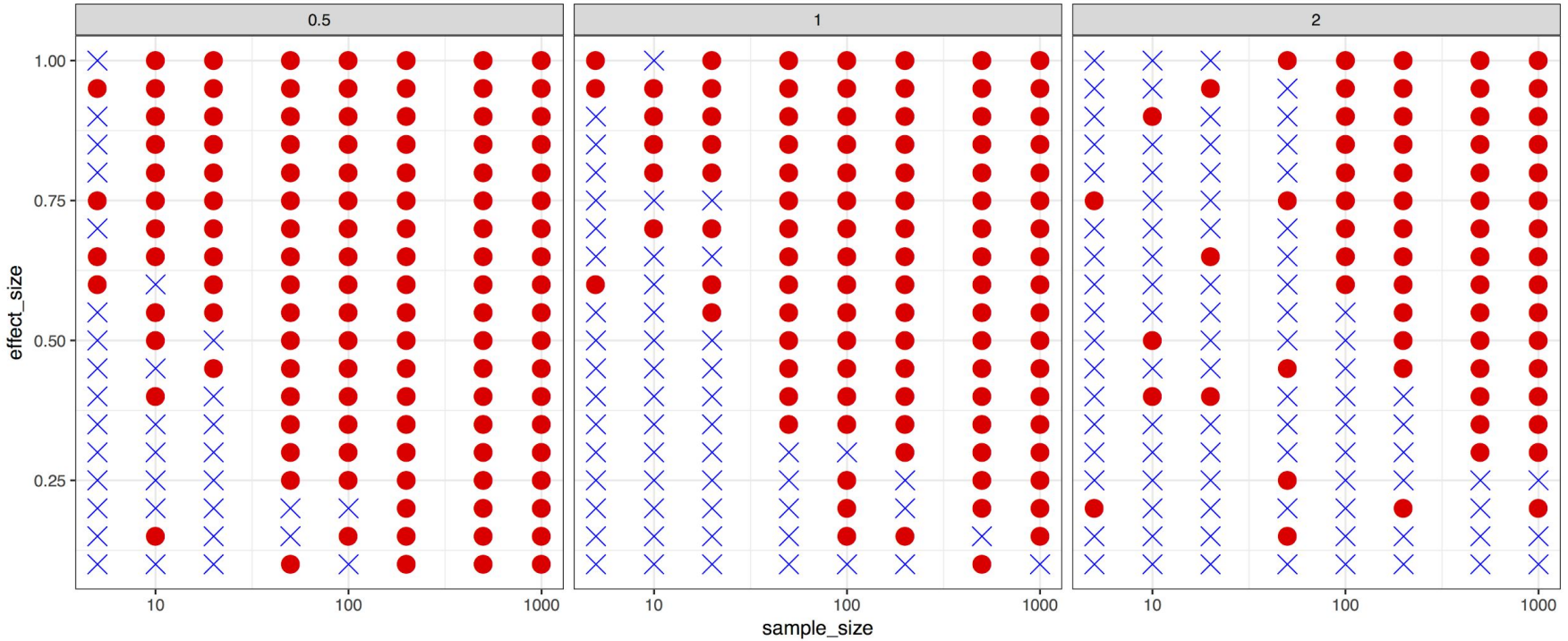
Day 04

Statistical power

- Statistical power
- Dependence on sample size, effect size, and significance threshold

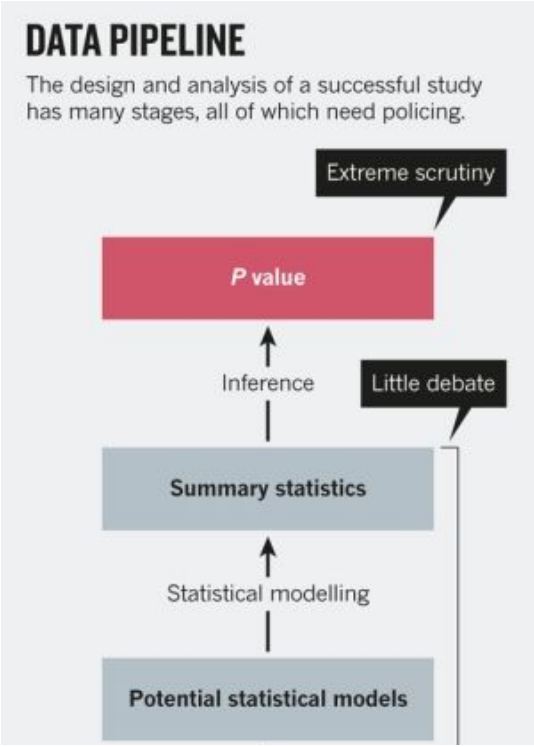
P-value

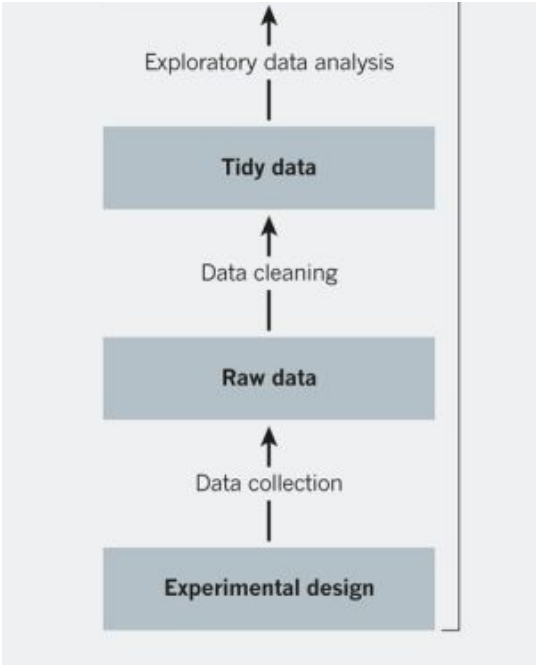
- P-values are dependent on: sample_size, effect_size, within-group variance



P-value

P values are just the tip of the iceberg!



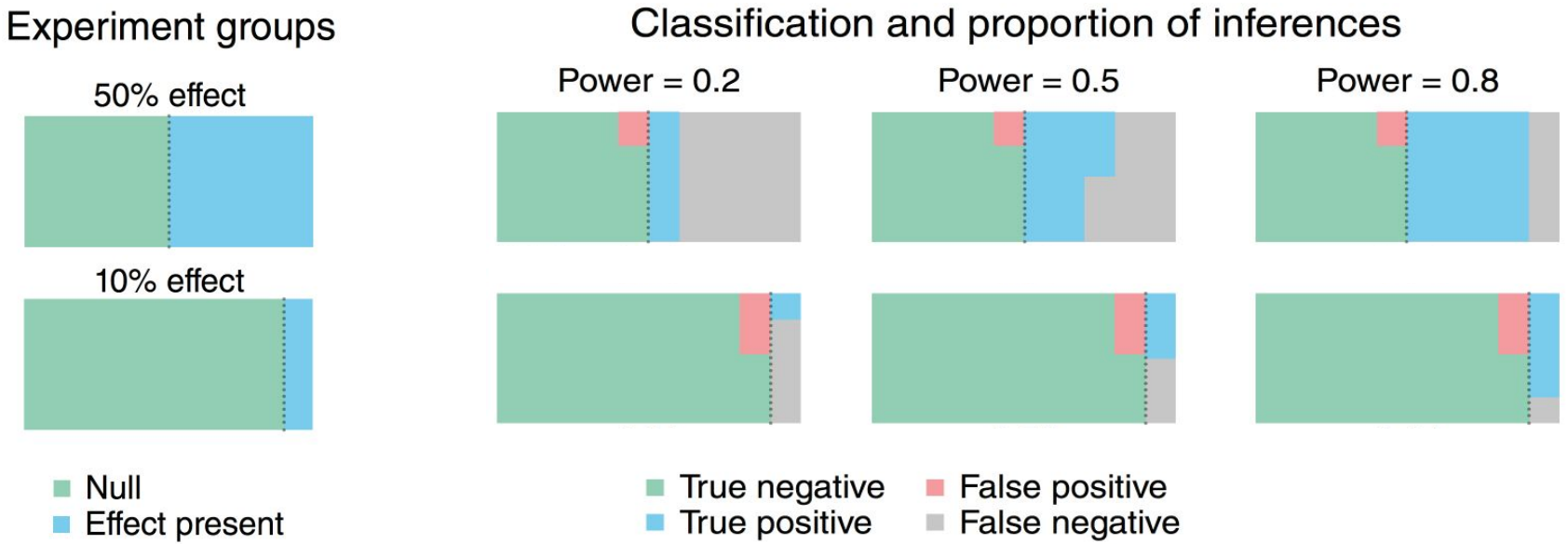


JT Leek, RD Peng http://www.nature.com/news/statistics-p-values-are-just-the-tip-of-the-iceberg-1.17412

Statistical power of a study

Probability that it can distinguish an effect of a given size from random chance

Power = True positive rate = Sensitivity = Recall

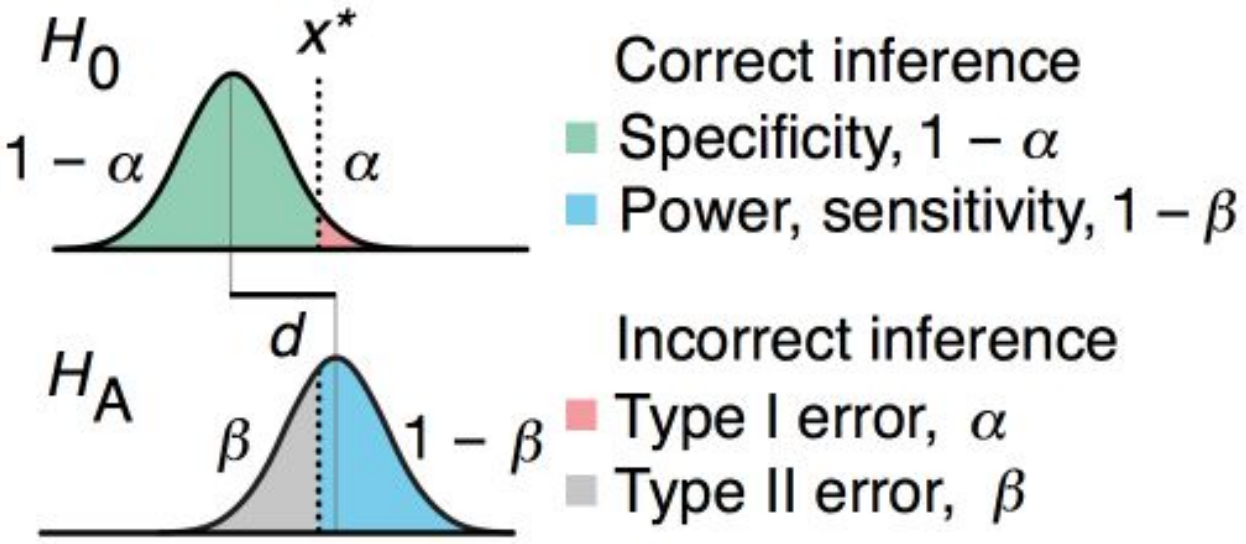


Most studies are underpowered ⟶ Waste of resources & Unethical

http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power

Null hypothesis



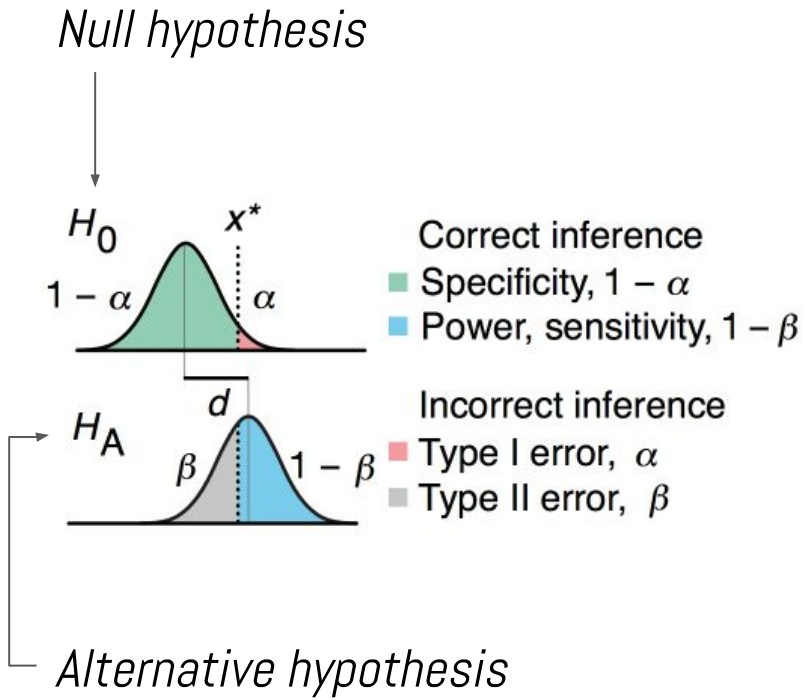
Alternative hypothesis

http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power

The power is the probability that the test correctly rejects the null hypothesis (H_0) when a specific alternative hypothesis (H_1) is true.

- Pr(reject H_0 | H_1 is true)
- H_1 has to be specific (cannot just be negation of H_0)
- The probability that it will yield a statistically significant outcome.

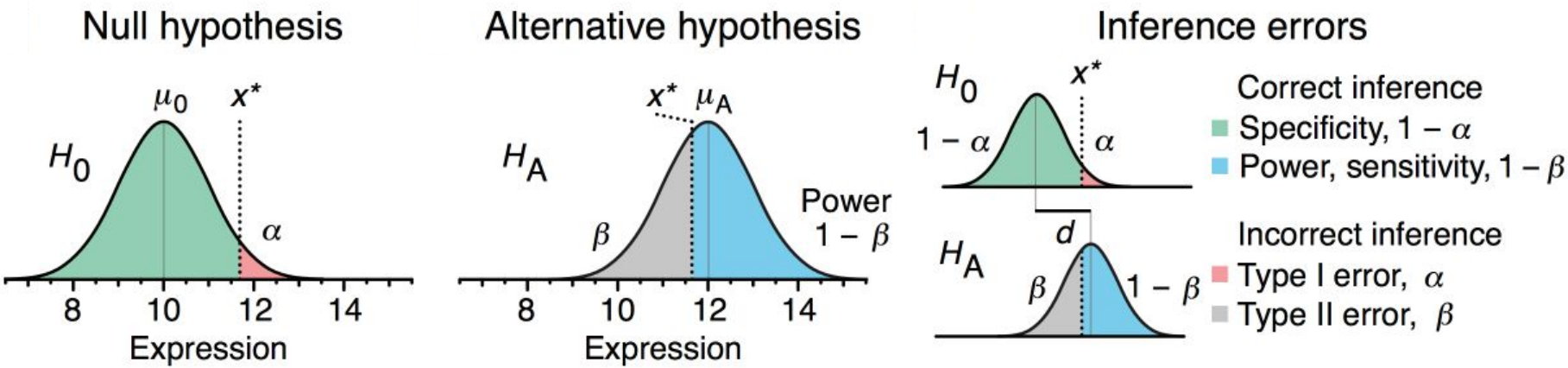


Power = $1 - \beta$

As power increases ⟶ Probability of making type II error (β) decreases.

http://www.nature.com/doifinder/10.1038/nmeth.2738

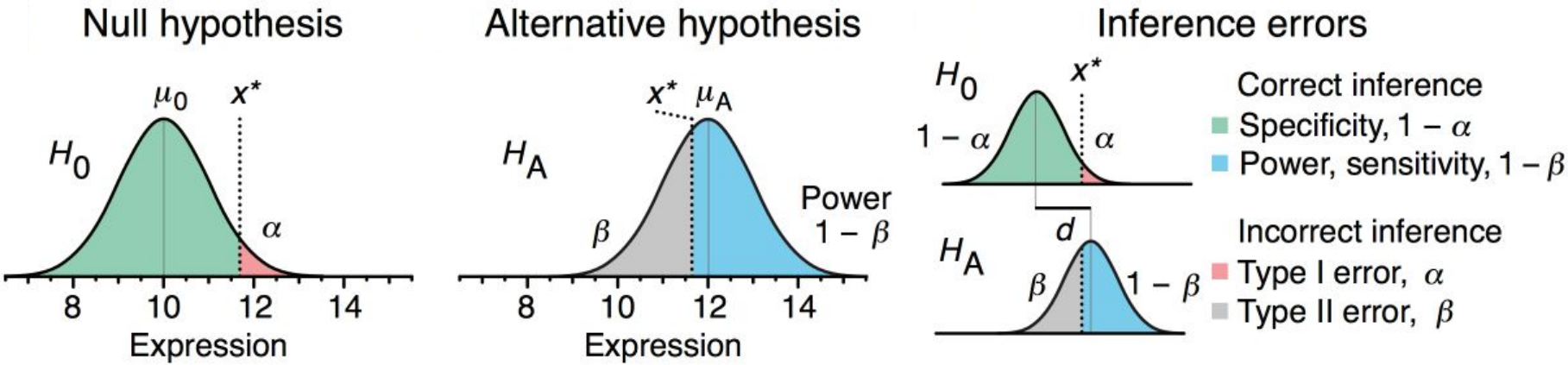
Statistical power



- Values sampled from $H_A < x^*$ do not trigger rejection of H_0 and occur at a rate β.
- Power (sensitivity; TRP) = 1 – β (blue area).
- Good to have low α (FPR) & low β (FNR), but:
  - The α and β rates are inversely related: ↓α → ↑β (& reduces power).

http://www.nature.com/doifinder/10.1038/nmeth.2738

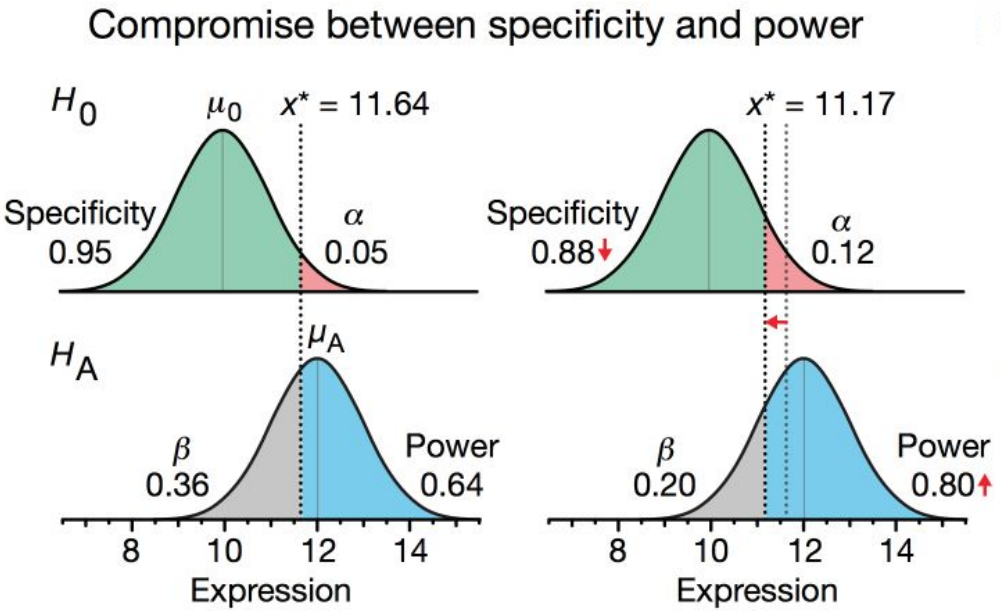
Statistical power

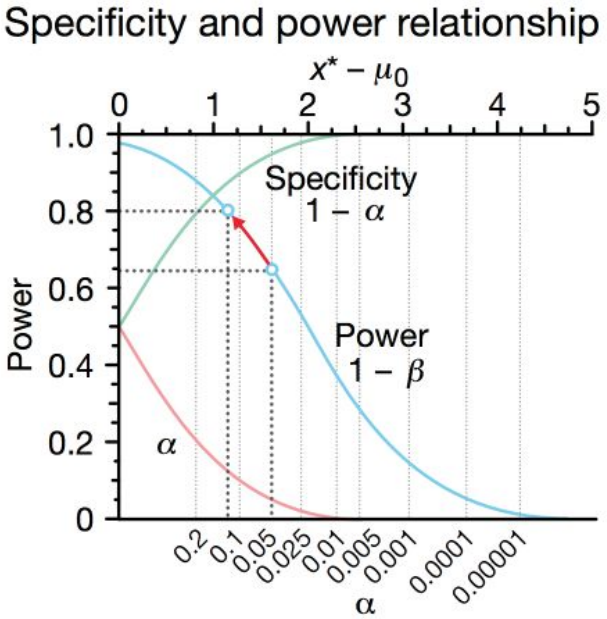


- Typically, α < β: consequences of FP (in an extreme case, a retracted paper) are more serious than those of FN (a missed opportunity to publish).
- But, the balance between α and β depends on the objectives:
  - If FP are subject to another round of testing but FN are discarded, β should be kept low.

http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power

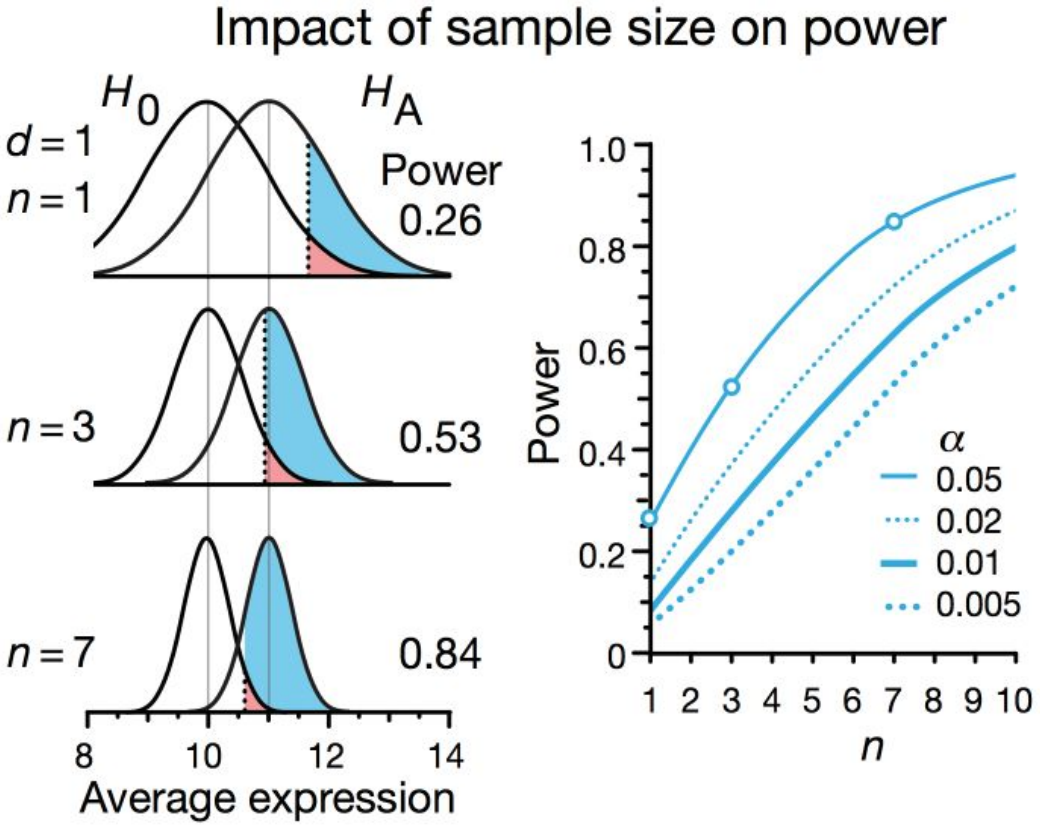




- Decreasing specificity (TNR) increases power (TPR)
- Can we improve our chance to detect increased expression from H_A (increase power) without compromising α (increasing FP)?

http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power

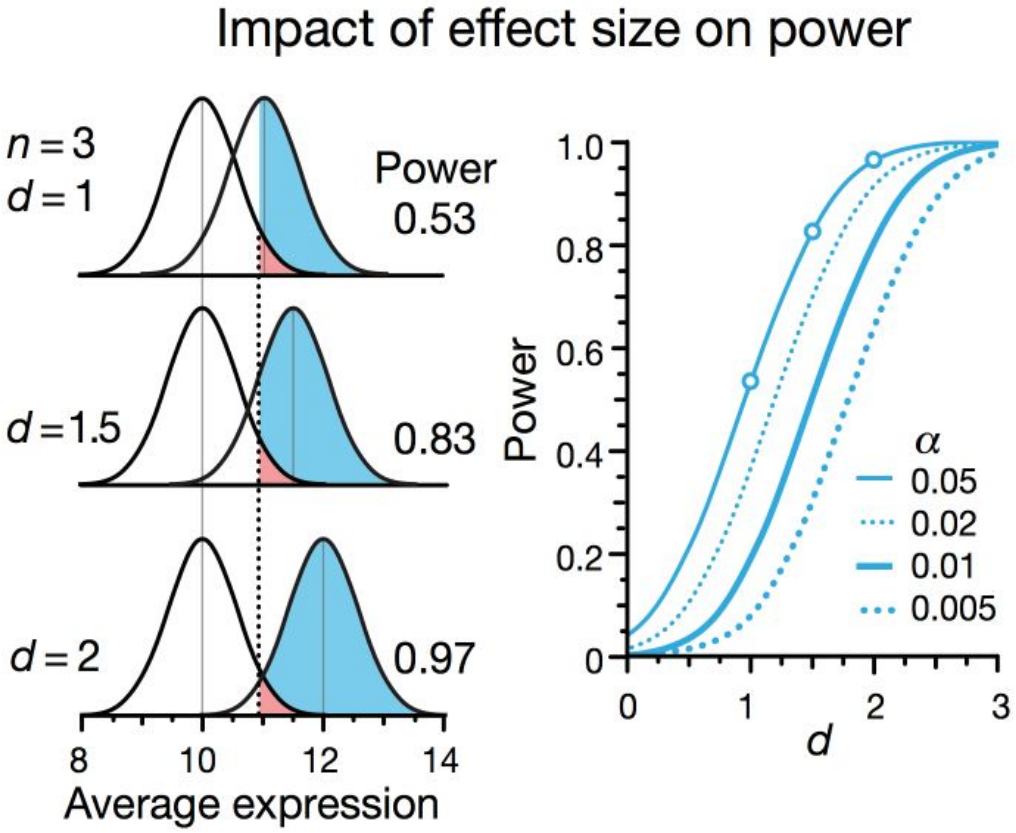


Control experimental conditions (e.g. using genetically identical orgs under lab conditions; adding precise amount of a drug) to reduce the variation b/w samples & compensate to some extent for small sample sizes.

In practice, because we estimate population σ from the samples, power is decreased and we need a slightly larger sample size to achieve the desired power.

http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power



http://www.nature.com/doifinder/10.1038/nmeth.2738

Statistical power

Power depends on:

- Statistical significance criterion: lesser conservative test (larger significance criterion) → more power
- Sample size: collecting more data → easier to detect small effects; relates to the efficiency of a given testing procedure, experimental design, or an estimator (sample size required for a given power)
- Size of the effect: larger the effect, easier it is to detect; (std. effect size better)

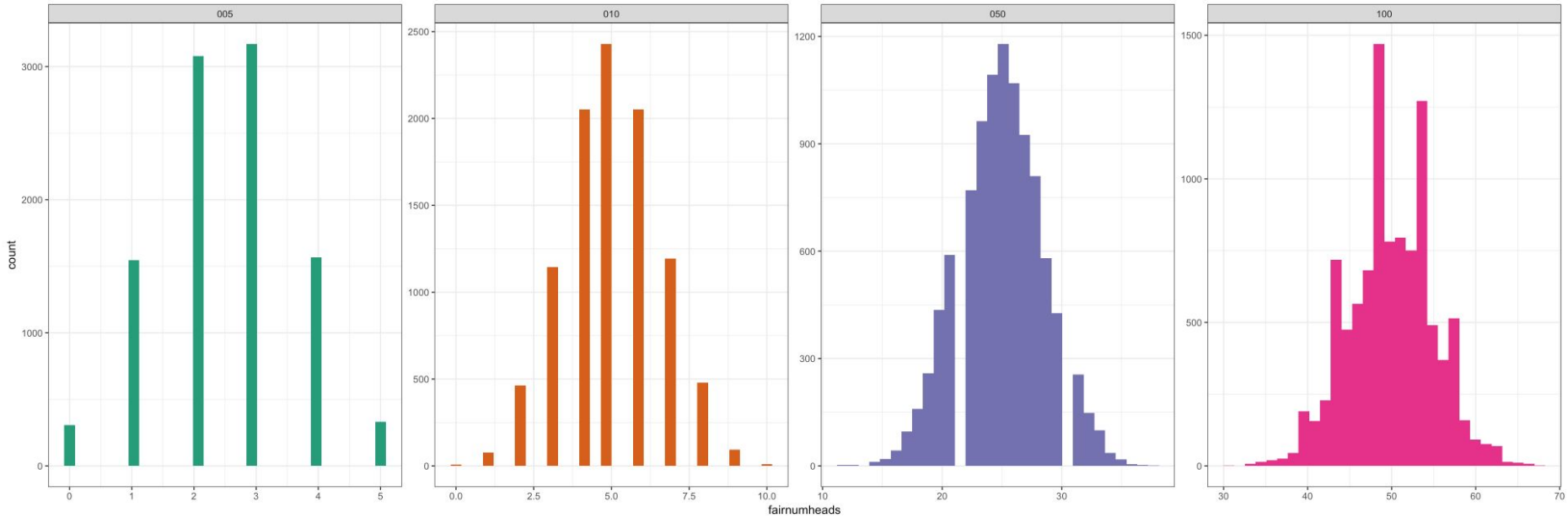
- Measurement error: counting cells vs. estimating level of fatigue/depression
- Experimental design: e.g. in a two-sample setting, optimal to have equal number

Statistical power

Let's examine some code to generate a power curve to detect unfair coins:

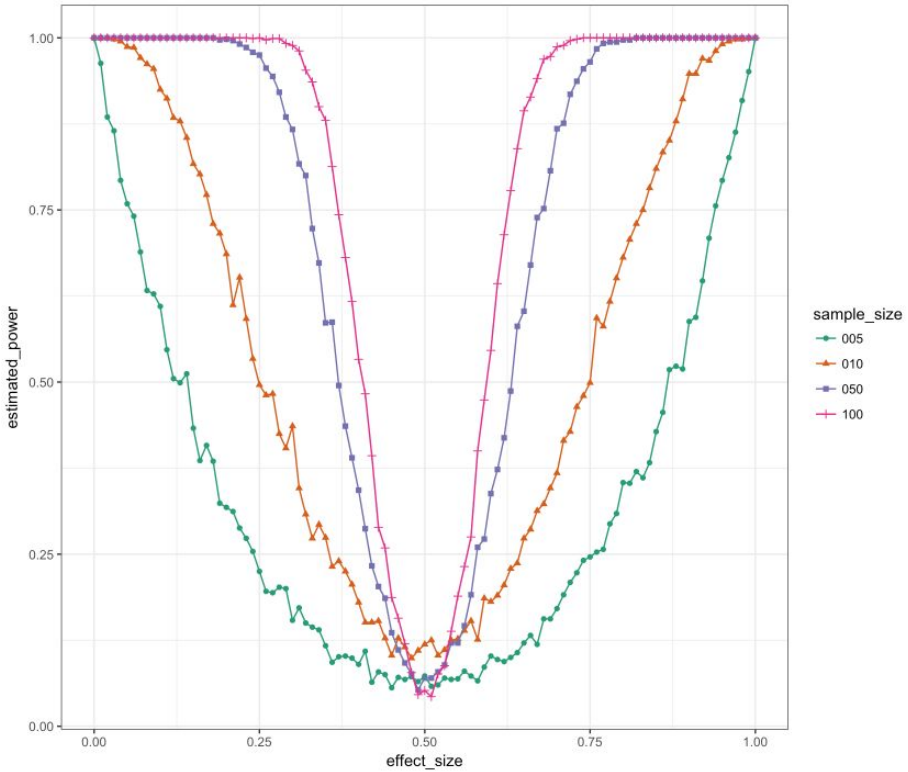
- You are given a coin and asked to detect if it is biased.
- Experiment: Flip the coin num_flips and take a call.
- Establish the null hypothesis (num_permutations = 10,000) for a given num_flips (sample_size)
- For a given bias (effect_size), find out how many times does an experiment like the one above can reject the null hypothesis.

Statistical power



Null distibutions for different sample sizes

Statistical power



Power curves for different sample sizes

Statistical power

Balancing sample size, effect size, and power is critical to good study design.

- First, set the values of type I error (α) and power ($1 - \beta$) to be statistically adequate:
  - Traditionally 0.05 and 0.80, respectively.
- Then determine sample size (n) on the basis of the smallest effect we wish to measure.
  - If the required sample size is too large → may need to reassess objectives or more tightly control the experimental conditions to reduce the variance.
- When the power is low, only large effects can be detected, and negative results cannot be reliably interpreted.

Sample size

- Clinical research (behavioral or drug treatments):
  - Need enough participants to represent all subtypes for which treatment might be used.
  - Some issues: lack reliable methods for diagnosis.
  - Rough rule of thumb: at least 100 people.
    - The actual number needed to find a valid effect depends on a range of factors, including the magnitude and frequency of the effect in the general population.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/

Sample size

- Brain imaging studies:
  - Historically included 20 or fewer participants. In the past 10 years, closer to 100 participants.
  - Studies that aim to trace developmental trajectories should also track the same few individuals over time, scanning their brains at regular intervals, rather than examining a cross-section of people of different ages at different sites.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/

Sample size

- Genetic studies (large no. of variants/genes, each making a small contribution):
  - Rare variants in coding regions: order of thousands of people.
  - Risk variants across the whole-genome: tens of thousands of individuals.
    - Millions of statistical tests, one per variant → increases FPR.
  - GWAS: hundreds of thousands of individuals
    - Common gene variants that contribute to the risk of a condition.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/

Sample size

- Preclinical research:
  - Underpowered animal studies for decades (cost and ethical issues).
  - Make up for their low numbers by analyzing a large number of cells or other samples from each animal → 'pseudoreplication.'
  - Can control lab animals' diets, ages and housing conditions, and scale doses or treatments by weight → sample sizes on the order of 10 animals to be acceptable. Should ≥15 per group to identify important biological effects.
  - In the past few years, push for larger numbers in animal studies.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/

Sample size

- Biomarker studies (physiological characteristics, such as patterns of eye movements, brain waves or activity, or blood chemistry):
  - Candidate biomarkers have often failed in subsequent studies.
  - Must draw samples from at least 100 individuals.
  - Clinical trials of biomarkers designed to flag people with disease → ≥ 1,000 participants. Researchers should also replicate the efficacy of a biomarker in an independent sample.
  - Some scientists are designing biomarker studies of thousands of participants that combine data from behavioral, imaging and genetic studies.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/

Sample size

- Field trials:
  - Variables that are hard to control, and so must include hundreds of individuals to yield meaningful results.
  - Needs more than an appropriate number of participants.
    - Representative mix of sexes and ages.

https://www.spectrumnews.org/news/studies-size-matters-let-us-count-ways/