A multi-scale model of virus pandemic: Heterogeneous interactive entities in a globally connected world

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Some reasonings on pandemic modeling

• Modeling approach should go far beyond deterministic population dynamics: Individual reactions are heterogeneous. Spatial dynamics is generated by interactions and transportation devices.

• The modeling ought to be developed within a multiscale vision: The dynamics of individuals depends on the dynamics at a smaller scale given by the competition between virus particles and the immune system.

• Applied mathematicians cannot tackle the modeling problem by a stand-alone approach: An interdisciplinary vision is necessary through mutually enriching and beneficial interactions with scientists in other fields as virology, epidemiology, immunology and biology in general.

• The scope of such a research project should not be confined only to "biological and medical sciences", but also be addressed to wider aspects of other communities in our society, e.g. economists and sociologists.

A multiscale vision of contagion and in-host dynamics

Contagion in crowds: Consider a population of N_0 individuals homogeneously distributed in space. A small number $\varepsilon\, N_0$ is initially infected, while $(1-\varepsilon)\, N_0$ is considered healthy. Contagion depends on the frequency of contacts, on the level of the infection within each individual, on the level of physical protection used by individuals aware of the risk of contagion, and on the so-called *social distance*. [1]

1. N. Bellomo, R. Bingham, M. A. J. Chaplain, G. Dosi, G. Forni, D. A. Knopoff, J. Lowengrub, R. Twarock, and M. E. Virgillito, **A multi-scale model of virus pandemic: Heterogeneous interactive entities in a globally connected world**, *Math. Models Methods Appl. Sci.*, **30**, 1591–1651, (2020).

A multiscale vision of contagion and in-host dynamics

A simple model of contagion: The contagion dynamics, followed by the competition for survival within each individual, can be modeled according to the following rationale:

1. The modeling is grounded on mathematical tools of the so-called *kinetic theory of active particles*
2. Individuals are viewed as *active particles* which are carriers of an internal state, called *activity*. The level of infection of each a-particle can progress (or regress) in time due to a prevalence (or lack of prevalence) of the virus aggressiveness over the immune defence.
3. Contagion depends on the *level of the infection* as well as on the *social distance* between individuals which is a constant parameter in the case of spatial homogeneity.
4. Dynamics within each individual depends on the heterogeneous *competition between a proliferative virus and the immune system*.

Functional subsystems

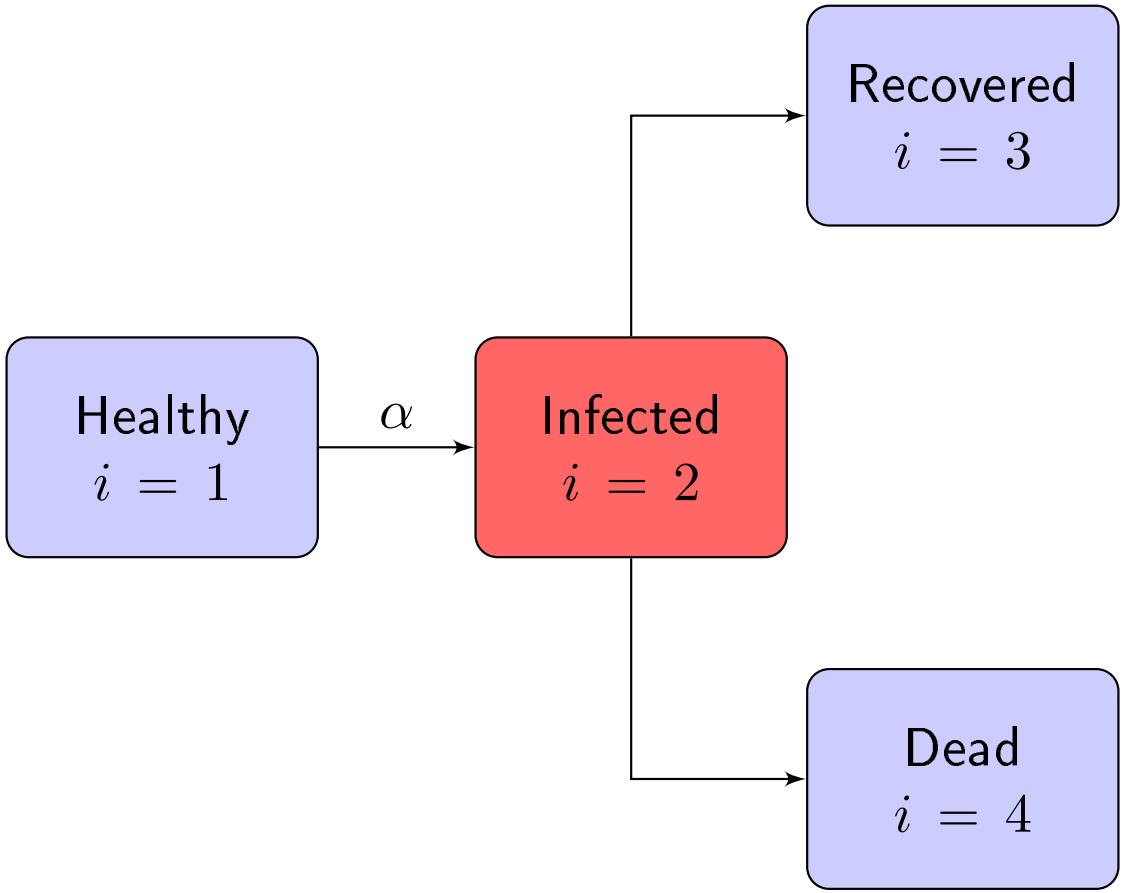


Figure – Transfer diagram of the model. Boxes represent functional subsystems and arrows indicate transition of individuals. The abbreviation i-FS is used to denote the i-th population viewed as a functional subsystem.

Flow chart of the systems approach

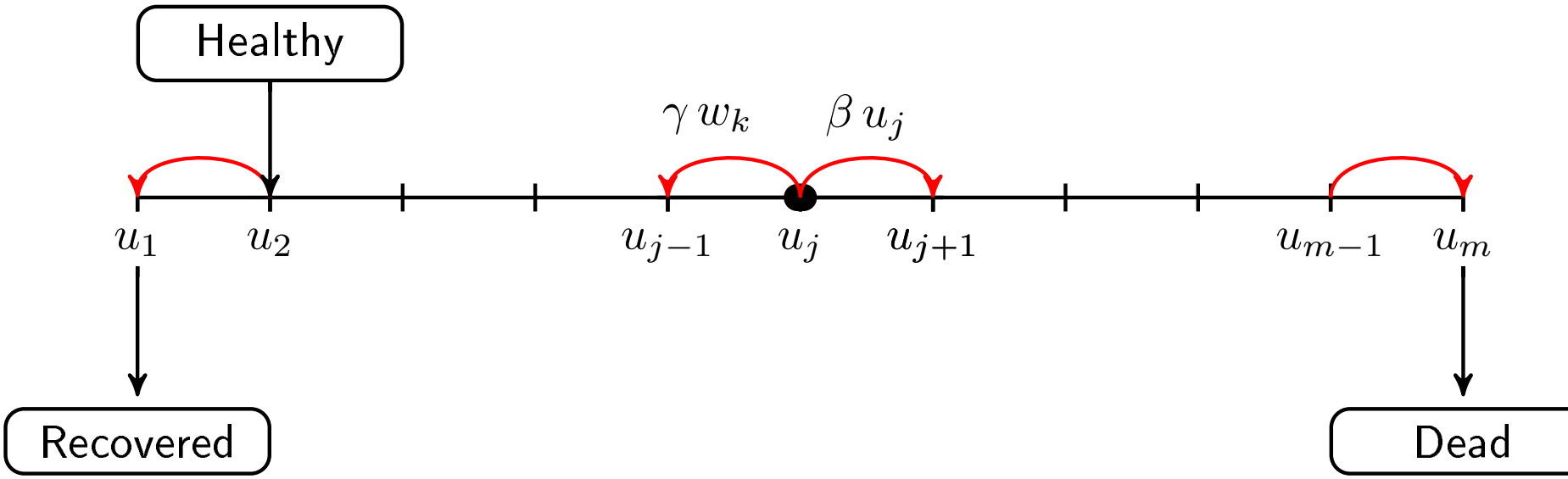


Figure – Dynamics within infected population.

The micro-state of a-particles includes two variables $u \in [0,1]$ and $w \in [0,1]$ corresponding, respectively, to the progression of virus invasion and to the level of activation of the immune defence.

$$\mathbf{u} = \{u_j = \frac{j-1}{m-1}, j = 1, \ldots, m\}, \quad \text{and} \quad \mathbf{w} = \{w_k = \frac{k-1}{n-1}, k = 1, \ldots, n\}.$$

A multiscale vision of contagion and in-host dynamics

Within host dynamics

- $i = 1$: Healthy individuals with distribution $f_1^{1,k}(t, u_1, w_k)$, where t is the time belonging to the interval $[0, T]$.
- $i = 2$: Infected individuals with distribution $f_2^{j,k}(t, u_j, w_k)$, with $1 < j < m$.
- $i = 3$: Individuals recovered from the infection with distribution $f_3(t)$, namely infected individuals that succeed in reaching back to the state $j = 1$.
- $i = 4$: $f_4(t)$ is the number of individuals of the infected population who do not succeed to recover, that are infected individuals who reach the state $j = m$.

A multiscale vision of contagion and in-host dynamics

Within host dynamics A general structure is reported as it provides the conceptual basis for these developments.

$$\begin{aligned}\partial_t f^r_{ij} &= G^r_{ij}(\mathbf{f}) - L^r_{ij}(\mathbf{f}) \\ &= \sum_{s=1}^{m} \sum_{h,k,p,q=1}^{n} \eta^{pq}_{hk}(r,s)(\mathbf{f}) \mathcal{A}^{pq}_{hk}(hk \to ij)(\mathbf{f}) f^r_{hk} f^s_{pq} \\ &\quad - f^r_{ij} \sum_{s=1}^{m} \sum_{p,q=1}^{n} \eta^{pq}_{ij}(\mathbf{f}) f^s_{pq},\end{aligned}$$

The subscripts h, k and p, q denote the micro-states corresponding to the r, s FSs which by interactions lead to the dynamics of f^r. In addition, η^{pq}_{hk}, η^{pq}_{ij}, denote the interaction rates, and $\mathcal{A}^{pq}_{hk}$ the transition rate into the micro-state i, j of the r-FS. The time dynamics are then ruled by a *gain* term of particles which at time t gain the state (i, j) and a *loss* term related to particles which lose such a state.

The mathematical model

$$
\begin{cases}
\partial_t f_1^{1,k}(t) = -\alpha \displaystyle\sum_{s=1}^{n} \sum_{j=2}^{m-1} u_j \, f_1^{1,k}(t) \, f_2^{j,s}(t), \\
\partial_t f_2^{j,k}(t) = \alpha \displaystyle\sum_{s=1}^{n} \sum_{j=2}^{m-1} u_j \, f_1^{1,k}(t) \, f_2^{j,s}(t) \, \delta_{2j} \; + \beta u_{j-1} \, f_2^{j-1,k}(t) \\
\qquad\qquad + \gamma \, w_k \, f_2^{j+1,k}(t) - \beta \, u_j \, f_2^{j,k}(t) - \gamma \, w_k \, f_2^{j,k}(t), \\
\partial_t f_3(t) = \gamma \displaystyle\sum_{k=1}^{n} w_k \, f_2^{2,k}(t), \\
\partial_t f_4(t) = \beta \, u_{m-1} \displaystyle\sum_{k=1}^{n} f_2^{m-1,k}(t).
\end{cases}
$$

Numerical simulations

How long should locking last? *Simulations show how delaying T_d reduces the peak, but increases the time interval of the persistence of the infection.*

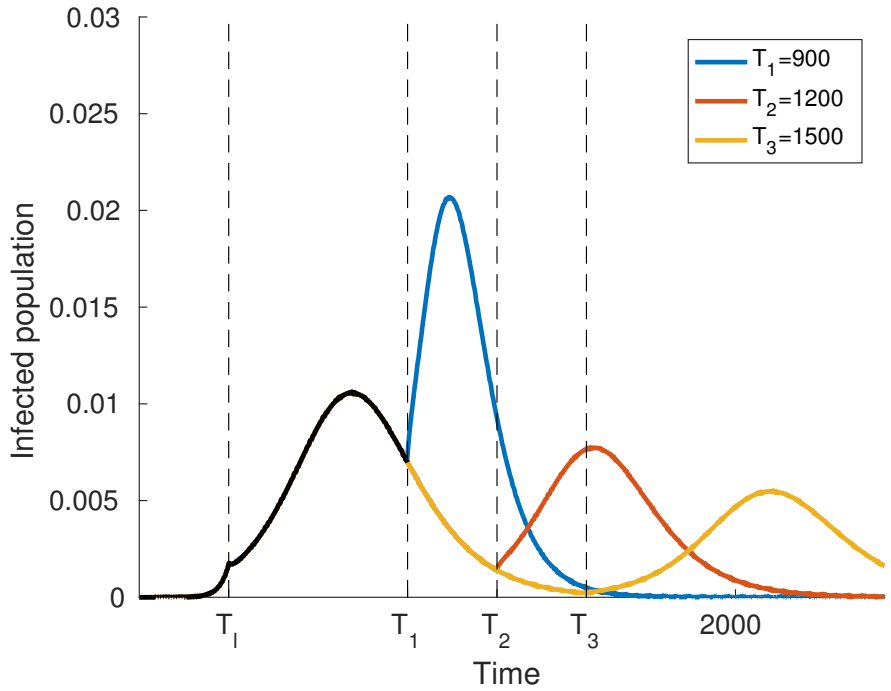


Figure – Varying lifting times. We take a fixed locking time $T_\ell = 300$, and three different reopening times $T_d = 900, 1200, 1500$. $\alpha = 0.4$ for $t \in [0, T_l) \cup [T_d, T_{max}]$ while $\alpha = 0.25$ during the locking interval.

Numerical simulations

How flexible shall lock-down relaxation be? *We study the influence of the relaxation level for fixed values of T_d and T_ℓ. Simulations show that a large relaxation can generate high level peaks.*

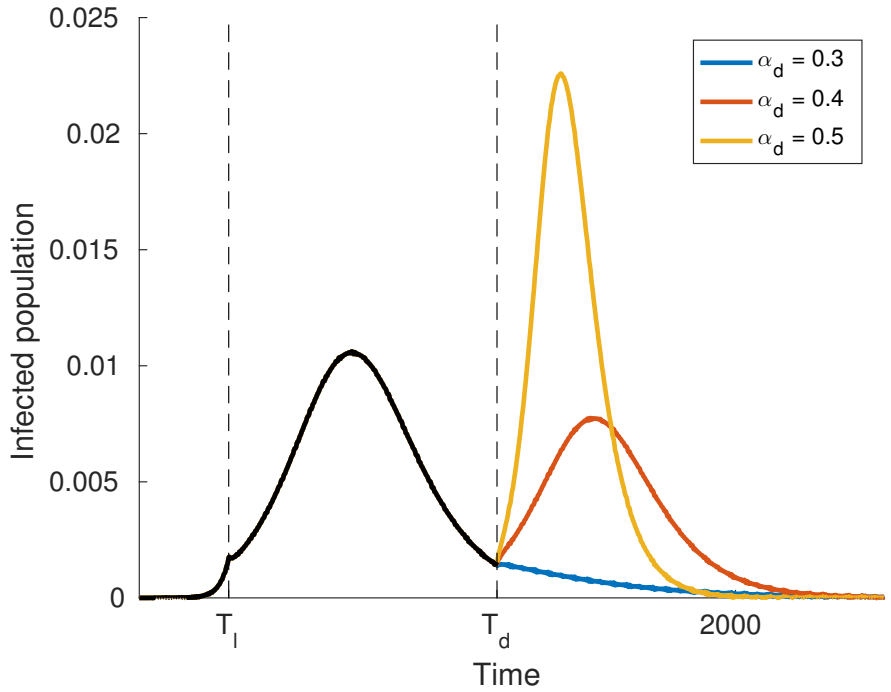
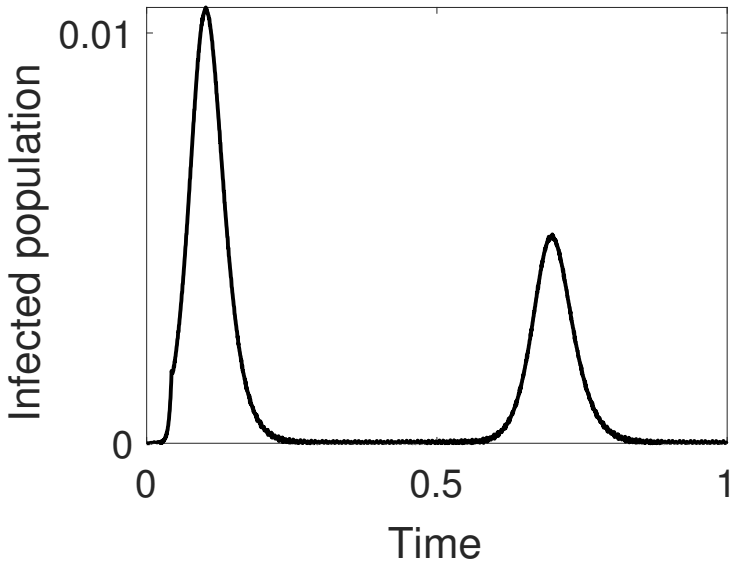
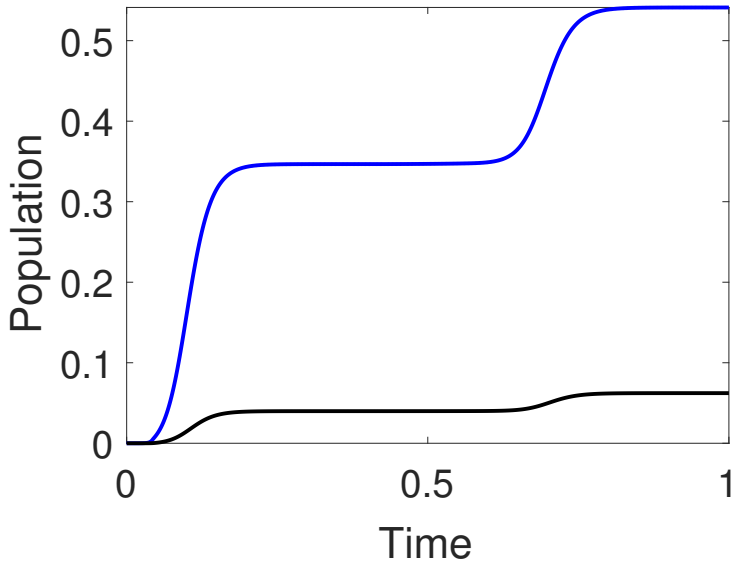


Figure – Varying the lifting value α_d. We take fixed locking and reopening times $T_l = 300$ and $T_d = 1200$, respectively. $\alpha = 0.4$ initially for $t \in [0, T_l)$ then reduced to $\alpha = 0.25$ during the locking interval and finally we consider three different reopening values $\alpha_d = 0.3, 0.4, 0.5$.

Numerical simulations

Which type of scenarios appear for the first and second wave?
After the lockdown, the increase of the infectivity parameter always creates a second wave. If there is a control on the size of the parameter, the second wave is lower than the first wave. On the right, dark grey for death and blue for recovered.

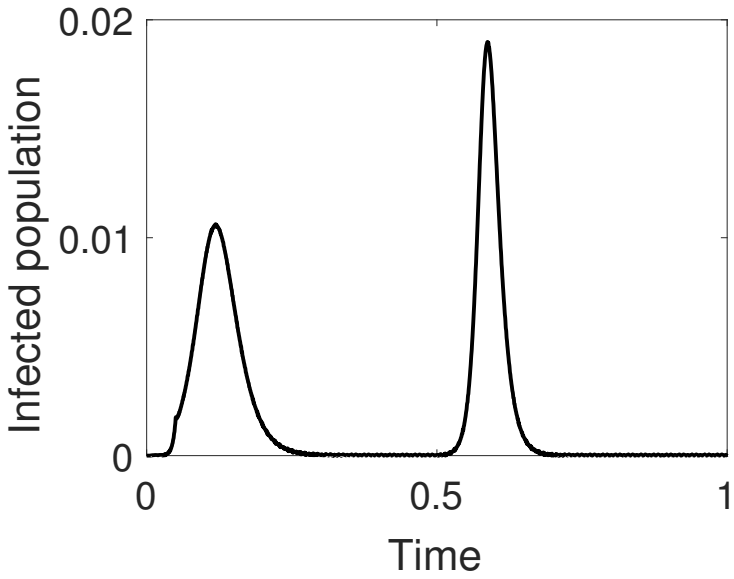


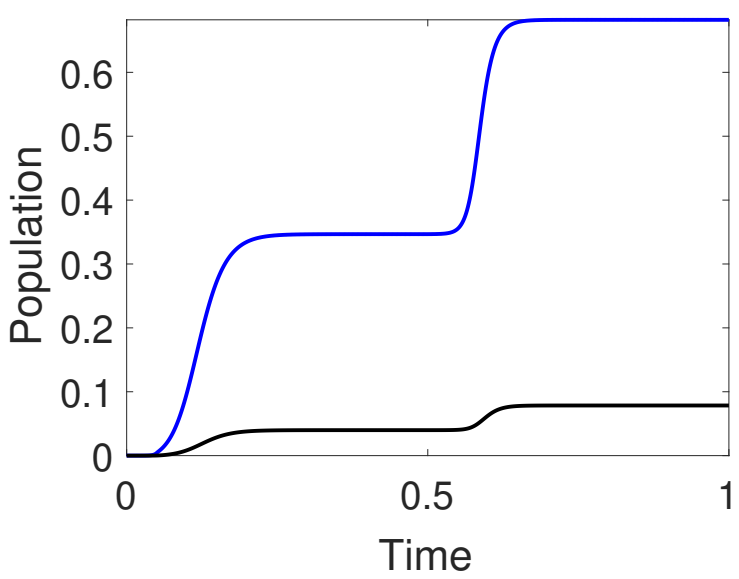


$0 \leq t \leq 300 : \ \alpha = 0.4; \quad 300 < t \leq 3000 : \ \alpha = 0.25; \quad 3000 < t \leq 4000 : \ \alpha = 0.35; \quad t > 4000 : \ \alpha = 0.4; \mu = 0.5.$

Numerical simulations

How the size of second wave refers to the level of confinement?
After the lockdown the increase of the infectivity parameter always creates a second wave. In absence of a control on the size of the parameter, the second wave can be higher than the first wave. On the right, dark grey for death and blue for recovered.

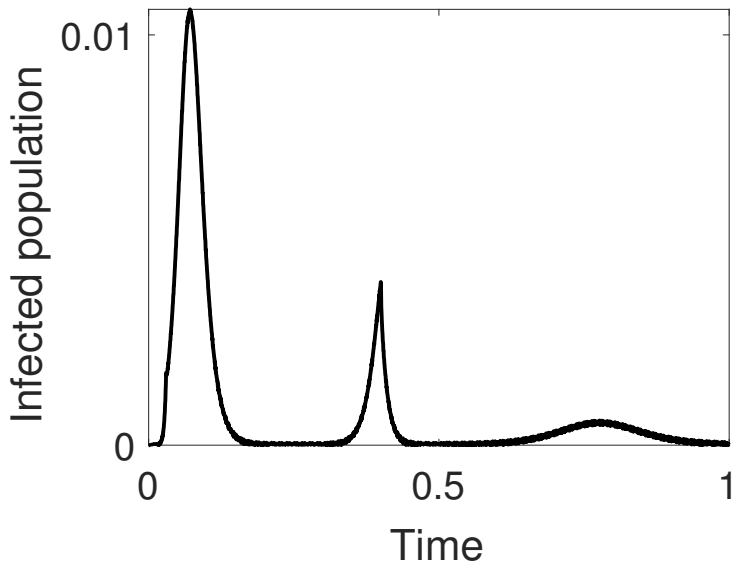


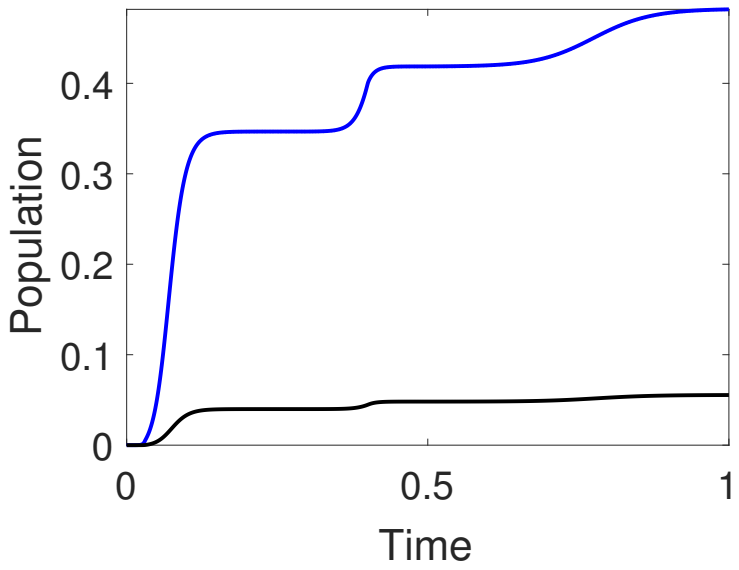


$0 \leq t \leq 300 : \ \alpha = 0.4; \quad 300 < t \leq 3000 : \ \alpha = 0.25; \quad t > 3000 : \ \alpha = 0.5; \quad \mu = 0.5.$

Numerical simulations

Can a third wave appear? After the lockdown, the increase of the infectivity parameter can create dynamics with multiple waves. On the right, dark grey for death and blue for recovered.





$0 \leq t \leq 300 : \ \alpha = 0.4; \quad 300 < t \leq 3000 : \ \alpha = 0.25; \quad 3000 < t \leq 4000 : \ \alpha = 0.4; \quad 4000 < t \leq 5000 : \ \alpha = 0.25; \quad t > 5000 : \ \alpha = 0.4; \mu = 0.5.$

Modeling strategy for corona virus pandemic

Key objectives

• Design of **a multiscale modeling approach towards simulations** with the capacity to explore crucial aspects of the spread of a pandemic.

• **Exploring the different scenarios corresponding to possible strategies to control a virus pandemic**.

• **Validation of models to make them predictive**, while models can be further developed to include additional details of the virus such as mutations, selection and evolution.

Closure

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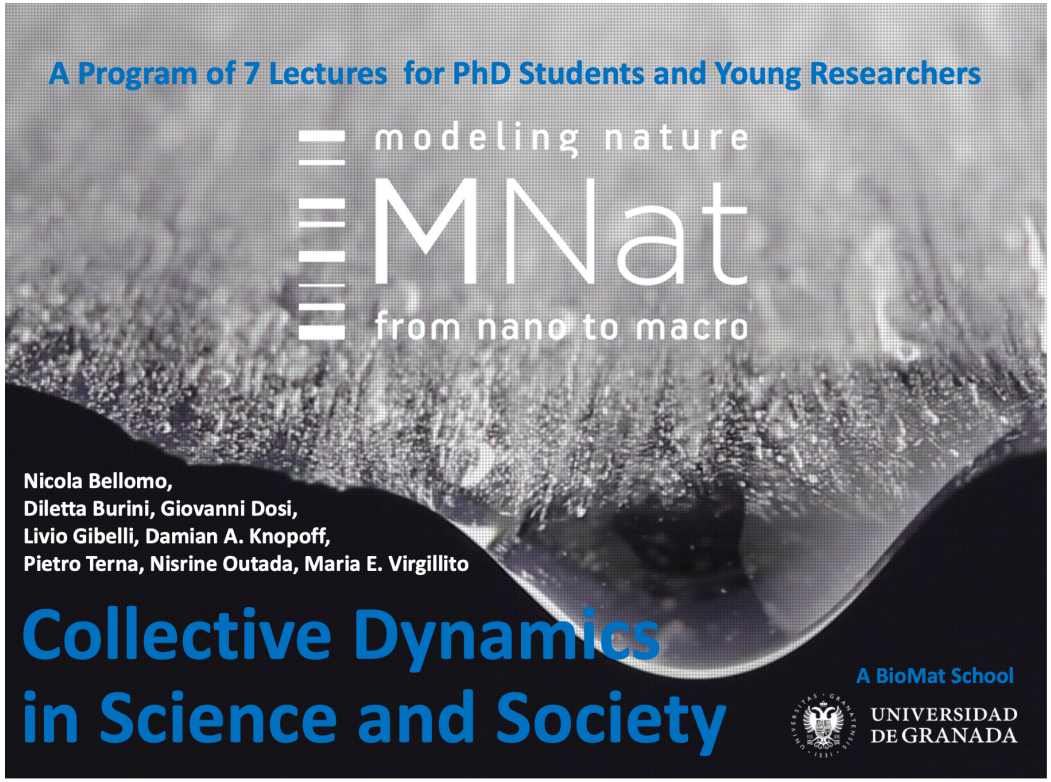

THANKS TO THE AUDIENCE