

Final report
for the project
Analysis and control of mathematical models for the evolution of epidemics,
tumors and phase field processes
Project period: 2023-2025

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I. Description of the research

The topic proposed in this project had both theoretical and practical relevance as it developed in a mathematical research direction of current international interest.

We aimed to develop new models based on nonlinear partial differential equations of parabolic and hyperbolic type for describing physical and biological processes of high interest and to find mathematical methods for their study. Moreover, we applied them for characterizing and predicting the possible evolution of these phenomena, mainly biological and physical processes including population dynamics, epidemic spread, with a special attention to SARS-CoV-2 propagation, tumor growth models and phase field processes.

The topics studied in this project had both a theoretical and practical importance, since the theoretical results were adapted and applied to concrete problems put by other sciences and faced towards a research line of current international interest. The models developed on the basis of these researches gave the possibility of a better understanding of some peculiarities of the concerned biological and physical processes.

II. Problems studied and results

The team focused on different mathematical models describing epidemic propagation with the following objectives:

1. Models and analysis of diffusion-reaction systems for a Susceptible-Exposed-Infected-Recovered-Susceptible (SEIRS) disease
2. Optimal control
3. Epidemics: global shape of the COVID-19 pandemic
4. Optimal epidemic control of an infection structured by class age with application to COVID-19 case study
5. A new approach of a control policy for COVID epidemics

First, the first two objectives were treated in **paper [1]** and regarded the well-posedness of a proposed model of a SEIRS epidemic and its optimal control through the transmission rate. The paper was concerned with the well-posedness and optimal control problem of a reaction-diffusion system for an epidemic Susceptible-Exposed-Infected-Recovered-Susceptible (SEIRS)

mathematical model in which the dynamics develops in a spatially heterogeneous environment. Using as control variables the transmission rates u_i and u_e of contagion resulting from the contact with both asymptomatic and symptomatic persons, respectively, the number of exposed and infected individuals at a final time T of the controlled evolution of the system is optimized. More precisely, the aim is searching for the optimal u_i and u_e such that the number of infected plus exposed does not exceed at the final time a threshold value Λ , fixed a priori. The existence of optimal controls is shown in a proper functional framework and the first-order necessary optimality conditions are derived in terms of the adjoint variables.

Paper [2] explored the solvability and the optimal control problem for a compartmental model based on reaction–diffusion partial differential equations describing a transmissible disease. The nonlinear model takes into account the disease spreading due to the human social diffusion, under a dynamic heterogeneity in infection risk.

The analysis of the resulting system provides the existence proof for a global solution, by preparing an intermediate result and successfully applying the Schauder fixed point theorem. We also discussed two uniqueness and continuous dependence results in a reduced setting. Moreover, we proved the conditions of optimality, which are of some help to reduce the concentration of the infected population in certain spatial areas.

Partial differential equation models for infectious disease have received renewed interest in recent years. Most models of this type extend classical compartmental formulations with additional terms accounting for spatial dynamics, with Fickian diffusion being the most common such term. However, while diffusion may be appropriate for modeling vector-borne diseases, or diseases among plants or wildlife, the spatial propagation of airborne diseases in human populations is heavily dependent on human contact and mobility patterns, which are not necessarily well-described by diffusion. By including an additional chemotaxis-inspired term, in which the infection is propagated along the positive gradient of the susceptible population (from regions of low to high density of susceptibles), one may provide a more suitable description of these dynamics. **Article [3]** introduced and analyzed a new mathematical model of infectious disease incorporating a modified chemotaxis-type term. The model was analyzed mathematically, and the well-posedness of the resulting PDE system was demonstrated. A series of numerical simulations were provided, demonstrating the ability of the model to naturally capture important phenomena

not easily observed in standard diffusion models, including propagation over long spatial distances over short time scales and the emergence of localized infection hotspots.

The objectives 3, 4 and 5 have been treated in a series of other papers. **Paper [4]** analyzed a global shape of a COVID disease by proposing a new mathematical model with age structure. Moreover, an optimal control by social distancing and vaccination was discussed. Motivated by the issue of COVID-19 mitigation, this work dealt with the general problem of optimally controlling an epidemic outbreak of a communicable disease structured by age since exposure, with the aid of two types of control instruments, namely social distancing and vaccination, by a vaccine at least partly effective in protecting from infection. By the analyses the existence of (at least) one optimal control pair has been proved. First-order necessary conditions for optimality have been derived and some useful properties of such optimal solutions have been inferred. It is a general model that can be specialized to include a number of subcases relevant for epidemics like COVID-19, such as, e.g., the arrival of vaccines in a second stage of the epidemic, and vaccine rationing, making social distancing the only optimizable instrument. A worked example provides a number of further insights on the relationships between key control and epidemic parameters.

The overall course of the COVID-19 pandemic in Western countries has been characterized by complex sequences of phases. In the period before the arrival of vaccines, these phases were mainly due to the alternation between the strengthening/lifting of social distancing measures, with the aim to balance the protection of health and that of the society as a whole. After the arrival of vaccines, this multi-phasic character was further emphasized by the complicated deployment of vaccination campaigns and the onset of virus' variants. To cope with this multi-phasic character, we proposed in **paper [5]** a theoretical approach to the modeling of overall pandemic courses, that we term *multi-period/multi-phasic*, based on a specific definition of phase. This allowed a unified and parsimonious representation of complex epidemic courses even when vaccination and virus' variants are considered, through sequences of weak ergodic renewal equations that become fully ergodic when appropriate conditions are met. Specific hypotheses on epidemiological and intervention parameters allow reduction to simple models. The framework suggested a simple, theory driven, approach to data explanation that allows an accurate reproduction of the overall course of the COVID-19 epidemic in Italy since its beginning (February 2020) up to *omicron* onset, confirming the validity of the concept.

In **paper [6]**, we proposed an optimal control model of an age-of-infection transmission model under a two-phases control regime where social distancing is the only available control tool in the first phase while the second phase also benefits from the arrival of vaccines. We analyzed the problem by an ad-hoc numerical algorithm under a strong hypothesis implying a high degree of prioritization to the protection of health from the epidemic attack that we term the 'low attack rate' hypothesis. The outputs of the model were also compared with the data from the Italian COVID-19 experience to provide a crude assessment of the goodness of the enacted interventions prior to the onset of omicron variant.

During the COVID-19 epidemic, episodes of increase-decrease of the number of infected can be observed as repeated waves with different amplitudes. This is the effect of public intervention to contain the disease through non-pharmaceutical measures such as distancing as well as through vaccination strategies. Actually, the experience of COVID-19 is quite paradigmatic and can be applied to any new emerging disease. Thus, specific mathematical efforts to investigate methods and strategies for controlling such diseases are of actual interest in the applied context. **In paper [7]**, we implemented a model by introducing a specific mechanism for the vaccination strategy depending on some parameters that are supposed to be chosen by governmental policy. The optimal control problem was then studied, and its existence was proven. Furthermore, optimality conditions were established, in view of possible use in applied simulations. Since the vaccination mechanism was defined through a Heaviside function our approach is naturally developed within the theory of monotone operators.

III. Published articles

- [1] P. Colli, G. Gilardi, G. Marinoschi, E. Rocca, Optimal control of a reaction-diffusion model related to the spread of COVID-19, **Analysis and Applications**, Vol. 22, No. 1 (2024) 111-136 <https://doi.org/10.1142/S0219530523500197>
- [3] P. Colli, G. Gilardi, G. Marinoschi, Global Solution and Optimal Control of an Epidemic Propagation with a Heterogeneous Diffusion, **Appl. Math. Optim.** 89, 1, 28, 1-27, 2024. <https://doi.org/10.1007/s00245-023-10094-2>
- [5] P. Colli, G. Marinoschi, E. Rocca, A. Viguerie, Chemotaxis-inspired PDE model for airborne infectious disease transmission: analysis and simulations, **J. Nonlinear Sci.** 35:28, 1-38, 2025. <https://doi.org/10.1007/s00332-024-10121-8>
- [4] A. d'Onofrio, M. Iannelli, P. Manfredi, G. Marinoschi, Optimal epidemic control by social distancing and vaccination of an infection structured by time since infection: The COVID-19 case study, **SIAM J. Appl. Math**, 84, 3, S199-S224, 2024. <https://doi.org/10.1137/22M14994>
- [5] A. d' Onofrio, M. Iannelli, P. Manfredi, G. Marinoschi, Multiple pandemic waves vs multi-period/multi-phasic epidemics: global shape of the COVID-19 pandemic, **J. Theoret. Biol.** 593, 111881, 2024. [10.1016/j.jtbi.2024.111881](https://doi.org/10.1016/j.jtbi.2024.111881)
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- [7] V. Barbu, M. Iannelli, G. Marinoschi, Optimal control of epidemics by alternating vaccination strategies, **Nonlinear Differ. Equ. Appl.** 32:87, 2025 <https://doi.org/10.1007/s00030-025-01094-y>