TOWARDS A DYNAMICAL MODEL OF SKELETAL MUSCLE

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An equation of motion for skeletal muscle is derived, one part of which is fixed, while the other is free. To the latter, active and passive external forces are applied. The obtained nonlinear inhomogeneous differential second-order equation for the muscle length change in time is analytically solved. It is shown that, depending on the parameter values of this equation, the skeletal muscle contraction can have both single and periodic (vibrational) behavior. It is proved that the isotonic muscle contraction begins at the moment, when the strain value of the stressed muscle equals the value of the stress. The limited stress value of the beginning of isotonic muscle contraction and the maximum possible muscular strain are found. In spite of the quantitative differences between theoretical and experimental results, one should notice their qualitative agreement within the framework of the presented model.

Introduction

Muscle, as a complex biophysical system, attracts attention of many researchers. It is conditioned mainly by newly received experimental data [1 – 4] on the analysis of muscle contraction, in particular, of a force which is developed by a skeletal muscle fiber under the influence of loading and electrical stimulation and its dependence on length, speed, and other physical parameters. However, the obtained experimental results did not quite correspond to the postulates of a skeletal muscle contraction model known as the theory of sliding [5 – 6]. Therefore, it is necessary to explain these experimental facts within the framework of a correct mechanism of contraction and to make adequate mathematical formulation.

First of all, it should be noted that all contraction models in one way or another are connected with the dynamics of myosin-actin complex within the sarcomere. For example, the active movable agent of the sliding model [5] is a heavy fraction of myosin (the head of a myosin molecule). Besides, the sliding model has two submodels, one of which is based on the inactivity of the light fraction of myosin and the activity of its heavy fraction, while the other one, on the contrary, is based on the contracting activity of the light fraction with the heavy fraction functioning as a link of myosin and actin filaments. There is another mechanism [7] which shows that the contraction of a skeletal muscle is a result of the twisting of myosin filaments into tubulin form like structures formed by actin filaments. The contraction is possible owing to interdomain motions in two heads of myosin molecules, which move in turn. Pollak's model [1] is based on the 'stepwise" contraction of a muscle fiber. Davydov's model [8] is grounded on motion as well, but that of a soliton which stimulates the reciprocal movement of both myosin and actin filaments. There is another model [9] which is based on the stimulation of α-helix segments of protein, but unlike Davydov's model, this model concentrates not on the soliton motion, but on the deformation reaction of an α-helix to stimulation.

Though the concepts concerning the mechanism of contraction considerably differ, all the existing models are, as stated above, connected with motion ('sliding", 'twisting", 'stepwise shortening"). In addition, this motion should be asynchronous in different parts of sarcomere and at different points of time to provide (during the process of contraction) a constant interaction between actin and myosin. Such an asynchrony means the simultaneous presence of all possible impulse values of moving elements in sarcomere, regardless of what is meant under the 'moving element", that is regardless of the model, and these elements can be considered as a one-dimensional gas of noninteracting particles (at least, in the first approximation). Therefore, it is obvious that in order to explain the experimental data cited in [1 – 4], one should use methods of statistical physics for a one-dimensional gas of noninteracting particles [10].

Model and its discussion

Let us consider a skeletal muscle, one part of which is rigid, while the other – the free one – is stressed M (Fig. 1). It is obvious that the strained muscle will be affected by three external forces: 1) active force as a function of muscle length $f(l)$; 2) force caused by a strain which varies depending on a change of muscle length. It can be, for example, the weight of a load. We label it as passive force $Q(l)$; 3) force of proper resistance of the muscle. It also plays a passive role and does not depend on length l. We denote it as q. Thus, the forces $Q(l)$ and q act as resistant forces to contraction, that is, counteract this contraction, while the active force $f(l)$ produce muscle contraction.

As follows from Fig. 1, the equation of motion of the free end of a muscle is

$$M \ddot{l} = q + Q(l) - f(l). \tag{1}$$

In the case where the stress M is constant, the straining force does not depend on l and has a constant value of Q. Then the equation becomes

$$M \ddot{l} = Q_0 - f(l), \tag{2}$$

where $Q + q = Q_0$ is the constant of the total passive force.

The expression for the active force $f(l)$ is set by the following formula [11]:

$$\varphi(L) = \frac{f(L)}{f_0} = \frac{1}{2L} \frac{L^3 - 0.43}{L^3 - 0.93L^2 + 0.21}. \tag{3}$$

Here, $L \equiv \dfrac{l}{l_0}$, where $l_0 = 2.5\,\mu m$ is the initial length of sarcomere; $f_0 = \dfrac{kT}{l_0}$, where k is the Boltzmann constant and T is the temperature.

However, we cannot use (3) because it is impossible to solve the problem analytically due to complexity of the differential equation (2). Thus, we will use an approximation, which would not lead to a noticeable variance in the definition of the given problem. In this case, the approximation will mean a power L decomposition of function (3) in the Taylor series to the quadratic term included, at the point of maximum $L = 1$. Then we have

$$\varphi(L) \approx 1 + 0.2(L - 1) - 7.3(L - 1)^2. \tag{4}$$

The curve calculated by (4) is presented in Fig. 2. Though this curve qualitatively reproduces the behavior of the dependence $\varphi(L)$, it quantitatively differs from the experimental result [1]. Apparently, the approximate curve does not have such a distinctive feature of the dependence $\varphi(L)$ as its skewness in regard to the maximum. In our case, the approximate curve in regard to the maximum is symmetric.

Using (4), we get

$$f(l) = f_0 \left\{ 1 + 0.2 \left(\frac{l}{l_0} - 1 \right) - 7.3 \left(\frac{l}{l_0} - 1 \right)^2 \right\}. \tag{5}$$
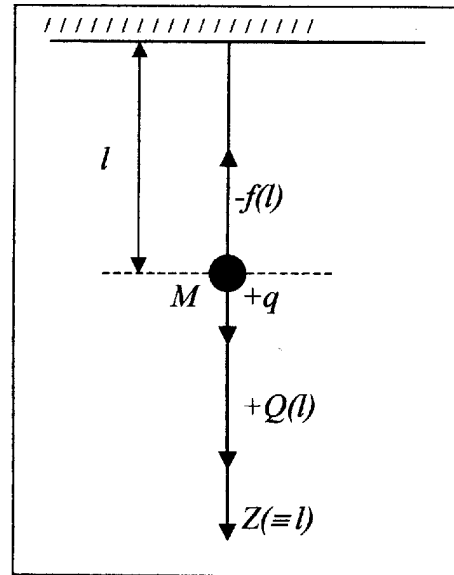

Fig. 1. External forces applied to the free end of a muscle, where l is the length of the muscle and M is the stress
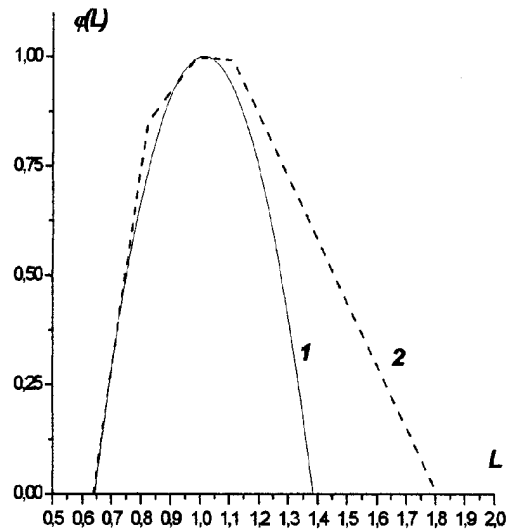

Fig. 2. Curve (1) is a graph of formula (4). Compare: one of the experimental curves (2) [1]

Substituting (5) into (2) gives the nonlinear inhomogeneous differential second-order equation for the function $f(t)$:

$$\ddot{l}(t) - \frac{7.3f_0}{M l_0^2} l^2(t) + \frac{14.8f_0}{M l_0} l(t) - \left\{ \frac{6.5f_0}{M} + \frac{Q_0}{M} \right\} = 0. \tag{6}$$
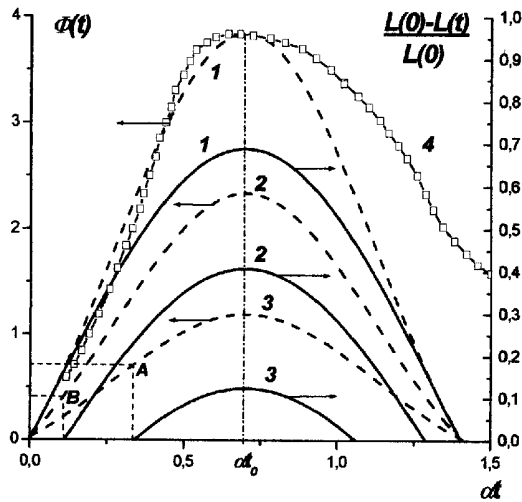
Fig. 3. Dotted curves are graphs of muscle strain, full curves are graphs of single isotonic contraction of a muscle found by formulas (15) and (14) at different values of stress: 1 – $Q_0 = 0$; 2 – $Q_0 = 0.4 f_0$ and 3 – $Q_0 = 0.7 f_0$. Curve 4 is the data of the experiment [5]

As the inhomogeneous part of this equation is a constant, $\left\{\dfrac{6.5 f_0}{M} + \dfrac{Q_0}{M}\right\}$, its solution can be written as

$$l(t) = A + \Psi(t), \tag{7}$$

where A is a constant and $\Psi(t)$ is the function to be determined. Substituting (7) into (6) and stipulating that the constant part of the equation is zero, we obtain an algebraic quadratic equation, from which one finds

$$A \approx l_0 \left(1 \pm 0.4 \sqrt{1 - \frac{Q_0}{f_0}} \right), \tag{8}$$

and the differential equation for the function $\Psi(t)$

$$\ddot{\Psi}(t) - G \Psi^2(t) + \lambda \Psi(t) = 0, \tag{9}$$

where

$$G \equiv \frac{7.3 f_0}{M l_0^2}, \quad \lambda \equiv \frac{14.6 f_0}{M l_0}\left(1 - \frac{A}{l_0}\right). \tag{10}$$

The following analysis of the solution will show which sign should be taken in formula (8).

The solution of (9) can be written as

$$\Psi(t) = \frac{C}{\mathrm{ch}^2(\alpha t)}, \tag{11}$$

where C and α are the constant parameters of the problem.

Substituting (11) into (9), we obtain two relations for the parameters C and α:

$$6\alpha^2 = -GC; \quad 4\alpha^2 = -\lambda, \tag{12}$$

whence

$$\alpha^2 = -\frac{\lambda}{4}; \quad C = 1.5\frac{\lambda}{G}. \tag{13}$$

The detailed analysis of Eq. (13) and solution (11) shows that, in the case of the muscle contraction which is considered as a single contraction – relaxation, we should take $\lambda < 0$ (when $\lambda < 0$, the process of contraction is periodic). In this case, (10) shows that $A > l_0$, and that is why we should leave the solution of (8) with the plus sign. Then we have

$$L(t) = 1 + 0.4 \sqrt{1 - \frac{Q_0}{f_0}}\left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_0)}\right), \tag{14}$$

where t_0 is the time of motion of a muscle (see below).

Substituting (14) into (4) and then into (2), where $M\ddot{l}(t) \equiv F(t)$, we obtain the dependence of the force F of a strained muscle on time:

$$\frac{F(t)}{f_0} \equiv \Phi(t) = \sqrt{1 - \frac{Q_0}{f_0}}\left\{\sqrt{1 - \frac{Q_0}{f_0}} \times\right.$$

$$\times \left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_{0)}}\right)^2 - 0.08\left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_{0)}}\right) -$$

$$\left. - \sqrt{1 - \frac{Q_0}{f_0}}\right\}. \tag{15}$$

Supposing $q \ll Q$, one obtains $1 - \dfrac{Q_0}{f_0} \approx 1 - \dfrac{Q}{f_0}$. Next, $Q = 0$, when the relaxed muscle contracts, then

$$\Phi(t) = 1.17\left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_0)}\right)^2 -$$

$$- 0.08\left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_{0)}}\right) - 1 \tag{16}$$

and

$$L(t) = 1 + 0.4\left(1 - \frac{3}{\mathrm{ch}^2 \alpha(t - t_0)}\right). \tag{17}$$

At the point $t = t_0$, function (16) has a maximum which satisfies the condition $\Phi'(t_0) = 0$. In addition,

the zero points of the function $\Phi(t) = 0$ are symmetric with respect to t_0, and let the left zero point concur with the zero point of time countdown. If $\Phi(t) = 0$, then $\alpha t_H = \alpha t_0 \pm 0.7$, where t_H are the zero points of the function $\Phi(t)$. We put $\alpha t_0 = 0.7$ getting $\alpha t_{H,1} = 0$ and $\alpha t_{H,2} = 1.4$.

The change of the muscle length in time is found according to the equation $\dfrac{L(0) - L(t)}{L(0)} \equiv$ $\equiv \dfrac{l(0) - l(t)}{l(0)}$. By analyzing formula (14), we find that the isotonic contraction does not take place $\left(\dfrac{L(0) - L(t)}{L(0)} = 0\right)$ if $Q_0 = 0.8 f_0$. By formula (15), we find the maximum strain of the muscle $F(t_0) = 0.81 f_0$.

Curves (14) and (15) in Fig. 3 show the isotonic contraction of a muscle at different stress values. Thus, we are able to say that the isotonic contraction begins at the very moment, when the strain value of a stressed muscle equals the value of the stress. Points A and B shown in Fig. 3 satisfy the equation $F(t) = Q_0 = 0.4 f_0$ and $F(t) = Q_0 = 0.7 f_0$, respectively. Comparing the theoretical dependence $\Phi(t)$ with the experimental data [5], it is possible to select the parameter value α. The maximum of the experimental curve which describes the muscle contraction when it is not stressed $(Q_0 = 0)$ is $t_0 \approx 0.2$ s. Then, to compare the theoretical and experimental results, α should equal 3.5 s^{-1}.

Thus, in spite of the quantitative differences between the theoretical and classical experimental results [1, 5], we should emphasize their qualitative agreement within the framework of the mathematical approximation which is analyzed in the thermodynamic model of single skeletal muscle contraction [11].

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