Regression analysis Two variables (Montgomery and Runger: ch 11 Brani Vidakovic: ch 14)

Reminder

Covariance Defined

Covariance is a number qunatifying average dependence between two random variables.

denoted as $\text{cov}\big(X,Y\big)$ or $\sigma_{_{XY}}$ is The covariance between the random v ariables X and Y,

$$
\sigma_{XY} = E\left[\left(X - \mu_X\right)\left(Y - \mu_Y\right)\right] = E\left(XY\right) - \mu_X\mu_Y \tag{5-14}
$$

The units of σ_{XY} are units of X times units of Y.

Unlike the range of variance, $-\infty < \sigma_{XY} < \infty$.

Correlation is "normalized covariance"

• Also called: Pearson correlation coefficient

*ρXY= ^σXY /^σXσ Y*is the covariance normalized to be *-1 ≤ ρXY≤ 1*

Karl Pearson (1852– 1936) English mathematician and biostatistician

Covariance and Scatter Patterns

Figure 5-13 Joint probability distributions and the sign of cov(*X*, *Y*). Note that covariance is a measure of linear relationship. Variables with non-zero covariance are correlated.

Regression analysis

• Many problems in engineering and science involve sample in which two or more variables were measured. They may not be independent from each other and one (or several) of them can be used to predict another

- Everyday example: in most samples height and weight of people are related to each other
- Biological example: in a cell sorting experiment the copy number of a protein may be measured alongside its volume
- Regression analysis uses a sample to build a model to predict protein copy number given a cell volume

Sir Francis Galton, (1822 -1911) was an English statistician, anthropologist, proto-geneticist, psychometrician, eugenicist, ("Nature vs Nurture", inheritance of intelligence), tropical explorer, geographer, inventor (Galton Whistle to test hearing), meteorologist (weather map, anticyclone).

Invented both correlation and regression analysis when studied heights of fathers and sons

Found that fathers with height above average tend to have sons with height also above average but closer to the average. Hence "regression" to the mean

Two variable samples

- •Oxygen can be distilled from the air
- • Hydrocarbons need to be filtered out or the whole thing would go kaboom!!!
- • When more hydrocarbons were removed, the remaining oxygen stays cleaner
- • Except we don't know how dirty was the air to begin with

 $Y = \beta_0 + \beta_1 \times + \epsilon$

Figure 11-1 Scatter diagram of oxygen purity versus hydrocarbon level from Table 11-1.

$$
Y=75115\cdot X+C
$$

Linear regression

The **simple linear regression model** is given by

$$
Y = \beta_0 + \beta_1 X + E = \hat{Y} + E
$$

is the **random error**

slope β_1 and intercept β_0 of the line are called **regression coefficients**

Note: $Y \cdot \hat{Y}$ X and E are random variables

Let's assume that $E(E | x)=0 \rightarrow$ $E(Y | x) = \beta_0 + \beta_1 x + E(E | x) = \beta_0 + \beta_1 x$

 $Y = \beta_0 + \beta_1 X + \epsilon$ $\int_{M} E(f|x) = 0$ \int_{M}
 H_{env} does one find β_0 $R\beta_1$. $Cov(Y, y) = Cov((\beta_{0} + \beta_{1}X + \epsilon)y)$ $= CoV(f_{10}x) + f_{1}Cov(x,x) + Cov(f_{2}x)$ $Cov(\beta_0, x)=0$ Since β_0 is constant $Cov(X,X)=E(X^{2})-E(X)^{2}=Var(X)$ $C_{\alpha\gamma}(f,X)=E(f\cdot X)-E(X)\cdot E(X)=E(f\cdot X)=\sum_{\alpha\in\mathbb{Z}}x\cdot E(f\cdot X)=0$ Thus $\beta_1 = \frac{Cov(X, V)}{Var(X)} \beta_0 = E(Y) - \beta_1 E(X)$

Method of least squares

• The **method of least squares** is used to estimate the parameters, β_0 and β_1 by minimizing the sum of the squares of the vertical deviations in Figure 11-3.

Figure 11-3 Deviations of the data from the estimated regression model.

> Figure $11-3$ Deviations of the data from the estimated regression model.

$$
y_i = \beta_0 + \beta_1 x_i + \epsilon_i, \qquad i = 1, 2, \dots, n \tag{11-3}
$$

and the sum of the squares of the deviations of the observations from the true regression line is

$$
L = \sum_{i=1}^{n} \epsilon_i^2 = \sum_{i=1}^{n} (y_i - \beta_0 - \beta_1 x_i)^2
$$
 (11-4)

The least squares estimators of β_0 and β_1 , say, $\hat{\beta}_0$ and $\hat{\beta}_1$, must satisfy

$$
\frac{\partial L}{\partial \beta_0}\Big|_{\beta_0, \beta_1} = -2\sum_{i=1}^n (y_i - \hat{\beta}_0 - \hat{\beta}_1 x_i) = 0
$$
\n
$$
\frac{\partial L}{\partial \beta_1}\Big|_{\beta_0, \beta_1} = -2\sum_{i=1}^n (y_i - \hat{\beta}_0 - \hat{\beta}_1 x_i)x_i = 0
$$
\n
$$
n\hat{\beta}_0 + \hat{\beta}_1 \sum_{i=1}^n x_i = \sum_{i=1}^n y_i
$$
\n
$$
\hat{\beta}_0 \sum_{i=1}^n x_i + \hat{\beta}_1 \sum_{i=1}^n x_i^2 = \sum_{i=1}^n y_i x_i
$$
\n(11-6)

Traditional notation

Definition

The least squares estimates of the intercept and slope in the simple linear regression model are

$$
\hat{\beta}_0 = \bar{y} - \hat{\beta}_1 \bar{x} \qquad (11-7)
$$
\n
$$
\hat{\beta}_1 = \frac{\sum_{i=1}^n y_i x_i - \frac{\left(\sum_{i=1}^n y_i\right)\left(\sum_{i=1}^n x_i\right)}{n}}{\sum_{i=1}^n x_i^2 - \frac{\left(\sum_{i=1}^n x_i\right)^2}{n}} = \frac{\mathcal{S}_{\mathcal{X}\mathcal{Y}}}{\mathcal{S}_{\mathcal{X}\mathcal{X}}} \qquad (11-8)
$$

where $\overline{y} = (1/n) \sum_{i=1}^n y_i$ and $\overline{x} = (1/n) \sum_{i=1}^n x_i$.

11-2: Simple Linear Regression

Definition

The least squares estimates of the intercept and slope in the simple linear regression model are

$$
\hat{\beta}_0 = \bar{y} - \hat{\beta}_1 \bar{x}
$$
\n
$$
\hat{\beta}_1 = \frac{\sum_{i=1}^n y_i x_i}{\sum_{i=1}^n y_i} - \frac{\left(\sum_{i=1}^n y_i\right)\left(\sum_{i=1}^n x_i\right)}{n^2}}{\sum_{i=1}^n x_i^2} - \frac{\left(\sum_{i=1}^n x_i\right)^2}{n^2}}
$$
\n
$$
\frac{\left(\sum_{i=1}^n x_i\right)^2}{\sqrt{q\sqrt{X}}}
$$
\n(11-8)\n
$$
\frac{\sum_{i=1}^n x_i^2}{\sqrt{q\sqrt{X}}}
$$

where $\overline{y} = (1/n) \sum_{i=1}^n y_i$ and $\overline{x} = (1/n) \sum_{i=1}^n x_i$.

11-4.2 Analysis of Variance Approach to Test Significance of Regression

The analysis of variance identity is

$$
\sum_{i=1}^{n} (y_i - \overline{y})^2 = \sum_{i=1}^{n} (\hat{y}_i - \overline{y})^2 + \sum_{i=1}^{n} (y_i - \hat{y}_i)^2
$$
 (11-24)

Symbolically,

$$
SS_T = SS_R + SS_E \tag{11-25}
$$

11-7: Adequacy of the Regression Model

11-7.2 Coefficient of Determination (R 2) VERY COMMONLY USED

• The quantity

$$
R^2 = \frac{SS_R}{SS_T} = 1 - \frac{SS_E}{SS_T}
$$

is called the **coefficient of determination** and is often used to judge the adequacy of a regression model.

- \bullet $0 \leq R$ $2 \leq 1;$
- We often refer (loosely) to R^2 as the amount of variability in the data explained or accounted for by the regression model.

11-7: Adequacy of the Regression Model

11-7.2 Coefficient of Determination (R 2)

• For the oxygen purity regression model, R^2

$$
R2 = SSR/SST= 152.13/173.38= 0.877
$$

• Thus, the model accounts for 87.7% of the variability in the data.

11-2: Simple Linear Regression

Estimating ε2

An **unbiased estimator** of σ_ε^2 is

$$
\hat{\sigma}_{\mathbf{E}}^2 = \frac{SS_E}{n-2} \tag{11-13}
$$

where SS_{E} can be easily computed using

$$
SS_E = SS_T - \hat{\beta}_1 S_{xy} \tag{11-14}
$$

11-3: Properties of the Least Squares Estimators

• Slope Properties

$$
E(\hat{\beta}_1) = \beta_1 \qquad V(\hat{\beta}_1) = \frac{\hat{\sigma}_{\epsilon}^2}{S_{xx}} = \frac{\hat{\delta}_{\epsilon}^2}{h \hat{\epsilon}_{\times}^2}
$$

\n• Intercept Properties\n
$$
L_{\text{cov}} g e \qquad n \Rightarrow \text{small}
$$
\n
$$
E(\hat{\beta}_0) = \beta_0 \quad \text{and} \quad V(\hat{\beta}_0) = \hat{\sigma}_{\epsilon}^2 \left[\frac{1}{n} + \frac{\bar{x}^2}{S_{xx}} \right] = \int_{\text{cov}_{\text{cov}}^2} \frac{\hat{\delta}_{\epsilon}^2}{h \hat{\epsilon}_{\times}^2}
$$
\n
$$
= \hat{\delta}_{\epsilon}^2 \left(1 + \frac{\gamma_{\kappa}^2}{\hat{\delta}_{\kappa}^2} \right) \cdot \frac{1}{h} \qquad \text{for} \qquad \text{if} \qquad \text{if} \qquad \text{if} \qquad \text{if} \qquad \text{if} \qquad \text{if} \quad \text{if} \quad
$$

Figure 11-5 The null hypothesis H $_0$: \upbeta_1 = 0 is accepted.

Figure 11-6 The $\boldsymbol{\mathsf{n}}$ ull $\boldsymbol{\mathsf{h}}$ ypothesis $\boldsymbol{\mathsf{H}}_\textbf{0}\text{: }\boldsymbol{\beta}_\textbf{1}=\boldsymbol{\mathsf{0}}$ is rejected.

11-4.1 Use of *Z***-tests for large n**

An important special case of the hypotheses of Equation 11-18 is

> $H_0: \beta_1 = 0$ H_1 : $\beta_1 \neq 0$

These hypotheses relate to the **significance of regression**. *Failure* to reject H₀ is equivalent to concluding that there is no linear relationship between *X* and *Y*.

11-4.1 Use of *t***-tests for smaller n.**

The number of degrees of freedom in **n-2**

One can always fit a straight line through two points so one needs n>=3

Multiple Linear Regression (Chapters 12-13 in Montgomery, Runger)

12-1: Multiple Linear Regression Model

12-1.1 Introduction

• Many applications of regression analysis involve situations in which there are more than one regressor variable X_{k} used to predict Y.

• A regression model then is called a **multiple regression model**.

Multiple Linear Regression Model

$$
Y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots \beta_k x_k + \varepsilon
$$

One can also use powers and products of other variables or even non-linear functions like $\mathsf{exp}(\mathsf{x_i})$ or $\mathsf{log}(\mathsf{x_i})$ instead of $\mathsf{x}_3 \, ... \, \mathsf{x}_\,$.

Example: the general two-variable quadratic regression has 6 constants:

 $Y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1)^2$ + β_4 (*x*₂)² + β_5 (*x*₁*x*₂) + ε

Nonlinear Regression Example: Logistic Regression

 $P(Y{=}1) = \sigma(X1{^*}w1+ x2{*}w2 + b)$

Linear regression analog

 $Y = X1 * b1 + X2 * b2 + b0$

How to know where to stop adding new variables or powers of old variables?

A Regression Problem

Linear Regression

Quadratic Regression

Join-the-dots

Also known as piecewise linear nonparametric regression if that makes you feel better

Which is best?

Why not choose the method with the best fit to the data?

What do we really want?

Why not choose the method with the best fit to the data?

> "How well are you going to predict future data drawn from the same distribution?"

1. Randomly choose 30% of the data to be in a test set2. The remainder is a training set

(Linear regression example)

1. Randomly choose 30% of the data to be in a test set 2. The remainder is a training set 3. Perform your regression on the training set

(Linear regression example) Mean Squared Error = 2.4

1. Randomly choose 30% of the data to be in a test set2. The remainder is a training set 3. Perform your regression on the training set 4. Estimate your future performance with the test set

(Quadratic regression example) Mean Squared Error = 0.9

1. Randomly choose 30% of the data to be in a test set2. The remainder is a training set 3. Perform your regression on the training set 4. Estimate your future performance with the test set

(Join the dots example) Mean Squared Error = 2.2 1. Randomly choose 30% of the data to be in a test set 2. The remainder is a training set 3. Perform your regression on the training set 4. Estimate your future performance with the test set

Human T cell expression data

- \bullet The matrix contains 47 expression samples from Lukk et al, Nature Biotechnology 2010
- •All samples are from T cells in different individuals
- Only the top 3000 genes with the largest variability were used
- \bullet The value is log2 of gene's expression level in a given sample as measured by the microarray technology

a T cell

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Affiliations | Corresponding author

Nature Biotechnology 28, 322-324 (2010) | doi:10.1038/nbt0410-322

Although there is only one human genome sequence, different genes are expressed in many different cell types and tissues, as well as in different developmental stages or diseases. The structure of this 'expression space' is still largely unknown, as most transcriptomics experiments focus on sampling small regions. We have constructed a global gene expression map by integrating microarray data from 5.372 human samples representing 369 different cell and tissue types, disease states and cell lines. These have been compiled in an online resource (http://www.ebi.ac.uk/gxa/array/U133A) that allows the user to search for a gene of interest and

"Let's Make a Deal" show with Monty Hall aired on NBC/ABC 1963-1986

Matlab exercise #1: "Wheel of Fortune"

- Each group gets a pair of genes that are known to be correlated.
- Each group also gets a random pair of genes selected by the "Wheel of Fortune". They may or may not be correlated
- Download (log-transformed) expression_table.mat
- \bullet Run command $fitlm(x,y)$ on assigned and random pairs
- Record β_0 , β_1 , R 2 , P-value of the slope $\boldsymbol{\beta}_1$ and write them on the blackboard
- Validate Matlab result for R ² using your own calculations
- \bullet Look up gene names (see gene_description in your workspace) and write down a brief description of biological functions of genes. Does their correlation make biological sense ?

Correlated pairs **plausible biological connection based on short description**

$$
1, 6 \quad g1=1994; \quad g2=188;
$$

$$
2, g1=2872; g2=1269;
$$

$$
3, g1=1321; g2=10;
$$

$$
4, g1=886; g2=819;
$$

$$
5, g1=2138; g2=1364;
$$

no obvious biological common function

g1=1+floor(rand.*3000); g2=1+floor(rand.*3000); disp([g1, g2])

Random pairs

>> g1=floor(3000.*rand)+1; g2=floor(3000.*rand)+1; $disp([g1,g2])$;

>> g1=floor(3000.*rand)+1; g2=floor(3000.*rand)+1; disp([g1,g2]);

>> g1=floor(3000.*rand)+1; g2=floor(3000.*rand)+1; disp([g1,g2]);

>> g1=floor(3000.*rand)+1; g2=floor(3000.*rand)+1; disp([g1,g2]);

Matlab code

- load expression_table.mat
- g1=2907; g2=288;
- x=exp_t(g1,:)'; y=exp_t(g2,:)';
- figure; plot(x,y,'ko');
- lm=fitlm(x,y)
- y_fit=lm.Fitted;
- hold on; plot(x,lm.Fitted,'r-');
- SST=sum((y-mean(y)).^2);
- SSR=sum((y_fit-mean(y)).^2);
- SSE=sum((y-y_fit).^2);
- R2=SSR./SST
- disp([gene_names(g1), gene_names(g2)]);
- disp(gene_description(g1)); disp(gene_description (g2));

