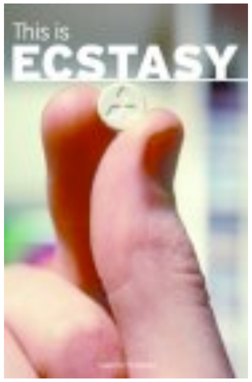
Researcher and statistician error

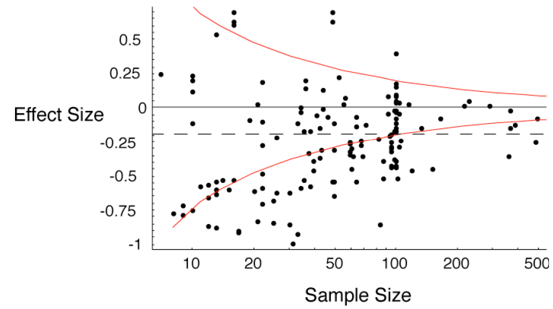


~8% of biomedical papers have substantial statistical flaws

Publication bias

Papers are more likely to be published if *P*<0.05

This causes a bias in the science reported in the literature.



Computer-intensive methods

- Hypothesis testing:
  - Simulation
  - Randomization
- Confidence intervals
  - Bootstrap

Simulation

- Simulates the sampling process on a computer many times: generates the null distribution from estimates done on the simulated data
- Computer assumes the null hypothesis is true

Example: Social spider sex ratios

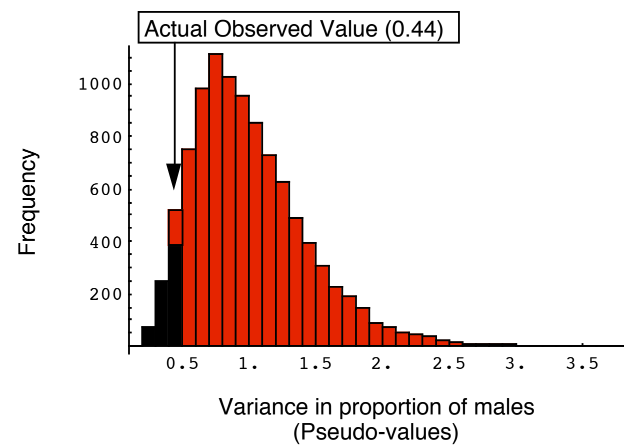
Social spiders live in groups

Example: Social spider sex ratios

- Groups are mostly females
- Hypothesis: Groups have just enough males to allow reproduction
- Test: Whether distribution of number of males is as predicted by chance
- Problem: Groups are of many different sizes
- Binomial distribution therefore doesn't apply

Simulation:

- For each group, the number of spiders is known. The overall proportion of males, p_m, is known.
- For each group, the computer draws the real number of spiders, and each has p_m probability of being male.
- This is done for all groups, and the variance in proportion of males is calculated.
- This is repeated a large number of times.



The observed value (0.44), or something more extreme, is observed in only 4.9% of the simulations. Therefore $P = 0.049$.

Randomization

- Used for hypothesis testing on measures of association
- Mixes the real data randomly
- Variable 1 from an individual is paired with variable 2 data from a randomly chosen individual. This is done for all individuals.
- The estimate is made on the randomized data.
- The whole process is repeated numerous times. The distribution of the randomized estimates is the null distribution.

Without replacement

- Randomization is done without replacement.
- In other words, all data points are used exactly once in each randomized data set.

Randomization can be done for any test of association between two variables

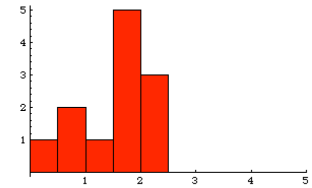
Example: Sage crickets

Sage cricket males sometimes offer their hind-wings to females to eat during mating.

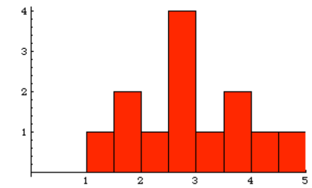
Do females who eat hind-wings wait longer to re-mate?

Waiting time to remating in sage cricket females after initial mating with either a wingless or winged male (presented in ln(days))

Male wingless	Male winged
0	1.4
0.7	1.6
0.7	1.9
1.4	2.3
1.6	2.6
1.8	2.8
1.9	2.8
1.9	2.8
1.9	3.1
2.2	3.8
2.1	3.9
2.1	4.5
	4.7



ln(Time to remating): First mate had no wings



ln(Time to remating): First mate had intact wings

Problems:
Unequal variance,
non-normal distributions

Real data: $\bar{Y}_1 - \bar{Y}_2 = -1.41$

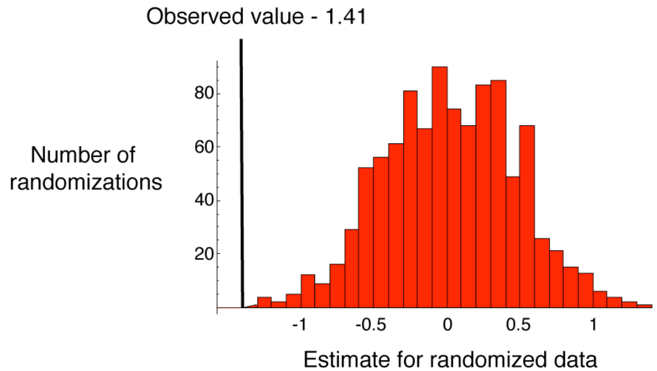
Male wingless	Male winged
0	1.4
0.7	1.6
0.7	1.9
1.4	2.3
1.6	2.6
1.8	2.8
1.9	2.8
1.9	2.8
1.9	3.1
2.2	3.8
2.1	3.9
2.1	4.5
	4.7

Randomized data: $\bar{Y}_1 - \bar{Y}_2 = 0.41$

Male wingless	Male winged
0.7	2.8
2.3	1.9
1.9	2.1
1.8	1.6
3.8	0
1.4	1.4
1.9	2.2
3.9	2.1
4.7	1.6
2.6	4.5
1.9	2.8
2.8	0.7
	3.1

Note that each data point was only used once

1000 randomizations



P < 0.001

Randomization: Other questions

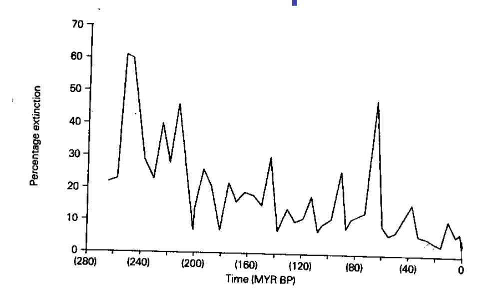


Figure 9.2 Plot of extinction rates against time (millions of years before the present) for marine genera.

Q: Is this periodic?

(yes)

Bootstrap

- Method for estimation (and confidence intervals)
- Often used for hypothesis testing too
- "Picking yourself up by your own bootstraps"

Bootstrap

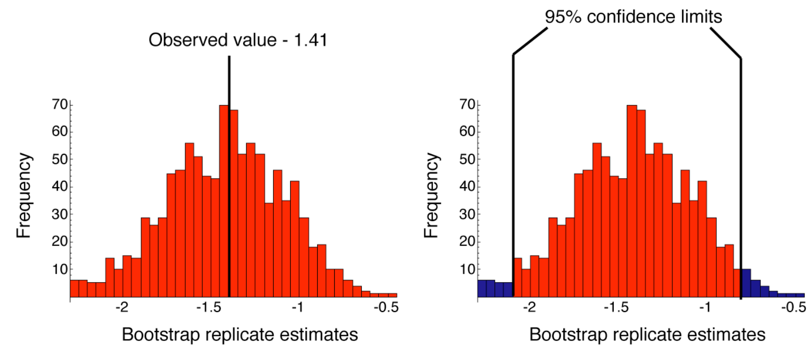
- For each group, randomly pick *with replacement* an equal number of data points, from the data of that group
- With this bootstrap dataset, calculate the estimate -- *bootstrap replicate estimate*

Real data: $\overline{Y}_1 - \overline{Y}_2 = -1.41$

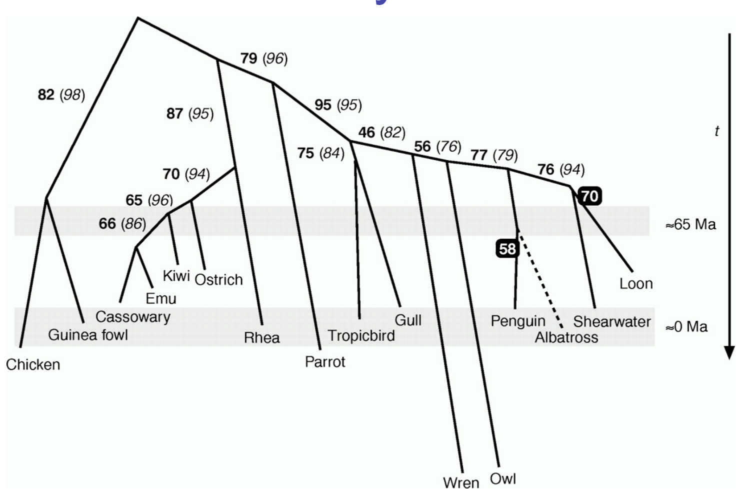
Male wingless	Male winged
0	1.4
0.7	1.6
0.7	1.9
1.4	2.3
1.6	2.6
1.8	2.8
1.9	2.8
1.9	2.8
1.9	3.1
2.2	3.8
2.1	3.9
2.1	4.5
	4.7

Bootstrap data: $\overline{Y}_1 - \overline{Y}_2 = -1.78$

Male wingless	Male winged
1.8	4.7
0.7	4.7
1.4	3.1
2.1	3.9
2.1	2.8
1.8	2.8
1.4	4.7
0.7	4.7
2.1	2.8
1.9	4.5
1.9	3.1
1.8	1.4
	1.4



Bootstraps are often used in evolutionary trees



Likelihood

$$L(hypothesis\ A \mid data) = P[data \mid hypothesis\ A]$$

Likelihood considers many possible hypotheses, not just one

Law of likelihood

A particular data set supports one hypothesis better than another if the likelihood of that hypothesis is higher than the likelihood of the other hypothesis.

Therefore we try to find the hypothesis with the *maximum likelihood*.

All estimates we have learned so far are also maximum likelihood estimates.

"Simple" example

- Using likelihood to estimate a proportion
- Data: 3 out of 8 individuals are male.
- Question: What is the maximum likelihood estimate of the proportion of males?

Likelihood

$$L(p = x) = P[3 \; males \; out \; of \; 8 \mid p = x]$$

where x is a hypothesized value of the proportion of males.

e.g., $L(p=0.5)$ is the likelihood of the hypothesis that the proportion of males is 0.5.

For this example only...

The probability of getting 3 males out of 8 independent trials is given by the binomial distribution.

$$L(p=x) = \Pr[data \mid p=x]$$
$$= \Pr[3\,out\,of\,8 \mid p=x]$$
$$= \binom{8}{3} x^3 (1-x)^{8-3}$$

How to find maximum likelihood hypothesis

1. Calculus

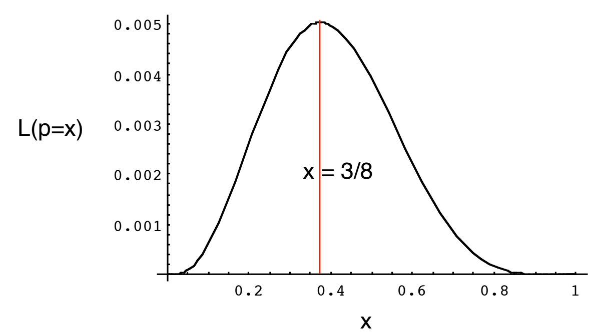
   or

2. Computer calculations

By calculus...

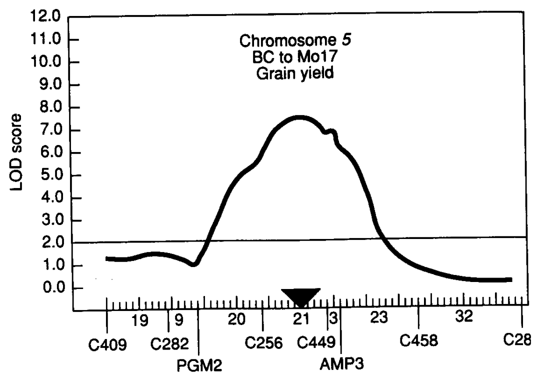
- Maximum value of $L(p=x)$ is found when $x = 3/8$.
- Note that this is the same value we would have gotten by methods we already learned.

By computer calculation...



Input likelihood formula to computer, plot the value of *L* for each value of *x*, and find the largest *L.*

Finding genes for corn yield:



Corn Chromosome 5

Hypothesis testing by likelihood

- Compares the likelihood of maximum likelihood estimate to a null hypothesis

Log-likelihood ratio =

$$\ln\left[\frac{Likelihood[Maximum\ likelihood\ hypothesis]}{Likelihood[Null\ hypothesis]}\right]$$

Test statistic

$$\chi^2 = 2\ \log\ likelihood\ \ ratio$$

With *df* equal to the number of variables fixed to make null hypothesis

Example:3 males out of 8 individuals

- H_0: 50% are male
- Maximum likelihood estimate $\hat{p} = \frac{3}{8}$

$$L[p = 3/8] = \binom{8}{3}(3/8)^3(1-3/8)^5 = 0.2816$$

Likelihood of null hypothesis

$$L[p = 0.5] = \binom{8}{3}(0.5)^3(1-0.5)^5 = 0.21875$$

Log likelihood ratio

$$\ln\left[\frac{L[p = 3/8]}{L[p = 0.5]}\right] = \ln\left[\frac{0.2816}{0.21875}\right] = 0.2526$$

$$\chi^2 = 2(0.2526) = 0.5051$$

We fixed one variable in the null hypothesis (*p*),
So the test has *df* = 1.

$\chi^2_{0.05,1} = 3.84$, so we do not reject H_0.