Bio-Thermo-Hydro-Mechanics: problems and perspectives

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A survey of the problems of biothermohydromechanics (BTHM) including the processes at the biomolecular, intracellular, cellular, tissue, systemic and organism levels is given. An importance of the coupling phenomena, a strong interconnection of the heat and mass exchange processes, local and long-distance biofluid transports is substantiated. Fruitfulness of the approaches of the non-equilibrium thermodynamics (NET) to the biosystems and biotechnological processes is shown. Some future perspectives of the NET in application to the BTHM phenomena are discussed.

Key Words: *Biosystems, Thermodynamics, Heat and mass transfer, Open systems, Biological Growth, Collective motion*

1 Introduction

Living organisms as well as their organs, tissues and cells are open thermodynamic systems, which are in a continuous exchange of mass, heat and energy with their environment and are in a non-equilibrium state. The life is supported by permanent mass, heat, charge and energy production accompanied by numerous coupled fluxes. As open thermodynamic systems the biological organisms can keep the total entropy S at some constant level ($S=S_0=const$) and even decrease it ($dS<0$) during the functioning, growth and development by increasing the order and producing highly structurized inhomogeneity via some active energy-depended mechanisms.

Biosystems could work in a steady state condition ($dS=0$) and some approaches consider life as permanent transitions between different steady states ($S_1 \rightarrow S_2 \rightarrow S_1$), e.g. the muscle contraction as a transition from the relaxed to the contracted states and vice versa; the same for the heart contraction with a series of substages; nerve signal transduction as transitions between the relaxed and excited states characterized by different transmembrane electric potentials. Both relaxed and excited states are considered as steady states with different energy dissipation and entropy production.

Heat and mass production in numerous bioelectrochemical reactions, heat transmission, radiation and transfer, cell divisions, tissue growth and development are tightly connected with acquisition of the new substances (food), delivery and distribution of the new matter via special long-distance transport systems and local tissue and cellular mechanisms (diffusion, osmosis, active membrane transport). In that way thermodynamics of biosystems must be considered in connection with a series of BTHM processes and some important examples are given in the paper.

2 Multiscale approach in BTHM

2.1 BIOMOLECULAR LEVEL

The biological molecules like proteins, lipoproteins, vitamins, enzymes, RNA and DNA, phospholipids of the cell membranes, receptor molecules and others are large and their conformation is important for the biochemical, electrical, adhesive and aggregation properties and abilities. Folding of the large molecules and their steady shapes are described by the minimal Gibbs energy $dG=0$, $d^2G>>0$ at given constant temperature and pressure. Unfolding of the large polymer molecules by the fluid flow is important for instance, for the fibrin polymerization and the blood clot formation. Folding and unfolding accompanied by the conformation changes and entropy variation resulted in different chemical and physical properties of the molecules. Visualization of the protein molecules is based on determination of the minimal Gibbs energy state of a long chain of amino acids. Determination of the Van-der-Vaals surface, position of the active centers are important for different biomedical and biotechnological applications including computer modeling of drags, fiber and structure formation, genetic modification technologies and tissue engineering.

Molecular motors like dynein, kinesin, myosin, actin, DNA and RNA polymerase, bacterial cilia and flagella consume energy, for instance the chemical free energy released by the ATP hydrolysis, and converts it into mechanical work. They operate at the conditions when the fluctuations due to thermal noise are not insignificant [1].

Motion of amebas is determined by the gel-sol phase transitions, contraction of the cytoskeleton and the motion of the liquid contents of the cell in certain direction forming a pseudopodium. Motion of the flagellates is determined by active deformation of the

flagellum/flagella, wave propagation along each flagellum sometimes accompanied by their rotation. Molecular motors are more energetically efficient than the man-made motors. The ratio of the wave propagation along the flagellum (U) and the cell velocity (V) for the unicellular is approximately U/V~0.2. The type of motion is very effective, so nature extended it to the multicellular organisms like threadlike worms (U/V~0.4), annelid worms, leech and water snakes (U/V~0.3).

Molecular motors are mechanochemical systems transforming chemical energy into mechanical work. The cyclic motion of actin and myosin bundles, sliding fibers in cilia and flagella, contraction of the cytoskeleton are examples of transformation of the chemical energy accumulated in ATP molecules into macroscopic motion and deformation. When the length L of a polymeric fiber depends on concentration of some chemicals and enzymes, pH of the solution or external electric field producing the tensile force f, the mechanical work is connected with variation of the internal energy U of the system

$$dU = TdS - pdV + fdL + \psi\, dE + \sum_j \mu_j dn_j$$

where T, S, p, V are the temperature, entropy, pressure and volume of the system, μ_j is the chemical potential of the j-th substance with concentration n_j, ψdE is electrical work.

If the work is provided by a single reactive component forming a fiber with varying length at p,T=const, the mechanochemical cycle can be described in both $\mu(n)$ and $f(L)$ variables and the efficiency of the work is

$$\theta = -\oint fdL / \oint \mu dn$$

and is quite high for the muscles, ~50% [2].

Then the Gibbs energy variation is

$$(dG)_{p,T} = fdL - Ad\xi$$

where A and ξ are affinity and extent of reaction, which gives that affinity depends on the length of the contracting fiber

$$\left(\frac{\partial f}{\partial \xi}\right)_L = -\left(\frac{\partial A}{\partial L}\right)_\xi$$

When electric field is important for the mechanochemical system, the electrochemical potential must be taken instead of μ. In experiments with contracting muscles and muscle cells the dependencies $f(L)$ and $f(v)$, where $v = dL/dt$ are preferable for measurements. The isotonic force-velocity relationship of the contracting muscle was founded by A.V. Hill

$$(P + a)(v + b) = const = (P_{\max} + a)b, \quad P_{\max} = P\big|_{v=0} \quad (1)$$

where P and $P_{\max}$ are external load and maximal isometric tension. The mechanical power produced by the muscle may be obtained from (1) in the form

$$\dot{W} = Pv = \frac{P_{\max} - P}{P + a} Pb$$

The heat produced by the contracting muscle consists of the activation heat Q_a connected with Ca - dependent activation of the actomyosin system, heat of contraction Q_c: $\Delta E = W + Q_a + Q_c$. When a muscle becomes shorter, the produced energy is bigger, than for the isometric contraction (Fenn effect) [3]. Then the efficiency is determined as $\theta = W/(W + Q)$. For the contraction phase $\theta \sim 45\%$ in frogs and $\theta \sim 75\%$ in tortoises, exhibiting significant importance of the molecular mechanics of muscle contraction on thermodynamics.

2.2 SUBCELLULAR AND CELLULAR LEVEL

The intracellular transport of the molecules, vesicles and organelles is provided by active transfer along the tubulin tubes, actin filaments and other fibers. It is high-order well-controlled energy-dependent transport, which thermodynamics is not fully known yet. The dynamical instability of the tubes which are in permanent assembling-disassembling state, a strong influence of the intracellular electric field and biochemical regulation are provided by interconnection of the mass, charge, heat and energy fluxes.

Each cell contains some 10-20 thousand chemicals and the concentrations of some of them are in periodical variations with different periods. The oscillation periods serve as biological clock determining the order in the intracellular processes.

The living cells are far from an equilibrium state. The entropy production dS_i due to the irreversible processes inside the cell and the entropy exchange dS_e through the cell membrane possess time variations and fluctuations resulting in permanent variation of the total entropy production $dS=dS_i-dS_e$. Transformation of a normal cell to a tumor cell is usually accompanied by noticeable variation in dS.

Some collective phenomena like directed motion of the cells towards some center/centers, aggregation and formation of the multicellular formations (like plasmodium) are interesting for BTHM and NET [4]. In suspensions of the moving and aggregating cells the concentric and spiral waves similar the ones in the “chemical clock” of the Belousov-Zabotinsky reaction can be observed. The unicellular algae can move towards the sunlight and form a hexagonal network on the water surface. The network covers the maximal sun-radiated surface at a given cellular mass. The light reception, energy transfer into the mechanical work, directed motion, aggregation and the network formation are interconnected via BTHM phenomena.

The motion of the cells in a water solution can be described as active diffusion in the concentration field $b(t,\vec{r})$ of the attractant. The simplest model of the concentration field C of the cells is [5]

$$\frac{\partial C}{\partial t} = \nabla \cdot D_b \nabla b + \alpha C$$
$$\frac{\partial b}{\partial t} = \nabla \cdot (D_C \nabla C - \delta \cdot b \nabla f(b)) + \beta - \gamma C b \quad (2)$$

where α is birth of cells, β is the source of the attractant, γ is adsorption of the attractant by the bacteria; δ is the chemotaxis rate, $\xi = \chi E_{chem}$ is kinetic energy of the bacteria movement due to accumulation of the chemical energy

E_{chem}, $f(b) = b/(b_0 + b)$ and $\alpha = \alpha_0 b/(b_0 + b)$

(from experiments). The diffusion coefficient D_b for the attractant is a temperature-dependent constant value, while cell diffusion coefficient D_C is determined by the abovementioned system parameters, fluid density ρ and viscosity μ and can be computed using the dimension analysis method in the form:

$$D_C = D_C(\gamma, b, \rho, R, \mu, \xi(T)) = \frac{\xi \gamma b}{\rho R} \cdot F\left(\frac{\xi \gamma b}{6\pi\mu\rho R}\right)$$

The equations (2) may be completed by the nonlinear terms of the cell birth and nutrition leading to the limiting cycle and stochastic solutions. Besides, some experimentally observed phenomena like cell concentration in the regions with high ∇b can be driven from (1) [5].

2.3 TISSUE LEVEL

Biological tissues consist of the cells and extracellular matter synthesized by the cells. For instance, the bones consist of the collagen produced by the bone cells and crystals of Ca salts. The polymerized collagen fibers are organized in the 5-level extracellular structures reinforced by the calcium crystals resulting in the compact and sponge bone tissue. The cellular contents are approx 4% of the dry bone matter [5]. The extracellular matrix is organized according to the directions of maximal extension and compression of the loaded bone exhibiting the optimal mechanical properties, i.e. maximal strength and durability at total lightweight design. The principles of reinforcement in plants and animals are similar: the rigid cell walls of the plant cells, the extracellular fibers in rigid and soft tissues, the blood vessel walls and airways are reinforced according to the principals of the stress tensor. Dynamical load conditions proper to all the tissues and organs demand remodeling of the inner structures according to the varying load. The remodeling in the bones and other collagen tissues is connected with piesoelasticity of collagen and interconnection of mechanical (stress and deformation), electrical (dependence of the cell activity on the produced electric potential) and hydromechanical (mass transfer to the reconstructing tissues), providing a strong coupling of the mass, heat, charge and entropy fluxes in living biological tissues.

The tissues are usually considered within the framework of thermodynamics of multicomponent and multiphase continua [5]. The continual models of cancellous and sponge bone gave rise to the models of adaptive materials (smart materials), which properties can be controlled and changed by external stimuli (stress, electric field, temperature, moisture contents, pH and others).

The balance equations for the rigid and soft biomaterials are based on the thermodynamic laws and theory of viscoelasticity:

$$\rho \frac{\partial^2 \vec{u}}{\partial t^2} = div \cdot \hat{P} + \vec{f}, \quad div \cdot \vec{u} = 0, \quad \rho c_V \frac{\partial T}{\partial t} = -\nabla \vec{q} + \dot{Q}$$

$$\rho \frac{\partial C_{\alpha\beta}}{\partial t} = Q_{\alpha\beta} + Q^e_{\alpha\beta} + M_\beta \sum_\gamma I^\gamma_\alpha \nu_{\beta\gamma} \quad (3)$$

where indexes α and β relate to the number of phase and component, $\vec{u}$ is displacement vector, $\hat{P}$ is the stress tensor, $\vec{f}$ is an external force, ρ is density, C_V is the heat capacity, $\vec{q}$ is the heat flux, $\dot{Q}$ is the heat production, $C_{\alpha\beta}$ is the mass concentration, $Q_{\alpha\beta}$ and $Q^e_{\alpha\beta}$ are mass exchange between the phases and with environment, M_β is molecular mass, I^γ_α is velocity of the $\gamma - th$ chemical reaction, $\nu_{\beta\gamma}$ is a stoichiometric coefficient.

For the contracting muscle as an active biological media two phases give a simple and effective model with an active phase $\alpha = 1$ (actin and myosin fibers) and a passive one $\alpha = 2$ (cell membranes, intracellular and extracellular structures, fascia, arteries and veins) [6]. The relationship between the thermodynamic fluxes and forces determines the reological model and the coupling between the fluxes:

$$P_{ik} = -p g_{ik} + \sigma_{ik}, \quad q_i = -\lambda_{ik} \nabla_k T,$$

$$A_{iklm} \frac{\partial \sigma_{lm}}{\partial t} + \sigma_{ik} = E_{iklm}\left(\varepsilon_{lm} + B_{lmjn} \frac{\partial \sigma_{jn}}{\partial t}\right),$$

$$\dot{Q}_T = \dot{Q}_0 + \dot{Q}^1_{klmn} \frac{\partial \Delta_{lm}}{\partial t} + \dot{Q}^2 Tr\left\{\frac{\partial \Delta_{ik}}{\partial t} \eta_{jklm} \frac{\partial \Delta_{lm}}{\partial t}\right\}, \quad (4)$$

$$Q_{1\beta} = \sum_p n^{p\beta}(\mu^{2p} - \mu^{1p}) + \sum_\gamma S_{\gamma\beta} A_\gamma,$$

$$I_\gamma = \Lambda^\gamma_{iklm} \frac{\partial \Delta_{lm}}{\partial t} + \sum_p S_{p\beta}(\mu^{2p} - \mu^{1p}) + \sum_\gamma k_{\gamma\beta} A_\gamma$$

where p is the pressure, g_{ik} is the metric, A, B_{iklm} are tensors of relaxation, E_{iklm} is elasticity tensor, σ_{ik} and ε_{lm} are stress and small strain tensors, $\Delta_{ik} = K_{iklm}\varepsilon_{lm} - M_{iklm}\sigma_{lm}$ are irreversible deformations of the active phase, M_{iklm} is compliance tensor for the active phase, η_{jklm} is the viscosity tensor.

At some simplifications the model (3)-(4) gives Hill's heat production in the contracting muscle (fourth equation in (4)). The cross-coupled phenomena in (4) describes the dependence of the mechano-chemical reactions on the irreversible strain rate $\partial \Delta_{ik} / \partial t$ and the gradient of interphase chemical potentials $\mu^{2p} - \mu^{1p}$, which is known for the muscles as dependence of the activity of the actomyosin system on the muscle

contraction rate and the concentrations of Na^+-K^+ATPase. In that way the continual macroscopic model describes the experimental data and empirical scalar dependences.

2.4 ORGAN AND SYSTEM LEVELS

Different tissues form organs which functions are based on the long-distance fluid flow, mass and heat exchange which are strongly coupled. Heat transfer is mainly provided by the fluid flow systems (blood and airflows). The 2d and 3d systems designed as distributed heat and mass exchangers. The branching bronchial tree divides up to the smallest airways covered by a "carpet" of alveoli. The area of that 2d surface is ~100m^2 in humans. It's an excellent example of a large exchange surfaces packed into a relatively small volume of chest. The blood circulation systems are also presented by the sets of tubes with optimal BTHM properties [7]. The structure principles of the conducting systems of animals can be used as a nature inspired engineering solutions in technical heat and mass exchangers [8].

Interconnection of the heat, mass and electric charge fluxes $\vec{J}_h, \vec{J}_m, \vec{J}_e$ at both long distance and local tissue levels are described by the thermodynamic relationships

$$\vec{J}_j = L_{jh}\vec{X}_h + L_{jm}\vec{X}_m + L_{je}\vec{X}_e$$

where $j = h, m, e$, $\vec{X}_{h,m,e}$ are the thermal, chemical and electric forces, $X_h = \nabla(T)^{-1}$, $X_m = -(T)^{-1}\nabla\mu$, $X_e = -(T)^{-1}\nabla\psi$. For the active biosystems additional forces and fluxes related to the active component can be added.

2.5 CROWD DYNAMICS

Contrary to the kinematic model (2) the dynamical models of the crowds of human beings, schools of fish, herds and flock at different external conditions are considered in NET. Mixture models are very successful for describing a collective motion of interacting individuals considered as particles with different properties (mean velocity, mass-inertia properties, activity, attraction/distraction laws). Different populations of particles can be described as continua with different temperatures and other thermodynamic properties. As a result a hydrodynamic-type system of equations have been obtained by both Boltzmann kinetic theory, momentum theory and mixture models. Here the model is presented for one type of particles and it can be generalized by substituting the corresponding indices:

$$\frac{\partial n}{\partial t} + div(n\vec{u}) = \sigma_n$$

$$n\frac{d\vec{u}}{dt} = -\nabla(nT) - div\hat{p} + n\left\langle\dot{\vec{v}}\right\rangle + \int \sigma_T(\vec{v}-\vec{u})d\vec{v}d\vec{z} \qquad (5)$$

$$n\frac{dT}{dt} = -\nabla(n\vec{\Gamma}) - 2nTdiv\vec{u} - 2p:\nabla\vec{u} + 2n\left\langle(\vec{v}-\vec{u})\dot{\vec{v}}\right\rangle + \int \sigma_T((\vec{v}-\vec{u})^2 - T)d\vec{v}d\vec{z}$$

where n is numerical concentration, $\vec{u}$ is velocity, $\vec{v} = \langle\vec{u}\rangle$ is the mean value, σ_n is the source term, $\hat{p}$ is the stress tensor

$$p_{ij} = nT\delta_{ij} + n\int(v_j - u_j)(v_i - u_i)d\vec{v}d\vec{z}$$

The model describes the crowd motion in a confined geometry: in the buildings, stadiums, squares, shopping centers. The motion of crowds looks like a fluid flow around the obstacles with certain stream lines, flow separation and secondary flows.

3 Conclusions

NET approaches work very well at different scales of biological systems exhibiting deep interconnection of the BTHM processes.

Acknowledgment

The authors would like to express thanks to the Hungarian Academy of Sciences and National Academy of Sciences of Ukraine for the financial support via the international cooperation research grant for 2010-2012.

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