

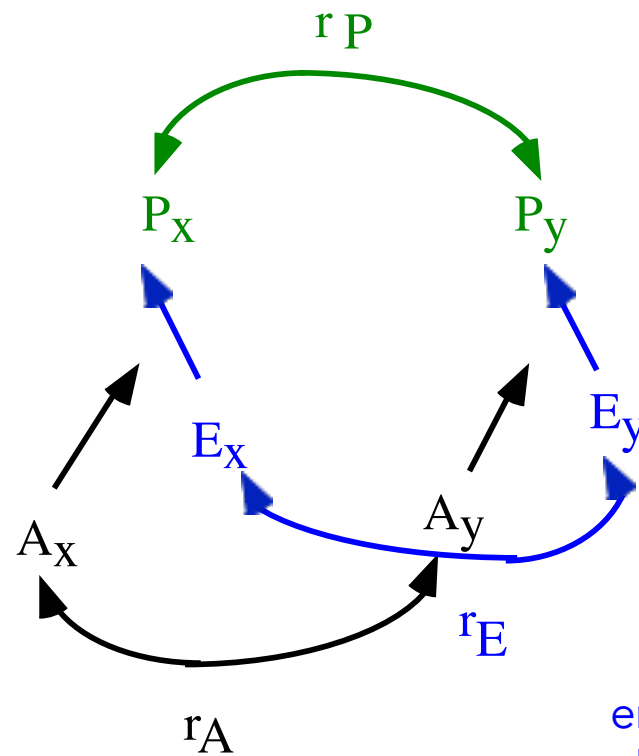
Lecture 6: Selection on Multiple Traits

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Introduction to Quantitative Genetics
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Genetic vs. Phenotypic correlations

- Within an individual, trait values can be positively or negatively correlated,
 - height and weight -- positively correlated
 - Weight and lifespan -- negatively correlated
- Such phenotypic correlations can be directly measured,
 - r_p denotes the phenotypic correlation
- Phenotypic correlations arise because genetic and/or environmental values within an individual are correlated.

The phenotypic values between traits x and y within an individual are correlated



Correlations between the breeding values of x and y within the individual can generate a phenotypic correlation

Likewise, the environmental values for the two traits within the individual could also be correlated

Genetic & Environmental Correlations

- r_A = correlation in breeding values (the **genetic correlation**) can arise from
 - pleiotropic effects of loci on both traits
 - linkage disequilibrium, which decays over time
- r_E = correlation in environmental values
 - includes non-additive genetic effects (e.g., D, I)
 - arises from exposure of the two traits to the same individual environment

The relative contributions of genetic and environmental correlations to the phenotypic correlation

$$r_P = r_A h_X h_Y + r_E \sqrt{(1 - h_x^2)(1 - h_Y^2)}$$

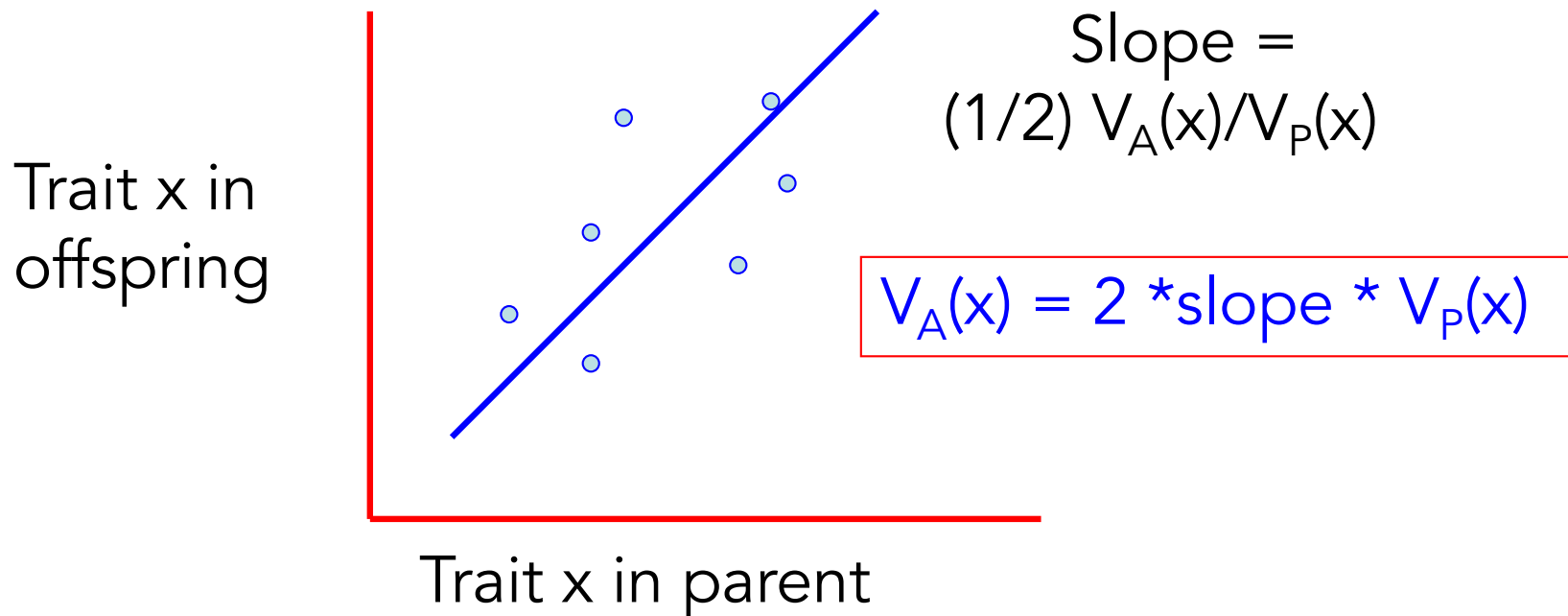
If heritability values are high for both traits, then the correlation in breeding values dominates the phenotypic correlation

If heritability values in EITHER trait are low, then the correlation in environmental values dominates the phenotypic correlation

In practice, phenotypic and genetic correlations often have the same sign and are of similar magnitude, but this is not always the case

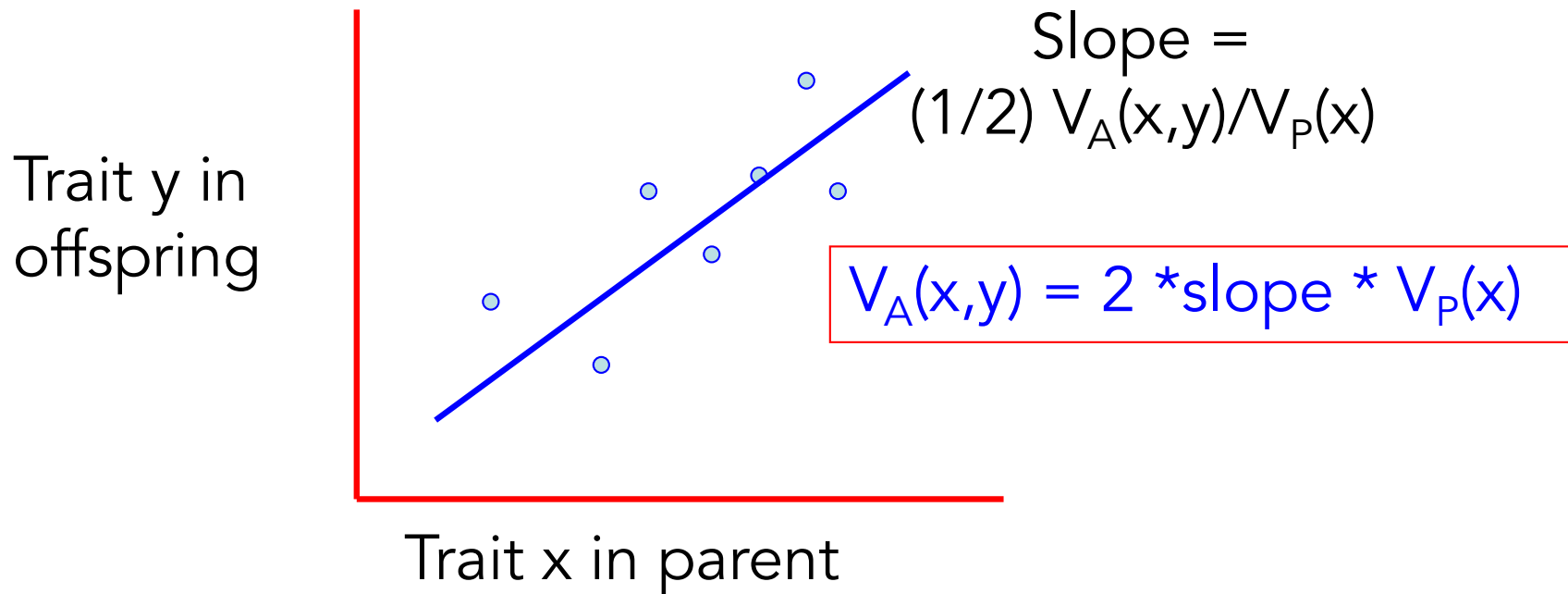
Estimating Genetic Correlations

Recall that we estimated V_A from the regression of trait x in the parent on trait x in the offspring,



Estimating Genetic Correlations

Similarly, we can estimate $V_A(x,y)$, the covariance in the breeding values for traits x and y , by the regression of trait x in the parent and trait y in the offspring



Thus, one estimator of $V_A(x,y)$ is

$$V_A(x,y) = \frac{2 * b_{y|x} * V_P(x) + 2 * b_{x|y} * V_P(y)}{2}$$

giving

$$V_A(x,y) = b_{y|x} V_P(x) + b_{x|y} V_P(y)$$

Put another way,

$$\text{Cov}(x_O, y_P) = \text{Cov}(y_O, x_P) = (1/2) \text{Cov}(A_x, A_y)$$

$$\text{Cov}(x_O, x_P) = (1/2) V_A(x) = (1/2) \text{Cov}(A_x, A_x)$$

$$\text{Cov}(y_O, y_P) = (1/2) V_A(y) = (1/2) \text{Cov}(A_y, A_y)$$

Likewise, for half-sibs,

$$\text{Cov}(x_{HS}, y_{HS}) = (1/4) \text{Cov}(A_x, A_y)$$

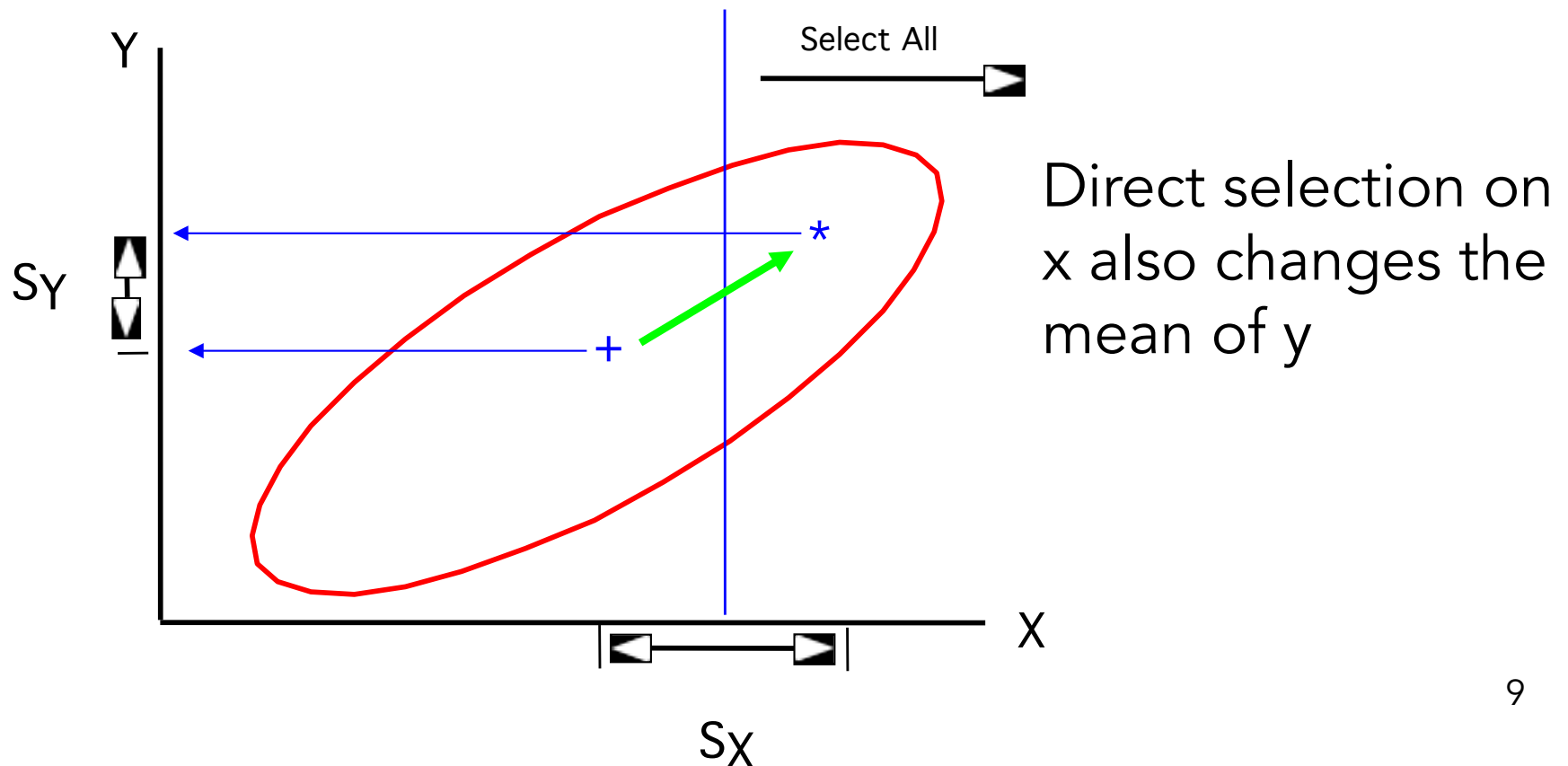
$$\text{Cov}(x_{HS}, x_{HS}) = (1/4) \text{Cov}(A_x, A_x) = (1/4) V_A(x)$$

$$\text{Cov}(y_{HS}, y_{HS}) = (1/4) \text{Cov}(A_y, A_y) = (1/4) V_A(y)$$

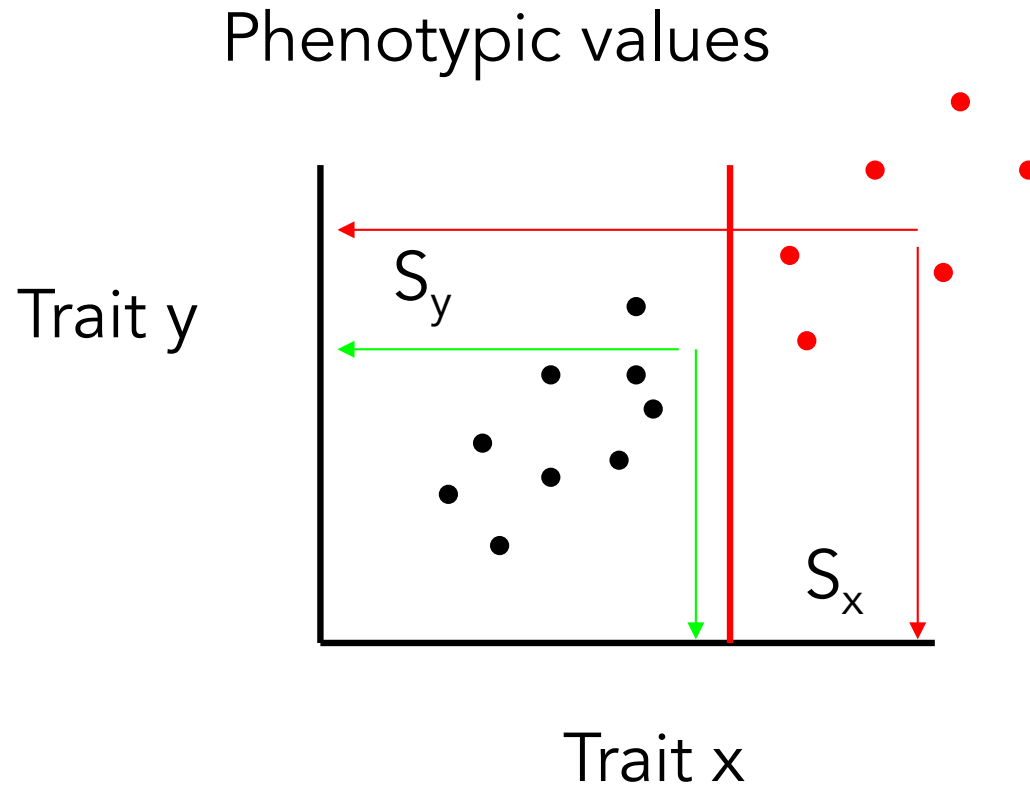
General: $\text{Cov}(x_i, y_j) = 2\Theta_{ij} \text{Cov}(A_x, A_y)$

Correlated Response to Selection

Direct selection of a character can cause a within-generation change in the mean of a phenotypically correlated character.



Phenotypic correlations induce **within-generation changes**

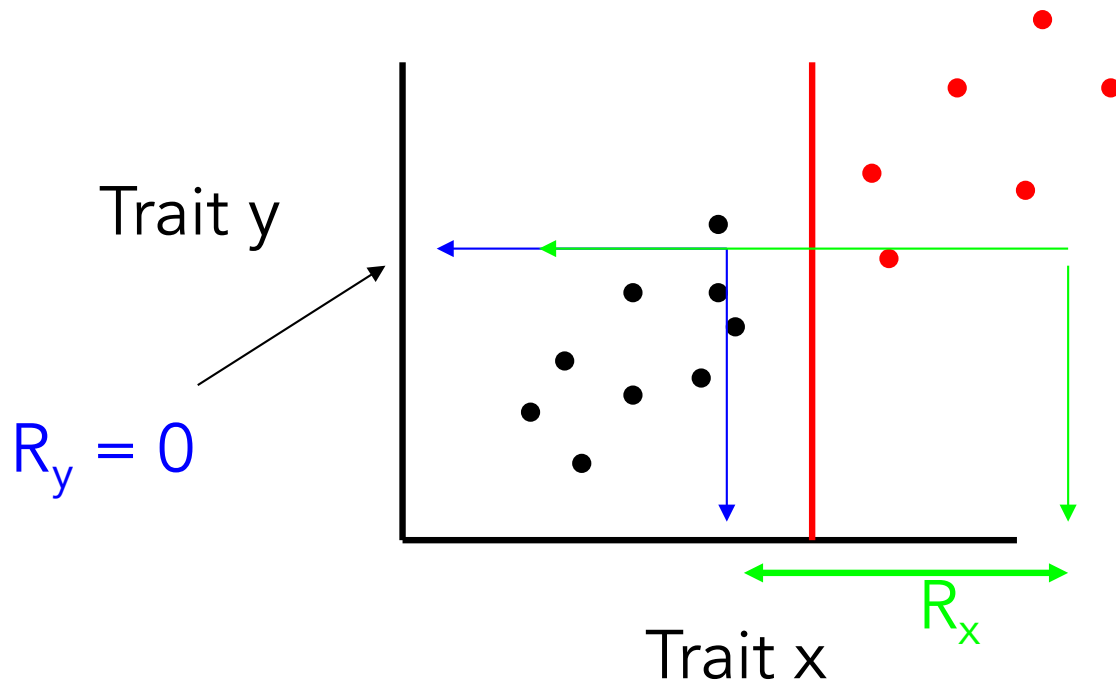


For there to be a **between-generation change**, the **breeding values must be correlated**. Such a change is called a **correlated response to selection**

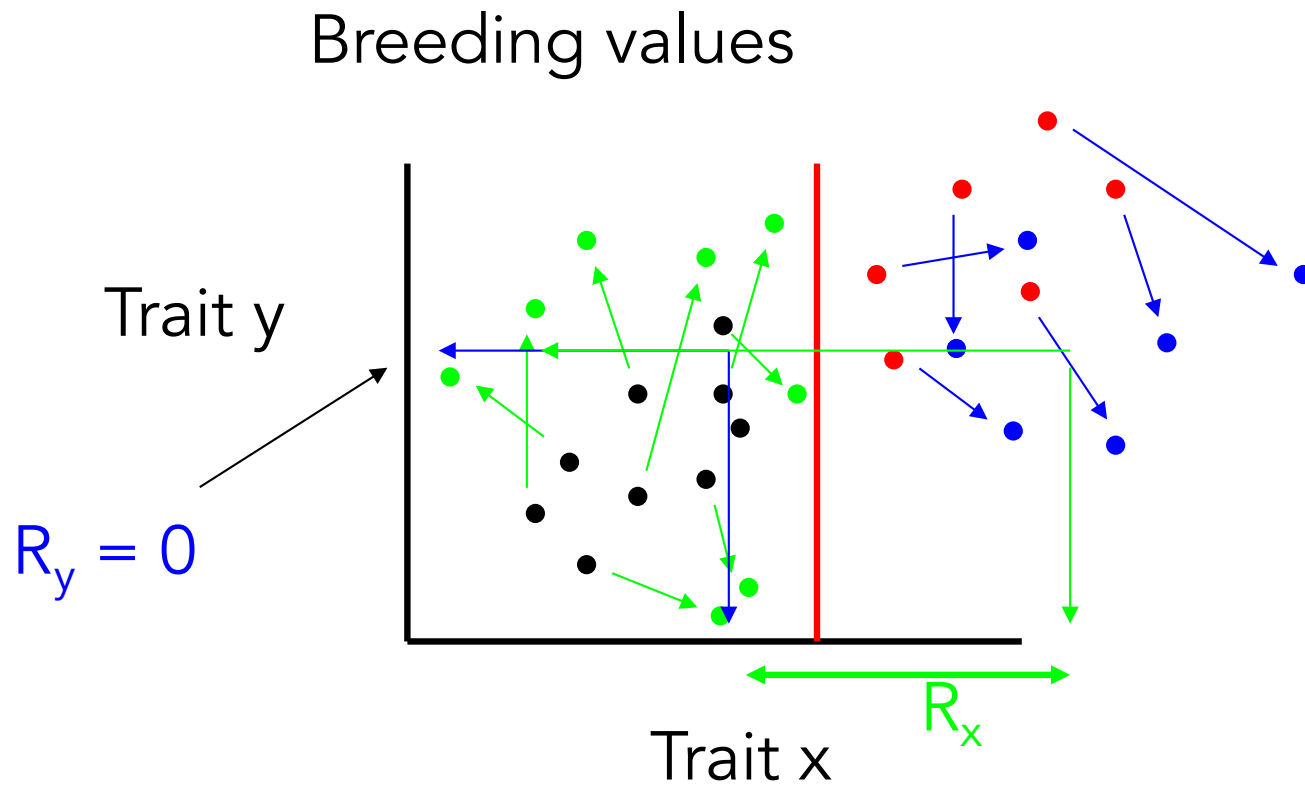
Example

- Suppose h^2 trait $x = 0.5$, h^2 trait $y = 0.3$
- Select on trait one to give $S_x = 10$
 - Expected response is $R_x = 5$
- Suppose $\text{Cov}(t_x, t_y) = 0.5$, then $S_y = 5$
- What is the response in trait 2?
 - is it $CR_y = 0.3 * 5 = 1.5$. NO!
 - Could be positive, negative, or zero
 - Depends on the Genetic correlation between traits x and y . Why??

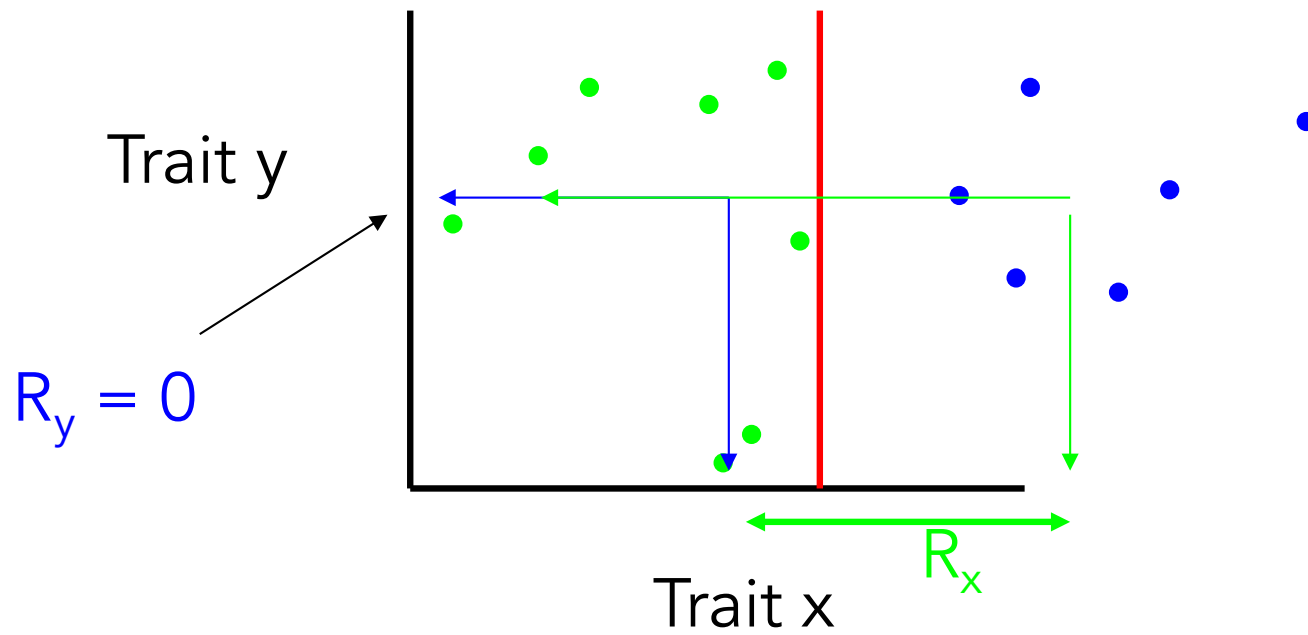
Phenotypic values

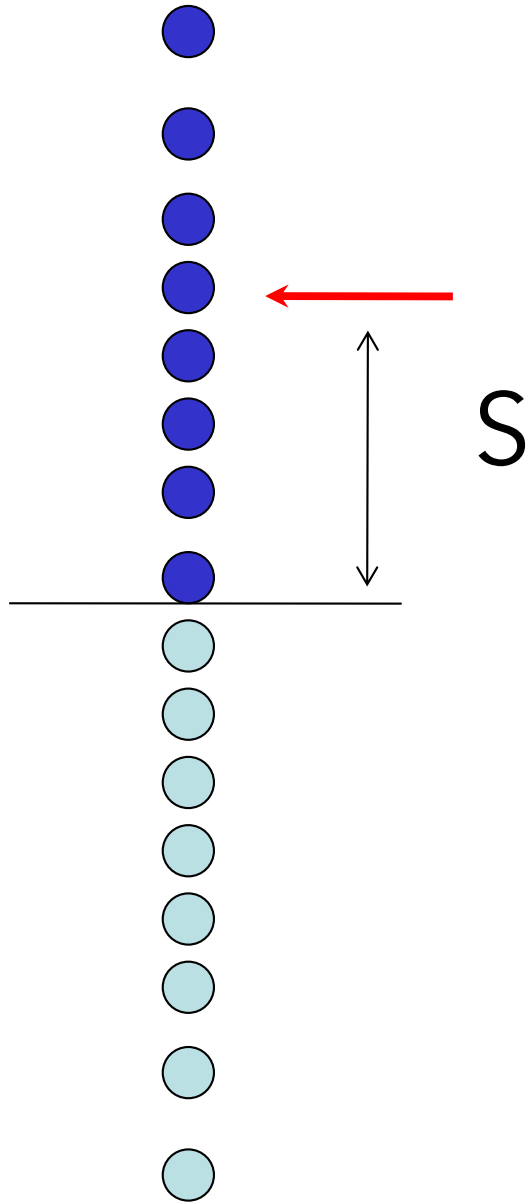


Phenotypic values are misleading, what we want are the breeding values for each of the selected individuals. Each arrow takes an individual's phenotypic value into its actual breeding value.

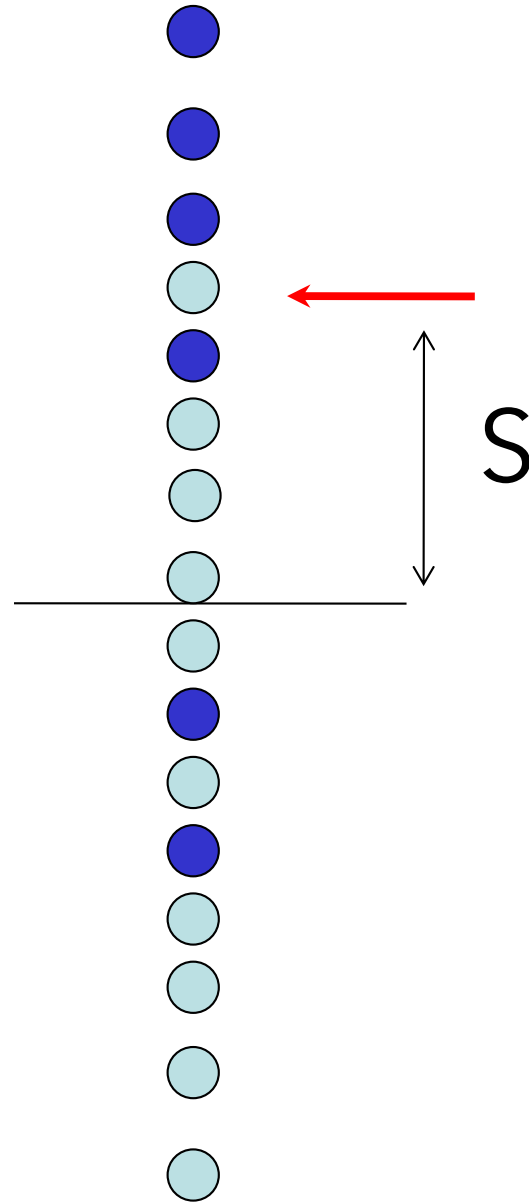


Breeding values





Direct selection



Indirect selection

Predicting the correlated response

The change in character y in response to selection on x is the regression of the breeding value of y on the breeding value of x ,

$$A_y = b_{A_y|A_x} A_x$$

where

$$b_{A_y|A_x} = \frac{\text{Cov}(A_x, A_y)}{\text{Var}(A_x)} = r_A \frac{\sigma(A_y)}{\sigma(A_x)}$$

If R_x denotes the direct response to selection on x , CR_y denotes the correlated response in y , with

$$CR_y = b_{A_y|A_x} R_x$$

We can rewrite $CR_y = b_{Ay|Ax} R_x$ as follows

$$\text{First, note that } R_x = h_x^2 S_x = i_x h_x \sigma_A(x)$$

↑
Recall that $i_x = S_x / \sigma_P(x)$
is the selection
intensity on x

$$\text{Since } b_{Ay|Ax} = r_A \sigma_A(x) / \sigma_A(y),$$

$$\text{We have } CR_y = b_{Ay|Ax} R_x = r_A \sigma_A(y) h_x i_x$$

Substituting $\sigma_A(y) = h_y \sigma_P(y)$ gives our final result:

$$CR_y = i_x h_x h_y r_A \sigma_P(y)$$

$$CR_y = i_x h_x h_y r_A \sigma_P (y)$$

Noting that we can also express the direct response as

$$R_x = i_x h_x^2 \sigma_P (x)$$

shows that $h_x h_y r_A$ in the corrected response plays the same role as h_x^2 does in the direct response. As a result, $h_x h_y r_A$ is often called the **co-heritability**

Direct vs. Indirect Response

We can change the mean of x via a direct response R_x or an indirect response CR_x due to selection on y

$$\frac{CR_x}{R_x} = \frac{i_y r_A \sigma_{AX} h_y}{i_x h_x \sigma_{AX}} = \frac{i_y r_A h_y}{i_x h_x}$$

Hence, indirect selection gives a large response when

$$i_y r_A h_y > i_x h_x$$

- The selection intensity is much greater for y than x . This would be true if y were measurable in both sexes but x measurable in only one sex.
- Character y has a greater heritability than x , and the genetic correlation between x and y is high. This could occur if x is difficult to measure with precision but y is not.

G x E

The same trait measured over two (or more) environments can be considered as two (or more) correlated traits.

If the genetic correlation $|\rho| = 1$ across environments and the genetic variance of the trait is the same in both environments, then no G x E

However, if $|\rho| < 1$, and/or $\text{Var}(A)$ of the trait varies over environments, then G x E present

Hence, dealing with G x E is a *multiple-trait problem*

Participatory breeding

The environment where a crop line is developed may be different from where it is grown

An especially important example of this is **participatory breeding**, wherein subsistence farmers are involved in the field trials.

Here, the correlated response is the yield in subsistence environment given selection at a regional center, while direct response is yield when selection occurred in subsistence environment. Regional center selection works when

$$i_Y r_A h_Y > i_X h_X$$

Matrices

$$\mathbf{A} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \quad \mathbf{B} = \begin{pmatrix} e & f \\ g & h \end{pmatrix} \quad \mathbf{C} = \begin{pmatrix} i \\ j \end{pmatrix}$$

Dimensions given by rows x columns (r x c)

The identity matrix \mathbf{I} , $\mathbf{I}_{2 \times 2} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$

Matrix Multiplication

$$\mathbf{AB} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} e & f \\ g & h \end{pmatrix}$$
$$= \begin{pmatrix} ae + bg & af + bh \\ ce + dg & cf + dh \end{pmatrix}$$

In order to multiply two matrices, they must conform

$$A_{r \times c} B_{c \times k} = C_{r \times k}$$

Matrix Multiplication

$$\mathbf{A} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \quad \mathbf{B} = \begin{pmatrix} e & f \\ g & h \end{pmatrix} \quad \mathbf{C} = \begin{pmatrix} i \\ j \end{pmatrix}$$

$$\mathbf{BA} = \begin{pmatrix} ae + cf & eb + df \\ ga + ch & gd + dh \end{pmatrix} \quad \mathbf{AC} = \begin{pmatrix} ai + bj \\ ci + dj \end{pmatrix}$$


The **identity matrix \mathbf{I}** serves the role of one in matrix multiplication: $\mathbf{AI} = \mathbf{A}$, $\mathbf{IA} = \mathbf{A}$

The Inverse Matrix, A^{-1}

For a square matrix A , define the **Inverse** of A , A^{-1} , as the matrix satisfying

$$\mathbf{A}^{-1} \mathbf{A} = \mathbf{A} \mathbf{A}^{-1} = \mathbf{I}$$

For $\mathbf{A} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$ $\mathbf{A}^{-1} = \frac{1}{ad - bc} \begin{pmatrix} d & -b \\ -c & a \end{pmatrix}$



If this quantity (the determinant) is zero, the inverse does not exist.

The inverse serves the role of division in matrix multiplication

Suppose we are trying to solve the system $Ax = c$ for x .

$A^{-1} Ax = A^{-1} c$. Note that $A^{-1} Ax = Ix = x$, giving $x = A^{-1} c$

The Multivariate Breeders' Equation

Suppose we are interested in the vector R of responses when selection occurs on n correlated traits

Let S be the vector of selection differentials.

In the univariate case, the relationship between R and S was the Breeders' Equation, $R = h^2S$

What is the multivariate version of this?

$$\mathbf{S} = \begin{pmatrix} S_1 \\ S_2 \\ \vdots \\ S_n \end{pmatrix} \quad \mathbf{R} = \begin{pmatrix} R_1 \\ R_2 \\ \vdots \\ R_n \end{pmatrix}$$

$$\mathbf{P} = \begin{pmatrix} \sigma^2(z_1) & \sigma(z_1, z_2) \\ \sigma(z_1, z_2) & \sigma^2(z_2) \end{pmatrix}$$

$$\mathbf{G} = \begin{pmatrix} \sigma^2(A_1) & \sigma(A_1, A_2) \\ \sigma(A_1, A_2) & \sigma^1(A_2) \end{pmatrix}$$

The multivariate breeder's equation

$$R = G P^{-1} S$$
$$R = h^2 S = (V_A / V_P) S$$

Natural parallels with univariate breeder's equation

$P^{-1} S = \beta$ is called the **selection gradient** and measures the amount of direct selection on a character

The gradient version of the breeder's equation is given by $R = G \beta$. This is often called the Lande Equation (after Russ Lande)

Sources of within-generation change in the mean

Since $\beta = P^{-1} S$, $S = P \beta$,
giving the j -th element as

Within-generation
change in trait j

Change in mean from
phenotypically
correlated characters
under direct selection

$$S_j = \underbrace{\sigma^2(P_j) \beta_j}_{\text{Change in mean from direct selection on trait } j} + \sum_{i \neq j} \sigma(P_j, P_i) \beta_i$$

Within-generation change in the mean

$$S_j = \sigma^2(P_j) \beta_j + \sum_{i \neq j} \sigma(P_j, P_i) \beta_i$$

Response in the mean

Between-generation
change (response) in
trait j

Indirect response
from genetically
correlated
characters under
direct selection

$$R_j = \sigma^2(A_j) \beta_j + \sum_{i \neq j} \sigma(A_j, A_i) \beta_i$$

Response from direct
selection on trait j

Correlated response

Direct response

Example in R

Consider three of these traits, z_1 = oil content, z_2 = protein content, and z_3 = yield. For these characters, Brim et al. estimated the covariance matrices as

$$\mathbf{P} = \begin{pmatrix} 287.5 & 477.4 & 1266 \\ 477.4 & 935 & 2303 \\ 1266 & 2303 & 5951 \end{pmatrix}, \quad \mathbf{G} = \begin{pmatrix} 128.7 & 160.6 & 492.5 \\ 160.6 & 254.6 & 707.7 \\ 492.5 & 707.7 & 2103 \end{pmatrix}$$

$$h^2_{\text{oil}} = 128.7/287.5 = 0.45, \quad h^2_{\text{protein}} = 254.6/935 = 0.27, \\ h^2_{\text{yield}} = 2103/5951 = 0.35.$$

Suppose you observed a within-generation change of -10 for oil, 10 for protein, and 100 for yield.

What is R? What is the nature of selection on each trait?

Enter G, P, and S

```
> P<-matrix(c(287.5,477.4,1266,477.4,935,2303,1266,2303,5951),nrow=3)
> P
      [,1] [,2] [,3]
[1,] 287.5 477.4 1266
[2,] 477.4 935.0 2303
[3,] 1266.0 2303.0 5951
> G<-matrix(c(128.7,160.6,492.5,160.6,254.6,707.7,492.5,707.7,2103),nrow=3)
> G
      [,1] [,2] [,3]
[1,] 128.7 160.6 492.5
[2,] 160.6 254.6 707.7
[3,] 492.5 707.7 2103.0
> S<-matrix(c(-10,10,100),nrow=3)
> S
      [,1]
[1,] -10
[2,] 10
[3,] 100
```

$$R = G P^{-1} S$$

```
> G %*% solve(P) %*% S
      [,1]
[1,] -13.57729
[2,] 12.28425
[3,] 65.14172
```

13.6 decrease in oil (breeder's -4.5)
12.3 increase in protein (breeder's 2.7)
65.1 increase in yield (breeder's 35.3)

S versus β : Observed change versus targets of Selection, $\beta = P^{-1} S$, $S = P \beta$,

$$S_j = \sigma^2(P_j) \beta_j + \sum_{i \neq j} \sigma(P_j, P_i) \beta_i$$

```
> solve(P) %*% S
      [,1]
[1,] -2.708160
[2,] -1.431750
[3,]  1.147009
```



```
> S
      [,1]
[1,]  -10
[2,]   10
[3,]  100
```

β : targets of selection

S: observed within-generation change

Observe a within-generation increase in protein, but the actual selection was to *decrease* it.

Quantifying Multivariate Constraints to Response

Is there genetic variation in the direction of selection?

Consider the following \mathbf{G} and $\boldsymbol{\beta}$:

$$\mathbf{G} = \begin{pmatrix} 10 & 20 \\ 20 & 40 \end{pmatrix}, \quad \boldsymbol{\beta} = \begin{pmatrix} 2 \\ -1 \end{pmatrix}$$

Taken one trait at a time, we might expect $R_i = G_{ii}\beta_i$

Giving $R_1 = 20$, $R_2 = -40$.

What is the actual response?

$$\mathbf{R} = \mathbf{G}\boldsymbol{\beta} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

Constraints Imposed by Genetic Correlations

While β is the directional optimally favored by selection, the actual response is dragged off this direction, with $R = G \beta$.

Example: Suppose

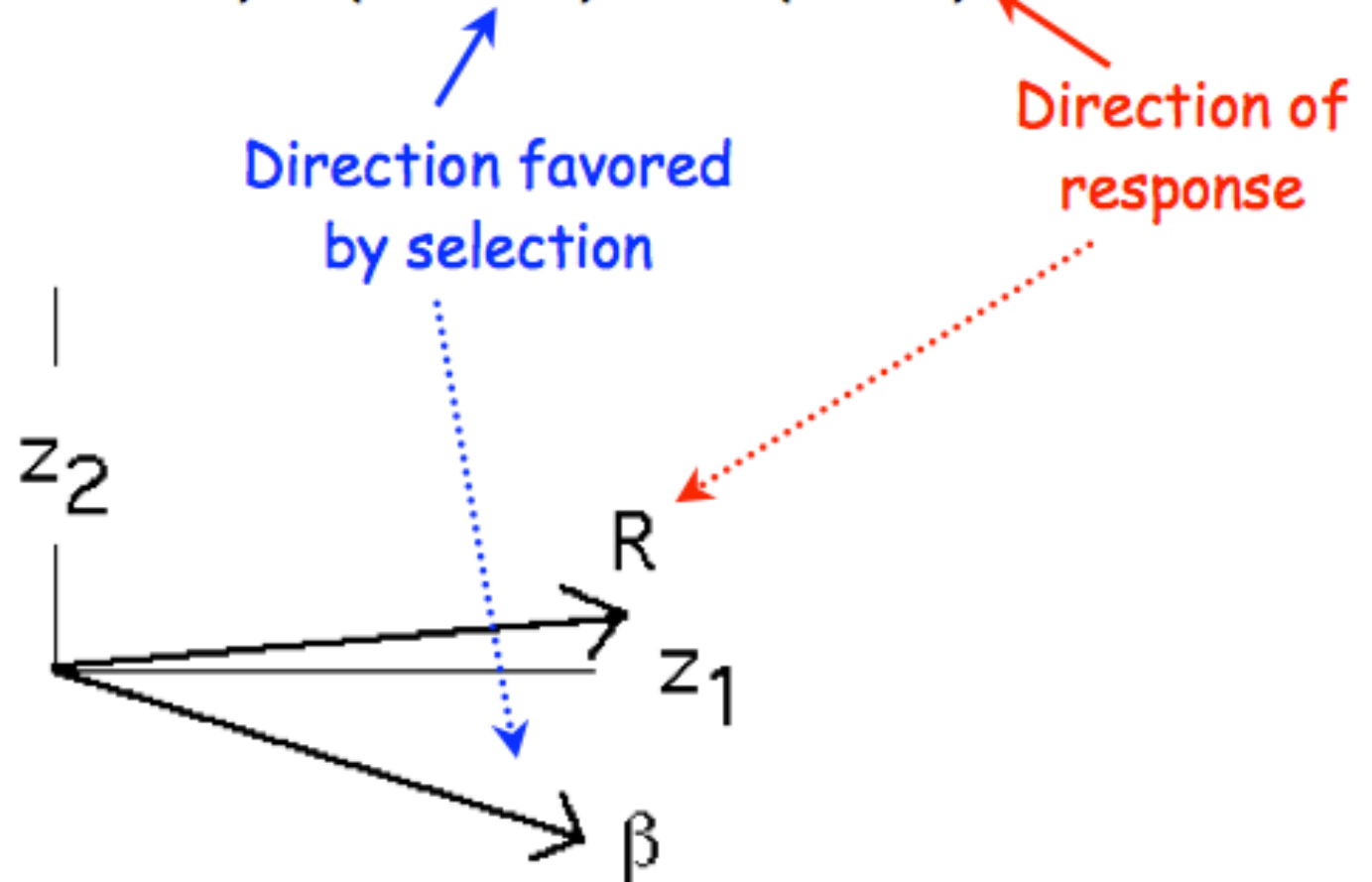
$$\mathbf{S} = \begin{pmatrix} 10 \\ -10 \end{pmatrix}, \quad \mathbf{P} = \begin{pmatrix} 20 & -10 \\ -10 & 40 \end{pmatrix}, \quad \mathbf{G} = \begin{pmatrix} 20 & 5 \\ 5 & 10 \end{pmatrix}$$

What is the true nature of selection on the two traits?

$$\beta = \mathbf{P}^{-1} \mathbf{S} = \mathbf{P}^{-1} \begin{pmatrix} 10 \\ -10 \end{pmatrix} = \begin{pmatrix} 0.43 \\ -0.14 \end{pmatrix}$$

What does the actual response look like?

$$\mathbf{R} = \mathbf{G}\boldsymbol{\beta} = \begin{pmatrix} 20 & 5 \\ 5 & 10 \end{pmatrix} \begin{pmatrix} 0.43 \\ -0.14 \end{pmatrix} = \begin{pmatrix} 7.86 \\ 0.71 \end{pmatrix}$$



Time for a short diversion: The Geometry of a matrix

A vector is a geometric object, leading from the origin to a specific point in n-space.

Hence, a vector has a length and a direction.

We can thus change a vector by both rotation and scaling

The length (or norm) of a vector \mathbf{x} is denoted by $\|\mathbf{x}\|$

$$\|\mathbf{x}\| = \sqrt{x_1^2 + x_2^2 + \cdots + x_n^2} = \sqrt{\mathbf{x}^T \mathbf{x}}$$

The (Euclidean) distance between two vectors \mathbf{x} and \mathbf{y} (of the same dimension) is

$$\|\mathbf{x}-\mathbf{y}\|^2 = \sum_{i=1}^n (x_i - y_i)^2 = (\mathbf{x}-\mathbf{y})^T (\mathbf{x}-\mathbf{y}) = (\mathbf{y}-\mathbf{x})^T (\mathbf{y}-\mathbf{x})$$

The angle θ between two vectors provides a measure for how they differ.

If two vectors satisfy $\mathbf{x} = a\mathbf{y}$ (for a constant a), then they point in the same direction, i.e., $\theta = 0$ (Note that $a < 0$ simply reflects the vector about the origin)

Vectors at right angles to each other, $\theta = 90^\circ$ or 270° are said to be orthogonal. If they have unit length as well, they are further said to be orthonormal.

Matrices Describe Vector transformations

Matrix multiplication results in a **rotation** and a **scaling** of a vector

The action of multiplying a vector x by a matrix A generates a new vector $y = Ax$, that has different dimension from x unless A is square.

Thus A describes a **transformation** of the original coordinate system of x into a new coordinate system.

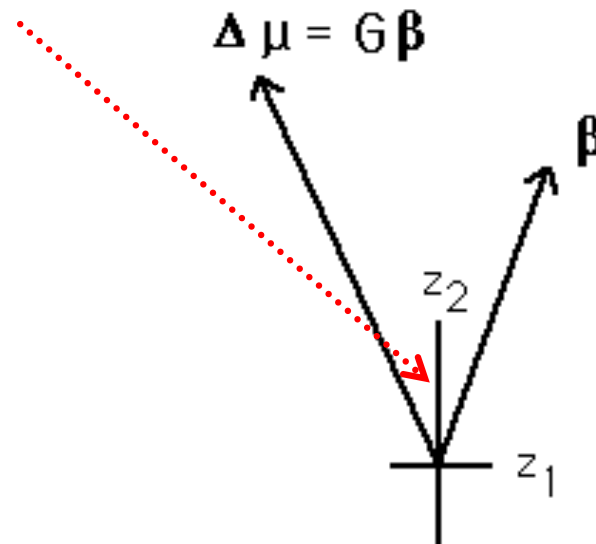
Example: Consider the following \mathbf{G} and β :

$$\mathbf{G} = \begin{pmatrix} 4 & -2 \\ -2 & 2 \end{pmatrix} \quad \beta = \begin{pmatrix} 1 \\ 3 \end{pmatrix}, \quad \mathbf{R} = \mathbf{G}\beta = \begin{pmatrix} -2 \\ 4 \end{pmatrix}$$

The resulting angle between \mathbf{R} and β is given by

$$\cos \theta = \frac{\beta^T \mathbf{R}}{\|\mathbf{R}\| \|\beta\|} = \frac{1}{\sqrt{2}}$$

For an angle of $\theta = 45^\circ$



Eigenvalues and Eigenvectors

The **eigenvalues** and their associated **eigenvectors** fully describe the geometry of a matrix.

Eigenvalues describe how the original coordinate axes are **scaled** in the new coordinate systems

Eigenvectors describe how the original coordinate axes are **rotated** in the new coordinate systems

For a square matrix A , any vector y that satisfies $Ay = \lambda y$ for some scalar λ is said to be an **eigenvector** of A and λ its associated **eigenvalue**.

Note that if y is an eigenvector, then so is a^*y for any scalar a , as $Ay = \lambda y$.

Because of this, we typically take eigenvectors to be scaled to have unit length (their norm = 1)

An **eigenvalue** λ of A satisfies the equation $\det(A - \lambda I) = 0$, where \det = determinant

For an n -dimensional square matrix, this yields an n -degree polynomial in λ and hence up to n unique roots.

Two nice features:

$\det(A) = \prod_i \lambda_i$ The determinant is the product of the eigenvalues

$\text{trace}(A) = \sum_i \lambda_i$. The **trace** (sum of the diagonal elements) is the sum of the eigenvalues

Note that $\det(A) = 0$ if and only if at least one eigenvalue = 0

For symmetric matrices (such as covariance matrices) the resulting n eigenvectors are mutually orthogonal, and we can factor A into its spectral decomposition,

$$\mathbf{A} = \lambda_1 \mathbf{e}_1 \mathbf{e}_1^T + \lambda_2 \mathbf{e}_2 \mathbf{e}_2^T + \cdots + \lambda_n \mathbf{e}_n \mathbf{e}_n^T$$

Hence, we can write the product of any vector x and A as

$$\begin{aligned} \mathbf{A}x &= \lambda_1 \mathbf{e}_1 \mathbf{e}_1^T x + \lambda_2 \mathbf{e}_2 \mathbf{e}_2^T x + \cdots + \lambda_n \mathbf{e}_n \mathbf{e}_n^T x \\ &= \lambda_1 \text{Proj}(\mathbf{x} \text{ on } \mathbf{e}_1) + \lambda_2 \text{Proj}(\mathbf{x} \text{ on } \mathbf{e}_2) + \cdots + \lambda_n \text{Proj}(\mathbf{x} \text{ on } \mathbf{e}_n) \end{aligned}$$

Example: Let's reconsider a previous G matrix

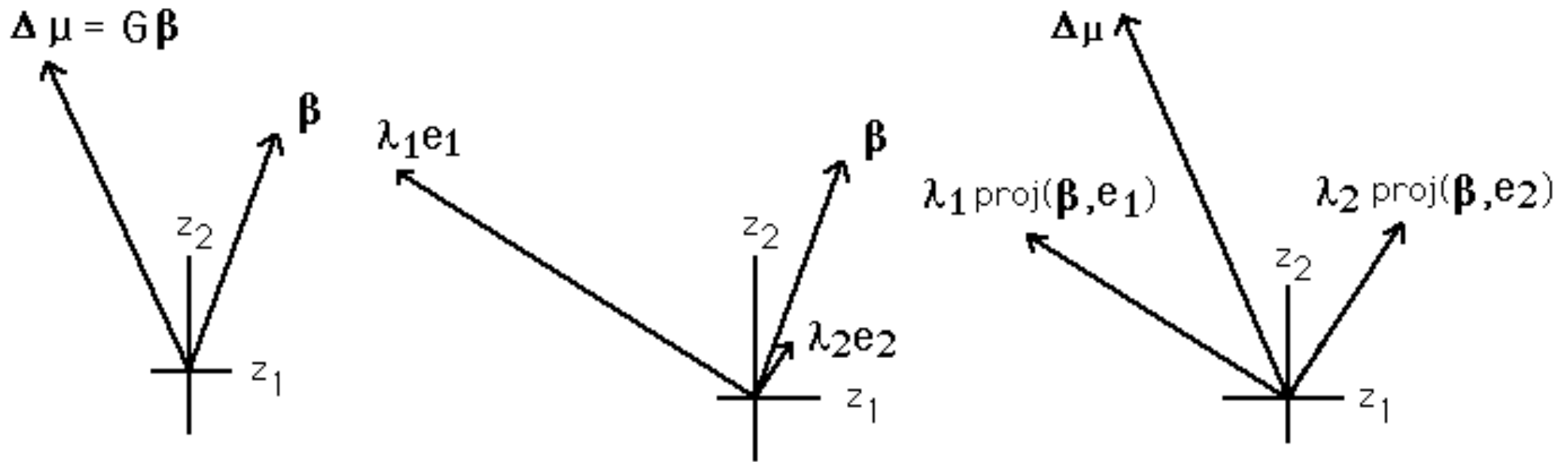
$$\begin{aligned} |\mathbf{G} - \lambda\mathbf{I}| &= \left| \begin{pmatrix} 4 - \lambda & -2 \\ -2 & 2 - \lambda \end{pmatrix} \right| \\ &= (4 - \lambda)(2 - \lambda) - (-2)^2 = \lambda^2 - 6\lambda + 4 = 0 \end{aligned}$$

The solutions are

$$\lambda_1 = 3 + \sqrt{5} \simeq 5.236 \quad \lambda_2 = 3 - \sqrt{5} \simeq 0.764$$

The corresponding eigenvectors become

$$\mathbf{e}_1 \simeq \begin{pmatrix} -0.851 \\ 0.526 \end{pmatrix} \quad \mathbf{e}_2 \simeq \begin{pmatrix} 0.526 \\ 0.851 \end{pmatrix}$$



Even though β points in a direction very close of e_2 , because most of the variation is accounted for by e_1 , its projection is this dimension yields a much longer vector. The sum of these two projections yields the selection response R .

Realized Selection Gradients

Suppose we observe a difference in the vector of means for two populations, $\mathbf{R} = \boldsymbol{\mu}_1 - \boldsymbol{\mu}_2$.

If we are willing to assume they both have a common \mathbf{G} matrix that has remained constant over time, then we can estimate the nature and amount of selection generating this difference by

$$\boldsymbol{\beta} = \mathbf{G}^{-1} \mathbf{R}$$

Example: You are looking at oil content (z_1) and yield (z_2) in two populations of soybeans. Population a has $\mu_1 = 20$ and $\mu_2 = 30$, while for Pop 2, $\mu_1 = 10$ and $\mu_2 = 35$.

Here

$$\mathbf{R} = \begin{pmatrix} 20 & -10 \\ 30 & -35 \end{pmatrix} = \begin{pmatrix} 10 \\ -5 \end{pmatrix}$$

Suppose the variance-covariance matrix has been stable and equal in both populations, with

$$\mathbf{G} = \begin{pmatrix} 20 & -10 \\ -10 & 40 \end{pmatrix}$$

The amount of selection on both traits to obtain this response is

$$\boldsymbol{\beta} = \begin{pmatrix} 20 & -10 \\ -10 & 40 \end{pmatrix}^{-1} \begin{pmatrix} 10 \\ -5 \end{pmatrix} = \begin{pmatrix} 0.5 \\ 0 \end{pmatrix}$$