

Fixed Linear Effects Models

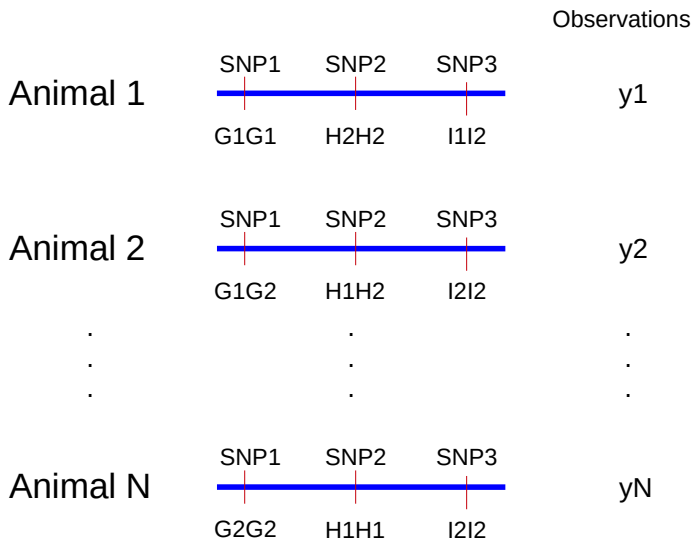
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Background

- ▶ Given a population of N animals
- ▶ Each animal has information on genotypes at loci G , H and I
- ▶ Each animal has an observation for one quantitative trait of interest y
- ▶ **Goal:** Predict genomic breeding values

Data



Two Types Of Models

1. **Genetic** Model: How can we decompose the phenotype into genetic part and non-genetic environmental part
2. **Statistical** Model: How to estimate unknown parameters from a dataset

Goals:

1. Use genetic model to show how observations and genetic information can be used to predict breeding values.
2. Use statistical techniques to do the prediction

Genetic Model

- ▶ simple model from quantitative genetics to split phenotypic observation into
 - ▶ genetic part g and
 - ▶ environmental part e

$$y = g + e$$

- ▶ environment: split into
 - ▶ known environmental factors: herd, year, ... (β)
 - ▶ unknown random error (ϵ)
- ▶ polygenic model: use a finite number of loci to model genetic part of phenotypic observation

Genetic Model (II)

Central Dogma
Of Molecular Biology

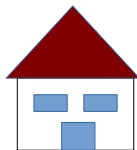
DNA 



RNA 



Protein 



Error



Genotype

Environment

Phenotype



Polygenic Model

- ▶ Component g can be decomposed into contributions g_j of single loci

$$g = \sum_{j=1}^k g_j$$

- ▶ Assume that loci are additive, hence genotypic values g_j depends on a_j with $d_j = 0$
- ▶ Genotypic values at locus j can either be $-a_j$, 0 or a_j
- ▶ Breeding values based on locus j depends on a_j .

Genotypic Value

- ▶ Genotypic value g_i for animal i over all loci

$$g_i = M_i \cdot a$$

where M_i is a row vector with elements -1 , 0 and 1 and a is the vector of all genotypic values of the positive homozygous genotypes of all loci.

Phenotypic Value

- ▶ Collecting all components for an observation y_i for animal i

$$y_i = W_i \cdot \beta + M_i \cdot a + \epsilon_i$$

- ▶ all animals in the population

$$y = W \cdot \beta + M \cdot a + \epsilon$$

- ▶ combining $b^T = \begin{bmatrix} \beta & a \end{bmatrix}$ and $X = \begin{bmatrix} W & M \end{bmatrix}$

$$y = X \cdot b + \epsilon$$

Statistical Model

- ▶ genetic model from statistics point of view
- ▶ phenotypic observation as response y
- ▶ vector b (known environment and genotypic values) as unknown parameter
- ▶ fixed predictor variables in matrix X
- ▶ vector ϵ as random error terms

→ Fixed Linear Effects Model

Parameter Estimation

- ▶ use regression model
- ▶ regression means both response and predictors are continuous
- ▶ example dataset: body weight on breast circumference

Regression Dataset

Animal	Breast Circumference	Body Weight
1	176	471
2	177	463
3	178	481
4	179	470
5	179	496
6	180	491
7	181	518
8	182	511
9	183	510
10	184	541

Regression Model

- ▶ response y : body weight
- ▶ predictor x : breast circumference
- ▶ model for observation y_i

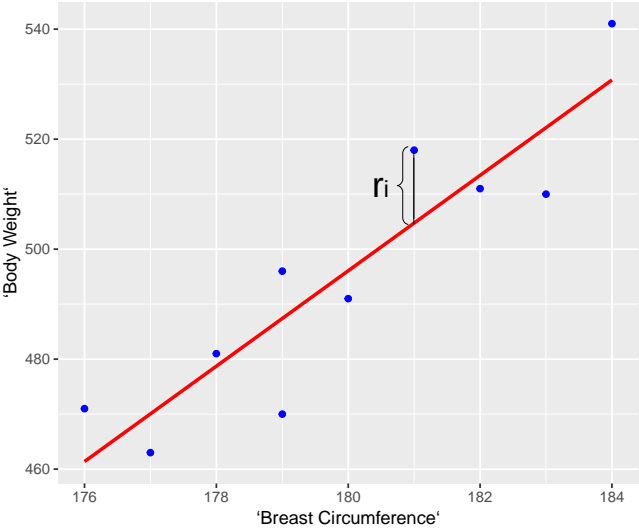
$$y_i = x_i * b + \epsilon_i$$

- ▶ meaning of b : change x_i by one unit $\rightarrow y_i$ changes on average by b units.
- ▶ use case: measure x_{N+1} for animal $N + 1$ with unknown weight and use b to predict y_{N+1}

Least Squares

- ▶ How to find b such that y is best approximated by x
- ▶ Residuals $r_i = y_i - x_i * \hat{b}$
- ▶ Minimization of sum of squared residuals (LS)
- ▶ Use \hat{b} at minimal LS as estimate

LSQ Diagram



Sum of squared residuals

$$LS = \sum_{i=1}^n r_i^2$$

- In matrix-vector notation with r denoting the vector of all residuals

$$LS = \|r\|^2 = r^T r$$

where $\|\cdot\|$ stands for the norm (“length in 2D”) of a vector

► Replacing r with $r = y - X\hat{b}$

$$LS = (y - X\hat{b})^T (y - X\hat{b}) = y^T y - y^T X\hat{b} - \hat{b}^T X^T y + \hat{b}^T X^T X\hat{b}$$

Minimization

- ▶ Set partial derivative of LS with respect to \hat{b} to 0

$$\frac{\partial LS}{\partial \hat{b}} = -X^T y - X^T y + 2X^T X \hat{b} = 0$$

- ▶ Take the \hat{b} that satisfies the above equation as the least squares estimate \hat{b}_{LS}

$$X^T X \hat{b}_{LS} = X^T y$$

- ▶ Solution

$$\hat{b}_{LS} = (X^T X)^{-1} X^T y$$

Variance of Error Terms

- ▶ Least Squares Procedure does not yield an estimate for σ^2
- ▶ The estimator based on the residuals

$$\hat{\sigma}^2 = \frac{1}{n-p} \sum_{i=1}^n r_i^2$$

Different Types of Regressions

- ▶ Regression through the origin

$$y_i = x_i * b + e_i$$

- ▶ Regression with intercept

$$y_i = b_0 + x_i * b + e_i$$

Predictions

- ▶ One of the use-cases for regression is **prediction**
- ▶ Prediction means that given a regression model with estimated regression coefficients based on a data set, values of responses are to be predicted for new predictor values (x_{new})

$$\hat{y} = x_{new} * \hat{b}$$

- ▶ No predictions outside of the range of x used to estimate \hat{b}

Multiple Linear Regression

- ▶ Use more than one predictor variable
- ▶ Example: Conformation traits BCS and HEI besides BC
- ▶ New model:

$$y_i = b_0 + BC_i * b_1 + BCS_i * b_2 + HEI_i * b_3 + e_i$$

- ▶ In matrix vector notation:

$$y = Xb + e$$

with $b^T = \left[b_0 \quad b_1 \quad b_2 \quad b_3 \right]$

New data set

Table 2: Dataset for Multiple Linear Regression

Animal	Breast Circumference	Body Weight	BCS	HEI
1	176	471	5.0	161
2	177	463	4.2	121
3	178	481	4.9	157
4	179	470	3.0	165
5	179	496	6.8	136
6	180	491	4.9	123
7	181	518	4.4	163
8	182	511	4.4	149
9	183	510	3.5	143
10	184	541	4.7	130

Goal

- ▶ Find solution for \hat{b}_{LS}
- ▶ Same principle of least squares as with simple linear regression
- ▶ Different dimensions for X and b

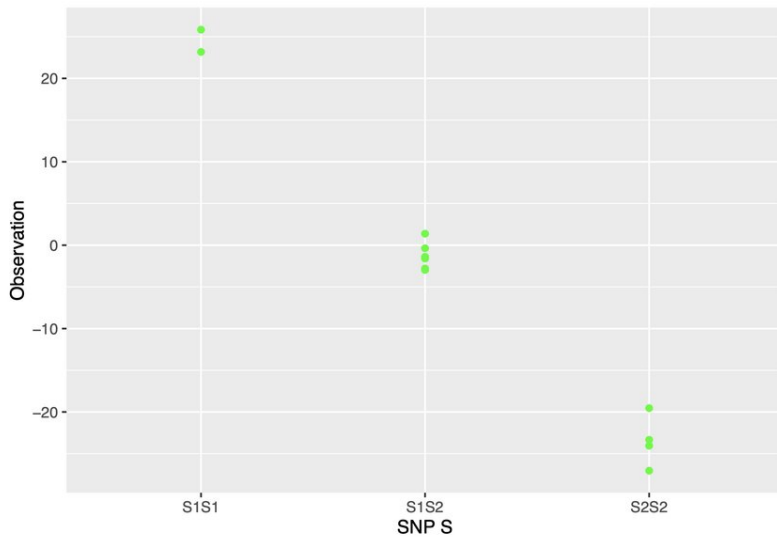
→ Problem 1 in Exercise 2

Regression on Dummy Variables

- ▶ What happens when predictor variables X are no longer continuous
- ▶ Examples: SNP-Genotypes
- ▶ X can only take a few discrete values, e.g., 0, 1 or $-1, 0, 1, \dots$

→ regression on dummy variables or just general fixed linear model.

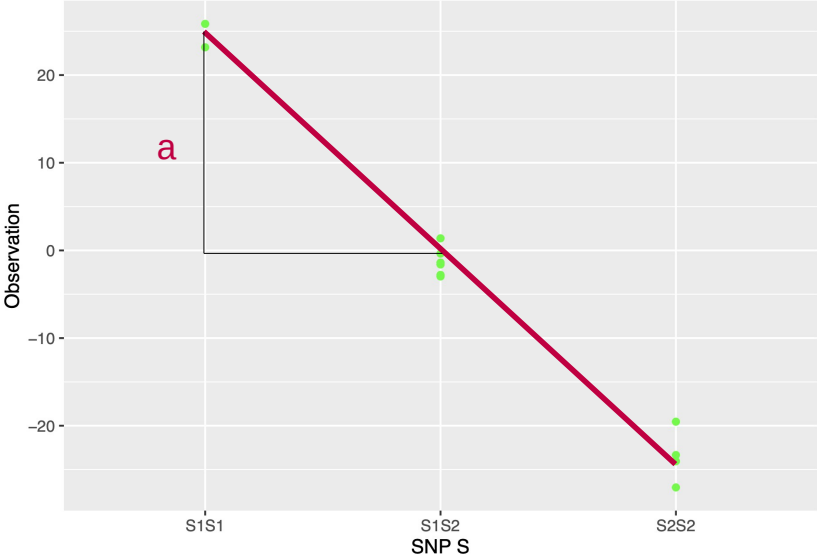
Example: SNP-Data



Goal

- ▶ Same as in linear regression: fit line through points such that least squares criterion holds
- ▶ Interpretation: Difference between effect levels
- ▶ For SNP-data: differences correspond to marker effects

Dummy Regression Line



Problem

- ▶ In many datasets X does not have full column-rank
- ▶ That means some columns of X show linear dependence
- ▶ As a consequence of that $(X^T X)$ cannot be inverted

Solution

- ▶ Use a generalised inverse $(X^T X)^-$ to get a solution \hat{b}_{LS} for least squares normal equations
- ▶ Use estimable functions of \hat{b}_{LS} which are independent of the choice of $(X^T X)^-$
- ▶ One example for estimable functions are differences between effect levels
- ▶ For example of SNP-data these correspond to marker effects.

Generalised Inverse

- ▶ Reminder: the (ordinary) inverse A^{-1} of A is given by $A^{-1}A = I$, but A^{-1} exists only, if A is of full rank.
- ▶ A generalised inverse G of matrix A satisfies: $AGA = A$
- ▶ For the system of equations $Ax = y$, the vector $x = Gy$ is a solution, if $AGA = A$
- ▶ For a generalised inverse G of A , the system of equation $Ax = y$ has solutions

$$\tilde{x} = Gy + (GA - I)z$$

for an arbitrary vector z .

Estimable Functions

- ▶ linear function of the parameter (b) that is identical to linear function of expected values of observations y , i.e.,

$$q^T b = t^T E(y)$$

- ▶ estimable functions are invariant (do not change) with different generalised inverses.