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DEFORMATION AND THE STRUCTURE OF CARTILAGE TISSUE

We propose a model of the structure of cartilage tissue which is considered as a set of local equilibrium regions. Every region is a lattice formed by plates (proteoglycan aggregates) and collagen fibers. A deformation of cartilage tissue under the action of an external load mainly occurs through the bending of chains entering the content of proteoglycan aggregates. Formulas for the shear and Young's moduli of cartilage tissue have been derived. It is shown that these parameters are reciprocal to the square of the collagen fiber diameter, and their values are equal to 10^6 *Pa by order of magnitude, which agrees with experimental data.*

K e y w o r d s: cartilage tissue, compliance tensor, shear modulus, Young's modulus.

1. Introduction

It is known that an important role in the vital activity of the human body is played by the ability of cartilage tissue to perform its inherent support function, i.e., its capability to sustain external loads. Therefore, challenging is the question "What is the physical nature of the processes of cartilage tissue deformation under the action of loads?" This paper is devoted to the search for a corresponding answer.

Three types of cartilage tissue are distinguished [1]: hyaline, fibrous, and elastic. In what follows, we talk about the first two types.

Bearing in mind the study of the nature of deformation processes, let us emphasize the following structural features of cartilage tissue [1, 2]:

1) cartilage tissue consists of cells (2%) and the intercellular substance (98%);

2) the main components of intercellular substance are water (75÷80%), collagen (10÷12%), and proteoglycans (7÷8%);

3) collagen and proteoglycans form the scaffold of cartilage tissue;

4) collagen chains are coiled into fibers;

5) proteoglycans exist in the form of aggregates, whose mass equals 10^7 Da by order of magnitude; the structure of such an aggregate (Fig. 1) is composed by a set of connected chains [3]; hyaluronic acid serves as the backbone (the main chain) of the aggregate; almost a hundred protein chains are connected with the latter; more than a hundred polysaccharide chains are connected to every of the protein chains.

Cartilage tissue is usually classified as a viscoelastic medium.

A rather large number of publications were devoted to the study of the physical nature of cartilage tissue deformation (see, for example, reviews [4–9] and references therein). Modern ideas concerning the structure of cartilage tissue are as follows. Car-

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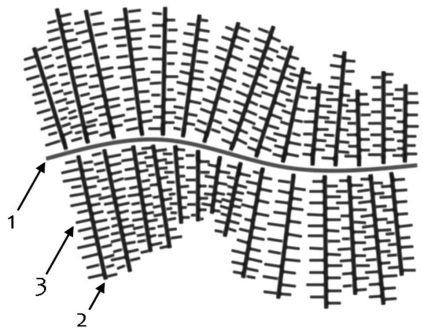

Fig. 1. The structure of proteoglycan aggregate: hyaluronic acid (*1*), protein chain (*2*), polysaccharide chain (*3*)

tilage tissue is considered as a continuous medium consisting of solid and liquid components. The former form a scaffold, and the latter is water with dissolved substances. In effect, cartilage tissue is considered as a porous medium, whose pores are filled with water. Under the action of an external load, water can move from one part of the medium to another. Here, we are talking about stresses of three types: the stresses arising in the scaffold, the stresses arising in water, and the stresses that are a consequence of the water motion. The appearance of the latter is due to the resistance created by the scaffold to the water motion.

The behavior of this model is described using the filtering theory [10]. This theory is based on the empirical relationship known as Darcy's law,

$$\mathbf{v} = -\kappa \nabla p, \tag{1}$$

where $\mathbf{v}$ is the velocity of the liquid, κ is the coefficient called the "liquid permeability", and p is the pressure.

2. Formulation of the Problem

It is customary [11] to describe the properties of a deformation of the physical system by considering the latter as a homogeneous solid medium and characterizing it using a certain rheological equation. For a viscoelastic medium, the rheological equation looks like

$$\hat{\epsilon} = \int\limits_{-\infty}^{t} \hat{F}(t') \frac{d\hat{\sigma}}{dt'} dt', \tag{2}$$

where $\hat{\epsilon}$ is the strain tensor, t is the time, $\hat{F}(t)$ is a tensor function called the "memory function", and $\hat{\sigma}$ is the stress tensor.

Actually, the issue of the physical nature of the cartilage tissue deformation is reduced to the establishment of an analytic relation between the memory function and the parameters of the medium structure. As one can see from the literature data, this problem remains unsolved. In this paper, we restrict the consideration to the case where the following inequality holds:

$$\tau_F \ll \tau_\sigma, \tag{3}$$

where τ_F and τ_σ are time intervals during which the functions $\hat{F}$ and $\hat{\sigma}$, respectively, change substantially. In this case, Eq. (2) takes the form

$$\hat{\epsilon} = \hat{S}\hat{\sigma}, \tag{4}$$

where $\hat{S}$ is a tensor that is commonly called the tensor of equilibrium (or static) elastic compliances (the compliance tensor). Accordingly, the elastic deformation that the cartilage undergoes under condition (3) is called equilibrium (or static).

The aim of this article is to create a physical model that would establish a relation between the tensor $\hat{S}$ and the structure of cartilage tissue. This paper is a continuation of the cycle of works [12–16], devoted to the study of liquid systems with cellulose derivatives (hydrogels). Unlike many other articles dealing with gels, standard thermodynamic approaches were used in the cited works. Namely, the gel formation was considered as a phase transition of the first kind, the properties of the interfacial layer and the phase separation were analyzed in terms of spinodal decomposition, and so forth. This tendency is inherent to this article too, where the deformation process is described on the basis of the local equilibrium concept, which is a key point in the thermodynamics of heterogeneous systems.

3. Structural Levels of Cartilage Tissue

As is known, every condensed system has to be characterized by at least four characteristic dimensions, that form the hierarchy

$$L_1 \ll L_2 \ll L_3 \ll L_4, \tag{5}$$

where L_1 is the size of a molecule, L_2 is the size of a supramolecular formation, L_3 is the size of the area, where the local equilibrium takes place, and L_4 is the size of the system. The regions with the sizes L_1,

L_2, and L_3 are the structural elements of different structural levels. A molecule is a structural element at the molecular (fine-scale) level, a supramolecular formation is a structural element at the supramolecular (medium-scale) level, and a region of local equilibrium is a structural element at the continual (large-scale) level.

Cartilage tissue is not an exception to the general rule: the same characteristic dimensions and the same structural levels are inherent to cartilage tissue as well. In this case, the size L_1 is equal (by order of magnitude) to the size of links in the polymer chains, water molecules, and other substances with low molecular weights; L_2 is the size of proteoglycan aggregates and the thickness of collagen fibers; and L_3 is the size of the region of local equilibrium. As the size L_4, we choose the size of the cartilage tissue region that plays the role of the morphofunctional unit of the organ.

4. Cartilage Tissue as a Randomly Inhomogeneous Continuum

Here, we consider the large-scale model of the structure. By definition, the existence of the large-scale level means that the system can be represented as a set of regions that are in local equilibrium states. Every state, as is known, is described using the parameters that characterize the region as a whole. One of those parameters is the tensor of statistical local compliances.

For the m-th region with the center of inertia located at the point described by the vector $\mathbf{r}^{(m)}$, let us denote the indicated tensor as $\hat{s}(\mathbf{r}^{(m)})$. Let us define the structure of the cartilage tissue system as a discrete set of the elements $\hat{s}(\mathbf{r}^{(m)})$, $m = 1, 2, ..., M$, where M is the number of regions with local equilibrium.

Let us determine the compliance tensor $\hat{S}$ of the cartilage tissue, which appears in formula (4), as the average value of the tensor $\hat{s}(\mathbf{r}^{(m)})$, i.e., by means of the formula

$$\hat{S} = \frac{1}{M} \sum_{m=1}^{M} \hat{s}(\mathbf{r}^{(m)}). \tag{6}$$

Substituting sum (6) by the integral, we obtain

$$\hat{S} = \frac{1}{V} \int\limits_{V} \hat{s}(\mathbf{r}) d\mathbf{r}, \tag{7}$$

where V is the volume of the system. This substitution means that the size L_3 is now considered as an infinitesimally small value, i.e., cartilage tissue is considered as a continual medium, a continuum. Since the tensor $\hat{s}(\mathbf{r})$ depends on the radius vector $\mathbf{r}$, then this continuum is inhomogeneous. Furthermore, the components of this tensor are random, so $\hat{s}(\mathbf{r})$ is a random tensor field. Thus, the large-scale model of cartilage tissue is a randomly inhomogeneous continuum.

5. The Ideal Scaffold of Cartilage Tissue

Let us consider the structure of cartilage tissue at the medium-scale level, i.e., the structure of a region with local equilibrium. In accordance with the current commonly used approach, we consider the tissue scaffold as a porous (foamed) medium. In the mechanics of such media, there is a concept of ideal media that are formed by rods [17] or plates [18]. Both of them are lattices. The former medium is formed by rods that are the edges of a unit cell, and the latter one by plates that are the faces of a unit cell. Let us use this idea and construct a scaffold model. It is obvious that collagen fibers have to play the role of rods.

From Fig. 1, it follows that proteoglycan aggregates cannot form fibers. Hence, bearing in mind the construction of an ideal porous scaffold, it is reasonable to assume that such aggregates should form plates. However, the scaffold includes both collagen and proteoglycans. Accordingly, an ideal scaffold has to include both rods and plates, and preserve a long-range order typical of a lattice.

The simplest version of an ideal scaffold that satisfies those conditions is shown in Fig. 2. As one can see from this figure, such a scaffold is a set of parallel plates that are permeated with fibers. In this model, proteoglycans connect collagen fibers with one another.

The lattice of an ideal scaffold (Fig. 2) corresponds to tetragonal syngonia. Let us determine the lattice periods a, b, and c. For this purpose, let us introduce the following notations. Let h be the plate thickness, D the fiber diameter, and θ_1 and θ_2 be the relative volumes occupied by the plates and fibers, respectively.

The number of plates N_1 per unit volume equals $N_1 = \theta_1/h$. Therefore, for the identity period $C = 1/N_1$ in the direction of axis 3, we obtain

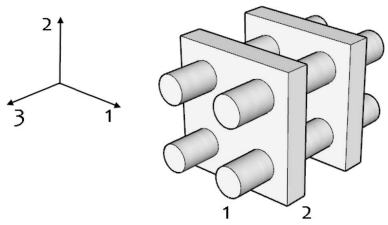

Fig. 2. Schematic diagram of the structure of ideal scaffold: collagen fibers (*1*), proteoglycan layers (plates) (*2*)

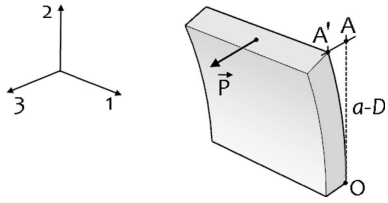

Fig. 3. Schematic diagram of deformation of ideal scaffold

the formula

$$C = h/\theta_1. \tag{8}$$

The number of fibers N_2 per unit volume is equal to $N_2 = 4\theta_2/(\pi D^2)$. The cross-section area per one fiber equals $S = 1/N_2$, so, the identity periods $a = b = \sqrt{S}$ in the directions of axes 1 and 2 are determined by the equality

$$a = b \simeq D/\sqrt{\theta_2}. \tag{9}$$

We will assume that the scaffolds of all regions with local equilibrium are ideal. However, every region has its own spatial orientation of symmetry axes 1, 2, and 3.

6. Local Compliance of Cartilage Tissue

For an ideal scaffold, axes 1, 2, and 3 are the principal axes of the tensor $\hat{S}$. Since we are talking about the tetragonal syngonia, the components of the tensor $\hat{S}$ in this coordinate system form the matrix [19] (here, we use the two-subscript notation)

$$\hat{S} = \begin{bmatrix} S_{11} & S_{12} & S_{13} & 0 & 0 & 0 \\ S_{12} & S_{11} & S_{23} & 0 & 0 & 0 \\ S_{13} & S_{23} & S_{33} & 0 & 0 & 0 \\ 0 & 0 & 0 & S_{44} & 0 & 0 \\ 0 & 0 & 0 & 0 & S_{44} & 0 \\ 0 & 0 & 0 & 0 & 0 & S_{66} \end{bmatrix}. \tag{10}$$

According to the introduced notations, S_{11} is the compliance in the direction of axes 1 and 2, S_{33} is the compliance in the direction of axis 3, S_{66} is the shear compliance in plane 12, and S_{44} is the shear compliance in planes 13 and 23. Taking the relatively large sizes of proteoglycan aggregates into account, it is reasonable to assume that the chain axes in those aggregates are located in planes that are parallel to plane 12. Provided this arrangement and due to the enhanced stiffness of the plates in plane 12, the values of the components S_{11}, S_{12}, and S_{66} have to be relatively small. The same is valid for the values of the components S_{33} and S_{13} owing to the considerable stiffness of the fibers.

From formula (8), the inequality

$$h \ll C \tag{11}$$

follows, which means that the plates cannot produce considerable resistance to the shift of the planes in which the fibers are located. In other words, the value of the component S_{44} is relatively large, namely,

$$S_{44} \gg (S_{11}, S_{12}, S_{13}, S_{33}, S_{66}). \tag{12}$$

In what follows, we consider the deformation behavior of the model in the zeroth approximation in the small parameters S_{11}/S_{44}, S_{12}/S_{44}, S_{13}/S_{44}, S_{33}/S_{44}, and S_{66}/S_{44}, which corresponds to the equality

$$S_{jk} = 0 \quad (j, k \neq 4). \tag{13}$$

Equality (13) excludes the elastic deformation of the fibers, and, according to this equality, the elasticity of cartilage tissue takes place owing to proteoglycans. This statement is consistent with the viewpoint, widespread in the literature [1], on the nature of cartilage tissue elasticity.

7. Mechanism of Cartilage Tissue Deformation

Let $\hat{\sigma}$ denote the local stress tensor. Let the stress σ_{32} induce a simple shear in a region with local equilibrium. Denoting the corresponding shift angle by γ_{32}, we have

$$\gamma_{32} = S_{44}\sigma_{32}. \tag{14}$$

Consider the deformation of a plate section in the form of a square with the sides of the length $a - D$

(Fig. 3). The force P that acts on the upper face of the section is calculated using the equality

$$P = \sigma_{32} h(a - D). \tag{15}$$

Under the action of this force, the section bends. As a result, the upper face shifts by $AA' = \Delta C$ in the direction of axis 3.

Inequality (3) means that all non-equilibrium processes, including the motion of water, have terminated, and the system is in the equilibrium state. In this state, the water is unable to counteract shear stresses; so, this is exclusively the tissue scaffold that does it. Taking all that into account, let us consider the section depicted in Fig. 3 as a beam the end of which undergoes the action of the force P. According to the theory of elasticity [20], we have

$$\Delta C = \frac{P(a - D)^3}{3g}, \tag{16}$$

where g is the bending stiffness of the beam.

According to Fig. 3, $\gamma_{23} = \angle AOA'$. Taking the smallness of elastic deformations into account, we may write the equality

$$\gamma_{23} = \frac{\Delta C}{a - D}. \tag{17}$$

Comparing formulas (17) and (14), we obtain

$$S_{44} = \frac{h(a - D)^3}{3g}. \tag{18}$$

As was indicated above, in the proposed model of an ideal scaffold, the axes of the chains in the proteoglycan aggregate (the plates) are located in planes that are parallel to the plate's surface. Due to the bending of the plate, the axes of those chains also bend. In the case of an isolated chain, its axis bends mainly due to the twist of the links that form the chain's backbone [21]. The energy change owing to such a rotation can be calculated using the force constant of torsional vibrations, K_φ.

Let g_c denote the bending stiffness of the chain, and a_c the link size. Tin view of the stiffness dimensionality, we write

$$g_c = K_\varphi a_c^3. \tag{19}$$

The number n of chains passing through the cross-section of the beam shown in Fig. 3 is determined by the equality

$$n = \frac{h(a - D)}{a_c^2}. \tag{20}$$

Therefore, for the bending stiffness of the beam, we have the expression

$$g = n g_c = K_\varphi a_c h(a - D), \tag{21}$$

and formula (18) takes the form

$$S_{44} = \frac{h(a - D)^2}{3K_\varphi a_c}. \tag{22}$$

Substituting equality (9) into formula (22) and taking the value of θ_1 into account, we obtain

$$S_{44} = \frac{4D^2}{3K_\varphi a_c}. \tag{23}$$

8. Relation between the Compliance and Structure of Cartilage Tissue

As was already mentioned above, the orientation of the principal axes of the tensor $\hat{S}$ is the only random parameter in the proposed model. At the same time, the values of the components of this tensor – they are determined in each of those systems of principal axes – remain constant. Therefore, averaging (7) over the volume can be replaced by averaging over the orientations of the systems of principal axes. Using the four-subscript notation for the tensor components, this operation looks like

$$\hat{S}'_{j'k'\ell'm'} = \hat{S}_{jk\ell m} \langle \alpha_{j'j}\, \alpha_{k'k}\, \alpha_{\ell'\ell}\, \alpha_{m'm} \rangle, \tag{24}$$

where $\alpha_{x'x}$ is the angle between the x'- and x-axes ($x = j, k, \ell, m$), and $\langle ... \rangle$ denotes the averaging operation. The right-hand side of formula (24) implies the summation over the repeating indices. Axes $1'$, $2'$, and $3'$ are the principal axes of the tensor $\hat{S}'$.

Let the possible orientations of the system of principal axes of the tensor $\hat{S}$ be equally probable. In this case, after the averaging over all regions with local equilibrium, cartilage tissue acquires the characteristics of an isotropic homogeneous continuum. Accordingly, after averaging (24) and taking equality (13) into account, the tensor $\hat{S}'$ takes the form

$$\hat{S}' = \frac{S_{44}}{15} \begin{bmatrix} 2 & -1 & -1 & 0 & 0 & 0 \\ -1 & 2 & -1 & 0 & 0 & 0 \\ -1 & -1 & 2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 6 \end{bmatrix}. \tag{25}$$

Formulas (23) and (25) give an answer to the question posed in Introduction about the relation of the tensor $\hat{S}'$ to the structure of cartilage tissue. The structural parameters affecting the tensor $\hat{S}'$ are as follows: K_φ is the power constant of torsional vibrations for the chains of proteoglycan aggregates, a_c is the size of the links in those chains, and D is the diameter of the collagen fiber.

According to expression (25), the following formulas hold for the shear, G, and Young's, E, moduli of cartilage tissue:

$$G = \frac{15}{6S_{44}} = \frac{15K_\varphi a_c}{8D^2}, \tag{26}$$

$$E = \frac{15}{2S_{44}} = \frac{45K_\varphi a_c}{8D^2}. \tag{27}$$

According to [22], $K_\varphi \sim 1$ N/m. Using the approximate values $a_c \approx 10^{-10}$ m and $D \approx 10^{-8}$ m, we obtain the following estimate for G:

$$G \simeq 10^6 \text{ Pa}, \tag{28}$$

which is consistent with experimental data [6].

9. Conclusions

The model proposed in this article describes static elastic deformation of cartilage tissue. This model is characterized by the following structural features.

The matter concerns three structural levels of cartilage tissue: (i) molecular, where the structural elements are links of polymer links, water molecules, and other low-molecular substances; (ii) supramolecular, where proteoglycan aggregates and collagen fibers act as structural elements; and (iii) continuum, where structural elements are regions with local equilibrium.

The structure of a region with local equilibrium is roughly represented in the form of a lattice formed by plates (proteoglycan aggregates) and rods (collagen fibers). At the continuum level, cartilage tissue behaves itself as a randomly heterogeneous continuum.

In the framework of the proposed model, the mechanism of deformation appearance looks as follows. At the molecular level, the chains entering the proteoglycan aggregates bend, but the chains composing the fibers practically do not undergo deformation. At the supramolecular level, the plates (proteoglycan aggregates) bend, whereas the fibers remain practically undeformed. At the continuum level, the values of the components of the local compliance tensor, which characterize the deformation behavior of a region with local equilibrium as a whole, are determined by the total deformation of the plates in this region.

The values of the components of the compliance tensor of cartilage tissue are the values of the corresponding components of the local compliance tensor that are averaged over all regions with local equilibrium. The values of the elastic moduli of cartilage tissue, which are calculated according to the formulas of the proposed model, are equal to 10^6 Pa by order of magnitude, which is consistent with experimental data. According to the presented formulas, these moduli are reciprocal to the square of the fiber diameter; in other words, an increase in the fiber diameter leads to a decrease in the cartilage tissue stiffness.

This result can be used in medical practice. The stiffness of cartilage tissue is known to grow with age. The obtained result suggests a possible way to deal with this phenomenon: a substance that can elevate the probability of formation of links between collagen chains, thus increasing the fiber diameter, has to be introduced into cartilage tissue.

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ДЕФОРМАЦІЯ І СТРУКТУРА
ХРЯЩОВОЇ ТКАНИНИ

Пропонується модель структури хрящової тканини, де остання розглядається як сукупність областей локальної рівноваги. Кожна така область є ґраткою, утвореною пластинами (протеоглікановими агрегатами) та колагеновими волокнами. Деформація хрящової тканини під дією зовнішнього навантаження зумовлена переважно вигином ланцюгів, що входять до складу протеоглікановых агрегатів. Отримано формули для модуля зсуву та модуля Юнга хрящової тканини. Показано, що ці модулі обернено пропорційні квадрату діаметра колагенового волокна, а їхні значення за порядком величини становлять 10^6 Па, що узгоджується з експериментальними даними.

Ключові слова: хрящова тканина, тензор податливостей, модуль зсуву, модуль Юнга.