



Uncertainty Quantification in Mechanistic Epidemic Models

Americo Cunha Jr

Rio de Janeiro State University — UERJ

International Colloquium on Mathematical Modelling in Epidemiology

Rio de Janeiro, August 14-17, 2023



Acknowledgments

► Collaborators



David A. W. Barton



Thiago G. Ritto

► Institutional and financial support



University of
BRISTOL



Conselho Nacional de Desenvolvimento
Científico e Tecnológico



CAPES



Fundação Carlos Chagas Filho de Amparo
à Pesquisa do Estado do Rio de Janeiro

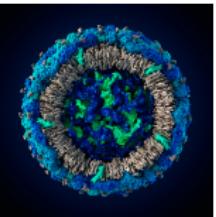


Engineering and Physical Sciences
Research Council

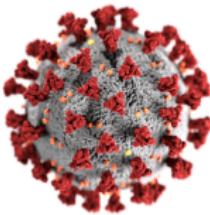
Epidemics are recurrent in history ...



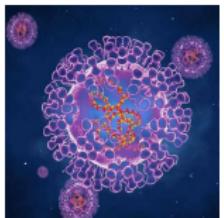
Dengue



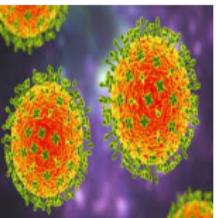
Zika virus



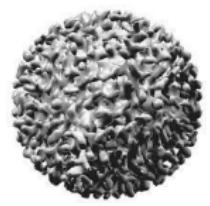
COVID-19



Monkeypox



Langya

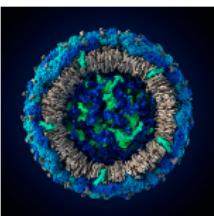


Next ?

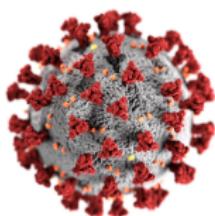
Epidemics are recurrent in history ...



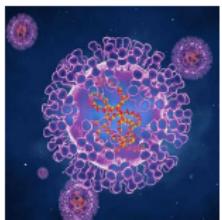
Dengue



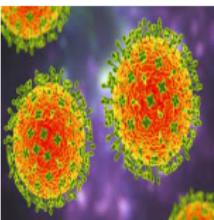
Zika virus



COVID-19



Monkeypox



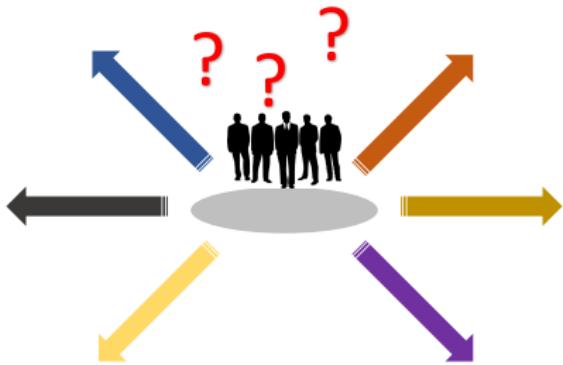
Langya



Next ?

They may cause a lot of trouble!

Tools to support for decision making



Computational Model + **Real World Data** = **Tool to aid with Decision Making**

Mathematical models are approximations!



"All models are wrong but some are useful"

George E. P. Box

Mathematical models are approximations!



"All models are wrong but some are useful"

George E. P. Box

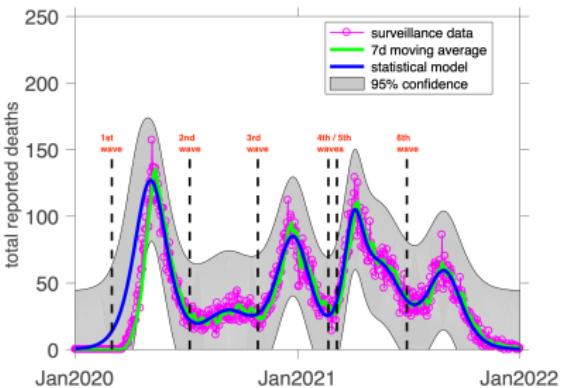


This idea has a more pronounced
meaning in computational epidemiology than in physics!
“First principles of epidemiology are unknown!”

For deaths records an algebraic model is effective!



$$I(t) = \sum_{i=1}^N \frac{r_i K_i e^{-r_i(t-\tau_i)}}{\left(1 + e^{-r_i(t-\tau_i)}\right)^2}$$



Chaos ARTICLE scitation.org/journals/cha

The starting dates of COVID-19 multiple waves

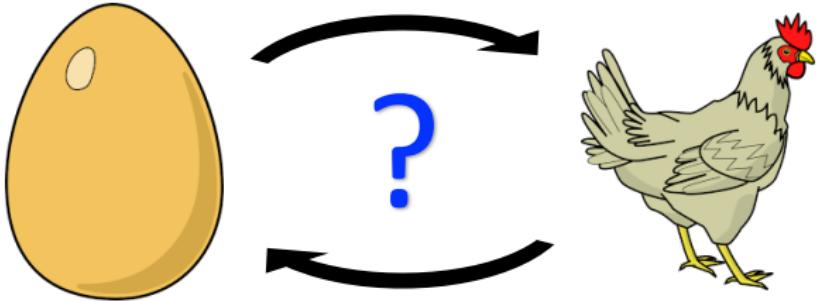
Cite as: Chaos **32**, 031101 (2022); doi: 10.1063/5.0079904
Submitted: 25 November 2021; Accepted: 9 February 2022;
Published Online: 3 March 2022

Paulo Roberto de Lima Gianfelice,¹ Ricardo Sovyk Oyarzabal,¹ Americo Cunha, Jr.,^{2,3} Jose Mario Vicensi Grzybowski,¹ Fernando da Conceição Batista,¹ and Elbert E. N. Macau¹

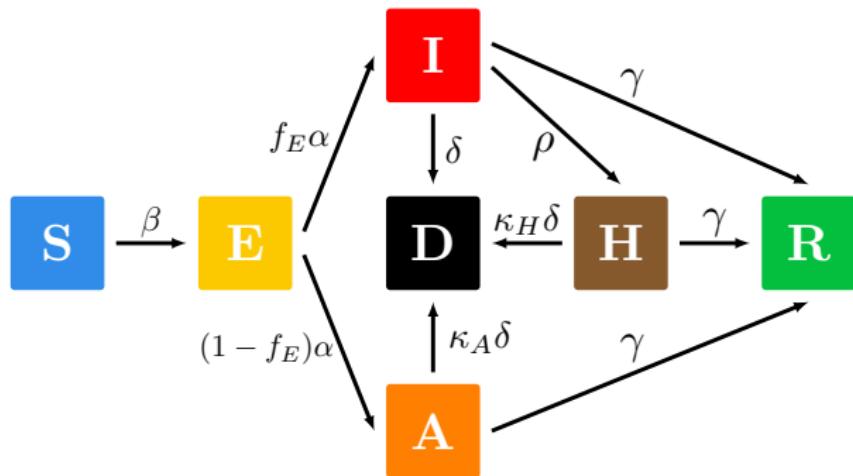


P. R. L. Gianfelice et al., *The starting dates of COVID-19 multiple waves*, **Chaos**, 32:031101, 2022

Mechanistic models are necessary!
(cause-effect relationship)



SEIR(+AHD) mechanistic epidemic model



SEIR(+AHD) $_{\beta}$ epidemic model

► Dynamic model:

$$\dot{S} = -\beta(t) S(I + A + \epsilon_H H)/N$$

$$\dot{E} = \beta(t) S(I + A + \epsilon_H H)/N - \alpha E$$

$$\dot{I} = f_E \alpha E - (\gamma + \rho + \delta) I$$

$$\dot{R} = \gamma (I + A + H)$$

$$\dot{A} = (1 - f_E) \alpha E - (\kappa_A \delta + \gamma)$$

+ initial conditions

$$\dot{H} = \rho I - (\gamma + \kappa_H \delta) H$$

$$\dot{D} = \delta (I + \kappa_A A + \kappa_H H)$$

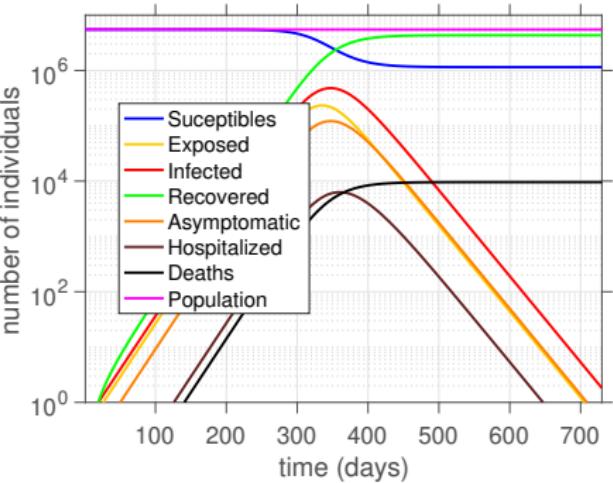
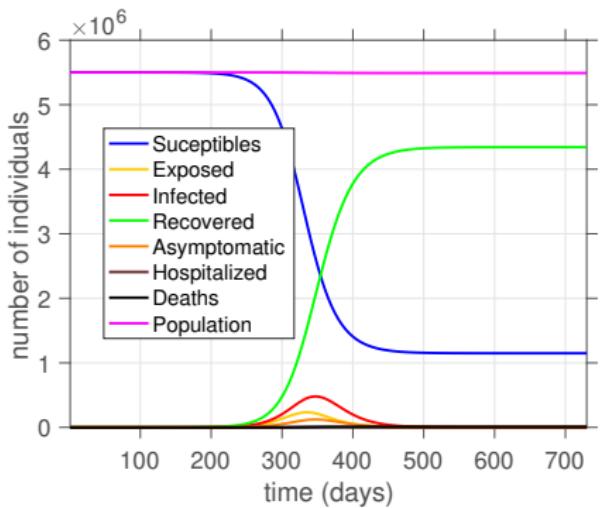
$$\dot{N} = -\dot{D}$$

► Rate of transmission:

$$\beta(t) = \beta_0 + \frac{(\beta_\infty - \beta_0)}{2} \left(1 + \tanh \left(\eta \frac{(t - t_\beta)}{2} \right) \right)$$

SEIR(+AHD) model response (virgin population)

In this example the transmission rate is fixed, i.e., $\beta(t) = \beta$



Abstraction of the epidemic model

- Dynamic model:

$$\frac{d}{dt} \mathbf{u}(t) = F(t, \mathbf{u}(t), \mathbf{x})$$

- Vector field:

$$(t, \mathbf{u}(t), \mathbf{x}) \in \mathbb{R} \times \mathbb{R}^8 \times \mathbb{R}^{12} \mapsto F(t, \mathbf{u}(t), \mathbf{x}) \in \mathbb{R}^8$$

- State vector:

$$\mathbf{u}(t) = (S, E, I, A, H, R, D, N)$$

- Parameters vector:

$$\mathbf{x} = (\beta_0, \alpha, f_E, \gamma, \rho, \delta, \kappa_A, \kappa_H, \epsilon_H, \beta_\infty, \eta, t_\beta)$$

- QoI vector:

$$\mathbf{y} = [H(t_1), \dots, H(t_n), D(t_1), \dots, D(t_n)]$$

- Computational model:

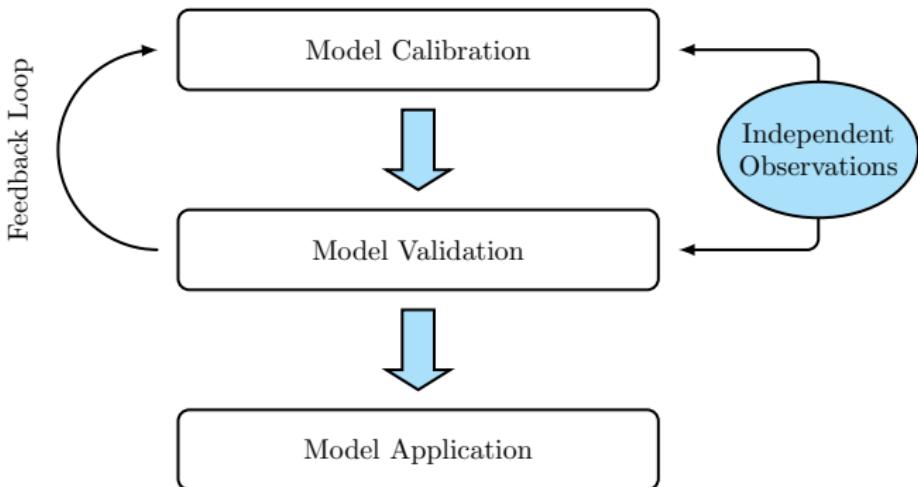
$$\mathbf{y} = \mathcal{M}(\mathbf{x})$$

Data-driven epidemic models

Model Parametrization: expert knowledge, literature, ansatz, etc

Model Calibration: data + model inversion

Model Validation: other data + error metrics



How to obtain consistent initial conditions ?



Initial conditions (almost surely) are unknown for epidemic systems!

How to obtain consistent initial conditions ?



Initial conditions (almost surely) are unknown for epidemic systems!

Ansatz → biased and inconsistent

How to obtain consistent initial conditions ?

Initial conditions (almost surely) are unknown for epidemic systems!

Ansatz → biased and inconsistent

Inversion → hard and expensive

How to obtain consistent initial conditions ?

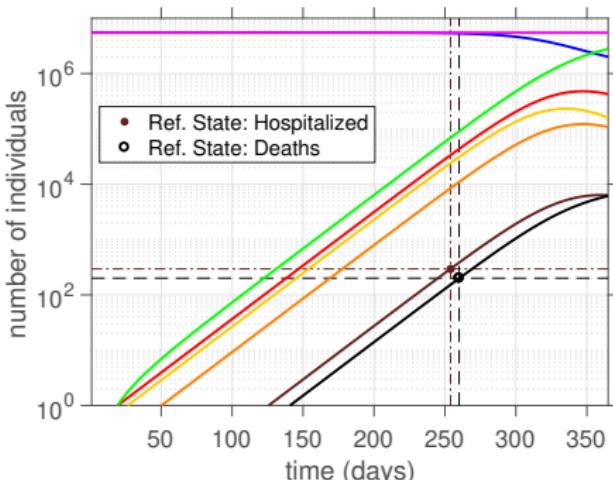
Initial conditions (almost surely) are unknown for epidemic systems!

Ansatz → biased and inconsistent

Inversion → hard and expensive

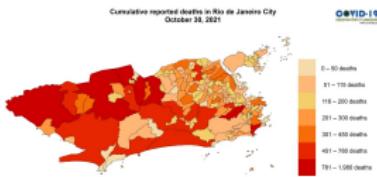
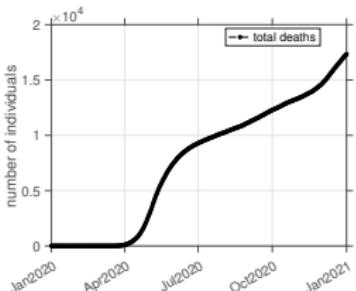
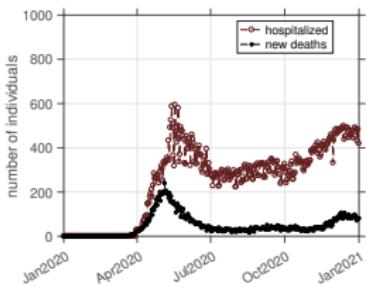
Dynamic inspired → $\mathbf{u}(0) = \omega \mathbf{u}(0)_{ref}^H + (1 - \omega) \mathbf{u}(0)_{ref}^D$

"convex combination of admissible reference states"



How to quantify model response and data similarity ?

- ▶ Surveillance data (Rio de Janeiro city):



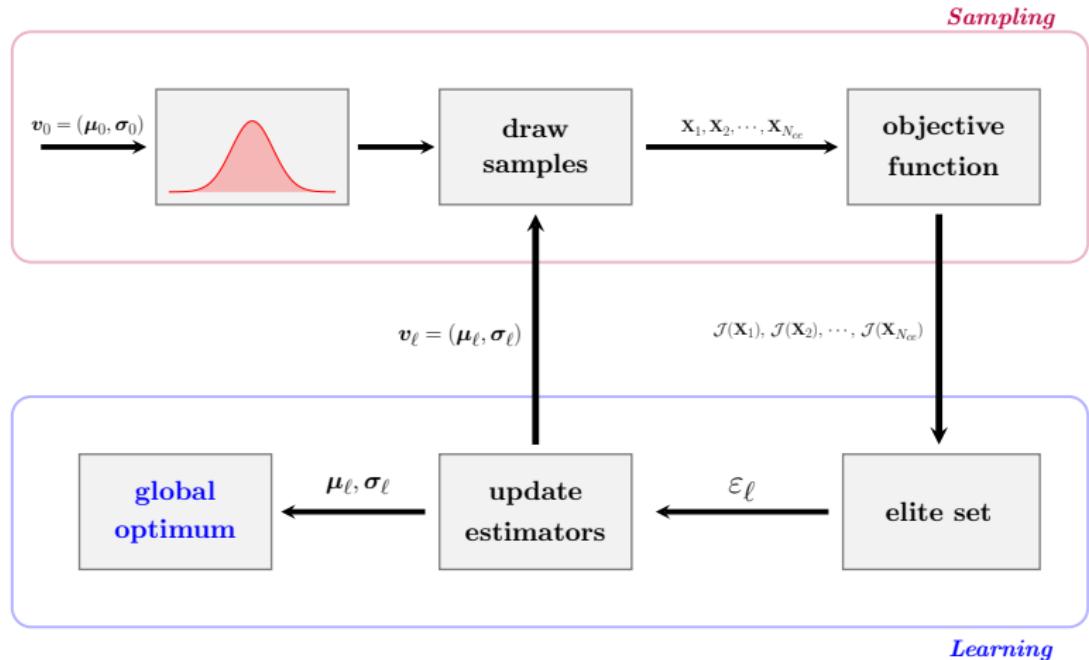
- ▶ Data partition:

$$\mathbf{y}_{\text{data}} = [\mathbf{y}_{\text{data}}^H \quad \mathbf{y}_{\text{data}}^D]$$

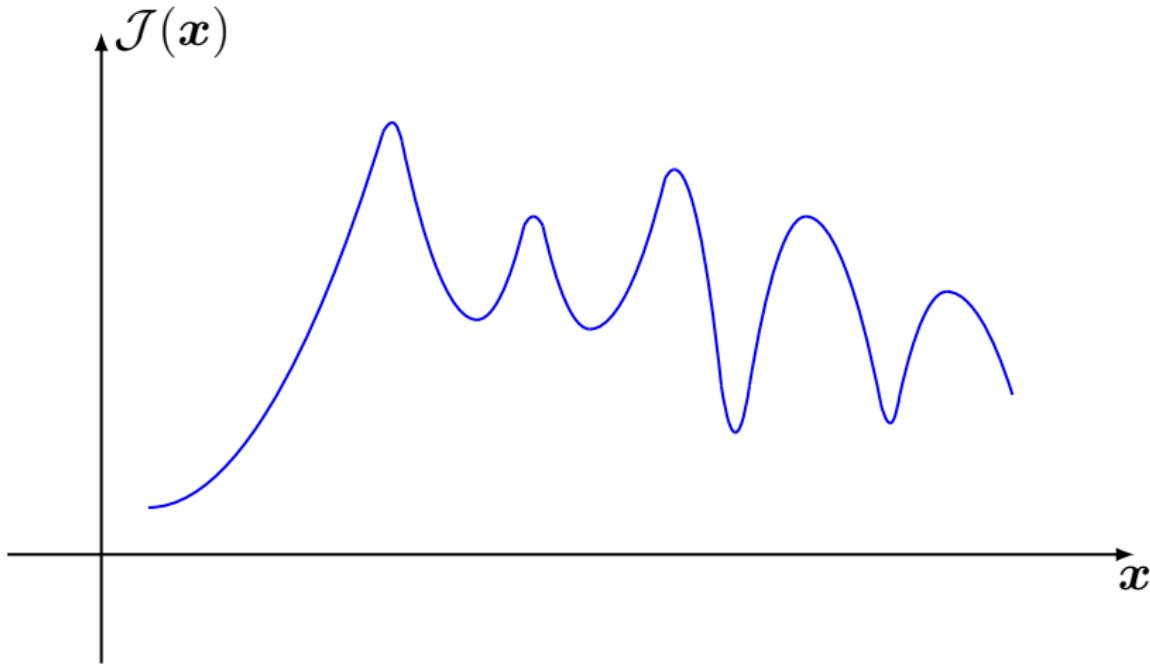
- ▶ Misfit function:

$$\mathcal{J}(\mathbf{x}) = \omega \frac{\|\mathbf{y}_{\text{data}}^H - \mathbf{y}^H(\mathbf{x})\|^2}{\|\mathbf{y}_{\text{data}}^H\|^2} + (1 - \omega) \frac{\|\mathbf{y}_{\text{data}}^D - \mathbf{y}^D(\mathbf{x})\|^2}{\|\mathbf{y}_{\text{data}}^D\|^2}$$

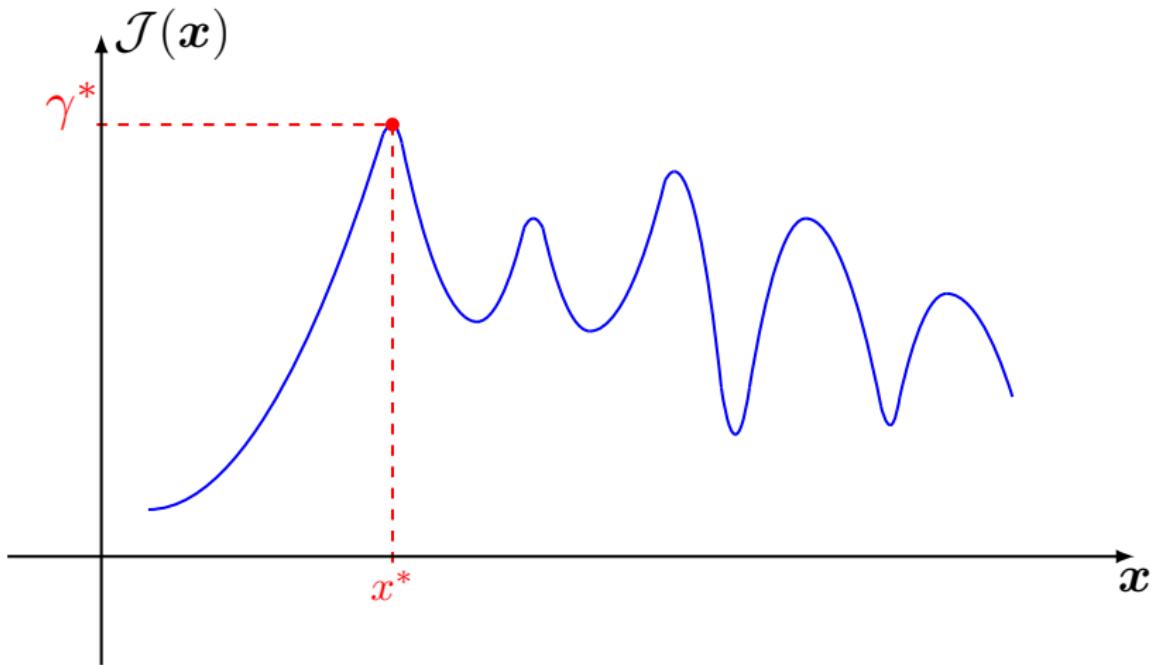
Non-convex optimization via Cross-Entropy method



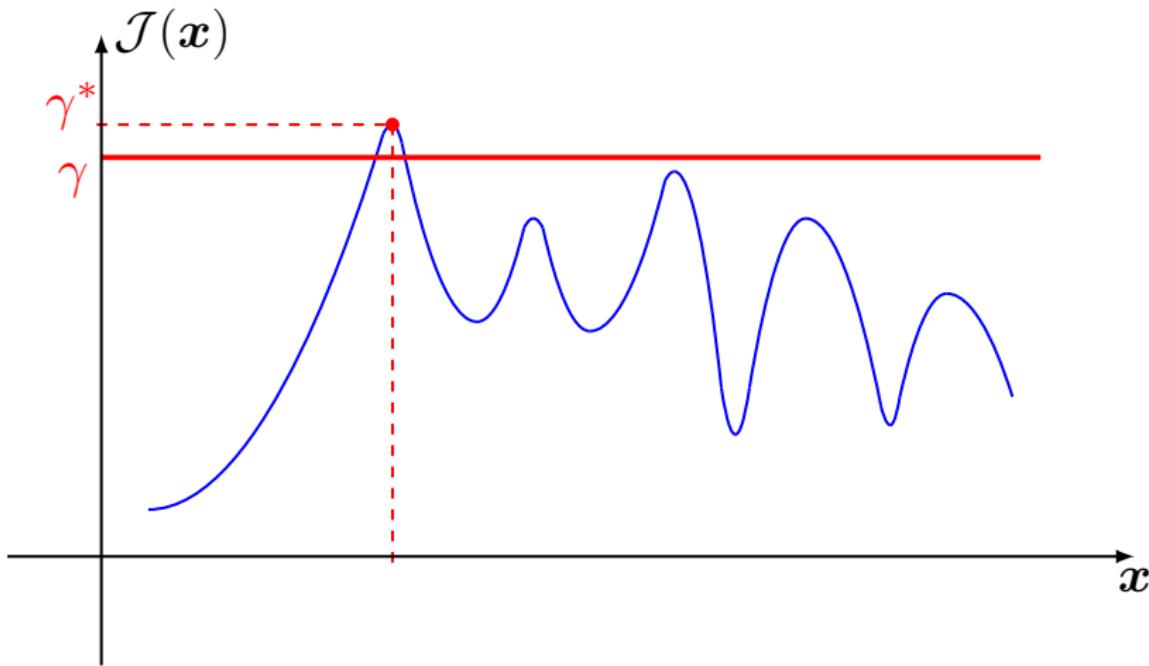
Cross-entropy method in action!



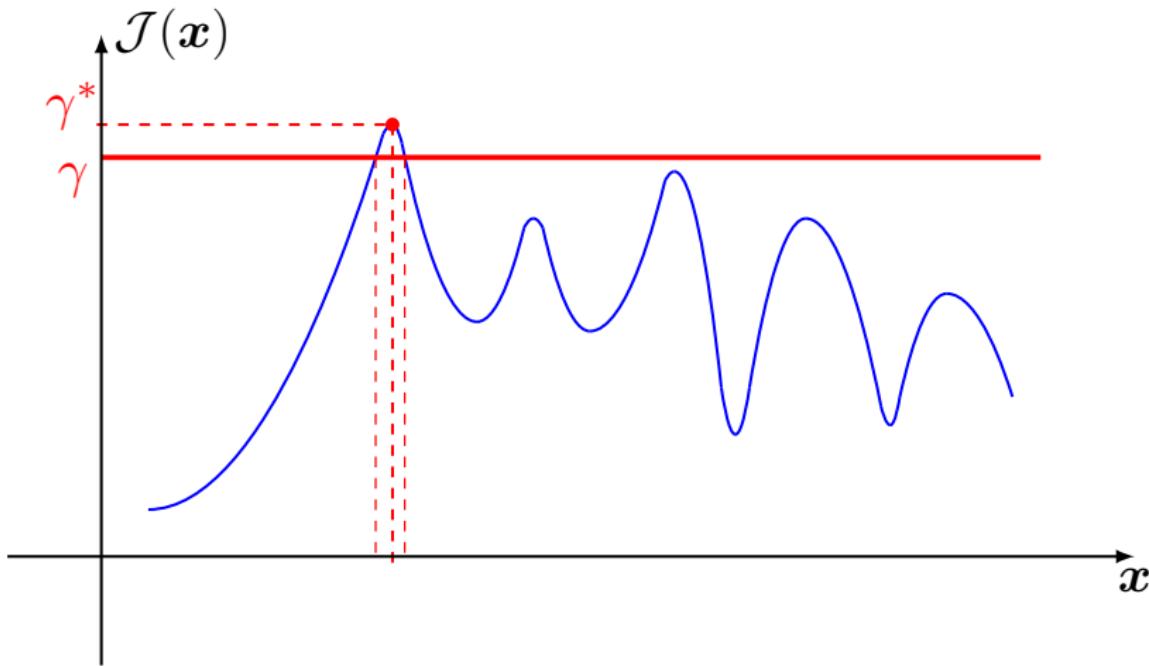
Cross-entropy method in action!



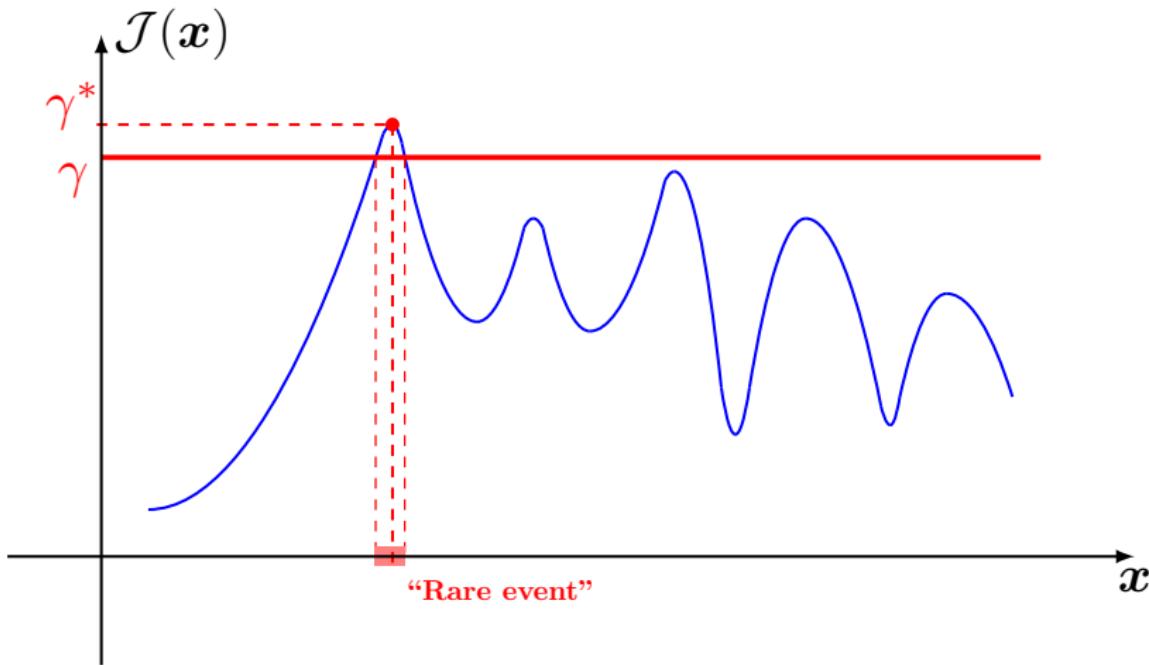
Cross-entropy method in action!



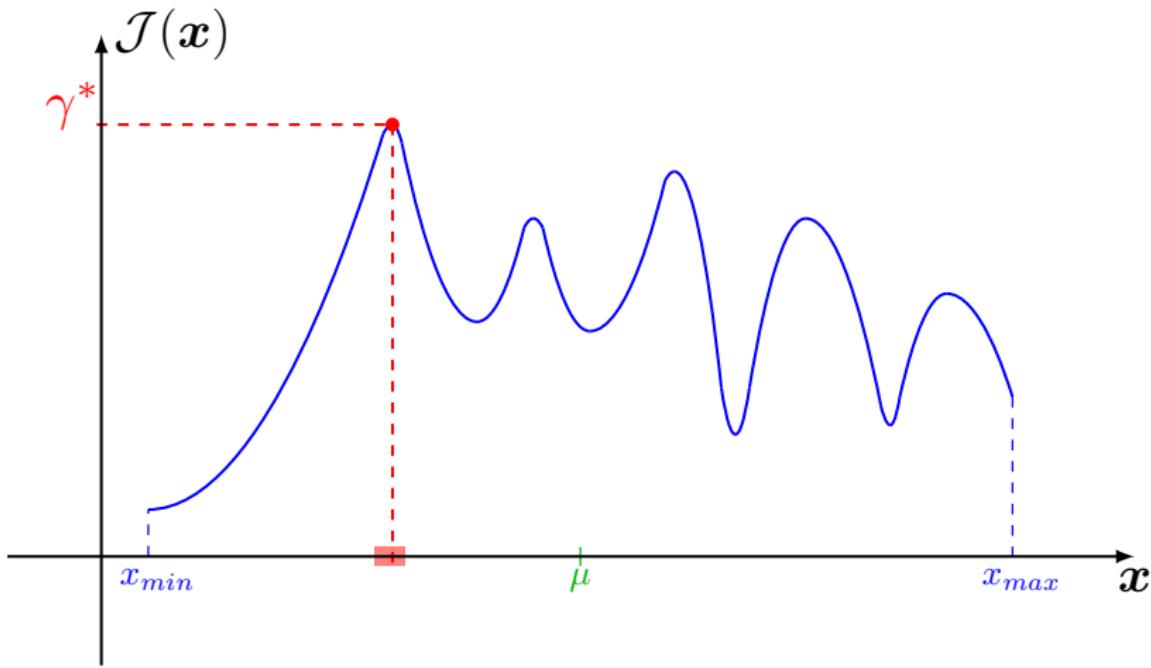
Cross-entropy method in action!



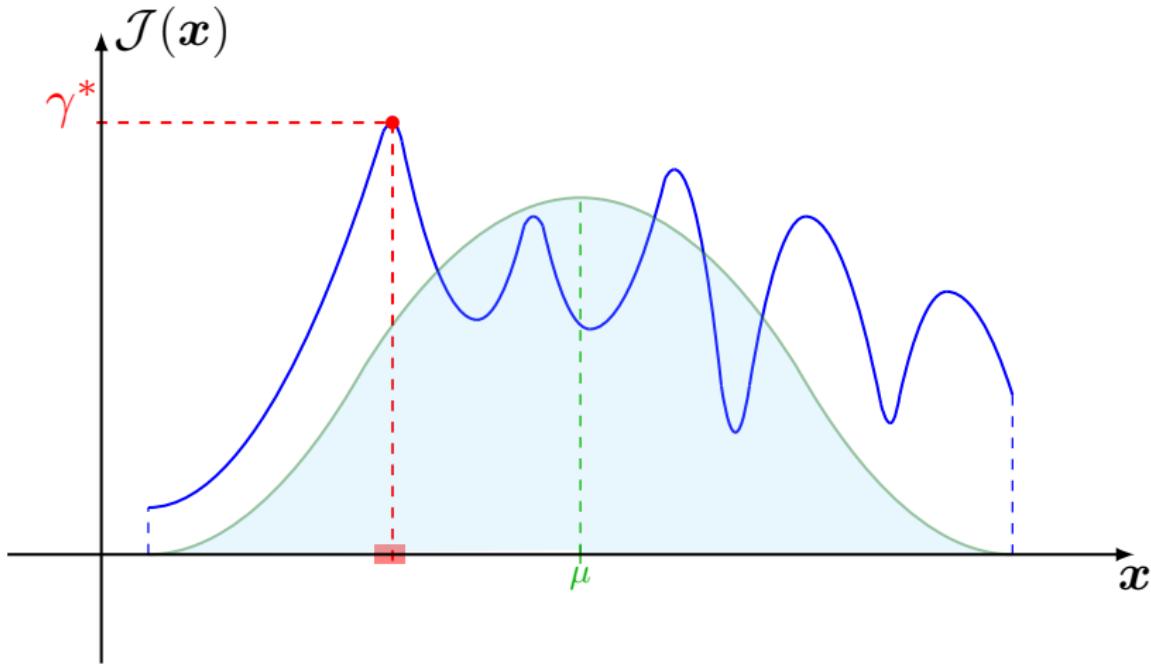
Cross-entropy method in action!



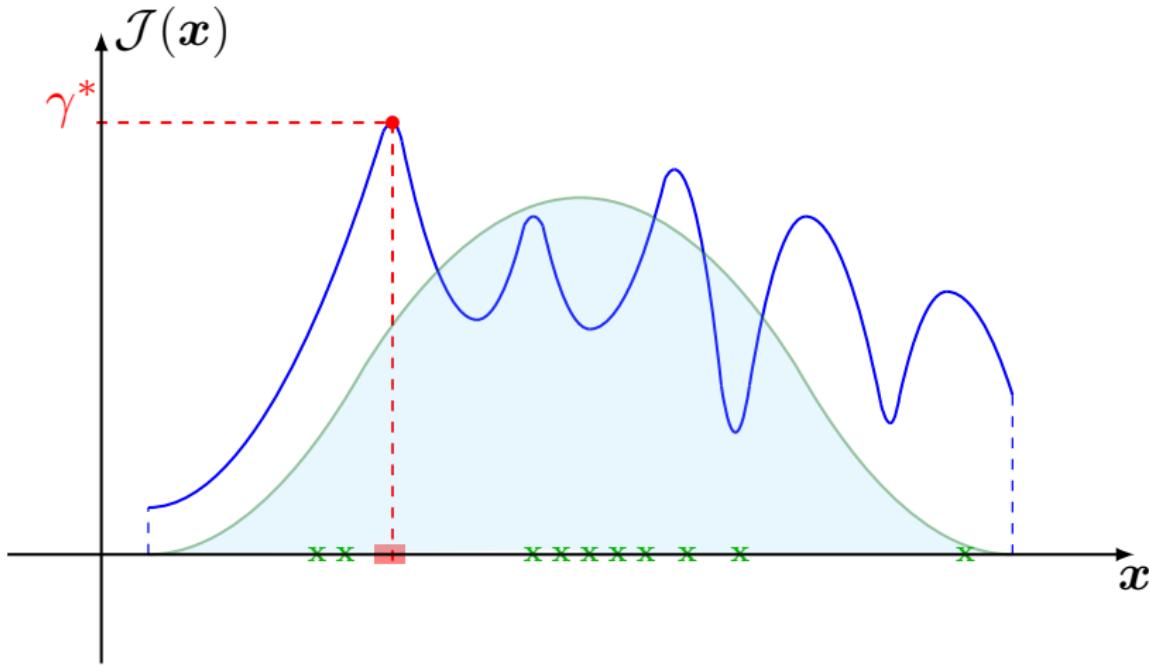
Cross-entropy method in action!



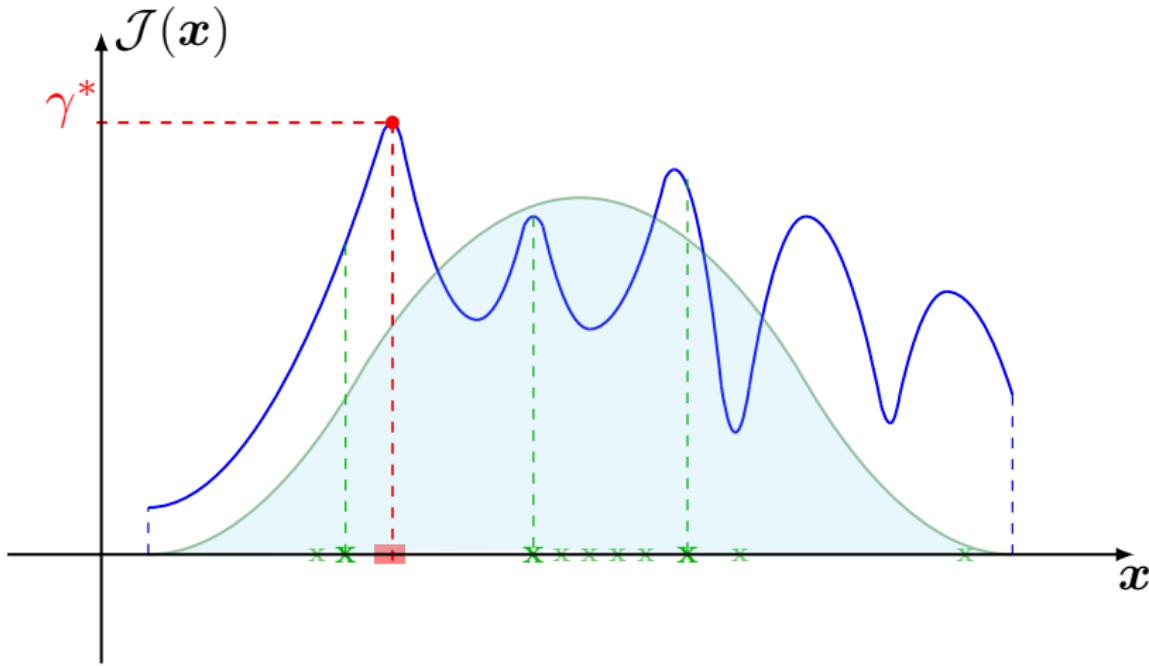
Cross-entropy method in action!



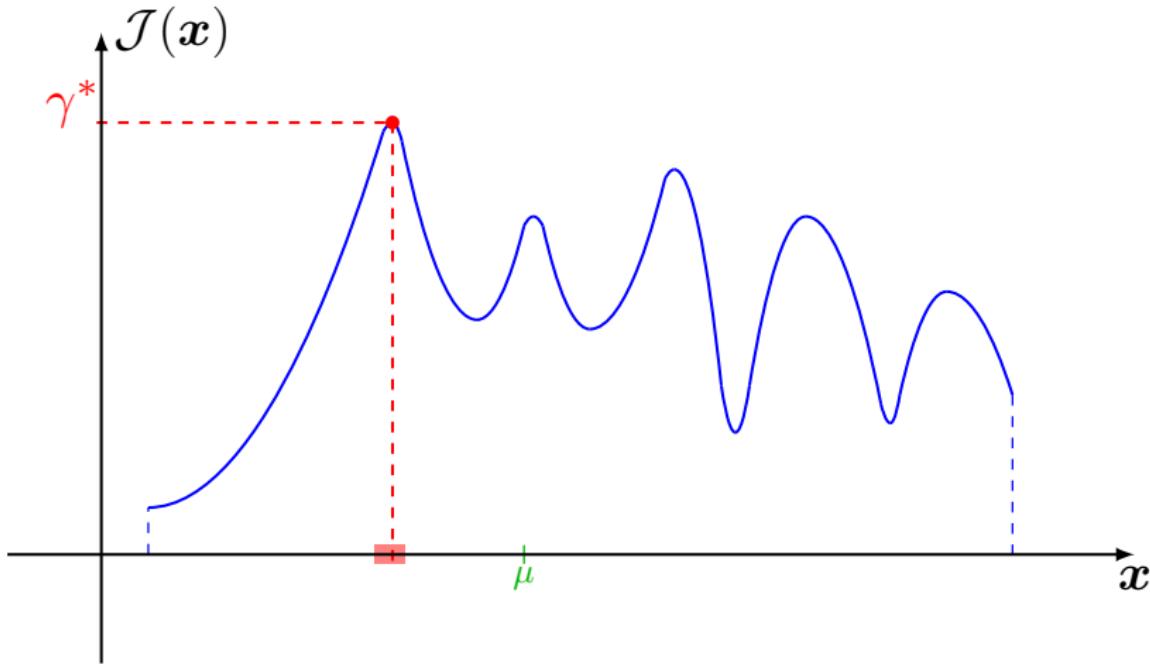
Cross-entropy method in action!



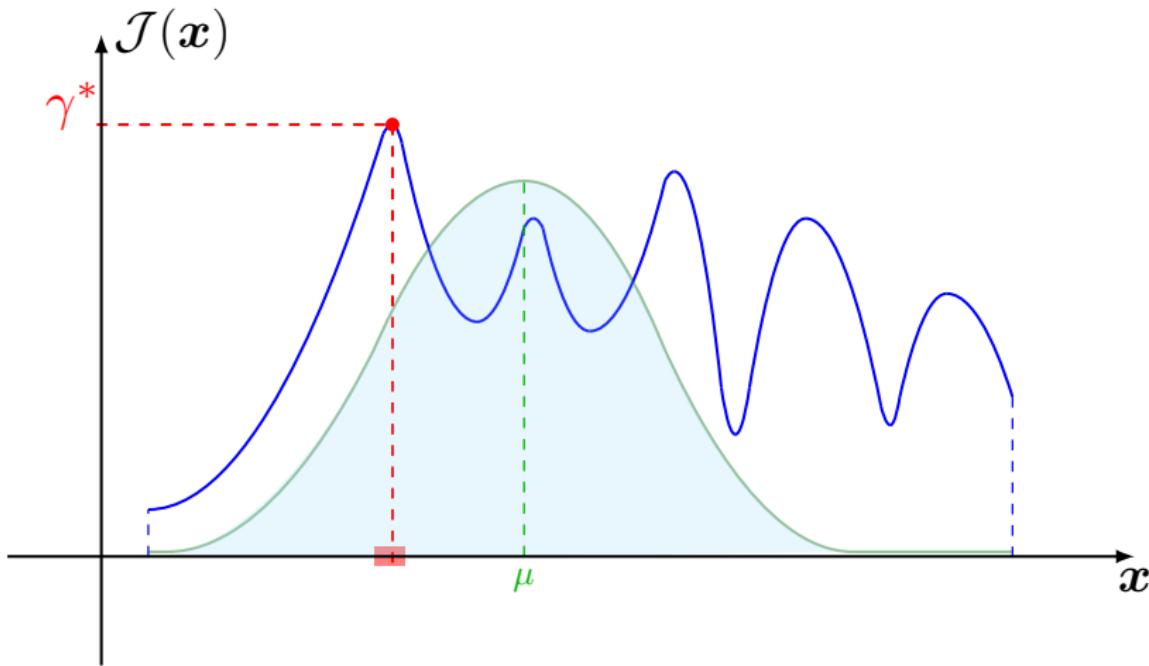
Cross-entropy method in action!



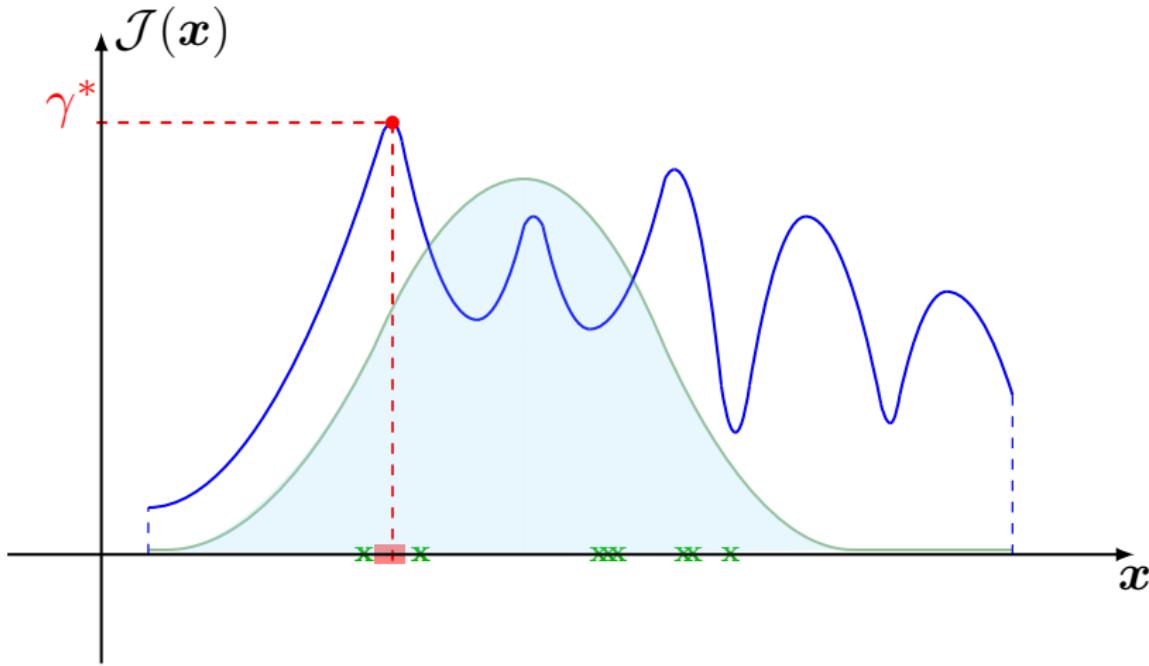
Cross-entropy method in action!



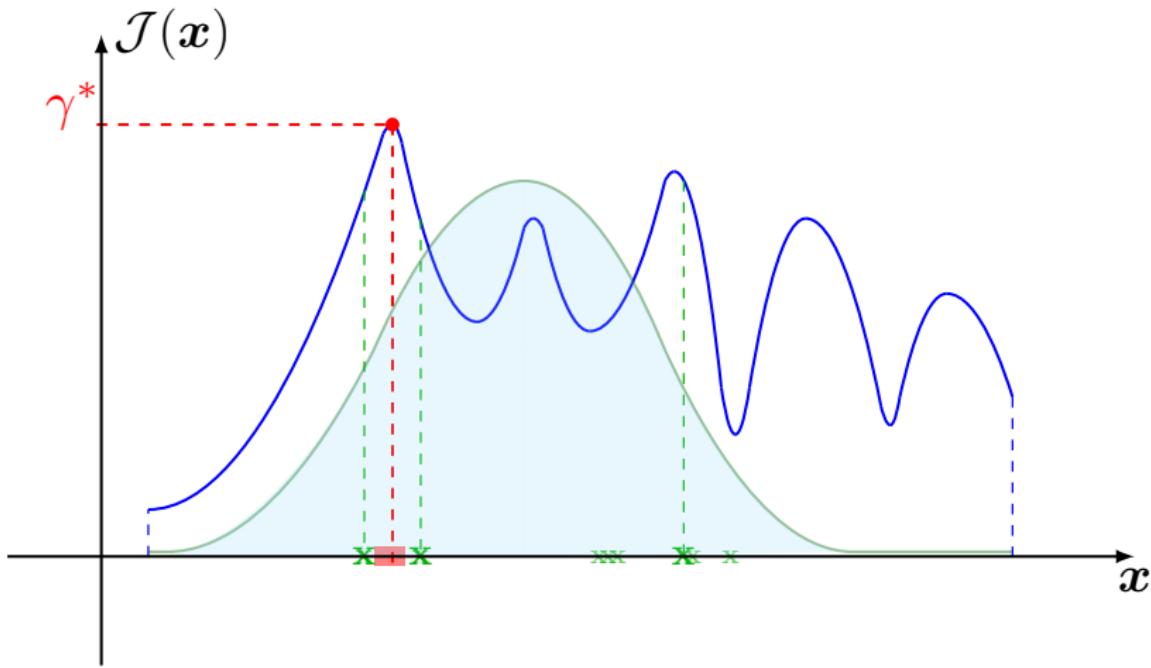
Cross-entropy method in action!



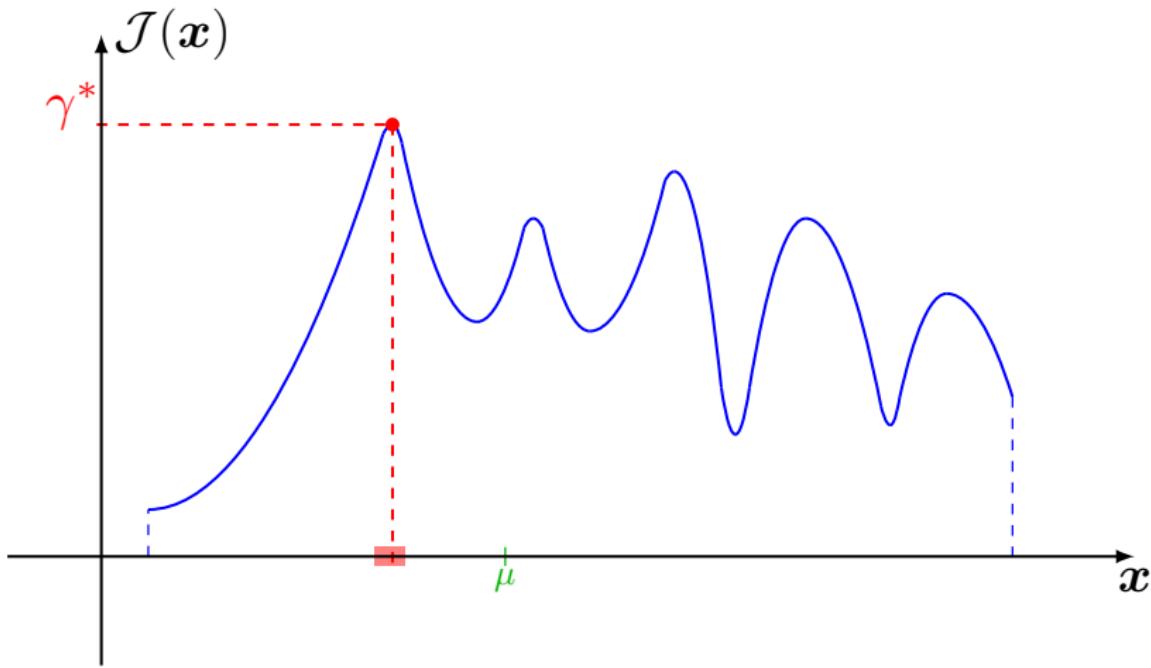
Cross-entropy method in action!



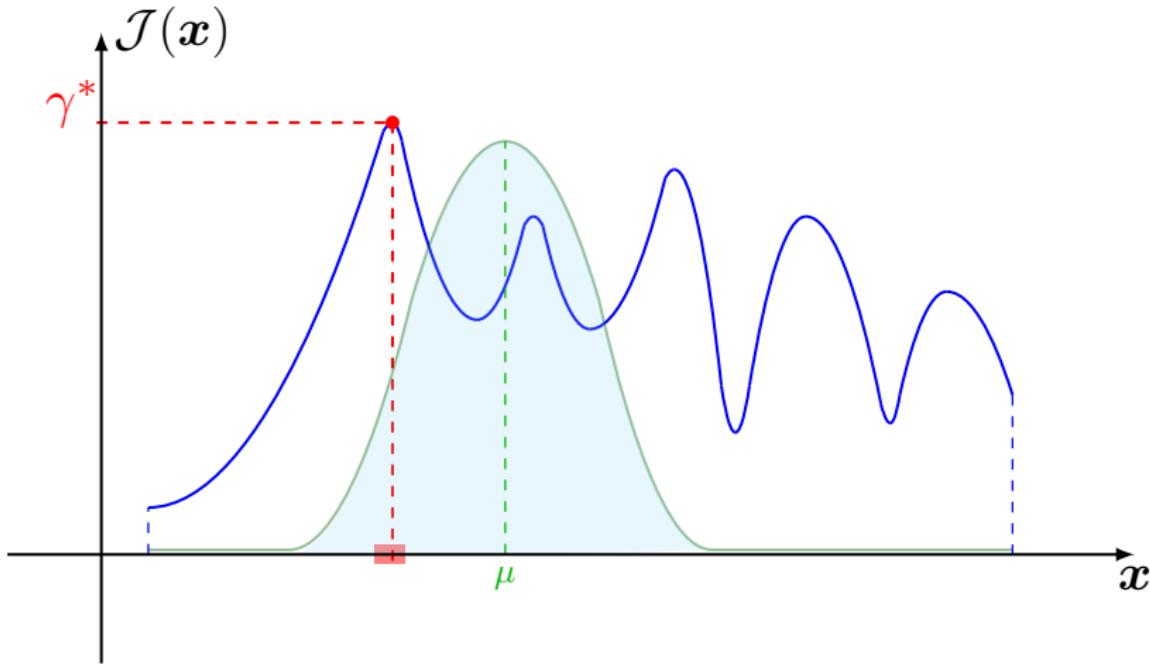
Cross-entropy method in action!



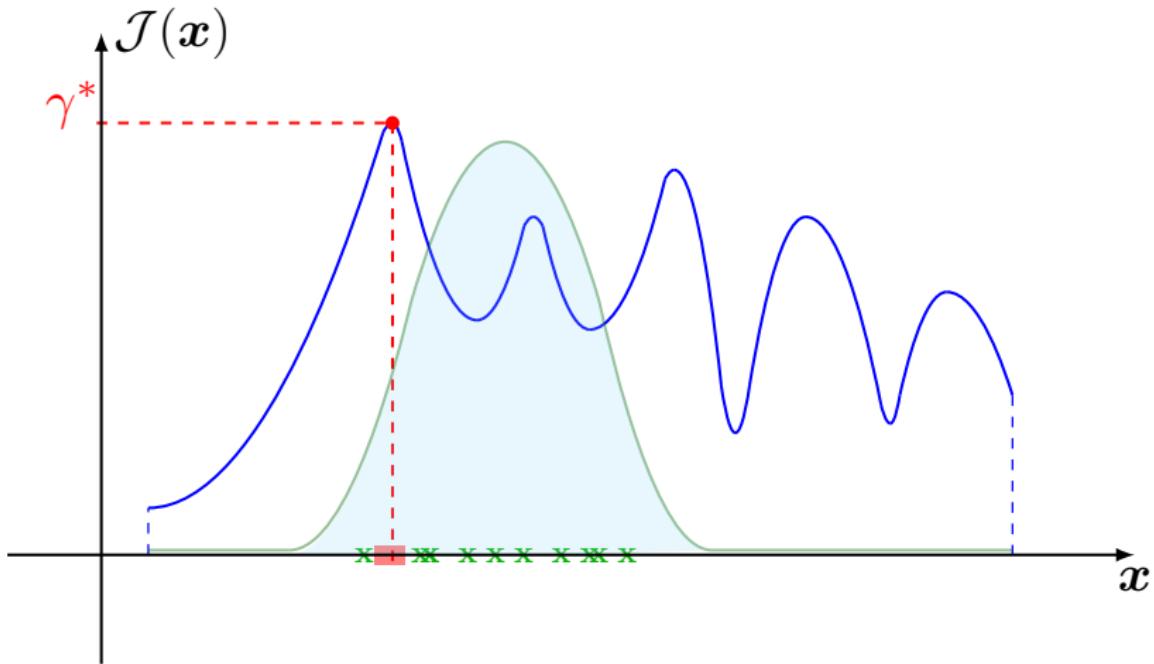
Cross-entropy method in action!



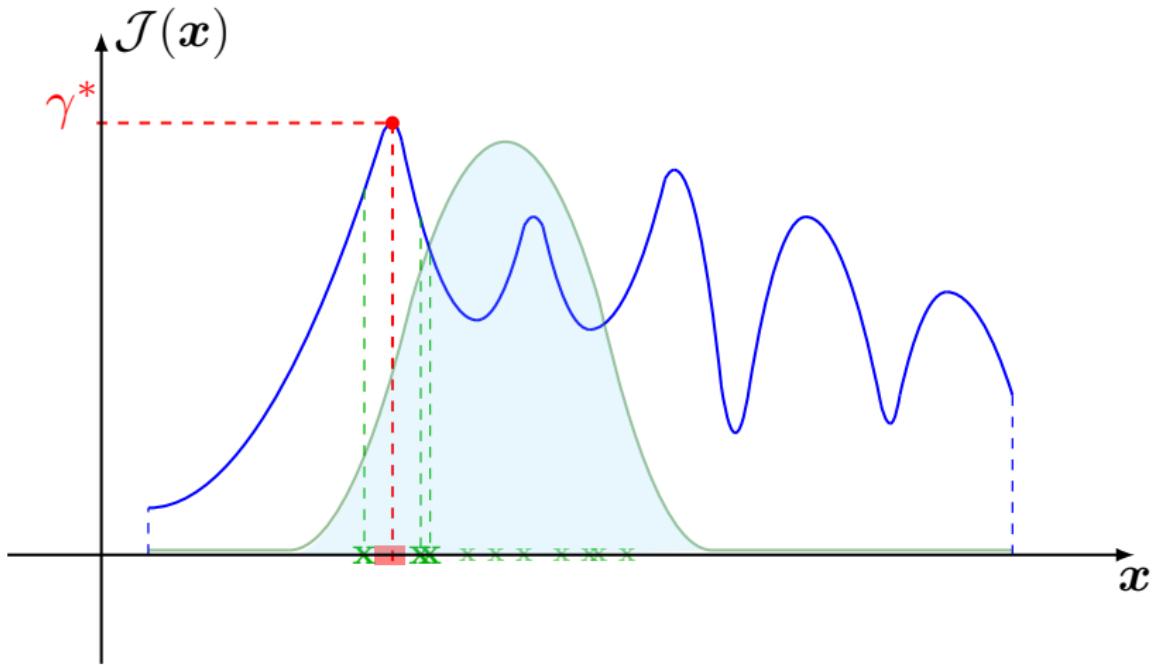
Cross-entropy method in action!



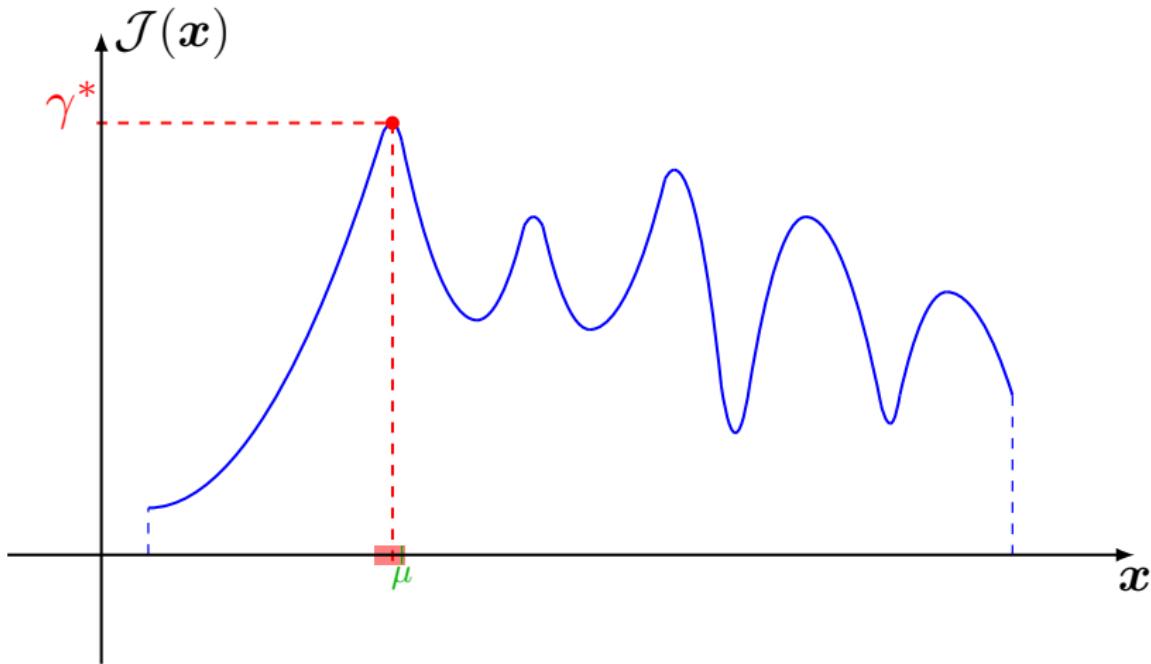
Cross-entropy method in action!



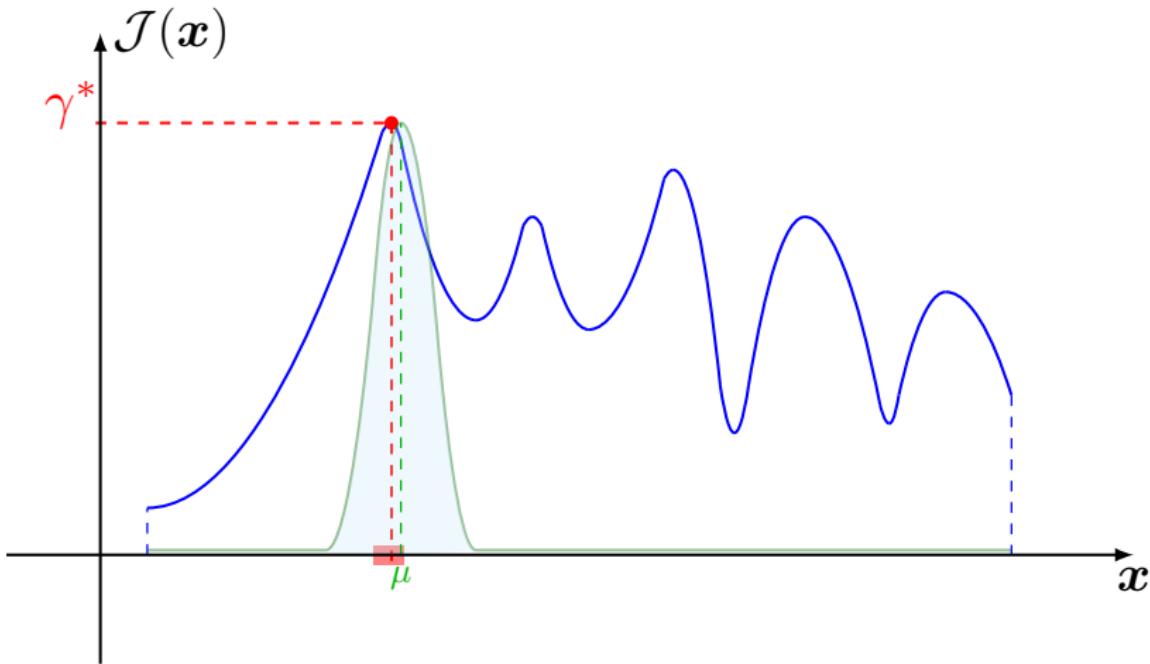
Cross-entropy method in action!



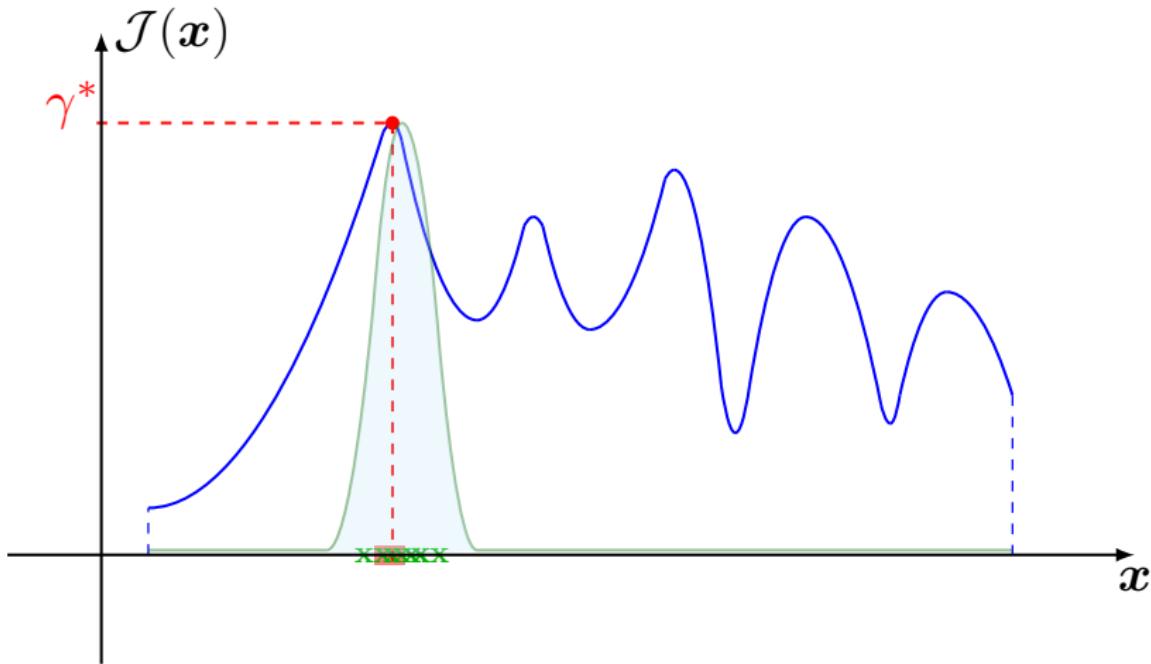
Cross-entropy method in action!



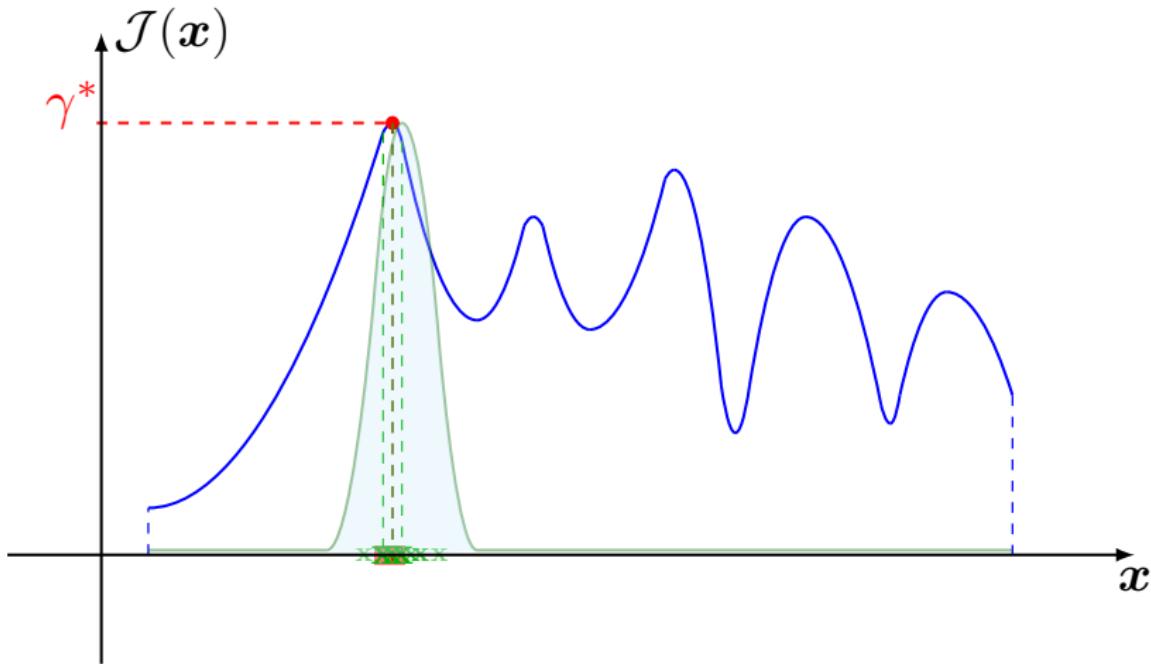
Cross-entropy method in action!



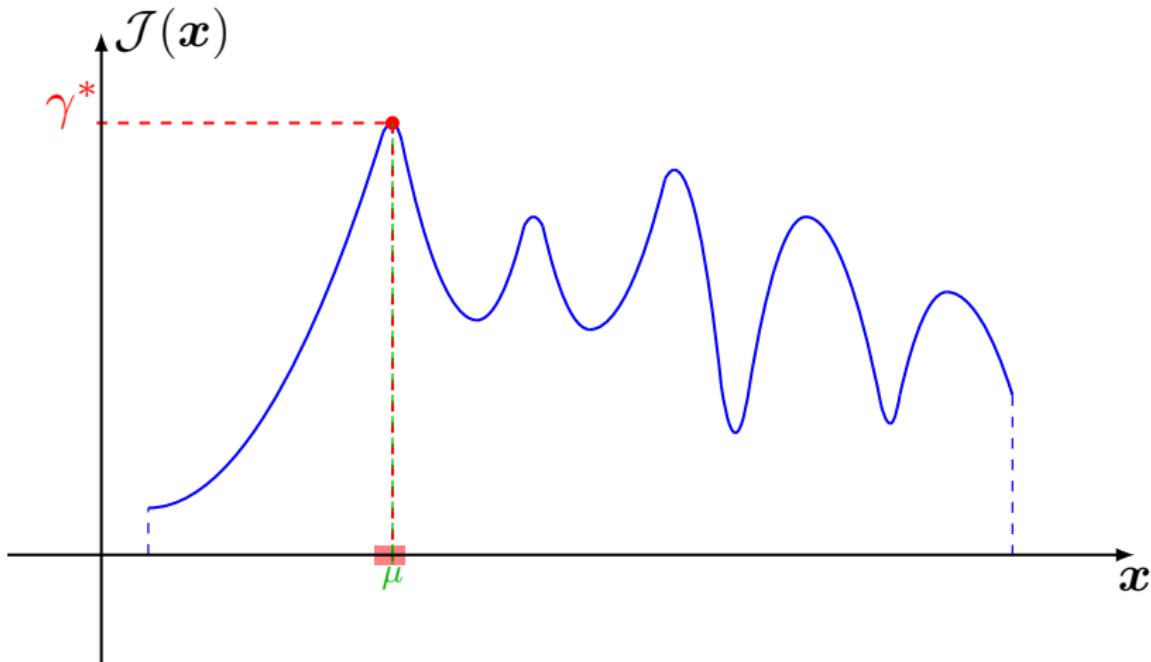
Cross-entropy method in action!



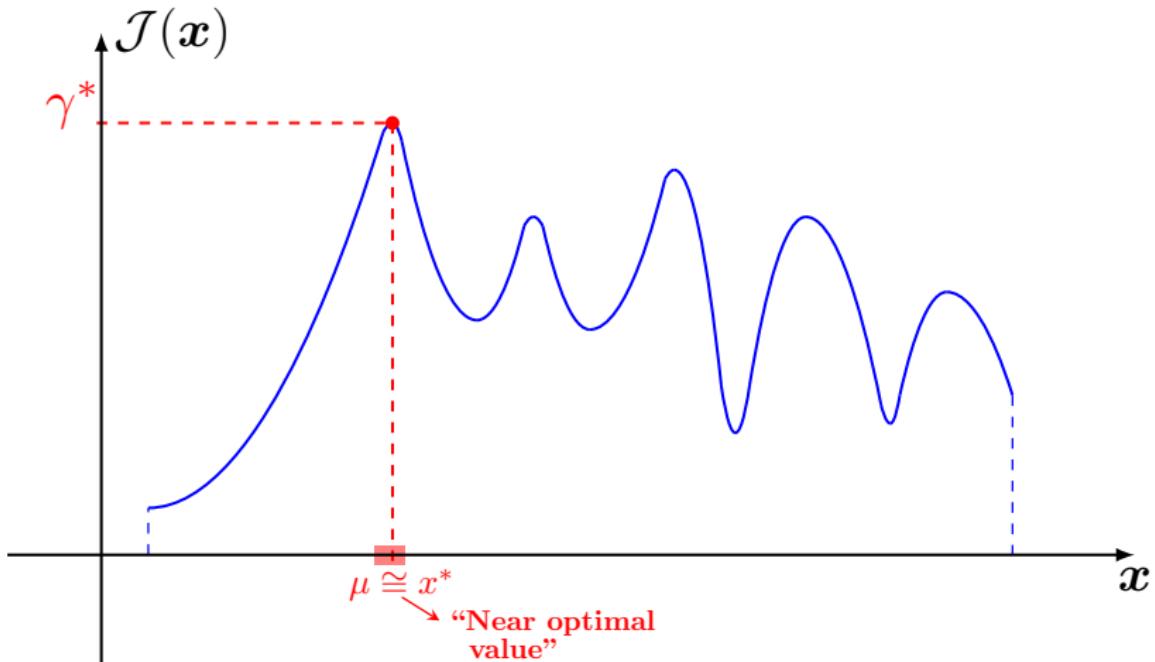
Cross-entropy method in action!



Cross-entropy method in action!



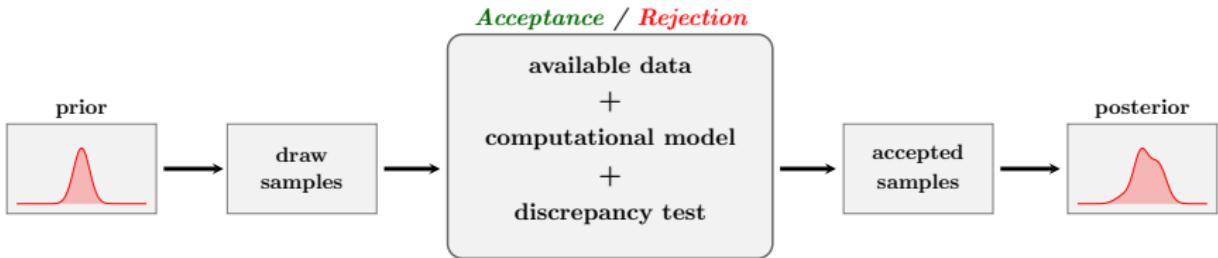
Cross-entropy method in action!



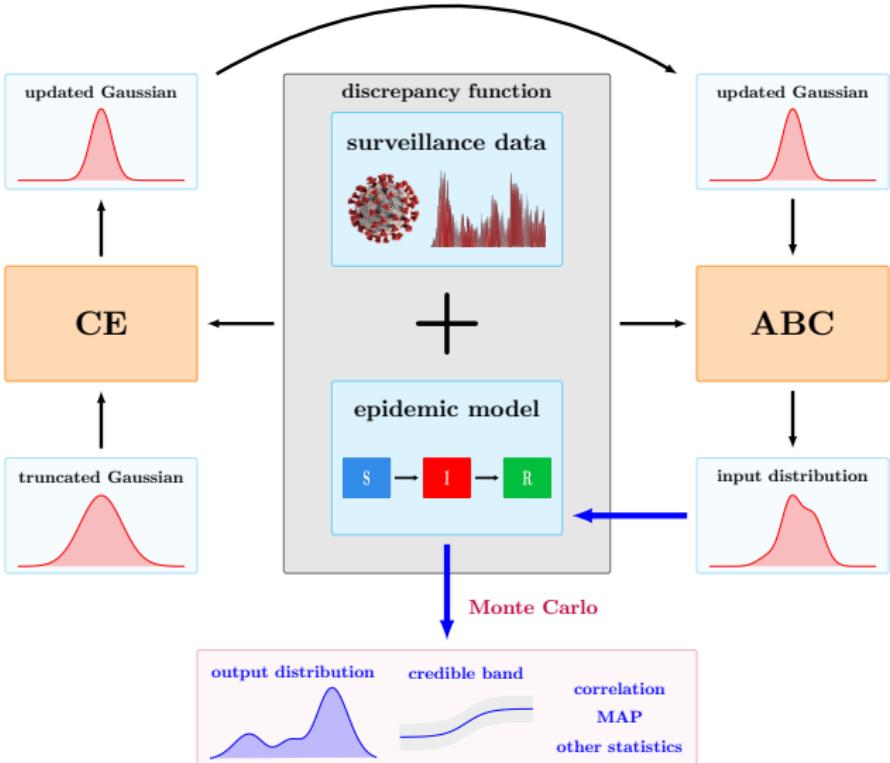
- ▶ Traditional Bayesian Computation

$$\underbrace{\pi(\text{model} \mid \text{data})}_{\text{posterior}} \propto \underbrace{\pi(\text{data} \mid \text{model})}_{\text{likelihood}} \times \underbrace{\pi(\text{model})}_{\text{prior}}$$

- ▶ Approximate Bayesian Computation

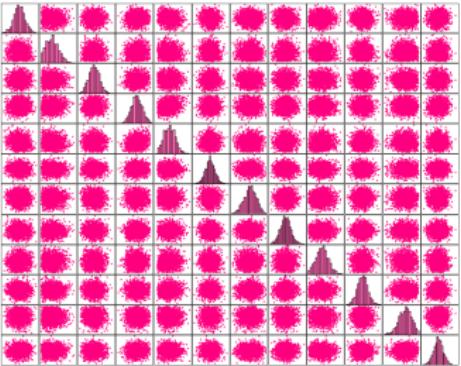


Cross-Entropy Approximate Bayesian Computation



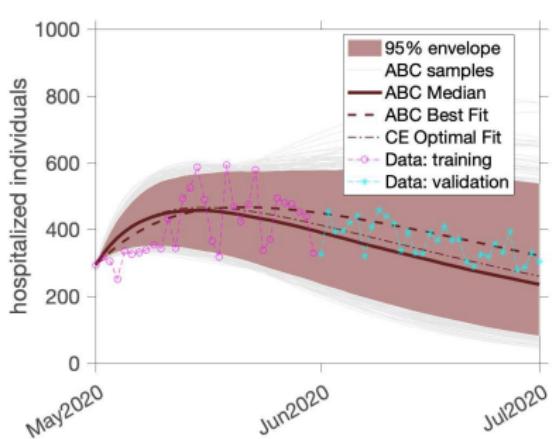
Calibration of the SEIR(+AHD) β model parameters

	Unit	CE Optimal	CE std dev	ABC Best	ABC std dev
β or β_0	1/day	0.12	0.02	0.13	0.02
α	1/day	0.20	0.07	0.27	0.06
f_E	—	0.81	0.03	0.84	0.03
γ	1/day	0.13	0.01	0.12	0.01
ρ	1/day	0.0006	0.0001	0.0005	0.0001
δ	1/day	0.0021	0.0004	0.0015	0.0004
κ_A	—	0.0026	0.0008	0.0027	0.0008
κ_H	—	0.0563	0.0130	0.0575	0.0128
ϵ_H	—	0.25	0.07	0.33	0.07
β_∞	1/day	0.31	0.06	0.43	0.06
η	1/day	5.8	1.9	6.2	1.8
τ_β	day	146	7	153	7

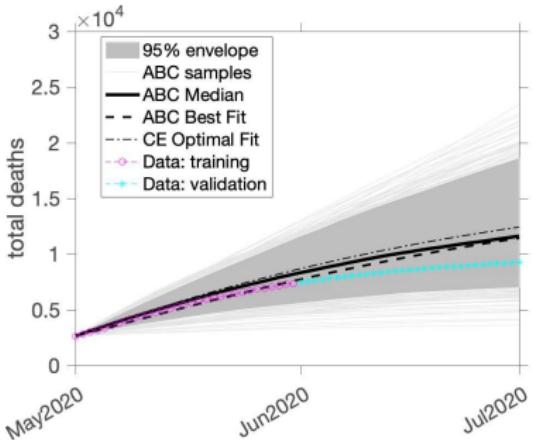


Model validation and uncertainty quantification

hospitalized



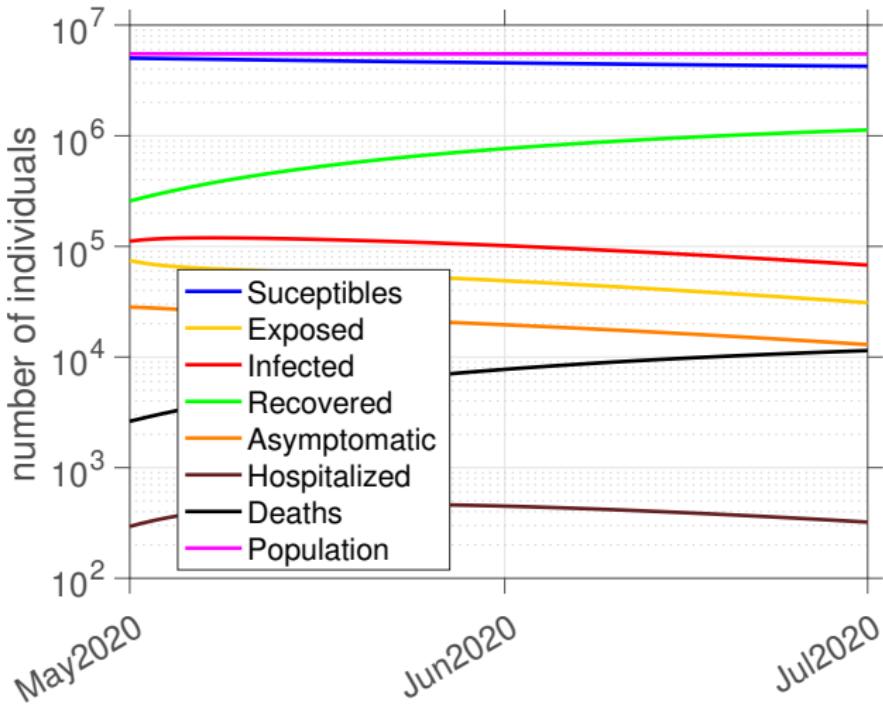
total deaths



$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

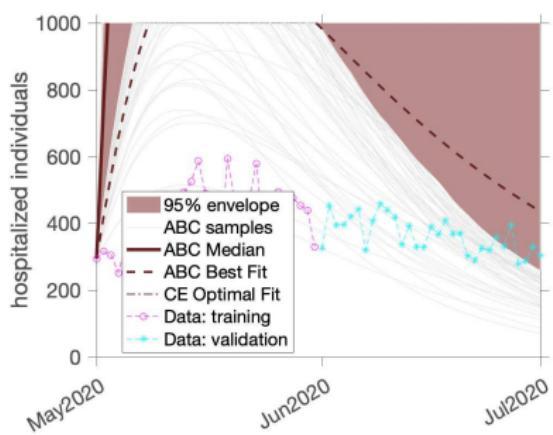
Acceptance rate: 87%

Model exploration of latent variables

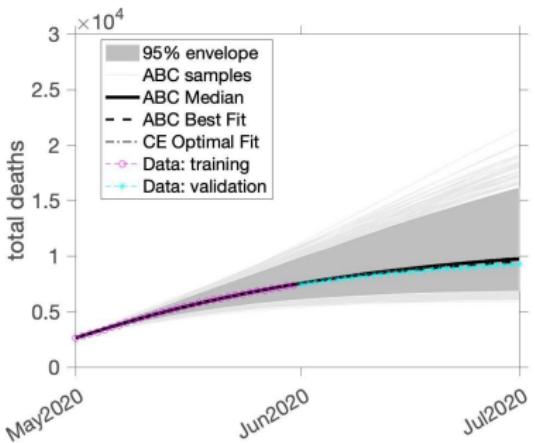


Influence of the weight parameter ω

hospitalized



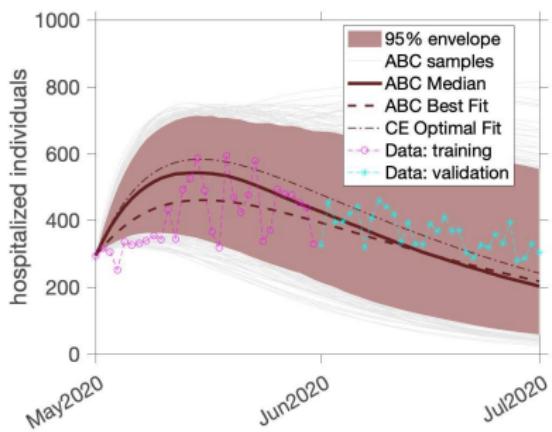
total deaths



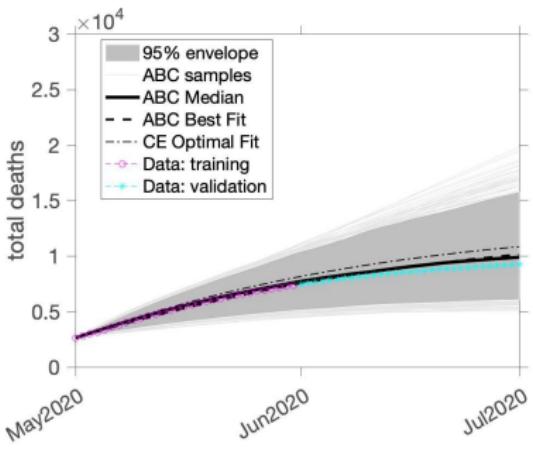
$$\omega = 0.00 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

Influence of the weight parameter ω

hospitalized



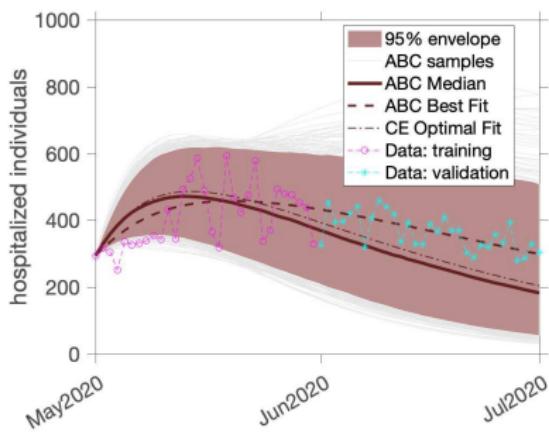
total deaths



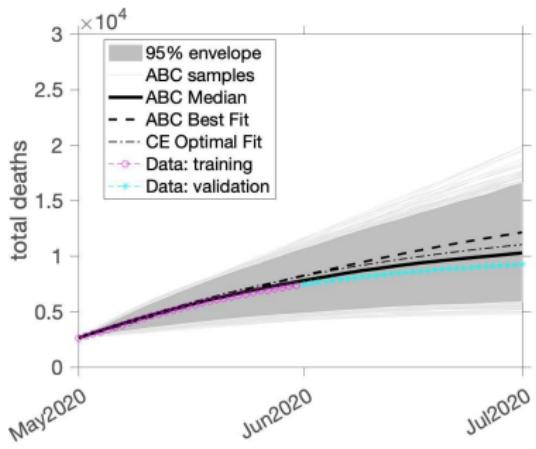
$$\omega = 0.25 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

Influence of the weight parameter ω

hospitalized



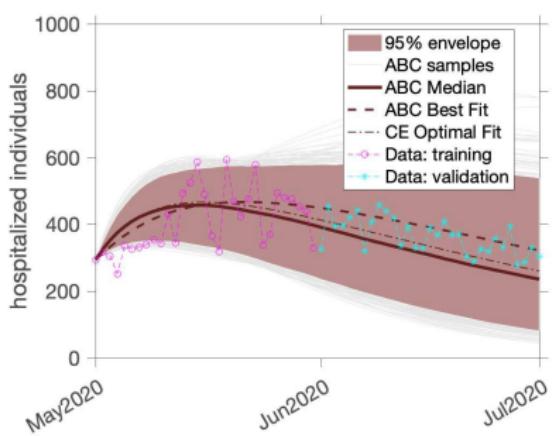
total deaths



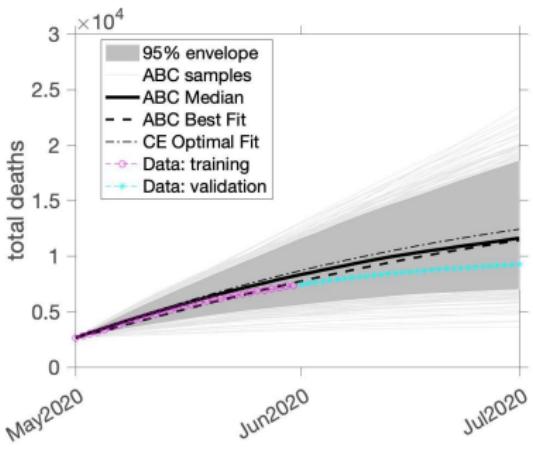
$$\omega = 0.50 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

Influence of the weight parameter ω

hospitalized



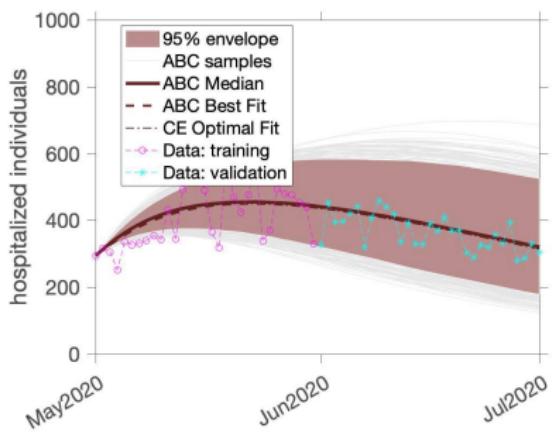
total deaths



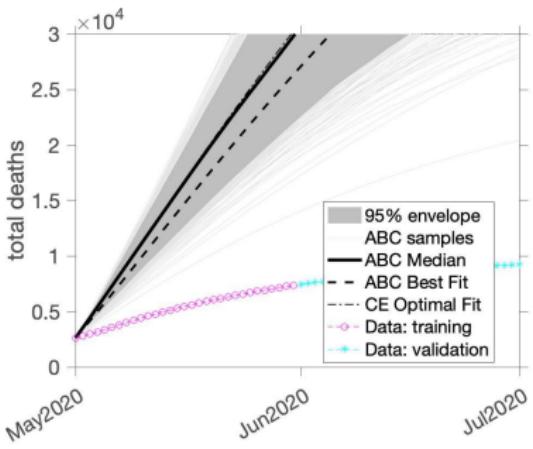
$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

Influence of the weight parameter ω

hospitalized



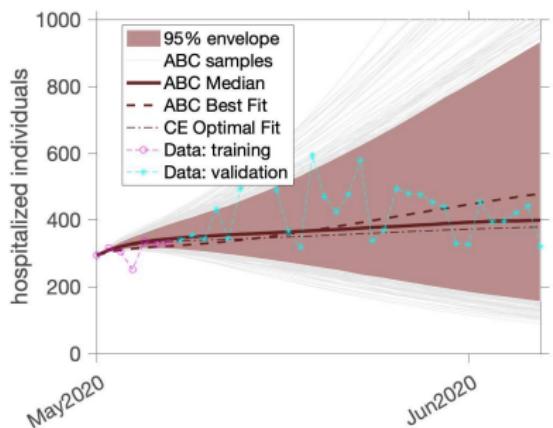
total deaths



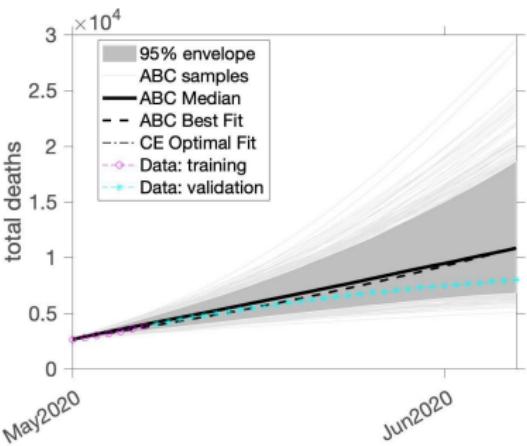
$$\omega = 1.00 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

Influence of the dataset size

hospitalized



total deaths

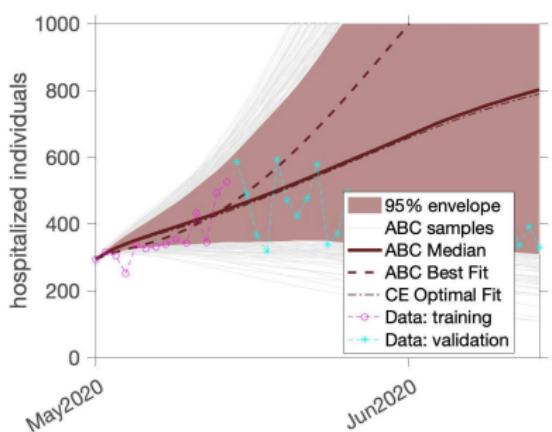


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

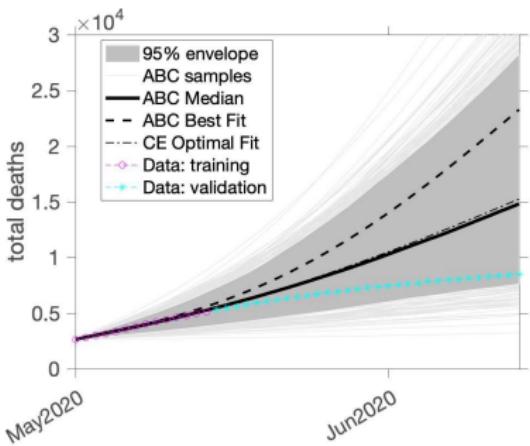
May 1 - May 7, 2020

Influence of the dataset size

hospitalized



total deaths

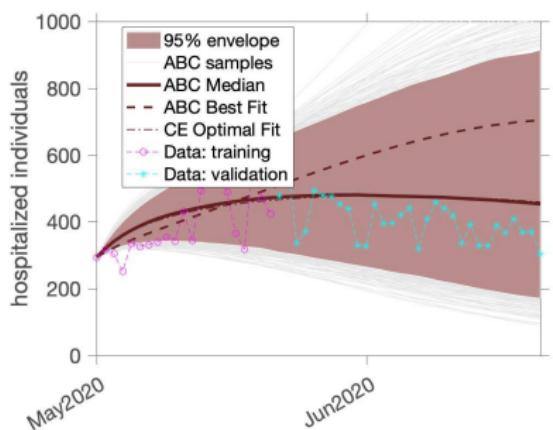


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

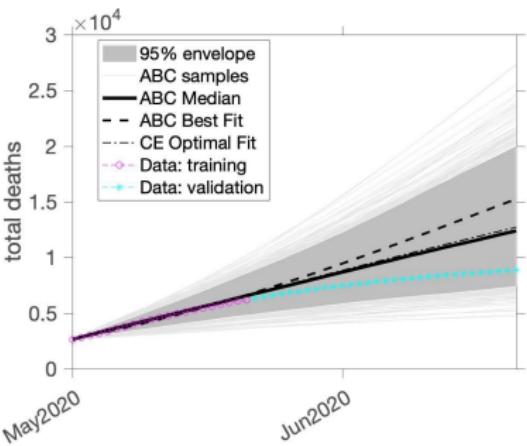
May 1 - May 14, 2020

Influence of the dataset size

hospitalized



total deaths

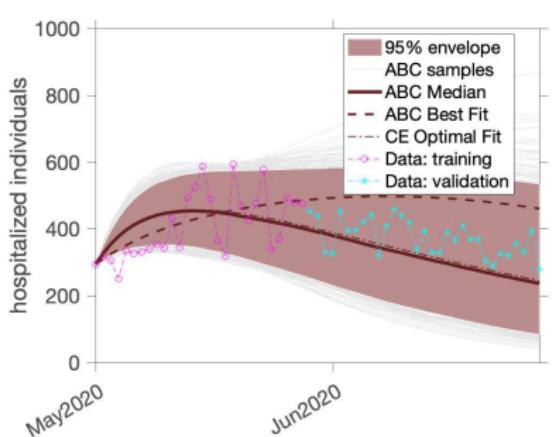


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

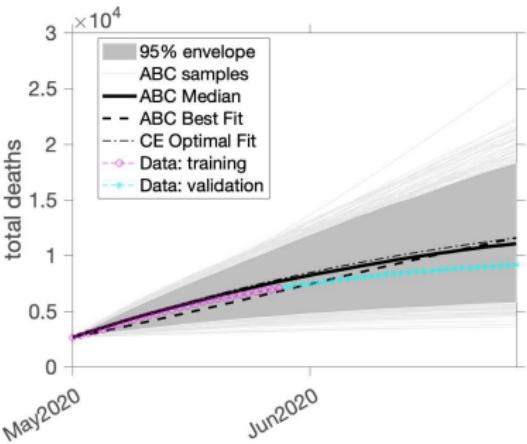
May 1 - **May 21**, 2020

Influence of the dataset size

hospitalized



total deaths

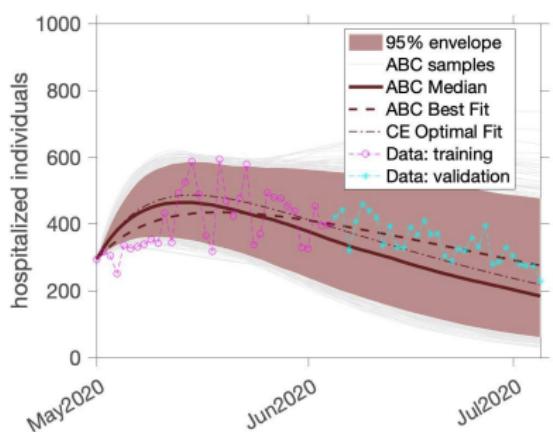


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

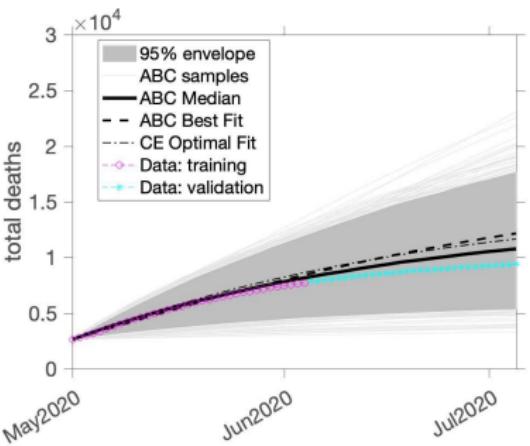
May 1 - **May 28**, 2020

Influence of the dataset size

hospitalized



total deaths

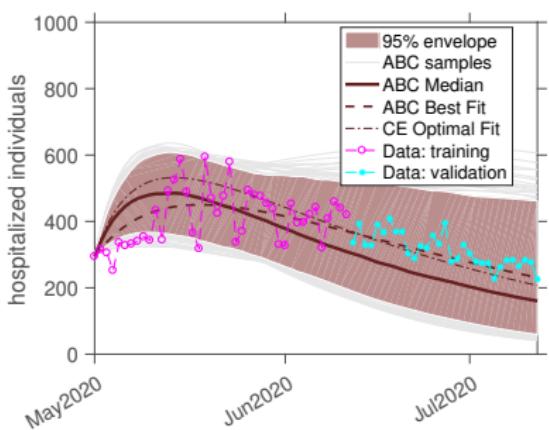


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

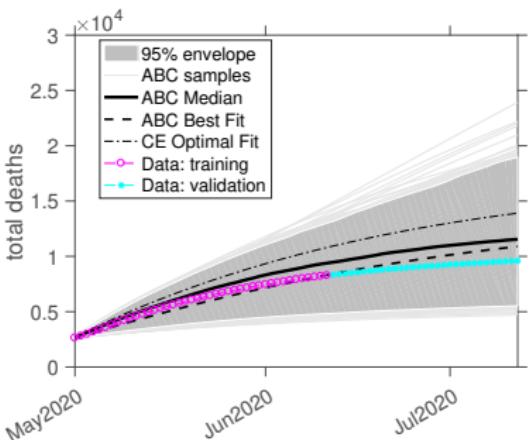
May 1 - June 4, 2020

Influence of the dataset size

hospitalized



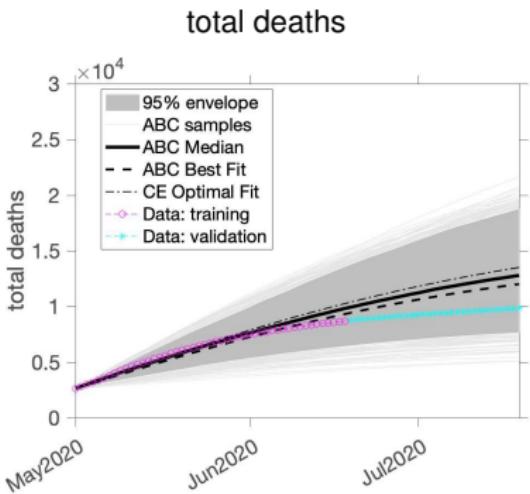
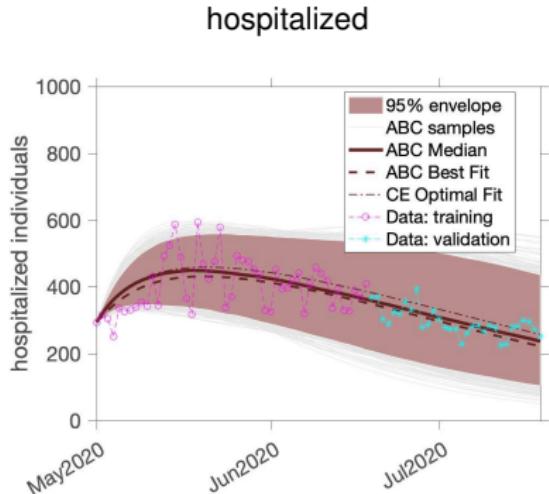
total deaths



$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

May 1 - June 11, 2020

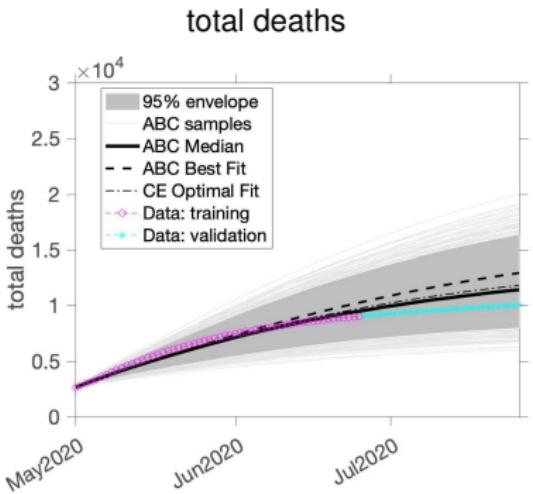
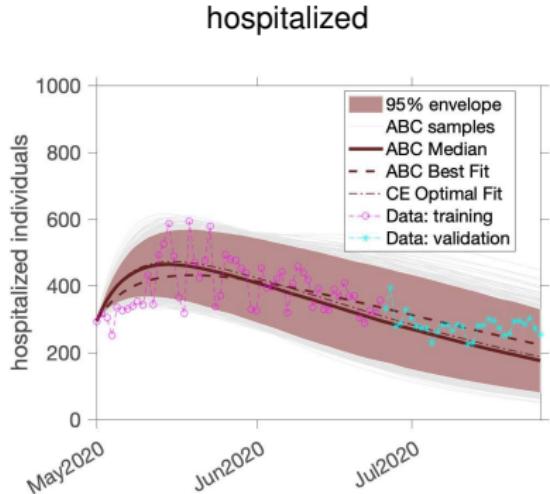
Influence of the dataset size



$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

May 1 - June 18, 2020

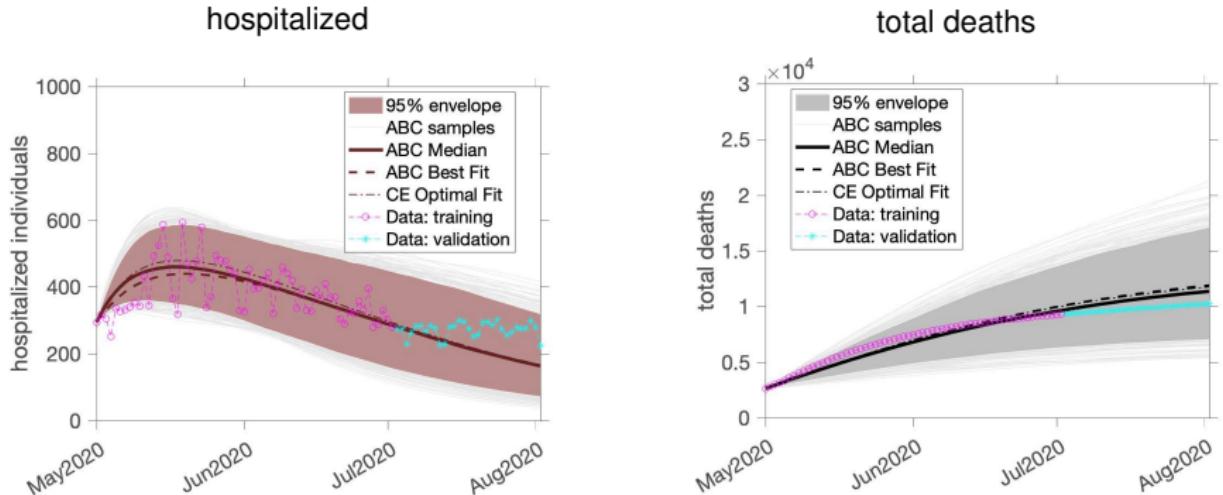
Influence of the dataset size



$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

May 1 - June 25, 2020

Influence of the dataset size

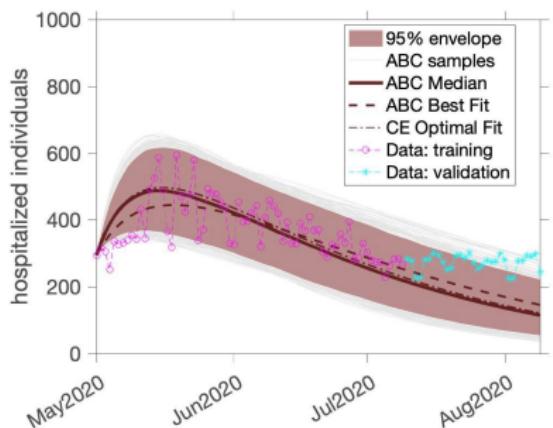


$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

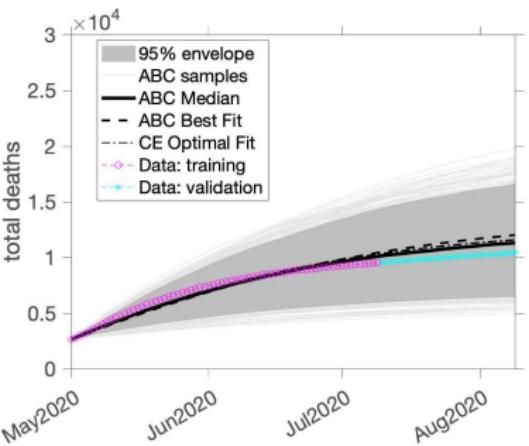
May 1 - July 2, 2020

Influence of the dataset size

hospitalized



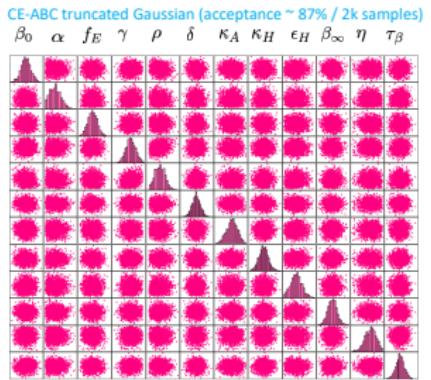
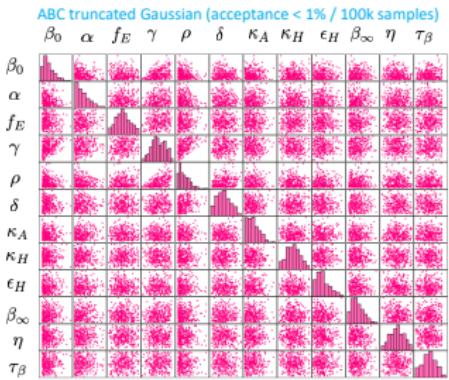
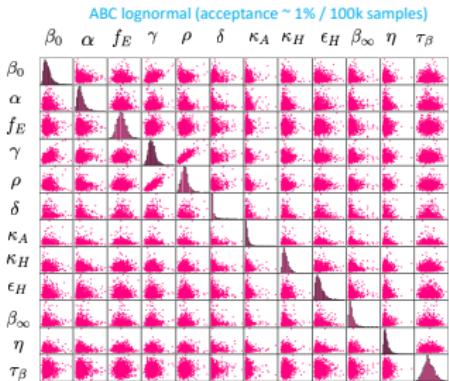
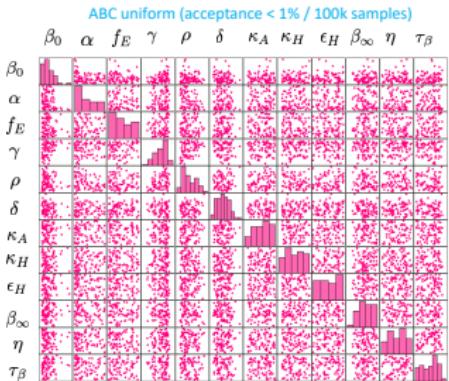
total deaths



$$\omega = 0.75 \quad N_{ce} = 100 \quad N_{abc} = 2000$$

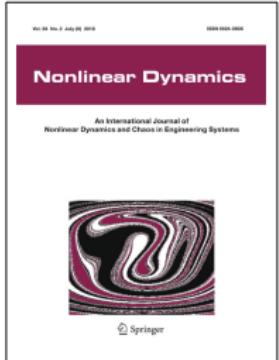
May 1 - July 9, 2020

Comparing CE-ABC and classical ABC



Final remarks

- ▶ Data-driven computational models may be a useful tool to aid with decision making during the course of an epidemic outbreak
- ▶ A Cross-Entropy Approximate Bayesian Computation (CE-ABC) framework for model calibration and uncertainty quantification is proposed
- ▶ CE-ABC + suitable dynamic model + reliable epidemic data may provide a very helpful insights (quantitative and qualitative) about an ongoing outbreak
- ▶ Our data-driven COVID-19 dynamic model for Rio de Janeiro:
 - ▶ “high-fidelity” predictability horizon: until one-week
 - ▶ “reasonable” predictability horizon: until one-month
- ▶ Model oriented decisions demand an interdisciplinary panel of experts:
 - ▶ Scientific
 - ▶ Ethical
 - ▶ Humanistic



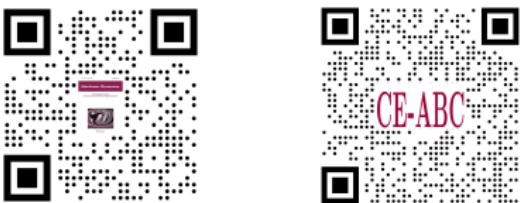
Nonlinear Dyn (2023) 111:9649–9679
<https://doi.org/10.1007/s11071-023-08327-8>

ORIGINAL PAPER



Uncertainty quantification in mechanistic epidemic models via cross-entropy approximate Bayesian computation

Americo Cunha Jr  · David A. W. Barton  ·
Thiago G. Ritto 



A. Cunha Jr, D. A. W. Barton and T. G. Ritto, *Uncertainty quantification in mechanistic epidemic models via cross-entropy approximate Bayesian computation*, *Nonlinear Dynamics*, 111:9649–9679, 2023

Thank you for your attention!

www.americocunha.org



 @AmericoCunhaJr

 @AmericoCunhaJr  @AmericoCunhaJr