STATISTICS FOR COMPUTATIONAL BIOLOGY PROJECTS

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INTRODUCTION TO STATS AND COMPUTATIONAL BIOLOGY

COMPUTATIONAL BIOLOGY AND ITS APPLICATIONS

Seeks to understand biological systems and their relationships through **data analysis**, **mathematical modeling**, and other **quantitative tools**.

Often applied to understand:

Population genomics	Evolutionary genomics & proteomics	Regulatory & metabolic networks	Gene-disease associations	Biomedical imaging analysis	Infectious disease dynamics	Many more!

STATISTICS IN COMPUTATIONAL BIOLOGY

Computational biology approaches typically generate **large amounts of data**.

Purpose of data analysis is to **identify patterns and trends** in biological data.

Allows us to **rigorously test hypotheses** about biological processes and their relationships.

Helps **estimate parameters, fit models, and validate** models and simulations.

Provides guidance on appropriate **experimental design**.

Can be used to **make predictions** and **guide future research** directions.

BEGINNING A PROJECT WITH STATISTICS IN MIND

Can provide advice about aspects of **experimental design**.

- Sample size
- Replication
- Randomization & Controls
- Batch effects

Important to plan appropriate analyses **before** an experiment begins.

- Increase power of analyses
- Reduce likelihood of Type II error ("false negatives")

BEGINNING A PROJECT WITH STATISTICS IN MIND

Important to plan appropriate analyses **before** an experiment begins.

A PRIORI ANALYSIS

- "Prospective", "planned"
- Hypothesis-driven
- Increased power against Type II error
- More thoughtful research design
- Not always possible

POST HOC ANALYSIS

- "Posteriori", "unplanned"
- Exploratory
- Provides insight and generates ideas
- Need to adjust significance value for multiple comparisons
- Interpret with caution
- Not advised for estimating treatment effect in randomized clinical trials

WORKSHOP OUTLINE

- Experimental Design
- Probability Distributions & Data Cleaning
- Statistical Inference
- Statistical Methods for Genomics
- Interpretation & Data Visualization
- Ethical Considerations & Challenges
- Wrap-up and Q&A

EXPERIMENTAL DESIGN

GENERAL CONSIDERATIONS FOR EXPERIMENTAL DESIGN

- Appropriate controls
- Sample size
- Replication
- Batch Effects

APPROPRIATE CONTROLS

Control minimize the effects of all variables other than the one(s) being tested.

How do we design an experiment with good controls?

Make observations	Know your study system	Have a clear hypothesis	Select a **specific, measurable** independent variable	Decide on appropriate control groups	Include randomization where appropriate	Monitor controls throughout experiment

SAMPLE SIZE & REPLICATES

- **Sample** = subset designed to represent the **population** being studied
- **Replicates** = multiple experimental runs under the same treatment
- Proper replication is an essential component of any experiment.
  - Ensures conclusions about experimental treatments are reliable
  - Provides information about natural variability in response variables

PSEUDOREPLICATION & BATCH EFFECTS

Psuedoreplication = "the use of inferential statistics to test for treatment effects with data from experiments where either **treatments are not replicated** (though samples may be) or **replicates are not statistically independent**." (Hurlbert 1984)

Should be avoided or, when unavoidable, statistically accounted for using a **repeated measures** test.

Example: A study participant's blood pressure is taken before being administered a blood pressure lowering drug. Their blood pressure is taken again 10 minutes and 60 minutes after the drug is administered.

POWER & EFFECTS SIZE

- **Power** = the probability that a statistical test will reject a false null hypothesis
- A larger sample size provides more power, meaning your statistical test is more likely to detect an effect.

- **Effect size** = the absolute difference between groups + variability

Cohen (1988) provides cutoffs for effect sizes as:

- Small ≥ 0.02,
- Medium ≥ 0.15
- Large ≥ 0.35

ACTIVITY 1: POWER ANALYSIS IN R

- The 'pwr' package (Champley 2020) can perform power analyses for a variety of common statistical test.
- Enter three of the four parameters (effect size, sample size, significance level, power) as well as your number of groups and the fourth is calculated.
- On the right is an example power analysis for ANOVA.
- Note that **sample size is per group**!

Input:

```
# load package
#install.packages("pwr")
library(pwr)
# calculate effect size
pwr.anova.test(k=2,
               n=20,
               sig.level=.05,
               power=.8)
```

Output:

```
Balanced one-way analysis of variance

         k = 2
         n = 20
         f = 0.4545483
 sig.level = 0.05
     power = 0.8
```

ACTIVITY 1: POWER ANALYSIS IN R

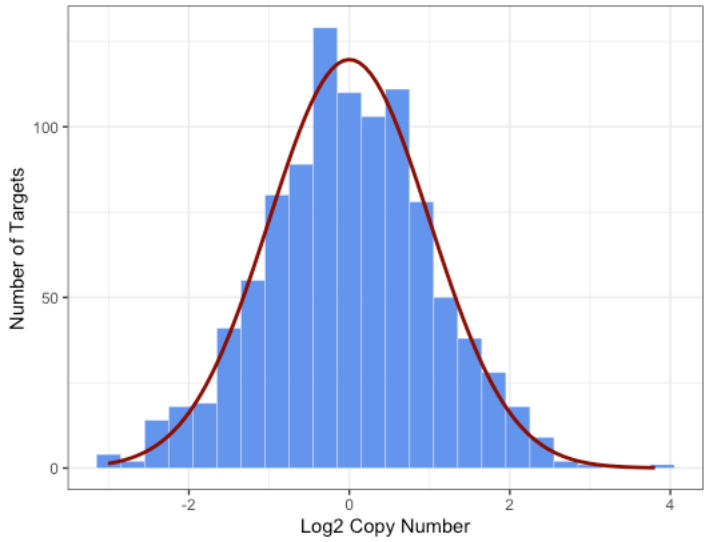
- The 'pwr' package (Champley 2020) can perform power analyses for a variety of common statistical test.
- Enter three of the four parameters (effect size, sample size, significance level, power) and the fourth is calculated.
- **Exercise:** Using the code provided in 'activities.R', determine how many participants you would need in each group (sample size) to have a power of 80% and a moderate effect size of 25% for each of the following tests.
  - **One-way ANOVA**
  - **GLM**
  - **Paired t-test (two tailed)**
  - **Independent t-test (one tailed – "greater")**
  - **X^2 test**

PROBABILITY, PROBABILITY DISTRIBUTIONS, AND DATA CLEANING

BASIC PROBABILITY CONCEPTS

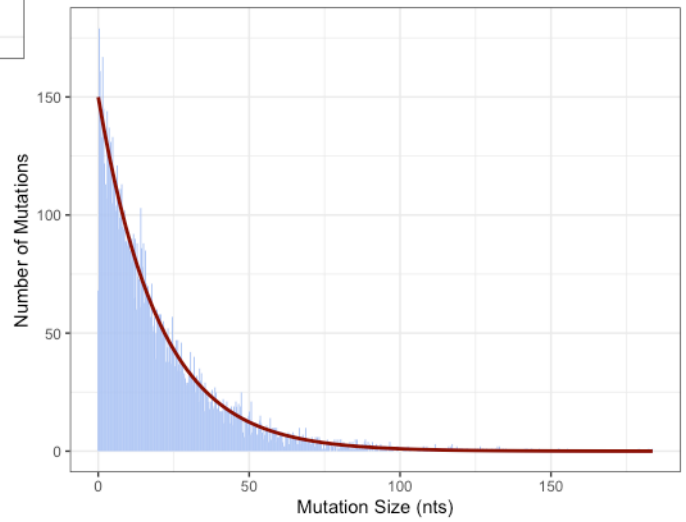
- **Probability** is an area of mathematics that deals with the likelihood of events occurring.
- Many statistical concepts are based upon probability including:
  - Sampling
  - Hypothesis testing
  - Significance values
  - Error & confidence
- Course GitHub includes suggested reading on probability.

PROBABILITY DISTRIBUTIONS



Normal Distribution
used to model log2 copy number ratios

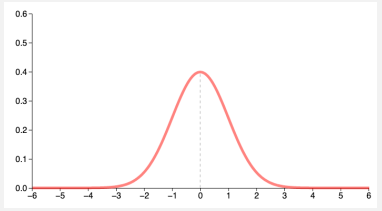
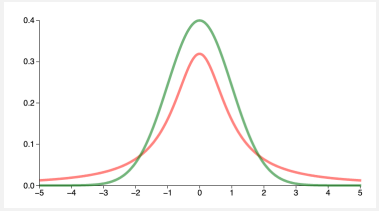
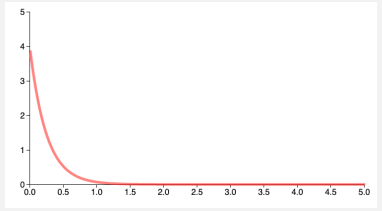
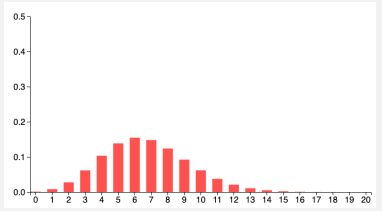
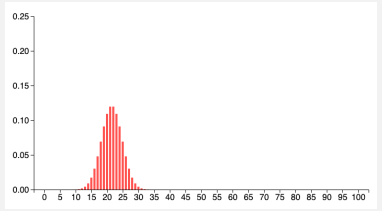
Exponential Distribution
used to model the size of mutations



- In statistics, we use **probability distributions** to model ”random” variables and quantify uncertainty.
- Fitting observed data to specific distributions allows for **predictions, inferences, and simulations** about populations.

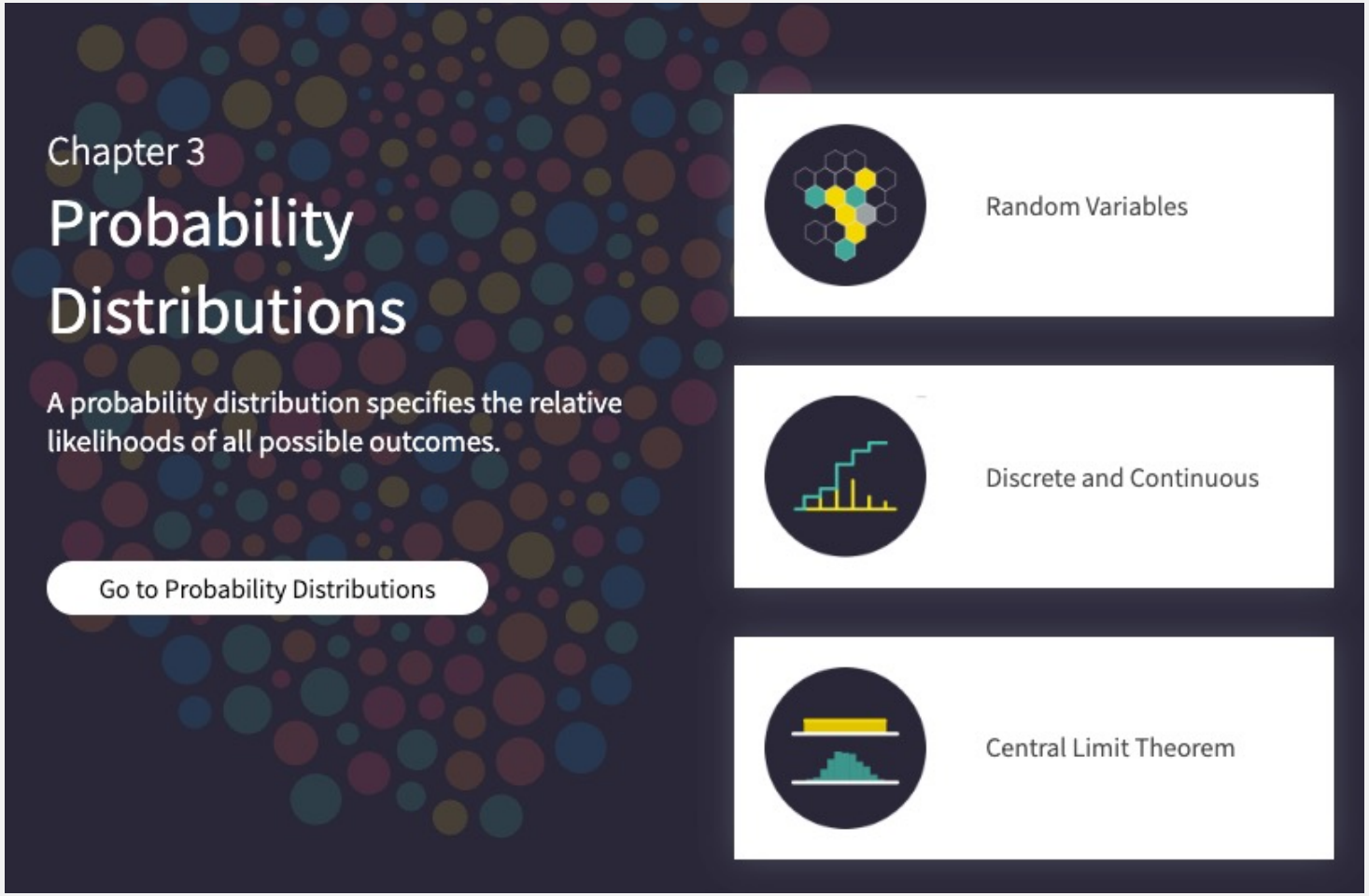
Adapted from S. Glen (2020)

COMMON PROBABILITY DISTRIBUTIONS IN COMPUTATIONAL BIOLOGY

	Continuous			Discrete	
Distribution	Normal	Student's T	Exponential	Poisson	Binomial
Appearance					
Characteristics	Bell shape	Shorter, wider	Long left tail	Integer values	Two outcomes
Example Data	Height, weight, test scores	Small sample size	Time between events	Number of events	"Coin toss"
Application	Least squares & uncertainty	Unknown variance	Continuous-time Markov chain	Waiting time between events	Anytime data is binary

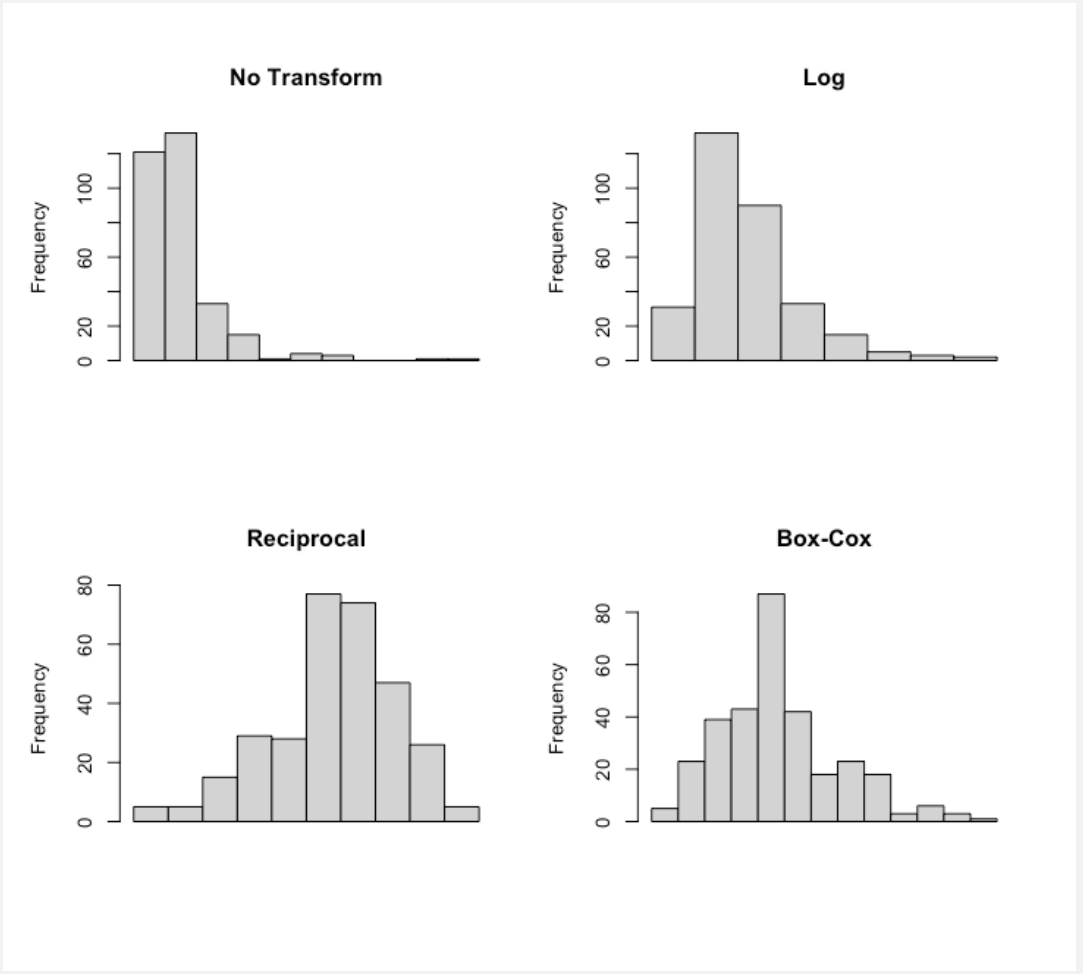
ACTIVITY 2: PROBABILITY IN COMPUTATIONAL BIOLOGY

- Interactive simulation
  - https://seeing-theory.brown.edu/probability-distributions/index.html
- Additional resource:
  - https://probstats.org/



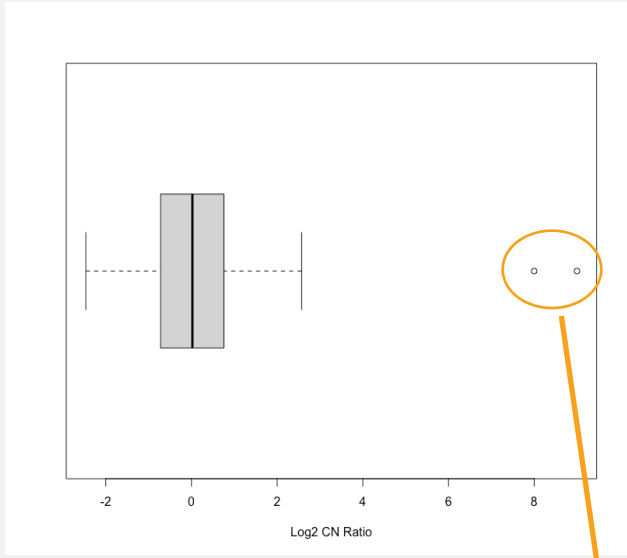
TRANSFORMATIONS

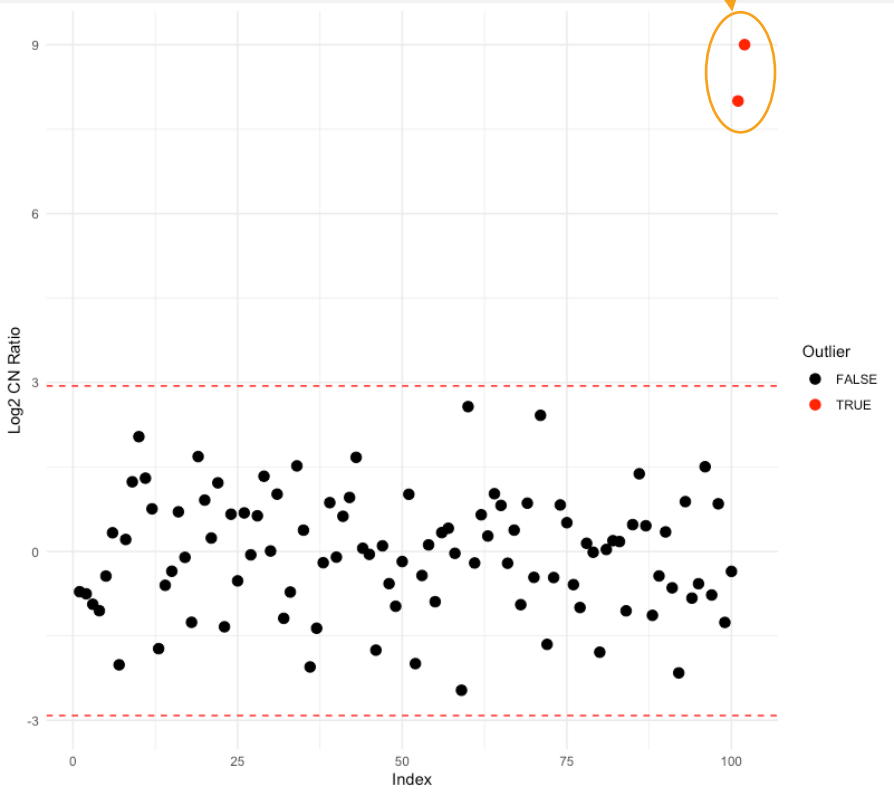
- **Data transformation** = applying the same deterministic function to all data points to facilitate statistical inference and/or interpretation
- For example, many statistical tests assume data is normally distributed.
- Right skewed distributions are the most common in biological data.
- Use tests such as Shapiro-Wilk to rigorously tests for deviations for normality.



OUTLIER ANALYSIS

- Outlier analysis seeks to identify and evaluate data points that are unusually far away from the mean of a dataset.
- Outliers may be caused by:
  - Experimental error
  - High variability (noise)
  - Something genuinely biologically interesting!
- Methods for detecting outliers:
  - **Descriptive: interquartile range (IQR), boxplot, Tukey**
  - Significance Tests: Grubbs', Dixon's, Rosner
  - Unsupervised Clustering: DBSCAN





Plots adapted from Diachkov (2024)

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```
        Grubbs test for one outlier

data:  right_outlier
G = 5.63483, U = 0.68252, p-value = 3.586e-08
alternative hypothesis: highest value 9 is an outlier
```

```
Results of Outlier Test
-------------------------

Test Method:                     Rosner's Test for Outliers

Hypothesized Distribution:       Normal

Data:                            right_outlier

Sample Size:                     102

Test Statistics:                 R.1 = 5.634825
                                 R.2 = 6.088720
                                 R.3 = 2.510327
                                 R.4 = 2.454923
                                 R.5 = 2.418916

Test Statistic Parameter:        k = 5

Alternative Hypothesis:          Up to 5 observations are not
                                 from the same Distribution.

Type I Error:                    5%

Number of Outliers Detected:     2

  i      Mean.i      SD.i     Value Obs.Num    R.i+1 lambda.i+1 Outlier
1 0  0.13115401 1.5739345  9.000000     102 5.634825   3.390825    TRUE
2 1  0.04334366 1.3067863  8.000000     101 6.088720   3.387474    TRUE
3 2 -0.03622291 1.0387812  2.571458      60 2.510327   3.384083   FALSE
4 3 -0.06256312 1.0099449  2.416773      71 2.454923   3.380651   FALSE
5 4 -0.08786247 0.9830997 -2.465898      59 2.418916   3.377176   FALSE
```

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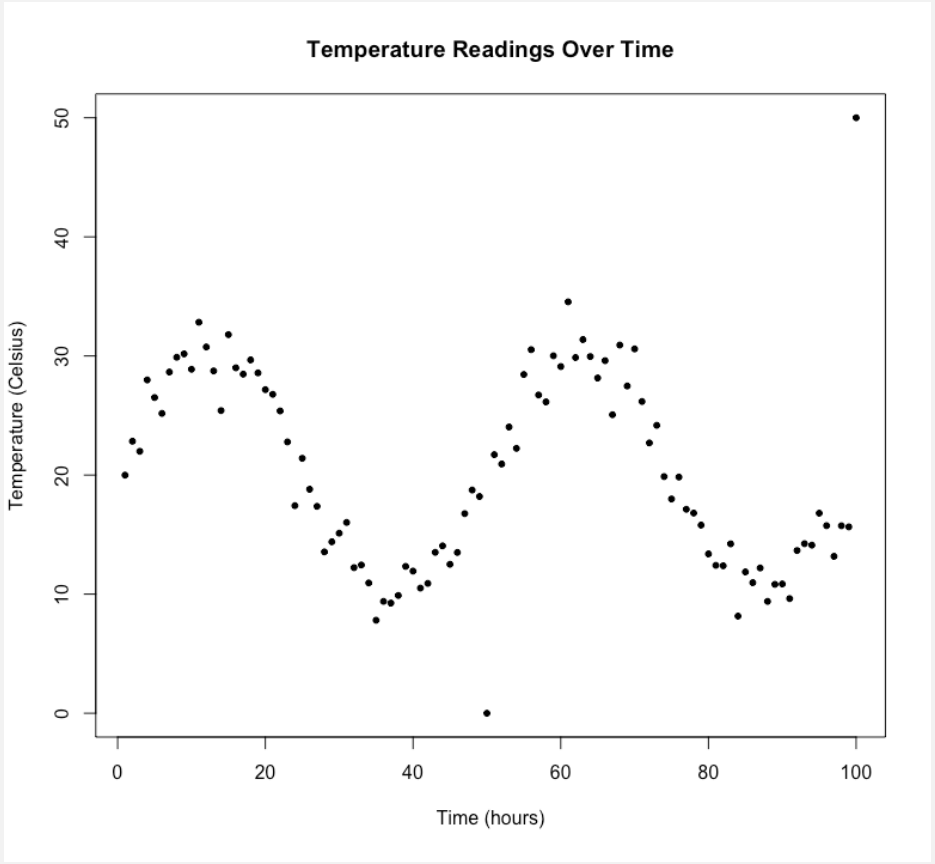
- Outlier analysis seeks to identify and evaluate data points that are unusually far away from the mean of a dataset.
- Outliers may be caused by:
  - Experimental error
  - High variability (noise)
  - Something genuinely biologically interesting!
- Methods for detecting outliers:
  - Descriptive: interquartile range (IQR), boxplot, Tukey
  - Significance Tests: Grubbs', Dixon's, Rosner
  - **Unsupervised Clustering: DBSCAN**

```
DBSCAN clustering for 100 objects.
Parameters: eps = 6, minPts = 4
Using euclidean distances and borderpoints = TRUE
The clustering contains 1 cluster(s) and 2 noise points.

 0  1
 2 98

Available fields: cluster, eps, minPts, dist, borderPoints
```



Plots adapted from Diachkov (2024)

ZERO-INFLATED DATA

- There are many reasons why your data may contain many zeros.
  - Zero adverse effects
  - Zero copy-number alterations
  - Zero expression of certain markers
- If the number of zeros in a dataset exceed what is expected by a Poisson distribution (or negative binomial), it is considered zero-inflated.
- There are many methods for dealing with zero-inflated data but lets like a look at one: generalized linear models (GLMs).

Review | Open access | Published: 21 January 2022

Statistics or biology: the zero-inflation controversy about scRNA-seq data

Ruochen Jiang, Tianyi Sun, Dongyuan Song & Jingyi Jessica Li

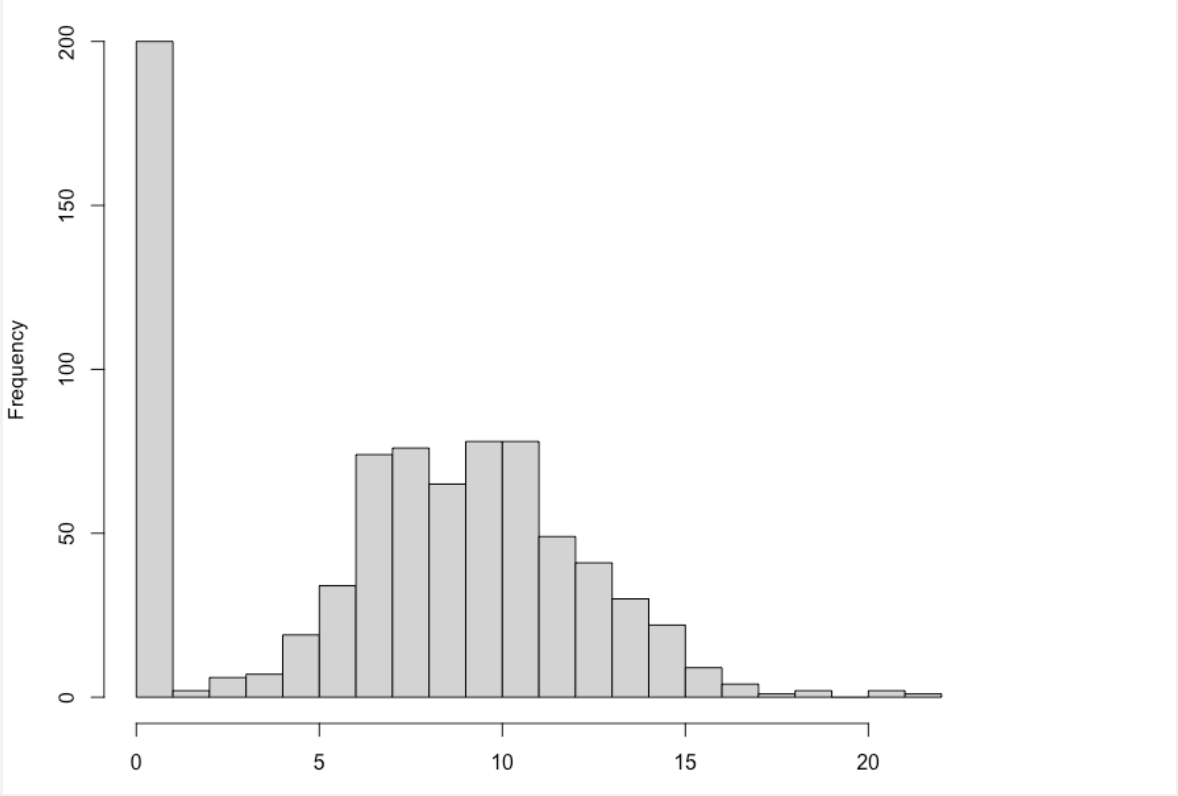
Genome Biology **23**, Article number: 31 (2022) | Cite this article

24k Accesses | **61** Citations | **78** Altmetric | Metrics

Abstract

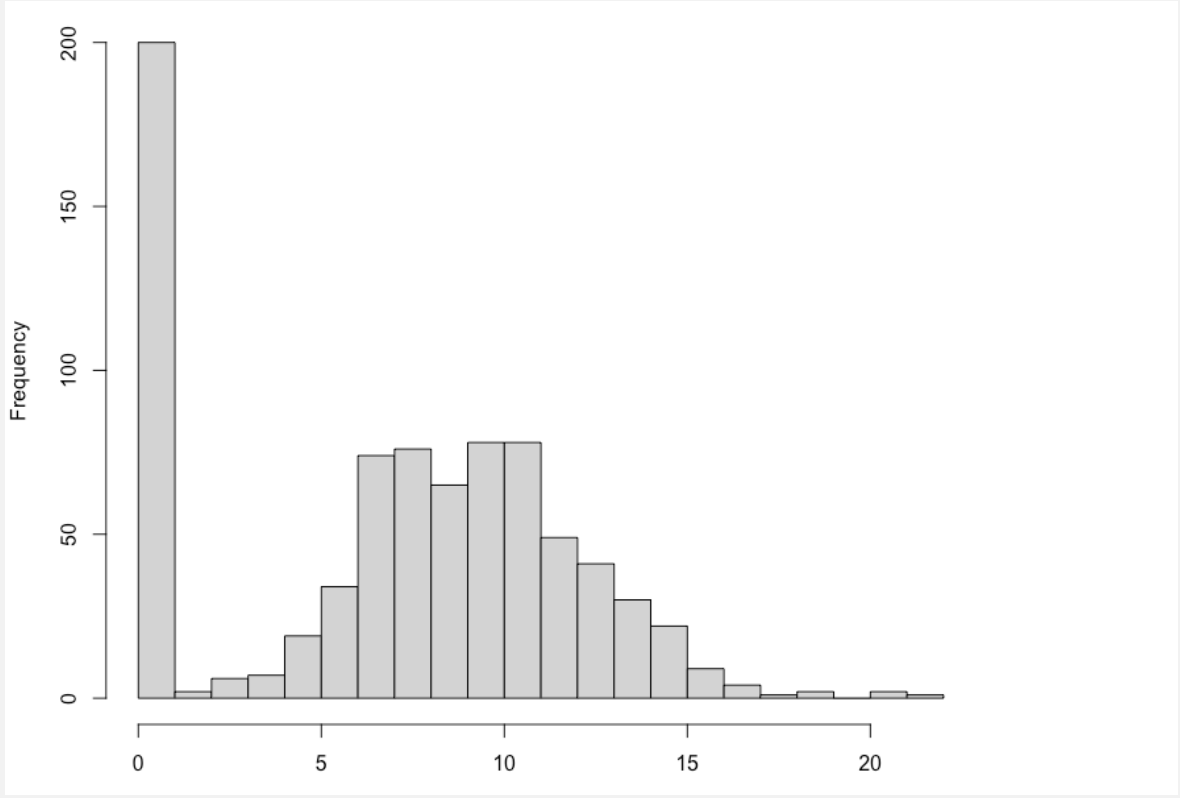
Researchers view vast zeros in single-cell RNA-seq data differently: some regard zeros as biological signals representing no or low gene expression, while others regard zeros as missing data to be corrected. To help address the controversy, here we discuss the sources of biological and non-biological zeros; introduce five mechanisms of adding non-biological zeros in computational benchmarking; evaluate the impacts of non-biological zeros on data analysis; benchmark three input data types: observed counts, imputed counts, and binarized counts; discuss the open questions regarding non-biological zeros; and advocate the importance of transparent analysis.

GLMS FOR ZERO-INFLATED DATA



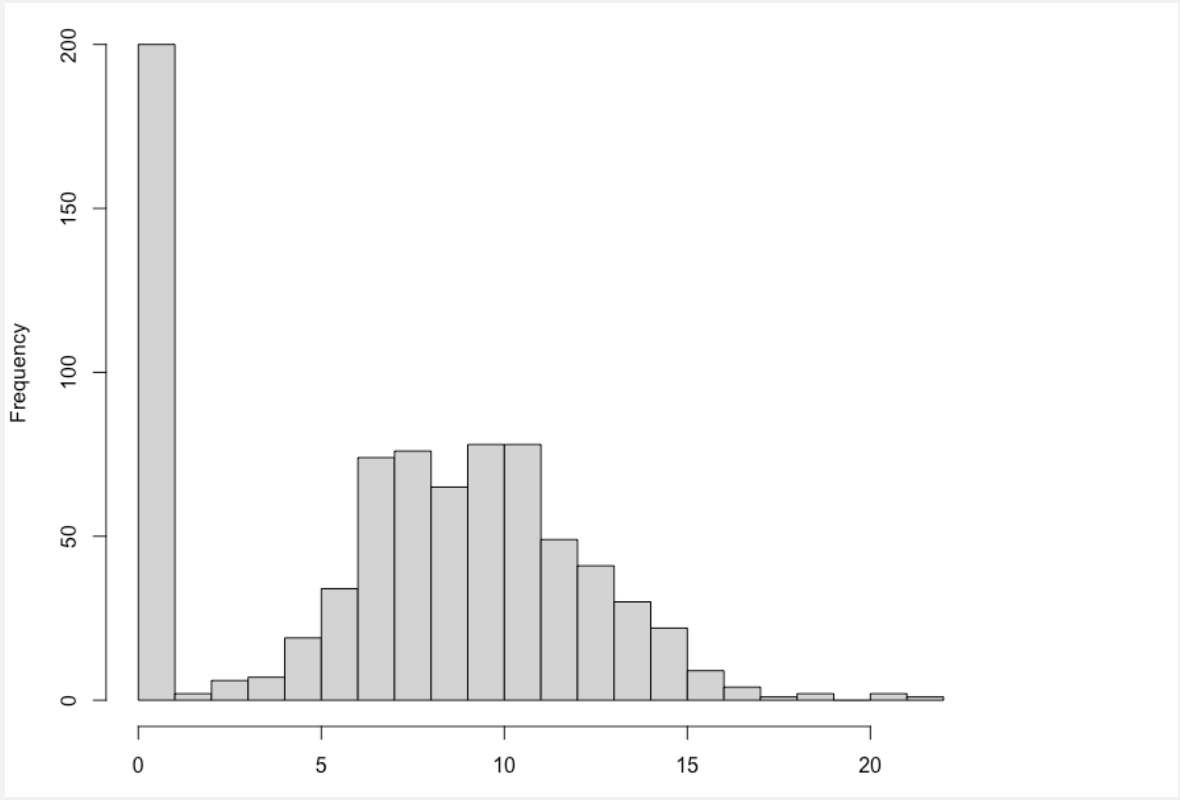

```
Call:
glm(formula = zero_inflated ~ predictor, family = "poisson",
    data = data1)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 0.207890   0.042142   4.933 8.09e-07 ***
predictor   0.147704   0.002919  50.595  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for poisson family taken to be 1)

    Null deviance: 3962.2  on 799  degrees of freedom
Residual deviance: 1159.1  on 798  degrees of freedom
AIC: 3617.8

Number of Fisher Scoring iterations: 5
```

GLMS FOR ZERO-INFLATED DATA




```
Call:
zeroinfl(formula = zero_inflated ~ predictor | predictor, data = data1, dist = "poisson")

Pearson residuals:
    Min      1Q  Median      3Q     Max
-1.3456 -0.1270 -0.0042  0.1563  2.0486

Count model coefficients (poisson with log link):
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 1.141551   0.054014   21.13   <2e-16 ***
predictor   0.086380   0.003818   22.63   <2e-16 ***

Zero-inflation model coefficients (binomial with logit link):
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   22.360      5.782   3.867 0.000110 ***
predictor     -4.166      1.118  -3.728 0.000193 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Number of iterations in BFGS optimization: 16
Log-likelihood: -1277 on 4 Df
```

GLMS FOR ZERO-INFLATED DATA




```
Likelihood ratio test

Model 1: zero_inflated ~ predictor
Model 2: zero_inflated ~ predictor | predictor
  #Df  LogLik Df  Chisq Pr(>Chisq)
1   2 -1806.9
2   4 -1276.8  2 1060.2  < 2.2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

Standard GLM

Zero-inflated GLM

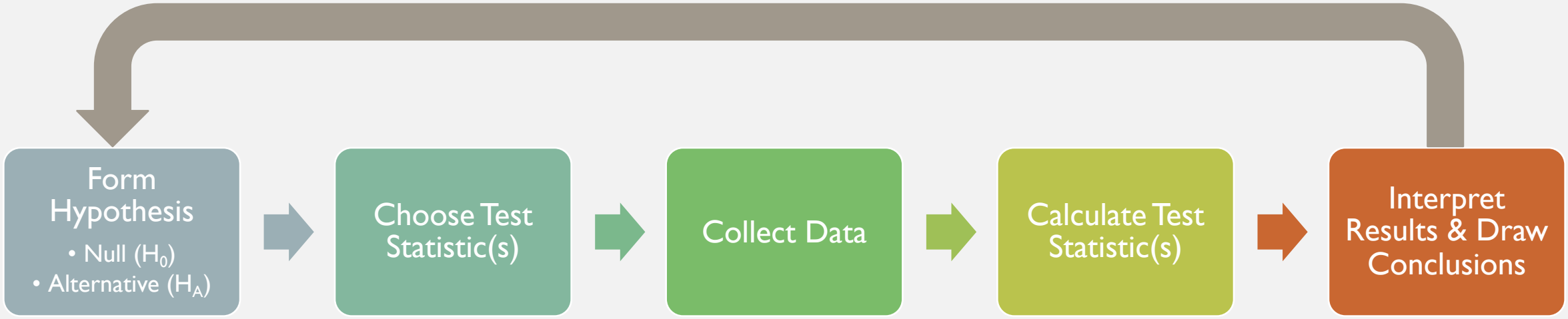
STATISTICAL INFERENCE

TESTING FOR DIFFERENCES

- One of the most common tasks in statistics is comparing 2+ sets of samples.
  - Healthy vs disease
  - Treatment vs placebo
- Simple taking the difference between means does not account for variability.
  - Small differences could be due to chance.
- Is the difference we observe between groups comparable to the difference we would see due purely to sampling (chance)?
- This is the basis for **hypothesis testing**.

BASICS OF HYPOTHESIS TESTING

- **Hypothesis testing** is the fundamental process by which we make inferences about a population based on sample data.



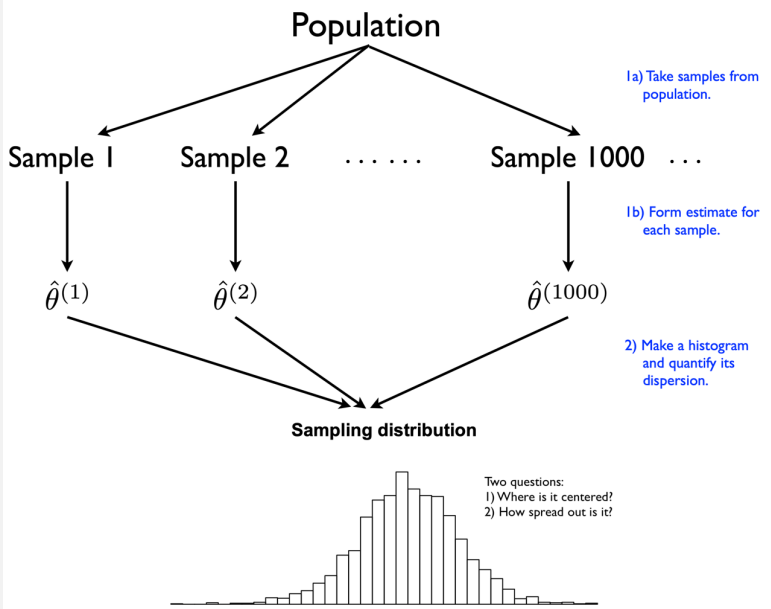


Fig 8.5 from J. Scott (2021)

UNCERTAINTY

- **Uncertainty** describes how much an estimate may differ from the true value.
- Fundamentally, it arises from the fact that we must use a **sample** to make inferences about a **population**.
- Mechanistically, uncertainty can arise through measurement/reporting error or variability that is intrinsic to individuals or processes.
- Quick demo: https://www.statcrunch.com/applets/type3&samplingdist

UNCERTAINTY

- How do we **quantify uncertainty**?
  - Variance/Standard deviation/**Standard error**
  - Confidence intervals
    - **Correct: A 95% confidence interval has a 95% chance of containing the true mean.**
    - Incorrect: There is a 95% probability that the true mean lies within the interval.

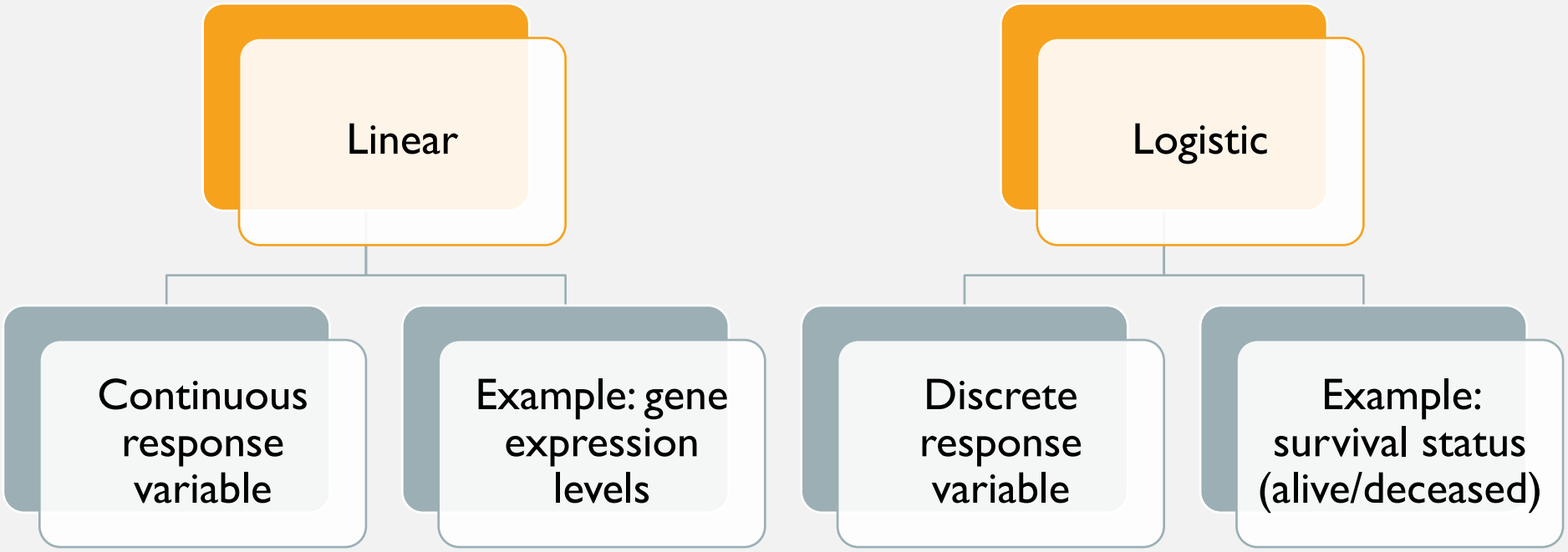
5-MINUTE BREAK

Stretch, use the restroom, grab a snack!

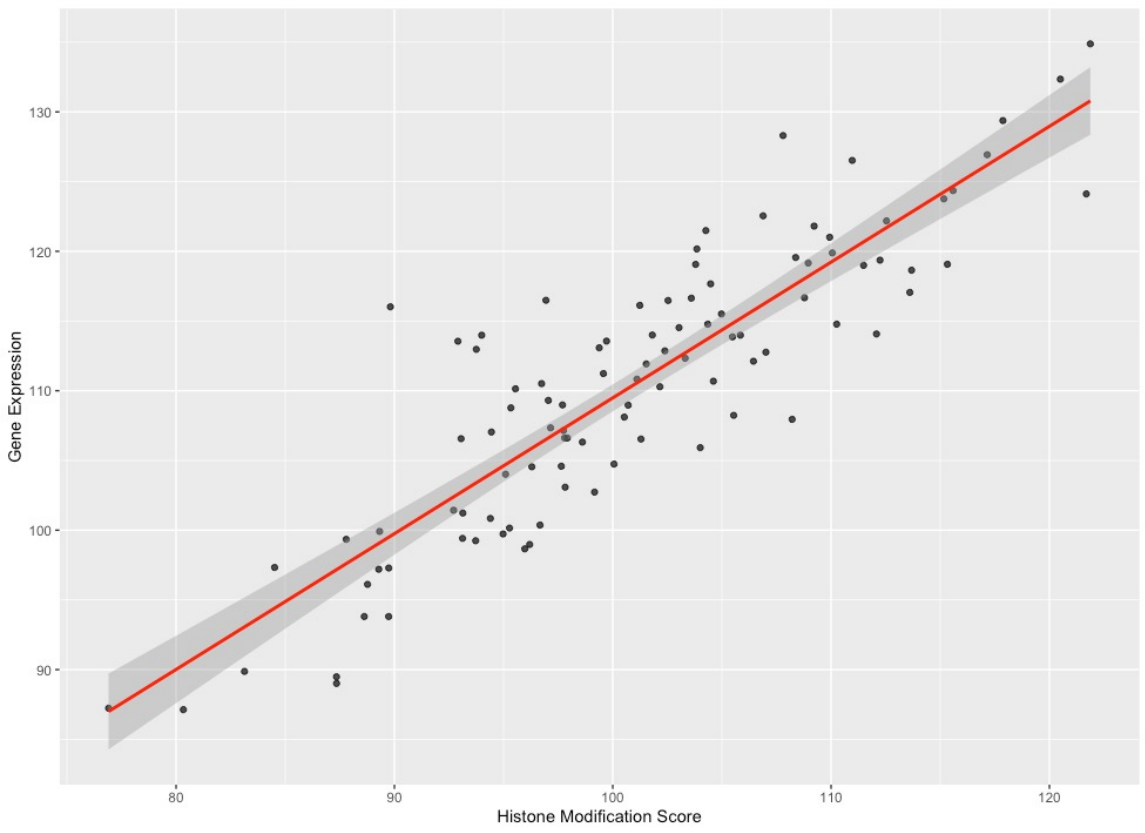
Meeting back here shortly.

STATISTICAL METHODS FOR GENOMICS

COMMON ANALYSIS METHODS: REGRESSION

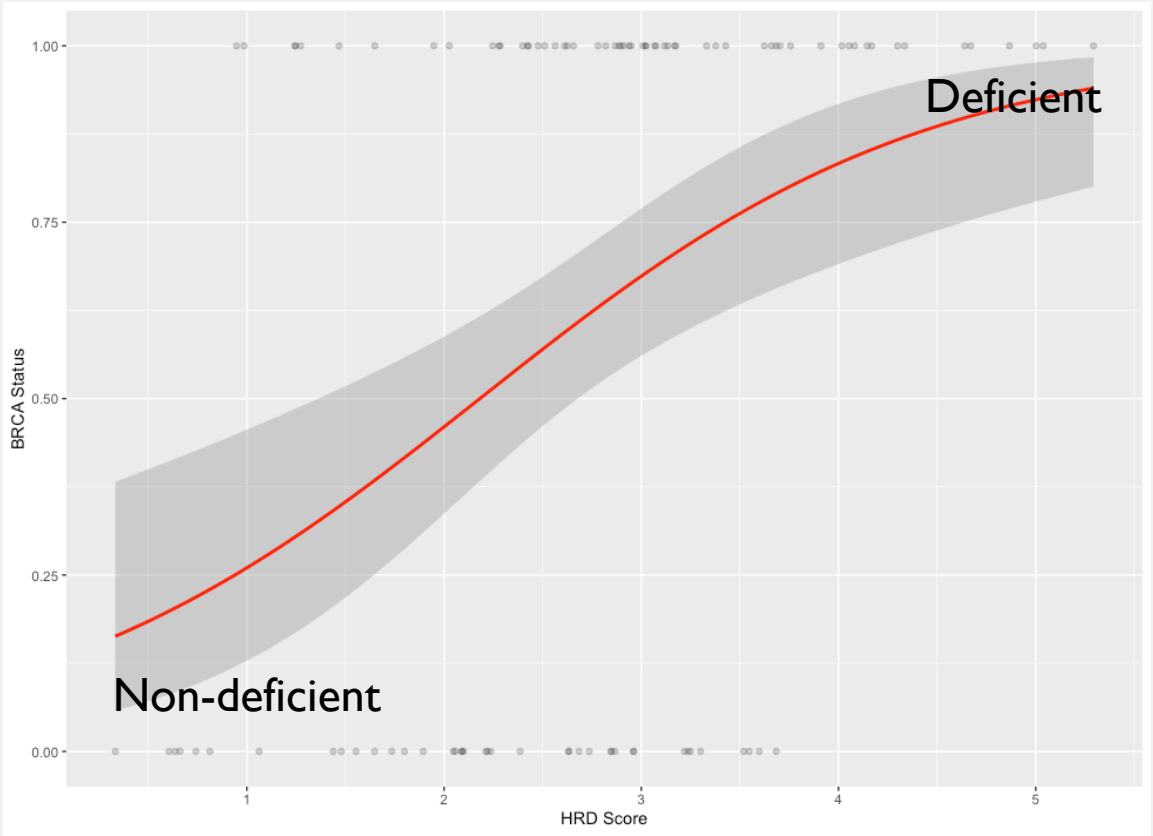


COMMON ANALYSIS METHODS: LINEAR REGRESSION




```
Call:
lm(formula = normal_data ~ predictor, data = data1)

Residuals:
     Min       1Q   Median       3Q      Max
-15.5723  -2.3947   0.0966   2.9096   9.8830

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 13.39292    4.82246   2.777  0.00657 **
predictor    0.79292    0.04351  18.222  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 4.38 on 98 degrees of freedom
Multiple R-squared:  0.7721,    Adjusted R-squared:  0.7698
F-statistic:   332 on 1 and 98 DF,  p-value: < 2.2e-16

> fit1$coefficients
(Intercept)   predictor
 13.3929240   0.7929152
```

COMMON ANALYSIS METHODS: LOGISTIC REGRESSION




```
Call:
glm(formula = binom_data ~ predictor, data = data1)

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) -0.05799    0.10925  -0.531    0.597
predictor    0.19520    0.04245   4.598 1.27e-05 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for gaussian family taken to be 0.2014385)

    Null deviance: 24.000  on 99  degrees of freedom
Residual deviance: 19.741  on 98  degrees of freedom
AIC: 127.54

Number of Fisher Scoring iterations: 2

> fit2$coefficients
(Intercept)   predictor
-0.05799028  0.19520065
```

```
binomial(link = "logit")
gaussian(link = "identity")
Gamma(link = "inverse")
inverse.gaussian(link = "1/mu^2")
poisson(link = "log")
quasi(link = "identity", variance = "constant")
quasibinomial(link = "logit")
quasipoisson(link = "log")
```

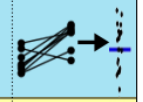
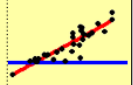
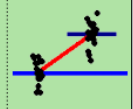
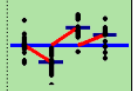
COMMON ANALYSIS METHODS: GENERALIZED LINEAR MODELS

- Generalized linear models (GLMs)
  - ”Non-parametric” in the sense that they do not assume that the response variable is normally distributed.
  - The **link function** relates the distribution of the response variable to the linear predictors of the model.
  - Does still assume:
    - Independence of response variable
    - Relationship between predictor and link-transformed response is linear
  - “Everything is a GLM!”

Common statistical tests are linear models

Last updated: 02 April, 2019

See worked examples and more details at the accompanying notebook: https://lindeloev.github.io/tests-as-linear

	Common name	Built-in function in R	Equivalent linear model in R	Exact?	The linear model in words	Icon
Simple regression: lm(y ~ 1 + x)	**y is independent of x** P: One-sample t-test N: Wilcoxon signed-rank	t.test(y) wilcox.test(y)	lm(y ~ 1) lm(signed_rank(y) ~ 1)	✓ for N >14	One number (intercept, i.e., the mean) predicts **y**. - (Same, but it predicts the *signed rank* of **y**.)	
	P: Paired-sample t-test N: Wilcoxon matched pairs	t.test(y_1, y_2, paired=TRUE) wilcox.test(y_1, y_2, paired=TRUE)	lm(y_2 - y_1 ~ 1) lm(signed_rank(y_2 - y_1) ~ 1)	✓ for N >14	One intercept predicts the pairwise $\mathbf{y_2}$-$\mathbf{y_1}$ differences. - (Same, but it predicts the *signed rank* of $\mathbf{y_2}$-$\mathbf{y_1}$.)	
	y ~ continuous x P: Pearson correlation N: Spearman correlation	cor.test(x, y, method='Pearson') cor.test(x, y, method='Spearman')	lm(y ~ 1 + x) lm(rank(y) ~ 1 + rank(x))	✓ for N >10	One intercept plus **x** multiplied by a number (slope) predicts **y**. - (Same, but with *ranked* **x** and **y**)	
	y ~ discrete x P: Two-sample t-test P: Welch's t-test N: Mann-Whitney U	t.test(y_1, y_2, var.equal=TRUE) t.test(y_1, y_2, var.equal=FALSE) wilcox.test(y_1, y_2)	lm(y ~ 1 + G_2)[A] gls(y ~ 1 + G_2, weights=…)[B][A] lm(signed_rank(y) ~ 1 + G_2)[A]	✓ ✓ for N >11	An intercept for **group 1** (plus a difference if **group 2**) predicts **y**. - (Same, but with one variance *per group* instead of one common.) - (Same, but it predicts the *signed rank* of **y**.)	
Multiple regression: lm(y ~ 1 + x_1 + x_2 +…)	P: One-way ANOVA N: Kruskal-Wallis	aov(y ~ group) kruskal.test(y ~ group)	lm(y ~ 1 + G_2 + G_3 +…+ G_N)[A] lm(rank(y) ~ 1 + G_2 + G_3 +…+ G_N)[A]	✓ for N >11	An intercept for **group 1** (plus a difference if group ≠ 1) predicts **y**. - (Same, but it predicts the *rank* of **y**.)	
	P: One-way ANCOVA	aov(y ~ group + x)	lm(y ~ 1 + G_2 + G_3 +…+ G_N + x)[A]	✓	- (Same, but plus a slope on **x**.) *Note: this is discrete AND continuous. ANCOVAs are ANOVAs with a continuous x.*	
	P: Two-way ANOVA	aov(y ~ group * sex)	lm(y ~ 1 + G_2 + G_3 + … + G_N + S_2 + S_3+ … + S_K + G_2*S_2+G_3*S_3+…+G_N*S_K)	✓	Interaction term: changing **sex** changes the **y ~ group** parameters. *Note: $\mathbf{G_{2\ to\ N}}$ is an indicator (0 or 1) for each non-intercept levels of the **group** variable. Similarly for $\mathbf{S_{2\ to\ K}}$ for sex. The first line (with G_i) is main effect of group, the second (with S_i) for sex and the third is the **group × sex** interaction. For two levels (e.g. male/female), line 2 would just be "S_2" and line 3 would be S_2 multiplied with each G_i.*	*[Coming]*
	Counts ~ discrete x N: Chi-square test	chisq.test(groupXsex_table)	**Equivalent log-linear model** glm(y ~ 1 + G_2 + G_3 + … + G_N + S_2 + S_3+ … + S_K + G_2*S_2+G_3*S_3+…+G_N*S_K, family=…)[A]	✓	Interaction term: (Same as Two-way ANOVA.) *Note: Run glm using the following arguments: `glm(model, family=poisson())`* *As linear-model, the Chi-square test is $log(y_i) = log(N) + log(\alpha_i) + log(\beta_j) + log(\alpha\beta_{ij})$ where α_i and β_j are proportions. See more info in the accompanying notebook.*	*Same as Two-way ANOVA*
	N: Goodness of fit	chisq.test(y)	glm(y ~ 1 + G_2 + G_3 +…+ G_N, family=…)[A]	✓	(Same as One-way ANOVA and see Chi-Square note.)	*1W-ANOVA*

List of common parametric (P) non-parametric (N) tests and equivalent linear models. The notation y ~ 1 + x is R shorthand for $y = 1 \cdot b + a \cdot x$ which most of us learned in school. Models in similar colors are highly similar, but really, notice how similar they *all* are across colors! For non-parametric models, the linear models are reasonable approximations for non-small sample sizes (see "Exact" column and click links to see simulations). Other less accurate approximations exist, e.g., Wilcoxon for the sign test and Goodness-of-fit for the binomial test. The signed rank function is `signed_rank = function(x) sign(x) * rank(abs(x))`. The variables G_i and S_i are "dummy coded" indicator variables (either 0 or 1) exploiting the fact that when $\Delta x = 1$ between categories the difference equals the slope. Subscripts (e.g., G_2 or y_1) indicate different columns in data. lm requires long-format data for all non-continuous models. All of this is exposed in greater detail and worked examples at https://lindeloev.github.io/tests-as-linear.

[A] See the note to the two-way ANOVA for explanation of the notation.

[B] Same model, but with one variance per group: `gls(value ~ 1 + G2, weights = varIdent(form = ~1|group), method="ML")`.

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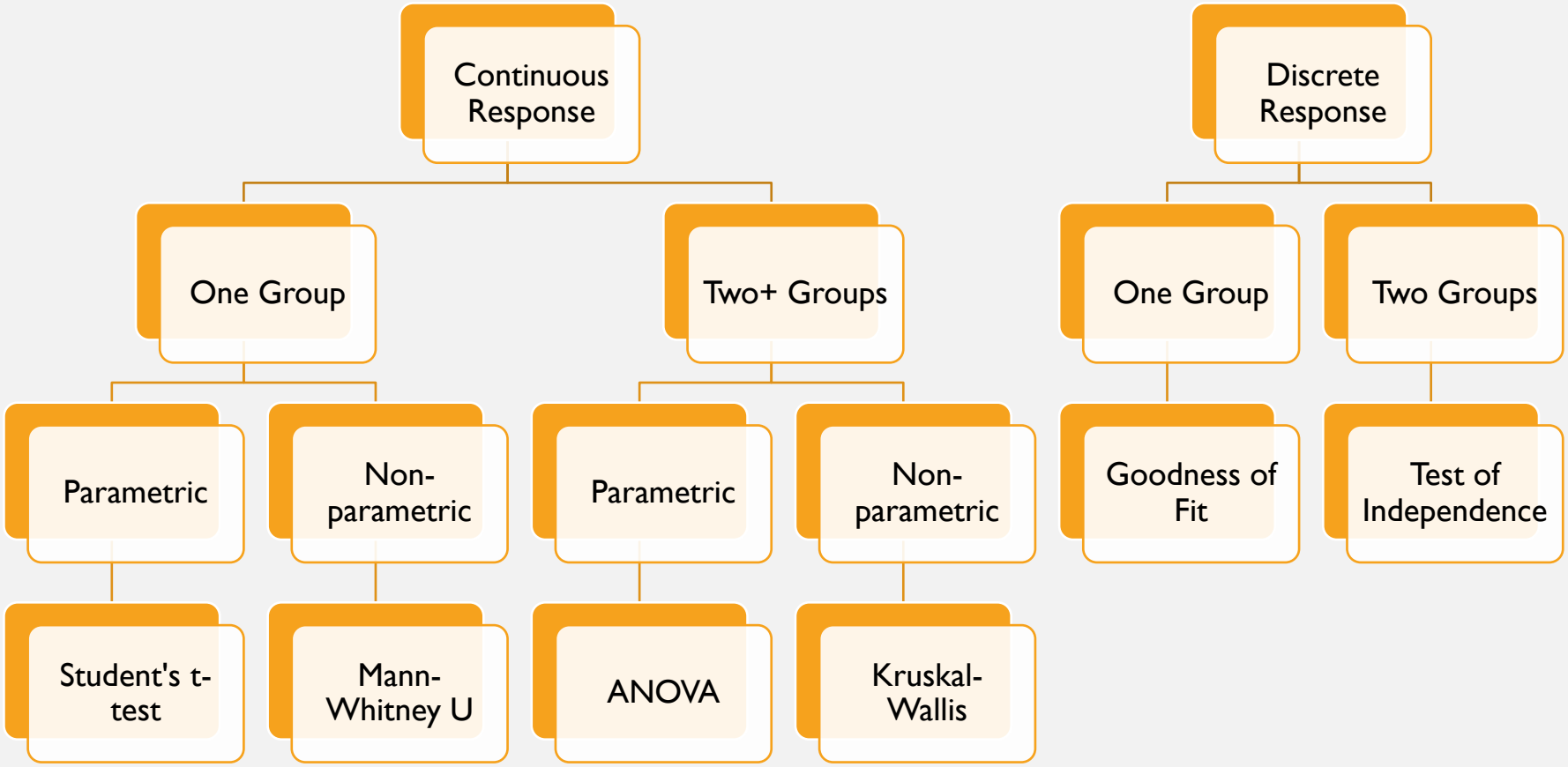
COMMON ANALYSIS METHODS: COMPARING MEANS



COMMON ANALYSIS METHODS: MULTIPLE COMPARISONS

- Hypothesis testing is not an error-free process.
- More tests on the same data = more type I errors (aka "false positives")
  - Example: Compare expression of 3226 genes between two mutational types (BRCA1 & BRCA2)
- To account for this, most methods "adjust" the p-value.

So what can we do in these cases?

Control the familywise error rate

- **Familywise error rate** = proportion of all tests that yield a false positive
- Bonferroni correction: p-value x number of tests
- This method is "harsh" in that they increase type II error (false negative) rates

Control the false discovery rate

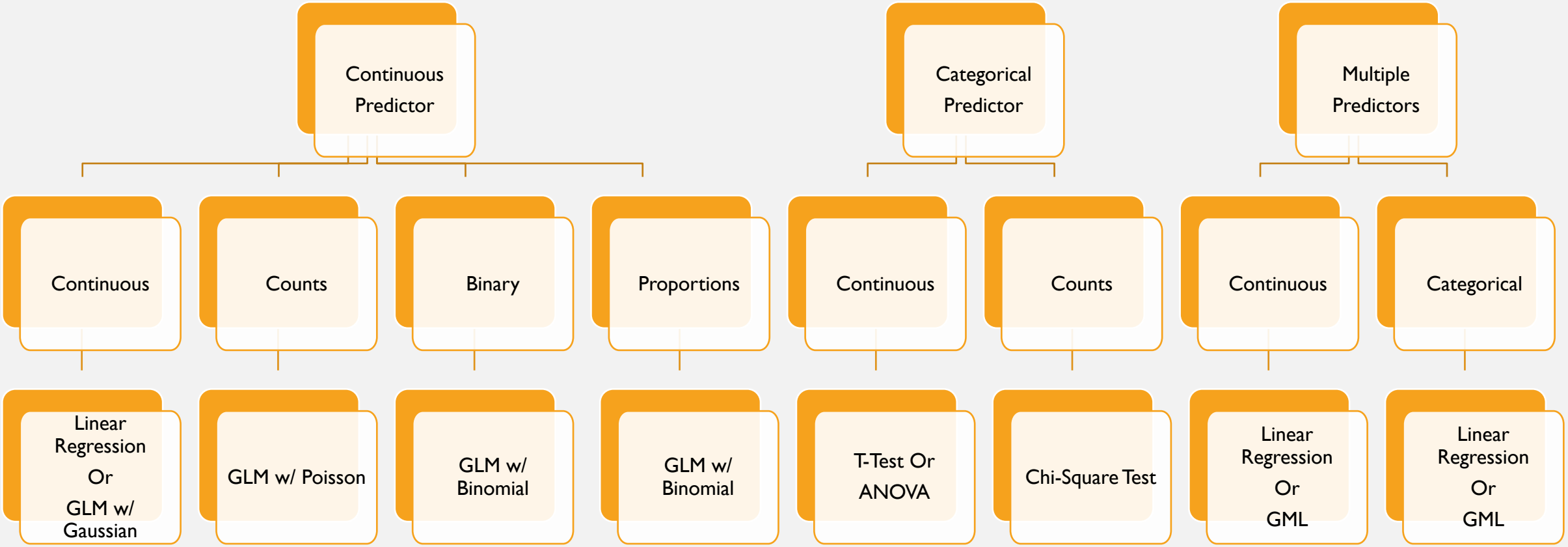
- **False discovery rate** = proportion of all significant tests that yield a false positive
- Benjamini-Hochberg (BH or FDR)

COMMON ANALYSIS METHODS: MULTIPLE COMPARISONS

ACTIVITY 3: MULTIPLE COMPARISONS

- Hands-on multiple comparisons analysis in R

CHOOSING AN APPROPRIATE TEST



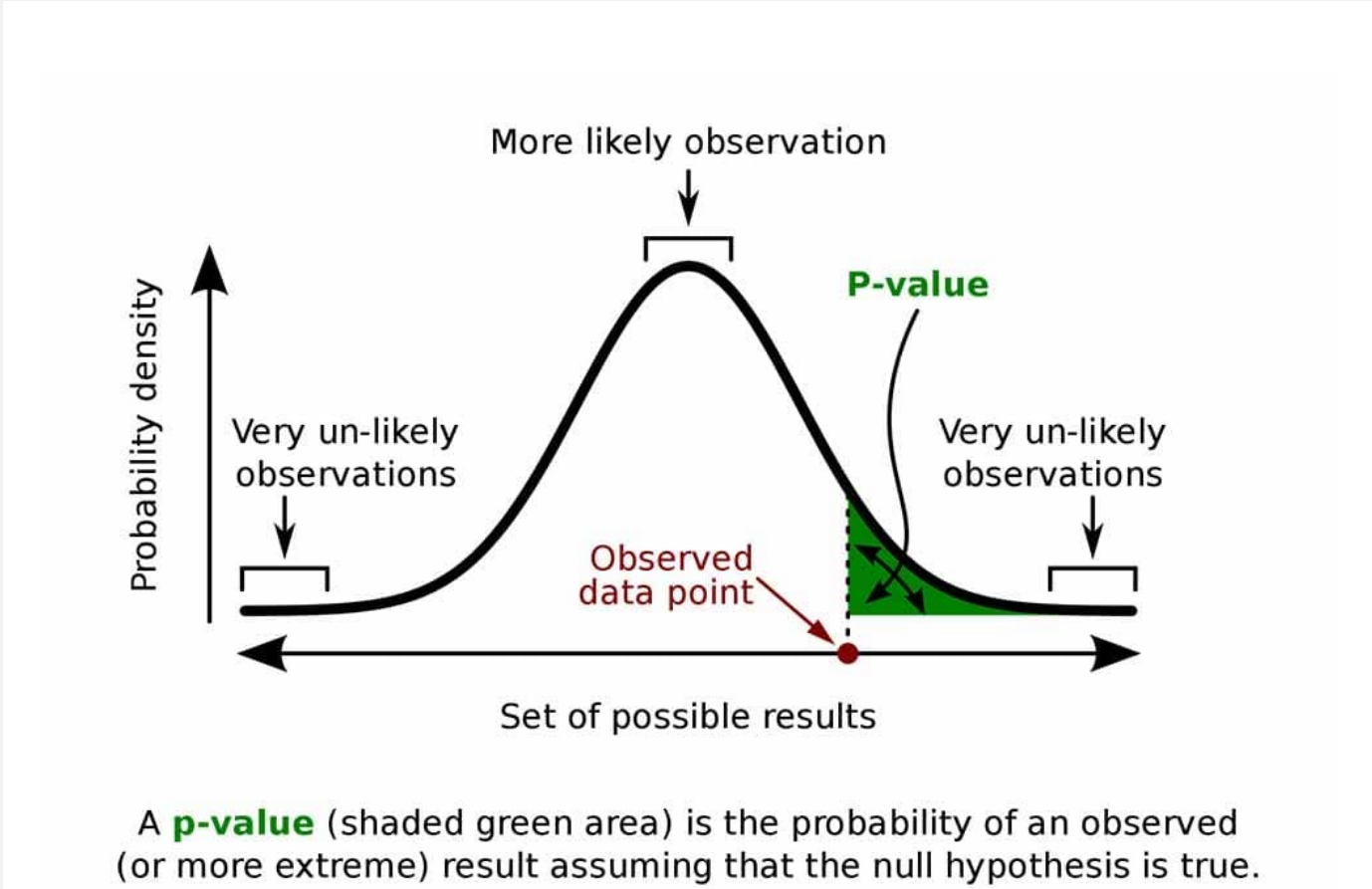
INTERPRETATION AND DATA VISUALIZATION

TYPES OF STATISTICAL ERROR

	True	**False**
Accept H_0	✓	Type II Error "False Negative"
Reject H_0	Type I Error "False Positive"	✓

WHAT IS A SIGNIFICANCE VALUE?

- **p-value** = what is the probability of observing a particular test statistic value given a particular distribution?
- Why is 0.05 commonly used as the threshold for statistical significance?
  - 1/20 chance of false positive
  - Convention



MEASURES OF EFFECT: DIRECTION AND MAGNITUDE

- Where **significance** tells us how likely it is that results are due to chance, measures of effect help us understand the **magnitude and direction** of differences.

J Grad Med Educ. 2012 Sep; 4(3): 279–282.
doi: 10.4300/JGME-D-12-00156.1
PMCID: PMC3444174
PMID: 23997866

Using Effect Size—or Why the *P* Value Is Not Enough

Gail M. Sullivan, MD, MPH and Richard Feinn, PhD

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Statistical significance is the least interesting thing about the results. You should describe the results in terms of measures of magnitude –not just, does a treatment affect people, but how much does it affect them.

-Gene V. Glass[1]

The primary product of a research inquiry is one or more measures of effect size, not P values.

-Jacob Cohen[2]

PRINCIPLES OF DATA VISUALIZATION

Color

Monochromatic, contrasting, complementary

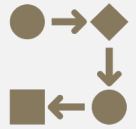
Colorblind friendly palettes

Keep it simple

Don't show too much data in one figure.

Keep it honest

Avoid confusing scales on axes.



Be clear

Decide exactly what you want to show and show **only** that.

Remain consistent.

Know your audience.

VISUALIZATION TECHNIQUES FOR GENOMICS & TRANSCRIPTOMICS

- Sequence Analysis
  - Tracks
    - UCSC Genome Browser/IGV
    - Circular maps
- Annotation
- Expression Profiles
  - Heat maps
- Gene Function
  - Gene Ontology (GO) https://geneontology.org/
- Molecular Pathways
  - Network maps

ACTIVITY 4: DATA VISUALIZATION

- Design and create visualization with real genomic data
- Group discussion on best practices and interpretation

ETHICAL CONSIDERATIONS AND CHALLENGES

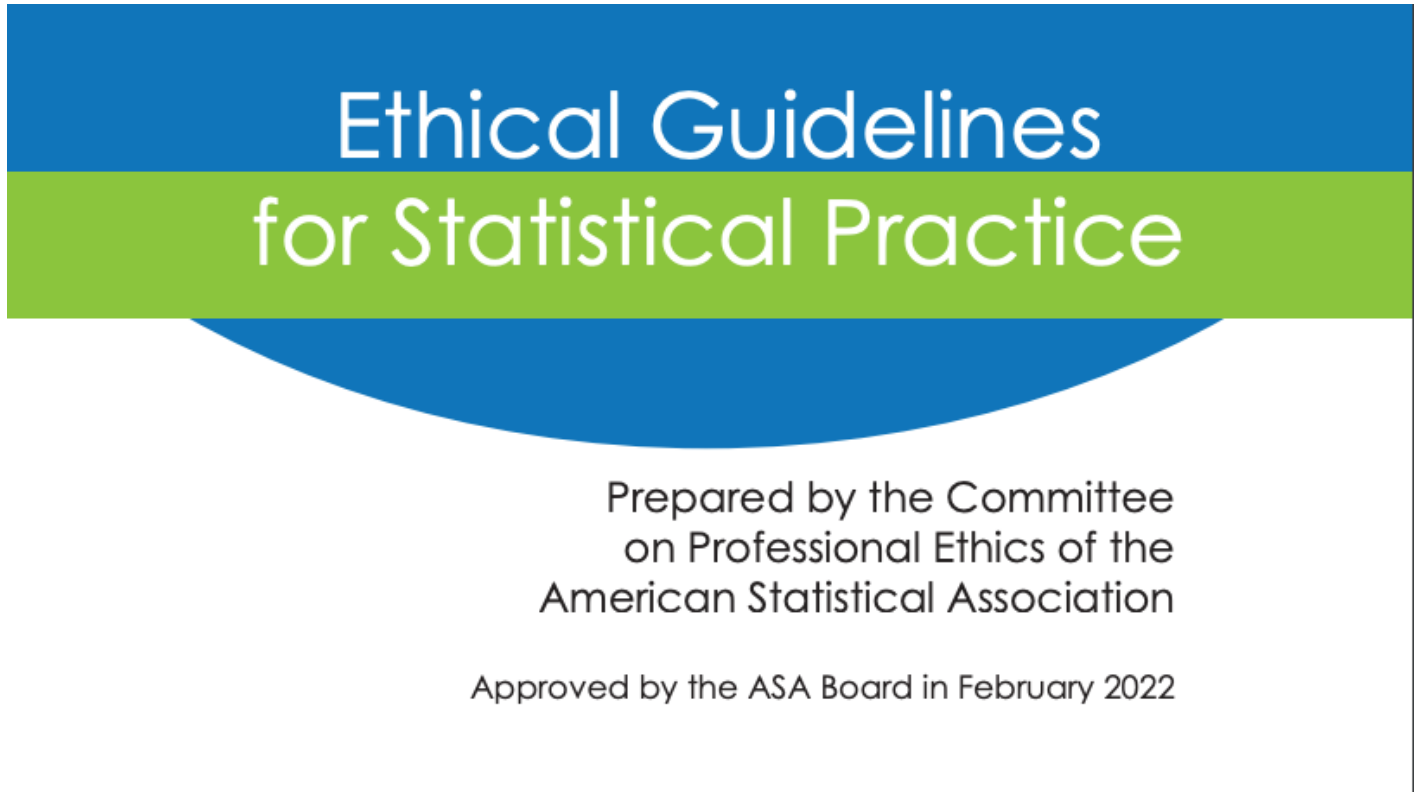
CHALLENGES AND LIMITATIONS

- Data Quality
- Interdisciplinary Collaboration
- Development & Optimization
- Education & Training
- Ethics & Communication

ETHICS OF HANDLING AND ANALYZING BIOLOGICAL DATA

- Ethical considerations are always important in science and statistics, especially when the data you are analyzing will be used to make individual and/or public health decisions.

AMERICAN STATISTICAL ASSOCIATION ETHICAL GUIDELINES



ACTIVITY 5: ETHICAL DILEMMAS

- Case study and group discussions

WRAP-UP AND Q&A

KEY TAKEAWAYS

- Statistics is one tool that computational biologist use to identify patterns in biological data and rigorously test hypotheses.
- It's important and beneficial to begin a project with statistics in mind.
- Use appropriate techniques to explore and improve the quality of data.
- Similarly, use appropriate statistical tests for the experimental design and data at hand.
- Careful interpretation and visualization and key to good scientific communication.
- As someone who handles data and analyses, you have ethical responsibilities to your colleagues, the scientific community, and society at large.

QUESTIONS?

Thank you!