Nonparametric Statistics

An Introduction

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Overview

- The Central Limit theorem revisited
- Nonparametric statistics in general
- The Wilcoxon signed-rank test
- The Wilcoxon rank sum test
- Multi-group testing
- Advantages and disadvantages

The Central Limit Theorem 2.0

Recall from Lecture 2:

Let X_i be observations from some probability distribution with mean μ and variance σ^2.

Then we can estimate the true mean of X ($E[X]$) using the sample mean:

$$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} X_i$$

Remarkably:

$$\bar{x} \sim N(\mu, \frac{\sigma^2}{n})$$

We've seen from Giorgio how this applies to the gamma distribution...how about others?.

Let's say we have a bunch of $\bar{x}$: $\{\bar{x}_1, \bar{x}_2, \ldots, \bar{x}_n\}$

How can we evaluate if the CLT applies?

Well

$$\bar{x}_i \sim N\left(\mu, \frac{\sigma^2}{n}\right) \rightarrow \sqrt{n}\frac{(\bar{x}_i - \mu)}{\sigma} \sim N(0,1)$$

(Can you show this?)

So let's check that the normalized $\bar{x}_i$ follow a standard normal distribution.

What does this look like in R?

Let's use the binomial distribution with n=100, p=0.25

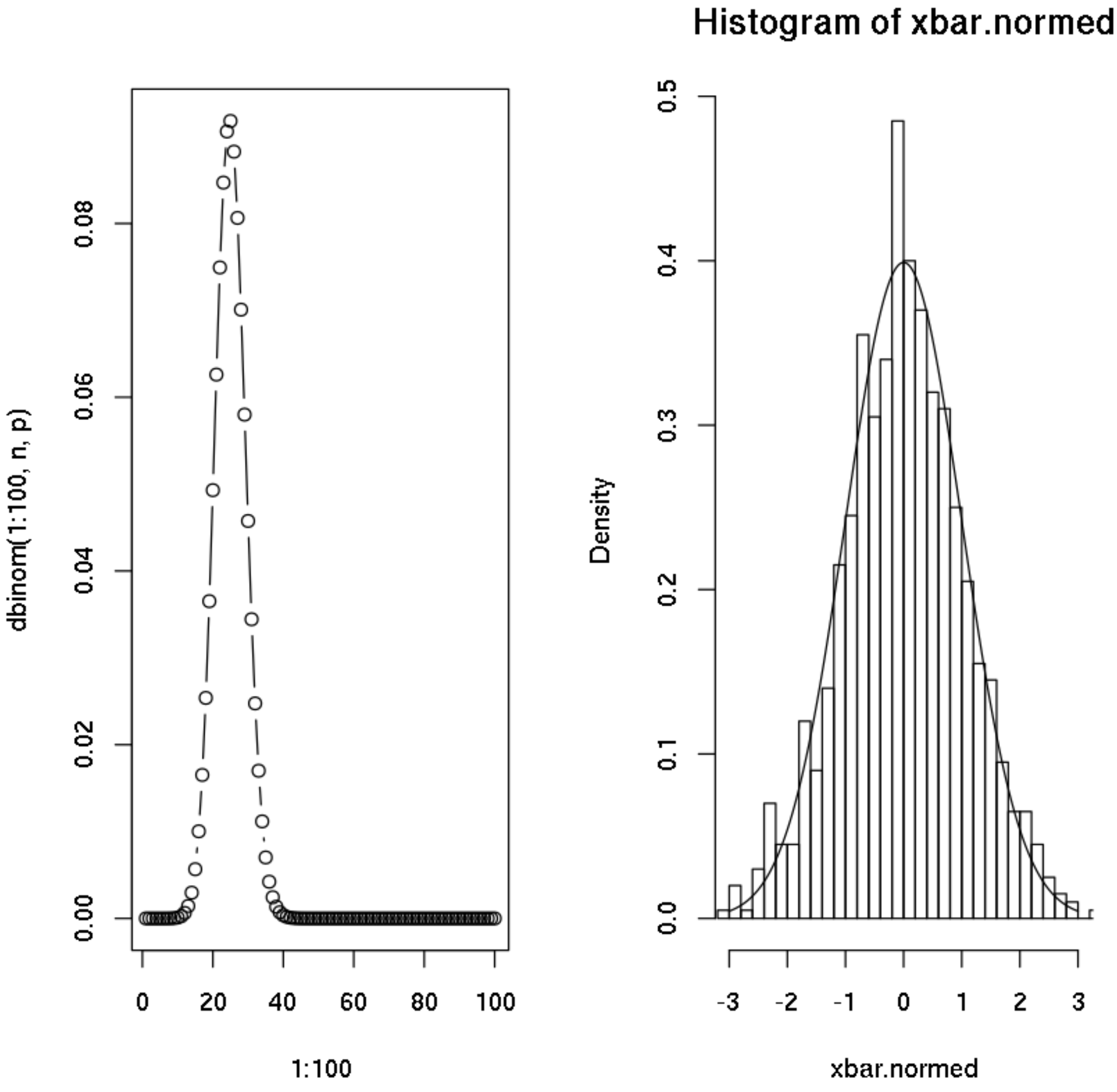
In [1]:

```
n   <- 100
p   <- 0.25
mu  <- n * p
var <- n * p * (1-p)
sig <- sqrt(var)

par(mfrow=c(1, 2))
plot(1:100, dbinom(1:100, n, p), type='b')  # plot the probability density function

n.outer <- 1000  # number of xbar
n.inner <- 50    # number of draws per xbar (n for sample mean calculation)

xbar.list <- sapply(1:n.outer, function(x) mean(rbinom(n.inner, n, p)))  # simulate from the
 binomial
xbar.normed <- sapply(xbar.list, function(x) sqrt(n.inner) * (x - mu) / sig) #
hist(xbar.normed, breaks=30, freq=F, xlim=c(-3, 3))
lines(seq(-3, 3, 0.01), dnorm(seq(-3, 3, 0.01)))
```



The Central Limit Theorem (formally)

Let $X_1, X_2, \dots, X_n$ be **independent and identically distributed** random variables **with** $E[X_i] = \mu < \infty$ and $Var(X_i) = \sigma^2 < \infty$

Define

$$\bar{X} = \frac{1}{n}\sum_{i=1}^{n} X_i.$$

Then

$$\lim_{n \to \infty} \sqrt{n}\frac{(\bar{X} - \mu)}{\sigma} \sim N(0, 1).$$

Why does the Cauchy distribution violate the CLT?

The standard Cauchy distribution has the probability density function:

$$f(x) = \frac{1}{\pi(1 + x^2)}$$

Let $X \sim f(x)$. It can be shown

1. $E[X]$ is undefined (not so easy)
2. $Var(X)$ is not finite (easy)

$$E[X^2] \propto \int_{-\infty}^{\infty} \frac{x^2}{1 + x^2} dx = \int_{-\infty}^{\infty} 1 - \frac{1}{1 + x^2} = \int_{-\infty}^{\infty} dx + \tan^{-1}(x)\Big|_{-\infty}^{\infty} = \infty$$

Nonparametric statistics overview

Beyond the Central Limit Theorem

When we have a small sample size, the t-test requires:

- the data are generated from a normal distribution.

When we have a large sample size, the CLT tells us everything is normal...except the central limit theorem can fail when:

- observations are not identically distributed (outliers).
- observations are not independent (correlation).
- Variance is not (obviously) finite.

What do we do if we have a small sample size and fear non-normality?
What do we do if we have a large sample size but fear the *iid* assumption is not valid?

Nonparametric statistics

What does "nonparametric" mean?

Parametric statistics: assume the data come from a distribution defined by the values of a finite number of parameters.

- We infer these parameters from the data itself.
- E.g. the t-test is a parametric model of mean (μ) and variance (S).

Nonparametric statistics: everything else

- Models with no parameters
- Models with an infinite number of parameters (yes, this is confusing)
- What nonparametric models have we already seen?

General approach of nonparametric methods

The steps are largely the same as parametric testing:

1. Record a random selection of observations
2. Specify null and alternate hypotheses
3. Calculate a test statistic
4. Accept or reject null based on extremity of test statistic

Major difference: nonparametric methods work with rank (or order) of observations relative to each other.

- Models specified based on how we expect the ranks to behave.
- Implementations often still rely on the Central Limit Theorem for numerical stability.

Wilcoxon Signed-Rank Test

What is the Wilcoxon Signed-Rank Test?

Nonparametric version of the paired t-test

Samples from two groups are paired; test if the two groups have the same mean location.

Example:

- We want to test if a certain gene is differentially expressed in tumor cells
- Collect normal cells and tumor cells from each patient
- Measure expression in each tumor-normal pair
- Is the expression level different?

Wilcoxon Signed-Rank Test method

In theory: If groups have the same mean, the difference between pairs should randomly be positive or negative. Many positive or negative pairs suggests different means.

In practice:

1. Calculate the difference between each pair, $D_i = X_i - Y_i$
2. Rank the pairs by absolute value of the differences from smallest to largest
    - If difference is zero, discard the pair and reduce n by 1.
    - Tied observations are assigned an average rank.
3. Sum the ranks with positive differences:
$$T^+ = \sum_i R_i \cdot 1(D_i > 0)$$

Wilcoxon Signed-Rank Test Statistic

$H_0 : D = 0 \qquad H_a : D \neq 0$

Under the null, the distribution of T^+ is complex, but it has finite mean and variance:

$$E[T^+] = \mu = \frac{n(n+1)}{4}$$
$$Var(T^+) = \sigma^2 = \frac{n(n+1)(2n+1)}{24}$$

So for n large(-ish) the Central Limit Theorem tells us:

$$Z = \frac{T^+ - \mu}{\sigma} \sim N(0,1)$$

An Example in R

Let's assume

- gene expression in tumor: $X_i \sim N(10, 5^2)$
- gene expression in normal: $Y_i \sim N(15, 5^2)$
- We have 25 pairs of observations

In [1]:

```
set.seed(123)  # set random seed so we always generate the same numbers

X.list <- rnorm(25, mean=10, sd=5)
Y.list <- rnorm(25, mean=15, sd=5)
D.list <- X.list - Y.list  # simulating from continous distributions, D_i will never be zero

df <- data.frame(X = X.list, Y=Y.list, D=D.list)  # make a dataframe
df.sort <- df[order(abs(D.list)), ]  # sort by absolute difference
df.sort$rank <- 1:nrow(df.sort)  # add the rank

T <- sum(df.sort$rank[df.sort$D > 0])  # manually calculate the T statistic
print(T)
```

```
[1] 27
```

In [2]:

```
w.test <- wilcox.test(X.list, Y.list, paired=T)  # Automatic calculation of T statistic with
 p-value
print(w.test)
```

```
	Wilcoxon signed rank test

data:  X.list and Y.list
V = 27, p-value = 7.498e-05
alternative hypothesis: true location shift is not equal to 0
```

Wilcoxon Rank Sum Test (Mann-Whitney U test)

What is the Wilcoxon Rank Sum Test?

Nonparametric version of the unpaired, *equal-variance* t-test.

We have observations from two independent groups; test if the two populations have the same location.

Intuitive motivation:

- If groups have the same location, then all observations should be approximately the same size. Once ordered, the rank sums of each group should be approximately proportional to their respective sizes.

Wilcoxon Rank Sum method

Suppose there are n_1 observations in group 1 and n_2 observations in group 2

1. Order all $n_1 + n_2$ observations.
2. Assign ranks from lowest to highest.
3. Sum the ranks belonging to group 2 observations:
$$W = \sum_{i}^{n_1+n_2} R_i \cdot 1(i \in \text{Group2}).$$
4. Calculate (Mann-Whitney):
$$U = n_1 n_2 + \frac{n_1(n_1+1)}{2} - W.$$

Wilcoxon Rank Sum statistic

For small sample sizes, the distribution of W can be calculated directly with elementary probability. For large sample sizes, we use the Central Limit Theorem:

$$Z = \frac{U - \mu}{\sigma}$$

where:

$$\mu = \frac{n_1 n_2}{2}$$
$$\sigma^2 = \frac{n_1 n_2 (n_1 + n_2 + 1)}{12}$$

An example in R

Suppose we are testing the effect of a new medication to decrease blood pressure.
Group 1 is given the medication.
Group 2 is given placebo.
We collect the following observations:

Group 1 Blood Pressure	Group 2 Blood Pressure
135	160
155	145
130	175
125	140

Is the treatment effective?

In [4]:

```
group.1 <- c(135, 155, 130, 125)
group.2 <- c(160, 145, 175, 140)
n1 <- length(group.1)
n2 <- length(group.2)
label.1 <- rep(1, n1)
label.2 <- rep(2, n2)

grouped <- c(group.1, group.2)  # Combined observations
labels <- c(label.1, label.2)   # Merge labels
labels.sort <- labels[order(grouped)]  # Sort labels based on order of observations

rank <- 1:length(grouped)
W <- sum(rank[labels.sort == 2])  # Sum the rank of group 2 observations (this is how R does
 it)
U <- n1*n2 + n1*(n1+1)/2 - W  # Manually determine U statistic
print(U)
```

```
[1] 2
```

In [5]:

```
# Automatically determine U statistic and p-value
wilcox.test(group.1, group.2)
```

```
        Wilcoxon rank sum test

data:  group.1 and group.2
W = 2, p-value = 0.1143
alternative hypothesis: true location shift is not equal to 0
```

In [6]:

```
t.test(group.1, group.2)
```

```
        Welch Two Sample t-test

data:  group.1 and group.2
t = -1.8235, df = 5.8071, p-value = 0.1197
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -44.114302   6.614302
sample estimates:
mean of x mean of y
   136.25    155.00
```

Multi-group testing

What if we have more than two groups to test?

- Parametric Statistcs: ANOVA
- Nonparametric Statistics: Kruskal-Wallis test

In summary:

- Paired t-test $\rightarrow$ Wilcoxon signed-rank test
- Unpaired (equal variance) t-test $\rightarrow$ Wilcoxon rank sum test (Mann-Whitney U Test)
- ANOVA $\rightarrow$ Kruskal-Wallis test

Advantages and Disadvantages

Advantages of nonparametric tests

Nonparametric methods work well under very general assumptions about the underlying probability distributions.

- Nonparametric tests are robust to non-normality
  - Less sensitive to measurement errors
  - Less sensitive to outliers

- Nonparametric tests can apply even when the CLT does not
  - Observations come from a variety of distributions
  - Observations are correlated

- Nonparametric tests can be used on difficult-to-quantify data
  - e.g. Subjective evaluations (physician notes on a patient)

Disadvantages of nonparametric tests

As a rule of thumb:

Fewer assumptions = Less power

If the data really do come from normal distributions:

Parametric	**Nonparametric**
More sensitive	Less sensitive
Confidence intervals easy	Confidence intervals hard
Easy to interpret	Can be difficult to interpret

Any questions?

Lecture notes and demos are available at https://github.com/msherman997/Useful-minis/tree/master/Central_Limit_Theorem (https://github.com/msherman997/Useful-minis/tree/master/Central_Limit_Theorem)