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# Modeling of muscle activity of human organism

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*Abstract:* Muscle contraction mechanism has been studied on microlevel (chemical reactions in a sarcomere) and macrolevel (consideration of the muscle as a whole). Parallel computations have been used for quantitative estimation for the systems' parameters. On microlevel muscle contraction mechanism is based on interaction between actin and myosin filaments and can be described by a chemical reaction which has a mathematical model in the form of ordinary differential equations system. The most effective for solution of inverse kinetic problem for this system is a parallel variant of genetic algorithm. Its correctness has been improved on a macrolevel during estimation of different fibers amount in the muscle.

## 1. Introduction

Studying of processes in contracting muscles is one of the most important and topical problems of biomechanics as all the functioning of a human organism is associated with muscular activity. Each muscle disfunction can cause different pathologies and even lethal outcome.

Investigation of any compound object can be implemented on several levels:

- megalevel (for our research it is the whole human organism);
- macrolevel (a separate muscle);
- mesolevel (a myofibril);
- microlevel (a sarcomere).

Authors started with investigation of microlevel.

## 2. Mechanism of sarcomere contraction

It can be seen under a microscope that each sarcomere consists of numerous parallel thick (myosin) and thin (actin) filaments. Thick and thin filaments cooperate by crossbridges which are located along thick filaments, and muscle length changes. Interaction between actin and myosin

filaments is realized due to energy released under ATP molecule degradation to ADP and phosphoric acid. This process can be described by reaction including 7 reversible stages and 10 agents [1]:

$$X_0 + 2X_1 \leftrightarrow 2X_2, \tag{1}$$

$$2X_2 \leftrightarrow 2X_3 + X_4, \tag{2}$$

$$2X_3 \leftrightarrow X_5, \tag{3}$$

$$X_5 \leftrightarrow X_6, \tag{4}$$

$$X_6 \leftrightarrow X_7 + 2X_9, \tag{5}$$

$$X_6 \leftrightarrow X_0 + 2X_8 + 2X_9, \tag{6}$$

$$X_7 \leftrightarrow X_0 + 2X_8. \tag{7}$$

Here $X_0$ is actin-myosin complex, $X_1$ – ATP, $X_2$ – complex of myosin and ATP, $X_3$ – complex of myosin, ATP and phosphorus, $X_4$ – hydrogen ion, $X_5$ – complex of actin-myosin, ADP and phosphorus, $X_6$ – energy-active conformation of $X_5$, $X_7$ – complex of actin-myosin and ADP, $X_8$ – ADP, $X_9$ – phosphorus.

A mathematical model for the chemical reaction of sarcomere contraction has been developed and implemented. It is based on mass action law and represents a Cauchy problem for the system of ordinary nonlinear differential equations:

$$\begin{cases}
\frac{dx_0}{dt} = -k_1 x_0 (x_1)^2 + \bar{k}_1 (x_2)^2 + k_6 x_6 - \bar{k}_6 x_0 (x_8)^2 (x_9)^2 + k_7 x_7 - \bar{k}_7 x_0 (x_8)^2; \\
\frac{dx_1}{dt} = -2k_1 x_0 (x_1)^2 + 2\bar{k}_1 (x_2)^2; \\
\frac{dx_2}{dt} = 2k_1 x_0 (x_1)^2 - 2\bar{k}_1 (x_2)^2 - 2k_2 (x_2)^2 + 2\bar{k}_2 (x_3)^2 x_4; \\
\frac{dx_3}{dt} = 2k_2 (x_2)^2 - 2\bar{k}_2 (x_3)^2 x_4 - 2k_3 (x_3)^2 + 2\bar{k}_3 x_5; \\
\frac{dx_4}{dt} = k_2 (x_2)^2 - \bar{k}_2 (x_3)^2 x_4; \\
\frac{dx_5}{dt} = k_3 (x_3)^2 - \bar{k}_3 x_5 - k_4 x_5 + \bar{k}_4 x_6; \\
\frac{dx_6}{dt} = k_4 x_5 - \bar{k}_4 x_6 - k_5 x_6 + \bar{k}_5 x_7 (x_9)^2 - k_6 x_6 + \bar{k}_6 x_0 (x_8)^2 (x_9)^2; \\
\frac{dx_7}{dt} = k_5 x_6 - \bar{k}_5 x_7 (x_9)^2 - k_7 x_7 + \bar{k}_7 x_0 (x_8)^2; \\
\frac{dx_8}{dt} = 2k_6 x_6 - 2\bar{k}_6 x_0 (x_8)^2 (x_9)^2 + 2k_7 x_7 - 2\bar{k}_7 x_0 (x_8)^2; \\
\frac{dx_9}{dt} = 2k_5 x_6 - 2\bar{k}_5 x_7 (x_9)^2 + 2k_6 x_6 - 2\bar{k}_6 x_0 (x_8)^2 (x_9)^2;
\end{cases} \tag{8}$$

with initial conditions:

$$x_i(t_0) = x_i^0. \tag{9}$$

Here $x_i$, $i=1,\ldots,9$ are concentrations of substances taking part in muscle contraction act; $k_i$ and $\bar{k}_i$ (i=1,…,7) are kinetic constants of direct and inverse stages correspondingly; $t$ is the time of reaction passing; $t_0$ is initial time.

Investigation of the muscle contraction process includes solution of direct and inverse problems. Direct problem consists in solution of the system (8)-(9) with fixed values of kinetic parameters, and inverse problem – recovery of model parameters on the base of experimental data.

Direct problem has been solved by Kutta-Merson method with automatic choice of integration step. Inverse problem solution for the system (8)-(9) reduces to series of direct problems consideration and discrepancy functional minimization:

$$F = \sum_{i=1}^{N} \sum_{j=1}^{n} \frac{1}{x_{ij}^{exp}} \left| x_{ij}^{calc} - x_{ij}^{exp} \right| \quad \left( x_{ij}^{exp} > 0 \right), \tag{10}$$

Here $x_{ij}^{calc}$ are calculated values, $x_{ij}^{exp}$ are experimental data, $N$ is the number of experiment points, $n$ is the number of reaction agents.

When solving the inverse problem the most effective is genetic algorithm. Authors have adapted this algorithm to considered problem solution (figure 1), and to accelerate the calculation it was decided to use technologies of parallel computations.

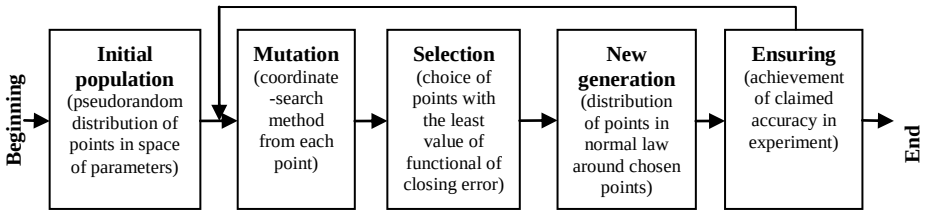


**Figure 1.** Genetic algorithm

To accelerate the calculation it was decided to use technologies of parallel computations. Paralleling of computing process is made at the stage of initial population forming when points in space of parameters are distributed to processors of multiprocessor computation system. Time of offline work of processors significantly exceeds time of their interaction at a selection stage that conditions efficiency of the given algorithm.

A computational experiment on the supercomputer MVS-100K of RAS Joint supercomputer center has been conducted. This multiprocessor computation system consists of 11680 processing cores and has peak performance about 140 TFlops.

Estimation of parallel program effectiveness showed that the most optimal at this point is use of 9-11 processors (figure 2).

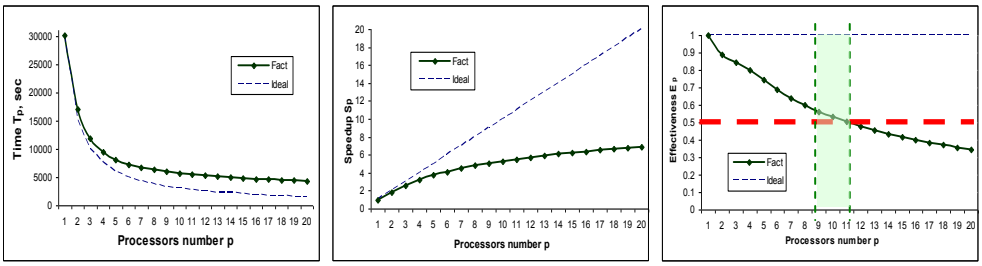


**Figure 2.** Analysis of parallel program effectiveness

These results are obtained on a model experiment. Having carried out the research at microlevel authors faced with a problem of experiment data absence and impossibility of its getting. It was decided to revert to the macrolevel and to investigate the muscle as a whole making experiments together with biologists of Bashkir state university.

## 2. Muscle fibers consideration

Today the most popular is three-component muscle model according to which a muscle consists of retractive component and elastic component, and elastic component subdivides into sequential and parallel parts (figure 3) [2].

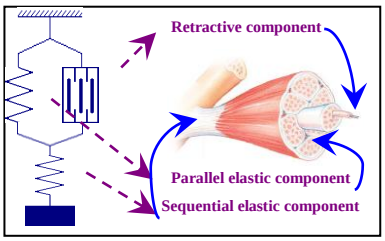


**Figure 3.** Three-component muscle model

One of the founders of muscle biomechanics A. Hill making experiments at a Sartorius muscle of a frog evolved the dependence between tension and contraction rate of a muscle [3]:

$$\frac{v}{l_0} = \frac{\frac{b}{l_0}\left(1 - \frac{P}{P_0}\right)}{P + a}. \qquad (11)$$

Here $P/P_0$ is the ratio of tension to the maximum tension under zero load, $a$ and $b$ are constants of the process (for frog's Sartorius $a/P_0=0.25$, $b/l_0=0.325$).

On the base of series of experiments Hill made a conclusion that muscle consists of fibers which differ essentially in their characteristic velocities that is maximum rates of shortening under zero load. All processes pass more quickly in fast fibers, active state develops and dams in them earlier.

To estimate distribution of muscle fibers by characteristic velocities Hill took several variants of distribution, put them to the formula and compared obtained results with the diagram. As a result he chose a symmetrical distribution (table 1). The total amount of fibers there was 82, and average velocity of the whole muscle equals 1.4.

**Table 1**

Distribution of muscle fibers by characteristic velocities

| ***v0, l0*/sec** | 2.4 | 2.2 | 2 | 1.8 | 1.6 | 1.4 | 1.2 | 1 | 0.8 | 0.6 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***n*** (Hill) | 1 | 3 | 7 | 13 | 17 | 17 | 13 | 7 | 3 | 1 |

Authors decided to test this hypothesis. At that characteristic velocities less than $1\ l_0$/sec were left out, because their presence hadn't been verified experimentally.

With the use of genetic algorithm we have found the closest distribution to the experiment (figure 4).

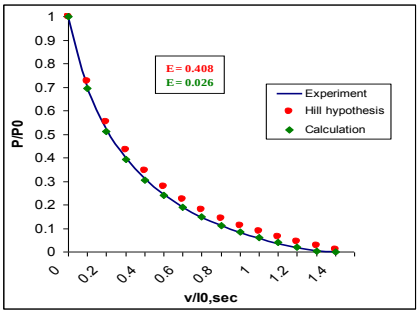


**Figure 4.** Comparison of calculation, Hill hypothesis and experiment

But specific character of considered problem is that the whole amount of probable distributions is finite, that is, using modern information technologies one can look through all the variants and don't miss any of them. So it was decided to look through all possible variants and thus to control the convergence of genetic algorithm. The authors have developed a "throwing over" algorithm which looks over just required variants of distribution (where the sum of fibers equals 82) and selects a

distribution minimizing deviation between calculated values and experimental curve which is presented on the figure 4.

A formula estimating the number of all probable variants has been elaborated.

$$\mathrm{vars}(m,N)=\frac{(N-1)!}{(N-m)!(m-1)!} \tag{12}$$

For considered case vars*(8,82) = 81!/(74*!7!) ≈ *3.5·10*$^9$. The program makes about *3.2·10*$^5$ iterations per second, so program execution time on *10* processors of the supercomputer MVS-100K is less than *30* minutes.

With the use of developed algorithm a muscle fibers distribution which provides the nearest approach to experimental curve has been found. It equals the distribution obtained with the use of genetic algorithm, and this shows that the latter is correct.

So by means of computational experiment it has been shown that the most part of a muscle is made up of fibers which have small characteristic velocities. But it also includes more fast fibers the velocity of which amounts to *2.4* $l_0$/sec.

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