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.

The covariance between the random variables X and Y, denoted as $\text{cov}(X,Y)$ or σ_{XY} is

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

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

$\rho_{XY}=\sigma_{XY}/\sigma_X\sigma_Y$
is the covariance normalized to be $-1 \leq \rho_{XY} \leq 1$

Karl Pearson (1852– 1936)
English mathematician and biostatistician

Covariance and Scatter Patterns

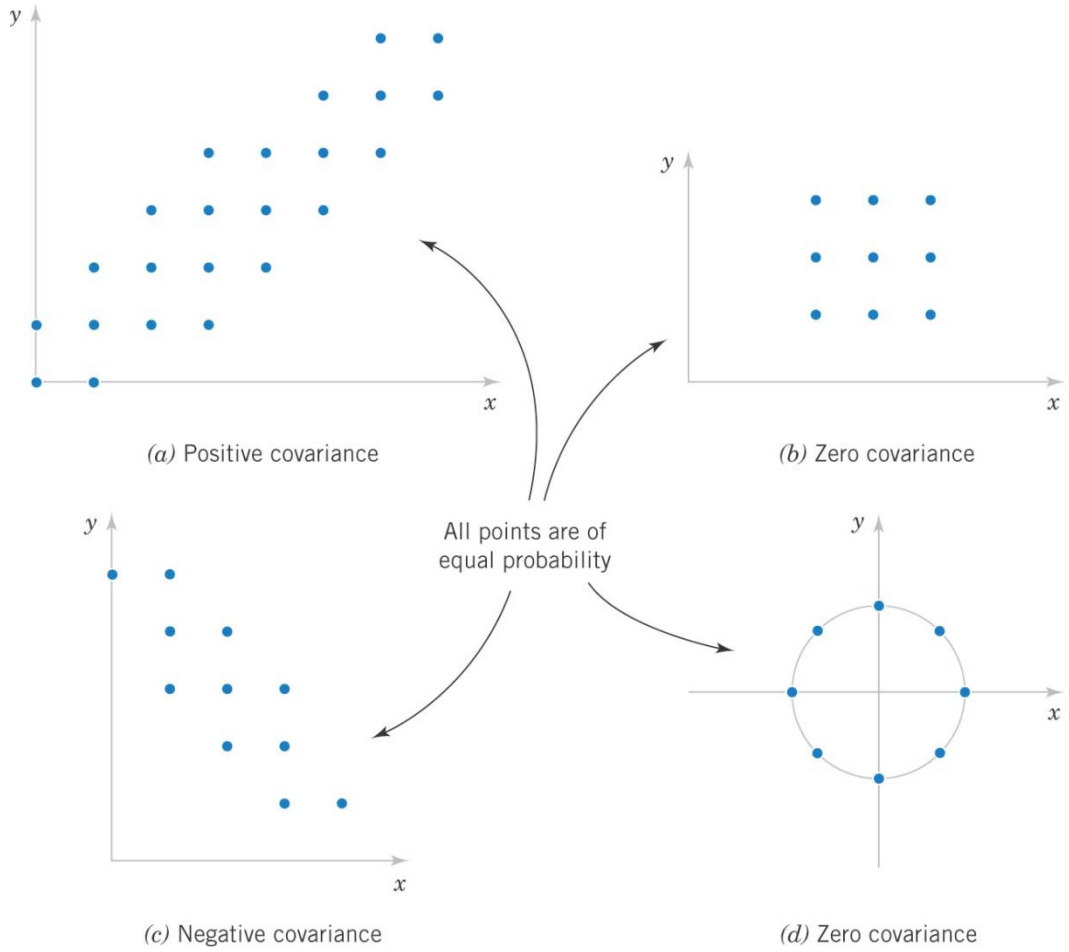

Figure 5-13 Joint probability distributions and the sign of cov(X, Y). Note that covariance is a measure of linear relationship. Variables with non-zero covariance are correlated.

Credit: XKCD comics

QUESTIONS
FOUND IN GOOGLE AUTOCOMPLETE

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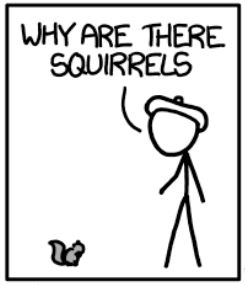
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WHY IS THERE NO GPS IN LAPTOPS
WHY DO KNEES CLICK
WHY AREN'T THERE E GRADES
WHY IS ISOLATION BAD
WHY DO BOYS LIKE ME
WHY DON'T BOYS LIKE ME
WHY IS THERE ALWAYS A JAVA UPDATE
WHY ARE THERE RED DOTS ON MY THIGHS
WHY IS LYING GOOD
WHY IS SEX SO IMPORTANT

WHY ARE THERE SLAVES IN THE BIBLE
WHY DO TWINS HAVE DIFFERENT FINGERPRINTS
WHY ARE AMERICANS AFRAID OF DRAGONS
WHY IS HTTPS CROSSED OUT IN RED
WHY IS THERE A LINE THROUGH HTTPS
WHY IS THERE A RED LINE THROUGH HTTPS ON FACEBOOK
WHY IS HTTPS IMPORTANT
WHY AREN'T MY ARMS GROWING

WHY ARE THERE WEEKS
WHY DO I FEEL DIZZY
WHY IS YKK ON ALL ZIPPERS
WHY ARE THERE SWARMS OF GNATS
WHY IS THERE PHLEGM
WHY ARE THERE SO MANY CROWS IN ROCHESTER, MN
WHY AREN'T ECONOMISTS RICH
WHY DO AMERICANS CALL IT SOCCER
WHY ARE MY EARS RINGING
WHY ARE THERE SO MANY AVENGERS
WHY ARE THE AVENGERS FIGHTING THE X MEN
WHY IS WOLVERINE NOT IN THE AVENGERS
WHY IS THERE LAVA
WHY IS PSYCHIC WEAK TO BUG
WHY DO CHILDREN GET CANCER
WHY IS POSEIDON ANGRY WITH ODYSSEUS
WHY IS THERE ICE IN SPACE
WHY ARE THERE ANTS IN MY LAPTOP
WHY IS EARTH TILTED
WHY IS SPACE BLACK
WHY IS OUTER SPACE SO COLD
WHY ARE THERE PYRAMIDS ON THE MOON
WHY IS NASA SHUTTING DOWN
WHY ARE THERE GHOSTS

WHY IS THERE AN OWL IN MY BACKYARD
WHY IS THERE AN OWL OUTSIDE MY WINDOW
WHY IS THERE AN OWL ON THE DOLLAR BILL
WHY DO OWLS ATTACK PEOPLE
WHY ARE AK 47S SO EXPENSIVE
WHY ARE THERE HELICOPTERS CIRCLING MY HOUSE
WHY ARE THERE GODS
WHY ARE THERE TWO SPOCKS
WHY IS MT VESUVIUS THERE
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WHY ARE OCEANS BECOMING MORE ACIDIC
WHY IS ARWEN DYING
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WHY AREN'T MY QUAIL EGGS HATCHING
WHY AREN'T THERE ANY FOREIGN MILITARY BASES IN AMERICA
WHY ARE CIGARETTES LEGAL
WHY ARE THERE DUCKS IN MY POOL
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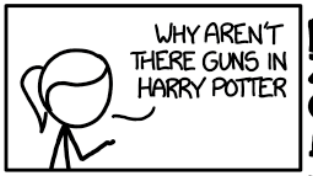
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Regression analysis

• Many problems in engineering and science involve sample in which two or more variables were measured

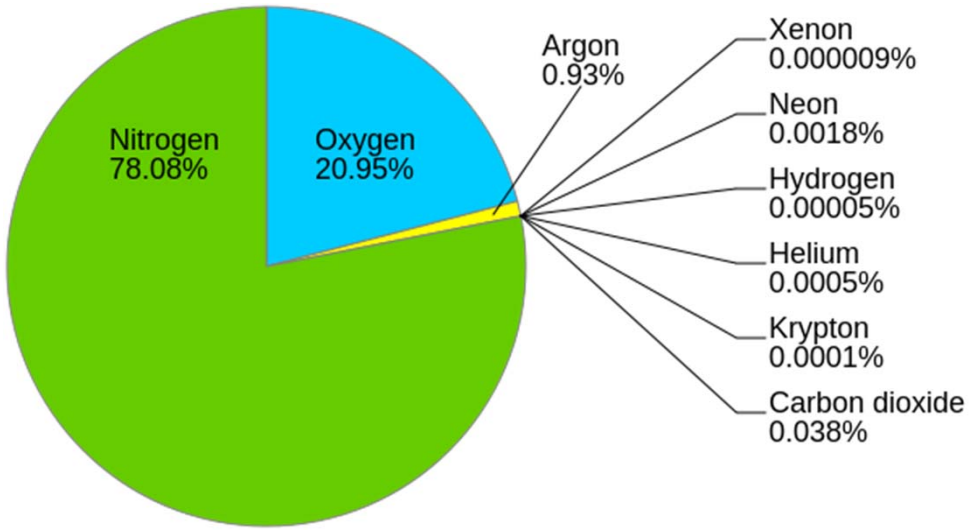
• **Regression analysis** is a statistical technique that is very useful for these types of problems

• 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

Two variable samples



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

Table 11-1 Oxygen and Hydrocarbon Levels

Observation Number	Hydrocarbon Level x (%)	Purity y (%)
1	0.99	90.01
2	1.02	89.05
3	1.15	91.43
4	1.29	93.74
5	1.46	96.73
6	1.36	94.45
7	0.87	87.59
8	1.23	91.77
9	1.55	99.42
10	1.40	93.65
11	1.19	93.54
12	1.15	92.52
13	0.98	90.56
14	1.01	89.54
15	1.11	89.85
16	1.20	90.39
17	1.26	93.25
18	1.32	93.41
19	1.43	94.98
20	0.95	87.33

Scatter plot to visually detect trends
Red line is called linear regression

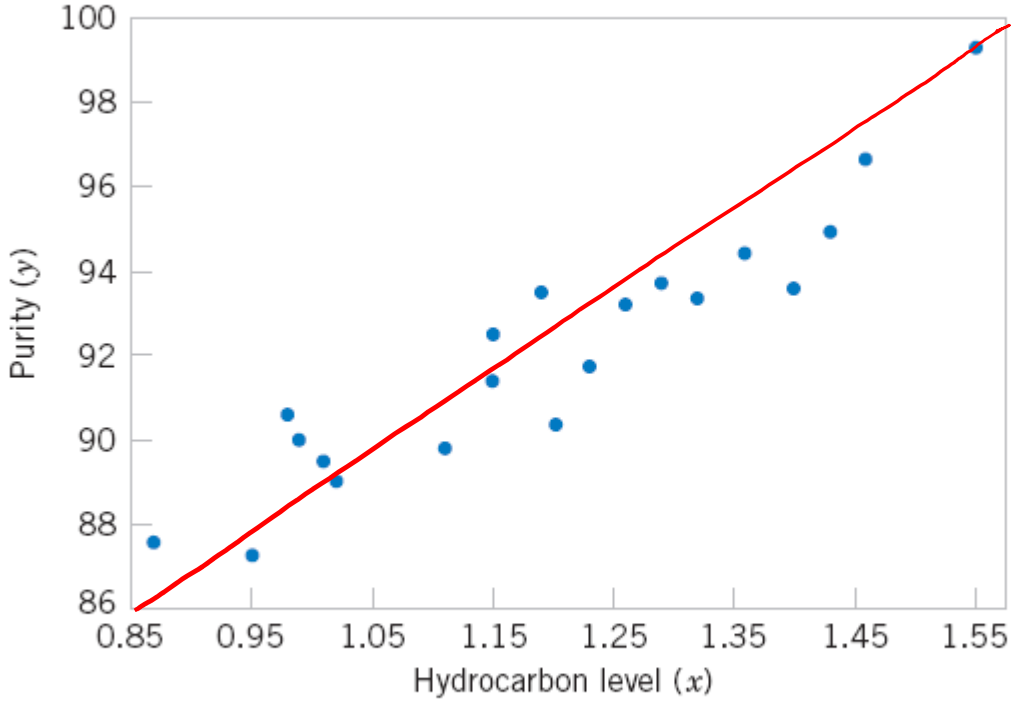
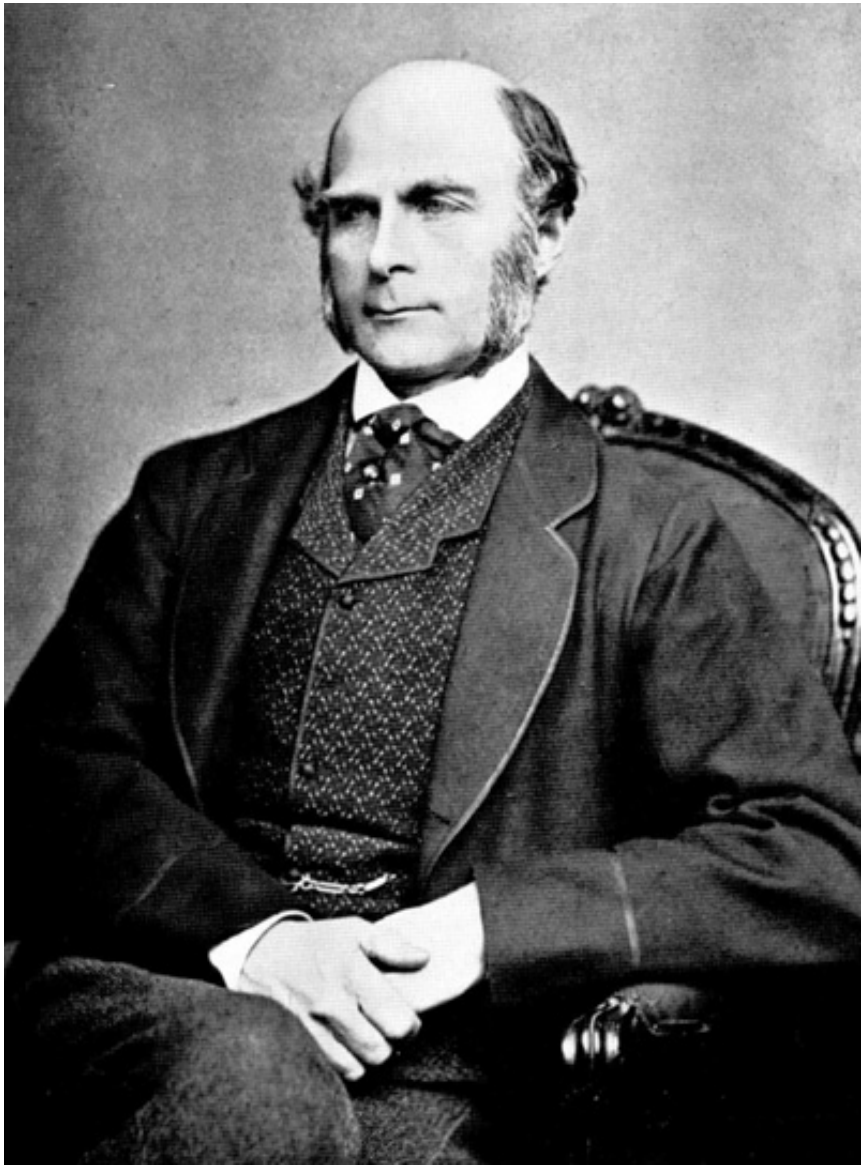


Figure 11-1 Scatter diagram of oxygen purity versus hydrocarbon level from Table 11-1.

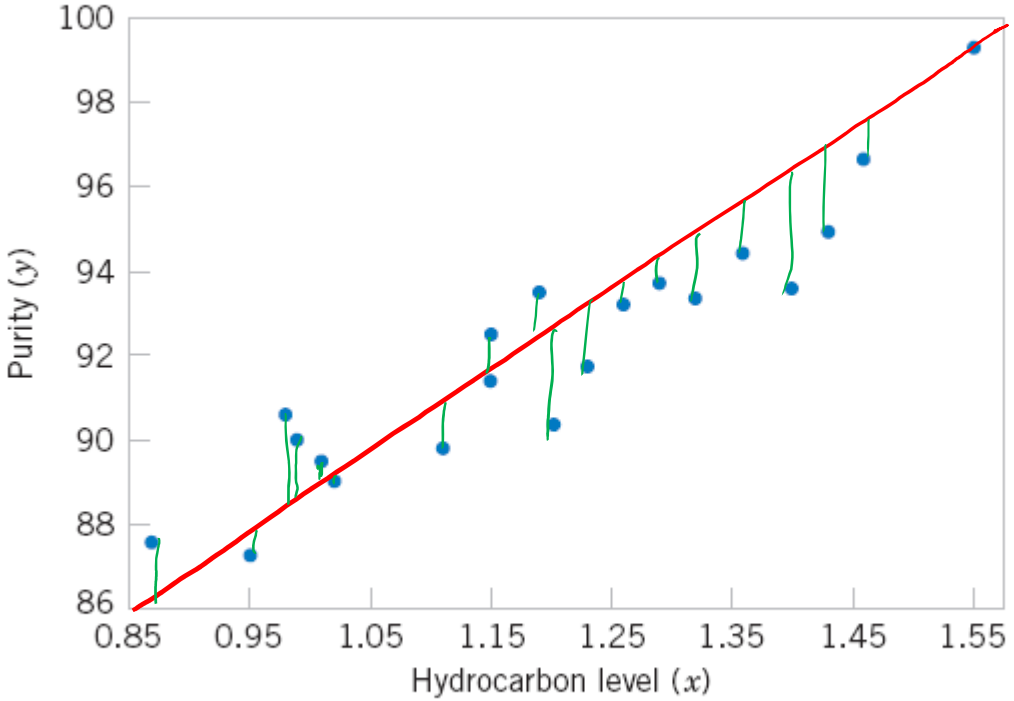


Sir Francis Galton,
(1822 -1911) was an English statistician, anthropologist, proto-geneticist, psychometrician, eugenicist, ("Nature vs Nurture", inheritance of intelligence), tropical explorer, geographer, inventor (Galton Whistle to test hearing), meteorologist (weather map, anticyclone).

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

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$



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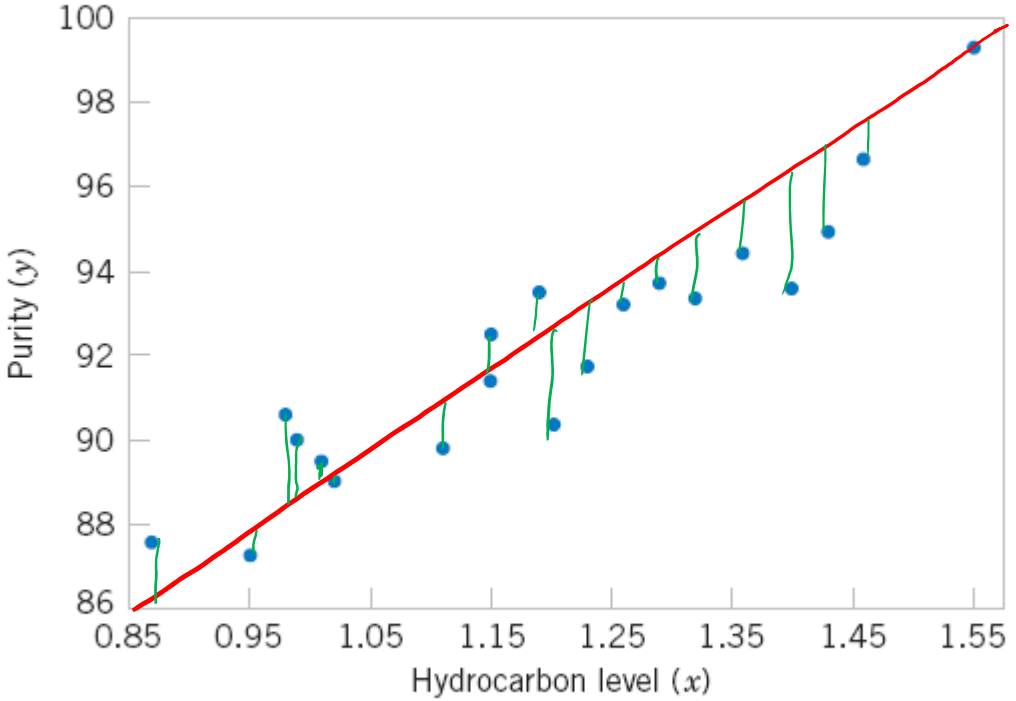


Figure 11-1 Scatter diagram of oxygen purity versus hydrocarbon level from Table 11-1.

Linear regression

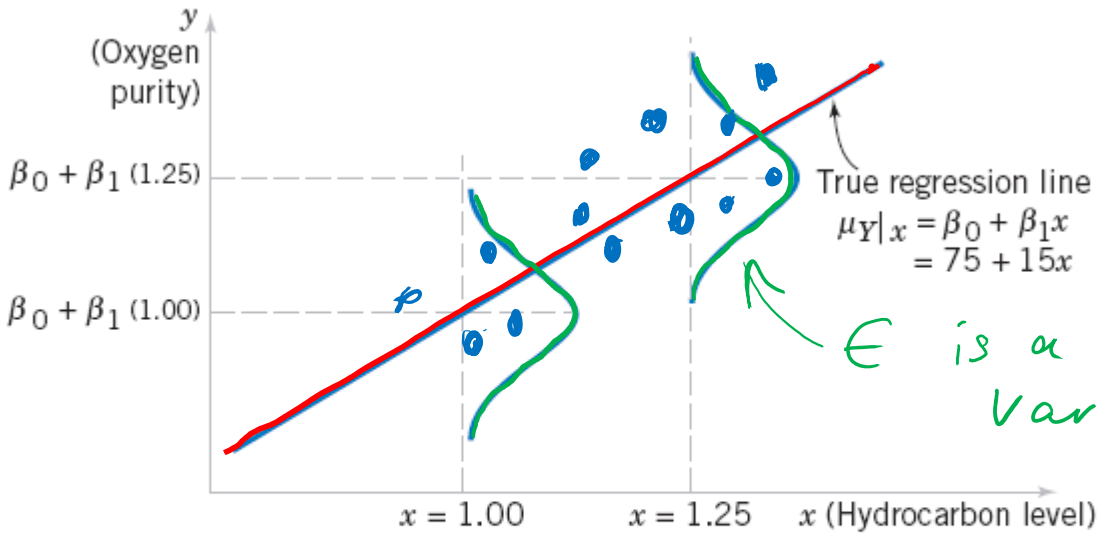
The **simple linear regression model** is given by

$$Y = \beta_0 + \beta_1 X + \varepsilon$$

ε is the **random error term**

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

Note: Y , X and ε are random variables
The minimal assumption: $E(\varepsilon \mid x)=0$ →
$E(Y \mid x) = \beta_0 + \beta_1 x + E(\varepsilon \mid x) = \beta_0 + \beta_1 x$



ϵ is a random variable given by

Figure 11-2 The distribution of Y for a given value of x for the oxygen purity–hydrocarbon data.

$$\epsilon = Y - \beta_0 + \beta_1 X$$

$$E(\epsilon \mid x) = 0 \quad \text{for all } x$$

$Y = \beta_0 + \beta_1 X + \epsilon$; $E(\epsilon | x) = 0 \quad \forall x$

How does one find β_0 & β_1?

$$Cov(Y, X) = Cov((\beta_0 + \beta_1 X + \epsilon), X) =$$

$$= Cov(\beta_0, X) + \beta_1 Cov(X, X) + Cov(\epsilon, X)$$

$Cov(\beta_0, X) = 0$ since β_0 is constant

$Cov(X, X) = E(X^2) - E(X)^2 = Var(X)$

$Cov(\epsilon, X) = E(\epsilon \cdot X) - E(\epsilon) \cdot E(X) =$

$= E(\epsilon \cdot X) = \sum_{all\ x} x \cdot E(\epsilon | x) = 0$

Thus $\boxed{\beta_1 = \frac{Cov(X, Y)}{Var(X)}}$ $\boxed{\beta_0 = E(Y) - \beta_1 E(X)}$

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.

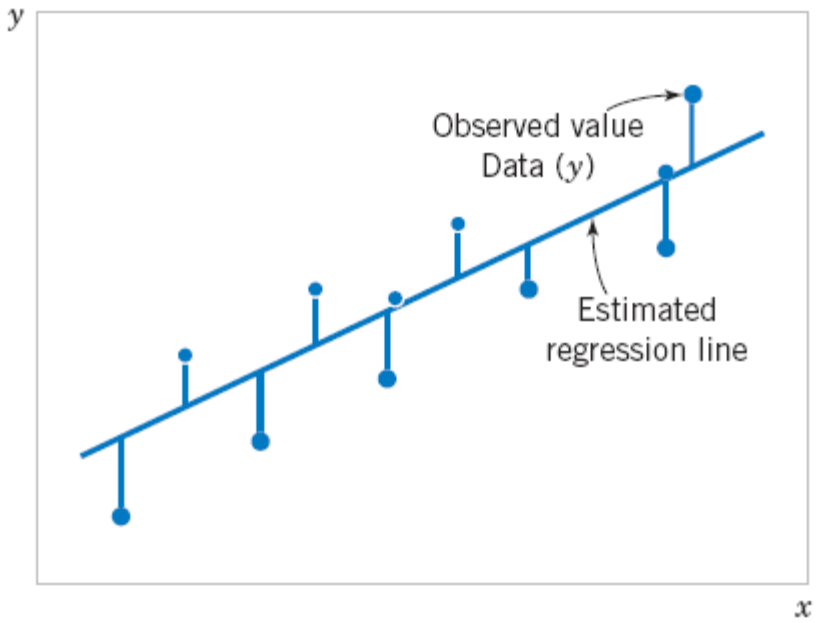


Figure 11-3 Deviations of the data from the estimated regression model.

Traditional notation

Definition

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

$$\hat{\beta}_0 = \bar{y} - \hat{\beta}_1 \bar{x} \tag{11-7}$$

$$\hat{\beta}_1 = \frac{\sum_{i=1}^{n} y_i x_i - \frac{\left(\sum_{i=1}^{n} y_i\right)\left(\sum_{i=1}^{n} x_i\right)}{n}}{\sum_{i=1}^{n} x_i^2 - \frac{\left(\sum_{i=1}^{n} x_i\right)^2}{n}} = \frac{S_{xy}}{S_{xx}} \tag{11-8}$$

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

11-2: Simple Linear Regression

Definition

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

11-4: Hypothesis Tests in Simple Linear Regression

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

The analysis of variance identity is

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

Symbolically,

$$SS_T = SS_R + SS_E \qquad (11\text{-}25)$$

11-7: Adequacy of the Regression Model

11-7.2 Coefficient of Determination (R^2) VERY USEFUL

- 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.

- $0 \le R^2 \le 1$;
- 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,

$$R^2 = SS_R/SS_T$$
$$= 152.13/173.38$$
$$= 0.877$$

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

11-2: Simple Linear Regression

Estimating σ^2

The error sum of squares is

$$SS_E = \sum_{i=1}^{n} e_i^2 = \sum_{i=1}^{n} (y_i - \hat{y}_i)^2 = (n-2)\hat{\sigma}^2$$

11-3: Properties of the Least Squares Estimators

- Slope Properties

$$E(\hat{\beta}_1) = \beta_1 \qquad V(\hat{\beta}_1) = \frac{\sigma^2}{S_{xx}} = \frac{\hat{\sigma}_\epsilon^2}{n\,\hat{\sigma}_x^2}$$

Large $n \rightarrow$ small variance of β_1

- Intercept Properties

$$E(\hat{\beta}_0) = \beta_0 \quad \text{and} \quad V(\hat{\beta}_0) = \sigma^2\left[\frac{1}{n} + \frac{\bar{x}^2}{S_{xx}}\right] =$$

$$= \hat{\sigma}_\epsilon^2\left[1 + \frac{\mu_x^2}{\hat{\sigma}_x^2}\right] \cdot \frac{1}{n}$$

11-4: Hypothesis Tests in Simple Linear Regression

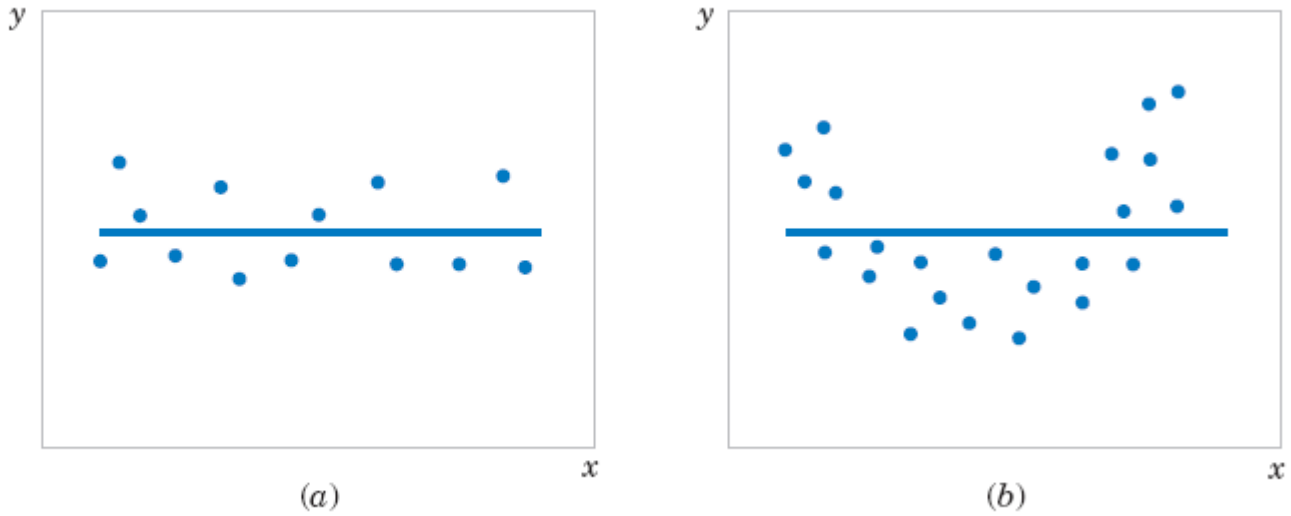


Figure 11-5 The hypothesis H_0: $\beta_1 = 0$ is not rejected.

Figure 11-5 The null hypothesis H_0: $\beta_1 = 0$ is accepted.

11-4: Hypothesis Tests in Simple Linear Regression

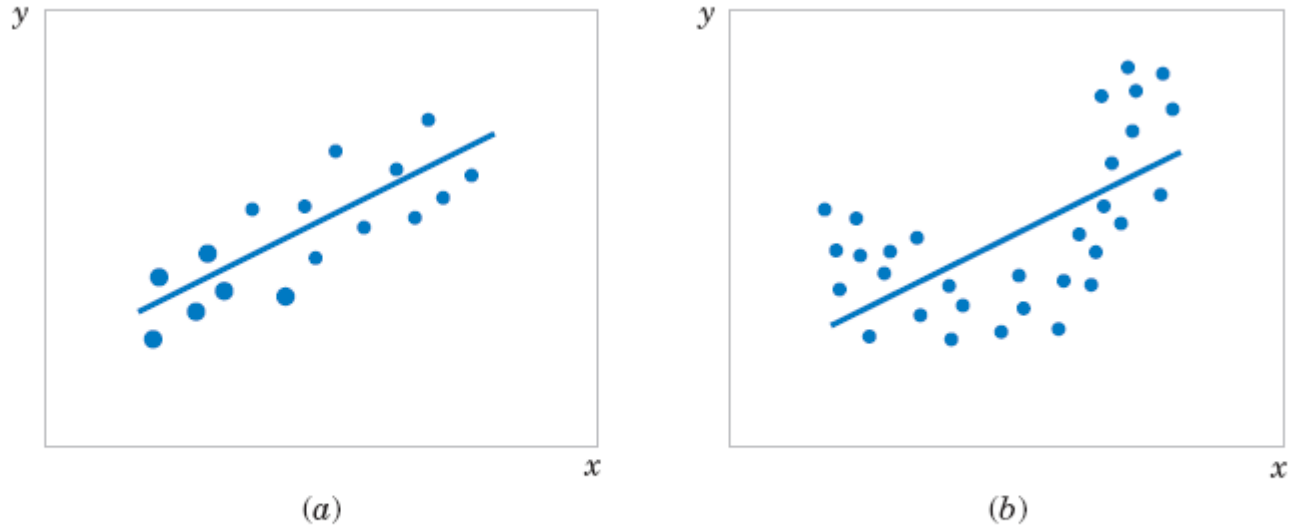


Figure 11-6 The hypothesis H_0: $\beta_1 = 0$ is rejected.

Figure 11-6 The **null hypothesis H_0: $\beta_1 = 0$ is rejected**.

11-4: Hypothesis Tests in Simple Linear Regression

11-4.1 Use of *t*-Tests

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 H_0 is equivalent to concluding that there is no linear relationship between *X* and *Y*.

11-4: Hypothesis Tests in Simple Linear Regression

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

Choose α (e.g. $\alpha = 5\%$ for 95% confidence in rejecting H_0)

$$Z = \frac{\hat{\beta}_1}{\frac{\hat{\sigma}_\epsilon}{\sigma_x} \cdot \frac{1}{\sqrt{n}}}$$

for $\alpha = 5\%$

Reject H_0 if $|Z| > Z_{\alpha/2} = 1.96$

T-cell expression data

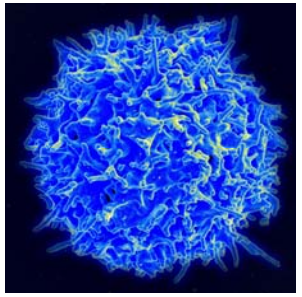
- The matrix contains 47 expression samples from Lukk et al, Nature Biotechnology 2011
- All samples are from T cells in different individuals
- Only the top 3000 genes with the largest variability were used
- The value is log2 of gene's expression level in a given sample as measured by the microarray technology

A global map of human gene expression

Margus Lukk, Misha Kapushesky, Janne Nikkilä, Helen Parkinson, Angela Goncalves, Wolfgang Huber, Esko Ukkonen & Alvis Brazma

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

Gene Expression "Wheel of Fortune"

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

Correlated pairs

2907	2881
1994	188
2274	1597
2982	1353
2872	1269
1321	10
2935	1654
2745	1695
886	819
2138	1364

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(g1,:)'; y=exp(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));

Credit: XKCD comics

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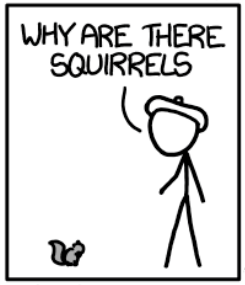
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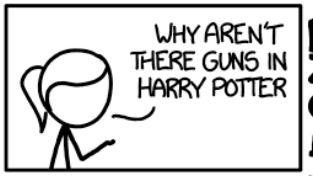
WHY DO SPIDER BITES ITCH
WHY IS DYING SO SCARY
WHY IS THERE NO GPS IN LAPTOPS
WHY DO KNEES CLICK
WHY AREN'T THERE E GRADES
WHY IS ISOLATION BAD
WHY DO BOYS LIKE ME
WHY DON'T BOYS LIKE ME
WHY IS THERE ALWAYS A JAVA UPDATE
WHY ARE THERE RED DOTS ON MY THIGHS
WHY IS LYING GOOD
WHY IS SEX SO IMPORTANT

WHY ARE THERE SLAVES IN THE BIBLE
WHY DO TWINS HAVE DIFFERENT FINGERPRINTS
WHY ARE AMERICANS AFRAID OF DRAGONS
WHY IS HTTPS CROSSED OUT IN RED
WHY IS THERE A LINE THROUGH HTTPS
WHY IS THERE A RED LINE THROUGH HTTPS ON FACEBOOK
WHY IS HTTPS IMPORTANT
WHY AREN'T MY ARMS GROWING

WHY ARE THERE WEEKS
WHY DO I FEEL DIZZY
WHY IS YKK ON ALL ZIPPERS
WHY ARE THERE SWARMS OF GNATS
WHY IS THERE PHLEGM
WHY ARE THERE SO MANY CROWS IN ROCHESTER, MN
WHY AREN'T ECONOMISTS RICH
WHY DO AMERICANS CALL IT SOCCER
WHY ARE MY EARS RINGING
WHY ARE THERE SO MANY AVENGERS
WHY ARE THE AVENGERS FIGHTING THE X MEN
WHY IS WOLVERINE NOT IN THE AVENGERS
WHY IS THERE LAVA
WHY IS PSYCHIC WEAK TO BUG
WHY DO CHILDREN GET CANCER
WHY IS POSEIDON ANGRY WITH ODYSSEUS
WHY IS THERE ICE IN SPACE
WHY ARE THERE ANTS IN MY LAPTOP
WHY IS EARTH TILTED
WHY IS SPACE BLACK
WHY IS OUTER SPACE SO COLD
WHY ARE THERE PYRAMIDS ON THE MOON
WHY IS NASA SHUTTING DOWN
WHY ARE THERE GHOSTS

WHY IS THERE AN OWL IN MY BACKYARD
WHY IS THERE AN OWL OUTSIDE MY WINDOW
WHY IS THERE AN OWL ON THE DOLLAR BILL
WHY DO OWLS ATTACK PEOPLE
WHY ARE AK 47S SO EXPENSIVE
WHY ARE THERE HELICOPTERS CIRCLING MY HOUSE
WHY ARE THERE GODS
WHY ARE THERE TWO SPOCKS
WHY IS MT VESUVIUS THERE
WHY DO THEY SAY T MINUS
WHY ARE THERE OBELISKS
WHY ARE WRESTLERS ALWAYS WET
WHY ARE OCEANS BECOMING MORE ACIDIC
WHY IS ARWEN DYING
WHY AREN'T MY QUAIL LAYING EGGS
WHY AREN'T MY QUAIL EGGS HATCHING
WHY AREN'T THERE ANY FOREIGN MILITARY BASES IN AMERICA
WHY ARE CIGARETTES LEGAL
WHY ARE THERE DUCKS IN MY POOL
WHY IS JESUS WHITE
WHY IS THERE LIQUID IN MY EAR
WHY DO Q TIPS FEEL GOOD
WHY DO GOOD PEOPLE DIE
WHY AREN'T THERE GUNS IN HARRY POTTER

WHY ARE ULTRASOUNDS IMPORTANT
WHY ARE ULTRASOUND MACHINES EXPENSIVE
WHY IS STEALING WRONG
WHY ARE DOGS AFRAID OF FIREWORKS
WHY IS THERE NO KING IN ENGLAND
WHY IS LIFE SO BORING
WHY ARE THERE FEMALE MR MIMES
WHY IS GPS FREE
WHY IS THERE HELL IF GOD FORGIVES
WHY DO IGUANAS DIE
WHY AREN'T THERE DINOSAUR GHOSTS