#### Imperial College London

# Maximum Likelihood Estimation CMEE MSc

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# Schedule (amended)

10-14 Feb: Maximum Likelihood & Selected topics in Statistics

- 17 Feb (next Monday): Austin on gene drive
- 18-20 Feb: gene drive modelling & simulations
- 21 Feb: Bhavin

### MSc Project

Desk / computer based projects available

• Email us

#### Learning outcome

- Define random variables, probability distributions, expectations, and associated concepts
- Understand the principles of Maximum Likelihood Estimation
- Perform statistical modelling, hypothesis testing, and parameter estimation under the likelihood framework (by hand or with R)
- Develop your own likelihood models

 Appreciate Statistics, and start to believe that it is more than a subject <sup>©</sup>

# Introductory lecture

Probability vs Statistics

Why do we need Statistics?

### Example 0: German Tank Problem

- During WW2, the Allies wanted to know the number of tanks the German side had produced
- Two methods: conventional intelligence vs Statistics
- Statistical estimation made use of the serial numbers on those captured or destroyed tanks
- What is my best guess, if I spotted a tank with serial number #40?
  - Statistics says around 40

- If multiple tanks were spotted, then
- $\widehat{N} = (largest \ serial \ number \ spotted) * \left(1 + \frac{1}{number \ of \ tanks \ captured}\right) 1$
- "The largest serial number plus the average gap between observations"

If we look at the real data:

Month	Statistical estimate	Intelligence estimate	German records
Jun 1940	169	1000	122
Jun 1941	244	1550	271
Aug 1942	327	1550	342

https://www.theguardian.com/world/2006/jul/20/secondworldwar.tvandradio

Statistical models/estimations could be useful (Of course!)

### **Probability vs Statistics**

- A Probabilistic question:
  - Given a fair coin, what is the probability of tossing three heads in a row?

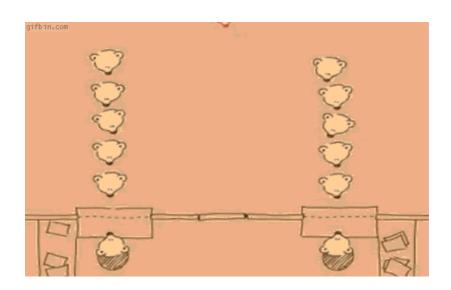
οccurrence of a certain event,
based on some (given) random

Λ Statistical question:
mechanisms.

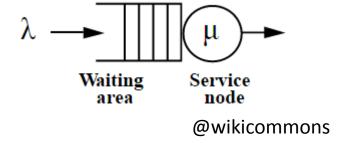
- A Statistical question:
  - I tossed three heads in a row, is the coin fair?

Given the observation, what inferences can we make about the underlying mechanism?

Queuing system in fast food shop



 Beer and nappies (and dad?) association...





- Wright-Fisher model
- If the current allele frequency is p, then the allele counts in the next generation due to drift will be binomially distributed with size 2N and prob p.
- For two populations with migration rate m, the mean population differentiation between them is  $F_{ST} \approx \frac{1}{1+4Nm}$

#### **EVOLUTION IN MENDELIAN POPULATIONS**

#### SEWALL WRIGHT University of Chicago, Chicago, Illinois

#### Received January 20, 1930

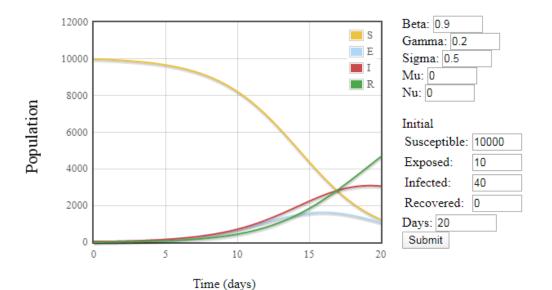
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heories of evolution	
ariation of gene frequency	
Simple Mendelian equilibrium	
Mutation pressure	
Migration pressure	
Selection pressure	
Equilibrium under selection	
Multiple allelomorphs	
Random variation of gene frequency	
Rate of decrease in heterozygosis	
The population number	
he distribution of gene frequencies and its immediate consequences.	
No mutation, migration or selection	
Nonrecurrent mutation	
Reversible recurrent mutation.	
Migration	
Irreversible recurrent mutation	-
Selection	
General formula	
The distribution curves	
The distribution curves	

• If I observed a certain amount of change in allele frequencies, what's my best guess of N?

• The data suggested  $F_{ST}=0.2$ . Can I rule out the nomigration scenario?

The use of epidemiological models to predict virus outbreak



$$\frac{dS}{dt} = \mu(N - S) - \beta \frac{SI}{N} - \nu S$$

$$\frac{dE}{dt} = \beta \frac{SI}{N} - (\mu + \sigma)E$$

$$\frac{dI}{dt} = \sigma E - (\mu + \gamma)I$$

$$\frac{dR}{dt} = \gamma I - \mu R + \nu S$$

$$N = S + E + I + R$$

Estimating  $R_0$  the basic reproductive number from infection data

Table 1: Best-case, central and worst-case estimates of 2019-nCoV human-to-human Ro compatible with either 4000 (top half of table) or 1000 (bottom half of table) total cases by 18/01/2020. Values of  $R_0 > 1$  represent self-sustaining human-to-human and are highlighted in red. Baseline estimates highlighted in bold.

Number of cases caused by zoonotic exposure	Assumed total number of cases by 18/01/2020	Best-case R <sub>0</sub>	Central (median) R <sub>0</sub>	Worst-case R <sub>0</sub>
40	4000	2.1	2.6	3.5
80	4000	1.8	2.2	2.7
120	4000	1.7	2.0	2.4
160	4000	1.6	1.8	2.2
200	4000	1.5	1.7	2.0
40	1000	1.4	1.9	2.7
80	1000	1.2	1.5	2.0
120	1000	1.1	1.3	1.7
160	1000	1.0	1.2	1.5
200	1000	0.9	1.1	1.3

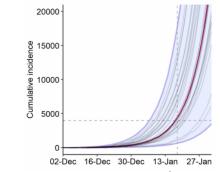


Figure 1: Illustration of estimation method for central estimate of Ro=2.6. Red curve represents median cumulative case numbers over time, calculated from 5000 simulated trajectories of the epidemic, assuming zoonotic exposure of 40 cases in December 2019 and the generation time and variability in infectiousness of SARS. The grey region indicates the 95 percentile range of trajectories - individual simulated epidemics (a random subset of which are shown as light grey curves) are highly variable, reflecting the random nature of disease transmission. Dotted lines indicate January 18th (vertical) and 4000 cumulative cases (horizontal).

Imai et al.

https://www.imperial.ac.uk/mrc-globalinfectious-disease-analysis/news--wuhan-

#### Statistical inference

- Point estimation
  - one-numbered estimate ("best guess")
- Interval estimation
  - 95% confidence interval

- Hypothesis testing
  - $-H_0$  vs  $H_1$
  - model selection

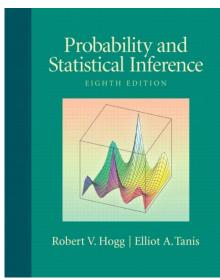
# Suggested readings

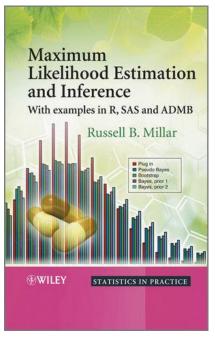
Hogg & Tanis, Probability and Statistical Inference.

 Millar, Maximum Likelihood Estimation and Inference.

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Crawley, The R Book.





"In war-time, truth is so precious that she should always be attended by a bodyguard of lies. " – Winston Churchill