PMM U.S.S.R.,Vol.46,pp.421-429
Copyright Pergamon Press Ltd.1983.Printed in U.K.

0021-8928/83/4 0421 $7.50/0

UDC 531:576.7+577.31

ON MODELS OF BIOLOGICAL CONTINUOUS MEDIA* (**)

S.A. REGIRER

The degree of study of biological objects within the framework of the continuum approach is characterized in comparison with practical demands. Features of the construction of models of biological continuous media are discussed, in particular, the role of thermodynamic and biological considerations. Certain timely research directions are considered.

1. Objects of investigation. Continuum representations (not necessarily formalized) are used for different biological objects, from subcellular formations (membranes, cytoplasmas) to ecological systems. Tissues consisting of cells and extracellular substances and sets of organisms, uni- and multicellular, lie between these limit cases on the averaging scales.

Rheological properties, expressible at least by effective viscosity and elasticity coefficients, are measured for many thousands of objects. A tissue or fluid not subjected to such investigation can hardly be found in the human body, for instance. Chemical, diffusion, electromagnetic, and thermal properties with which modern mechanics deals /1/, have also been studied experimentally for sets of biological objects which are especially distinctive by the close connection between phenomena of different physical nature. The number of literature sources containing appropriate information expressed in the language of continuum representations or useful for their development is in the tens of thousands.

Approximately 95% of the publications are devoted to the properties of blood, muscles, bones, biological membranes and biopolymer solutions. Hundreds of papers concern skin, cartilage, sinews, vascular walls, lung tissue, articular fluid, mucus, cytoplasm, plant tissue, etc. Single papers elucidate the results of investigating tears, lymph, hair, liver tissue, and sets of other objects, including the most exotic, for instance, the pedal slime of Gastropod mollusks.

On the whole, such a distribution correlates with the demands of biology, biophysics, and medicine in quantitative respects. But these requirements are not always satisfied:even for the objects studied most data of fundamental importance are often lacking. For instance, for muscles and a number of other anisotropic tissues, the elasticity coefficients are known only in one direction there are no satisfactory data on the architecture of the networks of the finest blood vessels penetrating them for many tissues. Not only difficulties in an experiment are the reason: no less important is the lack of governing theoretical models because it is often impossible to compare either the results of different authors or the properties of different objects.

The experimental data scattered in thousands of publications are not, as a rule, systematized and are frequently difficult to discover. Only recently have generalizing papers devoted to the properties of biological materials started to appear: the blood /2/, vascular walls /3/, bone tissue /4/, biological membranes /5/, and stimulable media /6,7/, articular cartilages and synovial fluid /4,8/, etc. (the references here and later reflect primarily domestic literature of recent years; further bibliographic information is contained in the citations; see /9-11/, also).

2. Theoretical approaches to the construction of models. Models of biological continuous media are the basis of not only computations (solutions of boundary value problems) but also of qualitative reasoning and rational performance of experiments. The independent heuristic value of models adduces special importance to the problem of their construction. Schemes to construct continuum models are known in mechanics, both founded on the analysis of phenomena in microscale, and operating directly with macroparameters /1,9,12-14/. The same schemes are used even for the description of biological objects. Here not the formal rigor

*Prikl.Matem.Mekhan.,46,No.4,pp.531-542,1982

**) Supplemented text of a report to the Fifth All-Union Congress on Theoretical and Applied Mechanics, Alma-Ata, May 27, 1981.

of the derivation or quantitative accuracy (only the accuracy of specific measurements is meaningful for live objects because of the individuality and variability of their properties), but the physical content of the model and the extraction of intrinsically biological regularities are essential.

2.1. Description at the microlevel. For biological objects, the description of processes at a microlevel with subsequent averaging is often realized successfully: the initial test data are ordinarily incomplete and allow too great a freedom in interpretation, but the averaging is fraught with exceptional mathematical difficulties. All the possibilities of such an approach have not been exhausted, and hence the attraction of the achievements of molecular biophysics and the solution of appropriate mechanical problems continue to be of interest. The averaging procedure for multiphase media continues to be the subject of discussion: the attraction of new mathematical ideas /14,15/ affords a hope for expansion of the class of models with explicitly defined correspondence between micro- and macro-variables.

Among the recent results we cite the research on the contribution of erythrocytes to the effective properties of blood. Thus, for erythorocyte aggregates of the "money column" type entrained by a flow, the probabilities of interaction, combination and exchange, are calculated as a function of the aggregate length, the shear velocity, and the bond strength /16,17/ (see Sect. 2.2.). In connection with the problem of describing mass transfer in blood (Sect. 3), O.F. Kuznetsova and the author solved the problem about the effective diffusivity of an erythrocyte rotating in a shear flow with chemical reactions taken into account.

A result of the solution is the formula $\mathbf{I} = f_0 I_0 \mathbf{e}_y + f_1 I_0 \boldsymbol{\omega} \times \mathbf{e}_y$, which predicts a change in the oxygen flow $\mathbf{I}$ through an erythrocyte as compared to the flow $I_0 \mathbf{e}_y$ (the external concentration gradient is along the y axis) in the absence of rotation and chemical bonding of the oxygen by hemoglobin Hb. Here $\boldsymbol{\omega}$ is the angular velocity, f_0, ωf_1 are functions of the mean O_2 concentration with respect to the surface, $\mathrm{Pe} = a^2\omega/D_{O_2}$ (a is the erythrocyte diameter), the ratio of the diffusion coefficients D_{O_2}/D_{Hb}, and the ratio of the characteristic diffusion and chemical reaction times. The theory agrees qualitatively with experiment, and correctly predicts the shear velocity level ($\sim 10^3$ s) starting with which the fine-scale erythrocyte motions noticeably affect the O_2 transfer in blood /2/.

2.2. Kinetic equations. Different distribution functions are introduced for media of complex composition, including a comprehensive one-particle function $f(t, \mathbf{r}, \mathbf{c}, \alpha_i)$ and its integrals with respect to $\mathbf{c}$ and α_i. Here $\mathbf{r}$ and $\mathbf{c}$ are the coordinate and velocity, α_i are parameters, some of which refer to the state of the molecule, and others to the state of the macro-particles containing this molecule. Underlying the continuum description is then the construction of kinetic equations in the distribution functions. Such an approach was developed for sets of live organisms, for instance /18,19/, muscle contracting protein /20,21/, elements of excitable media /6/, and erythocyte aggregates in moving blood /22/. Precisely for the closure of the aggregation equations can the above-mentioned probability characteristics of the interaction of money columns be used.

The equations of /22/ work allow of extension to the case of capture of the fluid (blood plasma) in the aggregate. For instance, for double interactions the function $\varphi(m, M, w, W)$ giving the number of aggregates with volumes in the interval dw and with volumes of pent-up fluid in the interval dW satisfies the equation

$$\begin{aligned}\frac{d\varphi}{dt} = {} & \frac{1}{2}\int \varphi(m, M)\,[\varphi(w - m - a, W - M - a)\,K(m, M, w, W, a) - \\ & 2\varphi(w, W)\,K(m, M, w + m + a, W + M + a)]\,dm\,dM da + \\ & \frac{1}{2}\int \varphi(m, M)\,[\varphi(m', M')\,E(m, M, m', M', w, W, a) - \\ & \varphi(w, W)\,E(m, M, w, W, m', M', a)]\,dm\,dM\,dm'\,dM'\,da + \\ & \int \varphi(m, M)\,F(m, M, w, W, a)\,dm\,dM\,da - \\ & \frac{1}{2}\int \varphi(w, W)\,F(w, W, m, M, a)\,dm\,dM\,da - \frac{\partial g\varphi}{\partial w} - \frac{\partial g\varphi}{\partial W}\end{aligned} \tag{2.1}$$

Here g is the rate of fluid capture, K, E, F are the probabilities of the acts of merger, exchange, and dissociation, and a is the fluid volume attached in one act. T.V. Chasova studied certain exact solution of (2.1) equation and its qualitative consequences.

2.3. Average variables; internal parameters. Moments of the distribution functions, including the means $\langle \alpha_i \rangle$, as well as different correlation characteristics occur as macroscopic variables in the averaging. The description of a medium of macroparticles with complex configuration evidently requires an expanded set of variables.

The successive development of the conception of "internal variables" /1,12/ was one of the

decisive circumstances assuring the possibility of applying mechanics to live objects. Microstrains, microstrain rates, and other kinematic quantities used to describe regular fine-scale motion in a volume element of the medium are from one of the important classes of internal variables. Another class is the parameters reflecting the state of an element of the medium, the mean size composition, and temperature of the macroparticle, say. A third class is the quasi-thermodynamic parameters describing chaotic fine-scale motion and having the same meaning with respect to the macroparticles as have the usual thermodynamic parameters with respect to molecules. Among this class is, in particular, the effective temperature of the macroparticle "gas".

The transport properties that ordinarily reflect the termal motion of molecules or Brownian particles, are often complicated in content for biological media since they exist as complex forms of thermal motion (for instance, bending vibrations of the cell membrane) and chaotic motions of a different nature associated with energy consumption: the wanderings of bacteria or people in a crowd, the random motions of blood cells in a shear flow, and during settling, opening and closing of the finest blood vessels because of spontaneous contraction of the vascular muscles or the random clogging by blood cells, etc. It is intuitively clear that quasi-thermodynamic variables can be introduced for the majority of the kinds of chaotic motion, but further analogies with ordinary thermodynamics require care.

2.4. Phenomenological approach, thermodynamics. The phenomenological approach to the construction of models of biological media uses known recipes, for which postulation of the governing parameters (including the quasi-thermodynamic), giving the internal energy as a function of these parameters, and indicating the dissipative processes in the media are common. To describe these latter, nonequilibrium thermodynamics methods are relied upon. Precisely thus were models of the blood, muscles, etc. constructed.

The thermodynamics of living systems is a subject far beyond the scope of this paper. It is just expedient to repeat the warning /9,23/ about the illegitimacy of formal transferral of the usual thermodynamic representations for simple systems to live objects. In particular, it is necessary to take into account that the media being studied are multiparametric, the media particles have internal dissipative mechanisms, and the media behavior is a complex combination of reversible and irreversible phenomena. In a number of cases (see Sect. 2.5, for instance) the equations of motion of the medium and the thermodynamic relations including the entropy balance equation, are written in terms of different sets of variables and turn out to be independent in this sence.

Unfortunately, examples of the incorrect comprehension of the real possibilities and limits of applicability of phenomenological nonequilibrium thermodynamics are not infrequent. As a rule, the question of internal parameters is not elucidated in reference texts; it is often forgotten that the Onsager theory does not yield a complete description of the medium, that the set of forces and flows characterizing nonequilibrium processes is not fixed once for all time, but depends on the details of the description, and that postulation of Onsager relations between arbitrarily selected forces and flows is not competent. Confusion in discussions on the linearity of models which is erroneously identified with the linearity of the dissipative governing relationships, is not rare, and it is, in turn, sometimes rejected unconditionally, sometimes postulated unconditionally.

2.5. On models of sets of organisms. New concepts must be introduced for the continuum description of the motion of sets of organisms; the aim of the motion, the program of the motion, etc. /24/. They are defined for one species, but upon satisfaction of a number of conditions, have continuum analogies which should be in the governing relations. Such analogies were used in the equations of motion of cell colonies, the flow of transport or crowds of people /9,18,19,25/.

The interaction of "particles" in such a continuum is accomplished in addition to the exchange of mass, momentum, and energy, also by the exchange of information, and this means that equations describing the change in the program of the motion with incoming information being taken into account should be formed.

The mass balance equation (or the number density) of "particles", which is closed by the "diffusion law" is principal in models of sets of organisms. The momentum and energy balance equations are not usually constructive,i.e., are satisfied identically. As a rule, the construction of such models is not related to thermodynamic considerations.

In a sufficiently general case, for sets of organisms in a certain fixed substrate, it is possible to set /9,25/

$$\partial C/\partial t = -\nabla_k j^k + Q, \quad \partial C_\alpha/\partial t = -\nabla_k j_\alpha{}^k + Q_\alpha \tag{2.2}$$

$$j^k = -D^{ik}\nabla_i C + \sum_\alpha \xi_\alpha^{ik}\nabla_i C_\alpha + j_*{}^k + \ldots, \; j_\alpha{}^k = \xi_\alpha^{ik}\nabla_i C - \sum_\beta D_{\alpha\beta}^{ik}\nabla_i C_\beta \tag{2.3}$$

Here C, j^k, Q are the concentrations, flow, and rate of generation of the organisms being considered, C_α, $j_\alpha{}^k$, Q_α are the same quantities for objects of the species α with which these organisms interact, $j_*{}^k$ is a part of the flow independent of $\nabla_i C, \nabla_i C_\alpha$. Since entropy production in such a system is not related directly to $j^k \nabla_k C$ (and is expressed in terms of the internal parameters not in (2.3)), the signs of D^{ik}, $\zeta_\alpha{}^{ik}$ are arbitrary and no symmetry of the coefficients is observed. Such freedom corresponds to a conceivable modification of the motion program. Let us say that the tendency of mushrooms to accumulate in one place in an "isotropic" forest is not inherent so that $D^{ik} \approx Dg^{ik}$, $D > 0$ while a random cluster in a homogeneous crowd attracts new idlers: $D < 0$. The signs of $\zeta_\alpha{}^{ik}$ are governed by whether the objects of the species α are attractive or repulsive; if they are fixed then $\xi_\alpha{}^{ik} = 0$, $D_{\alpha\beta}{}^{ik} = 0$ but $\zeta_\alpha{}^{ik} \neq 0$.

2.6. Utilization of biological representations. The actual complexity of live objects is so great that some observer data is often inadequate even to establish the topological characteristics, for instance, construction of tissue with a network of blood vessels. One of the ideas discussed now is to involve data on the development of the object in time or in its evolution: it is not excluded that it will turn out to be easier to comprehend the principle of the building process than the regularities in the architecture of a finished building. Construction of the model of a biological continuous medium relies even on other actual information of a biological nature: on the "purpose" of the tissue, the principles of the activity of its cells, etc. This is the common tendency for modern biomechanics to turn to fundamental biological representations. It is pertinent to add the following hypothetical reasoning as well. It is known that variational equations are utilized in constructing the models of continuous media /1,12/. On the other hand, assertions, expressed in variational form, about the optimality of organisms in a set of definite criteria /26/ occur in the study of biological evolution. Hence, it is not excluded that variational equations will successfully be allotted an additional, "historical" content for biological continua.

3. Blood. The question of a model for blood as a continuous medium can be considered solved on the whole. The model proposed in /27,28/ under certain natural assumptions (particularly about the Stokes nature of the flow around erythrocytes) reduces to the equations /9/

$$\rho\left(\frac{\partial v^i}{\partial t} + v^j \nabla_j v^i\right) = -g^{ij}\nabla_j p + \nabla_j \tau^{ij} + F^i, \quad \nabla_i v^i = 0 \tag{3.1}$$

$$\tau^{ij} = 2\eta(N, H, T_F)\, e^{ij}, \quad e_{ij} = \frac{1}{2}(\nabla_i v_j + \nabla_j v_i) \tag{3.2}$$

$$\rho\frac{dH}{dt} = -\nabla_k j^k + g, \quad \rho\frac{dN}{dt} = -\nabla_k\left(\frac{N}{H} j^k\right) + G, \quad \rho\frac{dC}{dt} = -\nabla_k\left(\frac{C}{H} j^k\right) \tag{3.3}$$

$$g = g(\eta, I, T_F, H, N, C), \quad G = G(\eta, I, T_F, H, N, C) \tag{3.4}$$

$$T_F = \Phi(\eta, I, H, N, C), \quad j_k = -\rho D \nabla_k H - \zeta \nabla_k T_F + \ldots$$

$$(I = (2e^{ij}e_{ji})^{1/2})$$

In addition to the standard notation, here we use the following: C is the true volume concentration of erythrocytes, H, N are the volume and number concentrations of aggregates (including single erythrocytes), g is the rate of capture of the liquid phase in the aggregate, G is the rate of generation of the aggregates, T_F is their fluctuation temperature. The functions g, G, Φ, D, ζ, η are hypothetically known from comparison with test, dimensional and other considerations, and require further refinement.

Equations (3.3) are the moment equations for the distribution functions in the kinetic equation, (2.1), say

$$C = \int (w - W)\varphi\, dwdW, \quad H = \int w\varphi\, dwdW, \quad N = \int \varphi\, dwdW$$

A more complete model than (3.1 – 3.4) takes account of the fractional composition, the rate of rotation ω, and the microstrain rate w^{ij} of the aggregates. Additional conservation equations and governing relations enter the model, and in addition, (3.2) and (3.4) for τ^{ij}, j^k, Φ /27/ are modified. This model contains internal parameters of all the classes named in Sect. 2.3, ω and w^{ij}; N and $H - C$; T_F.

A multivelocity model taking account of the compressibility and different plasma and erythrocyte densities was constructed by E.S. Losev to study sound propagation in blood, erythrocyte sedimentation /29,30/, etc. Erythrocyte aggregation in a rotation viscosimeter and their grouping in an ultrasonic field were also examined on the basis of this model with the participation of I.V. Orlova and I.A. Pichugina. In order to interpret the data about the apparent viscoelasticity of blood (partially due to thixotropic properties /31/), the investigated a model with the elastic shape changing of erythrocytes taken into account: this model

which contains the microstrain of erythrocytes as internal parameter, differs from that of Oldroyd /9/ and goes over into it in the case of a vanishingly small erythrocyte dimension.

Additions to the model, which are as yet unrealized, and would describe the physicochemical transformations in the blood, cell damage, coagulation and thrombus formation in the flow /2/, are of interest. Obscurities in questions of the adequacy of the adhesion conditions for the blood (for flows in narrow tubes and vessels) and on the role of the electrokinetic phenomena accompanying the motion of the blood are conserved. No complete description of the diffusion process for oxygen and other substances in the blood is given.

Oxygen transfer in the blood is ordinarily described by a system of the type

$$dC_1/dt = \nabla_i (D^{ik}\nabla_k C_1) - f(C_1, C_2),\ dC_2/dt = f(C_1, C_2) \tag{3.5}$$

where C_1, C_2 are molar concentrations of oxygen in the plasma and in the erythrocytes (including the chemically bonded). The diffusion coefficients D^{ik} are known approximately as functions of C_1, C_2 and the kinematic characteristics (see Sect. 2.1). Whether this approximation is satisfactory for quantitative computations is not clear. It is not known whether the description of the blood composition in terms of just C_1, C_2 is adequate in this sense; it is possible that it is sometimes necessary to consider free and chemically bond oxygen separately, and also the inhomogeneity of the local concentration within the erythrocytes. Furthermore, it is not known whether diffusion terms should not also be introduced even in the second equation of (3.5) with the dependence of the diffusion fluxes on $\nabla_i C_1$ and $\nabla_i C_2$ taken into account (since the erythrocyte concentration is high and collisions are frequent).

4. **Muscles.** The relationship which relates the stress in tissues p^{ij} to strains ε_{ij} and internal parameters $\gamma_1, \gamma_2, \ldots$ characterizing the muscle activity (activator concentrations, fraction of active cells, etc.)

$$p^{ij} = F^{ij}(\varepsilon_{kl}, A, \gamma_1, \gamma_2, \ldots, b_{kl}) \tag{4.1}$$

is central in continuum models of muscle tissue whose investigations started in /32,33/.

Here F^{ij} is a certain operator, A is the affinity of the reaction whereupon energy is liberated, b_{kl} is a characteristic of the anisotropy of the muscle. In the stationary states p^{ij} and ε_{ij} do not vanish simultaneously if the γ_i exceed a certain threshold and $A \neq 0$. Also important to the interpretation if the test data is the representation of the heat liberation rate in the muscle which is contained in the model: $q^* = \Phi(p^{ij}, \varepsilon_{ij}, A, \gamma_1, \gamma_2, \ldots, b_{ij})$.

The relationship (4.1) in /33/ is obtained in the form of a first order quasilinear differential equation (in time) with one given control parameter $\gamma = \gamma(t)$ for small strains and $b_{ij} = \text{const}$. For the smooth muscles of vessels it is apparently reasonable to consider $\gamma = \gamma(p^{ij}, \varepsilon_{ij})$ /34/ or $\gamma = \gamma(p^{ij}, \varepsilon_{ij}, e_{ij})$, but this latter version is studied only slightly. For the heart muscle $\gamma(t)$ is determined by differential equations reflecting the kinetics of calcium exchange /35–37/; this model is applied for a broad circle of specific computations. A model of a skeleton muscle with two control parameters is proposed in /38/.

One of the most recent problems is to construct models that would give a joint description of control signal and constraction propagation for the heart muscle, say, i.e., models of excitable media /6,7/ and mechanics of muscles with the influence of the mechanical factors on the excitation taken into account. Perfection of the muscle tissue model /9/ requires taking account of finite strains, heat and mass exchange with the blood, and the influence of blood filling on tissue stiffness, as well as the reverse influence (mechanical and through local regulation) of muscle contraction on its blood supply. Precisely here does information about the architecture of the vascular channel turn out to be necessary.

The continuum description of a branching microchannel network as a special phase of a multiphase continuum is of interest to the study of muscles and many other tissues, lung, bone, etc. The fundamental ideas of such a description, providing for the introduction of a fourth continuous coordinate in place of a discrete set of a large number of channel types, are presented in /9,39/; a quasi-one-dimensional model of a branching network is studied in /40/. Tissue models with vascular and other transport networks contribute to a meaningful interpretation of physiological measurement on the whole organ, even in the simplest versions.

Models of other contracting systems, for instance, cell cilia and flagella, that assure mobility because of the direct conversion of chemical into mechanical energy attract a great deal of attention among biologists, but are as yet represented by rather rough schemes /21,41, 42/.

5. **Bones.** Fluid motion in the networks of the finest channels and electromagnetic phenomena /4,9–11/ play a major role in the life-support of bones. Correspondingly, underlying the general models of bones is a representation of a two-phase material: a solid porous piezoelectric and a filtering fluid with ion conductivity. Among the governing relationships for such a medium are the generalized Hooke's, Darcy and Ohm's laws as well as the polarization

equation whose principal terms in the usual notation take the following form after manipulation /9,43/:

$$p^{ij} = -pg^{ij} + G^{ijkl}\varepsilon_{kl} - d^{kij}E_k + 2\eta^{ijkl}e_{kl} - \beta^{kij}E_k - \ldots$$
$$g^i = -k^{ij}\nabla_j p + \psi^{ij}E_j + \ldots$$
$$j^k = \sigma^{ki}E_i + \chi^{kijl}\nabla_l\varepsilon_{ij} + \beta^{kij}e_{ij} + \vartheta^{ki}\nabla_i p + \ldots$$
$$D^k = 4\pi d^{kij}\varepsilon_{ij} + \varkappa^{ki}E_i + \ldots$$

In particular, there hence follows that in the absence of current ($j^k = 0$) an electrical field proportional to the strain gradients can exist in the material so that the effective coupling of the induction D^i with ε_{kl} would seem to be nonlocal. It is also seen that because of cross effects the actual relation of p^{ij}, D^i to the strains and the electrical field E_i is nonsymmetric. Under isothermal conditions the relaxation processes are due to viscosity of the solid phase η^{ijkl}, filtration processes, and electrical resistance. The apparent viscoelasticity of the bone and the damping of the piezoelectrical signal can be due to all these factors.

The problems of practical medicine, particularly the development of methods of nondestructive diagnosis and electrostimulation of the healing of fractures, require both careful confirmation of existing bone models but also their extension to take account of compressibility (in connection with problems of high-frequency wave propagation) and reconstruction processes (see Sect.6). The question of whether or not piezoelectrical effects must be related to microstrains of the solid phase and changes in porosity remains unexplained.

The problem of a combined description of the strain, filtration, and electrical phenomena also occurs in studying articular cartilage. Especially essential for this is the dependence of the porosity and permeability on the stress, and visibly, on the ion composition of the fluid in the pores /8/.

6. Adaptation and growth. If tissue is seen as a porous material with porosity m and strain tensor ε_{kl} (governed by solid phase displacements), then changes in m, ε_{kl} in time are comprised, in the general case, of "fast" which follow a load change as in ordinary deformable bodies, and "slow" irreversible changes which correspond to accumulation (or dissipation) of the solid phase because of chemical reactions with the fluid and filtration. For instance, changes in m, ε_{kl} because of bone adaptation to loading or reconstructions conditions for healing last weeks for man, and growth changes in these quantities years. The individual development of a species is accompanied by cell differentiation processes (for multicellulars) and morphogenesis, which are partially characterized by the same variables m, ε_{kl} as well as internal parameters reflecting the kind of anisotropy of the tissue, cellular composition, etc.

Adaptation and growth changes in tissues, which are protracted relative to the characteristic times of the load change, depend substantially on the mean state of stress. A number of hypotheses about the nature of such a dependence is known, for instance, the adaptation properties of bones are treated as a result of the influence of electrical phenomena on mass exchange and the reaction rate, and electrical phenomena, through piezo- and pyroelectrical effects, are related directly to the stress.

Of exceptional interest to theoretical biology is the question of the growth in complexity of the object shape (morphogenesis), particularly, how changes not predetermined genetically (at least, directly), are accomplished. Widespread in the conception of dissipative structures /20,44/ and the formation of a complex shape because of the buckling of the simpler preceding shape. The instability mechanism is sought in the play of diffusion and nonlinear chemical reactions with the participation of hypothetical substances (activators and inhibitors), produced and absorbed cells, by considering that tissue construction follows the distributions of these substances. However, buckling can possibly be elastic in nature in the growing material, while dissipative processes determine the new shape.

If morphogenesis is considered as an irreversible spatially ordered strain, then the presence of factors assuring order must be acknowledge. The terminology "biopole", a compromise of parapsychologists, was introduced precisely to denote these factors. As mentioned above, the meaning of concentration fields of certain substances, and more rarely, stress fields or fields of electromagnetic nature (9,44/ are ascribed to them.

The opinion is sometimes expressed that the pathological development of tissue is also a kind of instability but too straight a treatment of this assertion results in paradoxes. This, an equally likely model, on the whole, for adapting bone tissue /45,46/ predicts that the existence of stable stationary states is achieved for absolute numerical agreement between two independent parameters. By such a theory any real tissue is evidently unstable. Not the presence of stable stationary states is apparently important but just a limitation on the

rates of specific processes in conformity with regulator and adaptable possibilities of the organism.

Study of the adaptation and growth phenomena generates the formulation of the general question about the mechanical development factors and about the rational description of developing objects on the language of continuum representations. Certain substantial elements of such a description were introduced in application to the growth of the spine (*) and in the model of bone tissue /43/. Special models of adaptive elastic material are proposed in /45,46/; a more general theory based on the variational equations of L.I. Sedov is developed in /47/. Let us note that the growth rate in /46/ was considered to depend directly on the stress, while in /47/ this dependence was introduced in terms of a completely definite internal parameter; the paper /43/ takes account of electrical factos also, in principle.

All such models are still far from perfect. In particular, whether a strong connection between the instantaneous values of the stress and the electrical quantities on the one hand, and the rates of growth changes on the other is valud is unclear, i.e. whether taking the difference in time scales for these two groups of elements is good.

7. Membranes. Life-support processes are assured to a considerable extent by the presence of biological membranes bounding the cell and the intercellular structure. The membrane properties make possible an ordered transfer of substance, the origination and propagation of electrical signals, the mobility and sorting of cells in tissue formation, etc.

Biological membranes consisting of several molecular layers (the thickness of each is ≈ 50 Å) are, as artificial bilayered membranes, two-dimensional (surface) continua possessing an abundant set of properties from the mechanics viewpoint. Thus, thermal motion is realized in a membrane not only in the form of chaotic molecule motion along a layer and infrequent transitions from one layer to another. Large-scale molecules in the membrane are in a state of two-dimensional Brownian motion. As a rule, the cell dimensions are sufficiently large so that their Brownian motion as a whole is negligible, but it is important for the finest membrane bubbles (vesicules) within the cell. Thermal fluctuations also appear in random flexible membrane deformations. Membranes are nonsymmetric in the sence that the layer configuration is dissimilar. This results in complex equilibrium modes of the membranes, in the dependence of its diffusion resistance on the transverse flow direction, in a dissimilar reaction to chemical agents coming in from different sides, etc.

A membrane is deformed and changes rheological properties in response to local changes in composition and temperature, chemical, electrical, and sometimes, magnetic effects. In turn, mass exchange, chemical, thermal, and electrical phenomena are interrelated and depend strongly on mechanical factors. Active transport, i.e., material transfer opposite to the diffusion gradient, and membrane motion performed because of the chemical reaction energy, as well as a change in membrane permeability and generation of an electrical potential because of mechanical effects have a special biological importance.

Until recently, the mechanics of membranes was limited by analogies to the theories of thin elastic shells and liquid films; the inadequacy of such an apporach is now evident /5,9, 48,49/. Further investigations have the aim of, firstly, giving an adequate description of kinematics of a membrane as a physically infinitely thin object alloted internal parameters, secondly, developing appropriate thermodynamic representations (let us emphasize that even the concept of membrane temperature has not been defined sufficiently clearly), thirdly, constructing governing relations with the observable mechanochemical and electromechanical effects taken into account by separating the regularities common to all membranes from the particular inherent to specialized membranes.

Representations of ordinary "three-dimensional" mechanics can be utilized to execute this program only partially because a membrane is not a "piece" of some three-dimensional material /5,9/. Hence, attempts have been undertaken to formulate conservation laws and governing relations directly for an open (in the thermodynamic sence) two-dimensional medium /5,50/. Sometimes, two-dimensional analogies between liquid crystals and Cosserat media are used here. There are also models describing trans-membrane mass transfer and certain other processes in membranes separately /6,21/.

Difficulties in constructing membrane models occur even in selecting the governing parameters which are not trivial even in particular problems about its equilibrium modes /48,49/. Possibly a rational approach to this question will be developed by starting from a preliminary description of the membrane as a system of interacting material surfaces with comparatively simple properties /51/.

---

*) Entov, V.M. On the mechanics of scoliosis. Preprint No.117, Institute of Problems of Mechanics of the U.S.S.R. Academy of Sciences, 1978.

8. Conclusion. The above-mentioned models are used to solve numerous and diverse biomechanical problems (see /2,5—11,52,53/, for example) and some have already been designated. The aims pursued in solving these particular problems are quite diverse, however, the results are almost always a confirmation and improvement on the initial model. In a number of cases, this was the main purpose of the investigation. In contrast, say, to a viscous gas or elastic body, biological objects possess such multivariate properties that almost unlimited possibilities (and requirements) for refinement, detailing, and extension of the models exist. Hence, none has nor will visibly have the status of a finally established, unique, and universal model in the near future.

The author is grateful to S.S. Grigorian, G.A. Liubimov, A.K. Tsaturian, and A.A. Shtein for useful discussions and critical remarks on many questions touched upon in the paper. The author happily remarks that the combined research of E.S. Losev and N.Kh. Shadrina contributed greatly to its writing.

REFERENCES

1. SEDOV L.I., Mechanics of a Continuous Medium. 3rd Ed., Vol.1, Vol.II, NAUKA, Moscow, 1976. (See also Pergamon Press Book Nos. 09878, 1965 and 10994, 1966 and A Course in Mechanics of Continuum, Wolters—Noordhoff, 1971.
2. LEVTOV V.A., REGIRER S.A., and SHADRINA N.Kh., Rheology of Blood. Meditsina, Moscow, 1982.
3. PURINIA B.A. and KAS'IANOV V.A., Biomechanics of Large Human Bloodvessels. Zinatne, Riga, 1980.
4. KNETS I.V. PFAFROD G.O., and SAULGOZIS Iu.Zh., Deformation and Rupture of Solid Biological Tissues. Zinatne, Riga, 1980.
5. EVANS E.A. and SKALAK R., Mechanics and Thermodynamics of Biomembranes. CRC Press, Boca Raton, Fla., 1980.
6. MARKIN V.S., PASTUSHENKO V.F. and CHIZMADZHEV Iu.A., Theory of Excitable Media, NAUKA, Moscow, 1981.
7. IVANITSKII G.R., KRINSKII V.I. and SEL'KOV E.E., Mathematical Biophysics of Cell, NAUKA, Moscow, 1978.
8. MOW V.C. and LAI W.M., Recent developments in synovial joint biomechanics. SIAM Review, Vol.22, No.3, 1980.
9. REGIRER S.A., Lectures on Biological Mechanics. Pt. 1, Izd-vo Moskovsk. Gosudarst. Univ., Moscow, 1980.
10. BRANKOV G., Principles of Biomechanics. MIR, Moscow, 1981.
11. FUNG Y.C., Biomechanics. Mechancial Properties of Living Tissues. Springer, New York, et al., 1981.
12. SEDOV L.I., Application of the variational basis equation to construct models of continuous media. In: Selected Questions of Modern Mechanics, Pt.1, Izd. Moskovsk, Gosudarst. Univ., Moscow, 1981.
13. NIGMATULIN R.I., Principles of Mechanics of Heterogeneous Media. NAUKA, Moscow, 1978.
14. BERDICHEVSKII V.L., Equations of mechanics of a fluid with particles. In: Problems of Averaging and Constructing Continuum Models in Mechanics of a Continuous Medium. Izd. Moskov. Gosudarst. Univ., Moscow, 1980.
15. KHINCHIN A.Ia., Mathematical foundation of statistical mechanics. In: Mathematical Modeling of Biological Processes. NAUKA, Moscow, 1979.
16. ZAIKO V.M., and ZARETSKAIA Iu.V., Determination of the velocities of effective collisions of erythrocyte aggregates in blood. Mekhan. Kompozitn. Materialov, No.3, 1981.
17. ZAIKO V. M. and ZARETSKAIA Iu.V., Aggregation equilibrium in blood. Mekhan., Kompositn. Materialov, No.1, 1982.
18. ALEKSEEV V.V., Biophysics of associates of live organisms. Usp. Fizich. Nauk, Vol.120, No. 4. 1976.
19. PRIGOGINE I. and HERMAN R., Kinetic Theory of Vehicular Traffic. Elsevier. New York, et al., 1971.
20. DESHCHEREVSKII V.I., Mathematical Models of Muscle Contractions. NAUKA, Moscow, 1977.
21. VOL'KENSHTEIN M.V., General Biophysics, NAUKA, Moscow, 1978.
22. POPEL' A.S., REGIRER S.A. and SHADRINA N.Kh., Equations of kinetics for aggregation processes in suspensions. PMM, Vol.39, No.1, 1975.
23. KNETS I.V. and REGIRER S.A., Certain modern problems of biorheology. In: Rheology (Polymers and Oil). Izd. Inst. Teplofiz. Sibirsk. Otdel. Akad. Nauk SSSR, Novosibirsk, 1977.
24. KORENEV G.V., Introduction to the Mechanics of Man, NAUKA, Moscow, 1977.
25. BABSKII V.G., Chemotaxis in bacteria from the viewpoint of molecular and mathematical biology, Molecular Biology, No.20, NAUKOVA DUMKA, Kiev, 1978.
26. KHANIN M.A., DORFMAN N.L., BUKHAROV I.B., and LEVADNYI V.G., Extremal Principles in Biology and Physilogy. NAUKA, Moscow, 1978.

27. REGIRER S.A. and SHADRINA N.Kh., On models of thixotropic fluids. PMM, Vol.42, No.5, 1978.
28. SHADRINA N.Kh., Erythrocyte aggregation and rheological properties of blood. In: Annotation to Reports to the Fourth All-Union Congress on Theoretical and Applied Mechanics, NAUKOVA DUMKA, Kiev, 1976.
29. LOSEV E.S., On the hydrodynamic theory of erythrocyte sedimentation. Mekhan. Kompositn. Materialov, No.1, 1980.
30. LOSEV E.S., Hydrodynamics of erythrocyte sedimentation. In: Annotation to Reports to the Fifth All-Union Congress on Theoretical and Applied Mechanics, NAUKA, Alma-Ata, 1981.
31. SHADRINA N.Kh., On shear flows of a thixotropic fluid. Izv. Akad. Nauk SSSR, Mekhan. Zhidk. Gaza, No.3, 1978.
32. NIKITIN L.V., Model of a bioelastic body, Izv. Akad. Nauk SSSR, Mekhan. Tverd. Tela, No.3, 1971.
33. USIK P.I., Continual mechanochemical model of muscular tissue, PMM, Vol.37, No.3, 1973.
34. REGIRER S.A., RUTKEVICH I.M. and USIK P.I., Model of Vascular tone, Mekhan. Polimerov, No.4, 1975.
35. TSATURIAN A.K. and IZAKOV V.Ia., Mathematical model connecting excitation to contraction in the heart muscle, BIOFIZIKA, Vol.23, No.5, 1978.
36. TSATURIAN A.K. and Zhelamskii S.V., On interaction between deformation and activation of the heart muscle, Mekhan. Kompozitn. Materialov, No.1, 1980.
37. TSATURIAN A.K., Model of the heart muscle. In: Annotation to Reports to the Fifth All-Union Congress on Theoretical and Applied Mechanics, NAUKA, Alma-Ata, 1981.
38. NIKITIN N.L., Model of muscle tissue with a variable number of operating fibers, Mekhan. Kompozitn. Materialov, No.1, 1980.
39. RUKHLIS V.E., Blood motion in a terminal vascular channel as filtration in a porous medium. In: Biomechanics of Blood Circulation, Respiration, and Biological Tissues, Zinatne, Riga, 1981.
40. D'IACHENKO A.I., Mechanics of a quasistationary one-dimensional flow in a bifurcated system of collapsible vessels, Trudy Moskov. Fiz.-Tekhn. Inst., No.11, 1979.
41. Motion of Non-muscle Cells and Their Components. NAUKA, Leningrad, 1977.
42. VOROB'EV M.M., PRIEZZHEV A.V. and ROMANOVSKII Iu.M., Mathematical model of protoplasma flow in a viscoelastic active cord of the plasmodium of Myxomycetes. BIOPHYSICS, Vol.25, No.3, 1980.
43. AVDEEV Iu.A. and REGIRER S.A., Mathematical model of bone tissue as a porous-elastic piezoelectrical material, Mekhan. Kompozitn. Materialov, No.5, 1979.
44. BELOUSOV L.V. and CHERNAVSKII D.S., Instability and stability in biological morphogenesis, Ontogenez, Vol.8, No.2, 1977.
45. COWIN S.C. and HEGEDUS D.H., Bone remodelling. 1. Theory of adaptive elasticity. J. Elast., Vol.6, No.3, 1976.
46. COWIN S.C. and VAN BUSKIRK W.C., Surface bone remodelling induced by a medullary pin. J. Biomech., Vol.12, No.4, 1979.
47. SHTEIN A.A., On continuum models of growing material, Mekhan. Kompozitn. Materialov, No.6, 1979.
48. MARKIN V.S., Organization of membranes in the plane of a layer and cell shape. Statistical approach, BIOFIZIKA, Vol.25, No.5, 1980.
49. MARKIN V.S., Organization of membranes in the plane of a layer and cell shape. Biological consequences of the theory, BIOFIZIKA, Vol.26, No.1, 1981.
50. PRIBYLEVA T.A., Conservation equations for a two-dimensional continuous medium as the model of a biological membrane. In: Abstract of Reports, Second All-Union Conference on Biomechanics Problems, Vol.1, Zinatne, Riga, 1979.
51. PRIBYLEVA T.A., Biological membrane as a two-dimensional continuum. In: Annotation of Reports to the All-Union Congress on Theoretical and Applied Mechanics, NAUKA, Alma-Ata, 1981.
52. GRIGORIAN S.S., Methods of the mechanics of continuous media in studies of respiration and blood circulation, Modern Problems of Theoretical and Applied Mechanics, NAUKOVA DUMKA, Kiev, 1978.
53. LIUBIMOV G.A., On hydrodynamic formulations of physiology and medicine problems, Izv. Akad. Nauk SSSR, Mekhan. Zhidk. Gaza, No.2, 1982.

Translated by M.D.F.