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ON A STRUCTURE OF MATHEMATICAL THEORY WHICH REFLECTS MULTISCALE ASPECTS AND INTEGRITY OF BIOLOGICAL SYSTEMS II

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Abstract

In this paper, considered as the second one of the two-part paper, we discuss a structure of mathematical theory which would be convenient for description of biological systems accentuating to more degree multiscale aspects of modelling. In the first part, we have discussed two levels of modelling. The first one has been related to electronic structure and the second one has been related to atomic level of description. The third level of description considered here is called functional and is related to scale larger than atomic one. Models related to such a scale are designed to description of selective functions of biological systems. In order to join of all descriptions introduced in both parts of the two-part paper, one proposes application of collection of dynamical systems with dimensional reduction as a multiscale method of modelling. Within this method, a scale of averaging applied in modelling is formalized. By this step, we

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obtain convenient conditions for unification of discrete and continuum descriptions and a framework for whole structure for theory describing biological systems. Role of mechanics of reactive nanostructures is accentuated. By this step, we try to change the point of view that biology is related predominantly to chemistry.

1. Introduction

In the first part [1] of the two-part paper, we have discussed methods of modelling related to electronic and atomic scales. Consequently, the paper [1] has been devoted to introduction of attractor responsible for selforganization of molecular structures considered at the most elementary level corresponding to dynamics of electrons. To this end, the description is based on vacuum medium mechanics instead of quantum mechanics. In the paper [1], one also discusses description related to atomic scale where biological structures are formed. One accentuates role of attractor and integrity of molecular structures within methods of modelling.

In this paper, one introduces the third level of modelling related to scale larger than atomic one and designed to description of functionality of molecular biological structures. Consequently, in this paper, one accentuates to larger degree role of multiscale aspects in theoretical description.

The most known multiscale method of modelling is related to mechanics of composites and allows us to average some structures from smaller scale to larger one. However, in case of biological structures, we have to do with various mechanisms close to atomic scale where dynamics of processes is large. Then traditional averaging over approximately static structure is not so appropriate.

We have also to do with another difficulty. Continuum mechanics which is applied usually to larger scales has infinite-dimensional fields. Thereby, when we average more complex processes described by molecular dynamics to more simple continuum description, we do not reduce the dimension of the problem. This inconvenience follows from fact that scale of averaging is not expressed formally.

Having in mind above obstacles on the way towards modelling of biological systems, we propose in this paper a method of multiscale modelling called *collection of dynamical systems* with dimensional reduction which seems to be appropriate to discussed ends. We distinguish furthermore particular scale of modelling by defining of reactive nanostructures. By this step, we try to indicate that biological processes are not related predominantly to chemistry but rather to stable structures which cooperate with chemical reactions in order to have at their disposal possibility of fluent change of structures.

2. Modelling of Processes at Functional Level of Description

2.1. Introductory remarks

Functional properties of molecular systems are manifested usually by groups of atoms. Then atoms within groups cooperate in order to realize a task. This cooperation frequently consists in organized change of conformations. Functionality is manifested at various scales. Let us mention role of muscles which are responsible for macroscopic motion. We can consider motion at single cell scale manifested by motion of a bacteria. We can also observe motion at molecular scale. Let us mention ATP synthase and rotation of their parts for instance.

Above discussion accentuates fact that functionality is related to various scales and particular tasks for this functionality can be represented by selective properties of molecular systems in relation to scale associated with external interaction.

Modelling of such a functionality with the aid of full atomic description could be enormously complex. Therefore, selective modelling should be applied to this end. Then we should be able to approximate our biological system in order to concentrate efforts on its chosen properties. However, maintaining of relations with more elementary descriptions is important.

Specificity of biological systems leads frequently to difficult questions. Let us mention a problem related to evolution. How a macroscopic function of a living organism appears as an adaptation property to environment.

In other words, how transmission of information from environment to mechanisms responsible for evolutionary changes happens.

Let us mention the simple question why the polar bear is white. The question is simple but the answer is in my opinion extremely difficult. We should determine mechanism of intention of such a change going through all scales related to mathematical models and ask which electronic process in molecules can express intention of corresponding reconstruction of the molecular system.

At this moment, we are not able to pose such a question since we have not at our disposal any theory which would be able to describe processes in all scales and would have determined the most elementary evolutionary mechanisms. In other words, now we have at our disposal descriptive evolution theory without any mechanisms responsible for such an evolution. Furthermore, modelling of selective functions is now rather arbitrary since methods of modelling are not unified. Let us mention an example.

Evolution of DNA by mutations applied also in theoretical models is in fact observed property which is introduced into model phenomenologically. However, physical mechanism of generation of mutations is not clear. Frequently, statistical approach is applied in order to justify this way of evolution. In order to treat stochasticity in mutations as mechanism of evolution, we should have justification of the stochastic distribution from smaller scale processes. By this point of view, one suggests that stochastic evolution is generated by lower scale physical laws which have stochastic manifestation at the atomic level.

The aim of this section is to characterize a methodology in construction of a multiscale theoretical description which would be able by its further development to approach to above discussed questions.

2.2. Collection of dynamical systems with dimensional reduction

Method of collection of dynamical system with dimensional reduction is previously elaborated for mechanics of materials [2]. In this paper, we adapt and include it into general concept of modelling of biological systems.

General aim of the collection of dynamical systems with dimensional reduction is to elaborate methods of dimensional reduction of an elementary dynamical system (*EDS*). The elementary dynamical system represents description of physical processes on an assumed elementary level and is characterized usually by considerable complexity. By means of the dimensional reduction, we obtain a simplified model based on theoretical foundations provided by the *EDS*.

Let $\boldsymbol{\varphi}$ be variables of *EDS* and $\mathbf{f}$ represents external interactions acting on such a system. Then we introduce the elementary dynamical system in the form

$$\dot{\boldsymbol{\varphi}} = L(\boldsymbol{\varphi}, \mathbf{f}). \tag{1}$$

Transition to a larger scale of averaging is connected with a simplification of this model, corresponding to reduction of degrees of freedom. Our concept of this simplification consists in division of the elementary dynamical system (1) into subsystems. Subsystems are distinguished by determination of groups of variables $\boldsymbol{\varphi}_h = \{\boldsymbol{\varphi}_{h\alpha}\}, \ \alpha \in I_{Ah}$. Then our initial variable takes the form $\boldsymbol{\varphi} = \{\boldsymbol{\varphi}_h\}, \ h \in I_P = \{1, ..., P\},$ where P is a number of subsystems.

Determination of subsystems allows one to introduce new variables. They have a reduced number of degrees of freedom and describe approximately behaviour of each subsystem. New variables are introduced by a mapping $\pi_T = V_T \to \overline{V}_T$ which transforms processes $\boldsymbol{\varphi}(t) \in V_T$ determined on a time interval T into processes determined on the reduced level of description $\mathbf{d}(t) \in \overline{V}_T$.

External interactions acting on the dimensionally reduced dynamical system have to correspond to those ones introduced for the elementary dynamical system. Such a correspondence is introduced by a mapping $\pi_{fT} : \mathcal{F}_T \to \overline{\mathcal{F}}_T$ which transforms processes of external interactions.

The dimensional reduction procedure $DR = \{\pi_T, \pi_{fT}, SDS, app\}$ consists of four elements. Determination of new variables and external

interactions with the help of π_T and π_{fT} is a first step in postulating of a skeletal dynamical system *SDS*. The $SDS(\mathbf{C})$ represents a set of dynamical systems with elements depending on constants $\mathbf{C}$. Final form of the dimensionally reduced dynamical system *RDS* is obtained by identification of the best constants $\overline{\mathbf{C}}$ by comparison of solutions of the elementary dynamical systems and solutions depending on $\mathbf{C}$ which are obtained from equations of the skeletal dynamical systems. Then we obtain $RDS = SDS(\overline{\mathbf{C}})$. The set of all methods of approximation and identification applied for obtaining $\overline{\mathbf{C}}$ is denoted by *app* and is viewed as fourth component of the dimensional reduction procedure.

Discussion of particular form of the dimensional reduction procedure will be carried out in next sections in relation to reactive nanostructures.

2.3. Balance of mass and energy for collection of dynamical systems

In order to postulate a form of the skeletal dynamical system, we have to introduce a set of assumptions which enable us to transfer fundamental physical laws expressed by balance of mass and energy equations into the reduced level. They are transferred from the *EDS* level.

Let $\mathcal{M}_\Pi = \{\{\boldsymbol{\varphi}_h\}\}$, $h \in I_P$ stand for space of solutions of the elementary dynamical system with distinguished groups of variables φ_h related to *h*th subsystem. We introduce the following set of assumptions:

1. There exists a function $\overline{m}_h(\boldsymbol{\varphi}_h) = \{m_{h1}, ..., m_{h\beta_h}\}$ which assigns a set of masses for the *h*th subsystem. The total mass of this subsystem is then $m_h = \sum_i m_{hi}$. We have also that $\sum_h \beta_h = N$, where *N* is the total number of masses in the whole system. The function $\tilde{m} : \mathcal{M}_\Pi \to R^P$ with property $\tilde{m}(\{\boldsymbol{\varphi}_h\}) = \{m_h\}$ determines distribution of masses in subsystems and $m : \mathcal{M}_\Pi \to R$, $m(\{\boldsymbol{\varphi}_h\}) = \Sigma m_h$ determines the total mass related to (1).

2. There exists a function $\tilde{E} : \mathcal{M}_\Pi \to R^P$, $\tilde{E}(\{\boldsymbol{\varphi}_h\}) = \{E_h\}$ which

determines distribution of energy assigned to subsystems and $E : \mathcal{M}_\Pi \to R$, $E(\{\varphi_h\}) = \sum_h E_h$ determines the total energy related to (1).

3. There exists a family of mappings $J_{ij} : \mathcal{M}_\Pi \to R, \quad i, j \in I_P$, $J_{ij}(\{\varphi_h\}) = J_{ij}$ called *flux of mass* from *j*th subsystem to *i*th subsystem and $J_{ij} + J_{ji} = 0, \ J_{ii} = 0$.

4. There exists a family of mappings $W_{ij} : \mathcal{M}_\Pi \to R, \quad i, j \in I_P$, $W_{ij}(\{\varphi_h\}) = W_{ij}$ called *flux of energy* from *j*th subsystem to *i*th subsystem and $W_{ij} + W_{ji} = 0, \ W_{ii} = 0$.

5. A source of mass is determined by a function $c : \mathcal{M}_\Pi \to R^p$, $c(\{\varphi_h\}) = \{c_i\}$. $c_i = \pi_i \circ c(\{\varphi_h\})$ can be considered for each subsystem of the whole system and stands for a source of mass in the *i*th subsystem.

6. A source of energy is determined by a function $R : \mathcal{M}_\Pi \to R^P$, $R(\{\varphi_h\}) = \{R_i\}$. $R_i = \pi_i \circ R(\{\varphi_h\})$ can be considered for each subsystem of the whole system and stands for a source of energy in the *i*th subsystem.

Let $I_G \subset I_P$ be a set of indexes which distinguishes a group of subsystem. Then $I_O = I_P - I_G$ determines subsystems which are external with respect to our group.

By means of above introduced assumptions, we are able to carry out analysis of interchange of mass between subsystems as well as to consider possible sources of mass which appear within subsystems. This leads to expressing the balance of mass equation for collection of dynamical systems in the following form:

$$\sum_{i \in I_G} (\dot{m}_i - c_i) + \sum_{i,\, j \in I_G} J_{ij} + \sum_{i \in I_G,\, j \in I_O} (J_{ij} + J_{ji})$$

$$+ \sum_{i,\, j \in I_O} J_{ij} + \sum_{i \in I_O} (\dot{m}_i - c_i) = 0. \tag{2}$$

Total sum of masses interchanged between subsystems, within the distinguished group by I_G, without any interchange with an external subsystem is equal to zero. Consequently, we obtain then $\sum_{i,\, j \in I_G} J_{ij} = 0$.

Option of I_G is arbitrary. Accordingly, we can express the balance of mass equation connected with an arbitrary group of subsystems represented by I_G with the help of the formula

$$\sum_{i \in I_G} \left(\dot{m}_i - c_i + \sum_{j \in I_O} J_{ij} \right) = 0. \tag{3}$$

The terms J_{ij} describe interchange of mass with an external system indexed by elements of I_O. As a result, equation (3) is not entirely determined. This, in turn, necessitates introducing an additional condition

$$J_{ij} = \bar{J}_{ij}, \quad j \in I_O, \tag{4}$$

where $\bar{J}_{ij}$ is given and expresses an assumed form of efflux of mass.

The balance of energy equation has similar structure as the balance of mass equation and is given by

$$\sum_{i \in I_G} \left(\dot{E}_i - R_i + \sum_{j \in I_O} W_{ij} \right) = 0 \tag{5}$$

with additional conditions

$$W_{ij} = \overline{W}_{ij}, \quad j \in I_O, \tag{6}$$

where $\overline{W}_{ij}$ represents an assumed form of efflux of energy.

Balance of mass and energy equations given by (3)-(6) is a starting point for postulating the skeletal dynamical system. This is realized by option of new variables and representations of functions which appear in (3)-(6). These functions are parameterized then by a set of constants which should be next identified.

2.4. Continuum skeletal dynamical system

Wide application of continuum mechanics in biology necessitates discussion of way of appearing of this theory within the collection of dynamical systems. Foundations of continuum mechanics have been discussed by many authors, see for instance [3, 4].

We would like to introduce fundamental notions of continuum mechanics in connection with the elementary dynamical system. Continuum is defined by means of geometrical terms. Therefore, we introduce an additional assumption related to properties of subsystems distinguished within *EDS* as follows:

Geometrical objects of various dimensions can be assigned to each subsystem by means of mappings $G_x = \mathcal{M}_\Pi \to E_e^P$, $G_L : \mathcal{M}_\Pi \to (2^{E_e})^P$, $G_S : \mathcal{M}_\Pi \to (2^{E_e})^P$, $G_V : \mathcal{M}_\Pi \to (2^{E_e})^P$, where 2^{E_e} stands for family of all subsets of the Euclidean space E_e. The map G_x assigns some distinguished points to subsystems, G_L introduces one-dimensional, G_S two-dimensional, G_V three-dimensional geometrical objects considered as subsets of E_e and accompanied by distinguished subsystems.

Assumption introduced above gives possibility of discussion of geometrical objects associated with *EDS*. In particular, we can discuss position vectors related to *EDS* by means of mappings G_x. This also gives a possibility of considering kinematics and other elementary notions of continuum mechanics in relation to the elementary dynamical system.

For defining a body, we consider the mapping $G_V(\{\varphi_h\}) = \{K_h\}$, where K_h is a three-dimensional subset of E_e. Let $\mathcal{K} = \{K_h, h \in I_P\}$ and $\mathcal{M}_K = \{\mathcal{K}\}$ stand for all families of K_h obtained by means of G_V. Then $G_V : \mathcal{M}_\Pi \to \mathcal{M}_K$. We assume also that $int K_g \cap int K_h = \varnothing$, $g, h \in I_P$, where *int* is operation of taking interior of a set.

Definition 1. The body associated with the elementary dynamical system $\dot{\boldsymbol{\varphi}} = L(\boldsymbol{\varphi}, \mathbf{f})$ is defined with the help of mapping G_V as $\mathcal{B}_\varphi = \bigcup_{h \in I_P} K_h$.

Deformation is connected with evolution of points with respect to reference configuration. In order to describe deformation, we consider the function G_x which assigns a distinguished point χ_h to each subsystem. Consequently, we have that $G_x : \mathcal{M}_\Pi \to \{\{\chi_h\}\}$. We interpret $\{\chi_h\}$ as distinguished positions associated with subsystems.

Let $H_{\chi h} = \{\chi_m, m \in I_h^a\}$ and V_{ah} be a linear space. The set I_h^a represents indexes of subsystems K_m which interact with K_h. Then we introduce the function $a_h : \{H_{\chi h}\} \to V_{ah}$ and $a : \{\{H_{\chi h}\}, h \in I_P\} \to \{\{a_h(\{\chi_m\})\}, h \in I_P\}$ as a function of kinematical dependence between subsystems. By this function, the gradient of deformation and strain tensor can be introduced.

The space $\overline{V}_D = \{\{\chi_h, a_h\}, h \in I_P\}$ characterizes deformation determined by a finite number of parameters. Let us define the space V_κ of deformation functions χ_κ of the body $\mathcal{B}$ with respect to a given configuration κ as $V_\kappa = \{\chi_\kappa : \chi_\kappa = \lambda \circ \kappa^{-1}, \lambda, \kappa \in \mathcal{C}\}$ in accordance with classical formulation of continuum mechanics [3]. Let furthermore, $\alpha_\chi : \overline{V}_D \to V_\kappa$ be a function and $\chi_\kappa^{\mathcal{K}} = \alpha_\chi(\{\chi_h, a_h\})$, $\chi_\kappa^{\mathcal{K}}(\mathbf{X}_h) = \chi_h$, where $\mathbf{X}_h$ is a value of χ_h in a reference configuration.

Definition 2. The deformation function associated with the distinguished family of subbodies $\mathcal{K}$ is a function $\chi_\kappa^{\mathcal{K}}$ which has the form $\chi_\kappa^{\mathcal{K}} = \alpha_\chi(\{\chi_h, a_h\})$.

Definition 3. The motion of the body $\mathcal{B}$ associated with the family of sets $\mathcal{K}$ is a continuous map $\chi_t : [0, T] \to \{\chi_\kappa^{\mathcal{K}}\}$.

Let us consider a function $\overline{T} : \mathcal{M}_K \to R^P$, $\overline{T}(\{K_h\}) = \{T_h\}$ which represents temperature. Let furthermore $I_h^b \subset I_P$ and $H_{Th} = \{T_n, n \in I_h^b\}$. Then we introduce function b_h by analogy to a_h as $b_h : \{H_{Th}\} \to V_{bh}$ and $b : \{\{H_{Th}\}\} \to \{\{b_h(T_n)\}\}$.

Determination of the value T_h is not so direct as defining χ_h. In the last case, we use geometrical interpretation. We cannot do this in the case of temperature. Discussed problem is connected with precise definition of the mapping π_T considered as component of the dimensional reduction procedure. Such a definition allows one to distinguish the part of evolution of the system which is responsible for definition of temperature.

Let $\overline{V}_{TM} = \{\{T_h, b_h\}, h \in I_P\}$, $V_{TM} = \{T(\mathbf{x}) : \mathbf{x} \in \chi(\mathcal{B})\}$. Let us consider a function $\alpha_T : \overline{V}_{TM} \to V_{TM}$ and $T^{\mathcal{K}} = \alpha_T(\{T_h, b_h\})$.

Definition 4. The temperature field $T^{\mathcal{K}}$ associated with the distinguished family of subbodies $\mathcal{K}$ is the field obtained with the help of the function α_T as $T^{\mathcal{K}} = \alpha_T(\{T_h, b_h\})$.

We have obtained definition of the body, deformation function and motion of the body using an elementary dynamical system. The mappings G_V, G_x determine connections between *EDS* and continuum description. Furthermore, temperature is connected with *EDS* by means of the mapping π_T.

The spaces $\overline{V}_D$ and $\overline{V}_{TM}$ are finite dimensional. As a result, we have obtained also finite-dimensional spaces $\alpha_\chi(\overline{V}_D)$ and $\alpha_T(\overline{V}_{TM})$. This follows that finite-dimensional fields are considered on continuum only.

In order to introduce a continuum skeletal dynamical system, we must have at our disposal balance of mass and energy equations also associated with the elementary dynamical system. Previously we have defined functions $\widetilde{m}$, $J_{\varphi ij}$, c_φ, E_φ, $W_{\varphi ij}$, R_φ which introduce masses, efflux of mass

between subsystems, source of mass, energy, efflux of energy and source of energy related to subsystems, respectively. These functions, indexed here by φ, are introduced in connection with the elementary dynamical system.

Let us consider the mapping $\widetilde{m} : \mathcal{M}_\Pi \to \{\{m_h\}\}$ which determines a set of masses related to collection of dynamical systems. Let $\mathcal{M}_M = \{\{M_h\}\}$ and $M : \mathcal{M}_K \to \mathcal{M}_M$ be a mapping which assigns masses to each K_h. Masses M_h related to continuum model are defined by means of the relation $M \circ G_V = i \circ \widetilde{m}$, where i is an identity mapping. Thereby, a system of masses related to continuum is introduced by means of the mapping $\widetilde{m}$ defined on elementary dynamical system.

We have defined body $\mathcal{B}$ associated with the elementary dynamical system. We define subbody also denoted by $\mathcal{B} = \bigcup_h K_h$, $h \in I_B$, where $I_B \subset I_P$ is an arbitrary subset of I_P. Let us introduce $M(\mathcal{B}) = \sum_{h \in I_B} M_h$. Thereby, mass related to subbodies is defined as a kind of measure on the body.

The function $\mathcal{E} : \mathcal{M}_K \to \{\{\mathcal{E}_h\}\}$ determines distribution of energy on the family $\{K_h\}$ and $\mathcal{E}_h = \pi_h \circ \mathcal{E}(\{K_h\})$ assigned to each K_h is defined by means of the relation $\mathcal{E} \circ G_V = i \circ E_\varphi$.

Source of mass $c_\varphi : \mathcal{M}_\Pi \to R^P$ and source of energy $R_\varphi : \mathcal{M}_\Pi \to R^P$ are defined now as $C : \mathcal{M}_K \to R^P$, $R : \mathcal{M}_K \to R^P$ by means of relations $C \circ G_V = i \circ c_\varphi$ and $R \circ G_V = i \circ R_\varphi$. These quantities can be defined for subbodies with the help of formulas $\mathcal{E}(\mathcal{B}) = \sum_h \mathcal{E}_h$, $C(\mathcal{B}) = \sum_h C_h$, $R(\mathcal{B}) = \sum_h R_h$.

We assume without discussion of details that $\mathcal{E} = E + \mathcal{T}$ is considered as a sum of internal energy and kinetic energy for continuum.

Interchange of mass and energy is described by efflux of mass $J_{\varphi ij} : \mathcal{M}_{\Pi} \to R$ and efflux of energy $W_{\varphi ij} : \mathcal{M}_{\Pi} \to R$. These quantities are defined for continuum as $J_{ij} : K_i \times K_j \to R$, where J_{ij} is determined by means of $J_{ij} \circ (G_{Vi} \times G_{Vj}) = i \circ J_{\varphi ij}$ and $W_{ij} : K_i \times K_j \to R$, where we obtain W_{ij} from $W_{ij} \circ (G_{Vi} \times G_{Vj}) = i \circ W_{\varphi ij}$.

Let us consider furthermore boundary of the body as $\partial\mathcal{B} = \partial \bigcup_h K_h$. We define $J(\partial\mathcal{B}) = \sum_{i \in I_B, m \in I_P - I_B} J_{im}$ and $W(\partial\mathcal{B}) = \sum_{i \in I_B, m \in I_P - I_B} W_{im}$ as quantities referred to boundary of the body. Let $\partial\mathcal{B}_s \subset \partial\mathcal{B}$ be defined as $\partial\mathcal{B}_s = \bigcup_{h \in I_s} (\partial K_h \cap \partial\mathcal{B})$, $I_s \subset I_B$. We assume that pair of indexes $\{i, m\}$ is associated with $\partial\mathcal{B}_s$ if $\partial\mathcal{B}_s$ is a border between subsystems *i* and *m*. Then $J(\partial\mathcal{B}_s) = \sum_{i,m} J_{im}$.

Using terms of continuum associated with the elementary dynamical system introduced above, we can express balance of mass equation for continuum which corresponds to (3) as

$$\dot{M}(\mathcal{B}) + J(\partial\mathcal{B}) - C(\mathcal{B}) = 0 \tag{7}$$

with the additional condition as a counterpart of (4) and satisfied for arbitrary $\partial\mathcal{B}_s \subset \partial\mathcal{B}$,

$$J(\partial\mathcal{B}_s) = \bar{J}(\partial\mathcal{B}_s) \tag{8}$$

for a given $\bar{J}(\partial\mathcal{B}_s)$.

The balance of energy equation corresponding to (5) and now expressed in terms of continuum is assumed in the following form

$$\dot{E}(\mathcal{B}) + \dot{T}(\mathcal{B}) + W(\partial\mathcal{B}) - R(\mathcal{B}) = 0 \tag{9}$$

with the additional condition corresponding to (6) and satisfied for arbitrary subboundary $\partial\mathcal{B}_s \subset \partial\mathcal{B}$ of the body $\mathcal{B}$,

$$W(\partial\mathcal{B}_s) = \overline{W}(\partial\mathcal{B}_s) \tag{10}$$

for a given $\overline{W}(\partial\mathcal{B}_s)$.

Considered above equations of balance of mass and energy are the first stage for postulating of form of the skeletal dynamical system. In the next step, we assume representations of quantities introduced in (7)-(10). They are parameterized by some constants which have to be identified. Identification of these constants is realized with the help of solutions of the elementary dynamical system.

Continuum fields on the body are introduced by means of previously determined discrete fields with the help of mappings similar to α_χ and α_T for deformation and temperature. They should fulfill well known integral relations between densities and discrete values of quantities on each subbody. Consequently, discussed here continuum mechanics is characterized by finite-dimensional spaces of fields. In classical case, such spaces are infinite-dimensional. This difference is important. Derived equations are finite-dimensional and we do not apply discretization methods. In discussed case, a continuum model with finite-dimensional fields is inherently connected with determination of degree of averaging what is expressed by option of sets K_h and the skeletal dynamical system. As a result we introduce by this, formalization of scale of averaging. Such a fact is important for description of processes associated with phenomena relating to several scales. Thereby this is also important for biological systems.

Introduced formulation of continuum mechanics admits integration of it with molecular dynamics. This integration consists in fact that we use *EDS* determined by molecular dynamics equations and continuum skeletal dynamical system in the framework of the dimensional reduction procedure.

Let us note that connections of molecular dynamics and continuum mechanics are discussed in literature. Such considerations are carried out usually in the context of statistical mechanical calculations supported by molecular dynamics [5, 6]. Considerable achievement for cooperation of both theories is given by Prrinello and Rahman in [7].

3. Mechanics of Reactive Nanostructures as a Functional Level for Modelling

3.1. Introductory remarks

Biological structures are frequently similar to solids. It means that role of chemical reactions is not so dominant as frequently is commented. Sometimes they say that biology is a chemistry. However, biological processes create very stable structures which are not similar to chemical reactions. Let us mention DNA for instance. The DNA molecule takes part in chemical reactions. However, this molecule is viewed predominantly as a relatively stable structure which can undergo some changes. We observe also that higher level of evolution is associated with creation of more dense molecular structures. We observe for instance in single cell increasing number of various compartments when evolution is continued. This makes structure of cell more dense and stable. In larger scale, an animal is perceived rather as solids like object than a chemically reacting system.

Above comments suggest a change of traditional point of view which treats biological systems predominantly as reacting system. On the other hand, stable structures within biological systems are characterized by large flexibility related to conformations and also with respect to possibility of changing this structure in order to evolve.

Possibility of fluent change of structures is realized just by chemical reactions. Thereby, we should see biological systems as a set of stable structures with possibility of realization of some structural changes, cooperating with chemical reactions. Thereby, this point of view suggests that chemical reactions are important but are considered now in a larger context. Accentuating role of stable structures, we introduce to larger degree molecular physics together with theoretical chemistry into description of biological systems.

Taking into account above discussion, we introduce concept of molecular reactive structure as an important object in mathematical modelling of biological systems.

3.2. Definition of the molecular reactive structure

Large part of molecules in cell does not change their chemical composition for a time. However, such molecules can undergo structural transformations and take part in chemical reactions. Thus, they are similar to catalysts. However, category of catalysts is functionally directed to controlling chemical reactions. We would like to define molecular reactive structures as all stable with respect to composition molecules which can take part in chemical reactions but their functions can be various. In particular, they can be enzymes or they can create larger, solids like structures.

We formulate definition of the molecular reactive structure considering molecule as a set of material points corresponding to nuclei of atoms. We introduce notation $S(\mathbf{R})$ for a system of the material points representing molecule and $\mathbf{R}$ for its current configuration. We introduce notation from the set theory for systems like S. Thus, two subsystems $S_1 \bigcup S_2 = S$ create a new molecule represented by S.

Let $\mathbf{R}_{RS} = \{\mathbf{R}_i\}, \ i \in I_{RS}$ stand for positions of material points within the reactive structure S_{RS}. The configuration $\mathbf{R}_{RS}$ can undergo transition between catchment regions during evolution. We admit, in general, transitions for the molecular reactive structure which do not destroy an admissible structure of interatomic bonds.

Let us introduce a relation $\mathcal{B}_\alpha \subset I_{RS} \times I_{RS}$ which consists of pairs of nuclei which are joined by interatomic bond $b(\mathbf{R}_i, \mathbf{R}_j)$. Existence of such bonds can be determined by means of methods of quantum chemistry [8] for instance.

Let $\mathcal{A}_B$ be a set of all relations $\mathcal{B}_\alpha$ which represents an admissible structure of interatomic bonds within S_{RS}. The term "admissible" corresponds to current requirements related to described structure. Thus, we can accept the case when the set $\mathcal{A}_B$ consists of one element only. Then all interatomic bonds cannot be changed with respect to the relation classifying them. However, we can accept the situation when a reorganization of interatomic bonds structure without unwanted changes happens.

With the help of the set $\mathcal{A}_B$, we introduce a relation between relations. Thus, $\mathcal{B}_\alpha \equiv_{\mathcal{A}} \mathcal{B}_{\alpha'}$, when $\mathcal{B}_\alpha, \mathcal{B}_{\alpha'} \in \mathcal{A}_B$.

We accept potential energy hypersurface and notion associated with it for further considerations. Domain $\mathcal{V}_C$ of the potential energy can be divided into catchment regions C_α connected with minima $\mathbf{c}_\alpha$ of V as $\mathcal{V}_C = \bigcup_\alpha C_\alpha$ [10, 11]. If the molecule S_{RS} interacts with other particles during a chemical reaction, then the configuration space is extended. As a result, the potential energy $V = V(\mathbf{R}_{RS}, \mathbf{R}_E)$ depends on additional variables $\mathbf{R}_E$ representing a system of external molecules S_E. Decomposition of $\mathcal{V}_C$ into catchment regions depends now on $\mathbf{R}_E$ and we have $C_\alpha = C_\alpha(\mathbf{R}_E)$.

Let us assume that $\{\mathbf{R}_{RS}, \mathbf{R}_E\}(t)$ represents process of a chemical reaction. At an initial instant t_I, the molecules S_{RS} and S_E are separated. At a final instant t_F, they are also separated. This can be expressed by the fact that $V(\mathbf{R}_{RS}, \mathbf{R}_E)|_{t_I, t_F} = V_{RS}(\mathbf{R}_{RS}) + V_E(\mathbf{R}_E)$ in a neighbourhood of initial and final positions of this molecular system. We introduce a set of admissible processes $\mathbf{R}_E(t) \in \mathcal{A}_{RS}$ satisfying discussed above conditions with respect to S_{RS} and which ensures realization of this reaction process.

Definition 5. We call a molecule S_{RS} the *molecular reactive structure* if configurations $\mathbf{R}_{RS}$ induced by all admissible processes $\mathbf{R}_E(t) \in \mathcal{A}_{RS}$ are contained within domain $\mathcal{V}_C = \bigcup_{\alpha \in I_C} C_\alpha(\mathbf{R}_E(t))$ between initial and final instants t_I and t_F. Furthermore, then we also have $\mathcal{B}_\alpha \equiv_{\mathcal{A}} \mathcal{B}_{\alpha'}$ for each pair $\alpha, \alpha' \in I_C$ which appears during evolution of the configuration $\mathbf{R}_{RS}$ through various catchment regions.

This definition expresses fact that the molecular reactive structure takes part in a chemical reaction but interatomic bonds can undergo evolution without destroying their admissible structure only. Thereby, deformation and structural transformations of the molecule S_{RS} are admissible.

3.3. Skeletal dynamical system for reactive nanostructures

We have introduced molecular reactive structures using atomic level of description. However, we can discuss reactive structures also by more averaged descriptions.

Let us consider behaviour of actin cytoskeleton [12, 9]. This molecular structure undergoes considerable reorganization in order to realize motility of cell. In particular, cytogel into cytosol transformation is realized by destruction of a meshwork of actin filaments. Assembly of contractile actin-myosin filaments is organized within cell for generation of active stress. Such a medium can be described by means of continuum models [9] in a very averaged way. Then the problem is to postulate form of constitutive equations taking into account high controllability of this medium.

Elementary mechanisms of reorganization of the actin cytoskeleton are related to single molecules. Actin filaments are assembled from monomers [12]. Protein molecules take part in regulation of these processes [9, 13, 14].

Above concise discussion suggests that considered here processes are related to single molecules or to a system of such molecules which can undergo a reorganization. Thus, evolution of this system depends on the properties of single molecules as well as on processes responsible for the reorganization.

Direct modelling of single molecules considering all atoms is too complicated for description of the multimolecular processes. Therefore, it seems to be the most appropriate to elaborate models of single molecules which describe evolution of groups of atoms within them in an averaged way. Then we have to use a nanoscale level of averaging properties of intramolecular processes. Furthermore, we should be able to describe mentioned above processes of reorganization as well as interactions with external chemical reactions.

We can encounter in literature some models which consider reduced number of degrees of freedom for describing evolution of molecules. Let us mention for instance the papers [15-17].

Particular properties of reactive nanostructures have to follow from smaller scale considerations. Consequently, reactive nanostructures should be placed in our multiscale method of modelling. We tend towards construction of a skeletal dynamical system for our reactive nanostructures. To this end, we should distinguish first a set of new variables related to the reduced level of description.

In many cases, during modelling, we are able to distinguish slowly and quickly varying processes realized within considered system. We assume that this is the case for evolution of our molecule modelled. Thus we consider thermal vibrations as quickly varying processes and structural transformation or a deformation of the molecule as the slowly varying one. Such division of processes, we call *SQ-decomposition*. We introduce variables which reflect this property, by means of a set of mappings defined to this end.

We consider, as previously, a molecule $S(\mathbf{R}_{RS})$ modelled by means of a set of material points. We distinguish subsystems within such a molecule as $S(\mathbf{R}_{RS}) = \bigcup_{h \in I_A} S_h(\{\mathbf{R}_{hj}\})$ composed of determined groups of atoms.

Let us note that many small molecules appear in biological systems repeatedly, what gives a hope to obtain a degree of universality in division into subsystems.

We introduce three kinds of variables on the dimensionally reduced level of description. The first one represents configurational variables $\mathbf{Q}_h = \{Q_{hp}\}$ and velocities $\mathbf{w}_h = \dot{\mathbf{Q}}_h$, which approximately describe evolution of the whole group of particles within *h*th subsystem. They describe slowly varying processes. We introduce also the configuration space $\overline{\mathcal{V}}_C = \{\mathbf{Q}\} = \{\{\mathbf{Q}_h\}\}$ and the corresponding phase space $\overline{\mathcal{V}}_D = \{\{\mathbf{Q}_h, \mathbf{w}_h\}\}$.

The second kind of variables θ_h describes in an averaged way quickly varying processes and is related directly to balance of energy equation. The third group of variables $\boldsymbol{\eta}_h$ is related to quickly varying processes and needs postulating additional evolution equations.

Let us introduce spaces of processes $\mathcal{V}_T = \{\{\mathbf{R}_i, \mathbf{v}_i\}(t) : i \in I_{RS}, t \in T\}$ related to atomic level of description and

$$\overline{\mathcal{V}}_{DT} = \{\{\mathbf{Q}_h, \mathbf{w}_h\}(t) : h \in I_A, t \in T\},$$

$$\overline{\mathcal{V}}_{\theta T} = \{\{\theta_h\}(t) : h \in I_A, t \in T\}, \quad \overline{\mathcal{V}}_{\eta T} = \{\{\boldsymbol{\eta}_h\}(t) : h \in I_A, t \in T\}$$

and $\overline{\mathcal{V}}_T = \overline{\mathcal{V}}_{DT} \times \overline{\mathcal{V}}_{\theta T} \times \overline{\mathcal{V}}_{\eta T}$, where T is a time interval.

New variables are obtained by means of the mappings $\pi_T : \mathcal{V}_T \to \overline{\mathcal{V}}_T$, $\pi_T = \pi_{ST} \times \pi_{QT}$ and $\pi_{ST} : \mathcal{V}_T \to \overline{\mathcal{V}}_{DT}$, $\pi_{QT} : \mathcal{V}_T \to \overline{\mathcal{V}}_{\theta T} \times \overline{\mathcal{V}}_{\eta T}$.

Structure of the mappings π_{ST} and π_{QT} is obtained by using decomposition of variables. In order to illustrate this, let us take a set of time instants $t_0 < t_1 < \cdots < t_k$ which belong to the time interval $T = [t_0, t_K]$, $t_K = t_0 + T$, and let $I_K = \{0, 1, ..., K\}$. By means of these instants, we divide the time interval into the sum $T = \bigcup_k T_k$, $T_k = [t_{k-1}, t_k]$, $k = 1, ..., K$. Then for each k, we can calculate the value of $\widetilde{\mathbf{R}}_k$ as

$$\widetilde{\mathbf{R}}_k = \frac{1}{T_k} \int_{T_k} \mathbf{R}(t) dt. \tag{11}$$

A value $\widetilde{\mathbf{R}}_0 = \mathbf{R}(t_0)$ is assigned to $k = 0$. With the aid of sequence of values $\{\widetilde{\mathbf{R}}_k\}$, $k \in I_K$, we can generate a function $\widetilde{\mathbf{R}}(t) = \mathcal{J}_R(\{\widetilde{\mathbf{R}}_k\})$, where $\mathcal{J}_R$ is an approximation procedure which tries to lower second order derivative as far as it is possible for $\widetilde{\mathbf{R}}(t)$. Now, we are able to decompose the variable $\mathbf{R}(t)$ into two summands

$$\mathbf{R}(t) = \widetilde{\mathbf{R}}(t) + \delta\mathbf{R}(t). \tag{12}$$

Thus, $\widetilde{\mathbf{R}}(t)$ represents the slowly varying part of $\mathbf{R}(t)$ and $\delta\mathbf{R}(t)$ its quickly varying part.

We assume that the mapping $\mathcal{J}_R$ satisfies the condition $\int_{T_k} (\mathbf{R} - \widetilde{\mathbf{R}}) dt = \int_{T_k} \delta\mathbf{R} dt \approx 0$, where "$\approx$" means equality with an admissible error. In

general, methods of determining of $\mathcal{J}_R$ are an open problem. In the paper [18], one considers a numerical example of procedure of such a decomposition.

Let $A_t(\{\mathbf{R}, \dot{\mathbf{R}}\}(t)) = \{\widetilde{\mathbf{R}}, \delta\mathbf{R}, \dot{\widetilde{\mathbf{R}}}, \delta\dot{\mathbf{R}}\}(t)$ be mapping which realizes *SQ*-decomposition. We assume further that there exist mappings π_S and π_Q which give direct assignation of new reduced variables to those obtained by means of A_t. We would say that π_S and π_Q take into account also a space averaging imposed on previously obtained time averaging introduced by A_t. As a result, we obtain

$$\pi_T = \{\pi_{ST}, \pi_{QT}\} = \{\pi_S \circ A_t, \pi_Q \circ A_t\}. \tag{13}$$

Similar *SQ*-decomposition can be carried out for forces **f**. To this end, we calculate the following time averaged quantities

$$\widetilde{\mathbf{f}}_k = \frac{1}{T_k}\int_{T_k} \mathbf{f}(t)dt. \tag{14}$$

Then we have $\widetilde{\mathbf{f}}(t) = \mathcal{J}_f(\widetilde{\mathbf{f}}_k)$ with the help of an approximation procedure $\mathcal{J}_f$. Finally, we obtain the decomposition

$$\mathbf{f}(t) = \widetilde{\mathbf{f}}(t) + \delta\mathbf{f}(t). \tag{15}$$

Let $B_t(\mathbf{f}(t)) = \{\widetilde{\mathbf{f}}(t), \delta\mathbf{f}(t)\}$ and $\pi_{Sf} \circ B_t(\mathbf{f}(t)) = \bar{\mathbf{f}}_S$, $\pi_{Qf} \circ B_t(\mathbf{f}(t)) = \bar{\mathbf{f}}_Q$. Thereby, we obtain the general form of the map π_{fT} by

$$\pi_{fT} = \{\pi_{Sf} \circ B_t, \pi_{Qf} \circ B_t\} \tag{16}$$

and $\pi_{fT}(\mathbf{f}(t)) = \{\bar{\mathbf{f}}_S, \bar{\mathbf{f}}_Q\}(t)$.

In general, it is expected that mappings π_T and π_{fT} are not entirely independent. We postulate that there exists a relation $\mathcal{R}_L(\pi_T, \pi_{fT})$ which joins considered two mappings. By this relation, we accentuate fact that it is possible that averaging methods applied to processes described by variables of the dynamical system and processes related to forces can be consistent to

some degree. At this moment, we do not analyse this possibility in details. In discussed here case, we assume that $\mathcal{R}_L = I$ or in other words, the same procedures are represented by π_T and π_{fT}.

Discussed above *SQ*-decomposition is similar to some degree to the Parinello Rahman method applied in molecular dynamics [7].

In order to construct a skeletal dynamical system, we have to postulate form of total energy $\mathcal{E}$ of the system modelled. We assume that

$$\mathcal{E} = \sum_h E_h = \sum_h (V_h + \mathcal{T}_h), \tag{17}$$

where $\mathcal{T} = \sum_h \mathcal{T}_h$ is kinetic energy corresponding to slowly varying processes and

$$\sum_h V_h = \sum_h (V_{Sh} + V_{Qh}) = \Phi + \mathcal{E}_Q \tag{18}$$

is decomposed into parts related to slowly and quickly varying processes. Furthermore, we assume that

$$V_{Sh} = C_{Sh\gamma}\Psi_{Sh\gamma}(\mathbf{Q}_h, a_{Qh}), \tag{19}$$

$$V_{Qh} = C_{Qh\delta}\Psi_{Qh\delta}(\theta_h, a_{\theta h}), \tag{20}$$

where a_{Qh} and $a_{\theta h}$ are functions of kinematical dependence between subsystems related to $\mathbf{Q}_h$ and θ_h correspondingly. They are defined in similar way as this is done in subsection related to continuum mechanics for deformation function and temperature. We admit dependence $C_{Sh\gamma}$, $C_{Qh\delta}$ on $\mathbf{Q}_h$, θ_h, $\boldsymbol{\eta}_h$ in the sequel.

Let us consider temporarily a given constant values of variables $\{\theta, \boldsymbol{\eta}\}$. By such a step, we can introduce the properties of the function $\widetilde{\Phi} = \Phi(\{\theta, \boldsymbol{\eta}\})(\mathbf{Q})$ defined in (18) which depends now on configurational variables only. We also assume that $\overline{\mathbf{Q}} = \{\overline{\mathbf{Q}}_h\}$ stands for minimum of this function.

Let $A_R : \overline{\mathcal{V}}_C \to \overline{\mathcal{V}}_C$, $A_T : \overline{\mathcal{V}}_C \to \overline{\mathcal{V}}_C$ be mappings which realize the same rotation and translation for each component of $\mathbf{Q}$ belonging to the configuration space $\overline{\mathcal{V}}_C$. Then the transformation

$$\mathbf{Q} = A_R(\overline{\mathbf{Q}}) + A_T(\overline{\mathbf{Q}}) \tag{21}$$

represents rigid transformation of the configuration $\overline{\mathbf{Q}}$. In other words, we have defined rigid motion of the molecule S on the dimensionally reduced level.

Let $[\overline{\mathbf{Q}}]$ stand for class of elements which are determined by using of all A_R and A_T in (21) for given $\overline{\mathbf{Q}}$ and $\mathcal{M}$ be set of all manifolds in $\overline{\mathcal{V}}_C$. We introduce a set of representatives of the equivalence classes in the form

$$H = \{\mathbf{Q} : \mathbf{Q}, \mathbf{Q}_1 \in H \Rightarrow [\mathbf{Q}] \neq [\mathbf{Q}_1], H \in \mathcal{M}\}. \tag{22}$$

The set H represents deformations of the molecule S determined on the dimensionally reduced level of description. H is viewed to be manifold since deformation of the molecule is considered as a continuous process.

The domain of the function $\widetilde{\Phi}$ can be expressed as a fiber bundle [19]:

$$\overline{\mathcal{V}}_C = H \times_f F_R(\mathbf{Q}), \quad \mathbf{Q} \in H, \tag{23}$$

where $\times_f$ stands for symbol of generalized Cartesian product of H and a chosen fiber $F_R(\mathbf{Q})$ identified with the equivalence class $[\mathbf{Q}]$. H is considered as basis of the fiber bundle.

We assume that the function Φ has the following properties for each given values of $\{\theta, \boldsymbol{\eta}\}$:

$$\Phi(\{\theta, \boldsymbol{\eta}\})(\mathbf{Q}) = \Phi(\{\theta, \boldsymbol{\eta}\})(\mathbf{Q}_1) \tag{24}$$

for all $\mathbf{Q}$, $\mathbf{Q}_1$ belonging to the same F_R and this is the case for all F_R. In other words, the function Φ does not change its value during a rigid motion.

Let $[0, s^*] \subset R$ be an interval. The steepest descent path $P(\mathbf{Q}, \cdot) : [0, s^*]$

$\to \overline{\mathcal{V}}_C$ with the origin $\mathbf{Q}$ is defined as a path tangent to the vector $\mathbf{g} = -\dfrac{\partial\widetilde{\Phi}}{\partial\mathbf{Q}}$. Then we assume also that $p(\mathbf{Q}, 0) = \mathbf{Q}$ and at the end of each path, we have a critical point $\mathbf{c} = p(\mathbf{Q}, s^*)$ and then $\dfrac{\partial\widetilde{\Phi}}{\partial\mathbf{Q}}(\mathbf{c}) = \mathbf{0}$.

Two points $\mathbf{Q}$, $\mathbf{Q}_1$ are called *equivalent* if $p(\mathbf{Q}, s^*) = p(\mathbf{Q}_1, s^*)$. In other words, equivalent points are origins of steepest descent paths having the same ends as a critical point.

Definition 6. Equivalence classes of the relation defined by the steepest descent path are called *catchment regions* associated with the function $\widetilde{\Phi}$.

As a result of defining the equivalence relation in $\overline{\mathcal{V}}_C$, we obtain decomposition of the domain of the function $\widetilde{\Phi}$ as follows:

$$\overline{\mathcal{V}}_C = \bigcup_{\alpha} C_\alpha(\{\theta, \boldsymbol{\eta}\}), \tag{25}$$

where C_α are the catchment regions.

The catchment regions depend on $\{\theta, \boldsymbol{\eta}\}$ since the function $\widetilde{\Phi}$ is defined for given $\{\theta, \boldsymbol{\eta}\}$. Thus, evolution of these variables can lead to qualitative changes of the catchment region division given in (25).

The kinetic energy term $\mathcal{T} = \mathcal{T}(\mathbf{w}_h, \dot{a}_{Qh})$ depends on slowly varying variables only and inertia characteristics. Let us calculate $\dot{\mathcal{T}}_h$. To this end, we assume that the function $\mathcal{T}_h$ has properties $\dfrac{\partial\mathcal{T}_h}{\partial w_{hp}} \approx \dfrac{\partial^2\mathcal{T}_h}{\partial w_{hp}\partial w_{hq}}(0) w_{hq}$, $\dfrac{\partial\mathcal{T}_h}{\partial\dot{a}_{Qh}} \approx \dfrac{\partial^2\mathcal{T}_h}{\partial\dot{a}_{Qh}^2}(0)\dot{a}_{Qh}$ expressed by means of the Taylor expansion. Finally, we obtain

$$\dot{\mathcal{T}}_h = \frac{\partial^2 \mathcal{T}_h}{\partial w_{hp} \partial w_{hq}}(0) w_{hq} \dot{w}_{hp} + \frac{\partial^2 \mathcal{T}_h}{\partial \dot{a}_{Qh}^2}(0) \frac{\partial \dot{a}_{Qh}}{\partial \dot{Q}_{jp}} \frac{\partial \ddot{a}_{Qh}}{\partial \ddot{Q}_{kq}} \dot{Q}_{jp} \ddot{Q}_{kq}$$

$$= M_{hpq} w_{hq} \dot{w}_{hp} + I_{hjqkr} \dot{Q}_{jq} \ddot{Q}_{kr}$$

$$= (M_{hpq} \dot{w}_{hp}) \dot{Q}_{hq} + (I_{hjqkr} \ddot{Q}_{kr}) \dot{Q}_{jq}. \tag{26}$$

We use usual summation by means of the symbol Σ for indexes of subsystems $h \in I_G$ and $m \in I_O$ which are related to main division into subsystems. For the remaining indexes, the summation convention is applied.

Taking into account *SQ*-decomposition, we modify the general balance of energy equation (5) into the form

$$\sum_{i \in I_G} \left(\dot{E}_i - R_{Si} - R_{Qi} + \sum_{i \in I_O} (W_{Sij} + W_{Qij}) \right) = 0. \tag{27}$$

Thereby, sources of energy considered within subsystems and efflux of energy are decomposed into two parts.

We assume that $C_{Sh\gamma}$ and $C_{Qh\delta}$ are constants at this stage of derivation. Furthermore, we postulate particular forms of $R_{Sh} = \bar{f}_{Shq} \dot{Q}_{hq}$ and $W_{Shm} = -\bar{f}_{Shmq} \dot{Q}_{mq}$. Then taking into account (17)-(20) and (26), the balance of energy (27) is now expressed by means of the formula

$$\sum_{h \in I_G} \left\{ \left[C_{Sh\mu} \frac{\partial \Psi_{Sh\mu}}{\partial Q_{hq}} \dot{Q}_{hq} + C_{Sh\mu} \frac{\partial \Psi_{Sh\mu}}{\partial a_{Qh}} \frac{\partial a_{Qh}}{\partial Q_{js}} \dot{Q}_{js} \right. \right.$$

$$\left. + C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial \theta_h} \dot{\theta}_h + C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial a_{\theta h}} \frac{\partial a_{\theta h}}{\partial \theta_j} \dot{\theta}_j \right]$$

$$+ (M_{hpq} \dot{w}_{hp}) \dot{Q}_{hq} + (I_{hjskr} \ddot{Q}_{kr}) \dot{Q}_{js} - \bar{f}_{Shq} \dot{Q}_{hq} - R_{Qh}$$

$$\left. + \sum_{m \in I_O} (-\bar{f}_{Shmq} \dot{Q}_{mq} + W_{Qhm}) \right\} = 0 \tag{28}$$

with additional conditions corresponding to (6),

$$W_{Qhm} = \overline{W}_{Qhm}, \quad h \in I_G, \quad m \in I_O. \tag{29}$$

Owing to particular form of W_{Shm} assumed, an additional condition for this quantity appears and will be discussed below.

At this moment, we admit again dependence of $C_{Sh\mu}$, $C_{Qh\nu}$ on previously considered variables. We assume that terms $\dot{C}_{Sh\mu}\Phi_{Sh\mu} \neq 0$ and $\dot{C}_{Qh\nu}\Phi_{Qh\nu} \neq 0$. We take into account these terms in the balance of energy equation. Consequently, next transformed version of (28) is given by

$$\begin{aligned}
\sum_{h\in I_G} \Bigg\{ \Bigg[& C_{Sh\mu} \frac{\partial \Psi_{Sh\mu}}{\partial Q_{hq}} + \sum_{h'} C_{Sh'\mu} \frac{\partial \Psi_{Sh'\mu}}{\partial a_{Qh'}} \frac{\partial a_{Qh'}}{\partial Q_{hq}} + M_{hpq}\dot{w}_{hp} \\
& + \sum_{h'} I_{h'hqkr}\ddot{Q}_{kr} - \bar{f}_{Shq} \Bigg] \dot{Q}_{hq} + C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial \theta_h} \dot{\theta}_h \\
& + C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial a_{\theta h}} \frac{\partial a_{\theta h}}{\partial \theta_j} \dot{\theta}_j + \dot{C}_{Sh\mu}\Psi_{Sh\mu} \\
& + \dot{C}_{Qh\nu}\Psi_{Qh\nu} - R_{Qh} + \sum_{m\in I_O} W_{Qhm} \Bigg\} \\
& + \sum_{m\in I_O} \sum_{h'\in I_G} I_{h'mqkr}\ddot{Q}_{kr}\dot{Q}_{mq} \\
& + \sum_{m\in I_O} \sum_{h\in I_G} \left(\frac{\partial V_{Sh}}{\partial Q_{mq}} - \bar{f}_{Shmq} \right) \dot{Q}_{mq} = 0,
\end{aligned} \tag{30}$$

where additional terms dependent on Q_{mq} are taken into account.

We would like to introduce friction terms as well as effects following from stochastic forces as a result of molecule-solvent interaction. Thus we

assume existence, on the dimensionally reduced level, of additional forces $\bar{c}_{hq} w_{hq}$. Furthermore, the function Φ can be modified by averaging of effects of the stochastic forces. This is postulated by extension of the function Φ into the function $\Phi_E = \Phi + \Phi_S$ in (18). Φ_S depends on Q_{hq} only for this derivation. This function will be plotted with variables θ, $\boldsymbol{\eta}$, $\boldsymbol{\eta}_S$ in the sequel, where $\boldsymbol{\eta}_S$ is an internal variable which takes into account solvent properties during evolution of the system.

Let us assume that time processes are independent. Then we obtain the equations describing slowly varying processes

$$C_{Sh\mu} \frac{\partial \Psi_{Sh\mu}}{\partial Q_{hq}} + \sum_{h'} C_{Sh'\mu} \frac{\partial \Psi_{Sh'\mu}}{\partial a_{Qh'}} \frac{\partial a_{Qh'}}{\partial Q_{hq}} + \frac{\partial \Phi_S}{\partial Q_{hq}}$$

$$+ \bar{c}_{hq} w_{hq} - \bar{f}_{Shq} + M_{hpq} \dot{w}_{hp} + \sum_{h'} I_{h'hqkr} \ddot{Q}_{kr} = 0 \tag{31}$$

with the additional condition

$$\sum_{h} \frac{\partial V_{Sh}}{\partial Q_{mq}} + \sum_{h} I_{hmqkr} \ddot{Q}_{kr} = \sum_{h} \bar{f}_{Shmq} \equiv \bar{f}_{Smq},\ h \in I_G,\ m \in I_O. \tag{32}$$

We introduce also the equation which expresses previously introduced notation in the form

$$\dot{Q}_{hq} = w_{hq},\quad h \in I_G. \tag{33}$$

The last term in (31) contains second time derivatives of Q_{kr} with index k which can be found in I_O. This induces necessity of considering furthermore the following additional condition

$$\dot{Q}_{mq} = \overline{w}_{mq},\quad m \in I_O \tag{34}$$

for determining values of $\dot{Q}_{mq}$ which do not belong to the system I_G.

We obtain also from (30), using (31) and (32), the equation describing averaged evolution of quickly varying processes

$$\sum_h \Bigg(C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial \theta_h} \dot{\theta}_h + C_{Qh\nu} \frac{\partial \Psi_{Qh\nu}}{\partial a_{\theta h}} \frac{\partial a_{\theta h}}{\partial \theta_j} \dot{\theta}_j + \dot{C}_{Sh\mu} \Psi_{Sh\mu} + \dot{C}_{Qh\nu} \Psi_{Qh\nu} - R_{Qh} + \sum_{m \in I_O} W_{Qhm} \Bigg) = 0 \tag{35}$$

with the additional condition

$$W_{Qhm} = \overline{W}_{Qhm}, \quad h \in I_G, \quad m \in I_O \tag{36}$$

motivated by considerations related to (6).

Since I_G is not defined precisely, we assume that equations (35), (36) are valid for all I_G and thereby for all parts of the molecule composed from distinguished subsystems. This necessitates in turn defining a family of conditions of type (36).

Let $\mathcal{H}_h = \{\mathbf{Q}_h, a_{Qh}, \theta_h, a_{\theta h}\}$. Above introduced equations have an excessive number of variables. Therefore, additional constitutive equations must be introduced. They are assumed in the following forms:

$$V_{Sh} = C_{Sh\mu}(\mathbf{C}_{Sh\mu}, \mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S) \Psi_{Sh\mu}(\mathbf{Q}_h, a_{Qh}), \tag{37}$$

$$V_{Qh} = C_{Qh\nu}(\mathbf{C}_{Qh\nu}, \mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S) \Phi_{Qh\nu}(\theta_h, a_{\theta h}), \tag{38}$$

$$\overline{W}_{Qhm} = \overline{W}_{Qhm}(\mathbf{C}_{Wh}, \mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S), \tag{39}$$

$$\dot{\boldsymbol{\eta}}_h = A_\eta(\mathbf{C}_{\eta h}, \mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S), \tag{40}$$

where $\boldsymbol{\eta}_S$ represents additional internal state variables which describe effects of interactions of the molecule with solvent. We introduce also the evolution equation for these internal state variables by

$$\dot{\boldsymbol{\eta}}_S = A_S(\mathbf{C}_S, \mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S). \tag{41}$$

Equations (31)-(41) determine skeletal dynamical system for the reactive nanostructure. Identification of introduced constants should be realized by means of comparison of solutions of molecular dynamics equations and *SDS* equations. The comparison of solutions can be carried out by means of a metric $\rho_{DR} : \overline{V}_T \times \overline{V}_T \to R_+ \cup \{0\}$ determined in space of processes $\overline{V}_T$. Then the function H_I defined by

$$H_I(\boldsymbol{\varphi}_0, \mathbf{f}) = \inf_{\mathbf{C}\in\mathcal{C}} \rho_{DR}(\pi_T(\boldsymbol{\varphi}(\boldsymbol{\varphi}_0, \mathbf{f})(t)), \mathbf{d}(\mathbf{C}, \pi(\boldsymbol{\varphi}_0), \pi_{fT}(\mathbf{f})(t))), \quad (42)$$

where **d** is a solution of *SDS* equations, should be weakly dependent on quantities $\boldsymbol{\varphi}_0$, **f** related to elementary dynamical system for obtaining a good approximation. $\mathcal{C}$ stands for a set of admissible constants **C**.

Let us note that there is a challenge to introduce for such a type of description of reactive nanostructures variables which would represent presence of attractor in electronic structure. We have done such a step previously in [1] for modification of potential in molecular dynamics description. Similar effect should be present in above discussed function having role of a potential.

3.4. Chemical reactions with reactive nanostructures

We distinguish two kinds of chemical reactions. The first one is related to reactions with particles which are not defined as reactive nanostructures. We would say that they influence behaviour of the nanostructure. As a result, we are interested mainly in effects which they cause. Therefore, description of such reactions is suggested by terms responsible for external interactions. Consequently, we introduce the following additional equations:

$$\bar{f}_{Smq} = \bar{f}_{Smq}(\mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S, \boldsymbol{\eta}_{RC}), \quad m \in I_O, \quad (43)$$

$$\overline{W}_{Qhm} = \overline{W}_{Qhm}(\mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S, \boldsymbol{\eta}_{RC}), \quad m \in I_O, \quad (44)$$

$$\dot{\boldsymbol{\eta}}_{RC} = A_{RC}(\mathcal{H}_h, \boldsymbol{\eta}_h, \boldsymbol{\eta}_S, \boldsymbol{\eta}_{RC}), \quad (45)$$

where $\boldsymbol{\eta}_{RC}$ represents internal state variables which describe process of

approaching, bonding and releasing of the external particles. They influence evolution of the system directly by $\bar{f}_{Smq}$ which can be viewed as a modifying factor related to Φ and also by interchange of energy expressed by $\overline{W}_{Qhm}$.

The second kind of chemical reactions is related to joining of various reactive nanostructures as well as various forms of reorganization or fragmentation within a system of them. Then we are interested in description of more detailed mechanisms governing such processes. Therefore, the notion of the molecular recognition should be transferred from atomic level of description into the nanoscale description.

We consider the reaction $a + b \rightarrow ab$ denoted by $\mathcal{R}$, and $\overline{C}_R$ is the corresponding catchment region defined on the reduced level of description.

Let us consider a set $\overline{U}_S \subset \overline{\mathcal{V}}_D$, $\overline{\mathbf{D}} = \{\mathbf{Q}, \mathbf{w}\}$ and $\overline{\mathbf{D}}_0 \in \overline{U}_S$ stand for an initial condition for evolution of $\overline{\mathbf{D}}$. Let $\boldsymbol{\lambda}(t) = \{\theta, \boldsymbol{\eta}, \boldsymbol{\eta}_S\}(t)$ stand for a process related to evolution of the remaining variables which have an effect on form of Φ and thereby also on the corresponding catchment region $\overline{C}_R$. Consequently, together with evolution of $\boldsymbol{\lambda}$, we consider also evolution of $\overline{C}_R(\boldsymbol{\lambda})$.

We define the set $\mathcal{A}(\overline{U}_S)$ as a set of all processes $\boldsymbol{\lambda}(t)$ which do not change qualitatively the catchment region $\overline{C}_R(\boldsymbol{\lambda}(t))$ during evolution and $\overline{\mathbf{D}}(\overline{\mathbf{D}}_0, t) \in \overline{U}_S$ for each t and $\boldsymbol{\lambda}(t)$ considered. This condition ensures that processes $\boldsymbol{\lambda}(t)$ do not disturb realization of the reaction $\mathcal{R}$.

Definition 7. We say that two molecules a and b undergo the molecular recognition with respect to reaction $\mathcal{R}$, with probability p, if they find themselves in a state $\overline{\mathbf{D}}_0 \in \overline{U}_S$, where $\overline{U}_S \subset \overline{\mathcal{V}}_D$ is a maximal set satisfying the condition that there exists t_k such that for each $\overline{\mathbf{D}}_0 \in \overline{U}_S$, we have $\mathcal{P}(\pi_C(\overline{\mathbf{D}}(\overline{\mathbf{D}}_0, \mathcal{L}(t))(t)) \in \overline{C}_R(\boldsymbol{\lambda}(\mathbf{t})) \wedge \{\theta, \boldsymbol{\eta}, \boldsymbol{\eta}_S\}(t) \in \mathcal{A}(\overline{U}_S)) = p \leq 1$ and $\mathcal{P}$

is a probability measure related to this problem. The set $\overline{U}_S$ is called the *range of selection*.

The probability p and stochastic forces $\mathcal{L}(t)$ applied in this definition express connections with solvent interactions. It also means that we admit a stochastic effect in equations describing evolution of the nanostructure.

The range of selection enables to formulate conditions for realization of the reaction $\mathcal{R}$ expressed in terms of the nanoscale model. Furthermore, it gives possibility of discussion of integrity in reactive nanostructures.

Form of the set $\overline{U}_S$ could be also considered as a phenomenological postulate. Then phenomenological, nanoscale models of assembling or reorganization of reactive nanostructures could be formulated neglecting detailed atomic processes.

4. Characterization of Integrity of Molecular Reacting Systems

We observe that chemical reactions in living organisms are highly organized and create an integrated system. The definition of the molecular recognition allows one to formulate integrity property for a chain of chemical reactions.

We define a chain of chemical reactions $\{CR_\alpha\}$ by means of the formula

$$a_\alpha + b_\alpha \to a_{\alpha+1} + \{d_{\alpha i}\}, \quad \alpha \in I_{CR}. \tag{46}$$

Thus, the characteristic property of the chain of reactions consists in fact that the product $a_{\alpha+1}$ of the reaction CR_α is a substrate for the next reaction $CR_{\alpha+1}$. The substrate $b_{\alpha+1}$ is taken from an environment.

Values of positions and velocities of nuclei of atoms belonging to molecules a_α and b_α at the time instant t are denoted by $\{\mathbf{R}, \mathbf{v}\}(\{a_\alpha, b_\alpha\})(t)$. Let U_α stand for the range of selection for the reaction CR_α. Let us consider a time interval $\Delta_\alpha = [t_{p\alpha}, t_{k\alpha}]$ connected with a stage of realization of the

chain of reactions. We assume that an instant for inception of the reaction CR_α belongs to Δ_α.

Definition 8. We say that the chain of the chemical reactions $\{CR_\alpha\}$, $\alpha \in I_{CR}$ has the *integrity property* if $\{\mathbf{R}, \mathbf{v}\}(\{a_\alpha, b_\alpha\})(t) \in U_\alpha$ for some $t \in \Delta_\alpha$ for each $\alpha \in I_{CR}$.

The range of selection is of fundamental importance for this definition. Each step of realization of the chain of reactions has to be preluded by molecular recognition. This has to be interpreted as a necessary condition for precise realization of this system of chemical reactions.

The mathematical definition of the molecular recognition enables us to discuss problem of integrity of larger system of chemical reactions. Thereby, we have accentuated role of notion of molecular recognition. We can define it for various systems and various scales as it was shown for reactive nanostructures.

At this stage of description, it seems that the integrity property needs further investigations. This is related especially to the case where we manifest in description variables related to lower scale. Let us mention again generalization of molecular dynamics towards potentials dependent on electronic variables considered in [1]. It is expected that similar step can be done for molecular structures in order to improve considerations related to properties of the system induced by presence of attractor on the most elementary level. Then integrity should find its manifestation in more averaged models.

5. Final Remarks

Two papers [1] and this one present a structure of theory which would be convenient for modelling of biological systems. This theoretical approach is created with intention of providing a possibility of description of biological systems which is especially adjusted to such objects. In particular, one accentuates necessity of considering of integrity and multiscale aspects

of biological systems. Furthermore, an effort is done in order to obtain a theoretical description which would be able to unify models of various phenomena which happen in biological systems within one theoretical scheme. This in turn can be important in a future when we expect to obtain possibility of doing of complex numerical simulations. They have to be based on stable theoretical foundations.

It is shown in the paper [1] how the most elementary theory called *vacuum medium mechanics* is developed in order to localize mechanisms of selforganization in molecular physics. At this stage of development, the chain state of electrons is considered as a driven force for evolution.

Furthermore, multiscale method of modelling considered in this paper called *collection of dynamical systems* with dimensional reduction is aimed at providing possibility of description of dynamics at various scales together with possibility of transition between them. Within this approach, the role of reactive nanostructures is accentuated as particularly convenient to description of functionality in molecular processes.

This multiscale method should be able to describe evolutionary properties of biological systems expressed in larger scales where hitherto constructed theories related to evolution usually act. In other words, evolutionary phenomena should be obtained by means of the dimensional reduction procedure having at the most elementary level mechanisms of selforganization based on vacuum medium mechanics.

Both mentioned above approaches are the main elements of structure of theory elaborated for modelling of biological systems.

Further development of this theoretical structure should be continued towards more detailed modelling of single electron in order to obtain the best quantitative theory as far as it is possible. Then construction of atomic and molecular physics on this basis would have good qualitative properties for description of evolution.

Multiscale modelling should be continued towards specification of more details of models at various scales. At the atomic level, we should construct models which take into account dependence of potentials on electronic variables. Nanoscale models should be able to select particular properties of molecular systems which are responsible for functionality.

Efficient transition between scales by dimensional reduction procedure is important. This is so since numerical simulations of complex molecular objects change type of dimensional reduction when change of quality of phenomena happens. This will happen frequently during chemical reactions and structural transformations. Consequently, we should elaborate also efficient transition between various dimensional reduction procedures on the same level of description during numerical simulations.

Summarizing, it is my hope that this way of construction of mathematical theory can be useful for further development of theoretical biology.

References

[1] J. Kaczmarek, On a structure of mathematical theory which reflects multiscale aspects and integrity of biological systems I, Far East J. Appl. Math. 76(2) (2013), 79-117.

[2] J. Kaczmarek, Collection of dynamical systems with dimensional reduction as a multiscale method of modelling for mechanics of materials, Interactions and Multiscale Mechanics 3(1) (2010), 1-22.

[3] C. Truesdell, A First Course in Rational Continuum Mechanics, Baltimore, Maryland, 1972.

[4] C. Truesdell and W. Noll, The Non-linear Field Theories of Mechanics, Handbuch der Physik III/3, S. Flúgge, ed., Springer, 1965.

[5] W. G. Hoover, Molecular dynamics, Lecture Notes in Physics 258, Springer-Verlag, 1986.

[6] G. Cicotti and W. G. Hoover, Molecular dynamics simulations of statistical mechanical systems, Proc. of the Int. School of Phys. Enrico Fermi, 1986.

[7] M. Parinello and A. Rahman, Polymorphic transitions in single crystals: a new molecular dynamics method, J. Appl. Phys. 52(12) (1981), 7182-7190.

[8] W. Kołos, Quantum Chemistry, PWN Warszawa, 1978.

[9] G. F. Oster and G. M. Odell, The mechanochemistry of cytogels, Phys. D 12 (1984), 333-350.

[10] P. G. Mezey, Potential Energy Hypersurface, Elsevier Science Publishers B.V., 1987.

[11] P. G. Mezey, Catchment region partitioning of energy hypersurface, Theor. Chim Acta (Berl.) 58 (1981), 309-330.

[12] M. C. Beckerle, Spatial control of actin filament assembly: lessons from listeria, Cell 95 (1998), 741-748.

[13] A. Hall, Rho GTPases and the actin cytoskeleton, Science 279 (1998), 509-514.

[14] K. E. Prehoda, D. J. Lee and W. A. Lim, Structure of the enabled/VASP homology 1, domain-peptide complex: a key component in the spatial control of actin assembly, Cell 97 (1999), 471-480.

[15] W. R. Rudnicki, G. Bakalarski and B. Lesyng, A mezoscopic model of nucleic acids. Part 1. Lagrangean and quaternion molecular dynamics, J. of Biomol. Str. and Dyn. 17(6) (2000), 1097-1108.

[16] V. Tozzini, Coarse-grained models of proteins, Current Opinion in Structural Biology 15 (2005), 144-150.

[17] Tap Ha-Duong, N. Basdevant and D. Borgis, A polarizable coarse-grained water model for coarse-grained protein simulations, Chem. Phys. Letters 468 (2009), 79-82.

[18] J. Kaczmarek, A method of integration of molecular dynamics and continuum mechanics for solids, TASK Quarterly 6(2) (2002), 253-271.

[19] C. von Westenholtz, Differential Forms in Mathematical Physics, North-Holland, 1981.