The Phylogenetic Regression

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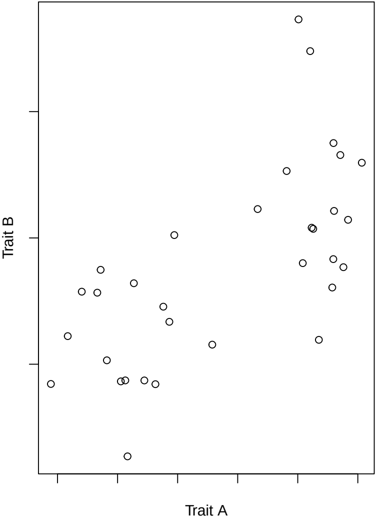
Phylogenetic Comparative Methods



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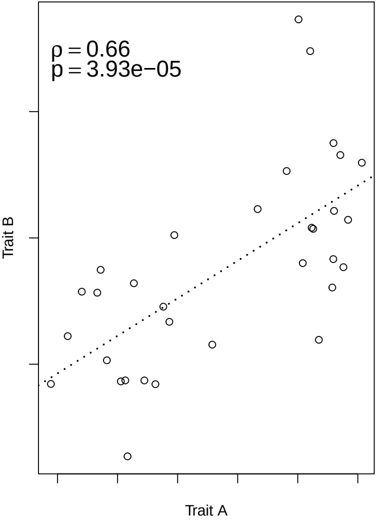

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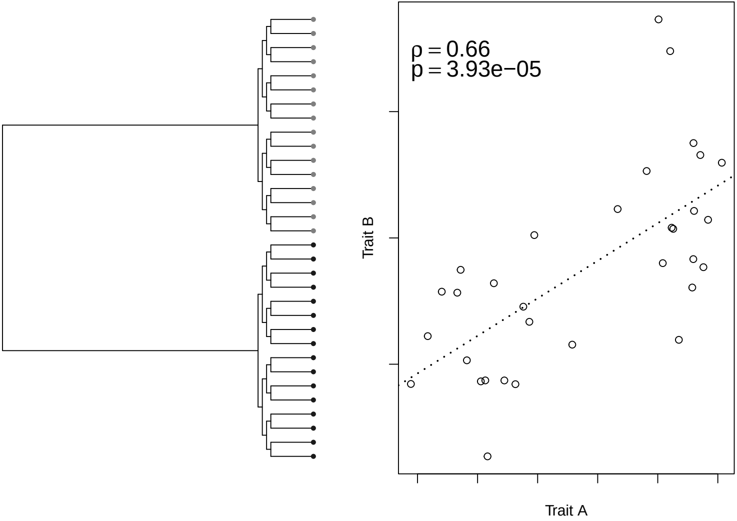

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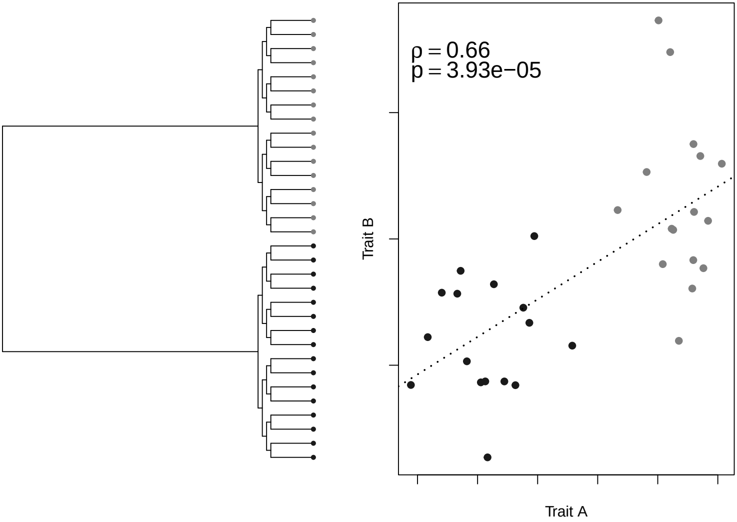

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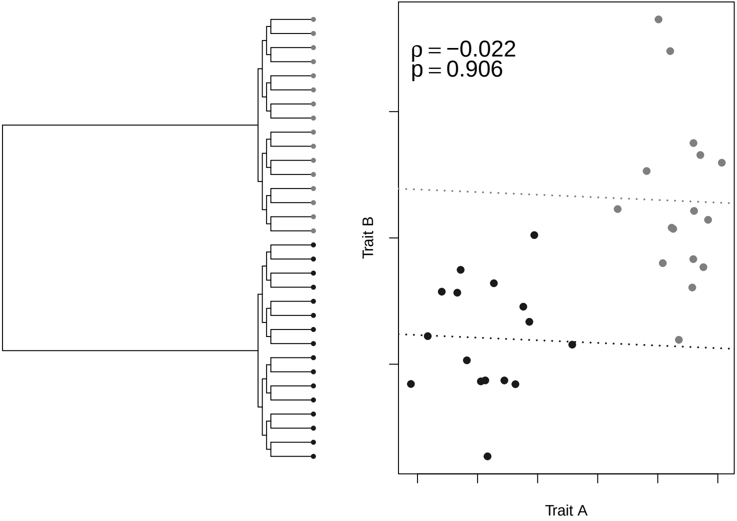

Outline

1. Linear Regression Framework
2. Efficient Computations
3. Phylogenetic Mixed Model

Outline

Simple Gaussian Regression

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i, \quad \forall 1 \leq i \leq n$$

- y_i: quantitative response for i
- x_i: quantitative predicting variable for i
- ϵ_i: "error" for i Gaussian random variable

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  - Centered: $\mathbb{E}[\epsilon_i] = 0$ for all i
  - Homoscedastic: $\mathbb{V}\text{ar}[\epsilon_i] = \sigma^2$ for all i
  - Independent: $\mathbb{C}\text{ov}[\epsilon_i; \epsilon_j] = 0$ for all $i \neq j$

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    - iid: $\boldsymbol{\epsilon} \sim \mathcal{N}(\mathbf{0}_n, \sigma^2 \mathbf{I}_n)$

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$$\begin{pmatrix} y_1 \\ \vdots \\ y_n \end{pmatrix} = \beta_0 \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} + \beta_1 \begin{pmatrix} x_1 \\ \vdots \\ x_n \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \vdots \\ \epsilon_n \end{pmatrix}$$

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- $\mathbf{Y} = (y_1, \dots, y_n)^T$ **random** vector of responses
- $\mathbf{1}_n = (1, \dots, 1)^T$ vector of ones
- $\mathbf{x} = (x_1, \dots, x_n)^T$ **non random** vector of predictors
- $\boldsymbol{\epsilon} = (\epsilon_1, \dots, \epsilon_n)^T$ **random iid Gaussian** vector of errors
- β_0, β_1 **non random, unknown** coefficients

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$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}$$

- $\mathbf{X}$ ($n \times 2$) matrix of regressors
- $\boldsymbol{\beta}$ (length 2) vector of coefficients

Multiple Gaussian Regression

$$\begin{pmatrix} y_1 \\ \vdots \\ y_n \end{pmatrix} = \beta_0 \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} + \beta_1 \begin{pmatrix} x_{11} \\ \vdots \\ x_{n1} \end{pmatrix} + \cdots + \beta_p \begin{pmatrix} x_{1p} \\ \vdots \\ x_{np} \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \vdots \\ \epsilon_n \end{pmatrix}$$

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$$\mathbf{Y} = \mathbf{X}\beta + \epsilon$$

- $\mathbf{X}$ ($n \times p$) matrix of regressors ($rg(\mathbf{X}) = p$)
- β (length p) vector of coefficients

Linear Regression

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\boldsymbol{\epsilon}$$

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$$\hat{\beta} = \underset{\beta \in \mathbb{R}^p}{\operatorname{argmin}} \sum_{i=1}^{n} \left(y_i - \sum_{j=1}^{p} x_{ij}\beta_j \right)^2 = \underset{\beta \in \mathbb{R}^p}{\operatorname{argmin}} \|\mathbf{Y} - \mathbf{X}\beta\|^2$$

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$$\hat{\sigma}^2 = \frac{1}{n-p} \sum_{i=1}^{n} (y_i - \hat{y}_i)^2 = \frac{1}{n-p} \|\mathbf{Y} - \hat{\mathbf{Y}}\|^2$$

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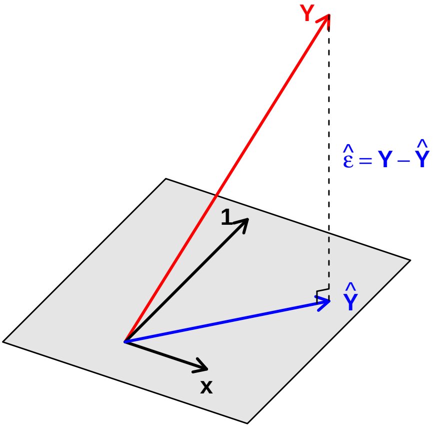

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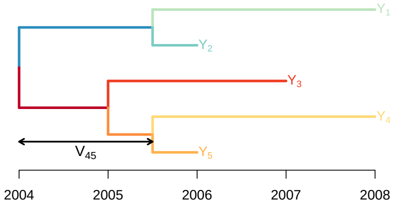
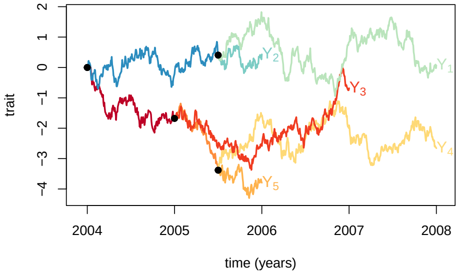
Distribution:

$$\frac{\hat{\beta}_k - \beta_k}{\sqrt{\hat{\sigma}^2[(\mathbf{X}^T\mathbf{X})^{-1}]_{kk}}} \sim \mathcal{T}_{n-p}$$
$$\frac{(n-p)\hat{\sigma}^2}{\sigma^2} \sim \chi^2(n-p)$$

Brownian Motion on a Tree





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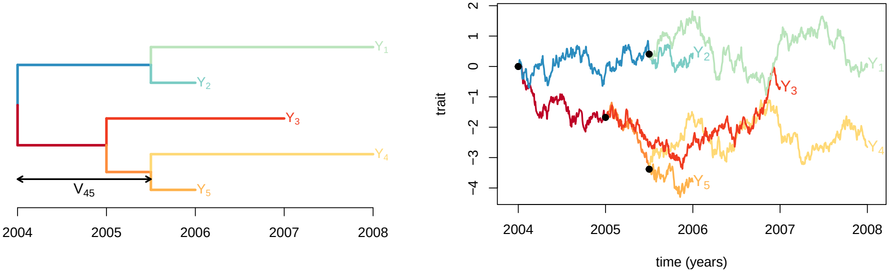

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- Expectation: μ

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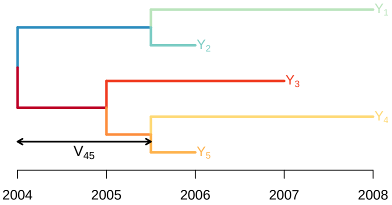

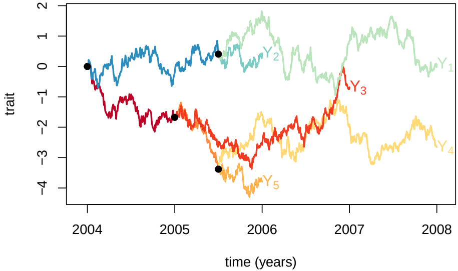

- Variance: $\mathbb{C}\mathrm{ov}(Y_i, Y_j) = \sigma^2 V_{ij}$
- Expectation: μ
- Distribution: $\mathbf{Y} = \mu\mathbf{1} + \sigma\mathbf{E}$, $\mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V})$.

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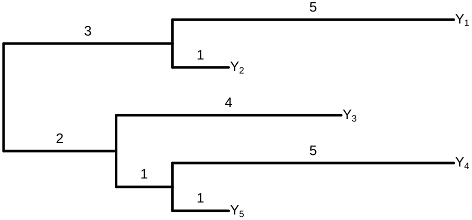
$$\mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V})$$

V informed by the tree and the trait model

Phylogenetic Linear Regression

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V})$$

BM on a tree:



$$\mathbf{V} = \begin{array}{c} \\ Y_1 \\ Y_2 \\ Y_3 \\ Y_4 \\ Y_5 \end{array} \begin{array}{c} \begin{array}{ccccc} Y_1 & Y_2 & Y_3 & Y_4 & Y_5 \end{array} \\ \begin{pmatrix} 8 & 3 & 0 & 0 & 0 \\ 3 & 4 & 0 & 0 & 0 \\ 0 & 0 & 6 & 2 & 2 \\ 0 & 0 & 2 & 8 & 3 \\ 0 & 0 & 2 & 3 & 4 \end{pmatrix} \end{array}$$

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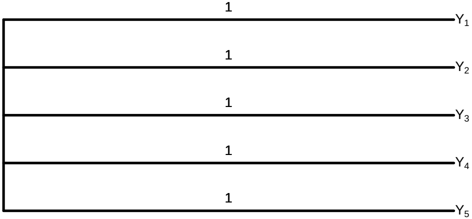
BM on a star tree:

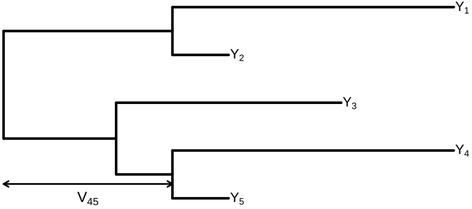


$$\mathbf{V} = \begin{array}{c} \\ Y_1 \\ Y_2 \\ Y_3 \\ Y_4 \\ Y_5 \end{array} \begin{array}{c} \begin{array}{ccccc} Y_1 & Y_2 & Y_3 & Y_4 & Y_5 \end{array} \\ \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \end{array}$$

Phylogenetic Linear Regression

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\alpha))$$

OU on a tree:

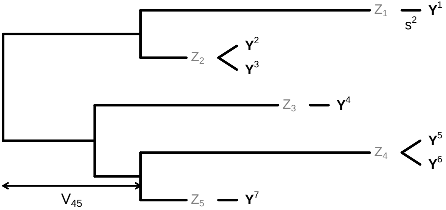


$$\mathbf{V}(\alpha)_{ij} = e^{-\alpha(V_i+V_j)}\frac{e^{2\alpha V_{ij}} - 1}{2\alpha}$$

Phylogenetic Linear Regression

$$\mathbf{Y} = \mathbf{X}\beta + \sigma \mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\phi)) \quad \phi = \frac{s^2}{\sigma^2}$$

BM with errors:



$$\mathbf{V}(\phi)_{ij} = V_{ij}$$
$$\mathbf{V}(\phi)_{ii} = V_{ii} + \phi$$

Generalized Least Squares

Assume that the tree and model ($\boldsymbol{\theta}$) is known.

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Cholesky Decomposition:

$$\mathbf{V} = \mathbf{L}\mathbf{L}^T$$

$$\mathbb{V}\text{ar}[\mathbf{L}^{-1}\mathbf{E}] = \mathbf{L}^{-1}\mathbf{V}[\mathbf{L}^{-1}]^T = \mathbf{I}$$

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De-correlated Regression:

$$\mathbf{L}^{-1}\mathbf{Y} = (\mathbf{L}^{-1}\mathbf{X})\beta + \sigma\mathbf{E}', \quad \mathbf{E}' \sim \mathcal{N}(\mathbf{0}_n, \mathbf{I})$$

Generalized Least Squares

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\boldsymbol{\theta}))$$

Generalized Least Squares

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\theta))$$

Estimators:

$$\hat{\beta} = (\mathbf{X}^T\mathbf{V}(\theta)^{-1}\mathbf{X})^{-1}\mathbf{X}^T\mathbf{V}(\theta)^{-1}\mathbf{Y}$$

$$\hat{\sigma}^2 = \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}(\theta)^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta}) = \frac{1}{n-p}\|\mathbf{Y} - \mathbf{X}\hat{\beta}\|^2_{\mathbf{V}(\theta)^{-1}}$$

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Distribution:

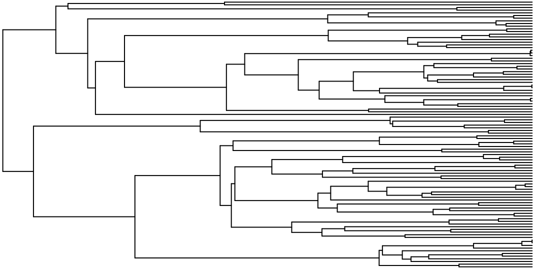
$$\frac{\hat{\beta}_k - \beta_k}{\sqrt{\hat{\sigma}^2[(\mathbf{X}^T\mathbf{V}(\boldsymbol{\theta})^{-1}\mathbf{X})^{-1}]_{kk}}} \sim \mathcal{T}_{n-p}$$

$$\frac{(n-p)\hat{\sigma}^2}{\sigma^2} \sim \chi^2(n-p)$$

Simulated Example

```r
library(ape)
library(phylolm)
```

```r
set.seed(18300718)
n <- 100
tree <- rphylo(n, birth = 0.1, death = 0)
plot(tree, show.tip.label = FALSE, no.margin = TRUE)
```



Simulated Example

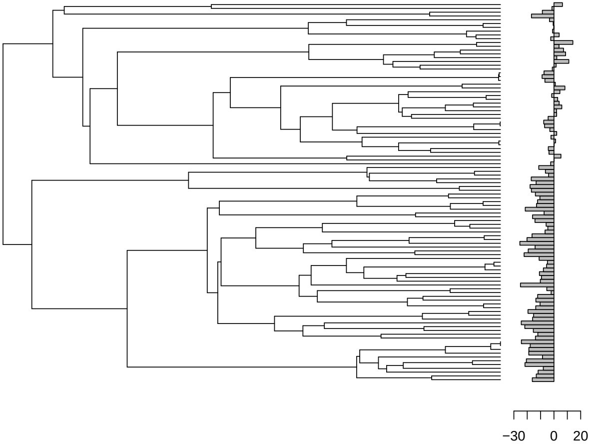
```r
# Regressor
x <- rnorm(n, mean = 0, sd = 4)

# Phylogenetic Noise
eps <- rTrait(n = 1, phy = tree, model = "BM",
              parameters = list(ancestral.state = 0, sigma2 = 2))

# Response variable
beta0 <- -10
beta1 <- 0.5
y <- beta0 + beta1 * x + eps
```

Simulated Example

```
par(mar = c(5, 0, 0, 0) + 0.1)
plot(tree, show.tip.label = FALSE, x.lim = 45)
phydataplot(y, tree, scaling = 0.1, offset = 4)
```



Simulated Example

```
# Standard linear regression
fit <- lm(y ~ x)
summary(fit)


##
## Call:
## lm(formula = y ~ x)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -20.0609  -6.4979   0.2226   7.3545  18.9895
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  -7.8921     0.8888  -8.880 3.25e-14 ***
## x             0.5032     0.2168   2.321   0.0224 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 8.887 on 98 degrees of freedom
## Multiple R-squared:  0.0521,Adjusted R-squared:  0.04243
## F-statistic: 5.387 on 1 and 98 DF,  p-value: 0.02236
```

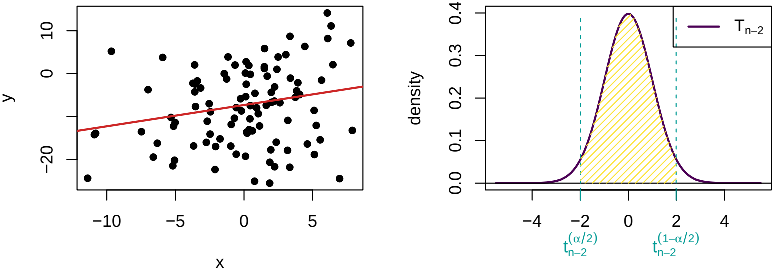
Simulated Example

```
# Phylogenetic linear regression
fitphy <- phylolm(y ~ x, phy = tree)
summary(fitphy)
```

```
##
## Call:
## phylolm(formula = y ~ x, phy = tree)
##
##    AIC logLik
##  573.2 -283.6
##
## Raw residuals:
##     Min      1Q  Median      3Q     Max
## -20.605  -7.110  -0.371   6.751  18.439
##
## Mean tip height: 37.22047
## Parameter estimate(s) using ML:
## sigma2: 1.968463
##
## Coefficients:
##              Estimate    StdErr t.value p.value
## (Intercept) -7.295577  3.075589 -2.3721 0.01964 *
## x            0.495603  0.010846 45.6953 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## R-squared: 0.9552 Adjusted R-squared: 0.9547
```

Simulated Example

$$\mathbf{y} = -10 \cdot \mathbf{1} + 0.5 \cdot \mathbf{x} + \boldsymbol{\epsilon}$$



With probability $1-\alpha$:

$$t_{n-2}(\alpha/2) \leq \frac{\hat{\beta}_1 - \beta_1}{\sqrt{\hat{\sigma}^2[(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X})^{-1}]_{11}}} \leq t_{n-2}(1-\alpha/2)$$

Outline

Generalized Least Squares

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\boldsymbol{\theta}))$$

Estimators:

$$\begin{aligned}
\hat{\beta} &= (\mathbf{X}^T\mathbf{V}(\boldsymbol{\theta})^{-1}\mathbf{X})^{-1}\mathbf{X}^T\mathbf{V}(\boldsymbol{\theta})^{-1}\mathbf{Y} \\
\hat{\sigma}^2 &= \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}(\boldsymbol{\theta})^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta}) \\
2L(\mathbf{y}|\boldsymbol{\theta}) &= n\log(2\pi) + \log\det\mathbf{V}(\boldsymbol{\theta}) + (\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}(\boldsymbol{\theta})^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})
\end{aligned}$$

Generalized Least Squares

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Naive Computation: Need to invert $\mathbf{V}(\boldsymbol{\theta}) \rightarrow$ worse than $O(n^2)$.

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$$\hat{\sigma}^2 = \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}(\boldsymbol{\theta})^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})$$

$$2L(\mathbf{y}|\boldsymbol{\theta}) = n\log(2\pi) + \log\det\mathbf{V}(\boldsymbol{\theta}) + (\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}(\boldsymbol{\theta})^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})$$

Naive Computation: Need to invert $\mathbf{V}(\boldsymbol{\theta}) \rightarrow$ worse than $O(n^2)$.

Three point structure:
Estimators computed in one traversal of the tree $\rightarrow O(n)$.

+

Three Point Structure Algorithm

(Ho and Ané, 2014)

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V})$$

Estimators:

$$\hat{\beta} = (\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X})^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Y}$$

$$\hat{\sigma}^2 = \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})$$

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Can be computed in linear time.

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\end{aligned}$$

Can be computed in linear time.

- Works for a BM on a tree

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- Works for a BM on a tree
- Implemented in phylolm

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\end{aligned}$$

Can be computed in linear time.

- Works for a BM on a tree
- Implemented in phylolm
- What about other models ? $\mathbf{V} = \mathbf{V}(\boldsymbol{\theta})$.

Tree Transformation Strategy

(Pagel, 1999)

Strategy

- See $\mathbf{V}(\theta)$ as a BM on a modified tree.

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Limits

- In general, only works for ultrametric trees.

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- See $\mathbf{V}(\boldsymbol{\theta})$ as a BM on a modified tree.
- For fixed $\mathbf{V}(\boldsymbol{\theta})$, use the fast algorithm.
- Optimize on $\mathbf{V}(\boldsymbol{\theta})$ numerically.

Limits

- In general, only works for ultrametric trees.
- Confidence intervals and tests only valid conditionally on $\boldsymbol{\theta}$.

$$\frac{\hat{\beta}_k - \beta_k}{\sqrt{\hat{\sigma}^2[(\mathbf{X}^T\mathbf{V}(\boldsymbol{\theta})^{-1}\mathbf{X})^{-1}]_{kk}}} \sim \mathcal{T}_{n-p}$$

Pagel's Lambda

Relax the BM variance structure:

$$\mathbf{V}(\lambda)_{ii} = \mathbf{V}_{ii}$$
$$\mathbf{V}(\lambda)_{ij} = \lambda \mathbf{V}_{ij}$$

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$$\begin{aligned}\mathbf{V}(\lambda)_{ii} &= \mathbf{V}_{ii}\\ \mathbf{V}(\lambda)_{ij} &= \lambda\mathbf{V}_{ij}\end{aligned}$$

Equivalent to running a BM on a modified tree with:

$$t(\lambda)_i = \begin{cases}\lambda t_i & \text{if } i \text{ internal node}\\ \lambda t_i + (1-\lambda)V_i & \text{if } i \text{ leaf}\end{cases}$$

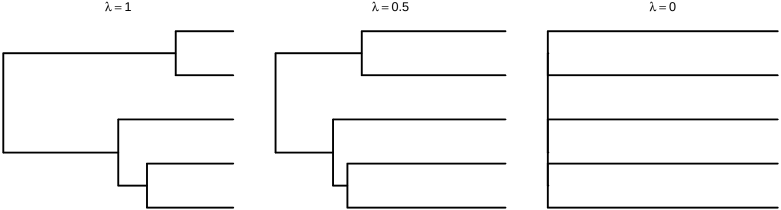
Pagel's Lambda

Relax the BM variance structure:

$$\mathbf{V}(\lambda)_{ii} = \mathbf{V}_{ii}$$
$$\mathbf{V}(\lambda)_{ij} = \lambda\mathbf{V}_{ij}$$

Equivalent to running a BM on a modified tree with:

$$t(\lambda)_i = \begin{cases} \lambda t_i & \text{if } i \text{ internal node} \\ \lambda t_i + (1-\lambda)V_i & \text{if } i \text{ leaf} \end{cases}$$



Pagel's Lambda

- Used a lot in practice.

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- Also exist Pagel's κ and δ.

Pagel's Lambda

- Used a lot in practice.
- Also exist Pagel's κ and δ.
- λ "phylogenetic heritability" (see below).

Ornstein-Uhlenbeck

Assuming a ultrametric tree with height T:

$$\mathbf{V}(\alpha)_{ij} = e^{-2\alpha T} \frac{e^{2\alpha V_{ij}} - 1}{2\alpha}$$

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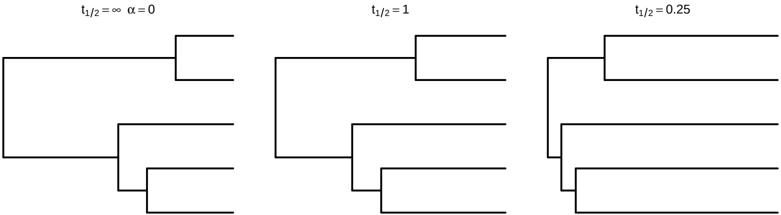

AC/DC

$$dX_t = \sigma_0 e^{rt/2} dB_t$$

$$\mathbf{V}(r)_{ij} = \frac{e^{rV_{ij}} - 1}{r}$$

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Assuming a ultrametric tree height T, equivalent to an OU with:

$$\begin{aligned} r &= 2\alpha \\ \sigma_0^2 &= \sigma^2 e^{-2\alpha T} \end{aligned}$$

AC/DC

$$dX_t = \sigma_0 e^{rt/2} dB_t$$

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Assuming a ultrametric tree height T, equivalent to an OU with:

$$r = 2\alpha$$
$$\sigma_0^2 = \sigma^2 e^{-2\alpha T}$$

Case $r < 0$ (EB) is a repulsing OU.

Outline

1. Linear Regression Framework
2. Efficient Computations
3. Phylogenetic Mixed Model
    - Mixed Models and BM Heritability
    - General Heritability
    - HIV Viral Load

Phylogenetic Mixed Model

(Lynch, 1991; Housworth et al., 2004)

Phylogenetic Regression

$$\mathbf{Y} = \mathbf{X}\beta + \sigma \mathbf{E}^p \quad \mathbf{E}^p \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V}(\theta))$$

Phylogenetic Mixed Model

(Lynch, 1991; Housworth et al., 2004)

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Phylogenetic Mixed Model

$$\mathbf{Y} = \mathbf{X}\beta + \sigma \mathbf{E}^p + s\mathbf{E}^e \quad \mathbf{E}^e \sim \mathcal{N}(\mathbf{0}_n, \mathbf{I})$$

Phylogenetic Mixed Model

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Distinction between:

- The heritable part of the trait

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Distinction between:

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  - Variance $\sigma^2\mathbf{V}(\boldsymbol{\theta})$ given by the trait evolution on the tree

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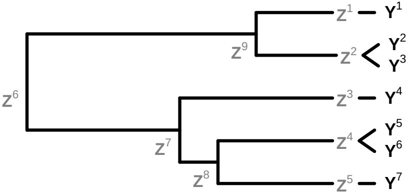
Distinction between:

- The heritable part of the trait
  - Variance $\sigma^2\mathbf{V}(\boldsymbol{\theta})$ given by the trait evolution on the tree
- The environemental part of the trait
  - Variance iid s^2 given by the error model

BM on a Ultrametric Tree

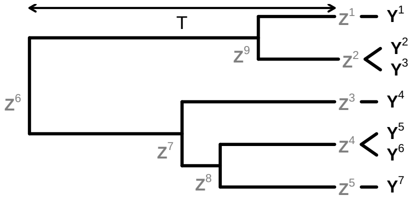


$$\mathbf{Z}^r = \boldsymbol{\mu} \qquad \text{root}$$

$$\mathbf{Z}^j \;\Big|\; \mathbf{Z}^{\mathrm{pa}(j)} \sim \mathcal{N}\left(\mathbf{Z}^{\mathrm{pa}(j)},\ \sigma^2 t_j\right) \qquad \text{nodes}$$

$$\mathbf{Y}^i \;\Big|\; \mathbf{Z}^{\mathrm{pa}(i)} \sim \mathcal{N}\left(\mathbf{Z}^{\mathrm{pa}(i)}, s^2\right) \qquad \text{obs}$$

BM on a Ultrametric Tree



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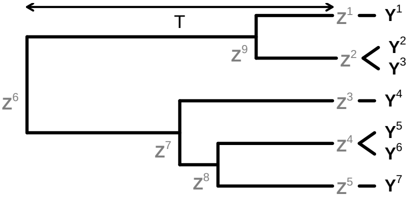
Ultrametric tree: Tip variance is constant equal to $\sigma^2 T$

BM on a Ultrametric Tree



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Ultrametric tree: Tip variance is constant equal to $\sigma^2 T$

Phylogenetic Heritability:

$$h^2 = \frac{\sigma^2 T}{\sigma^2 T + s^2}$$

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Assume a ultrametric tree with height T.

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BM PMM total variance is:

$$\sigma^2\mathbf{V} + s^2\mathbf{I} \quad \text{with}\, \text{Diag}(\mathbf{V}) = T\mathbf{I}$$

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To have both variances on the same scale, we write:

$$\sigma^2\mathbf{V} + s^2\mathbf{I} = \sigma^2 T\mathbf{V}/T + s^2\mathbf{I} \quad \text{with}\,\text{Diag}(\mathbf{V}/T) = \mathbf{I}$$

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The phylogenetic heritability is defined as:

$$h^2 = \frac{\sigma^2 T}{\sigma^2 T + s^2}$$

Pagel's lambda a Ultrametric Tree

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$$\sigma_\lambda^2 \mathbf{V}(\lambda) = \sigma_\lambda^2 \left[\lambda \mathbf{V} + (1 - \lambda) T \mathbf{I}\right]$$

Pagel's lambda a Ultrametric Tree

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The two models are equivalent with:

$$\lambda = \frac{\sigma^2 T}{\sigma^2 T + s^2} = h^2 \qquad \sigma_\lambda^2 = \sigma^2 + s^2/T$$

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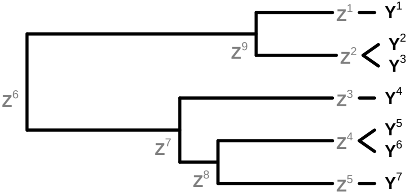
The two models are equivalent with:

$$\lambda = \frac{\sigma^2 T}{\sigma^2 T + s^2} = h^2 \qquad \sigma_\lambda^2 = \sigma^2 + s^2/T$$

λ is the heritability

BM on a Non-Ultrametric Tree



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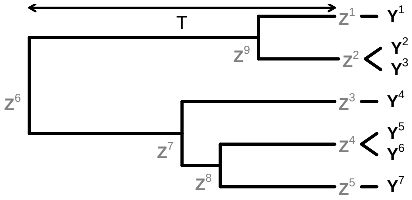
BM on a Non-Ultrametric Tree



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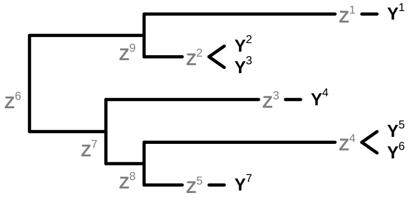

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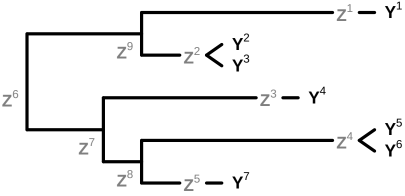

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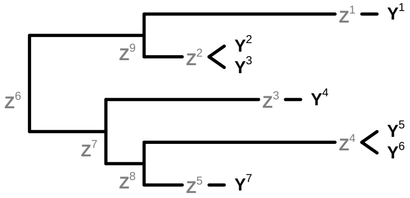

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Mitov and Stadler (2018) use $\bar{T}$ instead.
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Pagel's Lambda on a Non-Ultrametric Tree

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$$\sigma_\lambda^2\mathbf{V}(\lambda) = \sigma_\lambda^2\left[\lambda\mathbf{V} + (1-\lambda)\mathbf{V}^*\right]$$

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BM PMM with scaled variance is:

$$\sigma^2 \mathbf{V} + s_s^2 \mathbf{V}^*$$

Error accumulate in time (Leventhal and Bonhoeffer, 2016)
a tip further from the root has a larger error.

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λ is the heritability if the independent errors are scaled.

BM Heritability

Ultrametric Tree

$$h^2 = \frac{\sigma^2 T}{\sigma^2 T + s^2} = \lambda$$

Non Ultrametric Tree

$$h^2 = \frac{\sigma^2 T_{max}}{\sigma^2 T_{max} + s^2}$$

$$h^2 = \frac{\sigma^2 \bar{T}}{\sigma^2 \bar{T} + s^2}$$

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General Mixed Model

(Blanquart et al., 2017)

$$\mathbf{Y} = \mathbf{c} + \mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta}) + \mathbf{E}^e$$

with:

$\mathbf{c}$	vector of covariables
$\mathbf{m}(\boldsymbol{\theta})$	expectation of the phylogenetic model
$\mathbf{E}^p(\boldsymbol{\theta}) \sim \mathcal{N}(\mathbf{0}_n, \boldsymbol{\Sigma}(\boldsymbol{\theta}))$	variance of the phylogenetic model
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Example: BM

$$\mathbf{m}(\boldsymbol{\theta})_i = \mu$$
$$\boldsymbol{\Sigma}(\boldsymbol{\theta})_{ij} = \sigma^2 V_{ij}$$

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Example: OU

$$\mathbf{m}(\boldsymbol{\theta})_i = \mu e^{-\alpha V_i} + \beta(1 - e^{-\alpha V_i})$$

$$\boldsymbol{\Sigma}(\boldsymbol{\theta})_{ij} = \frac{\sigma^2}{2\alpha} e^{-\alpha(V_i+V_j)}(e^{2\alpha V_{ij}} - 1)$$

Empirical Phylogenetic Heritability (Blanquart et al., 2017)

$$\mathbf{Y} = \mathbf{c} + \mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta}) + \mathbf{E}^e$$

Empirical heritability

$$H^2_{emp} = \frac{\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]}{\mathbb{S}[\mathbf{Y}]}$$

with $\mathbb{S}$ the *empirical* variance: $\mathbb{S}[\mathbf{x}] = \frac{1}{n-1}\sum_{i=1}^{n}\left(x_i - \frac{1}{n}\sum_{i=1}^{n} x_i\right)^2$

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H^2_{emp} is a stochastic quantity.

Can be computed through simulations.

Mean Empirical Heritability (Blanquart et al., 2017)

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$$h^2_{emp} = \mathbb{E}\left[\frac{\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]}{\mathbb{S}[\mathbf{Y}]}\right] \approx \frac{\mathbb{E}\left[\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]\right]}{\mathbb{E}\left[\mathbb{S}[\mathbf{Y}]\right]}$$

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Expectation must be analytically computed for each model.

BM Mean Empirical Heritability

(Hassler et al., 2020)

$$\mathbf{Y} = \mu\mathbf{1} + \sigma\mathbf{E}^p + s\mathbf{E}^e$$

Mean Empirical Variance

$$\mathbb{E}\left[\mathbb{S}[\mathbf{Y}]\right] = \frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2$$

Mean Empirical heritability

$$h^2_{emp} \approx \frac{\left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2}{\frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2}$$

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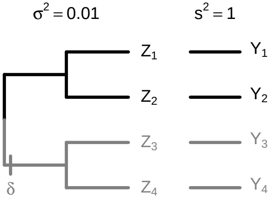
Mean Empirical heritability

$$h^2_{emp} \approx \frac{\left(\frac{1}{n} \operatorname{tr}(\mathbf{V}) - \frac{1}{n^2} \mathbf{1}^T \mathbf{V} \mathbf{1} \right) \sigma^2}{\frac{n}{n-1} s^2 + \left(\frac{1}{n} \operatorname{tr}(\mathbf{V}) - \frac{1}{n^2} \mathbf{1}^T \mathbf{V} \mathbf{1} \right) \sigma^2}$$

Yet again an other definition of the BM heritability.

Shifted BM Mean Empirical Heritability



$$\mathbf{Y} = \mu\mathbf{1} + \delta\mathbf{1}_{n/2} + \sigma\mathbf{E}^{p} + s\mathbf{E}^{e}$$

Mean Empirical heritability

$$h^2_{emp} \approx \frac{\left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}{\frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}$$

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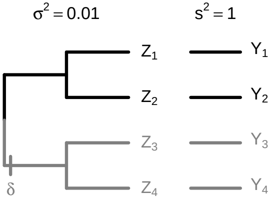

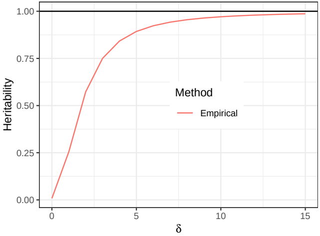

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Mean Empirical heritability

$$h^2_{emp} \approx \frac{\left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}{\frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}$$

Population Heritability

(Bastide et al., 2020)

$$\mathbf{Y} = \mathbf{c} + \mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta}) + \mathbf{E}^e$$

Mean Empirical heritability

$$h^2_{emp} \approx \frac{\mathbb{E}\left[\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]\right]}{\mathbb{E}\left[\mathbb{S}[\mathbf{Y}]\right]} \quad \text{with:} \quad \mathbb{S}[\mathbf{x}] = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2$$

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Population heritability

$$h^2_{pop} = \frac{\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]\right]}{\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{Y}]\right]}$$

with: $\mathbb{S}_{pop}[\mathbf{x}] = \frac{1}{n}\sum_{i=1}^{n}(x_i - \mathbb{E}[x_i])^2$ $\qquad$ $\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{x}]\right] = \frac{1}{n}\sum_{i=1}^{n}\mathbb{V}\mathrm{ar}[x_i]$

BM Population Heritability

(Bastide et al., 2020)

$$\mathbf{Y} = \mu \mathbf{1} + \sigma \mathbf{E}^p + s\mathbf{E}^e$$

Mean Population Variance

$$\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{Y}]\right] = \frac{1}{n}\sum_{i=1}^{n} \mathbb{V}\mathrm{ar}\left[Y_i\right] = \frac{1}{n}\sum_{i=1}^{n}(\sigma^2 T_i + s^2) = \sigma^2 \bar{T} + s^2$$

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$$h^2_{pop} = \frac{\sigma^2\bar{T}}{\sigma^2\bar{T} + s^2}$$

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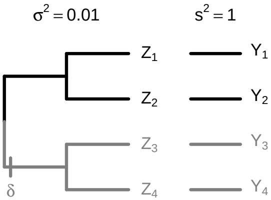
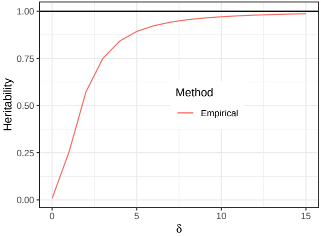
Population heritability

$$h^2_{pop} = \frac{\sigma^2\bar{T}}{\sigma^2\bar{T} + s^2}$$

Same definition as Mitov and Stadler (2018).

Shifted BM Population Heritability





Mean Empirical heritability

$$h^2_{emp} \approx \frac{\left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}{\frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}$$

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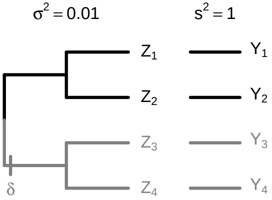
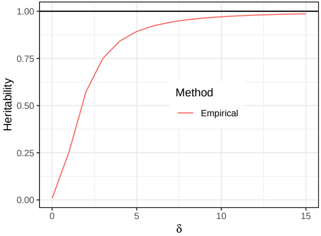




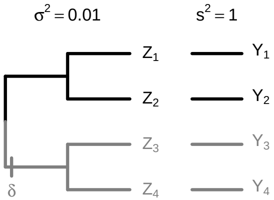
Mean Empirical heritability

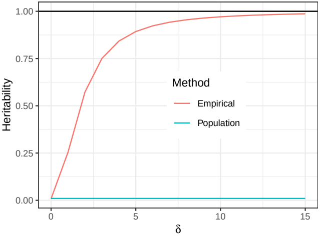
$$h^2_{emp} \approx \frac{\left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}{\frac{n}{n-1}s^2 + \left(\frac{1}{n}\operatorname{tr}(\mathbf{V}) - \frac{1}{n^2}\mathbf{1}^T\mathbf{V}\mathbf{1}\right)\sigma^2 + \frac{\delta^2}{4}}$$

Mean Population Variance unchanged by the shift

$$\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{Y}]\right] = \frac{1}{n}\sum_{i=1}^{n}\mathbb{V}\mathrm{ar}\left[Y_i\right] = \frac{1}{n}\sum_{i=1}^{n}(\sigma^2 T_i + s^2) = \sigma^2 \bar{T} + s^2$$

Shifted BM Population Heritability





Mean Empirical heritability

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Population heritability unchanged

$$h^2_{pop} = \frac{\sigma^2\,\bar{T}}{\sigma^2\,\bar{T} + s^2}$$

Heritability

$$\mathbf{Y} = \mathbf{c} + \mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta}) + \mathbf{E}^e$$

Empirical heritability: stochastic, affected by expectation

$$H^2_{emp} = \frac{\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]}{\mathbb{S}[\mathbf{Y}]} \quad \text{with:} \quad \mathbb{S}[\mathbf{x}] = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2$$

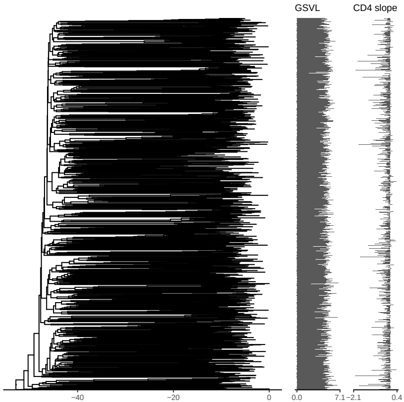
Mean Empirical heritability: affected by expectation

$$h^2_{emp} = \frac{\mathbb{E}\left[\mathbb{S}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]\right]}{\mathbb{E}\left[\mathbb{S}[\mathbf{Y}]\right]}$$

Population heritability: unaffected by expectation.

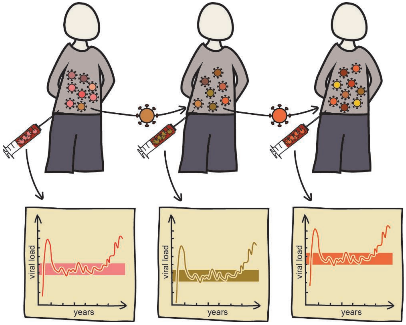
$$h^2_{pop} = \frac{\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{m}(\boldsymbol{\theta}) + \mathbf{E}^p(\boldsymbol{\theta})]\right]}{\mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{Y}]\right]} \quad \text{with:} \quad \mathbb{E}\left[\mathbb{S}_{pop}[\mathbf{x}]\right] = \frac{1}{n}\sum_{i=1}^{n}\mathbb{V}\text{ar}\left[x_i\right]$$

HIV Virulence Heritability (Alizon et al., 2010; Blanquart et al., 2017)



HIV-1, Sub-type B, MSM, 1171 tips

CD4: T cells decline rate
GSVL: viral load



Fraser et al. (2014)

Questions: Is virulence “heritable”? Which model of trait evolution?

HIV Virulence Heritability

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Data: Swiss HIV Cohort (MSM, $n = 134$)
Trait: spVL
Method: Pagel's lambda
Heritability: 51% [±27%]

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Trait: GSVL, CD4
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Heritability GSVL: 30% [8%, 44%] (OU)
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Hassler et al. (2020)
Data: BEEHIVE (MSM, $n = 1,171$)
Trait: GSVL, CD4
Method: BM, mean empirical
Heritability GSVL: 21% $[11\%, 30\%]$
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Bastide et al. (2020)
Data: BEEHIVE (MSM, $n = 1,171$)
Trait: GSVL, CD4
Method: OU-BM, population
Heritability GSVL: 43% [28%, 59%] (OU)
Heritability CD4: 27% [15%, 38%] (BM)

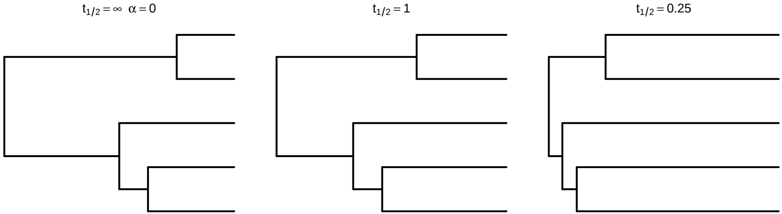
HIV Virulence Heritability

- Estimates vary a lot.
- Data is difficult to interpret (spVL, heritability).
- Various definitions of heritability are used.
- OU always give higher heritability estimates.

BM vs OU Heritability

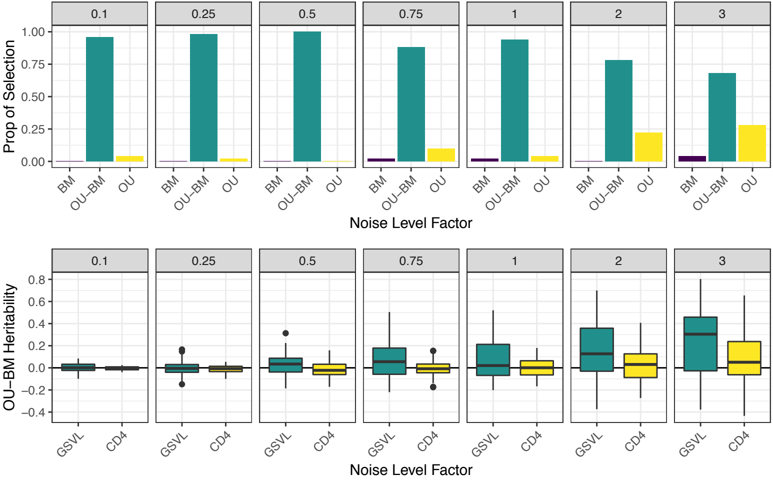
$$\mathbf{Y} = \mathbf{c} + \mathbf{m}(\theta) + \mathbf{E}^p(\theta) + \mathbf{E}^e$$

OU Phylogenetic Model allows for more individual variations.



→ heritability is higher for the OU.

OU-BM Simulations



Bibliography

Alizon, von Wyl, Stadler, et al. 2010. *PLoS Pathogens*. 6.

Bastide, Ho, Baele, et al. 2020. *Annals of Applied Statistics (in press)*. .

Blanquart, Wymant, Cornelissen, et al. 2017. *PLoS Biology*. 15:1–26.

Fraser, Lythgoe, Leventhal, et al. 2014. *Science*. 343:1243727–1243727.

Hassler, Tolkoff, Allen, et al. 2020. *Journal of the American Statistical Association*. pp. 1–15.

Ho, Ané. 2014. *Systematic Biology*. 63:397–408.

Hodcroft, Hadfield, Fearnhill, et al. 2014. *PLoS Pathogens*. 10.

Housworth, Martins, Lynch. 2004. *The American Naturalist*. 163:84–96.

Leventhal, Bonhoeffer. 2016. *Trends in Microbiology*. 24:687–698.

Lynch. 1991. *Evolution*. 45:1065–1080.

Mitov, Stadler. 2018. *Molecular Biology and Evolution*. 35:756–772.

Pagel. 1999. *Nature*. 401:877–884.

Vrancken, Lemey, Rambaut, et al. 2015. *Methods in Ecology and Evolution*. 6:67–82.

Thank you for listening

Institut Montpelliérain Alexander Grothendieck

Appendices

Three Point Structure Algorithm (Ho and Ané, 2014)

$$\mathbf{Y} = \mathbf{X}\beta + \sigma\mathbf{E} \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}_n, \mathbf{V})$$

Estimators:

$$\hat{\beta} = (\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X})^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Y}$$

$$\hat{\sigma}^2 = \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})$$

$$2L(\mathbf{y}|\boldsymbol{\theta}) = n\log(2\pi) + \log|\mathbf{V}| + (\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})$$

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Estimators:

$$\begin{aligned}
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\hat{\sigma}^2 &= \frac{1}{n-p}(\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta}) \\
2L(\mathbf{y}|\boldsymbol{\theta}) &= n\log(2\pi) + \log|\mathbf{V}| + (\mathbf{Y} - \mathbf{X}\hat{\beta})^T\mathbf{V}^{-1}(\mathbf{Y} - \mathbf{X}\hat{\beta})
\end{aligned}$$

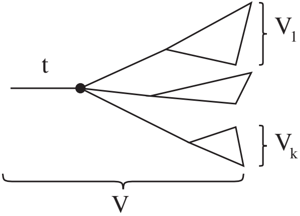
We need to compute:

- $\log|\mathbf{V}|$
- $\mathbf{Q} = \mathbf{X}^T\mathbf{V}^{-1}\mathbf{Y}$
- $p = \mathbf{1}^T\mathbf{V}^{-1}\mathbf{1}$, $\hat{\mu}_Y = \mathbf{1}^T\mathbf{V}^{-1}\mathbf{Y}/p$ and $\hat{\boldsymbol{\mu}}_X^T = \mathbf{X}^T\mathbf{V}^{-1}\mathbf{1}/p$

Three Point Structure Algorithm (Ho and Ané, 2014)

Three Points Structure:

$$\mathbf{V} = t\mathbf{1}^T\mathbf{1} + \begin{pmatrix} V_1 & & 0 \\ & \ddots & \\ 0 & & V_k \end{pmatrix}$$



Ho and Ané (2014)

Three Point Structure Algorithm (Ho and Ané, 2014)

Initialization : tree with a single tip of length t

- $\log |\mathbf{V}| = t$
- $\mathbf{Q} = \mathbf{x}^T y/t$
- $p = 1/t$, $\hat{\mu}_Y = y$ and $\hat{\boldsymbol{\mu}}_X^T = \mathbf{x}^T$

Three Point Structure Algorithm (Ho and Ané, 2014)

Propagation:

Woodbury and Sylvester formulas for $\mathbf{M} = \mathbf{A} + \mathbf{UCV}$

$$\mathbf{M}^{-1} = \mathbf{A}^{-1} - \mathbf{A}^{-1}\mathbf{U}(\mathbf{C}^{-1} + \mathbf{V}\mathbf{A}^{-1}\mathbf{U})^{-1}\mathbf{V}\mathbf{A}^{-1}$$

$$|\mathbf{M}| = |\mathbf{A}|\,|\mathbf{C}|\,\left|\mathbf{C}^{-1} + \mathbf{V}\mathbf{A}^{-1}\mathbf{U}\right|$$

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$$|\mathbf{M}| = |\mathbf{A}|\,|\mathbf{C}|\,\left|\mathbf{C}^{-1} + \mathbf{V}\mathbf{A}^{-1}\mathbf{U}\right|$$

Applied on $\mathbf{V} = \mathbf{A} + t\mathbf{1}^T\mathbf{1}$, with $\mathbf{A} = \begin{pmatrix} V_1 & & 0 \\ & \ddots & \\ 0 & & V_k \end{pmatrix}$:

$$\mathbf{V}^{-1} = \mathbf{A}^{-1} - \frac{t}{1 + tp_A}\mathbf{A}^{-1}\mathbf{1}\mathbf{1}^T\mathbf{A}^{-1}, \qquad p_A = \mathbf{1}^T\mathbf{A}^{-1}\mathbf{1} = \sum_{s=1}^{k} p_s$$

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$$|\mathbf{M}| = |\mathbf{A}|\,|\mathbf{C}|\,\left|\mathbf{C}^{-1} + \mathbf{VA}^{-1}\mathbf{U}\right|$$

Gives:

- $\log|\mathbf{V}| = \sum_{s=1}^{k} \log|\mathbf{V}_s| + \log(1 + tp_A)$
- $\mathbf{Q} = \sum_{s=1}^{k} \mathbf{Q}_s - \frac{tp_A^2}{1+tp_A} \hat{\boldsymbol{\mu}}_X^T \hat{\mu}_Y$
- $p = \frac{p_A}{1+tp_A}$, $\hat{\mu}_Y = \sum_{s=1}^{k} \frac{p_s}{p_A} \hat{\mu}_{Y,s}$ and $\hat{\boldsymbol{\mu}}_X^T = \sum_{s=1}^{k} \frac{p_s}{p_A} \hat{\boldsymbol{\mu}}_{X,s}$

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Gives:

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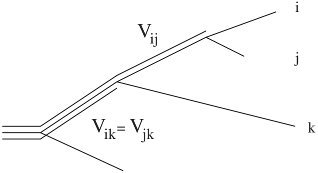
- $p = \frac{p_A}{1+tp_A}$, $\hat{\mu}_Y = \sum_{s=1}^{k} \frac{p_s}{p_A}\hat{\mu}_{Y,s}$ and $\hat{\boldsymbol{\mu}}_X^T = \sum_{s=1}^{k} \frac{p_s}{p_A}\hat{\boldsymbol{\mu}}_{X,s}$

Finalization : At the root of the tree.

Three Point Structure (Ho and Ané, 2014)

Three Points Structure: A matrix $\mathbf{V}$ has the 3-Point Structure if:

- it is symmetric non-negative
- for any i, j, k, the two smallest of V_{ij}, V_{ik} and V_{jk} are equal.



Ho and Ané (2014)

back

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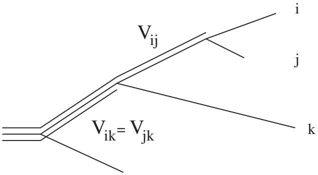

Ho and Ané (2014)

Theorem: $\mathbf{V}$ is 3-point structured if and only if it is the covariance matrix of a random variable at the tips of some rooted tree under a BM model.

back