

Lecture 41 Monte Carlo Simulation, Bootstrapping And Permutation Test

BIO210 Biostatistics

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LIFE SCIENCES

A Little History About Monte Carlo Simulations

Stanislaw Ulam



John von Neumann



ENIAC



Code name: Monte Carlo

https://en.wikipedia.org/wiki/Monte_Carlo_method

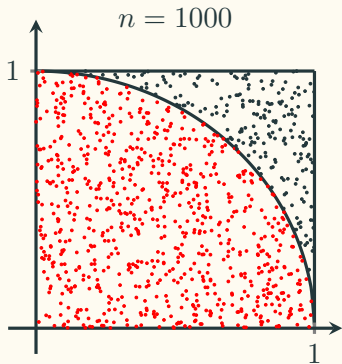
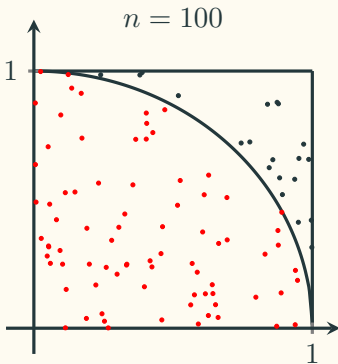
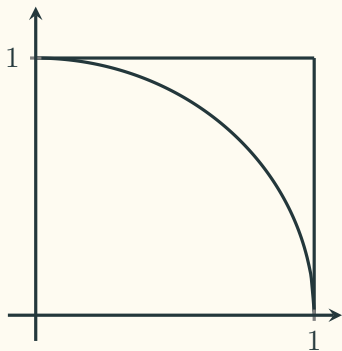
Monte Carlo Simulations

Casino de Monte-Carlo, picture taken on 26 Dec 2017.



A Monte Carlo Simulation To Calculate π

- **Monte Carlo Simulation:** a method of solving deterministic problems using a probabilistic analog.
 - An example to calculate π using Monte Carlo Simulation.



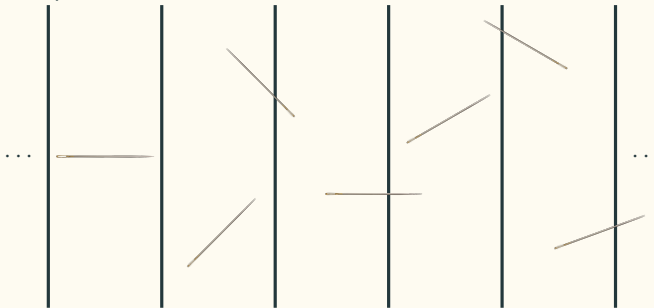
A Monte Carlo Simulation To Calculate π

Number of dots	Estimated π
10	2.0
100	3.0
1,000	3.124
10,000	3.1276
100,000	3.14112
1,000,000	3.141772
10,000,000	3.14163332
100,000,000	3.141831323

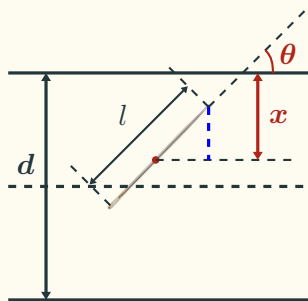
Buffon's Needle



- First Posed by Georges-Louis Leclerc, Comte de Buffon in 1733, and reproduced with solution in 1777.
- Suppose we have a floor made of parallel strips of wood, each the same width, and we drop a needle onto the floor. What is the probability that the needle will lie across a line between two strips?



Buffon's Needle



We have two random variables: X , Θ to describe the position of the needle:

$$0 \leq x \leq \frac{d}{2}$$

$$0 \leq \theta \leq \frac{\pi}{2}$$

Marginal PDF of X and Θ : $f_X(x) = \frac{2}{d}$, $f_\Theta(\theta) = \frac{2}{\pi}$

Joint PDF of X and Θ : $f_{X,\Theta}(x, \theta) = f_X(x)f_\Theta(\theta) = \frac{4}{\pi d}$

$A = \{ \text{the needle lies across a line between two strips} \}$

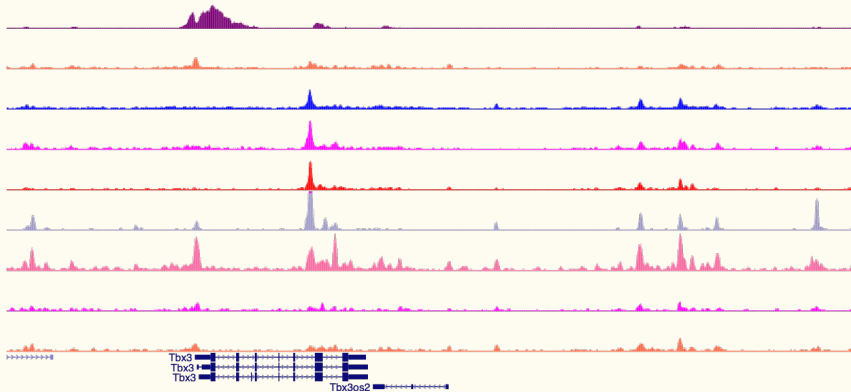
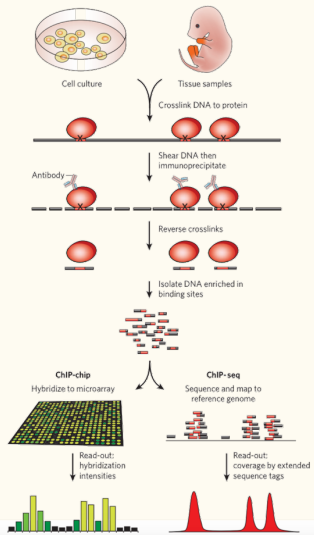
Event $A \Leftrightarrow$ red is shorter than blue $\Leftrightarrow 0 \leq x \leq \frac{l \cdot \sin \theta}{2}$

$$\begin{aligned} \mathbb{P}(A) &= \int_0^{\frac{\pi}{2}} \int_0^{\frac{l \cdot \sin \theta}{2}} f_{X,\Theta}(x, \theta) dx d\theta = \int_0^{\frac{\pi}{2}} \int_0^{\frac{l \cdot \sin \theta}{2}} \frac{4}{\pi d} dx d\theta \\ &= \int_0^{\frac{\pi}{2}} \left[\frac{4}{\pi d} \cdot x \right]_0^{\frac{l \cdot \sin \theta}{2}} d\theta = \int_0^{\frac{\pi}{2}} \frac{2l \cdot \sin \theta}{\pi d} d\theta = \frac{2l}{\pi d} \int_0^{\frac{\pi}{2}} \sin \theta d\theta = \frac{2l}{\pi d} \end{aligned}$$

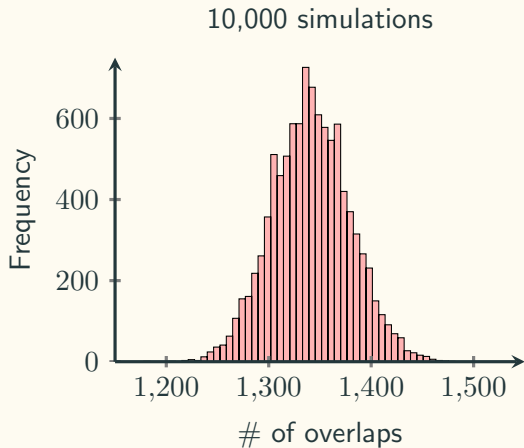
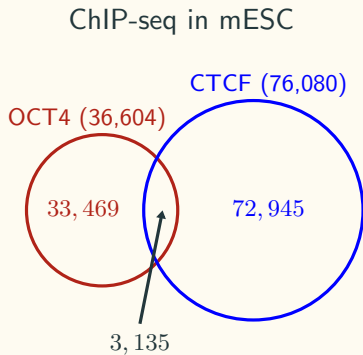
Buffon's Needle - Monte Carlo simulations to estimate π

Number of needles	Estimated π
10	3.333333
100	3.125
1,000	3.333333
10,000	3.22684737
100,000	3.13293023
1,000,000	3.14433768
10,000,000	3.14071042
100,000,000	3.14148011

Overlap of Transcription Factors



Overlap of OCT4 And CTCF In mESC



Bootstrapping

- Point/interval estimation of mean/median *etc.* from a population with very little information.
- How? - Bootstrapping methods.



{
parametric bootstraps
nonparametric bootstraps
weighted bootstraps
... ..

Steps of Bootstrapping

1. Replace the population with the sample
2. Sample **with replacement** B times. B should be large, say 1,000
3. Compute sample means/medians each time, M_i
4. Obtain the approximate distribution of the sample mean/median

Bootstrapping Example

Original sample ($n = 25$)

16.66	13.58	2.27	9.96	13.11
6.4	11.33	10.54	10.02	9.13
12.17	16.02	5.17	15.14	11.14
12.23	4.32	10.68	17.42	4.6
0.11	1.28	11.33	21.92	15.62

sampling
with replacement
with the same sample
size $n = 25$

Bootstrapping sample #1 ($n = 25$)

15.62	15.62	17.42	5.17	11.33
2.27	10.02	12.23	15.14	15.62
12.23	11.33	11.33	1.28	12.17
11.33	16.02	4.32	5.17	16.66
11.33	10.68	12.23	5.17	10.02

Bootstrapping sample #2 ($n = 25$)

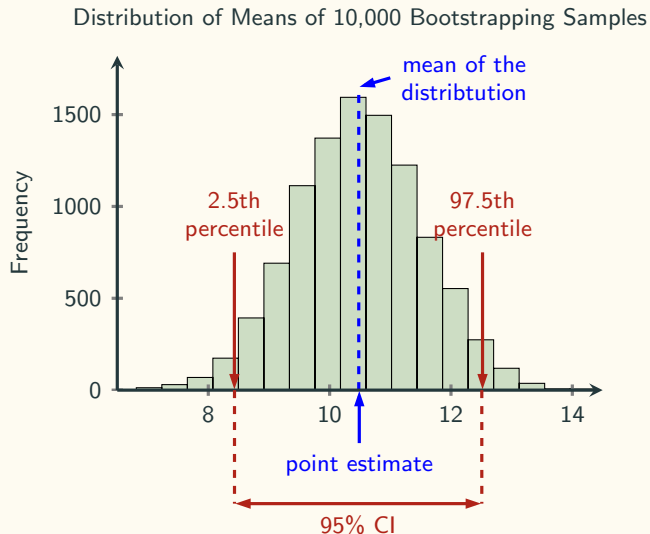
6.4	21.92	12.23	13.58	9.13
17.42	9.13	6.4	21.92	13.58
16.66	10.54	15.62	9.13	9.13
11.14	10.02	0.11	11.14	4.32
0.11	9.13	17.42	10.02	21.92

... ..

Bootstrapping sample #10,000 ($n = 25$)

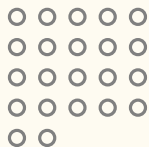
21.92	15.14	17.42	16.02	4.32
10.54	15.14	0.11	16.66	12.17
15.62	13.11	15.62	11.33	15.62
6.4	15.14	15.62	9.13	15.14
16.66	12.23	2.27	12.17	2.27

Bootstrapping - Point And Interval Estimation



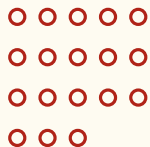
Permutation Tests

Control (X)



$$\bar{x} = 13.18$$

Treatment (Y)



$$\bar{y} = 9.50$$

$$H_0 : \mu_X - \mu_Y = 0$$

$$H_1 : \mu_X - \mu_Y \neq 0$$

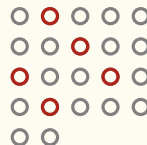
$$\text{Test statistic: } \bar{x} - \bar{y} = 3.68$$

How to assess statistic significance?

Using permutation
(shuffle the group labels):

$$\binom{40}{22} = 113,380,261,800$$

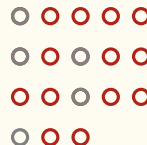
Control (X)



Permutation #1

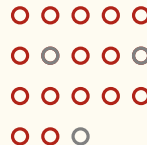
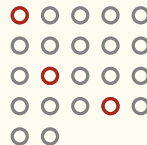
$$d_1 = \bar{x}_1 - \bar{y}_1$$

Treatment (Y)



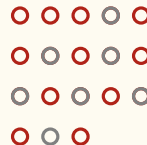
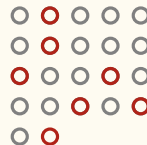
Permutation #1

$$d_2 = \bar{x}_2 - \bar{y}_2$$



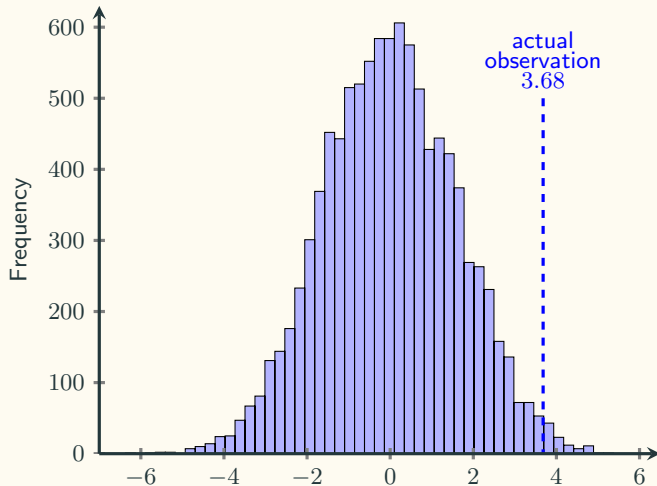
Permutation #1

$$d_3 = \bar{x}_3 - \bar{y}_3$$



Permutation Tests - p -value Calculation

Distribution of 10,000 Differences (d_1 to d_{10000})



p -value: probability of seeing the observation or more extreme given that H_0 is true!

$$p_{\text{one-sided}} = \frac{\# \text{ of simulations} \geq 3.68}{\text{total } \# \text{ of simulations}}$$

$$p_{\text{two-sided}} = 2 \times p_{\text{one-sided}}$$