This brief note is an introduction to the papers published in a special issue devoted to complex systems in life sciences. Out of this presentation some perspective ideas on conceivable future research objectives are extracted and brought to the reader’s attention. The final (ambitious) aim is the development of a mathematical theory for complex living systems.

**Keywords**: Swarming, emergent behaviors, self-organization, nonlinear interactions, flocking.

This special issue follows, in the journal M3AS, various previous ones devoted to the contribution of mathematics to the modeling, qualitative analysis, and simulation of complex living systems, more precisely large systems constituted by several living entities interacting in a nonlinear manner.

The focus of the previous issues was on specific topics such as biological systems \(^3\) and multi-particle systems \(^4\), related to the ambitious aim of contributing to a mathematical theory of complex systems. This present issue aims at contributing to the same objective by some speculations that link the contents to the said challenging objective.

A definition of complex systems, which is universally accepted by the scientific community, refers specifically to interactions and on their influence on collective emerging behaviors. The following definition can be quoted from paper \(^2\):

> The study of complex systems, namely systems of many individuals interacting in a non-linear manner, has received in recent years a remarkable increase of interest among applied mathematicians,
physicists as well as researchers in various other fields as economy or social sciences.

Their collective overall behavior is determined by the dynamics of their interactions. On the other hand, a traditional modeling of individual dynamics does not lead in a straightforward way to a mathematical description of collective emerging behaviors.

In particular, it is very difficult to understand and model these systems based on the sole description of the dynamics and interactions of a few individual entities localized in space and time.

Bearing all the above in mind, let us consider large systems of interacting entities, where the micro-scale refers to the state of individual entities, while the macro-scale is related to observable, locally averaged, quantities corresponding to the overall dynamics, and let us motivate the idea that modeling, qualitative analysis, and simulations can be regarded as a new challenging frontier of applied mathematics.

As already mentioned, living entities have the ability to express specific strategies without the application of any external organizing principle. In fact, living systems receive inputs from their environment and have the ability to learn from past experience to adapt themselves to the environmental conditions that evolve in time.

The presence of a strategy induces interactions that are nonlinearly additive, and involve immediate neighbors, but in some cases also distant particles. In fact, living systems have the ability to communicate and can choose different observation paths. An important contribution to understand nonlinearity in individual-based interactions is offered by the conjecture on the so-called topological interactions, given in paper and further analyzed in, also based on the interpretation of empirical data. More precisely, this conjecture states that living entities interact with a fixed number of surrounding entities independently on their localization rather than with all entities in a certain domain of influence. Paper provides a mathematical formalization of this conjecture with some additional concepts on this delicate issue.

Theoretical tools from game theory can contribute to the modeling of interactions. In fact, living entities play a game at each interaction with an output that is technically related to their strategy often connected to surviving and adaptation ability. The concept of evolutive games has to be introduced to take into account learning ability and evolution. Changes in the environment can, in some cases, induce modification of rational behaviors up to irrational ones.

An important feature is that the study of complex living systems always needs a multiscale approach, where the first step is the selection of the observation scale and of the related representation by mathematical variables and equations, while the second step is the search of the mathematical links between different scales used for the modeling approach. For instance, macroscopic equations should not (as far as possible) be postulated a priori, but related to the underlying scale of individuals.
Let us now consider the main difficulties that cause headaches to applied mathematicians. Hallmarks of a general modeling approach can be listed as follows:

- understanding the links between the dynamics of living systems and their complexity features;
- derivation of a general mathematical structure, consistent with the afore-said features, with the aim of offering the conceptual framework for the derivation of specific models;
- design of specific models that correspond to well defined classes of systems by implementing the said structure with suitable models of individual-based interactions connected to a detailed interpretation of the dynamics at the micro-scale;
- validation of models by comparison of the dynamics predicted by them with that resulting from empirical data;
- analysis of the gap between modeling and mathematical theory.

Applied mathematicians look at suitable developments of mathematical methods of statistical physics to model the collective behavior of complex living systems starting from their interactions at the low scales. Therefore, nowadays tools taken from this field are being used by both physicists and mathematicians focusing on the afore-said aim. However, the straightforward application of known methods do not generally lead to satisfactory results, unless suitable developments are introduced to take into account the complexity features that have been outlined above. More precisely, game theory, nonlinear interactions, and multiscale methods.

A delicate problem is the validation of models, which should be based on their ability to reproduce both phenomena observed in steady conditions and emerging behaviors observed in unsteady dynamics. In the first case the model is required to reproduce empirical data with the needed accuracy, while in the second case models should be able to reproduce the different qualitative dynamics of emerging behaviors which are generated by similar inputs but are very sensitive to small differences among them. In any case, the overall dynamics should be linked to models at the microscopic scale without artificially introducing phenomenological parameters into the models. Looking for the ability of models to depict special emerging behaviors motivates simulations made to understand how far this ability is effective, for instance in reproducing milling formations in various types of aggregates.\textsuperscript{8,18}

The contents of this special issue aim at contributing to the afore said topics and to offer new challenges to applied mathematicians without hiding the difficulty of the modeling tasks. The presentation of the various papers of this issue will specifically refer to the modeling of interactions. In fact, different ways of treating this topic distinguish the different strategies to deal with the modeling problem. At present, various strategies are in competition, and we hope that this special issue could possibly contribute to define the best way to design reliable models. Finally it is worth stressing that in particular four of the seven papers of this special issue
present models of dynamical systems on networks, which imply problems of coupling models at different scales. Indeed, this is a challenging problem of particular interest for real world applications.

A first group of three papers develops analytic and modeling topics for large systems of living interacting entities. In detail:

- Paper 13 presents a study of the one-dimensional motion of pedestrians in corridors moving in opposite directions. The authors first present a stochastic cellular automata model and subsequently derive a macroscopic model with corrected nonlinear flux properties. Numerical experiments compare the output of the different approaches.

- Paper 14 analyzes various properties of individual-based models of self-rotating particles interacting through local alignment. The model combines the Kuramoto model of synchronization with the swarming model by Vicsek. One of the objective consists, following 15, in developing an appropriate hydrodynamic limit based on two different scales. A new interesting hydrodynamic model is derived.

- Paper 7 focuses on different models of self-organized biological aggregation focusing specifically on a class of hyperbolic models with nonlocal interactions introduced in 16. The study leads to a detailed analysis of Hopf/Hopf bifurcations. A deep analysis on nonlinear interactions is particularly important in the case of the dynamics of large living systems as individuals have the ability of communicating at a distance 5.

The other four papers deal with the study of various differential models on networks focusing on the interaction of living entities modeled by differential equations. It is a new challenging frontier of applied mathematics that requires the solution of analytic problems at junctions in order to understand their interplay with the dynamics within each node and in the overall network. In detail:

- Paper 23 presents a new methodological approach to the modeling of social systems on networks by methods of the generalized kinetic theory. Interactions occur within each node and between them, as well as between individuals of each node with the overall system. The model couples individual based interactions and the interplay of individuals with the stream represented by mean value in the nodes. Moreover, individuals are also subject to the mean value of the whole network. The study focuses on opinion formation, with the additional target of understanding how this coupled interactions can lead to extreme events 26.

- Paper 10 presents a global model of vehicular traffic and pedestrian motion on a network. The authors provide a detailed analysis of the coupling of models at the macro-scale based on fundamental diagrams of pedestrians and traffic flow. A variety of simulations of several physical situations cor-
responding to interesting real transportation phenomena are presented in the last part of the paper.

- A scalar Keller-Segel model is, in paper 9, inserted in a network and studied in different geometries properly related to computational schemes. It is shown in this paper how the topic requires the simultaneous treatment of different problems such as revision of the model, including flux limited approaches, modeling of boundary conditions at junctions, and development of “ad hoc” computational schemes. The contents can guide future work in the field.

- Paper 17 focuses on a problem related to technology, namely achieving a common estimation of the signal of mixtures of sensors in a network. The paper proposes and algorithm to achieve the aforesaid objective and proves convergence. Appropriate simulations also related to alternative existing methods complete the paper.

A critical analysis can be briefly outlined from the contents of this special issue, which should hopefully contribute to future developments. Some indications are selected, according to the authors’ bias, among various ones. We do not naively claim that the following list is exhaustive, but simply hope it can contribute to reduce the “headaches” that might strike mathematicians who decide to operate in the challenging, and fascinating, field of modeling living (and hence complex) systems.

1. The modeling approach should tackle the conceptual difficulty that that, in the case of living systems, deterministic field theories are not available to generate classical causality principles that are typical of classical mechanics19;
2. Interactions are nonlocal as individual entities communicate and feel the presence of other individuals at a distance;
3. Interactions are nonlinearly additive and evolve in time due to the learning ability of living entities;
4. The study of networks poses a variety of conceptual problems related to the modeling of junctions and to the computational treatment of the overall system;
5. The dynamics on networks of social systems can be significantly influenced by communications between individuals and the mean field of the network that can be expressed by lower order moments.

It is plain that further reasonings can be added. Indeed this research field is far from having found a unified research approach. Future speculation will definitely contribute to a synergy between different personal quests. The great challenge remains what is, at present, simply a dream, namely the development of a mathematical theory of living systems.
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