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Editorial

Differential equations frameworks and models for the physics of biological systems

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Abstract: The modeling of biological systems has recently gained much attention considering the possibility to describe the time evolution of a biological system by employing differential equations. Different frameworks have been proposed depending on the number of dynamic variables. Ordinary differential equations (ODE) are employed if time is the only dynamic variable; partial differential equations (PDE) are proposed when, in addition to the time variable, space and/or velocity variables are considered. In the context of differential equation models, new frameworks have been proposed where stochastic terms are added to classical deterministic terms. A specific model is proposed when the differential equations are coupled to initial and/or boundary conditions. This editorial article deals with the topic of this special issue, which is devoted to the new developments in the multiscale modeling of complex biological systems with special attention to the interplay between different scholars.

Keywords: complexity; biomathematics; biomechanics; agent-agent models; multiscale approaches

Preface

In the last and in the present centuries the interest towards the biological systems has largely increased considering the recent progression in the natural sciences. Usually, the analysis of a biological system is expensive from the *in vivo and in vitro* experiments viewpoint. Indeed, in the case of an *in vivo* experiment the use of animals entails both ethical and availability issues [1]; in the case of an *in vitro* experiment, the results can be misleading considering that the normal biological

environment is limited [2]. A summary of the advantages and disadvantages of in vivo and in vitro methods can be found in [3].

Biological systems are composed by elements that, differently from the inert matter, can perform a strategy or a function. The interactions among the constituting elements occur at different levels and sometimes it is not necessary the contact because (cellular) signals are usually at the base of interactions [4]. The result of interactions can be also proliferation/destruction or mutation of the elements. Accordingly, the classical laws of physics can be broken. Moreover, biological systems are characterized by emerging collective behaviors that are not the simple linear combination of the interactions. The microscopic state of a component of a biological system thus is composed by the classical mechanical variables, e.g. space and velocity, but also by an internal-state variable, which models the strategy/function. According to the above-mentioned properties, a biological system has thus the structure of a complex system [5−7].

The analysis of a complex biological system requires also interactions among different research fields. A multidisciplinary approach needs to be employed and the development of such an approach demands the definition of specific frameworks and models.

The most developed approaches come from mathematics, physics and information sciences. It is worth stressing that the notion of model in the previous mentioned research fields is different from the classical notion of model in biology [8]. Indeed, the term model is employed in biology to identify a non-human species subjected to some experiments. Differently from biology, the term model in mathematics or physics represents a system of equations that describe the time evolution of a quantity related to the system under consideration.

As already mentioned, the collaboration between different scholars is an important issue in the modeling of a complex biological system. Recently three main multidisciplinary research domains have emerged: biomathematics [9], biophysics-biomechanics [10,11] and bioinformatics [12].

In biomathematics and biophysics, the term differential equation framework defines a differential equation, or a system of differential equations fulfilled by some quantities related to the system. A differential equation is an identity relating more functions and their derivatives. Each differential equation is defined by the introduction of some coefficients and functions.

A specific differential equation model is obtained once these parameters and functions are quantitatively defined and all the initial or boundary conditions are defined. Accordingly, a differential equation model is defined by recurring to a Cauchy and/or to a Dirichlet-Neumann-Robin problem, usually called initial-value and initial-boundary-value problems, respectively. Finally, a differential equation model is well-posed in the Hadamard sense if the solution exists, it is unique and depends continuously on the initial data.

Three main differential equation frameworks can be found in the pertinent literature: The ordinary differential equation (ODE) framework, the partial differential equation (PDE) framework and the integro-differential equation (IDE) framework. In the ODE-framework only the time evolution of the quantities is modeled whereas in the PDE-framework also the role of the mechanical and internal-state variables can be taken into consideration. An IDE-framework, which is defined by introducing both integrals and derivatives, can model either the time evolution or the time-space-velocity-internal-state evolution of the quantities under consideration.

In this century two new developments have been proposed:

●Stochastic differential equation (SDE) frameworks (see [13] and therein references) where the coefficients are random numbers, and the functions are random functions of the quantities under

consideration. Stochastic terms have been defined for ODE, PDE and IDE frameworks and models. Usually, game theory can be also defined in this framework [14].

●Fractional order differential equation (FODE) frameworks (see [15] and therein references) where the classical notion of integer-order derivative is replaced by the notion of fractional derivative which is obtained by unified the operations of differentiation and integration. This is a fruitful research domain that has recently gained much attention.

Bearing all above in mind, different approaches have been derived in the context of differential equation frameworks. Among others:

●Continuum mechanics approach where the differential equations are obtained by employing the fundamental balance or conservation laws that are related to the conservation of mass, linear momentum, angular momentum and energy. This approach is usually adopted for the analysis of biological material such as soft biological tissues at the macroscopic scale, see [16].

●Generalized kinetic theory approaches that are based on the classical Boltzmann equation for a dilute gas. However, in the context of biological systems the collision kernel is replaced by a probability density function which models the microscopic state changing during the interactions. Moreover, further operators are introduced to consider non conservative interactions related to proliferative/destructive and mutative events, see [17].

It is worth stressing that various mathematical theories have been involved in the modeling of complex biological systems, among others, the inverse theory, the non-equilibrium statistical mechanics theory, the information theory, the game theory, the asymptotic theory.

An important issue that needs to be considered when dealing with the complex biological systems is the scale problem. Indeed, each phenomenon can be analyzed at a different scale. Usually, three main representation scales have been identified: microscale, mesoscale and macroscale [18].

The following important question raises:

What is the most suitable differential equation framework at a specific scale?

The answer is not obvious considering that each framework can present advantages and disadvantage from the computational viewpoint and that each framework can require assumptions that can reduce the analysis of the biological phenomena. Indeed, considering the complexity of the biological system, a phenomenological analysis is necessary to identify the main actors, interactions and in particular to reduce the number of parameters of the model.

The most accredited classification establishes that usually phenomena occurring at:

●microscopic scales are modeled by stochastic games, the classical or fractional order ODE-framework;

●mesoscopic scales are modeled by the classical PDE-framework, generalized kinetic theory;

●macroscopic scales are modeled by the classical or fractional order PDE-framework, continuum mechanics.

It is worth pointing out that the differential equation framework is not the only modeling structure presented in the literature. Indeed, bioinformatics [19] has proposed further modeling approaches based on the so-called agent-based model that can be considered as a microscopic approach based on the definition of agent which is a discrete entity capable to perform a strategy. An agent modifies its behaviors regulated by specific rules defined in the model [20]. In this context, graph theory, cellular automata, lattice Boltzmann models have been also defined.

Is it worth stressing that even if the models of bioinformatics are not defined by differential equations, they can be used to tune some parameters/function of a differential equation model thus

constructing a hybrid model.

As already mentioned, a phenomenon at a specific scale can be modeled with a specific differential equation framework. However, each phenomenon obviously depends on other phenomena occurring at different scales. Accordingly, a multi-scale approach is necessary for linking the different interactions presented in the different scales. This is the most important issue that can be pursued by considering the interplay among the different scholars coming from the different research domains. Even if the interest in this research domain has increased, the results are not satisfactory and further developments are required.

Finally, a differential equation model needs to be validated with empirical or experimental data. The latter step demands a further interplay with scholars coming from the bioinformatics domain, see, among others, the paper [21].

References

1. Hirsch C, Schildknecht S (2019) *In vitro* research reproducibility: Keeping up high standards. *Front Pharmacol* 10: 1484. https://doi.org/10.3389/fphar.2019.01484
2. Lipatov VA, Kryukov AA, Severinov DA, et al. (2019) Ethical and legal aspects of in vivo experimental biomedical research. *I.P. Pavlov Russian Medical Biological Herald* 27: 80−92. https://doi.org/10.23888/PAVLOVJ201927180-92
3. National Research Council (1999) Summary of advantages and disadvantages of in vitro and in vivo methods, *Monoclonal Antibody Production*, Washington: National Academies Press.
4. Nair A, Chauhan P, Saha B, et al. (2019) Conceptual evolution of cell signaling. *Int J Mol Sci* 20: 3292. https://doi.org/10.3390/ijms20133292
5. Bar-Yam Y (1999) *Dynamics of Complex System (Studies in Nonlinearity)*, CRC Press.
6. Nicolis G, Nicolis C (2009) Foundations of complex systems: Nonlinear dynamics, *Statistical Physics, Information and Prediction*, Cambridge University Press. https://doi.org/10.1017/S1062798709000738
7. Bianca C, Bellomo N (2011) Towards a mathematical theory of complex biological systems, *Series in Mathematical Biology and Medicine*, World Scientific Publishing Co. Pte. Ltd.
8. Gunawardena J (2014) Models in biology: accurate descriptions of our pathetic thinking. *BMC Biol* 12: 29. https://doi.org/10.1186/1741-7007-12-29
9. Britton NF (2003) Essential mathematical biology, *Springer Undergraduate Mathematics Series,* Springer-Verlag London.
10. Glaser R (2012) *Biophysics: an Introduction*, Springer.
11. Hatze H (1974) The meaning of the term 'biomechanics'. *J Biomech* 7: 189−190. https://doi.org/10.1016/0021-9290(74)90060-8
12. Hogeweg P (2011) The roots of bioinformatics in theoretical biology. *PLoS Comput Biol* 7: e1002021. https://doi.org/10.1371/journal.pcbi.1002021
13. Barrera A, Román-Román P, Torres-Ruiz F (2020) Two stochastic differential equations for modeling oscillabolastic-type behavior. *Mathematics* 8: 155. https://doi.org/10.3390/math8020155
14. Perea A, Predtetchinski A (2019) An epistemic approach to stochastic games. *Int J Game Theory* 48: 181–203. https://doi.org/10.1007/s00182-018-0644-8

15. Bonyah E, Juga ML, Matsebula LM, et al. (2023) On the modelling of COVID-19 spread via fractional derivative: a stochastic approach. *Math Models Comput Simul* 15: 338−356. https://doi.org/10.1134/S2070048223020023
16. Chauvière A, Preziosi L, Verdier C (2010) *Cell Mechanics: from Single Scale-Based Models to Multiscale Modeling*, London: CRC Press.
17. Amar MB, Bianca C (2016) Towards a unified approach in the modeling of fibrosis: a review with research perspectives. *Phys Life Rev* 17: 61–85. https://doi.org/10.1016/j.plrev.2016.03.005
18. Castiglione F, Pappalardo F, Bianca C, et al. (2014) Modeling biology spanning different scales: an open challenge. *BioMed Res Inter* 2014: 902545. https://doi.org/10.1155/2014/902545
19. Bai Q, Ren F, Fujita K, et al. (2017) *Multi-agent and Complex Systems*, Singapore: Springer.
20. Van Liedekerke P, Palm MM, Jagiella N, et al. (2015) Simulating tissue mechanics with agent-based models: concepts, perspectives and some novel results. *Comput Part Mech* 2: 401–444. https://doi.org/10.1007/s40571-015-0082-3
21. Hasdemir D, Hoefsloot HCJ, Smilde AK (2015) Validation and selection of ODE based systems biology models: how to arrive at more reliable decisions. *BMC Syst Biol* 9: 32. https://doi.org/10.1186/s12918-015-0180-0

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