# Statistics for laboratory scientists II


## Karl W Broman

Department of Biostatistics, Johns Hopkins University

Office: E3612 SPH; Email: kbroman@jhsph.edu

http://www.biostat.jhsph.edu/~kbroman

**TA**: Qing Li (qli@jhsph.edu, E3035)


## Logistics

| | |
|---|---|
| Lectures: | MWF 10:30-11:30 (W2033 SPH) |
| Discussion/lab: | W 1:30-3:30 (W3025 first half; W2033 second half) |
| Office hours: | **Karl**: MF 1:30-2:30 (E3612 SPH)<br>**Qing**: by appointment (E3035 SPH) |
| Textbooks: | Samuels & Witmer (2002) Statistics for the life sciences<br>Gonick & Smith (1993) The cartoon guide to statistics. [recommended]<br>Dalgaard (2002) Introductory statistics with R statistics. [recommended] |

# Grading

Grade based on:

- 3 Computer labs (67%)
- 1 Final project (33%)

Other work:

- Homework
- Reading assignments
- Deep and careful thought
- Discussions

# Final project

- Obtain some real experimental data.
- Analyze the data
- Write a 4–8 page double-spaced paper describing the data, the goal, your analysis, and your results.
  (Use the usual Introduction – Methods – Results – Discussion format.)

## This term

- Goodness of fit
- Contingency tables
- Analysis of variance (Anova)
- More on multiple comparisons
- Linear regression
- More on design of experiments
- . . .

## Goodness of fit - 2 classes

| A | B |
|---|---|
| 78 | 22 |

Do these data correspond reasonably to the proportions 3:1?

## We could use what we learned last term. . .

During the previous quarter we discussed several options for testing $p_A = 0.75$:

- Exact p-value
- Normal approximation
- Randomization test

## Goodness of fit - 3 classes

| AA | AB | BB |
|---|---|---|
| 35 | 43 | 22 |

Do these data correspond reasonably to the proportions 1:2:1?

# The likelihood-ratio test (LRT)

Back to the first example:

| A | B |
|---|---|
| $n_A$ | $n_B$ |

We want to test $H_0 : (p_A, p_B) = (\pi_A, \pi_B)$ versus $H_a : (p_A, p_B) \neq (\pi_A, \pi_B)$.

MLE under $H_a$: $\hat{p}_A = n_A/n$ where $n = n_A + n_B$.

Likelihood under $H_a$: $L_a = \Pr(n_A | p_A = \hat{p}_A) = \binom{n}{n_A} \times \hat{p}_A^{n_A} \times (1 - \hat{p}_A)^{n - n_A}$

Likelihood under $H_0$: $L_0 = \Pr(n_A | p_A = \pi_A) = \binom{n}{n_A} \times \pi_A^{n_A} \times (1 - \pi_A)^{n - n_A}$

Likelihood ratio test statistic: LRT = $2 \times \ln(L_a/L_0)$

If $H_0$ is true, then LRT follows a $\chi^2$(df=1) distribution (approximately).

# Likelihood-ratio test for the example

We observed $n_A = 78$ and $n_B = 22$.

$H_0 : (p_A, p_B) = (0.75, 0.25)$

$H_a : (p_A, p_B) \neq (0.75, 0.25)$

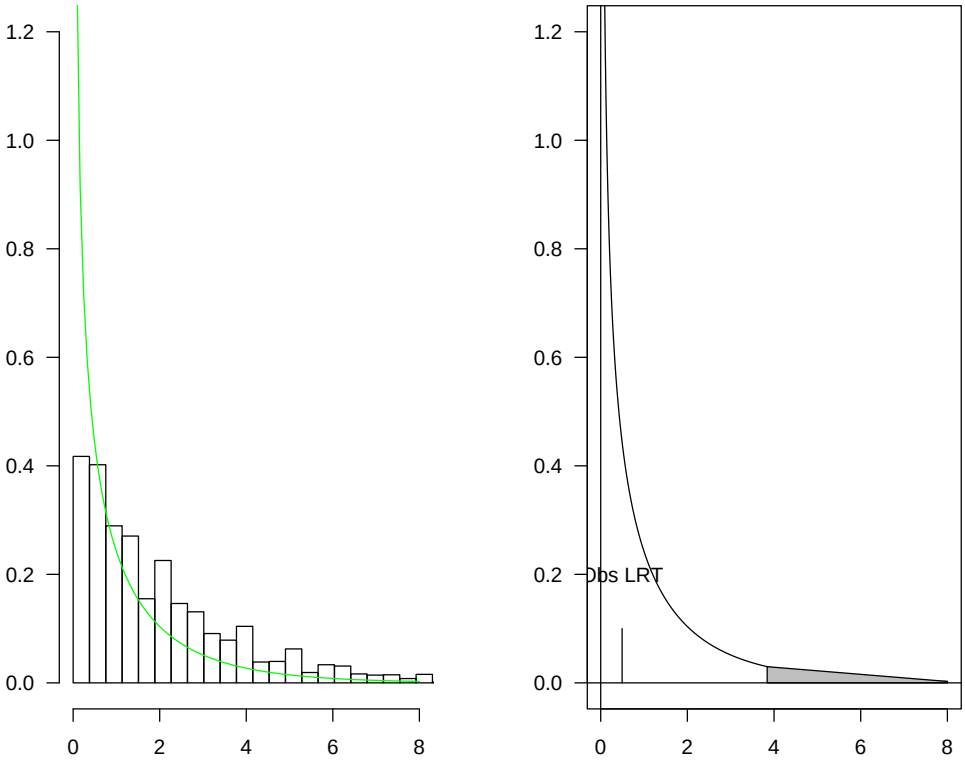
$L_a = \Pr(n_A = 78 \mid p_A = 0.78) = \binom{100}{78} \times 0.78^{78} \times 0.22^{22} = 0.096.$

$L_0 = \Pr(n_A = 78 \mid p_A = 0.75) = \binom{100}{78} \times 0.75^{78} \times 0.25^{22} = 0.075.$

LRT = $2 \times \ln(L_a/L_0) = 0.49$. Using a $\chi^2$(df=1) distribution, we get a p-value of 0.48.

In R: p-value = `1 - pchisq(0.49, 1)`

We therefore have no evidence against the hypothesis $(p_A, p_B) = (0.75, 0.25)$.




# A little math ...

$n = n_A + n_B, \quad n_A^0 = E[n_A \mid H_0] = n \times \pi_A, \quad n_B^0 = E[n_B \mid H_0] = n \times \pi_B.$

Then $L_a/L_0 = \left(\frac{n_A}{n_A^0}\right)^{n_A} \times \left(\frac{n_B}{n_B^0}\right)^{n_B}.$

Or equivalently $LRT = 2 \times n_A \times \ln\left(\frac{n_A}{n_A^0}\right) + 2 \times n_B \times \ln\left(\frac{n_B}{n_B^0}\right).$

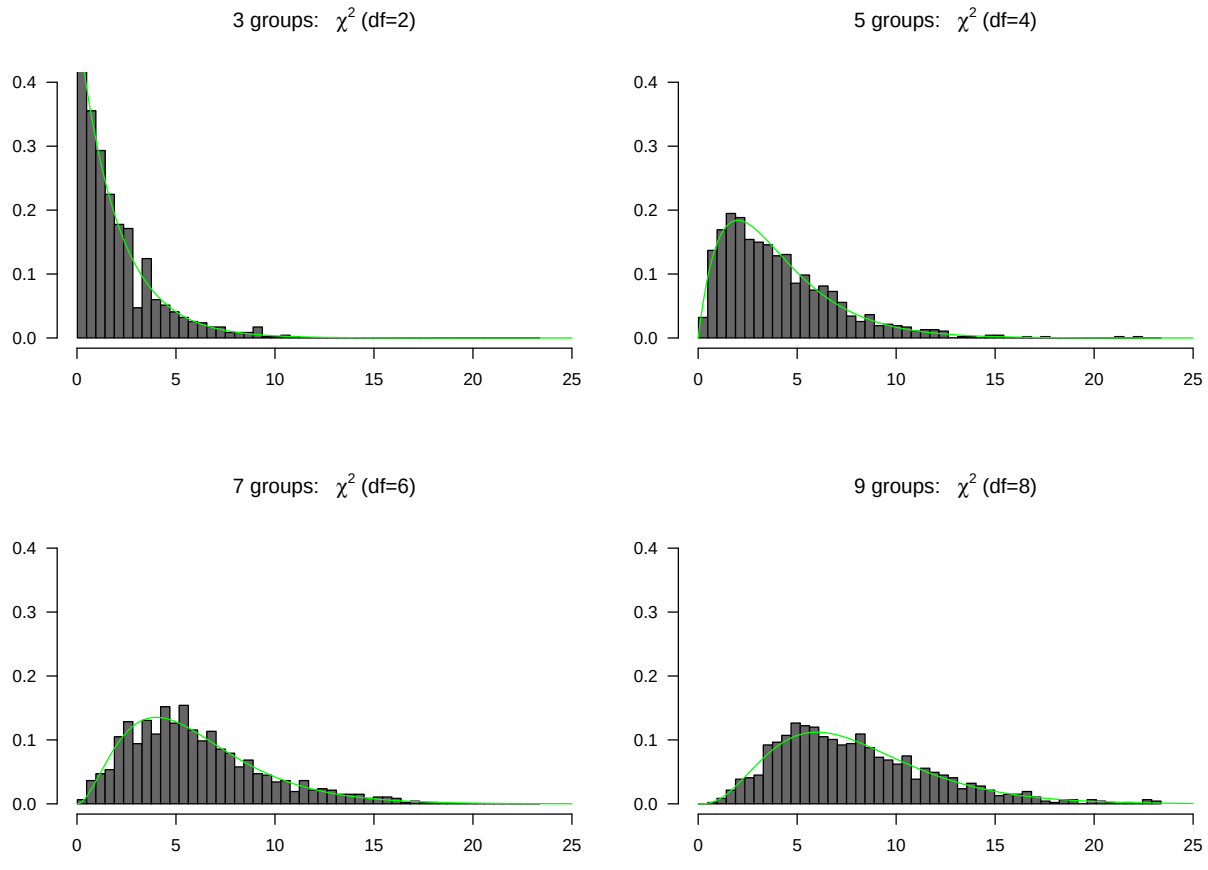
Why do this?

# Generalization to more than two groups

If we have k groups, then the likelihood ratio test statistic is

$$LRT = 2 \times \sum_{i=1}^{k} n_i \times \ln\left(\frac{n_i}{n_i^0}\right)$$

If $H_0$ is true, $LRT \sim \chi^2(df=k-1)$.

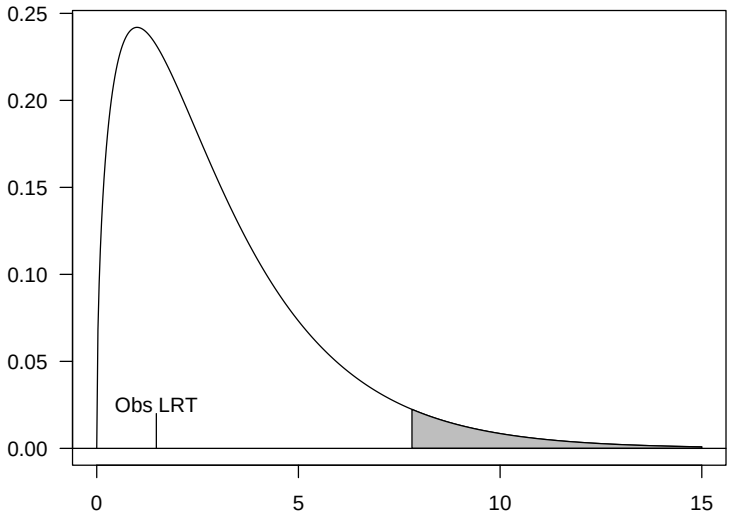


# Example

In a dihybrid cross of tomatos we expect the ratio of the phenotypes to be 9:3:3:1. In 1611 tomatos, we observe the numbers 926, 288, 293, 104. Do these numbers support our hypothesis?

| Phenotype | $n_i$ | $n_i^0$ | $n_i/n_i^0$ | $n_i \times \ln(n_i/n_i^0)$ |
|---|---|---|---|---|
| Tall, cut-leaf | 926 | 906.2 | 1.02 | 20.03 |
| Tall, potato-leaf | 288 | 302.1 | 0.95 | -13.73 |
| Dwarf, cut-leaf | 293 | 302.1 | 0.97 | -8.93 |
| Dwarf, potato-leaf | 104 | 100.7 | 1.03 | 3.37 |
| Sum | 1611 | | | 0.74 |

# Results




The test statistics LRT is 1.48. Using a $\chi^2$(df=3) distribution, we get a p-value of 0.69. We therefore have no evidence against the hypothesis that the ratio of the phenotypes is 9:3:3:1.

# The chi-square test

There is an alternative technique. The test is called the chi-square test, and has the greater tradition in the literature. For two groups, calculate the following:

$$X^2 = \frac{(n_A - n_A^0)^2}{n_A^0} + \frac{(n_B - n_B^0)^2}{n_B^0}$$

If $H_0$ is true, then $X^2$ is a draw from a $\chi^2$(df=1) distribution (approximately).

# Example

In the first example we observed $n_A = 78$ and $n_B = 22$. Under the null hypothesis we have $n_A^0 = 75$ and $n_B^0 = 25$. We therefore get

$$X^2 = \frac{(78\text{-}75)^2}{75} + \frac{(22\text{-}25)^2}{25} = 0.12 + 0.36 = 0.48.$$

This corresponds to a p-value of 0.49. We therefore have no evidence against the hypothesis $(p_A, p_B) = (0.75, 0.25)$.

Note: using the likelihood ratio test we got a p-value of 0.48.

## Generalization to more than two groups

As with the likelihood ratio test, there is a generalization to more than just two groups.

If we have k groups, the chi-square test statistic we use is

$$X^2 = \sum_{i=1}^{k} \frac{(n_i - n_i^0)^2}{n_i^0} \sim \chi^2(\text{df=k-1})$$

## Tomato example

For the tomato example we get

$$X^2 = \frac{(926\text{-}906.2)^2}{906.2} + \frac{(288\text{-}302.1)^2}{302.1} + \frac{(293\text{-}302.1)^2}{302.1} + \frac{(104\text{-}100.7)^2}{100.7}$$

$$= 0.43 + 0.65 + 0.27 + 0.11 = 1.47$$

Using a $\chi^2$(df=3) distribution, we get a p-value of 0.69. We therefore have no evidence against the hypothesis that the ratio of the phenotypes is 9:3:3:1.

Note: using the likelihood ratio test we also got a p-value of 0.69.