UNIVERSITY of WASHINGTON

BIOE 498 / BIOE 599: Computational Systems Biology for Medical Applications

CSE 599V: Advancing Biomedical Models

Lecture 9: Estimating Confidence in Models and Parameters: I

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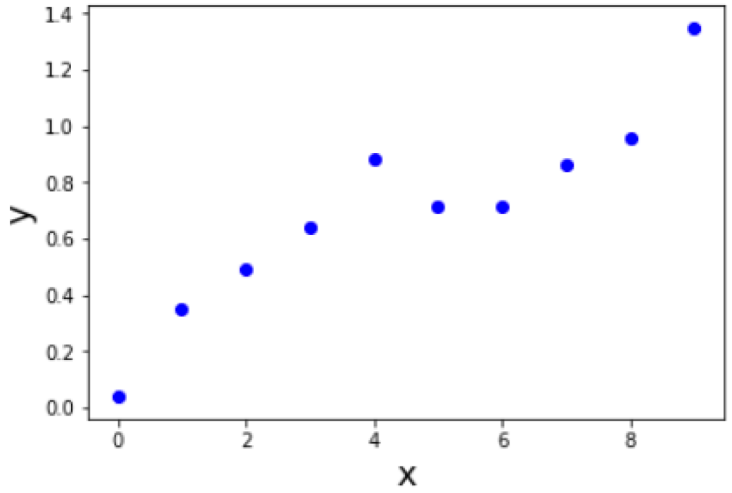
**BioEngineering

Agenda

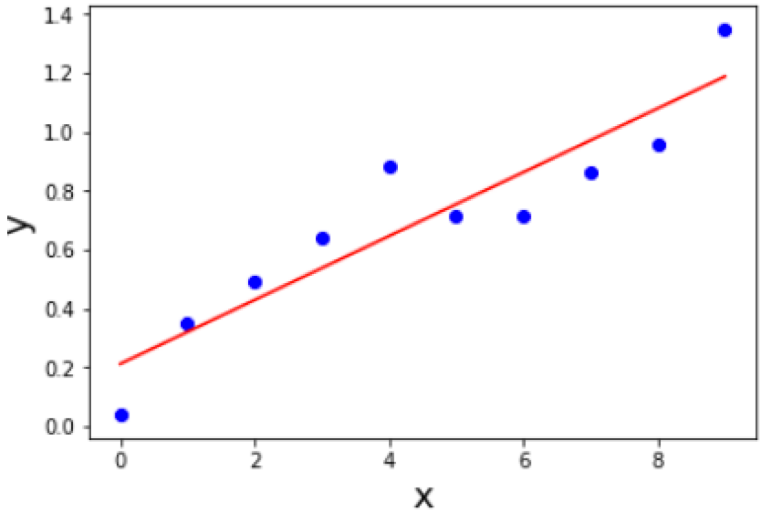
- Residual analysis
- Parameter fitting and evaluation of a mathematical model using least squares regression
- Hypothesis testing to evaluate models

What is A Good Model?

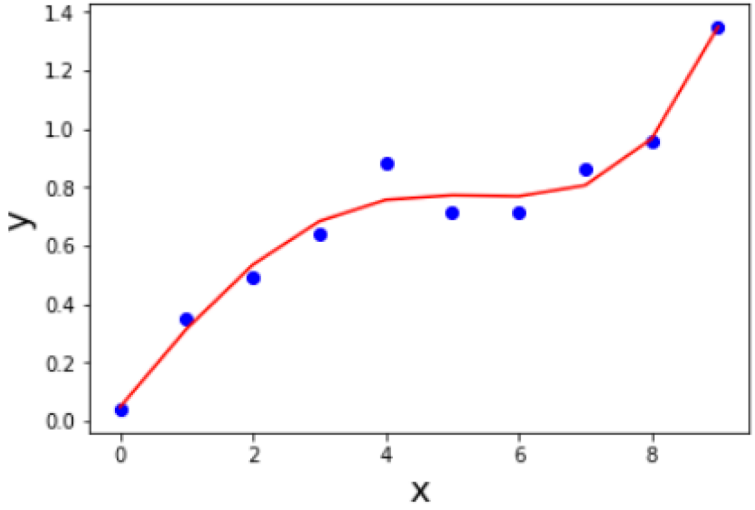
Measured Data



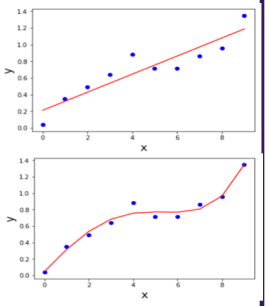
$y = ax + b$



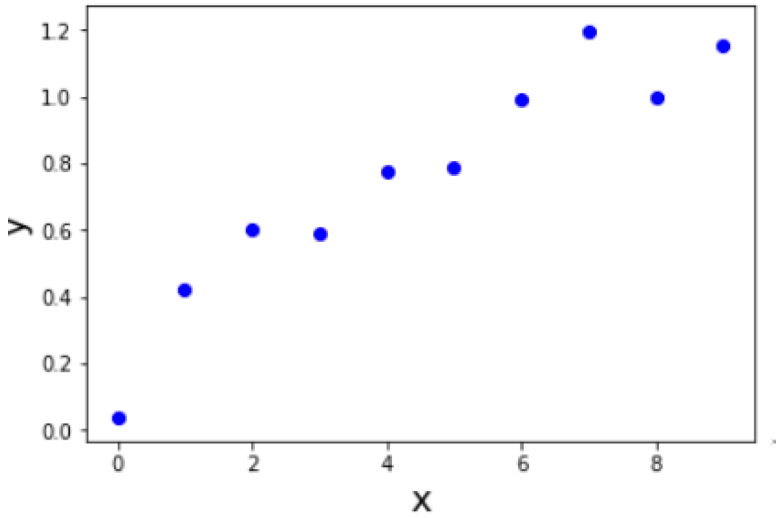
$y = a_1x + a_2x^2 + a_3x^3 + a_4x^4 + b$



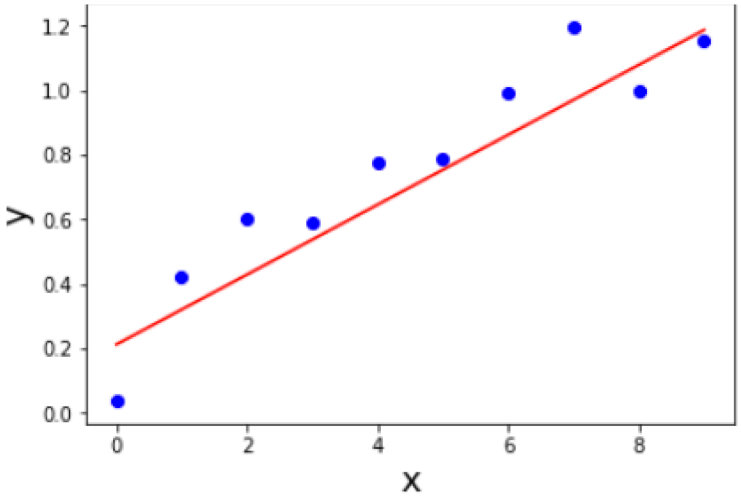
Generalizing Model to New Data

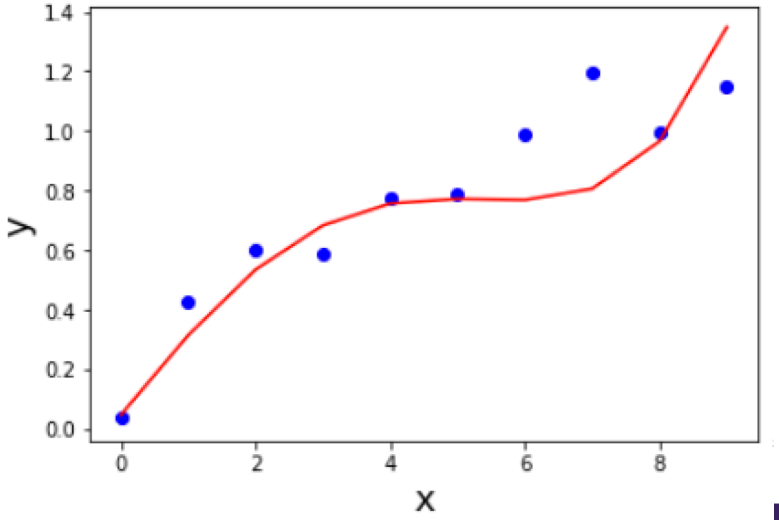


Data 2



Which is the better model now?

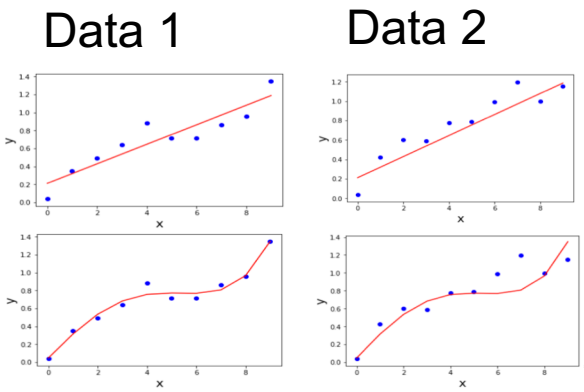




What is A Good Model?

$$y = ax + b$$

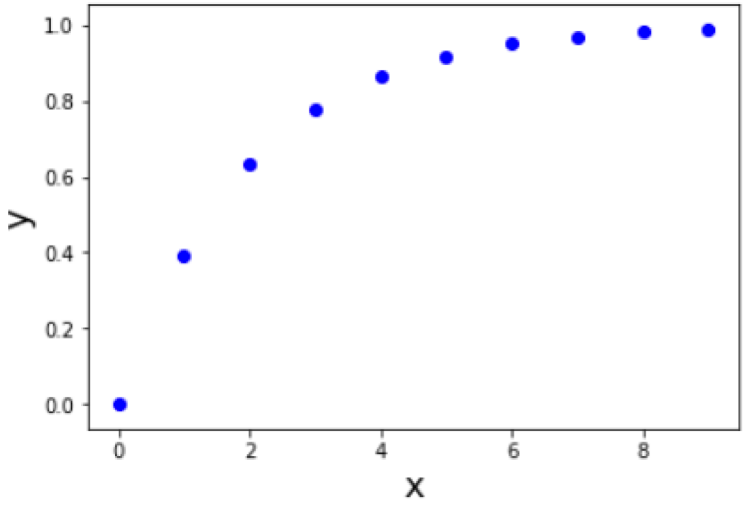
$$y = a_1x + a_2x^2 + a_3x^3 + a_4x^4 + b$$

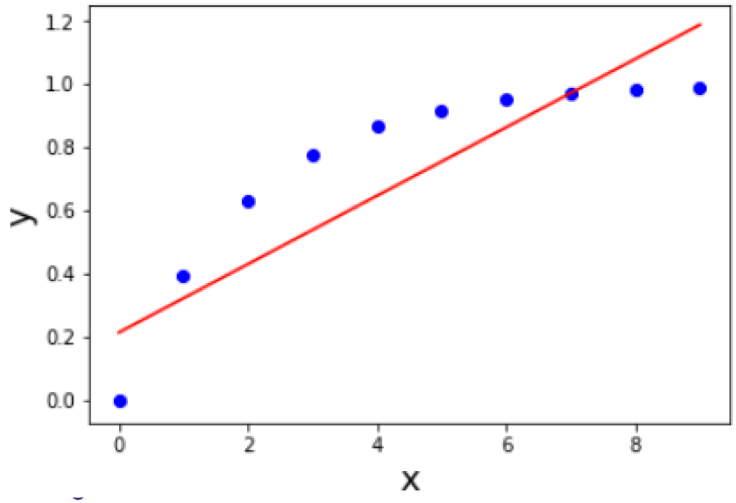


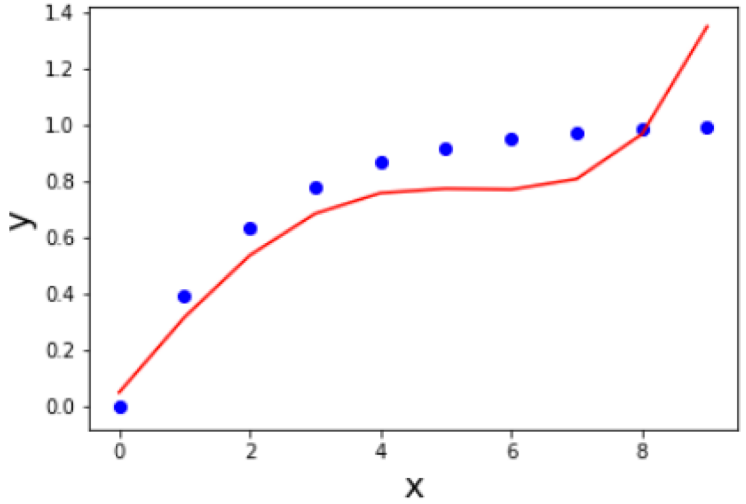
- Fits measurement data
- Simple (e.g., few parameters)
- Generalizes to new measurement data

We Never Know if a Real World Model is Correct!

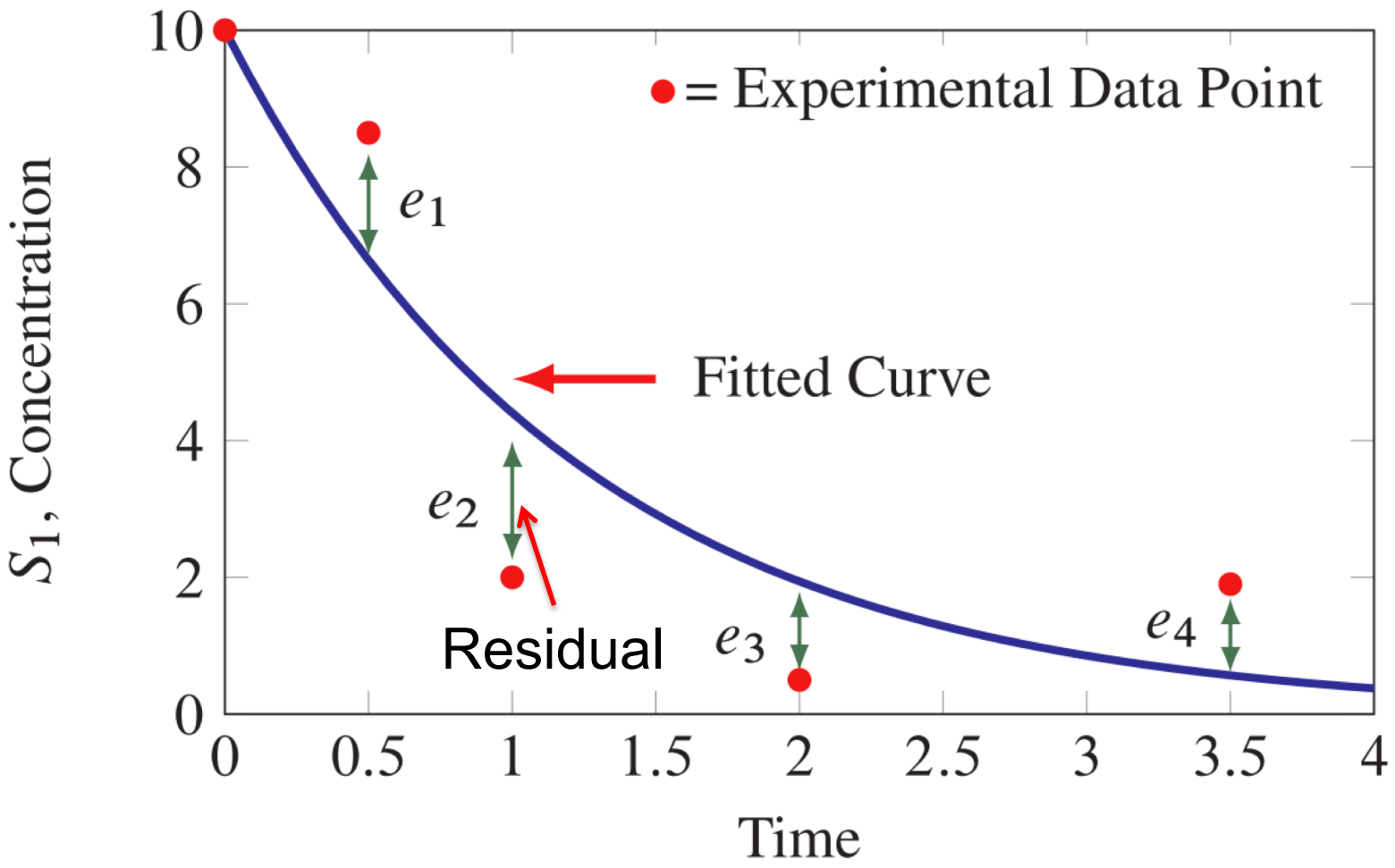
Data Without Measurement Errors



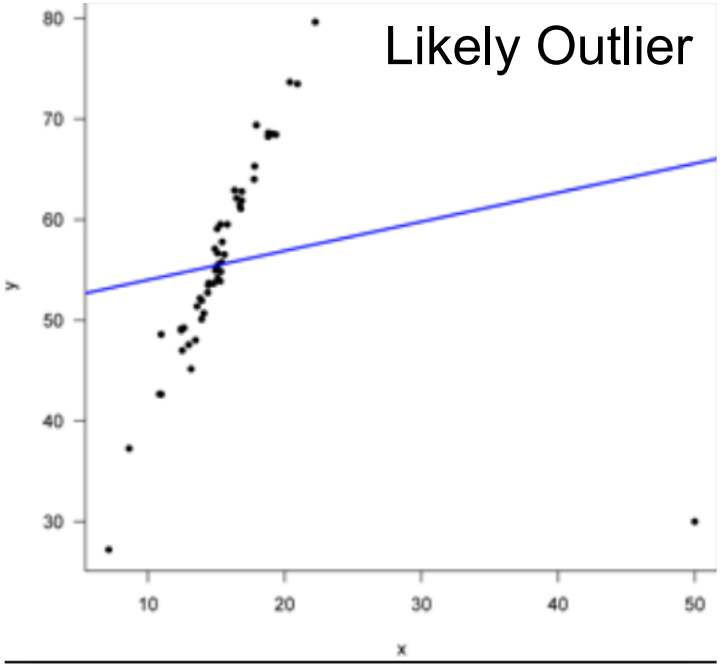




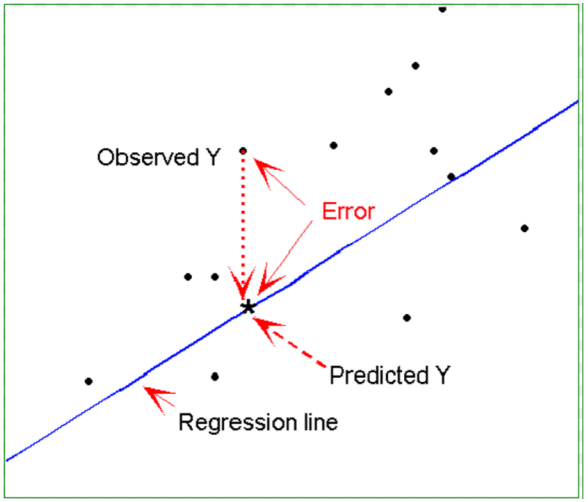
Residuals = Experimental - Fitted

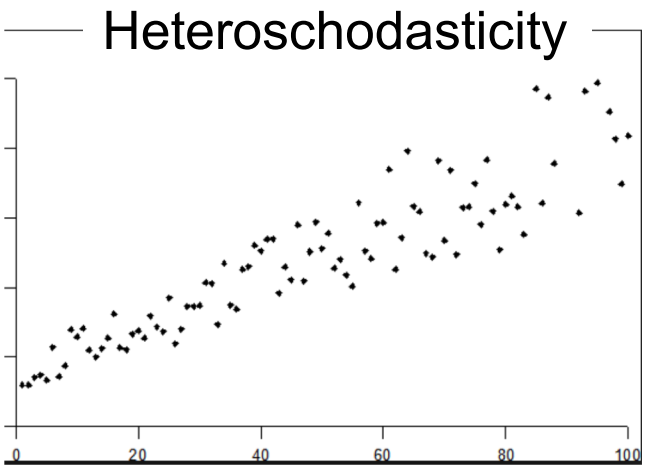


What Residuals Tell Us About Models



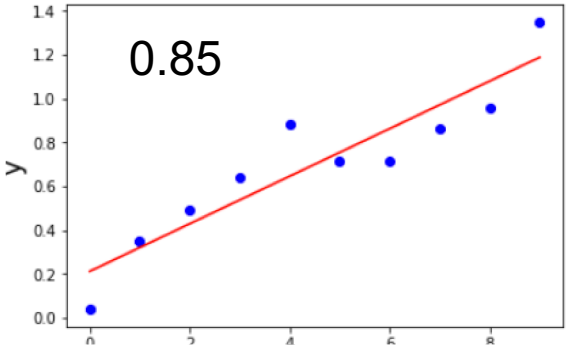
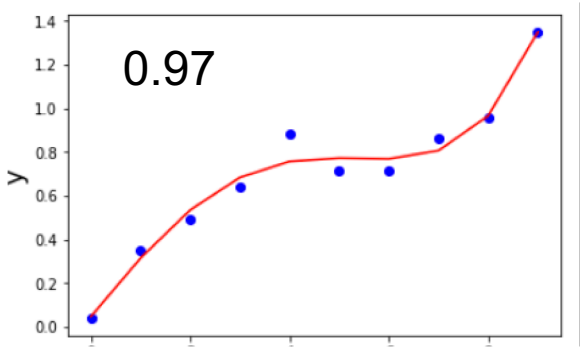
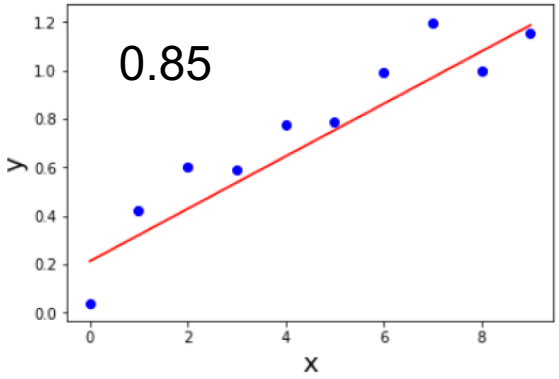
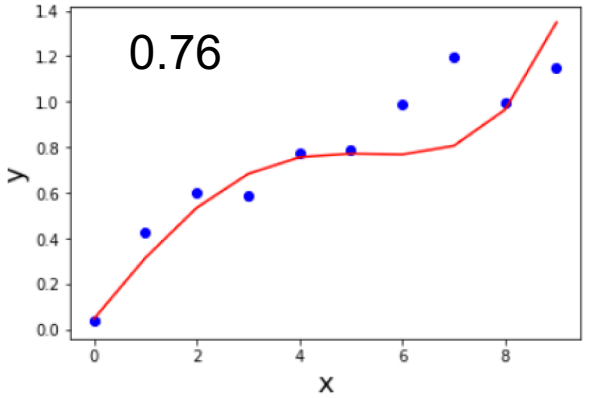
Functional Bias





Quantifying Model Quality: R^2

$$R^2 = \frac{var(fitted)}{var(observed)} = 1 - \frac{var(residuals)}{var(observed)}$$

	$y = ax + b$	$y = a_1x + a_2x^2 + a_3x^3 + a_4x^4 + b$
Data 1		
Data 2		

Exercise: Compare Models Using Residuals

Model 1

$$\rightarrow A; v_0$$
$$A \rightarrow B; k_a A$$
$$B \rightarrow C; k_b B$$
$$C \rightarrow; k_c C$$

$$v_0 = 10; k_a = 0.4;$$
$$k_b = 0.32; k_c = k_a$$

Model 2

$$\rightarrow B; v_0$$
$$B \rightarrow; k_b C$$

1. Simulate both models
2. Using Model 1 as the "observations" and Model 2 as the "predicted values", compute the residuals. (Hint: `simulate` returns a matrix of values.)
3. Compute the R^2 of Model 2 with respect to Model 1.
4. Do we achieve the same steady state values?
5. Where are errors the largest? Why?

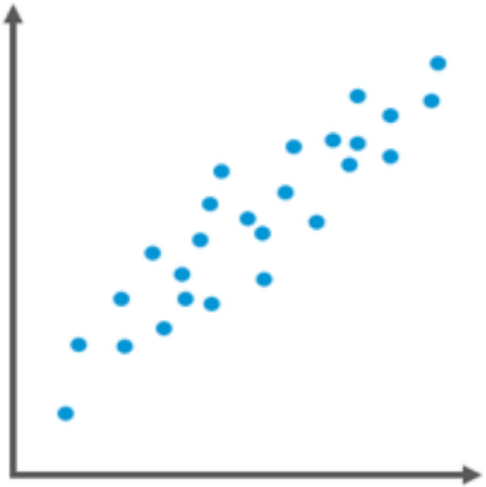
Linear Least-Squares Regression
The Work Horse of Most Modeling Procedures

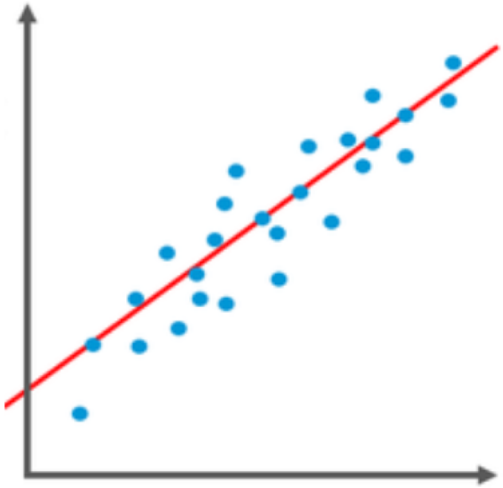
- Given dependent variable y, with values $y(i)$, and predictor variables $x_1, \cdots x_N$ with values $x_n(i)$.
- Estimate y by $\hat{y} = \sum_n k_n x_n$
- Find the values of k_n that minimize

$$\sum_i \left(y(i) - \hat{y}(i)\right)^2$$

- $r(i) = y(i) - \hat{y}(i) = y(i) - k_n x_n(i)$ are the residuals of the regression model.

How Least Squares Fits a Line to Data

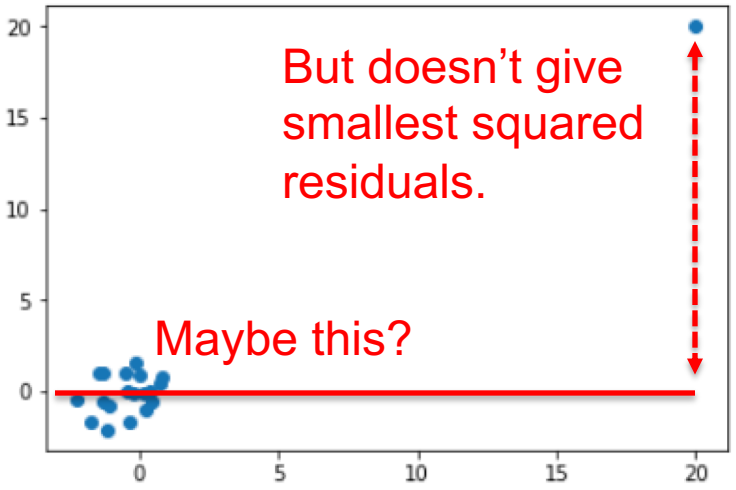


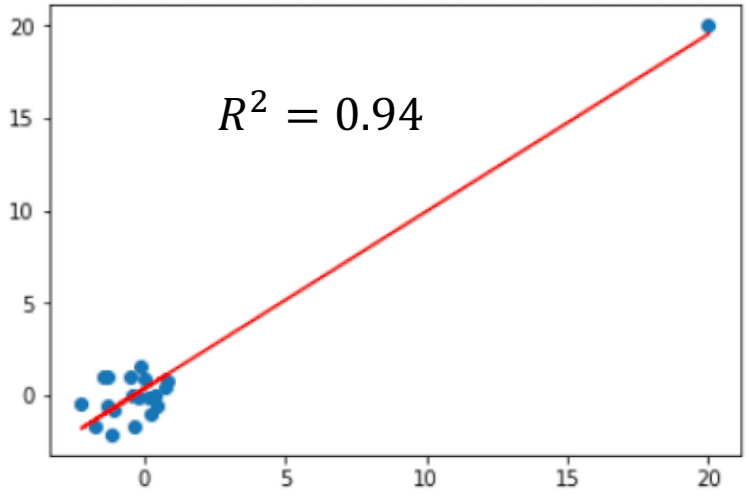


Line minimizes the sum of the squared residuals.

Limitations of Least Squares

What's the least squares fit for these data?

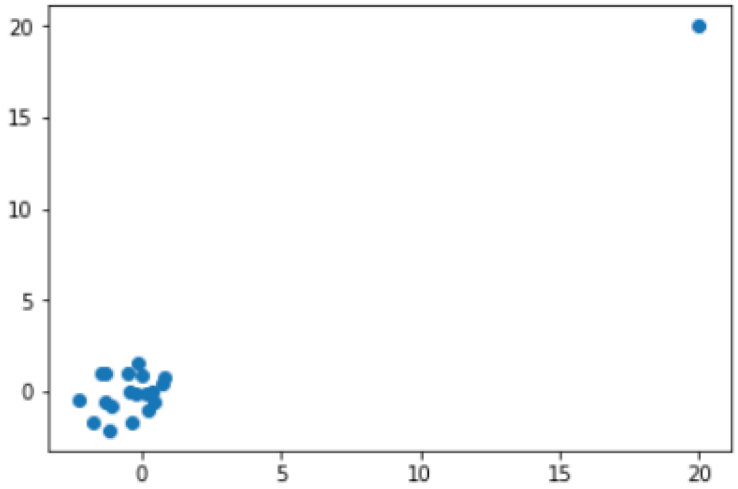




Need outlier detection.

Linear Regression in Python

Prepare the Data




```
LENGTH = 20
STD = 1
# Construct vectors with 19 random values and a 20
xv = np.random.normal(0, STD, LENGTH - 1)
xv = np.concatenate([xv, np.array([LENGTH])])
yv = np.random.normal(0,STD, LENGTH - 1)
yv = np.concatenate([yv, np.array([LENGTH])])
# Construct a matrix (has 1's in the first column)
mat = np.matrix([np.repeat(1, LENGTH), xv])
mat = mat.transpose() # Transpose to 20 X 2
```

Linear Regression in Python

Fit, Predict, Find Constants, Evaluate

```
from sklearn import linear_model
from sklearn.metrics import mean_squared_error,
r2_score
# Fit, find constants evaluate
regr = linear_model.LinearRegression()
regr.fit(mat, yv)
# Predicted values
y_preds = regr.predict(mat)
# R-squared
rsq = r2_score(yv, y_preds)
# Values of the constants
coefs = regr.coef_
#
print("Predictions: ", y_preds)
print("RSQ: ", rsq)
print("Coeficients: ", coefs)
```

Exercise: Evaluate a Mathematical Model of A System

Model 1

$$\rightarrow A; v_0$$
$$A \rightarrow B; k_a A$$
$$B \rightarrow C; k_b B$$
$$C \rightarrow; k_c C$$

$$v_0 = 10; k_a = 0.4;$$
$$k_b = 0.32; k_c = k_a$$

Mathematical Model

$$B = K(1 - e^{-kt})$$

1. Use the simulation of the Model 1 as "observations" by adding a normally distributed error term $N(0,1)$.
2. Construct training data and test data using different arrays of normally distributed errors
3. For the mathematical model, estimate K, k from the training data.

Hint for Estimating K, k

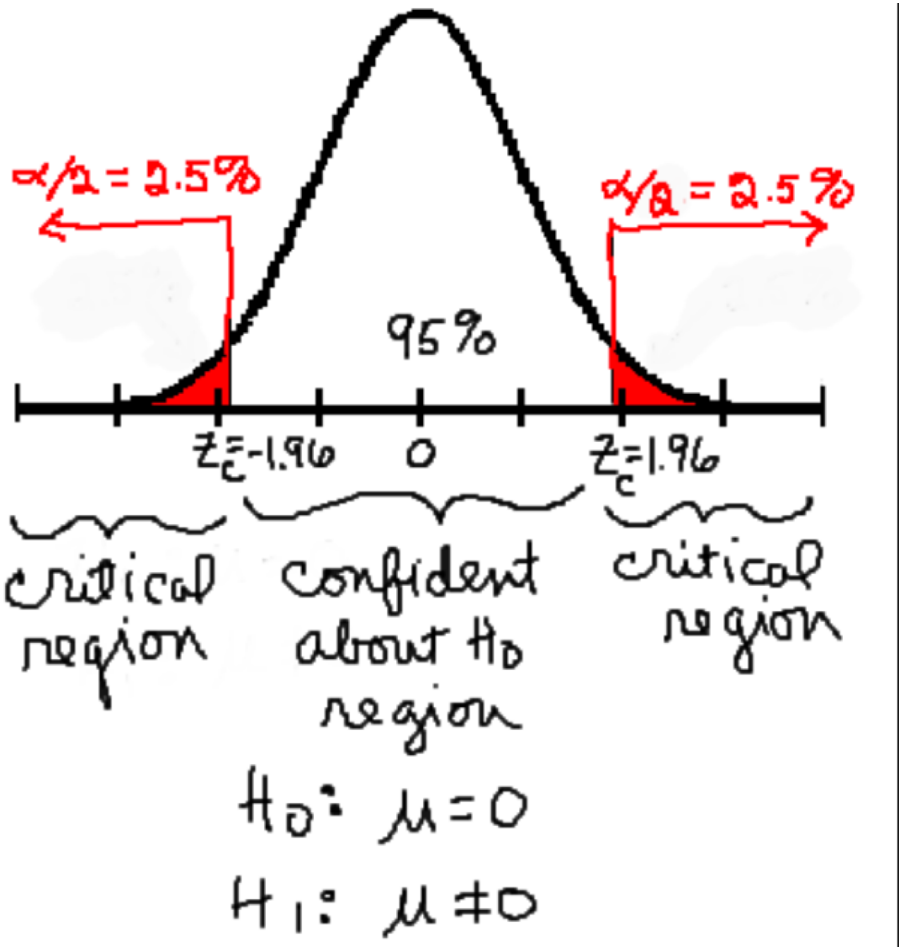
Mathematical Model

$$B = K(1 - e^{-kt})$$

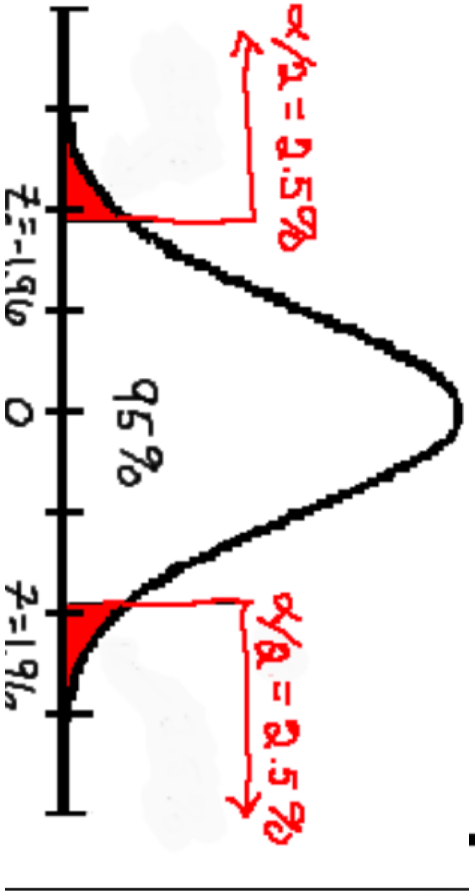
1. The training data contains values of B.
2. Note that K is the steady state value of B. We can estimate K from the training data, taking the last n observations. Call this $\widehat{K}$.
3. With a little arithmetic, $\ln\left(\widehat{K} - B\right) = \ln\left(\widehat{K}\right) - kt$. k can be estimated using linear regression.

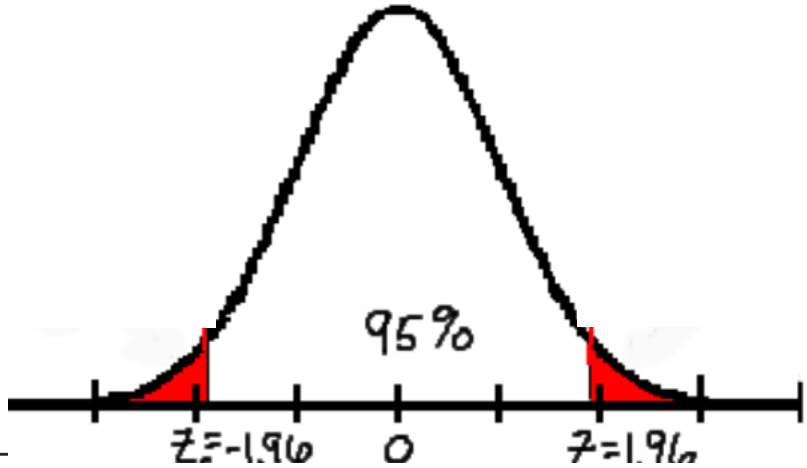
Hypothesis Testing Basics

1. Null Hypothesis: No change from baseline
2. Assume data come from a known distribution (e.g., normal).
3. Calculate a test statistic based on this distribution.
4. If test statistic is near 0 (not in a critical region), do not reject the Null Hypothesis.
5. Otherwise, reject the Null Hypothesis.



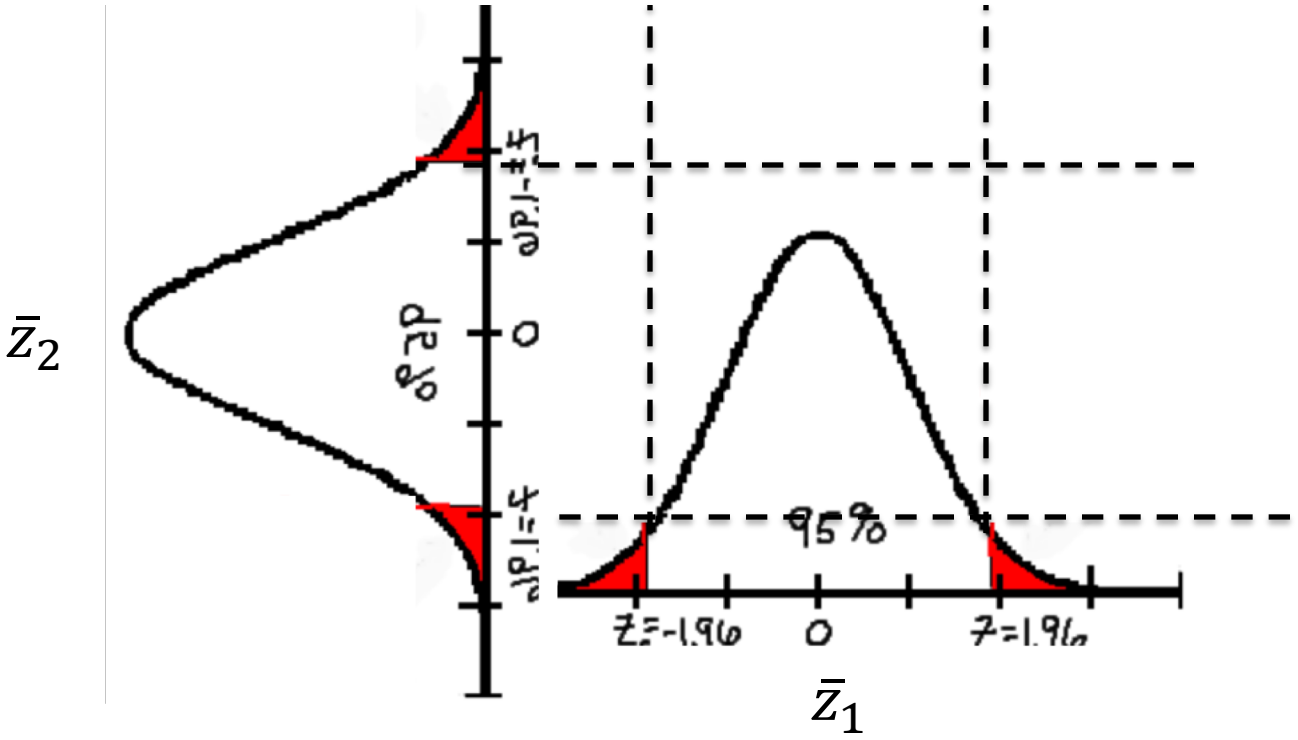
The Multiple Hypothesis Problem





The Multiple Hypothesis Problem

Test the hypothesis that $\mu_1 = 0$ or $\mu_2 = 0$



Approaches: Reject the Null Hypothesis if

1. ~~$\bar{z}_1$ **or** $\bar{z}_2$ is in its critical region.~~
2. ~~$\bar{z}_1$ **and** $\bar{z}_2$ is in its critical region.~~
3. Use the joint distribution of the test statistics.