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Short communication

How do mutative events modify moments evolution in thermostatted kinetic models? ☆

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ABSTRACT

This short communication aims at developing a thermostatted kinetic framework which includes conservative and nonconservative interactions. Specifically nonconservative interactions refer to proliferative/destructive and mutative events. The thermostatted kinetic framework is a set of autonomous partial integro-differential equations with quadratic nonlinearity. How the moments evolution is modified by mutative interactions is explored in the present communication. Applications refer to the cancer-immune system competition.

1. Introduction

The evolution of biological system, especially cancer-immune system competition, is characterized by interactions among the cells. Specifically cells are able to proliferate and mutate as consequence of interactions among themselves and with the outer environment. Indeed during the competition, if the immune system is activated then the immune system cells are able to proliferate and can be able to deplete cancer cells, see paper [1] and the references cited therein. The role of genetic mutations is an important topic in cancer modeling because they are responsible of evolutionary dynamics as stressed by Nowak [2].

Recently the thermostatted kinetic framework has been proposed for the modeling of nonequilibrium physical and living systems subjected to external force fields, see the review paper [3]. This framework includes a mathematical term that controls the magnitude of lower-order moments (such as density and energy) in order to prevent the uncontrolled increase of them. Moreover it considers only the role of conservative interactions among particles, namely interactions that modify the microscopic state of the particle but not the density. However the thermostatted kinetic frameworks reviewed in [3] cannot be applied for the modeling of biological systems characterized by proliferative/destructive and mutative events.

This short communication aims at introducing the role of mutative events in the thermostatted kinetic framework proposed in [4,5] and to analyze how the evolution equations of the moments change. Specifically the mathematical model refers to complex biological systems decomposed into functional subsystems each of them constituted by particles which perform the same strategy (progression towards high-values of aggressiveness in cancer cells, activation and recognition in immune system cells). An external force field acts on the system thereby moving it away from equilibrium and a mathematical thermostat is inserted in order to control the time evolution of lower-order moments. The particle-function is modeled by inserting a scalar variable (activity) into the particle-microscopic state; the evolution equations of the functional subsystems are obtained by considering the interactions in the activity variable.

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The mathematical framework here proposed consists of a partial integro-differential equations system with quadratic nonlinearity. The framework here proposed is certainly worth of future research activity concerning both its qualitative analysis (such as the existence and uniqueness theorem of classical and mild solutions [4], the existence of stationary solutions [5], the convergence towards nonequilibrium stationary states [7]) and quantitative comparison (such as the tuning of a specific model, within this framework, with in vitro and in vivo experimental data [1]). Finally the derivation of macroscopic tissue equations from the thermostatted kinetic framework proposed in the paper by performing asymptotic limits is a further research perspective, see, among others, [6,8]. This is an important topic considering the difficult to link the dynamics of a biological system at different levels and scales (genetic, cellular, organ and tissue scales).

It is worth stressing that thermostatted Kac and Boltzmann equations have been considered by various authors, see papers [8–10], but these equations cannot be applied directly to biological systems and are different from the framework presented in this communication.

The contents of the present paper are divided into two more sections which follow this introduction. In details, Section 2 highlights the essential mathematical settings. Section 3 deals with the analysis of the moments evolution and how mutative events modify the evolution equations.

2. The thermostatted kinetic framework with mutative interactions

This section deals with the introduction of mutative interactions into the thermostatted kinetic framework proposed in [3]. Specifically we consider a complex system decomposed into a finite number $n \in \mathbb{N}$ of functional subsystems and subjected to external force fields. Each subsystem is composed by particles whose microscopic state includes the activity variable $u \in D_u \subset \mathbb{R}$, where D_u is a compact set of $\mathbb{R}$, which models the function expressed by particles.

The time evolution of the system refers to the vector $\mathbf{f}(t,u) = (f_1(t,u), f_2(t,u), \ldots, f_n(t,u))$, where $f_i = f_i(t,u) : [0,\infty[\times D_u \to \mathbb{R}^+$, for $i \in \{1,2,\ldots,n\}$, is the distribution function of the ith functional subsystem, which is a differentiable function with respect to the variables t and u. Setting

$$\widetilde{f}(t,u) = \sum_{i=1}^{n} f_i(t,u)\,du \tag{2.1}$$

and under the assumption that $u^p \widetilde{f}(t,u) \in L^1(D_u)$, the pth order moment of the whole system reads:

$$\mathbb{E}_p[\mathbf{f}](t) = \int_{D_u} u^p \widetilde{f}(t,u)\,du, \quad p \in \mathbb{N}. \tag{2.2}$$

In general $\mathbb{E}_0[\mathbf{f}]$ represents the particles density of the system and $\mathbb{E}_2[\mathbf{f}]$ the activation energy. In particular the pth order moment of each functional subsystem f_i reads:

$$\mathbb{E}_p[f_i](t) = \int_{D_u} u^p f_i(t,u)\,du, \quad p \in \mathbb{N}. \tag{2.3}$$

The time evolution equation of each distribution f_i is obtained by considering the interactions occurring among the active particles. Mutual interactions refer to test particles, whose distribution function is denoted by $f_i(t,u)$, candidate particles (with distribution function denoted by $f_i(t,u_*)$) and field particles (with distribution function denoted by $f_i(t,u^*)$). Candidate particles can acquire in probability the microscopic state of the test particle after interactions with field particles. The possibility of interactions among the particles is measured by the nonnegative function $\eta_{ij}(u_*,u^*)$ which represents the interaction rate between the subsystem u_* particle of f_i and the u^* particle of subsystem f_j.

The probability that after the interaction, the candidate particle undergoes a change in its microscopic state (that of test particle) is measured by the nonnegative function:

$$\mathscr{A}_{ij}(u_*,u^*,u) : D_u \times D_u \times D_u \to \mathbb{R}^+,$$

which is a probability density with respect to u and then

$$\int_{D_u} \mathscr{A}_{ij}(u_*,u^*,u)\,du = 1, \quad \forall\ u_*,u^* \in D_u. \tag{2.4}$$

Bearing all above in mind, summing up with respect to the all candidate and field particles, and assuming that $\eta_{ij}(u_*,u^*)\mathscr{A}_{ij}(u_*,u^*,u) f_i(t,u_*) f_i(t,u^*)$ is an integrable function with respect to the elementary measure $du_*\,du^*$, we obtain the following operator $\mathscr{G}_i[\mathbf{f}] = \mathscr{G}_i[\mathbf{f}](t,u)$, which models the gain of test cells:

$$\mathscr{G}_i[\mathbf{f}] = \sum_{j=1}^{n} \int_{D_u \times D_u} \eta_{ij}(u_*,u^*)\mathscr{A}_{ij}(u_*,u^*,u) f_i(t,u_*) f_j(t,u^*)\,du_*\,du^*$$

and, similarly, the lost of test cells $\mathscr{L}_i[\mathbf{f}] = \mathscr{L}_i[\mathbf{f}](t,u)$ is modeled by the following operator:

$$\mathscr{L}_i[\mathbf{f}] = f_i(t,u) \sum_{j=1}^{n} \int_{D_u} \eta_{ij}(u,u^*) f_j(t,u^*)\,du^*, \tag{2.5}$$