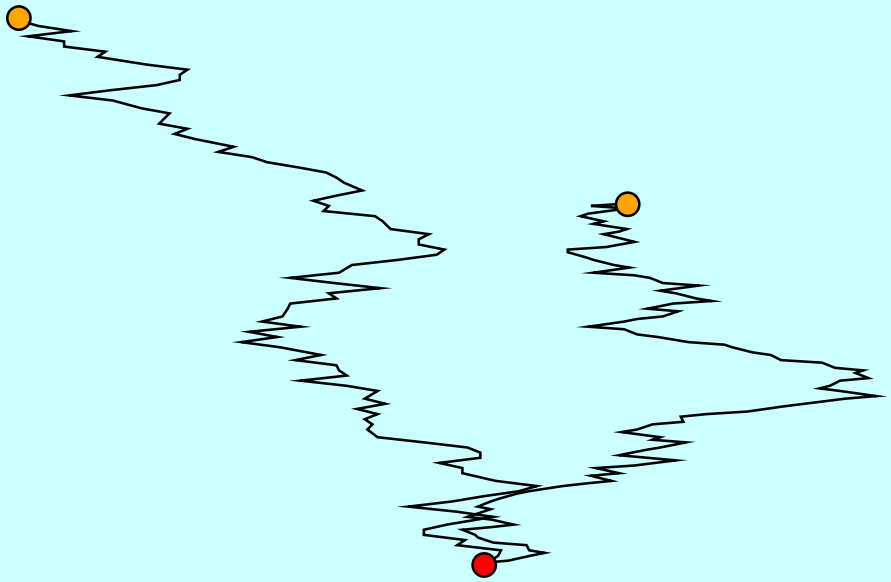
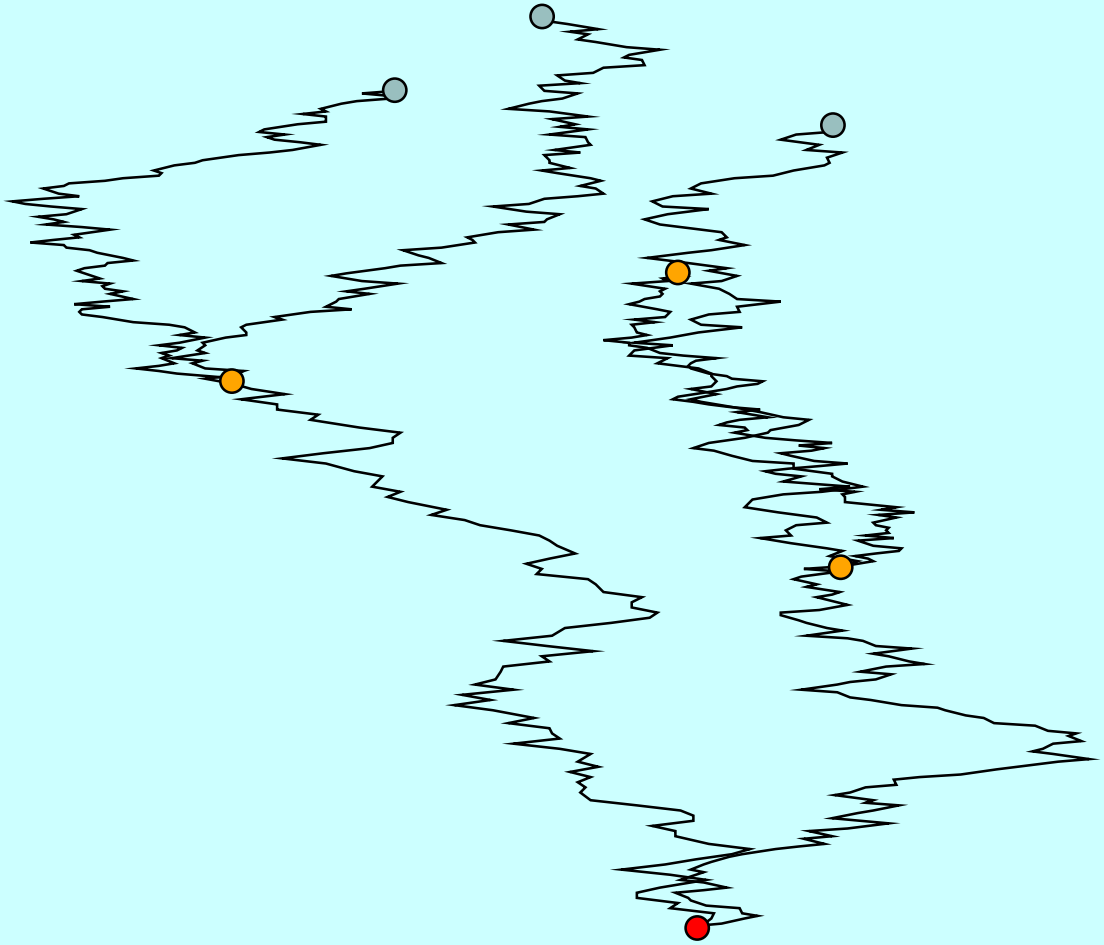


An outcome of Brownian motion on a 5-species tree



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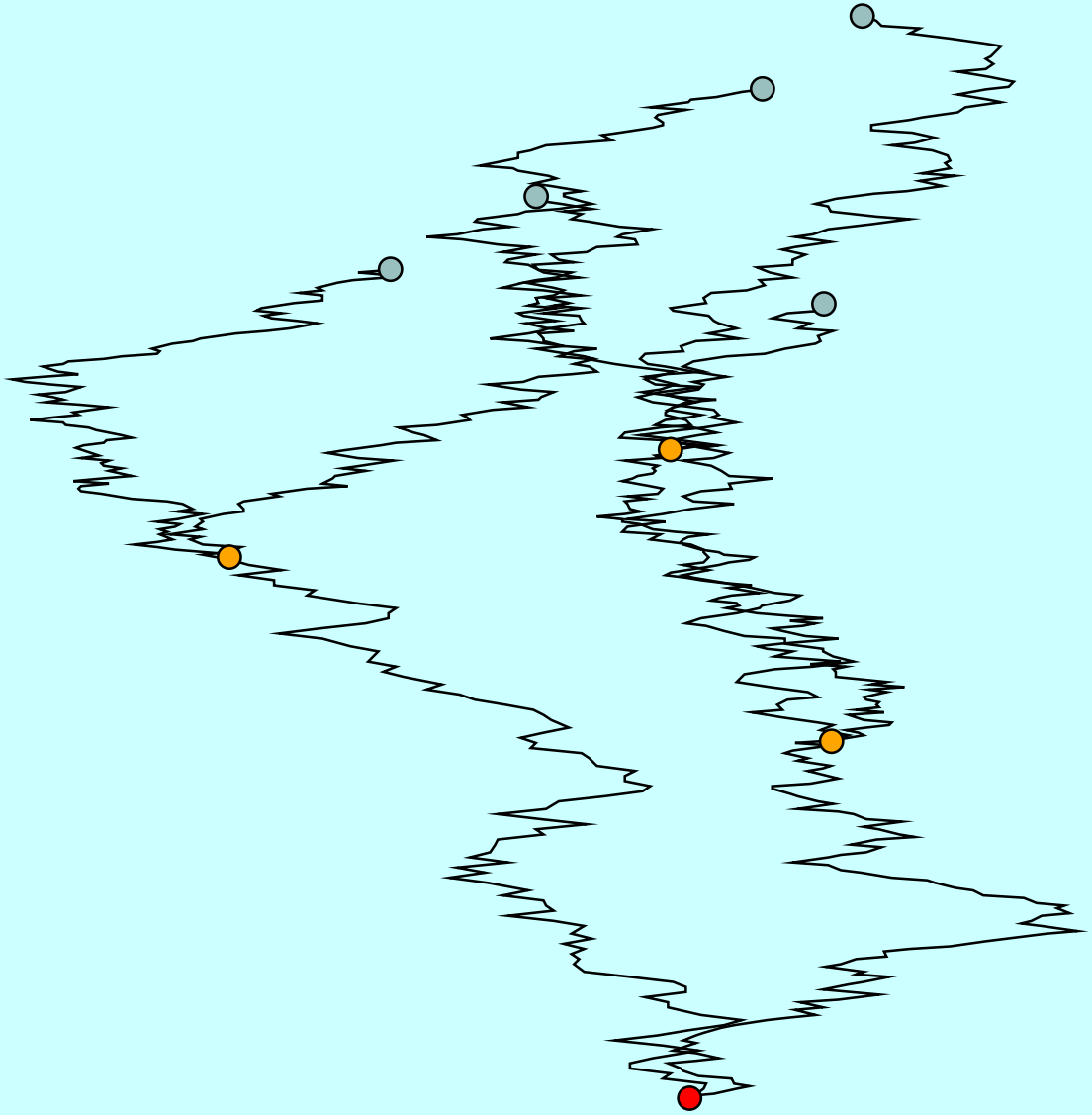


“Pruning” a tree in the Brownian motion case

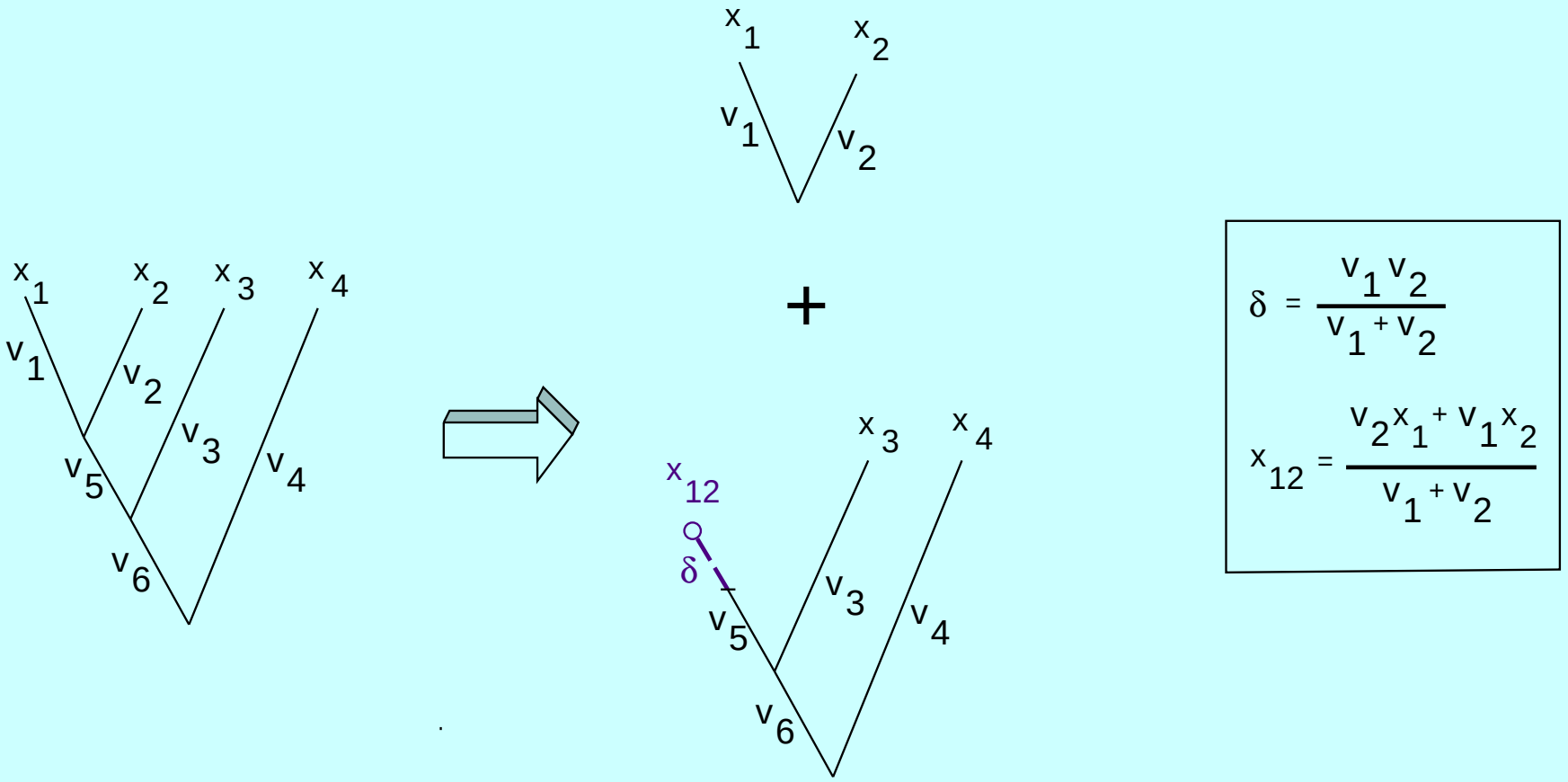
One can take two neighboring tips, and consider their difference $x_1 - x_2$ as well as a weighted average $ax_1 + (1-a)x_2$. Using weights $a : 1-a = 1/v_1 : 1/v_2$, the weighted average is independent of the difference, and the difference is also independent of the rest of the tree.

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.

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

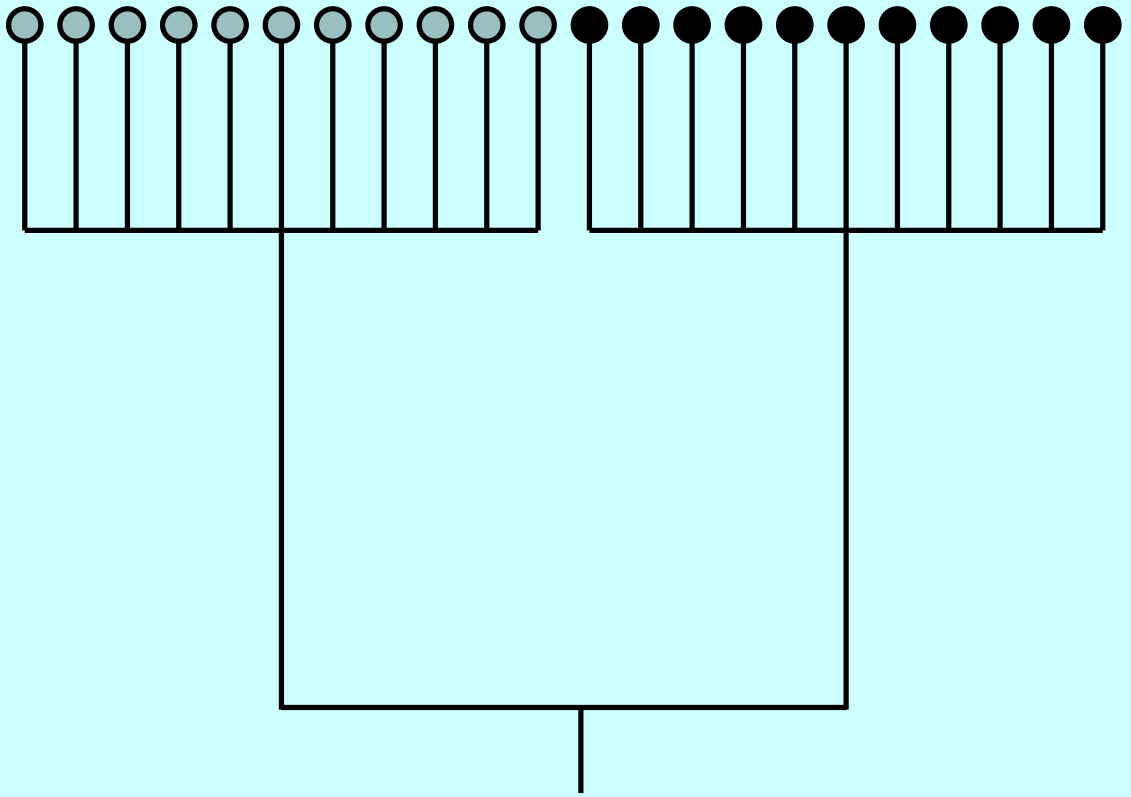
so in effect, a small extra amount of branch length is added.

“Pruning” a tree in the Brownian motion case

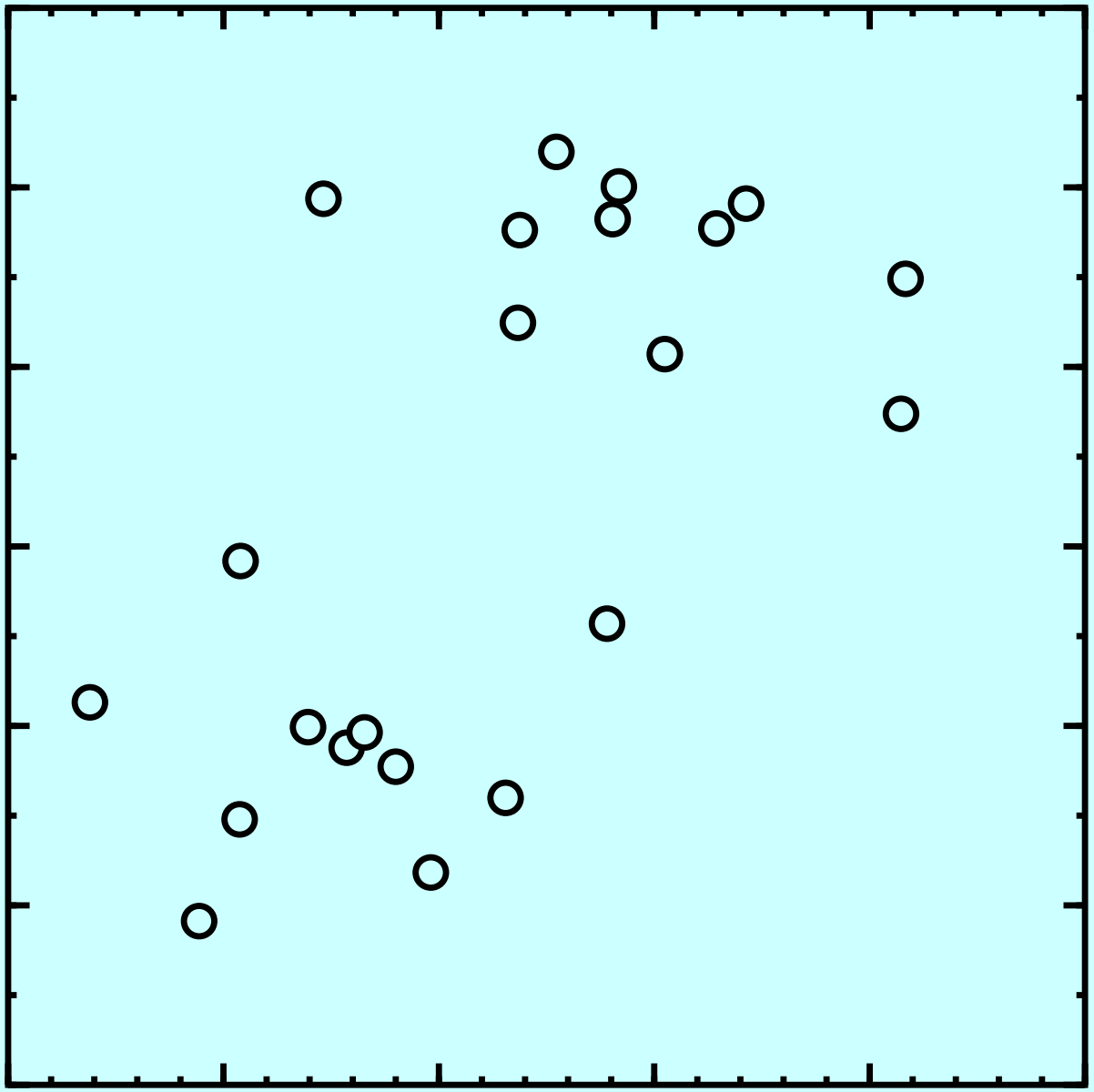


(True in the sense that the log-likelihoods – which are a bit different than the usual likelihoods – add up, since the likelihoods multiply).

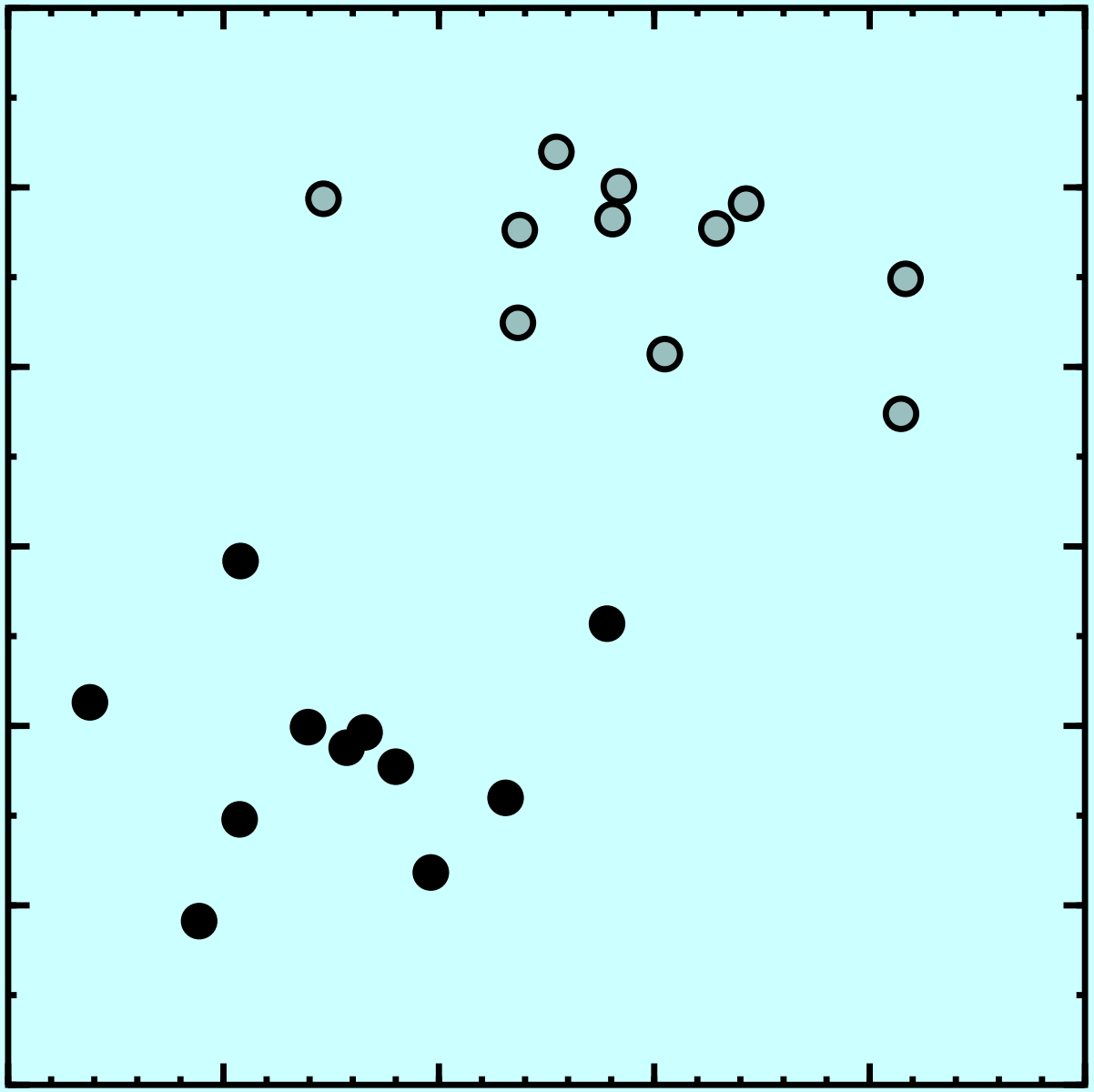
A simple case to show effects of phylogeny



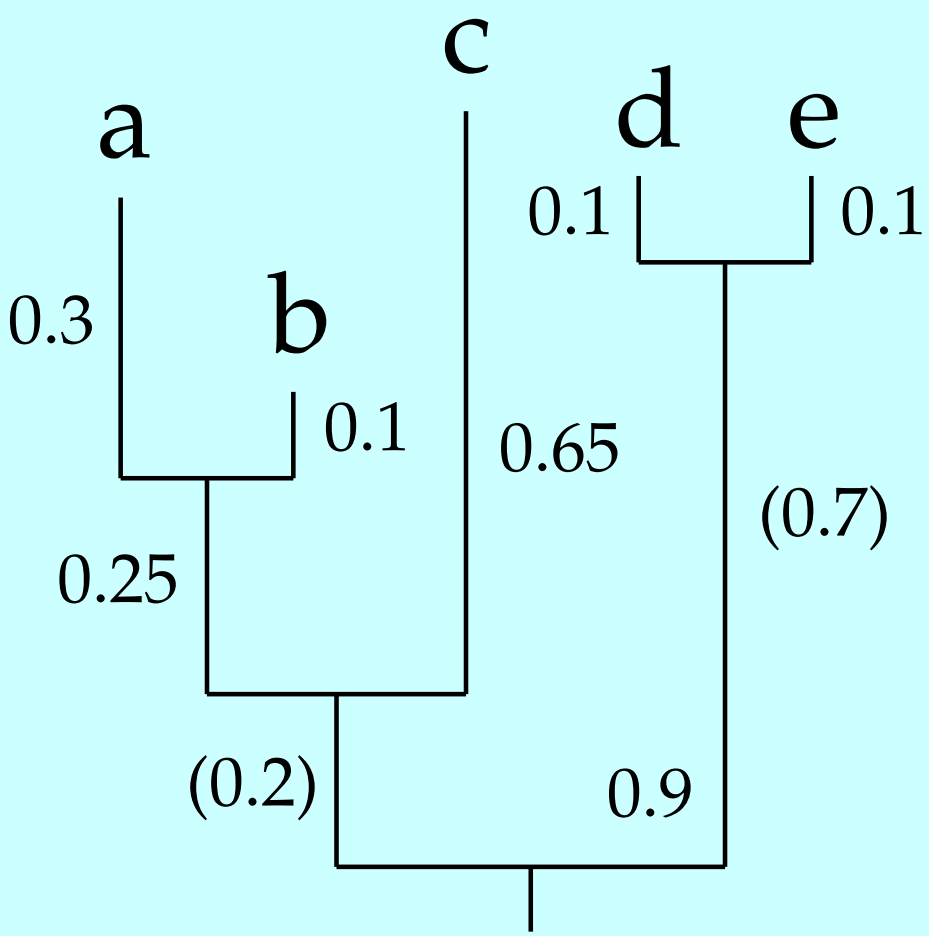
Two uncorrelated characters evolving on that tree



Identifying the two clades



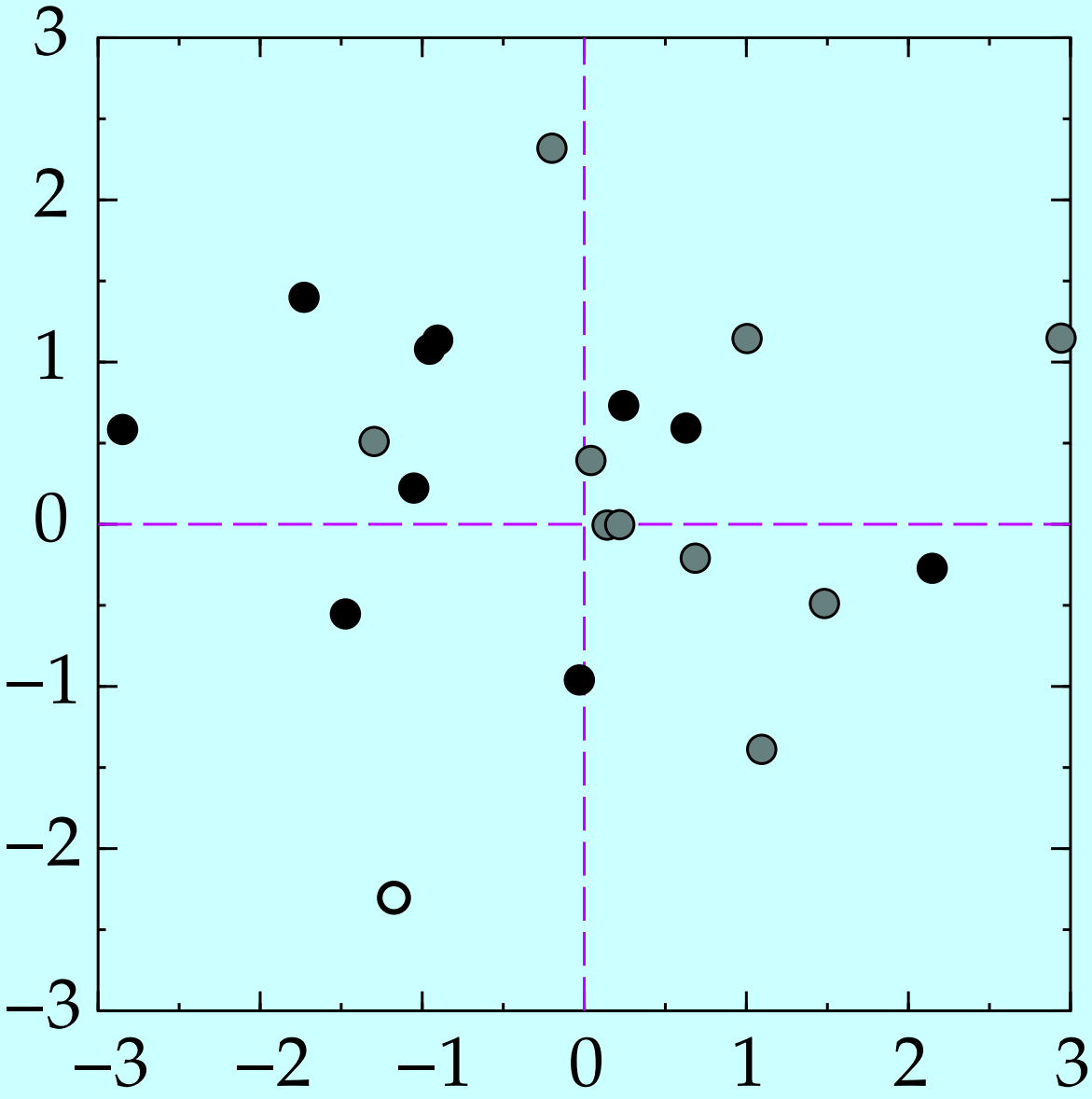
A tree on which we are to observe two characters



Contrasts on that tree

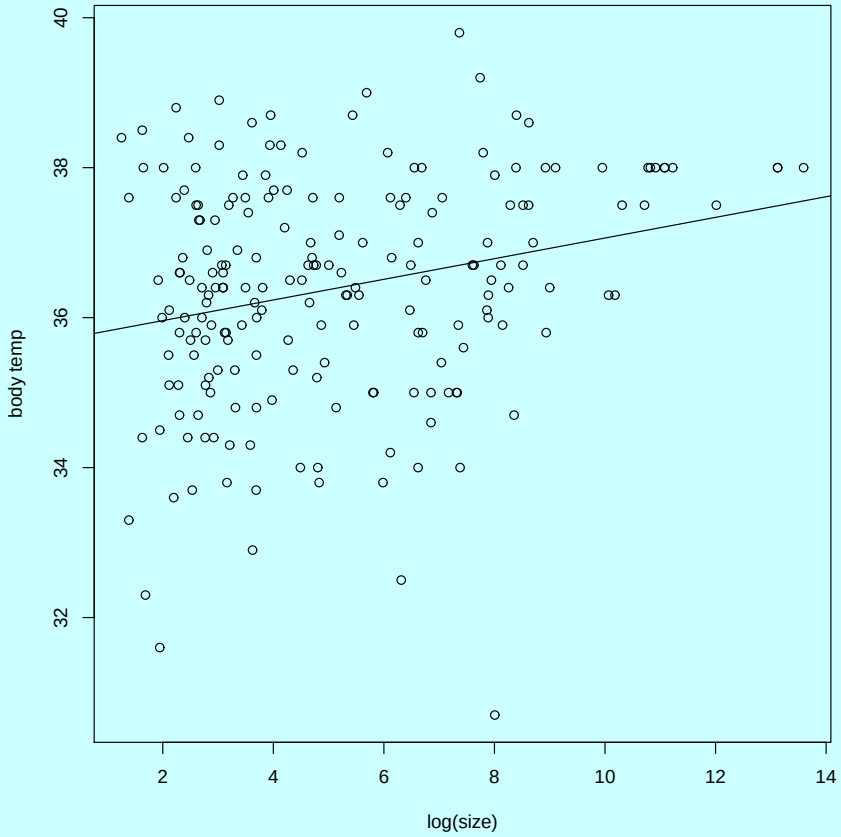
Contrast												Variance proportional to
y_1	$=$	x_a	$-$	x_b								0.4
y_2	$=$	$\frac{1}{4}\,x_a$	$+$	$\frac{3}{4}\,x_b$	$-$	x_c						0.975
y_3	$=$						x_d	$-$	x_e			0.2
y_4	$=$	$\frac{1}{6}\,x_a$	$+$	$\frac{1}{2}\,x_b$	$+$	$\frac{1}{3}\,x_c$	$-$	$\frac{1}{2}\,x_d$	$-$	$\frac{1}{2}\,x_e$		1.11666

Contrasts for the 20-species two-clade example

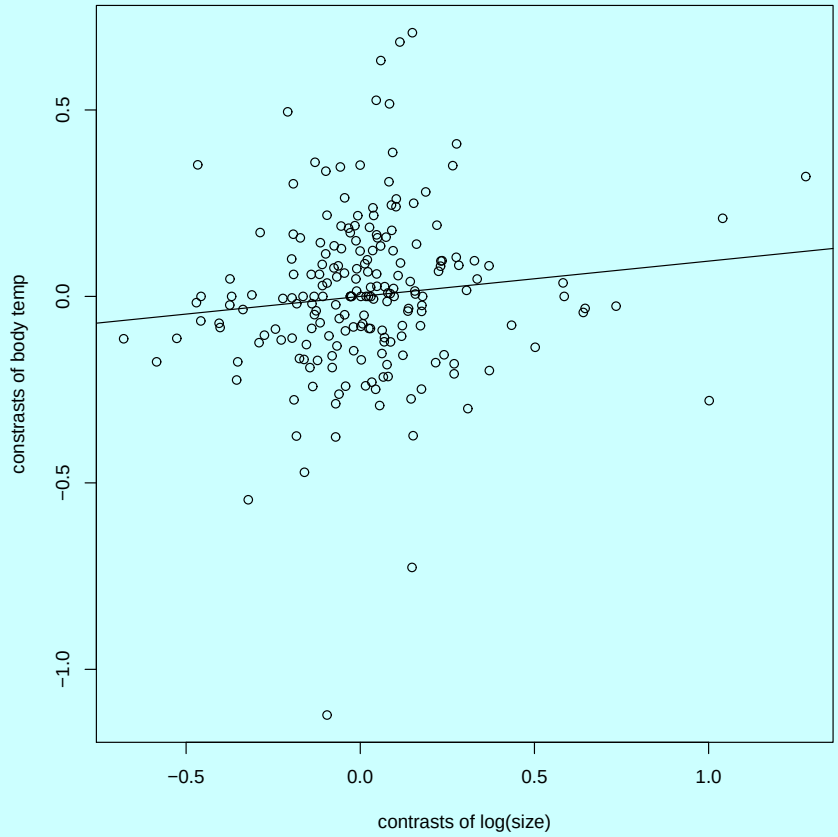


An example: Riek and Geiser, 2013

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)



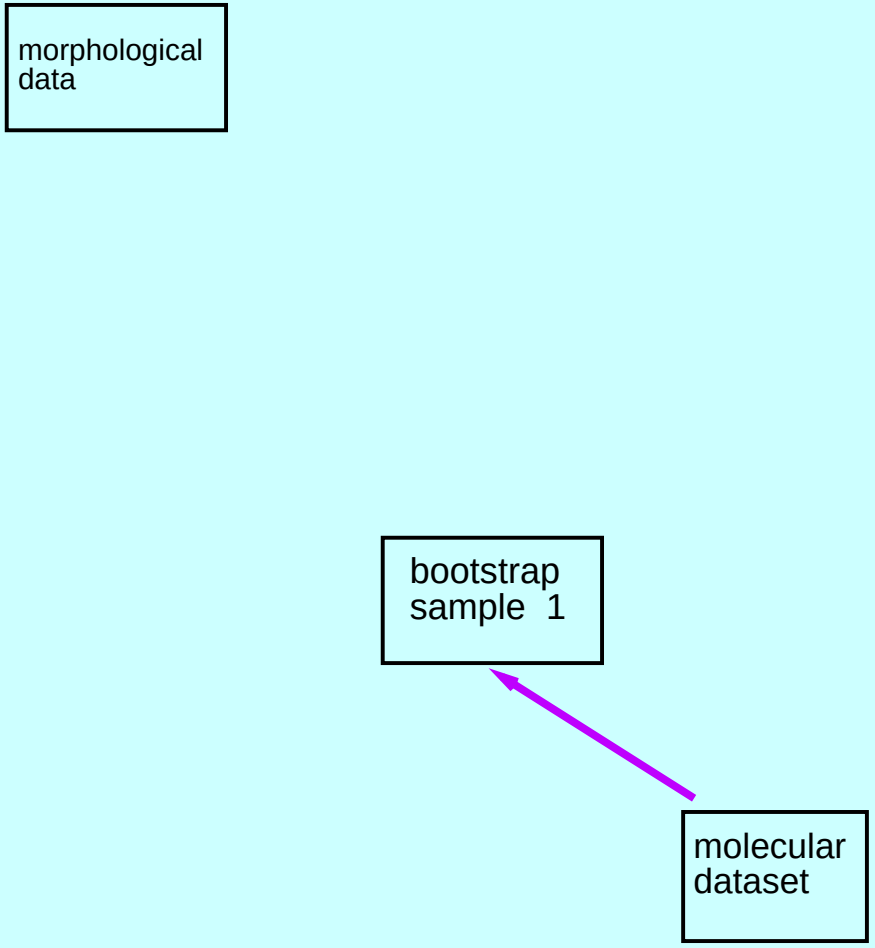
contrasts vs. contrasts
(P for slope $\neq 0$ is 0.116)

When the tree is noisy: Propagating bootstrap sampling

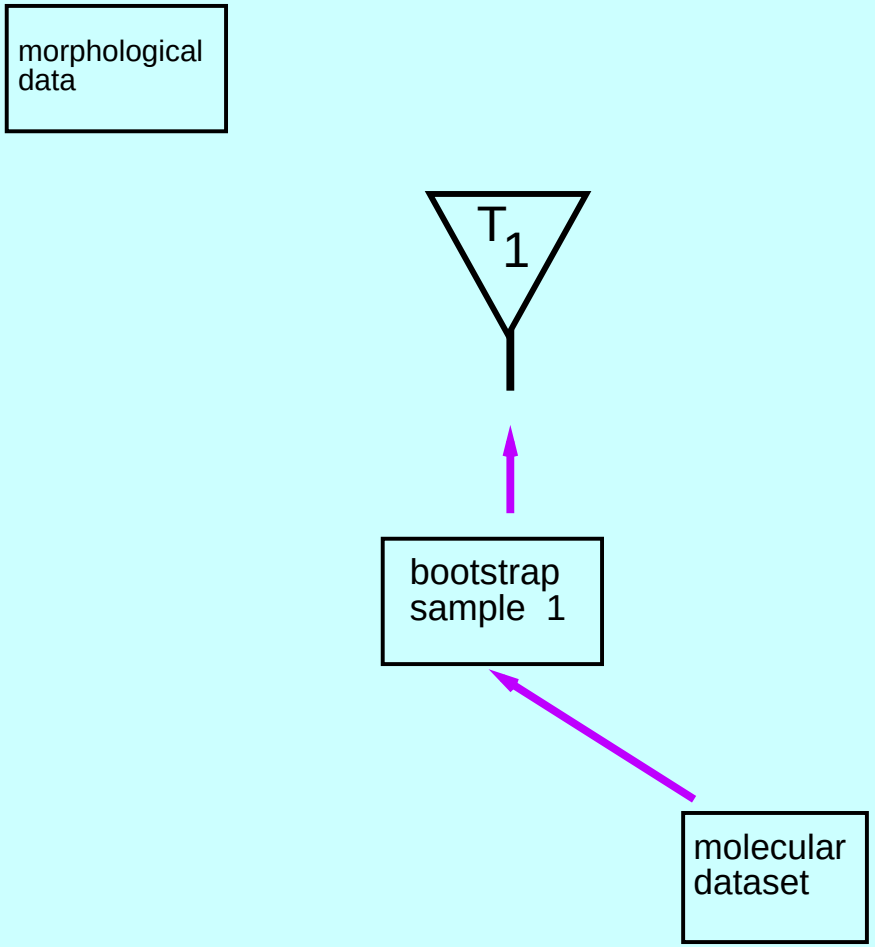
morphological data

molecular dataset

Propagating bootstrap sampling



Propagating bootstrap sampling



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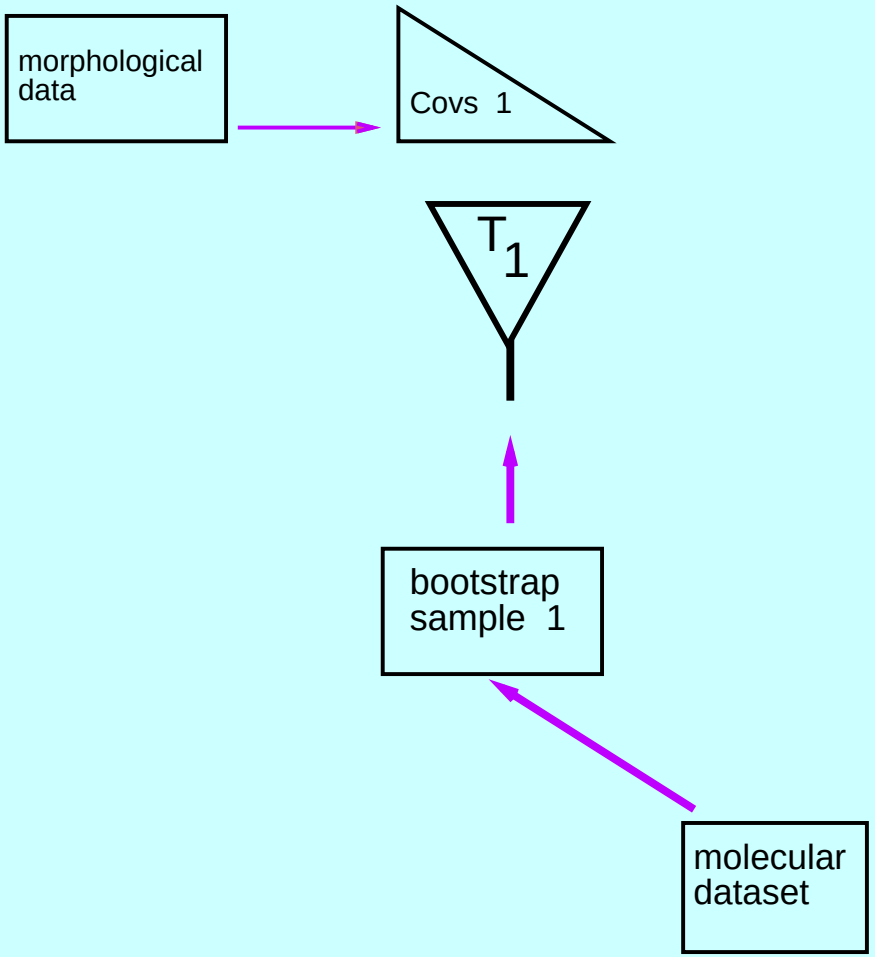

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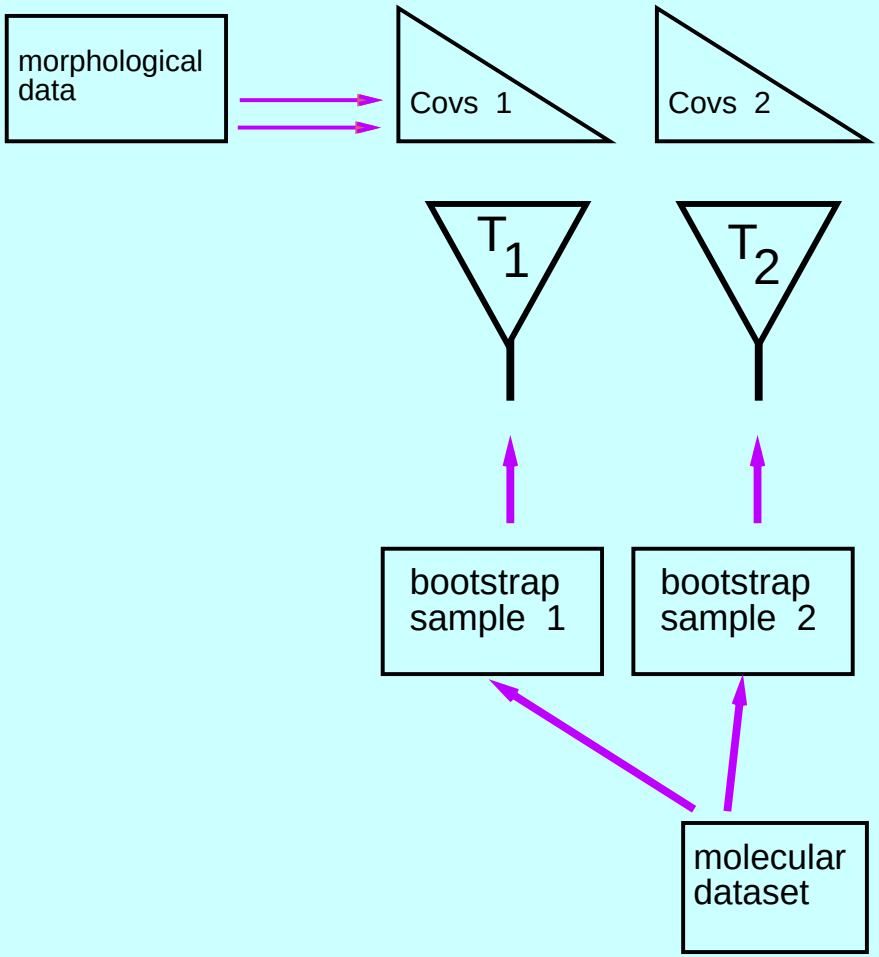

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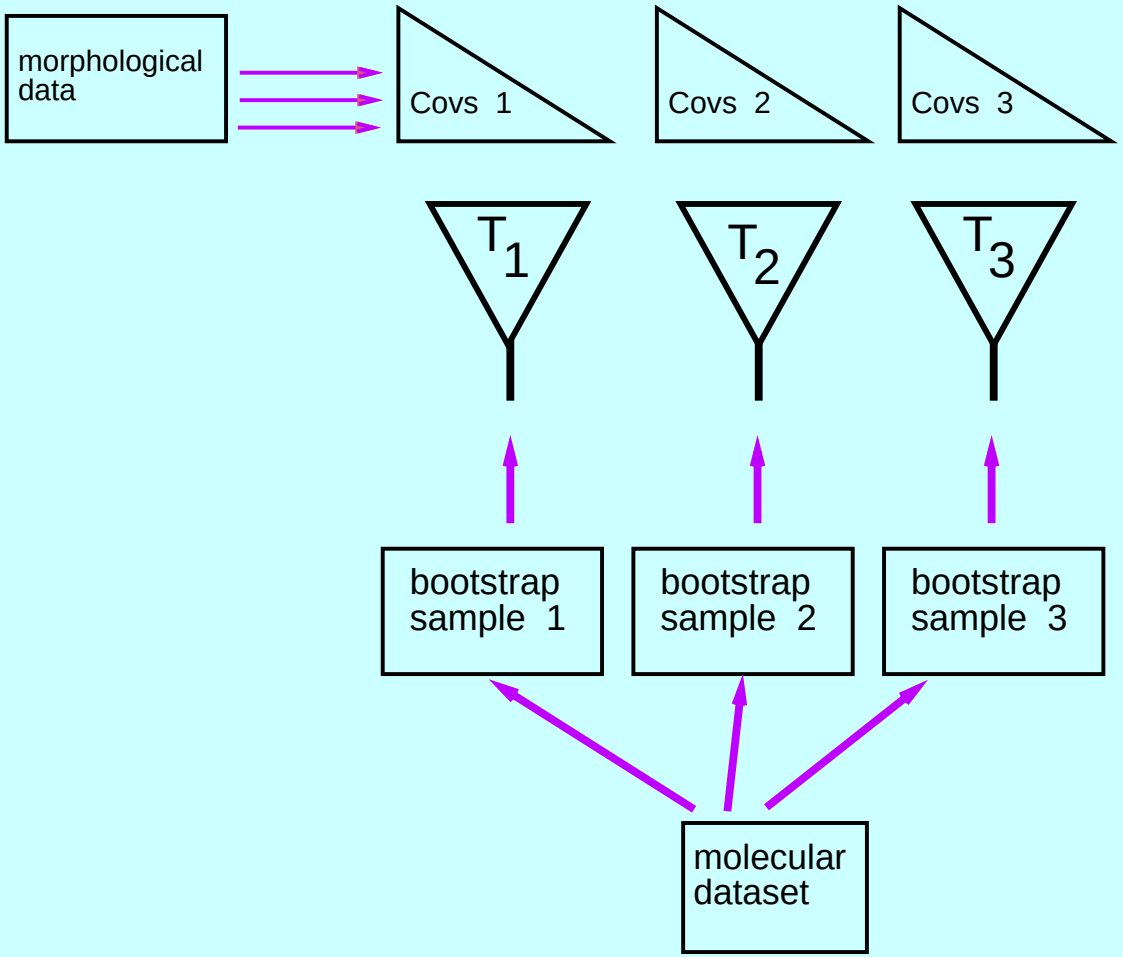

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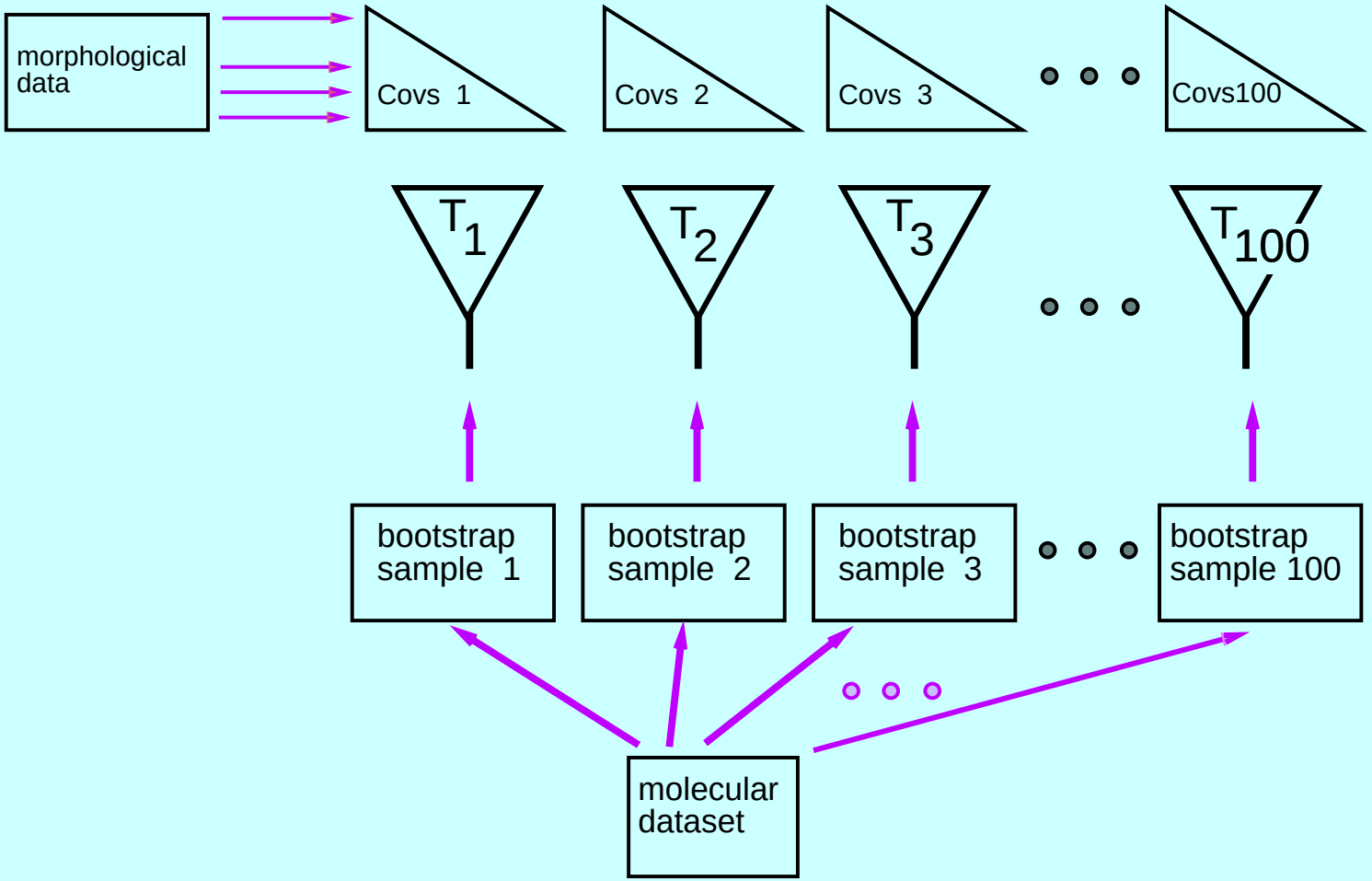
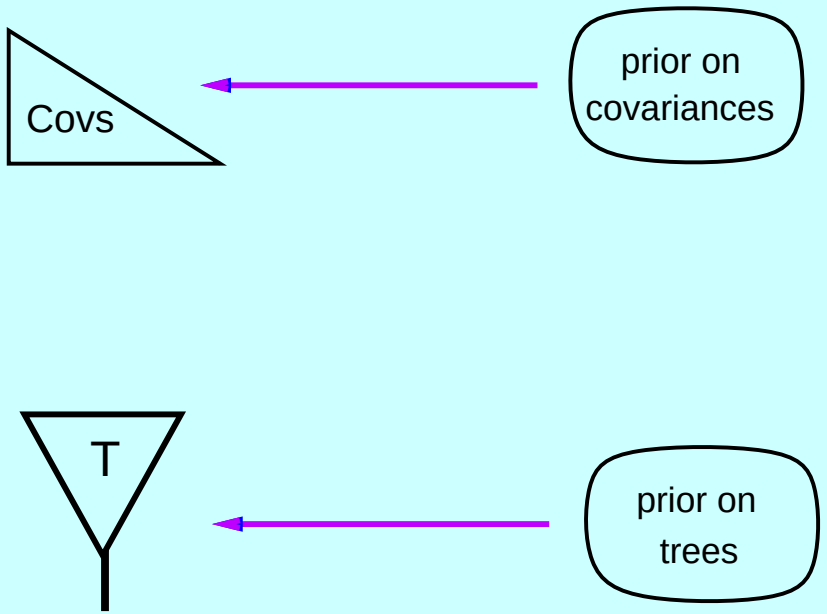


A Bayesian model



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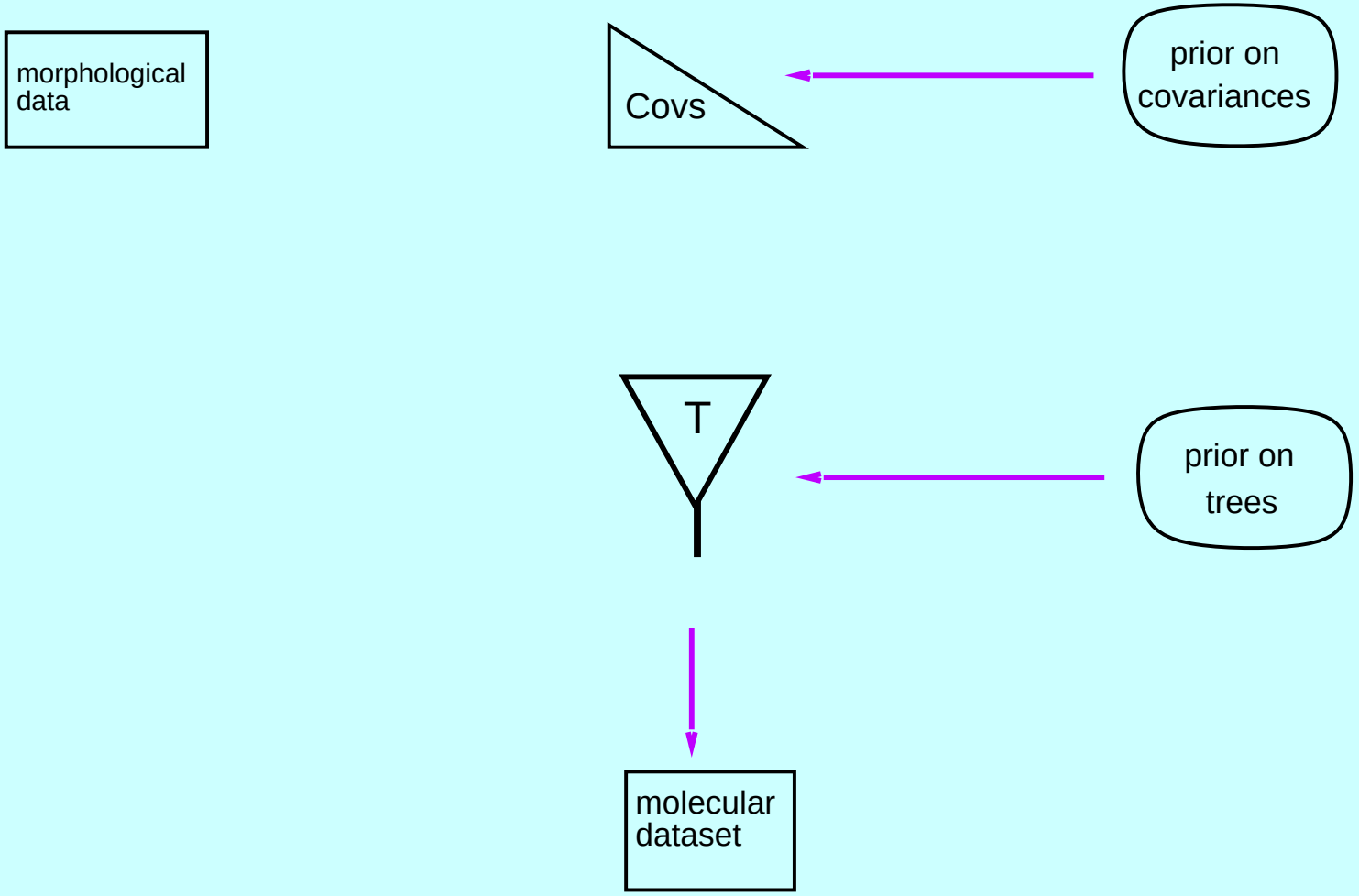

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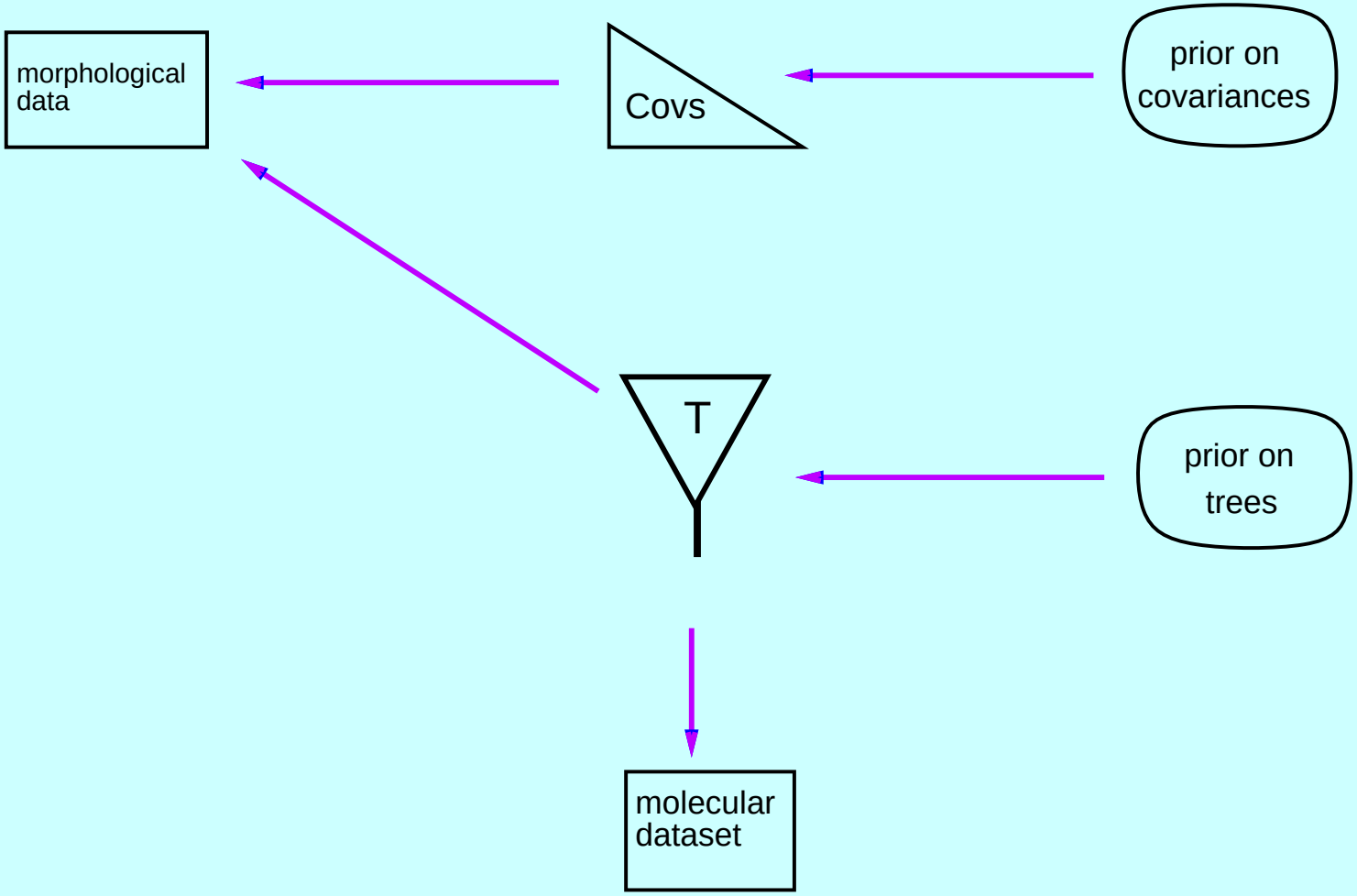
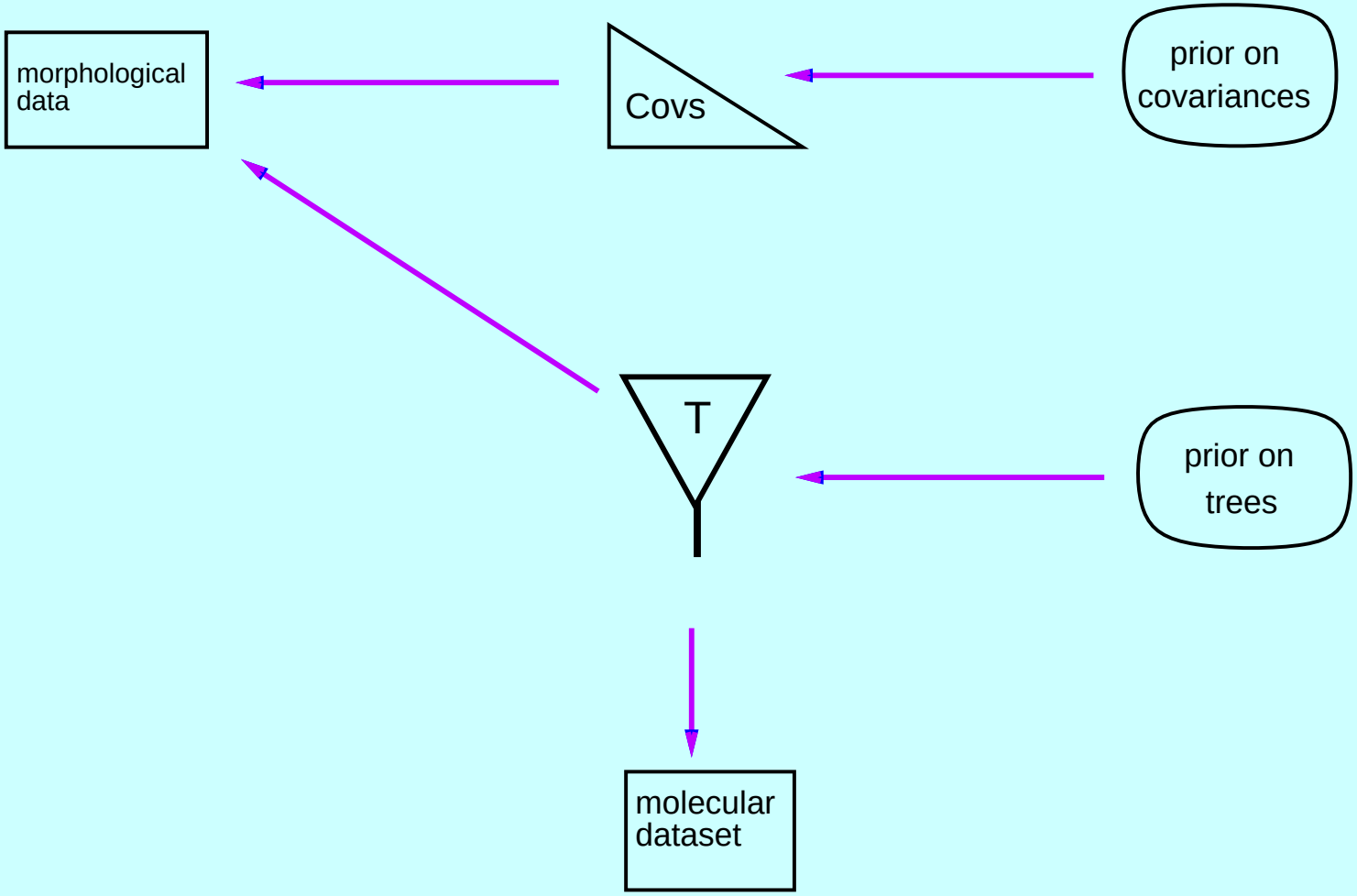


Bayesian MCMC

Markov Chain Monte Carlo



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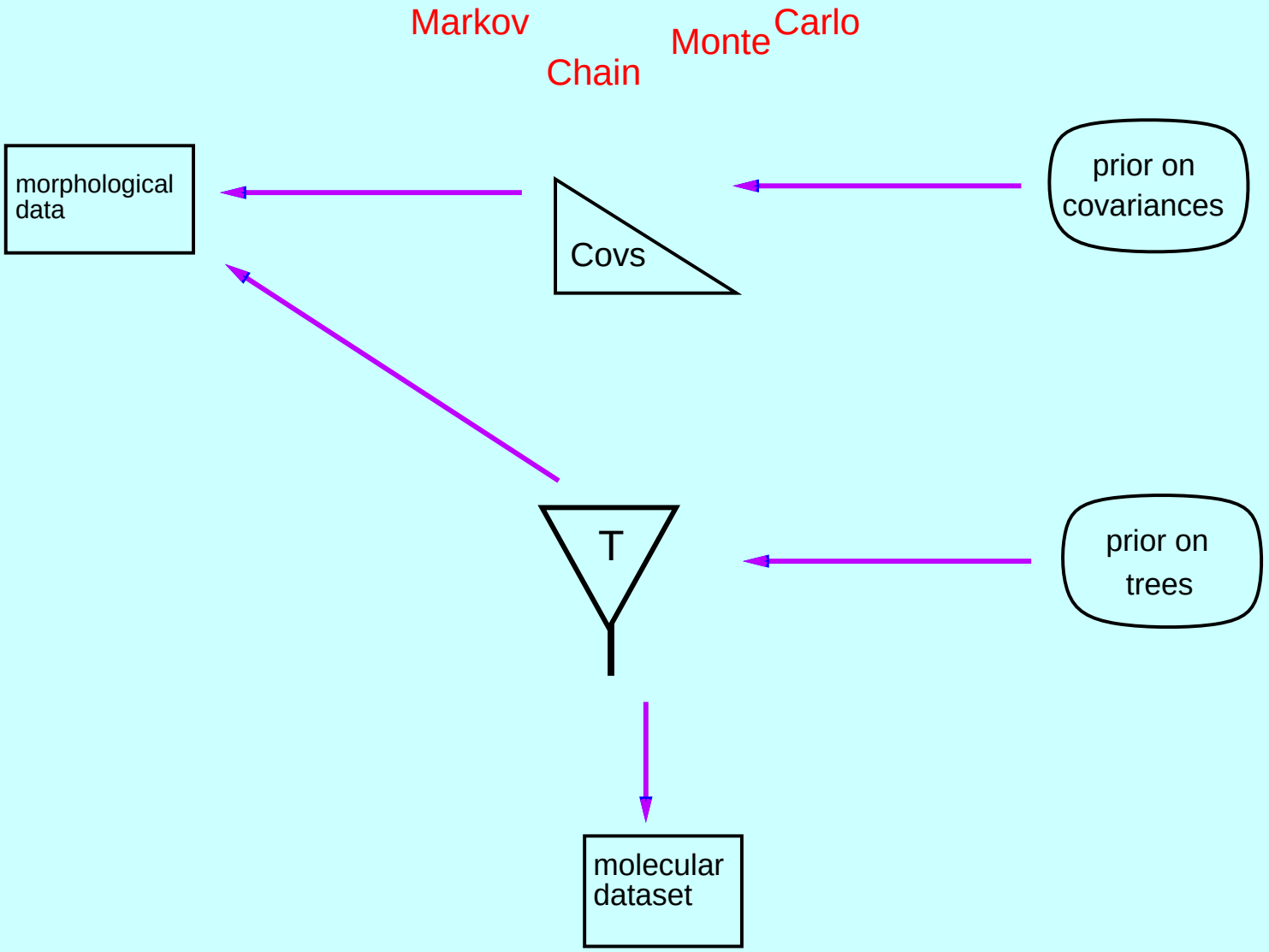

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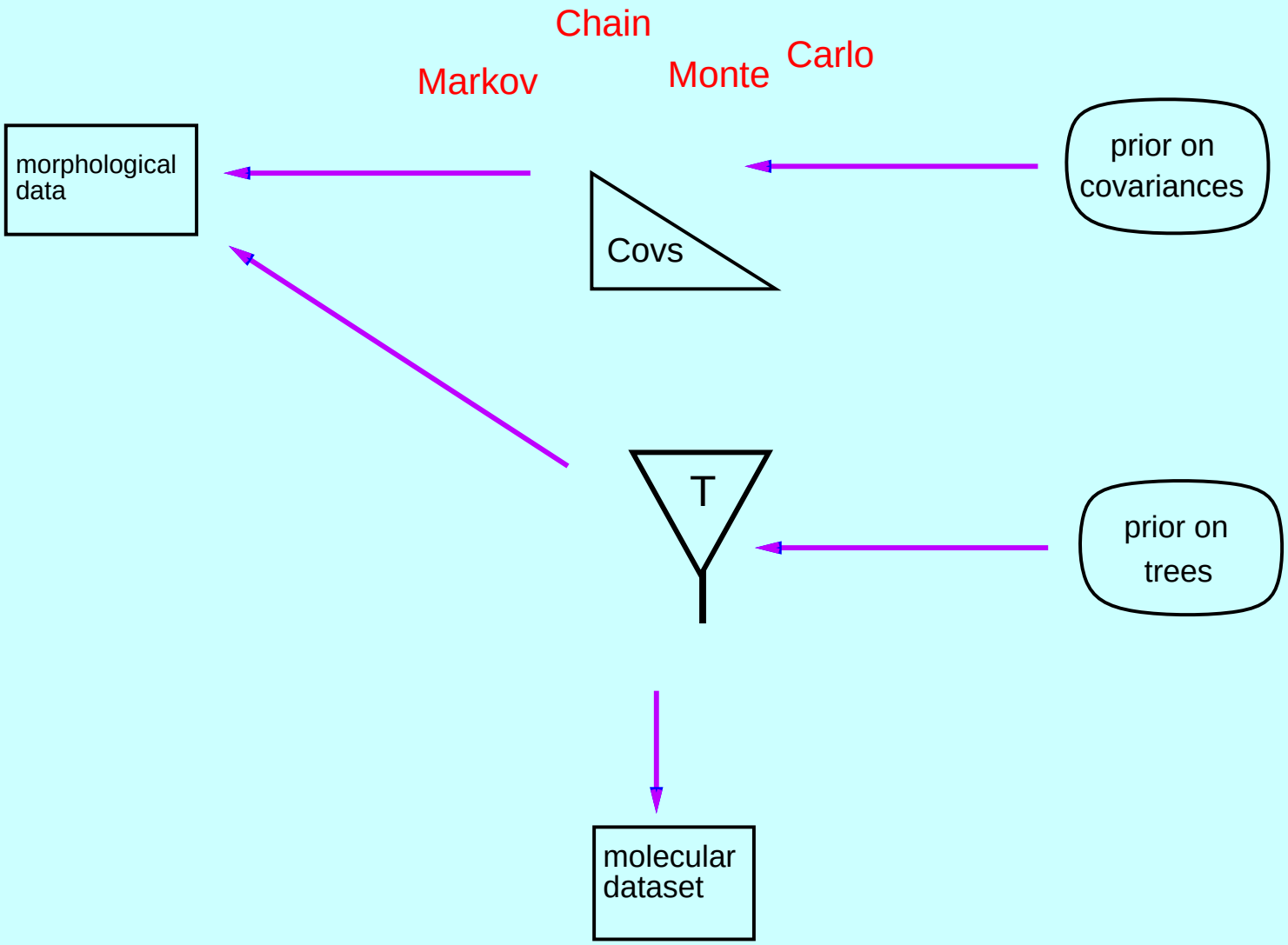

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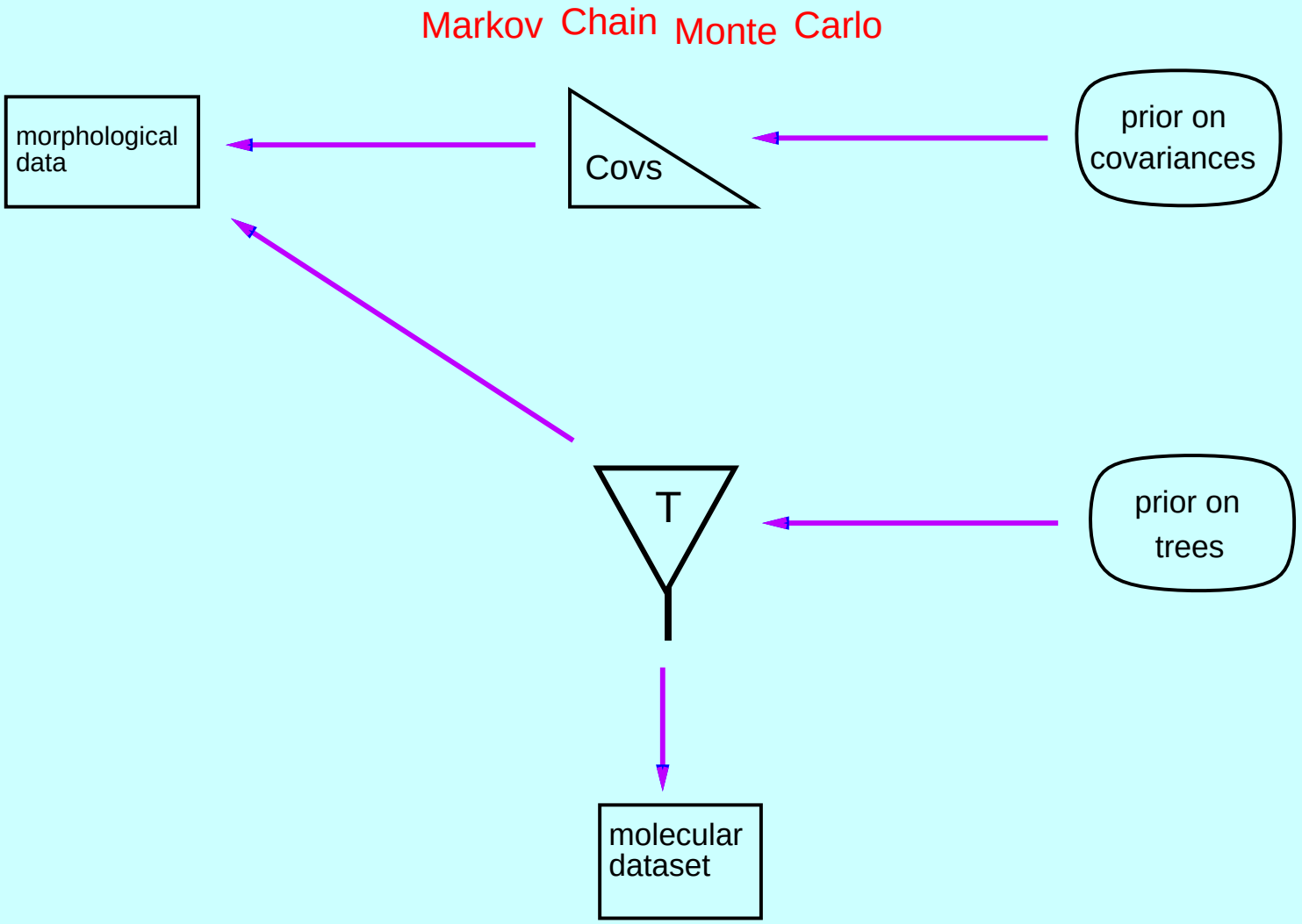

Some complications

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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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