

COMBINED FIELDS

GENERAL THERMODYNAMIC THEORY FOR ACTIVE BIO-CONTINUUM

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ABSTRACT. Molecular motors are nanometric protein-based devices, essential for the movement in living organisms. The aim of the present study is to offer a general thermodynamic theory for the active bio-continua considered as composition including continually distributed assemble of molecular motors. The restrictions following from Clausius-Duhem inequality formulation of Second principle of Thermodynamics on the constitutive equations are under consideration. The capability of the new theory to model active bio-mechanical processes is demonstrated for muscle mechanics by unifying the well known classical heuristic models. Also it is shown that the theory is able to offer an active extension of the classical diffusion model as well.

KEY WORDS: active, diffusion, continuum, thermodynamics, thermomechanics, muscle, mixture.

1. Introduction

The human body is composed of about 60 trillion cells. A close galaxy order (10^{19}) is valid for all mammals. To be in stable condition such enormous system needs an extremely high organization, specialization and communication. An important role for the shape of the biological body, considered as bio-continuum, play the so called molecular motors. They represent protein based nanometric devices transforming the free energy, released by the hydrolysis of Adenosine TriPhosphate (ATP), in mechanical work [1]. The molecular motors are responsible for the muscle force, for the shape and structural reconstruction of the cells at mitosis, adaptive reconstruction of the connective tissues, organs and for the transportation of nutrients, waste products and

other important fractions. Their activity is controlled by the central and peripheral nerve system with nerve signals, hormones and other mediators. Some substances as alkaloids, alcohols, drugs are also able to affect the molecular motors.

Our attempts to construct general thermodynamic theory for active bio-continua started 1978 with a model of the skeletal muscle tissue as actin-myosin composition [2]. In 1982 we, for first time in literature [3], offered a model for externally controlled mono continuum. The rapid progress in the field of nanoscience, for the last decade, makes the idea for modelling the activity of the bio-continua on the basis of molecular motors composition actual and very attractive.

The principle aim of the present study is extension of the limit of the classical field mixture theory [3, 4, 5] in a way to be able to model the biomechanical activity on tissue level.

2. Basic principles

The present study is based on the following principles:

1. The active bio-continuum is characterized by multiple reference state;
2. The moment reference state is dependant on the molecular motor activity;
3. The control on the activity of the molecular motors is subjected to Le Chatelie–Brown principle: “Under the action of external factors the system reacts in a way to reduce the effect of the external action”. So the inputted by the activation signals entropy should be non positive in order to reduce the chaotic increase caused by the external factors;
4. The activation signals are not a principal source of internal energy, but of encoded bio-information, informational entropy and consequently, informational free energy. The inputted by the activation signal internal energy is negligibly small in respect to the inputted “informational” free energy;
5. The dissipation of the energy inputted by the activation signal is a negligibly small value in respect to the dissipation of the energy associated with the mechanical work done by the molecular motors;
6. The molecular motor at each moment could be in one of the two possible discreet states – active or inactive, in excited or in reference state;
7. Each closed volume of the active bio-continuum is an open multi-phase thermodynamic system exchanging with surroundings metabolic products and activating informational signals.

3. Kinematics

The motion of each phase is described by the equation:

$$(1) \quad x_k = \varphi_k^{(l)}(X_K^{(m)}, t) \quad l = 1, 2, \dots, n,$$

where x_k are Cartesian coordinates at moment t of the l^{th} phase particles, occupying at the initial moment a position in the material coordinate system with Cartesian coordinates $X_K^{(l)}$.

The total mass density is sum of the partial densities:

$$(2) \quad \rho = \sum_{l=1}^n \rho^{(l)}.$$

The barycentric velocity is expressed by the individual phase velocities:

$$(3) \quad v_k = \sum_{l=1}^n C^{(l)} v_k^{(l)}, \quad C^{(l)} = \frac{\rho^{(l)}}{\rho}.$$

The relative constituent's velocities and fluxes are:

$$(4) \quad u_k^{(l)} = v_k^{(l)} - v_k; \quad J_k^{(l)} = \rho^{(l)}(v_k^{(l)} - v_k) \quad l = 1, 2, \dots, n.$$

We denote with $l = 1$ the dominating constituent of the tissue, which is composed by the protein tissue skeleton, the cell fluid, the bounded to the cytoskeleton water and other immovable in respect to the skeleton fluids. Taking into account that because of the drag the diffusion fluxes and the microcirculatory rates should be small values, we reformulated the relative rates and the fluxes as:

$$(5) \quad u_k^{(1)} = 0, \quad u_k^{(l)} = v_k^{(l)} - v_k^{(1)}, \quad J_k^{(l)} = \rho^{(l)}(v_k^{(l)} - v_k^{(1)}) \quad l = 2, 3, \dots, n.$$

4. Conservation principles

The conservation principles, for the continua under consideration, are presented by the equations:

a) mass balance –

$$(6) \quad \rho \frac{d}{dt} C^{(1)} = \hat{\rho}^{(1)},$$

$$(7) \quad \rho \frac{d}{dt} C^{(l)} + J_{k,k}^l = \hat{\rho}^{(l)}, \quad l = 2, 3, \dots, n,$$

$$(8) \quad \sum_{l=1}^n \hat{\rho}^{(l)} = 0,$$

$$(9) \quad \frac{d}{dt} \rho + \rho v_{k,k} = 0,$$

where $C^{(l)}$ and $\hat{\rho}^{(l)}$ are l^{th} constituent concentration and the respective rate of the partial mass production.

b) momentum, moment of momentum and energy balance –

$$(10) \quad \rho \frac{d}{dt} v_k = T_{lk,l} + \rho f,$$

$$(11) \quad T_{lk} = T_{kl},$$

$$(12) \quad \rho \frac{d}{dt} e = T_{lk} v_{k,l} + h_{k,k} + \rho e^* + \rho \hat{e},$$

where T_{kl} , h_k , e , e^* and \hat{e} are the Cauchy stress tensor, the heat flux, the rate of energy density, the rate of the internal heat supply density, and the rate of the bio-informational energy density contributed by the control signal.

5. Second Law of Thermodynamics

The Clausius-Duhem formulation of the Second thermodynamic law, for mixture of n constituents, is:

$$(13) \quad \rho \frac{d}{dt} \eta - \left(\frac{h_k + \sum_{l=2}^n \mu^{(l)} J_k^{(l)}}{\theta} \right)_{,k} - \frac{\rho e^*}{\theta} - \rho \hat{\eta} \geq 0,$$

where η , $\mu^{(l)}$, θ and $\hat{\eta}$ are, respectively, the entropy density, the chemical potential of l^{th} constituent, the absolute temperature, and the rate of density of the entropy inputted by the activation signal. With the help of Legendre transformation we introduce the free enthalpy:

$$(14) \quad F = e - \theta \eta - \frac{1}{\rho_0} T_{KL} E_{KL},$$

where ρ_0 , T_{KL} and E_{KL} are the initial mass density, the second stress tensor of Piola and the Lagrangian strain tensor. Substituting (6, 7, 9, 10, 12, 14) into (13) we reformulate the Second law of thermodynamics for the mixture under consideration in the form:

$$(15) \quad \rho \frac{d}{dt} F + \rho \eta \frac{d}{dt} \theta - \frac{\rho}{\rho_0} E_{KL} \frac{d}{dt} T_{KL} - \sum_{l=2}^n \rho \mu^{(l)} \frac{d}{dt} C^{(l)} + \sum_{l=2}^n \theta \left(\frac{\mu^{(l)}}{\theta} \right)_{,k} J_k^l \\ + \sum_{l=2}^n \mu^{(l)} \hat{\rho}^{(l)} - \frac{\theta_{,k} h_k}{\theta} - \rho \hat{\psi} \leq 0,$$

where

$$(16) \quad \hat{\psi} = \hat{e} - \theta \hat{\eta}$$

is the rate of the density of the free energy inputted by the activation signal.

6. Kinetic equations

The following form for the kinetics of the molecular motors and of the biochemical reactions rate is supposed:

$$(17) \quad \frac{d}{dt} C^{(a.m.)} = \Omega(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta) + \Theta(C_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta, \alpha) \alpha,$$

$$(18) \quad \hat{\rho}^{(r)} = \hat{\rho}_{(0)}^{(r)}(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta) + \chi^{(m)}(C_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta, \alpha) \alpha,$$

$$r, l = 1, 2, \dots, n,$$

where α is a nonnegative parameter representing the activating signal, and $C^{(a.m.)}$ is the concentration of the active motors (**a.m.**). The values Ω and $\hat{\rho}_{(0)}^{(l)}$ are the first terms of the respective Taylor series of $\hat{\rho} \wedge^{(l)}$ in terms of powers of α .

7. Restriction following from the Second thermodynamic law on the constitutive equations

As thermodynamic state parameters we assume Piola's stress tensor T_{KL} , the constituent concentrations $C^{(l)}$, the gradients of concentrations $C_{,K}^{(l)}$,

the density of the active molecular motors $C^{(a.m.)}$, and the temperature θ . So for the constitutive equations we have:

$$(19) \quad F = F(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta),$$

$$(20) \quad E_{MN} = E_{MN}(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta),$$

$$(21) \quad J_N^{(m)} = J_N^{(m)}(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta),$$

$$(22) \quad \mu^{(m)} = \mu^{(m)}(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta),$$

$$(23) \quad h_N^{(m)} = h_N^{(m)}(T_{KL}, C_{,K}^{(l)}, C^{(l)}, C^{(a.m.)}, \theta), \quad l, m = 2, 3, \dots, n.$$

Taking into account (19)–(23) in (15) we obtain:

$$(24) \quad \rho \left(\frac{\partial F}{\partial \theta} + \eta \right) \frac{d\theta}{dt} + \rho \left(\frac{\partial F}{\partial T_{KL}} + \frac{1}{\rho_0} E_{KL} \right) \frac{dT_{KL}}{dt} + \rho \frac{\partial F}{\partial C^{(1)}} \frac{dC^{(1)}}{dt} \\ + \rho \frac{\partial F}{\partial C^{(a.m.)}} \frac{dC^{(a.m.)}}{dt} + \rho \sum_{l=2}^n \left(\frac{\partial F}{\partial C^{(l)}} - \mu^{(l)} \right) \frac{dC^{(l)}}{dt} + \rho \sum_{l=2}^n \frac{\partial F}{\partial C_{,K}^{(l)}} \frac{dC_{,K}^{(l)}}{dt} \\ + \sum_{l=2}^n \theta \left(\frac{\mu^{(l)}}{\theta} \right)_{,k} J_k^{(l)} - \theta_k h_k + \sum_{l=2}^n \mu^{(l)} \hat{\rho}^{(l)} - \rho \hat{\psi} \leq 0.$$

The necessary and sufficient conditions for the validity of the inequality (24), under the assumptions done, are:

$$(25) \quad \eta = -\frac{\partial F}{\partial \theta},$$

$$(26) \quad E_{KL} = -\rho_0 \frac{\partial F}{\partial T_{KL}},$$

$$(27) \quad \mu^{(l)} = \frac{\partial F}{\partial C^{(l)}}, \quad \frac{\partial F}{\partial C_{,K}^{(l)}} = 0 \quad l = 2, \dots, n,$$

$$(28) \quad \mu^{(1)} = \frac{\partial F}{\partial C^{(1)}} \quad (\text{by definition}).$$

Next, for simplicity, we shall consider the partial mass density of the tissue skeleton as a constant $C^{(1)} = \text{const}$ (there is no growth), and the biological continuum as an isothermal medium. So we obtain from (24) and (25)–(28) the following dissipation inequality:

$$(29) \quad \sum_{l=2}^n \mu_{,k}^{(l)} J_k^{(l)} + \sum_{l=1}^n \mu^{(l)} \hat{\rho}^{(l)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \frac{dC^{(a.m.)}}{dt} - \rho \hat{\psi} \leq 0.$$

By substituting (16)–(18) into (28, 29) we obtain:

$$(30) \quad \sum_{l=2}^n \mu_{,k}^{(l)} J_k^{(l)} + \sum_{l=1}^n \mu^{(l)} \hat{\rho}_{(0)}^{(l)} + \rho \frac{\partial F}{\partial M} \Omega + \sum_{l=1}^n \mu^{(l)} \chi^{(l)} \alpha + \rho \frac{\partial F}{\partial C_{am}} \Theta \alpha - \rho \hat{\psi} \leq 0.$$

As this inequality is necessary to be satisfied for all admissible values of α , it splits to the following two independent inequalities:

$$(31) \quad \sum_{l=2}^n \mu_{,k}^{(l)} J_k^{(l)} + \sum_{l=1}^n \mu^{(l)} \hat{\rho}_{(0)}^{(l)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \Omega \leq 0,$$

$$(32) \quad \left(\sum_{l=1}^n \mu^{(l)} \chi^{(l)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \Theta \right) \alpha - \hat{\psi} \leq 0.$$

According to the basic principles (3), (4)

$$(33) \quad -\theta \hat{\eta} \gg \hat{e} \quad \Rightarrow \quad \hat{\psi} \approx -\theta \hat{\eta} \geq 0,$$

$$(34) \quad \left(\sum_{l=1}^n \mu^{(l)} \chi^{(l)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \Theta \right) \alpha = \hat{\psi}.$$

Consequently,

$$(35) \quad \sum_{l=1}^n \mu^{(l)} \chi^{(l)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \Theta \geq 0.$$

To illustrate the capability of the theory to model active bioprocesses in bio-continua we consider the following two cases:

A. Application of the theory to skeletal muscle mechanics

The contraction of muscles is realized by muscle myofibrils. Each of them is with diameter of $1 \mu\text{m}$ and contains 2500 actin-myosin filaments, which represent nanometric molecular motor. The pathway for the filament activation is:

- a) in the moment at which the electric nerve signal reaches the myofibril, specific meditative substances diffuse through the myofibril membrane. The respective penetration time is about 1 ms;
- b) the diffused mediators generate the so called action membrane potential;
- c) the action potential is the reason for release of the bounded within the sarco- plasmatic reticulum Ca^{++} ions, which activate the actin-myosin protein motors to contract.

Following the theoretical model under consideration and the above pathway process consequence, we consider a simple linear model represented by the free enthalpy potential:

$$(36) \quad F = \frac{1}{2}D\sigma^2 + \frac{1}{2}S(C^{(a.m.)})^2 + \frac{1}{2}G(C^{(++)})^2 + R\sigma C^{(a.m.)} + MC^{(a.m.)}C^{(++)},$$

where $C^{(++)}$ is the concentration of the Ca^{++} ions, and D, E, G, R, M are functions of the homeostatic state variables $\sigma^0, C^{0(a.m.)}, C^{0(++)}$ satisfying the stability condition $D+E+G-(2R+2M) \geq 0$. The first term in (36) represents the internal energy due to the elastic deformation, the second the internal energy contributed by the active molecular motors, the third the contribution due to the Ca^{++} ions, and the fourth and the fifth terms internal energy of the couple interaction between the stress, molecular motors activity and Ca^{++} ions. Following the relations (26)–(36) we have:

$$(37) \quad \varepsilon = D\sigma + RC^{(a.m.)},$$

$$(38) \quad \frac{\partial F}{\partial C^{(a.m.)}} = R\sigma + SC^{(a.m.)} + MC^{(++)},$$

$$(39) \quad \mu^{(++)} = MC^{(a.m.)} + GC^{(++)},$$

$$(40) \quad \mu^{(++)}\hat{\rho}_{(0)}^{(++)} + \rho \frac{\partial F}{\partial C^{(a.m.)}} \Omega \leq 0,$$

$$(41) \quad \sum_{l=1}^n \mu^{(++)}\chi^{(++)} \geq 0, \quad \Theta = 0,$$

$$(42) \quad \rho \frac{d}{dt} C^{(a.m.)} = \Omega,$$

$$(43) \quad \rho \frac{d}{dt} C^{(++)} = \hat{\rho}_{(0)}^{(++)} + \chi^{(++)} \alpha,$$

where σ , ε , $C^{(a.m.)}$, $C^{(++)}$ are, respectively, the one dimensional stress and strain, the concentration of the active actin-miosin motors, and the concentration of the released calcium ions. Basing on the Onsager's theory [3] and on the idea of the linear dependence between the generalized thermodynamic rates and the generalized thermodynamic forces we have:

$$(44) \quad \hat{\rho}_{(0)}^{(++)} = -L_{11}\mu^{(++)} - L_{12} \frac{\partial F}{\partial C^{(a.m.)}},$$

$$(45) \quad \rho\Omega = -L_{12}\mu^{(++)} - L_{22} \frac{\partial F}{\partial C^{(a.m.)}},$$

$$(46) \quad \chi^{(++)} = K\mu^{(++)},$$

$$(47) \quad L_{11} + L_{22} - 2L_{12} \geq 0, \quad K \geq 0.$$

By substitution of (44)–(46) into (42), (43) we obtain:

$$(48) \quad \hat{\rho}_{(0)}^{(++)} = -(GL_{11} + ML_{12})C^{(++)} - (ML_{11} + SL_{12})C^{(a.m.)} - L_{12}R\sigma,$$

$$(49) \quad \rho\Omega = -(GL_{12} + ML_{22})C^{(++)} - (ML_{12} + SL_{22})C^{(a.m.)} - L_{22}R\sigma,$$

$$(50) \quad \chi^{(++)} = K(MC^{(a.m.)} + GC^{(++)}),$$

$$(51) \quad \left(\frac{d}{dt} + \frac{1}{\tau^{(a.m.)}} \right) C^{(a.m.)} = - \frac{GL_{12} + ML_{22}}{\rho} C^{(++)} - \frac{L_{22}R}{\rho} \sigma,$$

$$(52) \quad \left(\frac{d}{dt} + \frac{1}{\tau^{(++)}} \right) C^{(++)} = - \left(\frac{ML_{11} + SL_{12} - KM\alpha}{\rho} \right) C^{(a.m.)} - \frac{L_{12}R}{\rho} \sigma,$$

where

$$(53) \quad \tau^{(a.m)} = \frac{\rho}{ML_{12} + SL_{22}}, \quad \tau^{(++)} = \frac{\rho}{GL_{11} + ML_{12} - G\alpha}$$

are the relaxation times responsible for transition of the molecular motors in active state and for release of the calcium ions from sarco-plasmatic reticulum. One can see that these two phenomena are conjugated as it is predicted from cell physiology and experimental data [6, 7].

In the experimental and theoretical studies, rectangular electric potential impulse is usually used as an activating signal:

$$(54) \quad \alpha = \text{const}H((t - t_1)(1 - H(t - t_2))) \quad t_2 > t_1.$$

One can see two intriguing peculiarities of the model from equations (51, 52): the first one is the dependence of the calcium release relaxation time on the activation signal, and the second one is the presence of the stress as an effective parallel activation signal. The last is experimentally existing fact and it is called myogenic effect. One can see also that the present theory is able to model different kinds of experimental features including the influence of the activation on the relaxation times and the accumulative effect of stimulation as well. The present illustrative application to muscle mechanics unifies the classical heuristic models [8-14]. By the use of this illustrative example we have the ambition just to demonstrate the ability of the theory as an appropriate analytical tool.

B. Application to the nutrient transport within the lacunar-canalicular system of cortical bone

The passive diffusion of glucose in the lacunar-canalicular system of cortical bone was studied by Petrov and Pollack in [15]. It was demonstrated analytically that few orders are lacking in such a passive transport mechanism to sustain the vitality of bone cells (osteocytes). On the basis of this analytical result and on the fact that the cell processes within the canalicular canal are rich of actin filaments, the authors offered the hypothesis for the presence in active canalicular transport. One year later, in an experimental study Takai *at al.* [16] concluded that the theoretical findings of Petrov and Pollack are consistent with their experimental results. Next we shall demonstrate the ability of the theory to model qualitatively the active diffusion problems in one dimensional microcanal (model of bone canaliculae).

As state variables we consider the concentration of the diffusing substance $C^{(diff.)}$ and the concentration of the active molecular motors $C^{(a.m.)}$.

So, following the general theory, for the present case in its linear simplification we have:

$$(55) \quad F = F(C^{(diff.)}, C^{(a.m.)}),$$

$$(56) \quad J_K^{(diff.)} = J_K^{(diff.)}(C_{,R}^{(diff.)}, C^{(a.m.)}),$$

$$(57) \quad \rho \frac{d}{dt} C^{(a.m.)} = \Omega + \Theta \alpha, \quad \rho = 1,$$

$$(58) \quad F = \frac{1}{2} S (C^{(a.m.)})^2 + \frac{1}{2} G (C^{(diff.)})^2 + M C^{(a.m.)} C^{(diff.)},$$

$$(59) \quad \frac{\partial F}{\partial C^{(a.m.)}} = S C^{(a.m.)} + M C^{(diff.)},$$

$$(60) \quad \frac{\partial F}{\partial C^{(diff.)}} = M C^{(a.m.)} + G C^{(diff.)},$$

$$(61) \quad \left(\frac{\partial F}{\partial C^{(diff.)}} \right)_{,K} J_K^{(diff.)} + \frac{\partial F}{\partial C^{(a.m.)}} \Omega \leq 0,$$

$$(62) \quad \frac{\partial F}{\partial C^{(a.m.)}} \Theta \geq 0,$$

$$(63) \quad J_K^{(diff.)} = -L_{KL}^{11} \left(\frac{\partial F}{\partial C^{(diff.)}} \right)_{,L} - L_K^{12} \frac{\partial F}{\partial C^{(a.m.)}},$$

$$(64) \quad \Omega = -L_K^{12} \left(\frac{\partial F}{\partial C^{(diff.)}} \right)_{,K} - L^{22} \frac{\partial F}{\partial C^{(a.m.)}},$$

$$(65) \quad \Theta = H \frac{\partial F}{\partial C^{(a.m.)}},$$

$$(66) \quad J_K^{(diff.)} = -L_{KL}^{11} (M C^{(a.m.)} + G C^{(diff.)})_{,L} - L_K^{12} (S C^{(a.m.)} + M C^{(diff.)}),$$

$$(67) \quad \Omega = -L_K^{12}(MC^{(a.m.)} + GC^{(diff.)})_{,K} - L^{22}(SC^{(a.m.)} + MC^{(diff.)}),$$

$$(68) \quad \Theta = H(SC^{(a.m.)} + MC^{(diff.)}),$$

where $\begin{pmatrix} \{L_{KL}^{11}\} & \{L_K^{12}\} \\ \{L_K^{12}\} & \{L^{22}\} \end{pmatrix}$ is non negatively defined matrix, and H is non negative constant.

We have physical reasons to believe that the principle part of the active diffusive flux is depending on the active molecular motors concentration, but not on the concentration of the diffusing constituent. That is why we substitute in the above relations M equal to zero. As a result we obtain the following equation describing the active diffusion problem in the active bio-continuum under consideration:

$$(69) \quad J_K = -L_{KL}^{11}GC_{,L}^{(diff.)} - L_K^{12}SC^{(a.m.)},$$

$$(70) \quad \frac{d}{dt}C^{(a.m.)} = -(L^{22}S - HS\alpha)C^{(a.m.)} - L_K^{12}GC_{,K}^{(diff.)}.$$

In the case of steady state active diffusion we have:

$$(71) \quad C^{(a.m.)} = \frac{L_K^{12}G}{S(H\alpha - L^{22})}C_{,K}^{(diff.)}.$$

In Cartesian coordinate system with first axis parallel to the canal axis we obtain:

$$(72) \quad J_1 = -D^{(diff.)}C_{,1}^{(diff.)}, \quad D^{(diff.)}(\alpha) = -G \left(L_{11}^{11} + \frac{L_1^{12}L_1^{12}}{H\alpha - L^{22}} \right).$$

In non activated state the value of the diffusion constant is minimal

$$(73) \quad D^{(diff.)} = -G \left(L_{11}^{11} - \frac{L_1^{12}L_1^{12}}{L^{22}} \right), \quad L_{11}^{11}L^{22} \geq L_1^{12}L_1^{12},$$

and increases with the increase of the activation signal amplitude. Other peculiarity could be seen if we consider the response of the diffusion flux in respect to variation of the activation signal as step function:

$$(74) \quad \frac{d}{dt}C^{(a.m.)} = -\frac{1}{\tau^{(a.m.)}}C^{(a.m.)} - L_1^{12}GC_{,1}^{(diff.)}, \quad \tau^{(a.m.)} = \frac{1}{S(L^{22} - H\alpha)}.$$

Solving (74) in respect to concentration of the active motors and substituting the result into (69) we obtain:

$$(75) \quad J_1(t) = -L_{11}^{11}GC_{,1}^{(diff.)}(t) - (L_1^{12})^2SG \int_0^t \exp\left(\frac{-(t-t')}{\tau^{(a.m.)}}\right) C_{,1}^{(diff.)}(t')dt'.$$

The first term of this equation could be considered as a passive diffusion part and the second as an active diffusion term. When the activation is applied as a rectangular signal, then the relaxation time according to (74) decreases, and, in such way, assists for the quick start of the molecular motors activity; when the signal is released the relaxation time increases and supports the slow turn out of the molecular motors. It is an attractive result following from the theory. Similar result is valid for the activation and deactivation of muscle contraction.

8. Conclusive remarks

The key moment in the present theory is the generalized formulation of the Clausius-Duhem inequality, in which the entropy carried by the activation signals is taken into account.

The capability of the new theory to model active bio-mechanical processes is demonstrated for muscle mechanics by unifying the well known classical heuristic models [6–14]. Moreover, it is demonstrated that the theory offers possibilities for active extensions of the passive classical diffusion models with application to the canalicular diffusion transport in cortical bone.

Our efforts to find some bibliographic information about other studies concerning active bio-continua model based on the assumption for molecular motors activity and activation signal entropy influx were not successful. It seems that the offered in the present study thermodynamic model would be the first steps in this direction.

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