Biophysical Chemistry 118 (2005) 113 – 117

Biophysical Chemistry

http://www.elsevier.com/locate/biophyschem

Cooperative behaviour of the elementary sarcomere units and the cross-bridge step size

Enrico Grazi *, Cristina Di Bona

Dipartimento di Biochimica e Biologia Molecolare, Università di Ferrara, Via Borsari 46, 44100 Ferrara, Italy

Received 18 June 2005; received in revised form 15 July 2005; accepted 15 July 2005

Abstract

We present a model of muscle contraction based on purely physical grounds and modulated by a parameter, k, related to the visco-elastic hindrances of the contractile apparatus. The model predicts a strong cooperation among sarcomere units and proposes that viscous hindrance is a fundamental component of the economy of the contraction. The concept of cross-bridge step size is also discussed and it is concluded that the step size is of various and probably undeterminable length.

Keywords: Sarcomere; Units; Cooperativity

1. Introduction

The relationship between load and rate of muscle contraction is usually explained by the Eyring's theory [1] of the visco-elastic behaviour of high molecular weight polymers and by the Kramers' theory of chemical reactions [2]. Essentially the rate constant of the contraction, k_+, is assumed to depend exponentially on the free energy required to attain the transition state and that this free energy barrier changes with the elastic energy associated with the load. Thus the rate constant, k_+, depends on the load. On the contrary the rate constant for the reverse reaction, k_-, is independent on the load. On these grounds fairly accurate models were presented suitable to describe even subtleties of muscle contraction [3–5].

Our present aim is to describe muscle contraction on purely physical grounds. The energy made available by the hydrolysis of ATP promotes the sliding of the thin filament and of the attached load. The rate of the contraction is modulated by a parameter, k, related to the visco-elastic hindrances of the contractile apparatus. The model, perhaps naïve, reproduces the force–velocity curve and demonstrates that contractile mechanisms are inescapably influenced by viscous hindrance. The model also predicts a strong cooperation among sarcomere units. The concept of cross-bridge step size is also discussed and it is concluded that the step size is of various and probably indeterminable length.

2. The model

2.1. The elementary unit of the sarcomere

We define as the elementary unit of the sarcomere each thick filament with the surrounding crone of the six thin filaments. During contraction thin filaments move towards the center of the sarcomere. The thin filaments are anchored to the Z-disc so that, when sarcomere shortens, Z-disc and the thin filament move, all together, toward the center of the sarcomere [25]. The linear rate of the Z-disc and of the thin filaments is therefore the same as the rate of sarcomere shortening. Thus, although the elementary units can be considered separately, these in fact belong to a single, coherent system, the whole sarcomere.

---

* Corresponding author. Tel.: +39 0532 291421; fax: +39 0532 202723.
E-mail address: gre@unife.it (E. Grazi).

0301-4622/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.bpc.2005.07.005

The sarcomere is assumed to be composed by $n = 2000$ elementary units [6], its cross-section is,

$$s_S = n\ 3\ \sqrt{3}/2\ r^2, \tag{1}$$

and the fraction of the half sarcomere mass, m_1, which might move with the Z-lines, thin filaments and sarcoplasm separating thin from thick filaments, is,

$$m_1 = n\left(\rho\ 3\ \sqrt{3}/2\ r^2\ l_S/2 - 300\ \mathrm{MW_M}/(2N)\right), \tag{2}$$

where $\rho = 1.035\ \mathrm{g\ cm^{-3}}$ is the density of frog sartorius muscle [7]; $r = 25$ nm is the distance between the centers of two adjacent actin filaments; $l_s = 2.7\ \mu\mathrm{m}$ is the sarcomere length; 300 is the number of the myosin molecules in the tick filament; $\mathrm{MW_M}$ is the molecular mass of myosin, 407 kDa [10]; and N is the Avogadro's number.

2.2. The power stroke

The power stroke is powered by the hydrolysis of ATP, which, in muscle conditions, releases approximately 7.44 10^{-8} pJ per molecule (E_{ATP}) [8]. Power strokes occur randomly and the sequence of these events produces muscle contraction.

Energy and force delivered by the power stroke are linked by,

$$E_{\mathrm{ATP}} = F_1 l, \tag{3}$$

where F_1 is the average force over the distance l at the beginning of the contraction and l is the sliding of thick and thin filaments past each other, provided that E_{ATP} is used up completely and that the movement occurs without hindrance.

In the presence of a load per unit area, P, the opposing force, F_2, is

$$F_2 = 2 s_S P, \tag{4}$$

(the factor of 2 accounts for the fact that only about half of the total cross-section of the fiber is occupied by the contractile machinery [9]) and the driving acceleration is,

$$a_d = (F_1 - F_2)/(m_1 + m_2), \tag{5}$$

m_2 is the mass of the load pertaining to the sarcomere section,

$$m_2 = s_S P/a_L, \tag{6}$$

where a_L is the acceleration associated with the load, not necessarily the acceleration of gravity.

2.3. The effect of the power strokes in the absence of any hindrance

The force generated by a single power stroke is about 8 pN [9,11] and, in general, it is much lower than F_2 so that it is necessary to sum up the energy delivered by the power strokes. This is possible if the frequency of the power strokes exceeds a given level, so that not all the energy provided by a power stroke is used up before the following power stroke, performed by another attached cross-bridge, occurs. This condition is fulfilled if the space, l_A, traveled in the time between two power strokes, is lower than $l = E_{\mathrm{ATP}}/F_1$, so that the fraction left of the original energy, $|l_A|/l$, adds to the energy provided by the subsequent power stroke. To summarize, l is constant, its value is defined by Eq. (3), where the value of F_1 is that at the starting of the contraction. In the transient phase of the contraction both F_1 and l_A change. At the steady state both F_1 and l_A are constant the driving acceleration, a_d, approaches zero. Thus bound cross-bridges make a translation of $|l_A| < l$ whose value changes with the progress of the contraction and becomes fairly constant at the steady state

The iteration procedure is as follows,

The energy left after the $(i-1)$th cycle is,

$$E_{R(i-1)} = E_{T(i-1)} |l_{A(i-1)}|/l, \tag{7}$$

the total energy available in the ith cycle is,

$$E_{T(i)} = E_{\mathrm{ATP}} + E_{R(i-1)}, \tag{8}$$

$$F_{1(i)} = E_{T(i)}/l, \tag{9}$$

$$a_{d(i)} = \left(F_{1(i)} - F_2\right)/(m_1 + m_2), \tag{10}$$

l_A is given by,

$$l_{A(i)} = v_{(i-1)} t_{AT} + a_{d(i)} t_{AT}^2/2, \tag{11}$$

and the velocity $v_{(i)}$,

$$v_{(i)} = v_{(i-1)} + a_{d(i)} t_{AT}, \tag{12}$$

where t_{AT} is the time between the power strokes.

Thus at any cycle the energy available, the contractile force and the driving acceleration change. In the first cycle, $E_T = E_{\mathrm{ATP}}$ and $v = 0$.

2.4. The effect of the power stroke in the presence of viscous hindrance

According to Szymanski [12] and Muller [13], in the presence of a viscous hindrance, an hyperbolic form is assigned to the velocity, v_V, of the masses, m_1 and m_2, which move under the effect of the force F_1

$$v_V = k\ a_d\ t/(k + t), \tag{13}$$

where the reciprocal of the constant, k, defines the hindrance. In our system, since driving acceleration is changing at every cycle,

$$v_{Vi} = v_{v(i-1)} + i_{vv}, \tag{14}$$

where i_{vv} is the increment of velocity in the time t_{AT} is,

$$\begin{aligned} i_{vv} = {} & k\ a_d\ i\ t_{AT}/(k + i\ t_{AT}) - k\ a_d\ (i-1)\ t_{AT} \\ & /(k + (i-1)\ t_{AT}), \end{aligned} \tag{15}$$