

# WHAT STOCHASTIC MECHANICS IS RELEVANT TO THE STUDY OF LIVING SYSTEMS?

Eugen Mamontov, Krzysztof Psiuk-Maksymowicz\*, and Andrei Koptioug\*\*

Department of Physics, Faculty of Science, Gothenburg University, SE-412 96 Gothenburg, SWEDEN,  
E-mail: yem@physics.gu.se

\* Department of Physics, Faculty of Science, Gothenburg University, SE-412 96 Gothenburg, SWEDEN,  
E-mail: psiuk@physics.gu.se

\*\* Department of Information Technology and Media, Mid Sweden University, SE-831 25 Östersund, SWEDEN,  
E-mail: Andrei.Koptioug@mim.se

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*Biologists have identified many features of living systems, which cannot be studied by the application of fundamental statistical mechanics (FSM). The present work focuses on some of these features. By discussing all of the basic approaches of FSM, the work formulates the extension of the kinetic-theory paradigm (based on the reduced one-particle distribution function) that possesses all of the considered properties of the living-systems. This extension appears to be a model within the generalised kinetic theory developed by N. Bellomo and his co-authors. In connection with this model, the work also stresses some other features necessary for making the model relevant to living systems. An example is discussed, which is a generalised kinetic equation coupled with the probability-density equation representing the varying component content of a living system. The work also suggests directions for future research.*

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## 1. INTRODUCTION

The minimal unit of life is a living cell. A system that does not include living cells can be termed a nonliving system. Nonliving systems are studied in most of areas of physics, chemistry, and engineering. These fields are endowed with a great variety of experimental methods and theoretical treatments, including fundamental statistical mechanics (FSM) (e.g., Résibois and De Leener, 1977; Bogolubov and Bogolubov, 1994; Balescu, 1997; Liboff, 1998). FSM proved to be a powerful tool in the analysis of problems in nonliving matter. Subsequently, there has been an irresistible temptation to apply the first-principle mechanical theory to virtually every new problem, in particular, to living-system problems that appear similar to the ones successfully resolved by the nonliving-matter sciences in the previous decades.

However, there are some opposing opinions. One of them comes from biology (Hartwell *et al.*, 1999, p. C49):

Biological systems are very different from the physical or chemical systems analysed by statistical mechanics or hydrodynamics. Statistical mechanics typically deals with systems containing many copies of a few interacting components, whereas cells contain from million to a few copies of each of

thousands of different components, each with very specific interactions.

Further,

... The macroscopic signals that a cell receives from its environment can influence which genes it expresses — and thus which proteins it contains at any given time — or even the rate of mutation of its DNA, which could lead to changes in the molecular structures of the proteins. This is in contrast to physical systems where, typically, macroscopic perturbations or higher-level structures do not modify the structure of the molecular components.

The present work analyses in what specific respect FSM does not allow for the above features and what stochastic mechanics instead of FSM can enable them. The work also identifies the most relevant version of stochastic mechanics, among the available alternatives, in the study of living systems.

## 2. MATERIALS AND METHODS

The methods used in the present work are those commonly used in statistical or stochastic mechanics including the published results of various authors related to the topic of the work (e.g. Résibois and DeLeener, 1977; Balescu, 1997; Arlotti *et al.*, 2002).

### 3. RESULTS AND DISCUSSION

Biologists have described many features of living systems, which cannot be studied by the application of FSM (see Sections 1 and 3.1). The main result of the present work is the following. By discussing all of the basic approaches of FSM (see Sections 3.2–3.6), the work formulates (see Section 3.6) the extension of the kinetic-theory paradigm (based on the reduced one-particle distribution function) that possesses all of the properties of the living systems considered in the work. This extension appears to be a model within the generalised kinetic theory developed by N. Bellomo and his co-authors (e.g., Bellomo and Lo Schiavo, 2000; Arlotti *et al.*, 2003; see also Arlotti *et al.*, 2002; Bellomo *et al.*, 2003a, 2003b; Willander *et al.*, 2004). In connection with this model, the work also stresses (see Section 3.7) some other features necessary in making the model relevant to living systems. An example (see Section 3.8) is discussed, which is a generalised kinetic equation coupled with the probability-density equation representing the varying component content of a living system. The work also suggests directions for future research (in Section 3.8).

#### 3.1. Implications from biology: Formulation in terms of FSM

The objections of Hartwell *et al.* (1999) on the differences of biological and physical systems (see the citations in Section 1) can be formulated in terms of FSM. We consider a population of particles occupying a bounded or unbounded domain (i.e. open connected set) in  $\mathbb{R}^3$  where  $\mathbb{R} = (-\infty, \infty)$ , say, domain  $X(t) \subset \mathbb{R}^3$  where  $t \in \mathbb{R}$  is the time. Let the population comprise

$$M \geq 1 \quad (1)$$

components, i.e. (different if  $M \neq 1$ ) groups of identical particles, and let  $N_i$  such that

$$N_i \geq 1, \quad i = 1, \dots, M, \quad (2)$$

be the number of the particles in the  $i$ th component. The total number  $N$  of the particles in the population is expressed as

$$N = \sum_{i=1}^M N_i. \quad (3)$$

Obviously,

$$N \geq M. \quad (4)$$

The equality  $N = M$  corresponds to the case when every component comprises exactly one particle or, equivalently, all the particles are pairwise different. This can take place in a living system. It follows from the first citation in Section 1 (Hartwell *et al.*, 1999) that  $M$  and  $N_i$  in (1) and (2) are not limited to any specific intervals, i.e.

$$\text{number } M \text{ in (1) can take any value from very low, such as a unit or a few units, to a few millions (or greater),} \quad (5)$$

$$\text{every number } N_i \text{ in (2) can take any value from very low, such as a unit or a few units, to a few thousands (or greater).} \quad (6)$$

The second citation in Section 1 (Hartwell *et al.*, 1999) implies that, generally speaking, the numbers in (5) and (6) depend on time  $t$ , i.e.

$$M = M(t) \quad (7)$$

and

$$N_i = N_i(t), \quad i = 1, \dots, M. \quad (8)$$

The latter implies

$$N = N(t) \quad (9)$$

because of (3).

The four sections below analyse if the models within FSM allow the features (5)–(8).

#### 3.2. Phase-space models

In FSM, each particle is described with the three-dimensional position vector in domain  $X(t)$  (see above) and the three-dimensional momentum vector. Thus, the phase-space for one particle is  $\mathbb{R}^6$ . Subsequently,

the phase-space models in FSM consider the  $N$ -particle population in the phase space  $\mathbb{R}^d$  where  $d = 6N$ . (10)

The corresponding key notion is the *phase-space probability density* (e.g., Balescu, 1997, (3.7), (3.8), and p. 25)

$$\varphi(N, t, x_1, p_1, \dots, x_N, p_N) \quad (11)$$

where variables  $x_j \in X(t)$  and  $p_j \in \mathbb{R}^3$  represent the position and momentum vectors, respectively, of the  $j$ th particle. Density (11), as a function of  $x_j$  and  $p_j$ ,  $j = 1, \dots, N$ , at every fixed  $N$  and  $t$ , is also the *joint probability density* of the positions and momenta of  $N$  particles at time  $t$ .

The phase-space models form the *core* of FSM. They include the Liouville equation (e.g., Balescu, 1997, (3.15)), the formal master equation (e.g., Résibois and De Leener, 1977, (VIII.2), (VIII.21)), the molecular-dynamics equation systems, and other formalisms.

Along with this, it is unclear how to use the phase-space settings (10) under condition (9). Generally speaking, this prevents application of the phase-space models to living systems.

To resolve the problem, one chooses a phase space such that its dimension is independent of varying number (9). The simplest way to do that is discussed in Section 3.3.

### 3.3. One-particle reduced distribution function: One-component population

The simplest way to make the phase-space dimension independent of  $N(t)$  (cf., (9)) is by using the six-dimensional space for one particle as the phase space for the entire population. In this respect, the 6  $N(t)$ -dimensional space (see (9) and (10)) is *reduced* to the 6-dimensional space. However, the reduction can be done only under a special condition. This is considered below.

The joint probability density (11) enables one to introduce the functions  $\rho_j$  with equalities

$$\rho_j(N(t), t, x_j, p_j) = \int_{[X(t)] \times \mathbb{R}^{3M(t)-1}} \varphi(N(t), t, x_1, p_1, \dots, x_{N(t)}, p_{N(t)}) \times \prod_{k=1, k \neq j}^{N(t)} (dx_k dp_k), \quad j=1, \dots, N(t). \quad (12)$$

If the density function  $\varphi$  at every fixed  $t$  is symmetric with respect to *all* pairs  $(x_k, p_k)$  (e.g., Balescu, 1997, (4.7)) or, because of (12),

$$\rho_1(N(t), t, x, p) \equiv \rho_2(N(t), t, x, p) \equiv \dots \equiv \rho_{N(t)}(N(t), t, x, p) \quad (13)$$

then the  $N(t)$ -particle population can be described with the *reduced one-particle* distribution function (e.g., Balescu, 1997, (4.9))

$$f_1(t, x, p) = N_1(t) \rho_1(N_1(t), t, x, p) \quad (14)$$

where identity

$$N(t) \equiv N_1(t) \quad (15)$$

holds, since it, in view of (3) and (9), is equivalent to

$$M = 1 \quad (16)$$

which in turn is equivalent to condition (13).

In kinetic theory, the distribution function  $f_1$  in (14) is regarded as a solution of a kinetic equation (e.g., Balescu, 1997, p. 55). In this way, the terms on the right-hand side of (14) are determined by means of this function as follows

$$N_1(t) = \int_{[X(t)] \times \mathbb{R}^3} f_1(t, x, p) dx dp, \quad \rho_1(N_1(t), t, x, p) = f_1(t, x, p) / N_1(t). \quad (17)$$

The condition that all the particles are identical (see (15) or (16)) disagrees with feature (5) of living systems and is eliminated in Section 3.5. The next section discusses why the most important extension of the above paradigm is also irrelevant to modelling of living systems.

### 3.4. Two- and multi-particle reduced distribution functions: One-component population

This section considers the *one*-component particle population, i.e. when (15) or (16) holds. The one-component settings in the previous section can be regarded as a quite par-

ticular case of a more refined treatment, the Bogoliubov–Born–Green–Kirkwood–Yvon (BBGKY) equation chain (e.g., Balescu, 1997, p. 45), which is based on the reduced  $l$ -particle distribution functions,  $l \geq 1$ . The case in Section 3.3 corresponds to  $l = 1$ . The case when  $l > 1$  is discussed in the present section.

The well-known normalisation condition for the reduced  $l$ -particle distribution function at  $l > 1$  (e.g., Balescu, 1997, (4.14) and (4.18)) is equivalent to relation (e.g., Balescu, 1997, p. 41)

$$N(t)[N(t)-1] \dots [N(t)-l+1] = [N(t)]^l, \quad N(t) \geq l > 1 \quad (18)$$

One can show that the relative error  $\varepsilon$  of this approximation is inversely proportional to  $N(t)$ ,

$$\varepsilon \sim [N(t)]^{-1}. \quad (19)$$

Since the BBGKY description is traditionally regarded as the *first-principle* model, approximate equality (18) should hold with a very low relative error  $\varepsilon$ , say, on the order of tenths or hundredths of one percent, i.e.  $\varepsilon = 10^{-3} - 10^{-4}$ . Application of these values to (19) requires  $N(t) \sim 10^3 - 10^4$ .

This limitation sharply disagrees with feature (6) of living systems (see also (15)). Subsequently, the reduced  $l$ -particle distribution functions at  $l > 1$  and any model which employs at least one of them (e.g., the BBGKY equation chain or the so-called correlation functions (e.g., Balescu, 1997, Section 3.4)) are in general not suitable to describe living systems. One has to come back to the reduced one-particle distribution function in Section 3.3.

### 3.5. One-particle reduced distribution function: Multi-component population

The common extension of the identical-particle treatment in Section 3.3 to the case when the particles do not need to be identical involves the notion of a multicomponent population. Indeed, no matter if  $M = 1$  or  $M > 1$ , one can without a loss of generality assume that the first  $M$  particles in the  $N(t)$ -particle population (cf., (4)) are pairwise different and any other particle is identical to one of the mentioned  $M$  particles. In so doing, number  $N_i(t)$  in (2) and (8), turns out to be the total number of the particles identical to the above  $i$ th particle where  $i = 1, \dots, M$ . The corresponding generalisation of (14) is

$$f(t, x, p) = \sum_{i=1}^M f_i(t, x, p) \quad (20)$$

where

$$f_i(t, x, p) = N_i(t) \rho_i(N_i(t), t, x, p), \quad i = 1, \dots, M. \quad (21)$$

and  $f_i$  are the reduced one-particle distribution functions for the components.

In kinetic theory, the distribution functions  $f_1, \dots, f_M$  in (21) are obtained as a solution of a system of  $M$  kinetic equations

(e.g., Liboff, 1998, Section 3.2.2). (Note, however, that the derivation of this system from representation (20) is not always included in the corresponding textbooks.) Solutions of the system have values in set  $[0, \infty)^M$ . Applying (7) to this set, one encounters the difficulties analogous to those described in Section 3.2 in connection with substitution of (9) into the expression for  $d$  in (10). Thus, the above multi-component treatment underlying (20) is generally irrelevant to modelling of living systems.

The problem can be overcome if one leaves the scope of FSM. This is the topic of the next section.

### 3.6. One-particle reduced distribution function: Time-dependent number of components. Generalized distribution function

As stressed above, the notion of a multicomponent population is inherently associated with the features of the particles that are either identical or different. The latter is resolved by comparing the component-specific values of the related parameters of the particles, for example, the particle mass, size, shape, electric charge, or other physical quantities. They can be regarded as the entries of a vector variable, say,  $u \in \mathbb{R}^m$  (where  $m \geq 1$ ) such that

- the  $i$ th component,  $i = 1, \dots, M$ , corresponds to value  $u_i$  of  $u$
  - and all the values  $u_1, \dots, u_M \in \mathbb{R}^m$  are pairwise different, i.e.
- $$u_i \neq u_j, \quad i \neq j, \quad i, j = 1, \dots, M. \quad (22)$$

The treatment below follows the single-distribution-function approach to multicomponent populations proposed in Bellomo *et al.* (2003a) and Willander *et al.* (2004). Accordingly,  $M$  functions  $f_i(t, x, p)$  in (21) can be regarded as  $M$  values  $\bar{f}(t, x, p, u_i)$  of single function  $\bar{f}(t, x, p, u)$  where vector  $u$  varies in a bounded or unbounded, generally time-dependent domain in  $\mathbb{R}^m$ , say,  $U(t) \subset \mathbb{R}^m$ . This transforms (20) into

$$f(t, x, p) = \sum_{i=1}^M \bar{f}(t, x, p, u_i). \quad (23)$$

In so doing, the functions  $N_i$  and  $\rho_i$  in (21) are also determined in terms of function  $\bar{f}(t, x, p, u)$ , namely

$$N_i(t) = \bar{N}(t, u_i), \quad \rho_i(N_i(t), t, x, p) = \bar{\rho}(\bar{N}(t, u_i), t, x, p, u_i), \quad i = 1, \dots, M, \quad (24)$$

where (cf., (17))

$$\bar{N}(t, u) = \int_{X(t) \times \mathbb{R}^m} \bar{f}(t, x, p, u) dx dp, \quad (25)$$

$$\bar{\rho}(\bar{N}(t, u), t, x, p, u) = \bar{f}(t, x, p, u) / \bar{N}(t, u). \quad (26)$$

Thus, the reduced one-particle distribution function  $f$  (see (23)) for the multicomponent population and other basic characteristics of the components, for example, (24)–(26) are completely described by means of the single distribution

function  $\bar{f}$ . The latter can be determined in the way discussed in the next section. The rest of the present section analyses how the distribution function  $\bar{f}$  can integrate the feature (7) of living systems.

The above set  $\{u_1, \dots, u_M\}$  can be regarded as a sample for a random variable defined on domain  $U(t)$  and described with a probability density, say,  $\lambda(t, \cdot)$ . In the simplest case, i.e. when the random variable is defined on  $\mathbb{R}^m$  and discrete, namely

$$\lambda(t, u) \equiv \sum_{i=1}^M M^{-1} \delta(u - u_i), \quad u \in U(t), \quad U(t) \equiv \mathbb{R}^m, \quad (27)$$

where  $\delta(\cdot)$  is the  $M$ -dimensional Dirac delta-function, expression (23) is equivalent to

$$f(t, x, p) = M \int_{U(t)} \bar{f}(t, x, p, u) \lambda(t, u) du$$

According to the approach of Bellomo *et al.* (2003a) and Willander *et al.* (2004), one applies the latter equality even when (7) holds and both domain  $U(t)$  and probability density  $\lambda(t, \cdot)$  are not necessarily of the particular form (27), i.e.

$$f(t, x, p) = M(\lambda(t, \cdot)) \int_{U(t)} \bar{f}(t, x, p, u) \lambda(t, u) du \quad (28)$$

In so doing, the component number  $M(\lambda(t, \cdot))$  specifies the  $t$ -dependence (7). The time-dependent component number can be interpreted in various ways. The discussions in Bellomo *et al.* (2003a, Sections 5 and 7) and Willander *et al.* (2004, Section 4.3 and Appendix) suggest to read it as the number of the *modes* of probability density  $\lambda(t, \cdot)$ . These modes may be viewed as the spread out, nonzero-widths and finite-height peaks analogous to those in (27). Along with this, we present a more general and somewhat more precise definition of  $M(\lambda(t, \cdot))$ .

**Definition 1.** Let the components of a population of particles be described with vector parameter  $u \in \mathbb{R}^m$ . Let also the number of these components be denoted with  $M(\lambda(t, \cdot))$ . We term any *path-connected subset* of set

$$Y(\lambda(t, \cdot)) = \{u \in \mathbb{R}^m : \lambda(t, u) > 0\} \quad (29)$$

the *component-parameter subset* of the population. The particles in a component of the population are the ones corresponding to the values of  $u$  in a component-parameter subset. Subsequently, number  $M(\lambda(t, \cdot))$  is the number of the component-parameter sets of set (29).

If set (29) includes more than one component-parameter subset, then, obviously, all these subsets are mutually non-intersecting. This feature generalises condition (22), which is valid in the case of (27) when the component-parameter subsets are single-point sets  $\{u_1\}, \dots, \{u_M\}$ .

Importantly, Definition 1 is more general than the mode-based definitions developed in Bellomo *et al.* (2003a) and Willander *et al.* (2004). Indeed, any collection of the population particles that is a component in the sense of the present definition comprises at least one collection which is a component in the sense of the previous definitions.

**Remark 1.** As it is well-known (Gove, 1993, p. 1306), life is “the principle or force by which animals and plants are maintained in the performance of their functions and which distinguishes by its presence animate from inanimate matter; the state of a material complex or individual characterised by the capacity to perform certain functional activities including metabolism, growth, reproduction, and some form of responsiveness or adaptability”. The probability density  $\lambda$  in (28) and its component characteristics in Definition 1 are the very quantities that can be the *core* in the representing of the above metabolism, growth, reproduction, and responsiveness or adaptability.

Expression (28) shows that the entire multicomponent population is modeled in terms of a single, *generalised* reduced one-particle distribution function

$$f(t, x, p, u) = M(\lambda(t, \cdot)) \bar{f}(t, x, p, u) \lambda(t, u) \quad (30)$$

that describes not only the stochastic position and momentum of a particle (represented with  $x$  and  $p$ , respectively) but also its stochastic parameter vector (represented with  $u \in U(t)$ ), which determines the particle content of the population. In the context of (28) and (30),  $\bar{f}$  is the *conditional* distribution function for  $(x, p)$  conditioned with value  $u$ ,  $f$  (see (28)) is the *marginal* distribution function for  $(x, p)$ ,  $\bar{\rho}$  (see (26)) is the *conditional* probability density for  $(x, p)$  conditioned with values  $u$  and  $\bar{N}(t, u)$  (see (25)), and  $\lambda$  is the *marginal* probability density for  $u$ . The generalised distribution function (GDF) (30) is of the type underlying the generalised-kinetics (GK) theory developed by N. Bellomo and his co-authors (e.g., Bellomo and Lo Schiavo, 2000; Arlotti *et al.*, 2003; see also Arlotti *et al.*, 2002; Bellomo *et al.*, 2003a, 2003b; Willander *et al.*, 2004).

All the aforementioned issues can be summarised in the following way.

**Remark 2.** Definition 1, the single generalised reduced one-particle distribution function (30), and related expressions (24)–(26), (28) enable one to take into account not only (5), (6), and (8) but also (7), i.e. all the above features (5)–(8) of living systems. Among the stochastic-mechanics models considered in the present work, representation (30) and the related expressions are the only treatment that can allow for (5)–(8). Subsequently, if a population of living particles can be modelled by a stochastic-mechanics approach, then the latter is based on (30). In other words, application of GDF (30) is the necessary condition for modelling living systems by stochastic mechanics.

The next section derives one more condition that the model in Remark 2 should meet to properly describe the mechanics of the living-particle population.

### 3.7. Other properties of living systems formulated in terms of the present model

Stochastic variables  $(x, p)$  and  $u$  represent the *mechanics* and *component content*, respectively, of a population of liv-

ing particles. The mechanical evolution described with  $\bar{f}$  can be recognised as part of a living system only if the properties of the particles (e.g., those in Definition 1) influence the above evolution. This means that  $\bar{f}$  must depend on  $\lambda$ ,

$$\bar{f}(t, x, p, u) = \bar{f}(t, x, p, u, \lambda). \quad (31)$$

The corresponding corrections should be taken into account in (25), (26), (28), and (30).

Because of homeorhesis (Waddington, 1957, p. 32; Waddington, 1968, p. 526), the time-dependent specification of homeostasis, GDF  $f$  (see (30)) can not be stationary, i.e. independent of  $t$ , in a living system. Along with this, a living system may in principle be *mechanically* stationary, i.e. the  $t$ -independence of  $\bar{f}$  may be the case, at least as an approximation. In view of this and (30), the probability density  $\lambda$  is always nonstationary, i.e. depends on  $t$ . Haus and Smolensky (1999) discuss the corresponding examples of experimental results. Other details on homeorhesis in connection with (30) can be found in (Willander *et al.*, 2004, Section 4.1).

Numerous observations of mature (non-embryonic) living systems show that, in any sufficiently short time intervals, living systems behave similar to nonliving bodies, namely those with the  $t$ -independent  $\lambda$ . For instance, if the time needed for a driver to stop a car from avoiding collision with an immobile obstacle is less than one second, i.e. the typical time for the driver reaction, then the collision is inevitable. In a short time interval, when the mechanical-dynamics function  $\bar{f}$  noticeably varies, the driver action associated with  $\lambda$  remains unchanged. In specific terms, this means that, if a mature living system is modelled with (30), then

$$1 \ll \tau_\lambda(u) / \tau_{\bar{f}}(u) < \infty, \quad u \in U(t) \cap Y(\lambda(t, \cdot)), \quad (32)$$

where set  $Y(\lambda(t, \cdot))$  is described with (29),  $\tau_\lambda(u)$  is the characteristic time of changes in  $\lambda(\cdot, u)$ ,  $\tau_{\bar{f}}(u) = \sup_{(x,p)} \{\tau(x, p, u)\}$  and  $\tau(x, p, u)$  is the characteristic time of changes in  $\bar{f}(\cdot, x, p, u, \lambda)$  (see (31)). The time scales in living systems are discussed, for example, in (Willander *et al.*, 2004, Section 3.4).

The above issues can be summarised as follows.

**Remark 3.** If a living system is adequately described with the model in Remark 2, then:

- the conditional distribution function  $\bar{f}$  depends on probability density  $\lambda$ , i.e. (31) holds;
- the probability density  $\lambda$  depends on  $t$ ;
- the inequality (32) is valid.

If any of the above conditions does not hold, then the system is nonliving.

This summary lists the features to be accounted in development of specific models for GDF (31).

### 3.8. Generalised kinetic equation and related models. Directions for future research

The conditional distribution function  $\bar{f}(t, x, p, u, \lambda)$  in (30), (31) can be obtained as a solution of the following generalised kinetic equation (GKE) (Willander *et al.*, 2004, (3.15))

$$\begin{aligned} \frac{\partial \bar{f}(t, x, p, u, \lambda)}{\partial t} + \sum_{i=1}^3 \frac{\partial \bar{f}(t, x, p, u, \lambda)}{\partial x_i} \frac{p_i}{\mu(u)} + \\ \sum_{i=1}^3 \frac{\partial \bar{f}(t, x, p, u, \lambda)}{\partial p_i} F_i(t, x, p, u, \lambda, \bar{f}) = \\ J_1(t, x, p; u, \bar{f}(t, x, \cdot, u, \lambda)) + \\ M(\lambda(t, \cdot)) \int_{U(t)} J_2(t, x, p, \lambda; u, \bar{f}(t, x, \cdot, u, \lambda), w, \\ \bar{f}(t, x, \cdot, w, \lambda)) \lambda(t, w) dw, \\ x \in X(t), \quad p \in \mathbb{R}^3, \quad u \in U(t) \cap Y(t) \end{aligned} \quad (33)$$

where scalar  $\mu(u)$  is the mass of a particle in the population component corresponding to  $u$  and vector  $F(t, x, p, u, \lambda, \bar{f})$  is the nondissipative force acting on a particle. The nondissipativity means that force  $F(t, x, p, u, \lambda, \bar{f})$  is linear in  $p$  and matrix  $\partial F(t, x, p, u, \lambda, \bar{f}) / \partial p$  is independent of  $p$  and skew-symmetric.

If one of the entries of vector  $u$ , say,  $u_1$  represents the charge of a particle, then an example of a nondissipative force is the Lorentz force  $F(t, x, p, u, \lambda, \bar{f}) = u_1 [E(t, x, \lambda, \bar{f}) + [p/m(u)] \times B(t, x, \lambda, \bar{f})]$  where vectors  $E(t, x, \lambda, \bar{f})$  and  $B(t, x, \lambda, \bar{f})$  are the electric and magnetic fields, respectively. They are determined from the corresponding Maxwell equations. In particular, vector  $E(t, x, \lambda, \bar{f})$  is described with Coulomb's equation

$$\begin{aligned} \varepsilon_0 \varepsilon \sum_{i=1}^3 \frac{\partial E(t, x, \lambda, \bar{f})}{\partial x_i} = \\ M(\lambda(t, \cdot)) \int_{U(t)} u_1 [\int \bar{f}(t, x, p, u, \lambda) dp] \lambda(t, u) du \end{aligned}$$

where  $\varepsilon_0$  is the electric permittivity of a vacuum and  $\varepsilon$  is the relative electric permittivity of the particle population.

The term  $J_1(t, x, p; u, \bar{f}(t, x, \cdot, u, \lambda))$  in (33) is the collision integral due to the collisions of the particles of one component, i.e. the one corresponding to  $u$ , with the surrounding. The term  $J_2(t, x, p, \lambda; u, \bar{f}(t, x, \cdot, u, \lambda), w, \bar{f}(t, x, \cdot, w, \lambda))$  in (33) is the collision integral due to the collisions of the particles of two different components, i.e. the ones corresponding to  $u$  and  $w$ . The three- and multi-component collisions are not included in GKE (33). Further details regarding this equation can be found in (Willander *et al.*, 2004, Section 3.3). We only note that, in the case of (27), GKE (33) becomes a common kinetic-equation system for a multicomponent particle population (cf., Liboff, 1998, Section 3.2.2).

**Remark 4.** GKE (33) is an example of a model that can provide the first feature of the living-system mechanics discussed in Remark 3. Note that, in the GK theory, the condi-

tional distribution function  $\bar{f}(t, \cdot, \cdot, u, \lambda)$  may depend not only on the entries of the component-content vector  $u$  but also on other scalar parameters. The latter can be determined by means of the methods of the GK theory (see the references in the text above Remark 2).

New effects can be accounted for GKE (33) if one incorporates into the right-hand side the "memory"-based collision term, which includes an integral in  $t$  in line with the approach of (Sjögren, 1978, 1980). This enables to allow for the phenomena usually under-represented in kinetic theory and especially difficult to model in living systems, for example, the soft-glassy-material analogy of cellular populations observed in experiments (e.g., Fabry *et al.*, 2003). The distinguishing advantages of the mentioned theoretical approach is a consistent modelling paradigm and a distinct physical meaning of every involved term.

Another direction for future research is a detailed treatment of many-body collisions in multicomponent populations of living particles. This presumes a detailed reading of the terms on the right-hand side of GKE (33) and complementing them with the corresponding additional terms. A possible way in this direction is discussed in (De Angelis and Grünfeld, 2003; Grünfeld, 2000).

The general form of the model for probability density  $\lambda$  is equation (Willander *et al.*, 2004, (3.16)).

$$\partial \lambda(t, \cdot) / \partial t = \Lambda(t, u, \bar{f}(t, \cdot, \cdot, \cdot, \lambda)) \lambda(t, \cdot), \quad u \in U(t) \quad (34)$$

Equations (33) and (34) form the equation system for  $\bar{f}(t, \cdot, \cdot, u, \lambda)$  and  $\lambda(t, u)$ . Solutions of this system are supposedly of the second and third properties of the living-systems mechanics in Remark 3.

It follows from (5) that equation (34) can be fairly complex. The fact that (34) must be regarded in conjunction with GKE (33) to make the model closed, fully agrees with the well-known issues (Hartwell *et al.*, 1999, p. C49):

... the components of physical systems are often simple entities, whereas in biology each of the components is often a microscopic device in itself, able to transduce energy and work far from equilibrium. As a result, the microscopic description of the biological system is inevitably more lengthy than that of a physical system, and must remain so, unless one moves to a higher level of analysis.

The form of function  $\Lambda$  in (34) is still unknown. Until now, the models used for living systems (e.g., Koptioug *et al.*, 2004; Mamontov *et al.*, 2005; Psiuk-Maksymowicz and Mamontov, 2005) do not allow (7) and employ (27), in fact applying the nonliving-systems paradigm. More research is needed to specify function  $\Lambda$ . One of the fields for future study is associated with the fact that  $\lambda$  is assigned to represent the component structure due to biochemical reactions in the particle population. Subsequently, the results on the complex nature of these reactions (e.g., Bernasconi, 1986) may contribute to derivations of function  $\Lambda$ .

A discussion on equation (34) is also included in Willander *et al.* (2004, Section 3.4). We add only a few issues.

One of the simplest cases of equation (34) is the Kolmogorov forward, or Fokker-Planck, (KFFP) equation (e.g., Mamontov and Willander, 2001, and the references therein). Research on the KFFP reading of (34) can be facilitated by a series of the recent results. For example, the KFFP-based *nonstationary invariant* probability densities may appropriately describe homeorhesis, the time-dependent generalisation of homeostasis (cf., the text below (31)). A fairly general treatment for these densities is reported by Mamontov (2005b). The text by Mamontov and Willander (2001) includes a group of analytical-numerical methods developed for KFFPs with nonlinear coefficients in the high-dimensional case, i.e. when dimension  $m$  of vector  $u$  in (34) is high.

A promising and interesting topic in future development of equations for  $\lambda$  includes more capable models than KFFPs (or Itô's stochastic differential equations), for example, those studied by Y. Tsarkov (Tsarkov, 1989; Katafygiotis and Tsarkov, 1999; Tsarkov, 2002). These results may be especially helpful since they are related to dissipation (interpreted in a wider sense than the one common in physics), nonrecurrence, and stability, i.e. the features inherent in living systems. Moreover, the *functional-differential* nature of the above models may help to overcome certain limitations of the KFFP (and hence Markov) approach in modelling the population-component characteristics in Definition 1. This modelling is one of the most challenging fields of research on GK systems (33), (34).

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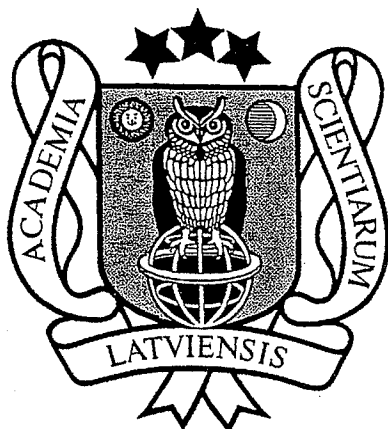
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#### VAI STOHAŠTISKĀ MEHĀNIKA IR PIELIETOJAMA DZĪVES SISTĒMU PĒTĪŠANĀ?

Dzīves sistēmām ir dažas īpatnības, kas to pētīšanai neļauj lietot fundamentālo statistisko mehāniku. Rakstā ir formulēts kinētiskās teorijas paradigmas paplašinājums, kas apmierina visām dzīves sistēmas īpašībām. Rakstā izvirzīti arī citi nosacījumi, kas padara modeli lietojamu attiecībā uz dzīves sistēmām. Apskatītais piemērs ir vispārināts kinētiskais vienādojums kopā ar varbūtību blīvuma vienādojumu. Darbā piedāvāti virzieni turpmākiem pētījumiem.





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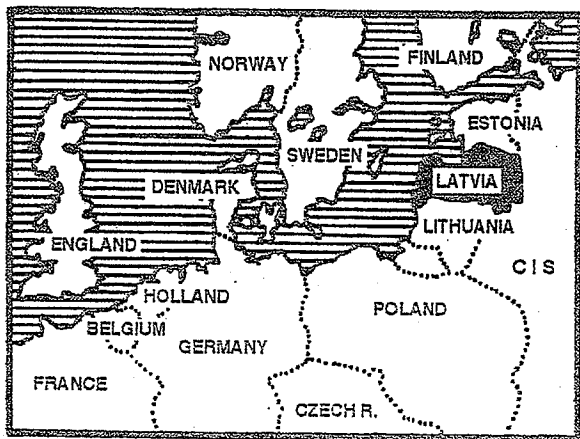
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