Large population limit for a wide class of individual-based epidemic models

Amaury Lambert & SMILE group

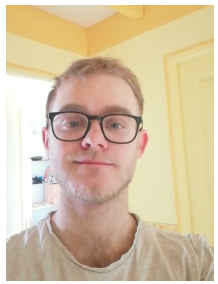
amaury_upmc

SMAI 2021
La Grande-Motte
June 22, 2021

SMILE : An interdisciplinary group in Paris

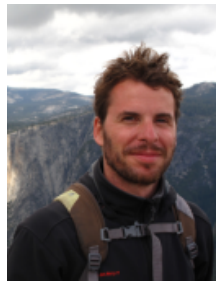
Jasmine 12/01

François 15/01

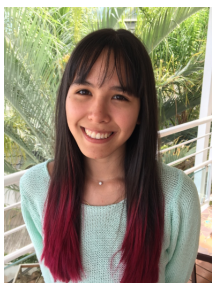


Guillaume T. 25/02

Pete 29/03



Emmanuel 18/04



Laura 21/05

Jean-Jil 24/05

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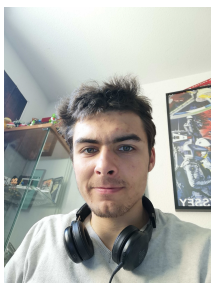
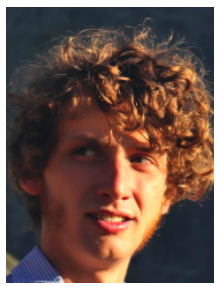


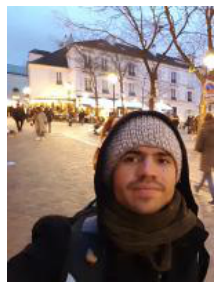
Léo 07/11

Guillaume A. 09/12

Amaury 16/12



Philibert 30/12



Alejandro

SMILE = **S**tochastic **M**odels for the **I**nference of **L**ife **E**volution

* Félix = Félix Foutel–Rodier, ** Emmanuel = Emmanuel Schertzer

Compartmental models

Kermack-McKendrick 1927

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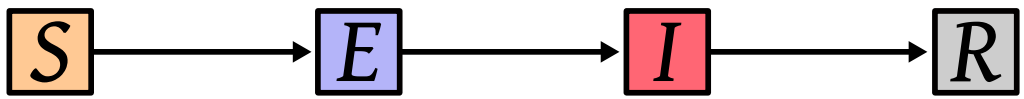

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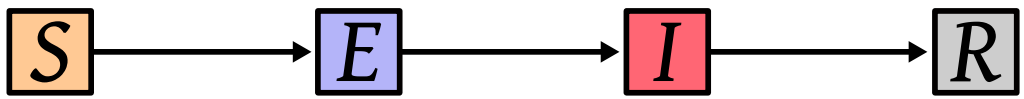

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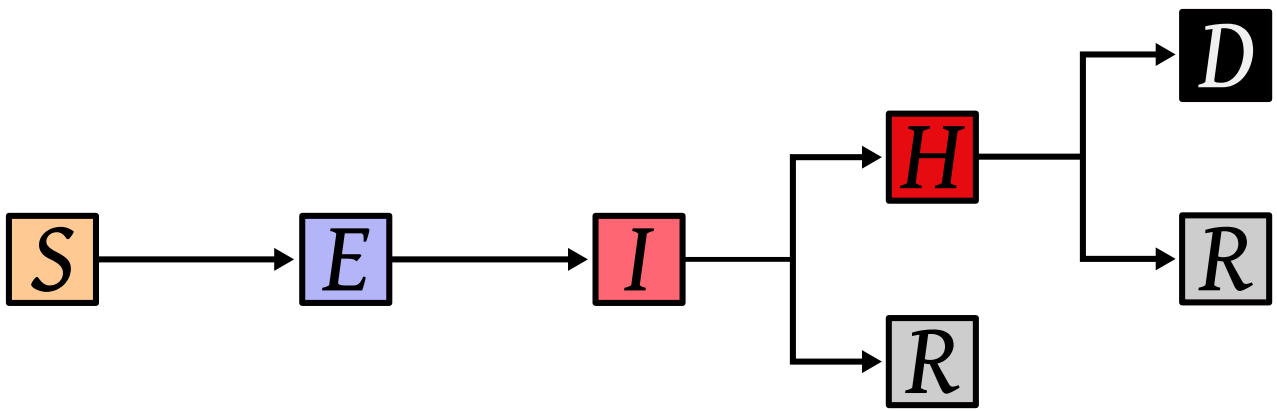

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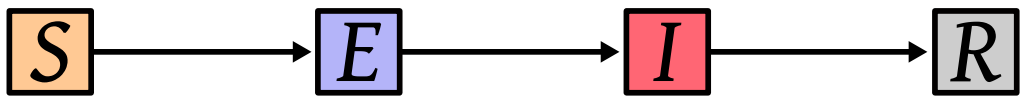

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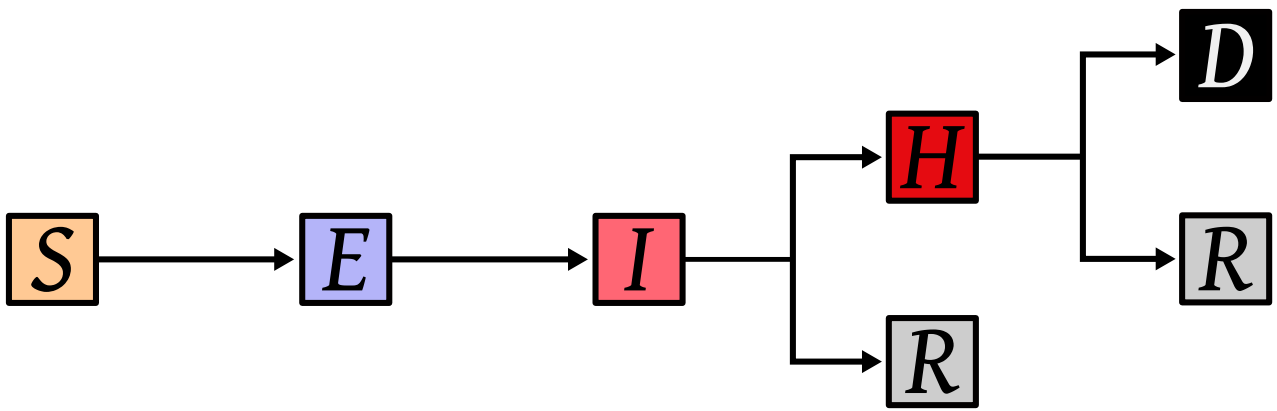


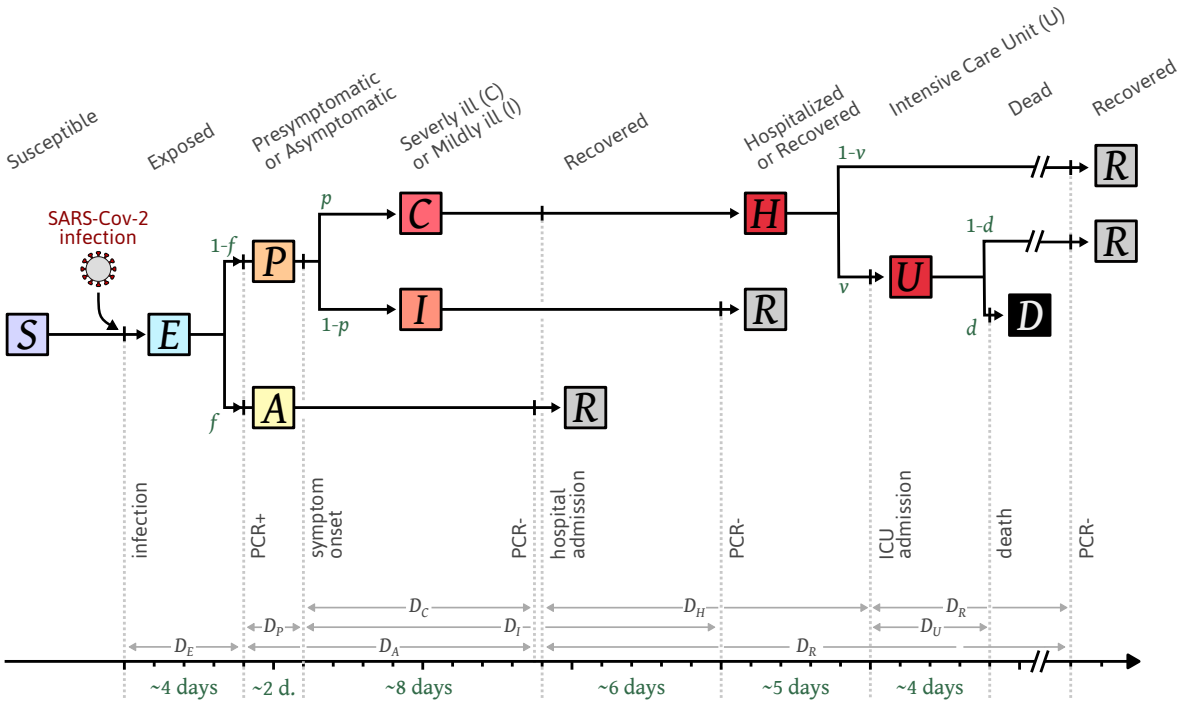
- ...Classes/compartments are structuring variables which are observable or play a role in transmission (health condition, employment category, age...)

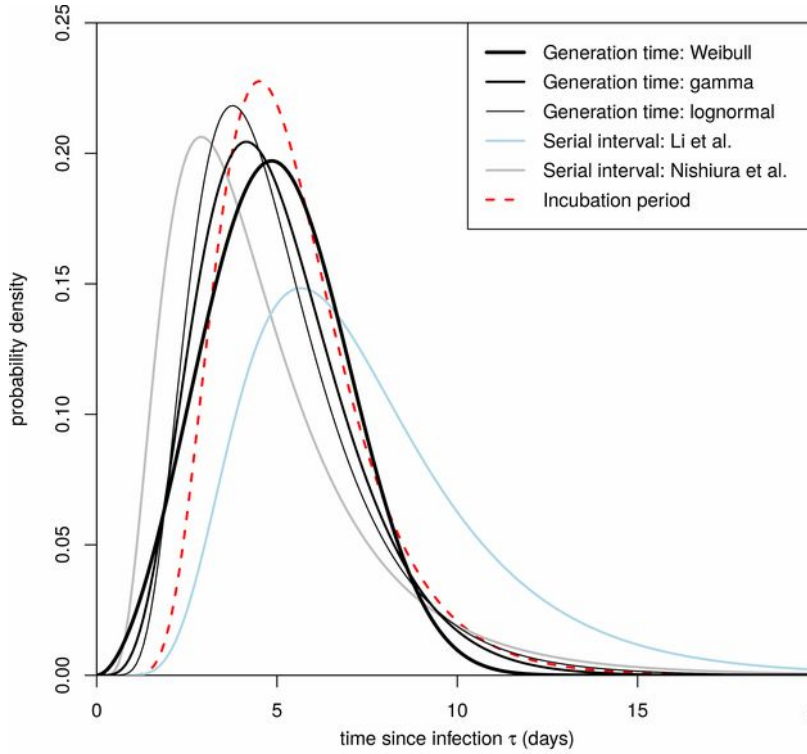
Compartmental models

- Under the assumption of large populations and...
- Lack of memory property of
  - the time spent in each compartment
  - the time between consecutive infections
- ...Compartmental models typically lead to systems of ODEs of the type

$$\begin{cases} \dot{E} &= \beta SI - \eta E \\ \dot{I} &= \eta E - \gamma I \\ \dot{S} &= -\beta SI \end{cases}$$

Life cycle of SARS-Cov2...





Ferretti et al *Science* 2020

- Requires a large number of compartments
- Non-exponential durations spent in each compartment and between infections
- **Q1.** How can we avoid using high-dimensional systems of ODEs (large pop limit)?
- **Q2.** How can we take advantage of the spontaneous growth to large pop?

A general branching process model

- Susceptibles in excess (branching process assumption)
- Each individual is identified by her **age a = time elapsed since her infection**
- Each infected individual is characterized by
  - (i) A stochastic life-history process $(X(a); a \geq 0)$ where
    $$X(a) = \text{ state of ind at age } a$$
  - (ii) A stochastic infection point process $\mathcal{P}$ encoding the times of transmission of the disease to susceptibles
- Example : the SEIR model is recovered by setting

$$X(a) = \begin{cases} E & \text{if } a \in [0, T_I) \\ I & \text{if } a \in [T_I, T_R) \\ R & \text{if } a \in [T_R, \infty) \end{cases} \quad \text{and} \quad \mathcal{P}_k = \mathbb{1}_{[T_I, T_R)} P$$

  where P is a rate β Poisson point process.
- Each newly infected individual draws a pair $(X, \mathcal{P})$ in the same distribution, independently of donor state and age

A word on assumptions

- Susceptibles in excess (branching process model)
- No re-infection
- No spatial/social structure (mean-field model)
- Independence of receiver and donor (contact matrix with identical rows)
- Allows for any type of correlation and temporal auto-correlation of $(X, \mathcal{P})$
- Additional feature : each new infection occurring at time t is successful with probability $c(t)$ (lockdown, masks, social distancing...)

Additional notation

- Average attack rate

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$$R_0 \int_0^\infty \tau(t)\, e^{-\alpha t} dt = 1.$$
- Define the empirical measure of the population as
$$\begin{aligned} \mu_t(da \times \{i\}) &:= \#\{ \text{ infected ind's at time } t, \text{ in state } i \text{ and of age} \in da \ \} \\ &= \sum_k \delta_{t-\sigma_k}(da)\, \mathbb{1}_{\chi_k(t-\sigma_k)=i} \end{aligned}$$

  where σ_k is the birth time of individual k.

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where σ_k is the birth time of individual k.
- Also define
$$\begin{aligned} Y_t(i) &:= \#\{\text{ infected ind's at time } t, \text{ in state } i \,\} = \int_{a=0}^\infty \mu_t(da \times \{i\}) \\ Z_t &:= \#\{\text{ infected ind's at time } t \,\} = \sum_i Y_t(i) \end{aligned}$$

A law of large numbers

- Start with N infected individuals at time 0.
- Assume that the ages of the initial individuals $(A_k)_k$ are iid with density g.
- The initial life-cycle and infection processes are iid $(\widetilde{X}_k, \widetilde{\mathcal{P}}_k)_k$, where

$$\widetilde{X}_k(a) = X_k(A_k + a), \quad \widetilde{\mathcal{P}}_k(da) = \mathcal{P}_k(A_k + da).$$

Theorem (Foutel–Rodier et al, 2020)

As $N \to \infty$, for any t,

$$\frac{1}{N}\mu_t^N(da \times \{i\}) \longrightarrow n(t,a)\, p(a,i)\, da$$

where $p(a,i) = \mathbb{P}(X(a) = i)$ and n is the solution to the McKendrick–von Foerster PDE

$$\frac{\partial n}{\partial a} + \frac{\partial n}{\partial t} = 0,$$

with boundary condition

$$n(t,0) = c(t) \int_0^\infty n(t,a)\tau(a)\, da,$$

and initial condition

$$n(0,a) = g(a).$$

A law of large numbers : consequences

- The age structure converges to the solution to a PDE that only depends on τ
- The class structure $Y_t^N(i)$ converges to

$$\int_0^\infty n(t,a)\, p(a,i)\, da$$

  which only depends on $p(a,i) = \mathbb{P}(X(a) = i)$.

- Structuring by age...
  - decouples transmission and life history
  - decouples time and class structure.
- Drawbacks :
  - requires assuming large initial population size
  - requires specifying age profile g, which is not observable.

Branching process counted with its characteristic

- Branching process counted with the random characteristic χ

$$Z_t^{\chi} := \sum_k \chi_k(t - \sigma_k),$$

where σ_k = infection time of ind k and sum is taken over all ind's in the course of the epidemic.

- Examples

$$\chi_k(t) = \begin{cases} 1 & \text{if } k \text{ is in state } i \text{ at time } t \\ 0 & \text{otherwise.} \end{cases} \qquad \Longrightarrow Z_t^{\chi} = Y_t(i)$$

$$\chi_k(t) = \begin{cases} 1 & \text{if } t \geq a \\ 0 & \text{otherwise.} \end{cases} \qquad \Longrightarrow Z_t^{\chi} = \#\{ \text{ ind's of age} \geq a \text{ at time } t \}.$$

A.s. limit theorems

Jagers 74, Nerman 81, Jagers & Nerman 84

Theorem (Jagers 74, Nerman 81, Jagers & Nerman 84)

Assume $\alpha > 0$. Then there is a single random variable W_∞ such that for all random characteristics χ simultaneously, with probability 1,

$$\lim_{t\to\infty} e^{-\alpha t} Z_t^\chi = \frac{\mathbb{E}\left(\widehat{\chi}(\alpha)\right)}{\alpha\beta} W_\infty,$$

where $\beta := R_0 \int_0^\infty t\,\tau(t)\,e^{-\alpha t}dt$ and

$$\widehat{\chi}(\alpha) := \alpha \int_0^\infty \chi(t)\,e^{-\alpha t}dt,$$

where it is implicit that $\chi(t)$ is the characteristic of the ancestor, 'born' at time 0. In particular, if we take $\chi(t) = \mathbb{1}_{t\geq a}$, we get

$$\lim_{t\to\infty} \frac{\#\{\text{ ind's of age} \geq a \text{ at time } t\}}{Z_t} = e^{-\alpha a}.$$

A second law of large numbers

- Start with 1 infected individual at time 0.
- Assume $\alpha > 0$.
- Let T_K be a random time such that $\lim_{K\to\infty} T_K = \infty$, e.g., time when $> K$ infected.
- $c(t) \leftarrow c(T_K + t)$.

Theorem (Foutel–Rodier et al, 2020)

Recall Z_t denote the total number of infected by time t. As $K \to \infty$, for any t,

$$\frac{1}{Z_{T_K}} \mu^K_{T_K+t}(da \times \{i\}) \longrightarrow n(t,a)\mathbb{P}(X(a) = i)da \quad a.s.,$$

where n is the solution to the McKendrick–von Foerster PDE

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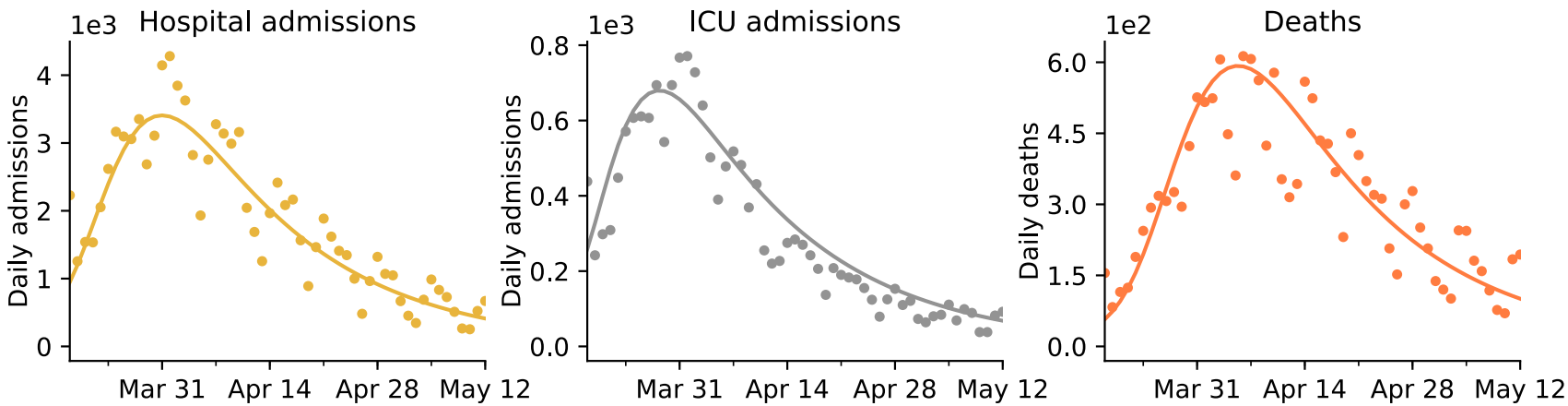
$$n(t,0) = c(t) \int_0^\infty n(t,a)\tau(a)\, da,$$

and initial condition

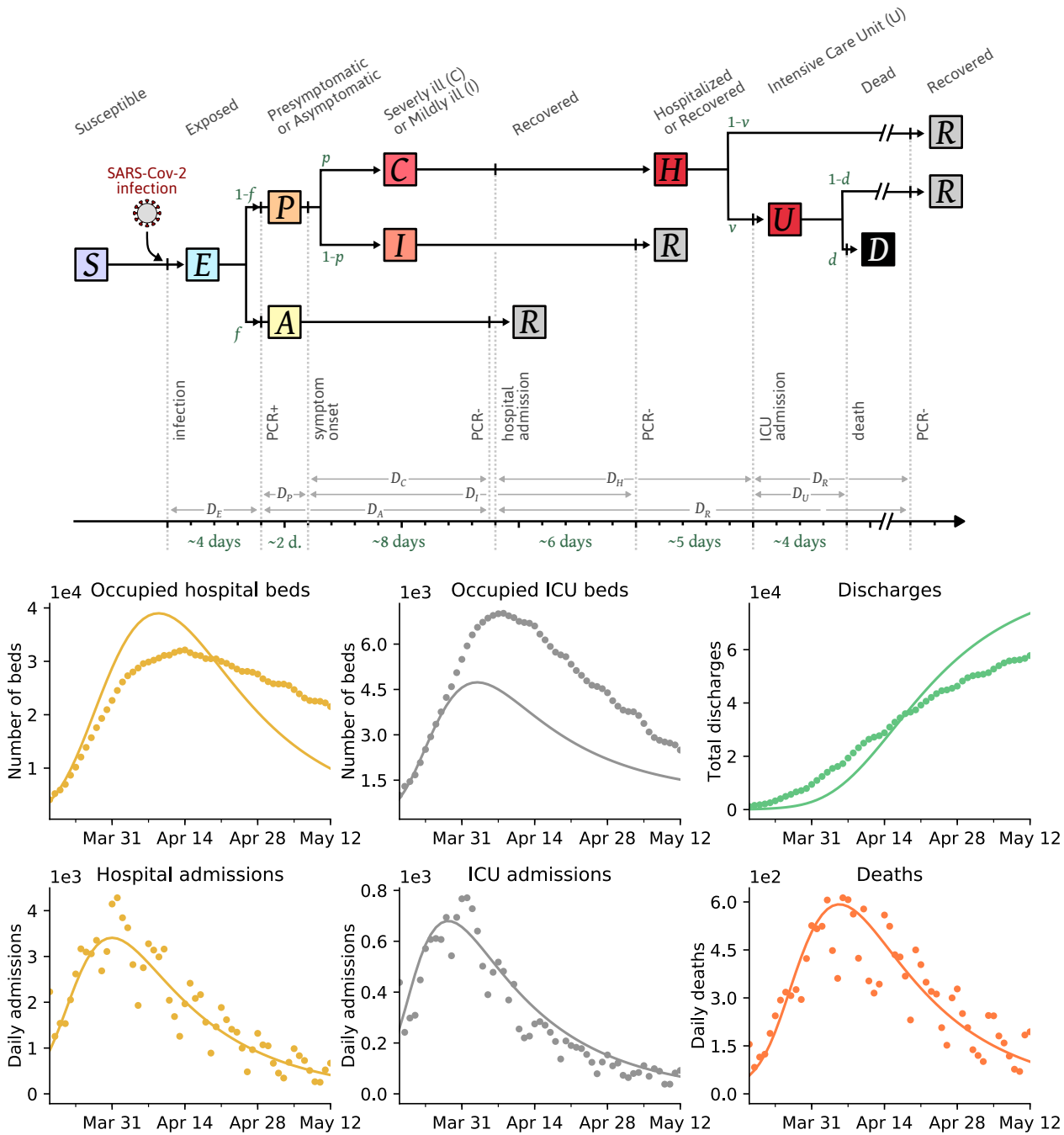
$$n(0,a) = \alpha e^{-\alpha a}.$$

Application to the COVID-19 epidemic in France

- Given the profile of τ, a compartmental model and a parameter set :
  - α is estimated as the initial growth rate
  - the PDE is solved numerically
  - the one-dimensional marginals $\mathbb{P}(X(a) = i)$ can be computed assuming Gamma distributed sojourn times
  - the observations are assumed to follow a Poisson distribution centered on the predicted value
- The best parameter set is obtained by maximum likelihood



Fitting the incidence curves



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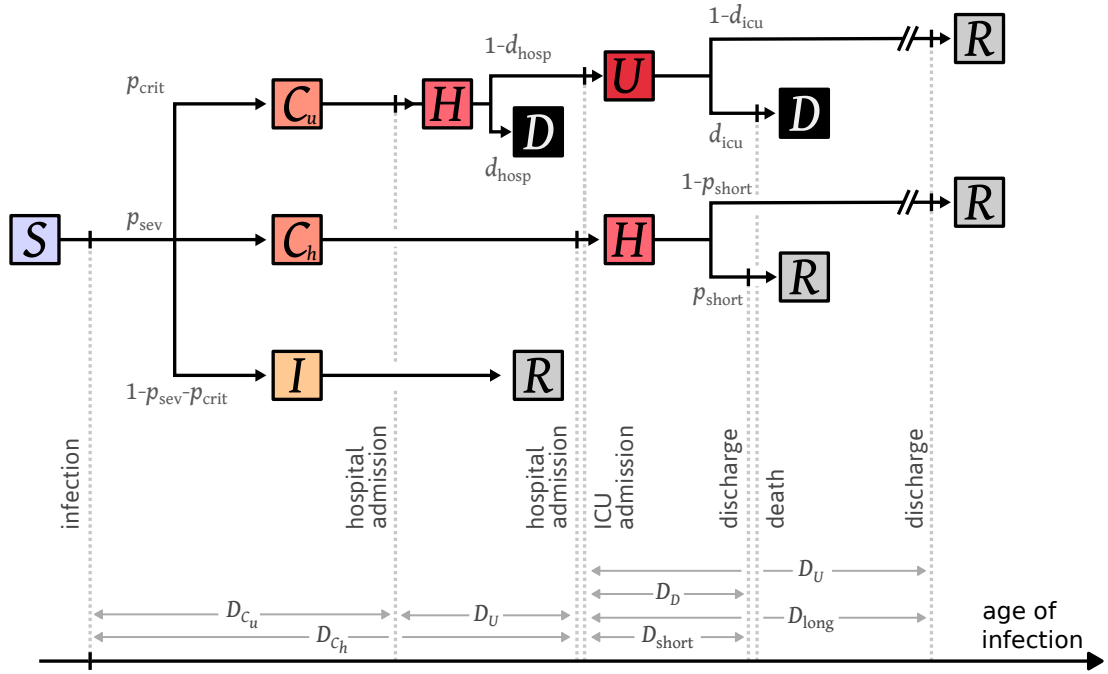

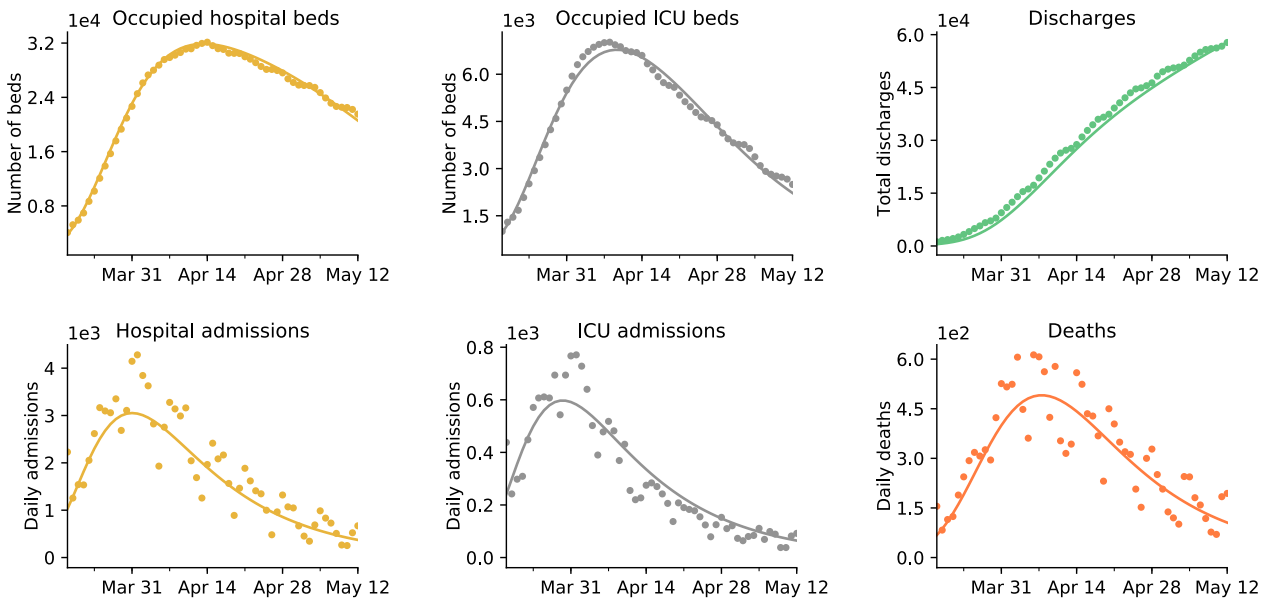

Discussion

- A general, stochastic, individual-based model for the spread of complex diseases
- Law of large numbers as a result of spontaneous growth, with emerging age structure
- Limit in the form of an age-structured McKendrick-von Foerster PDE decoupling time/class structure and transmission/life history.
- Model is tractable enough to be used for inference.
- Preprint : “From individual-based epidemic models to McKendrick-von Foerster PDEs : A guide to modeling and inferring COVID-19 dynamics”, by

  Foutel-Rodier* F, Blanquart F, Courau P, Czuppon P, Duchamps JJ, Gamblin J, Kerdoncuff E, Kulathinal R, Régnier L, Vuduc L, Lambert** A & Schertzer** E (2020).

  * first author, ** co-last authors
  `https://arxiv.org/abs/2007.09622`

- See also :

  JY Fan, K Hamza, P Jagers, F Klebaner. Convergence of the age structure of general schemes of population processes. *Bernoulli* 2020.

  K Hamza, P Jagers, F Klebaner. The age structure of population- dependent general branching processes in environments with a high carrying capacity. *Proceedings of the Steklov Institute of Mathematics*, 2013.

  VC Tran. Large population limit and time behaviour of a stochastic particle model describing an age-structured population. *ESAIM : Probability and Statistics*, 2008.

Acknowledgements

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DE FRANCE
1530

MODCOV19

...Et merci pour votre attention !

Notation	Description	Value	Source
R_0	Basic reproduction number during lockdown	0.734	E
W	Total number of infections before March 17 2020	9.52×10^5	E
$p_{\mathrm{crit}} + p_{\mathrm{sev}}$	Probability of being hospitalized	0.036	S
$\frac{p_{\mathrm{crit}}(1-d_{\mathrm{hosp}})}{p_{\mathrm{crit}}+p_{\mathrm{sev}}}$	Probability of entering ICU conditional on being at the hospital	0.19	S
$\frac{d_{\mathrm{hosp}}+(1-d_{\mathrm{hosp}})d_{\mathrm{ICU}}}{1+p_{\mathrm{sev}}/p_{\mathrm{crit}}}$	Death probability conditional on being hospitalized	0.181	S
d_{ICU}	Probability of death conditional on being in ICU	0.709	E
p_{short}	Probability of a short stay at hospital	0.701	E
D_{C_h}	Delay between severe infection and hospital admission	14.5 days	E
D_{short}	Delay between hospital admission and quick discharge	7.36 days	E
D_{long}	Delay between hospital admission and slow discharge	47.5 days	E
D_{C_u}	Delay between critical infection and hospital admission	11.0 days	E
D_H	Delay between hospital admission and ICU admission	1.5 days	S
D_U	Delay between ICU admission and discharge	28.2 days	E
D_D	Delay between ICU admission and death	9.90 days	E
γ	Scale parameter common to all Gamma distributions	0.316	E

TABLE – Inferred parameter set for the occupancy model. The values indicated for the durations correspond to the means of the Gamma distributions. In the “Source” column, “E” = estimated, “F” = taken from Salje et al (2020).