# Al buio non si trova

# Biostatistics in the 21st century

Luiz Max Carvalho lmax.fgv@gmail.com

Available from: https://github.com/maxbiostat/presentations/



# Le dirò con due parole, chi son

#### Personal

- Born and raised in Petrópolis-RJ;
- Eldest of three kids;
- Married and father of two sassy girls;
- Mais Querido supporter.

#### Academic

- BSc in Microbiology & Immunology (UFRJ, 2012);
- PhD Evolutionary Biology (Edinburgh, 2018);
- Post doctoral researcher at ENSP/Fiocruz (2019);
- Lecturer (Assistant Professor) at EMAp since Jan/2020.

# E che faccio

#### Applications of Statistics/Mathematics

Applications in Epidemiology, (Molecular) Biology, Ecology, Psychology, Linguistics, etc.

# **Applied Statistics**

Markov Chain Monte Carlo, Model combination and selection, Statistical Phylogenetics.

# Junior colaborators (Or, you know, students) I

# Mentoring/Honours

- Yure Oliveira: "Bayesian consistency under the normalised power prior";
- Rodrigo Kalil: "Extending joint models".

# Junior colaborators (Or, you know, students) II

#### MSc

- Ezequiel Braga (MSc) "Principled Bayesian analysis under the normalised power prior";
- Eduardo Adame (MSc) "Exact MCMC methods for the normalised power prior";
- Iara Castro (MSc) "Using survival analysis to understand cancer treatment outcomes";
- Wellington Silva (MSc) "Adaptive truncation of infinite series: applications to Statistics";
- Igor Michels (MSc) "Calibration of Bayesian player-level models for Brazilian football".

# Junior colaborators (Or, you know, students) III

#### **PhD**

- Felipe Schardong (PhD) "Mathematical modelling of antimicrobial resistance";
- Atilio Pellegrino (PhD) "Model combination for epidemiological forecasting".

#### **Postdocs**

- Fernanda Valente: "Spatio-temporal modelling of dengue and its vectors";
- Rodrigo Alves: "Tree-valued stochastic processes".

# Problem I: efficiently utilising available information

# Loads of historical data: how to build informative priors?

Let  $y_0 = (y_{01}, \dots, y_{0n_0})$  and  $y = (y_1, \dots, y_n)$  be **historical** and **current** data, respectively.

#### Question: how do I build a prior that

- $\odot$  Uses information in  $y_0$  efficiently but also
- Does not lead to borrowing too much information when the data sets are not compatible?

Applications: clinical trials, quality control, policy-making.

# I got the power

#### Normalised power prior<sup>1</sup>

$$\tilde{p}(\theta, \eta \mid \boldsymbol{y}_0) := \frac{L_0(\boldsymbol{y}_0 \mid \theta)^{\eta} \pi_0(\theta \mid \psi) \pi_A(\eta \mid \phi)}{c(\eta; \psi, \phi)}$$

- ⊚ How pick  $\pi_A$  such that prediction error (say) is minimised?
- How to efficiently compute

$$c(\eta; \psi, \phi) = \int_{\Theta} L(y_0 \mid t)^{\eta} \pi(t \mid \psi) \, d\mu(t)$$

by leveraging its special properties as function of  $\eta$ ?

<sup>&</sup>lt;sup>1</sup>https://doi.org/10.1002/sim.9124

# Open problems

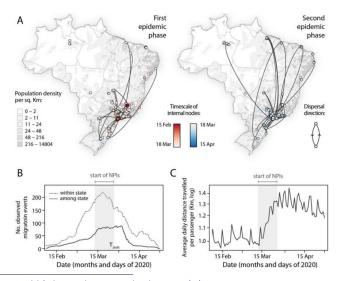
What happens to the posterior

$$p(\theta, \eta \mid \boldsymbol{y}_0, \boldsymbol{y}) \propto L(\boldsymbol{y} \mid \theta) \tilde{p}(\theta, \eta \mid \boldsymbol{y}_0),$$

- ⊚ in various asymptotic regimes (e.g.  $n \to \infty$  with  $n/n_0 = r$ )?
- ⊚ For finite  $(n, n_0)$  when  $dist(y_0, y) > \delta$ ?
- © Can we sample exactly from this doubly-intractable distribution?
- ⊚ How to pick  $\pi_A(\cdot | \phi)$ ?

# Problem II: dealing with huge complex data

#### Where did this virus come from?<sup>2</sup>



<sup>&</sup>lt;sup>2</sup>https://doi.org/10.1126/science.abd2161

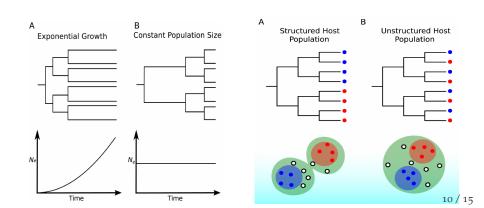
# Motivation

# Phylodynamics of fast-evolving viruses

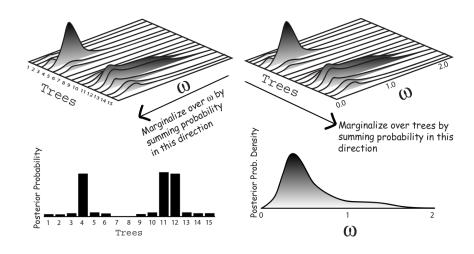
Inferring spatial and temporal dynamics from genomic data:

# Phylogenies\*!

\* plus complicated models

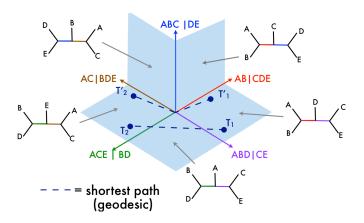


# The end product



# This place is weird..

# Traversing cubic complexes efficiently<sup>3</sup>



Applications: Molecular Epidemiology, Evolutionary Biology.

<sup>3</sup>https://youtu.be/h9bWRQ6aeKA

# Open problems in MCMC for phylogenies

#### Open problems:

- How can we construct more efficient proposals? How to exploit structure? Geometry!
- How to quantify exploration of the target? (Custom) Tools!
- Optimal scaling: what's the optimal acceptance probability?

# Take home

#### A light in the dark

Maths gives us methods with provable guarantees

#### Computational methods are key

Learn to program and learn Computational Statistics<sup>4</sup>

#### Maths at the service of Science

My research employs: combinatorics, probability theory, basic calculus, optimisation and classical **and** Bayesian Statistics.

# We've got loads to do!

Biomedical statistics is where most of the cool data and problems with actual impact are.

<sup>&</sup>lt;sup>4</sup>Here's a place to start:

THE END