## 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.


Publication bias with true effect size 0.05


## Publication bias with true effect size 0.05



Publication bias with true effect size 0.05


# Computer intensive methods 

Chapter 19

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



## Simulation:

For each group, the number of spiders is known. The overall proportion of males, $p_{\mathrm{m}}$, is known.

For each group, the computer draws the real number of spiders, and each has $p_{\mathrm{m}}$ 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.

## 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


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

## Bootstrap

Method for estimation (and confidence intervals)

Often used for hypothesis testing too
"Picking yourself up by your own bootstraps"

## Revisting the Sage crickets



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

Do females who eat hindwings wait longer to remate?

## 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 - the bootstrap replicate estimate.

Real data: $\bar{Y}_{1}-\bar{Y}_{2}=-1.41$

| Male <br> wingless | Male <br> 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: $\quad \bar{Y}_{1}-\bar{Y}_{2}=-1.78$

| Male <br> wingless | Male <br> 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

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

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.

$$
\begin{aligned}
L(p=x) & =\operatorname{Pr}[\operatorname{data} \mid p=x] \\
& =\operatorname{Pr}[3 \text { out of } 8 \mid p=x] \\
& =\binom{8}{3} x^{3}(1-x)^{8-3}
\end{aligned}
$$

## 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.

How to find maximum likelihood hypothesis

1. Calculus

> or
2. Computer calculations

By computer calculation...


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

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 =

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

## Example:3 males out of 8 individuals

$\mathrm{H}_{0}$ : $50 \%$ 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 $d f=1$.
$\chi_{0.05,1}^{2}=3.84$, so we do not reject $\mathrm{H}_{0}$.

