Sensitivity of the amplitude of the single muscle fibre action potential to microscopic volume conduction parameters

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Abstract—A microscopic model of volume conduction was applied to examine the sensitivity of the single muscle fibre action potential to variations in parameters of the source and of the volume conductor, such as conduction velocity, intracellular conductivity and intracellular volume fraction. The model results show that the sensitivity to the intracellular and extracellular conductivity depends on the distance from the source. The action potential amplitude is strongly influenced by the intracellular volume fraction. In this frequency-dependent model the amplitude is influenced by the conduction velocity to a smaller degree than predicted by previous studies, which use a noncapacitive homogeneous volume conductor model.

Keywords—Conduction velocity, Extracellular conductivity, Intracellular action potential, Intracellular conductivity, Membrane impedance, Single-fibre action potential, Volume conduction

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1 Introduction

AT MICROSCOPIC scale skeletal muscle tissue as an electrical conductor is characterised by the intra- and extracellular conductivities (σ_i and σ_e , respectively), the impedance of the muscle fibre membrane Z_m and by parameters which describe the tissue structure. In model studies extracellular action potentials are often simulated with a macroscopic approximation in which skeletal muscle tissue is assumed to be a noncapacitive, homogeneous, anisotropic volume conductor (NANDEKAR and STÅLBERG, 1983; ROSENFALCK, 1969). In such an approach the tissue is electrically characterised by parameters observed at large, macroscopic scale, namely the conductivities normal and parallel to the fibre direction (EPSTEIN and FOSTER, 1983; ZHENG *et al.*, 1984).

ALBERS *et al.* (1986) introduced a microscopic volume conductor model which accounts for the tissue structure and the microscopic electrical parameters. Conduction of current normal to the fibre direction occurs almost solely through the extracellular medium, owing to the high value of the membrane impedance. Parallel to the muscle fibre direction and close to the site of current injection a major part of current is conducted through the extracellular medium. However, at larger distances from the source,

current is redistributed over the intra- and extracellular medium. Owing to the larger volume of intracellular space at larger distances the intracellular properties play a more dominant role. Single-fibre action potentials (SFAPs) simulated with this microscopic model differed significantly from results obtained with a homogeneous volume conductor model within a range of 300 μm from the excited muscle fibre (ALBERS *et al.*, 1988b).

In the present paper the sensitivity of the SFAP to microscopic volume conductor properties is studied in relation to variation of source and conductor parameters. The results of this study allow conclusions as to the degree in which any uncertainty in the model parameters is reflected in simulated single-fibre electromyographic signals. This is of importance as there is considerable scatter in the literature concerning experimentally determined parameter values.

2 Simulation model

The microscopic volume conductor model has been described in detail by ALBERS *et al.* (1986). It is summarised in Fig. 1. The muscle fibre membrane is represented by a parallel circuit of the membrane conductance and the membrane capacitance. The current source is a discrete representation of a small part of an excited muscle fibre. The frequency-dependent potential distribution in the network is solved numerically.

The current through a membrane part with length L is given by

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Fig. 1 Model structure of the microscopic volume conductor model. In the figure the transformation into an electrical network representation is also illustrated. Current is injected at the six extracellular nodes of the central fibre (nodes indicated with arrows). The parameters of the model are: σ_i , σ_e : intra- and extracellular conductivities; G_m , C_m : membrane conductance and membrane capacitance. $2A$: fibre diameter; d : thickness of extracellular layer around the fibres. The intracellular volume fraction p is defined as the intracellular volume divided by the total volume. For this model structure $p = (A/(A + d))^2$

$$I_m(z) = \pi A^2 L \sigma_i \frac{\partial^2 V_i(z)}{\partial z^2} \quad (1)$$

with $z = Ut$ the position along the excited fibre, U is the conduction velocity and t the time. σ_i is the intracellular conductivity and $2A$ is the fibre diameter (see Fig. 1)

An empirical expression (after ROSENFALCK, 1969) was used to calculate the intracellular action potential V_i :

$$V_i(z) = \alpha z^3 \exp(-\beta z) - \gamma \quad (2)$$

The parameters α , β and γ determine the shape of the intracellular action potential.

Expressed in the time domain eqn. 1 transforms to

$$I_m(t) = \frac{\pi A^2 L \sigma_i}{U^2} \frac{\partial^2 V_i(t)}{\partial t^2} \quad (3)$$

Note that variation of the conduction velocity U causes no changes in $V_i(z)$ but only in $V_i(t)$.

3 Parameter values

Parameter values used in this sensitivity analysis were based on experimental data from rat EDL muscle. A reference set of parameters and the range in which these parameters were varied is given in Table 1. A number of

experimental methods are reported in the literature to determine the extracellular space in skeletal muscle. The different methods result in a wide range of values for the intracellular volume fraction p (Fig. 1). In the present analysis the reference value ($p = 0.90$) as well as the variation of this parameter was based on KOBAYASHI and YONEMURA (1967), who reported the extracellular space in rat EDL muscle to vary between 6 and 16 per cent of the entire muscle volume.

For the intracellular conductivity σ_i in rat EDL muscle KUYOHARA and SATO (1967) measured a value of $0.57 (\Omega \text{ m})^{-1}$. A reliable value for σ_e in the *in vivo* situation is not available. The expressions for the low frequency limit of the homogeneous transverse conductivity σ_r and the homogeneous axial conductivity σ_z (GIELEN *et al.*, 1986)

$$\sigma_r = \frac{1-p}{1+p} \sigma_e$$

$$\sigma_z = (1-p)\sigma_e + p\sigma_i$$

offer the possibility to relate a choice of σ_i and σ_e with actual measurements of σ_r and σ_z . With the range for σ_i and σ_e indicated in Table 1, and with $p = 0.90$, σ_r varies between 0.10 and $0.13 (\Omega \text{ m})^{-1}$ and σ_z varies between 0.59 and $0.93 (\Omega \text{ m})^{-1}$. These values of σ_r and σ_z are consistent with data reported by GIELEN *et al.* (1984, in rat EDL), and with measurements of EPSTEIN and FOSTER (1983) and ZHENG *et al.* (1984) carried out in dog, rabbit and chicken muscle.

With respect to the membrane capacitance DULHUNTY *et al.* (1984) found a value of $C_m = 0.067 \text{ F m}^{-2}$ for rat

Fig. 2 Two intracellular action potentials used in the simulations. Action potential I: $\alpha = 1800 \times 10^6 \text{ V m}^{-3}$; $\beta = 3 \times 10^3 \text{ m}^{-1}$; $\gamma = 0.075 \text{ V}$. Action potential II: $\alpha = 536 \times 10^6 \text{ V m}^{-3}$; $\beta = 2 \times 10^3 \text{ m}^{-1}$; $\gamma = 0.075 \text{ V}$. In all figures usage of these action potentials will be indicated by the symbols I and II

Table 1 Parameter set

	Parameter	Reference value	Range	Unit
Intracellular conductivity	σ_i	0.75	0.45–0.75	$\Omega^{-1} \text{ m}^{-1}$
Extracellular conductivity	σ_e	1.80	1.80–2.50	$\Omega^{-1} \text{ m}^{-1}$
Membrane conductance	G_m	1.0		$\Omega^{-1} \text{ m}^{-2}$
Membrane capacitance	C_m	0.01	0.005–0.04	F m^{-2}
Fibre radius	A	25		μm
Thickness of extracellular layer	d	1.35		μm
Intracellular volume fraction	p	0.90	0.85–0.95	—
Conduction velocity	U	5	3–7	m s^{-1}

EDL muscle. This value includes the capacitance of the transverse tubular membrane, whereas it is not clear in how far the latter takes part in volume conduction. In analysing their results, DULHUNTY *et al.* (1984) assumed a value of 0.01 F m^{-2} , for the surface membrane. In this paper a value of 0.01 F m^{-2} is used as the reference value. The conduction velocity in rat EDL muscle varied between the experimentally observed values of about 3 and 7 m s^{-1} (ALBERS, 1987).

Two intracellular action potential shapes, calculated with eqn. 2, were used (Fig. 2), giving rise to two membrane currents with different amplitude. For these action potentials, if converted to time functions, the risetime is approximately $140 \mu\text{s}$ if the conduction velocity has a value of 4 m s^{-1} for action potential I and 6 m s^{-1} for action potential II. This value for the risetime is consistent with data of the rat EDL reported by WALLINGA-DE JONGE *et al.* (1985).

4 Results

Parameter values are varied as indicated in Table 1. If the value of a parameter is not specified, its value of the reference set is accepted (Table 1).

4.1 Intra- and extracellular conductivities

Fig. 3a shows two SFAPs at a radial distance of $53 \mu\text{m}$ from the centre of the excited fibre, simulated with different values of σ_i . In this figure V_{tt} and V_1 are defined. For these simulations intracellular action potential I from Fig. 2 was used. Fig. 3b and 3c show the amplitude V_{tt} as a function of σ_i for radial distances of $53 \mu\text{m}$ and $279 \mu\text{m}$. The value of the intracellular conductivity σ_i influences both the volume conductor and the amplitude of the membrane current (eqn. 1).

Fig. 3b shows that close to the fibre the relative variation in the SFAP amplitude is comparable to the relative variation in σ_i . Hence, almost the entire variation in V_{tt} can be explained by source variations, due to the different values of σ_i (see eqn. 1). At a larger radial distance (Fig. 3c) this dependence of the source on σ_i is still the same; nevertheless the relative increase in V_{tt} is much less than the increase in σ_i . This reflects the increasing influence with radial distance of the volume conductor effect of σ_i . Comparison of Fig. 3b and 3c also shows that the influence of a variation in σ_e becomes slightly smaller for increasing radial distance.

Fig. 3 (a)

Fig. 3 (a) SFAPs simulated at a distance of $53 \mu\text{m}$ from the centre of the excited muscle fibre with different values of σ_i . The values of σ_i are given in $(\Omega \text{ m})^{-1}$. Intracellular action potential I from Fig. 2 was used. V_{tt} and V_1 are defined in this figure. (b) The peak-to-peak amplitude of the SFAP as a function of σ_i , for intracellular action potentials I and II of Fig. 2 and simulated with different values of σ_e (in $(\Omega \text{ m})^{-1}$). The radial distance is $53 \mu\text{m}$. (c) As in (b), for a radial distance of $279 \mu\text{m}$

4.2 Muscle membrane capacitance and conduction velocity

The value of the membrane capacitance C_m determines the sensitivity of the SFAP amplitude to the conduction velocity and the action potential type (I and II). Results are shown in Fig. 4. The conduction velocity only slightly

Fig. 4 Sensitivity to the conduction velocity at (a) 53 μm and (b) 234 μm from the excited fibre and for different values of the membrane capacitance C_m (given in 10^{-3} F m^{-2}). Broken lines: intracellular action potential I; Solid lines: intracellular action potential II

influences the SFAP amplitude in the case of a combination of a high value for C_m and a slow intracellular action potential (type II).

The conduction velocity affects the time course of the membrane current (eqn. 3) and also, but in an opposite way, the transfer function between source and position of extracellular registration. The latter function contains the properties of the conducting medium as well as the effects of propagation of the intracellular action potential along

Fig. 5 Peak-to-peak amplitude as a function of the intracellular volume fraction for two values of σ_e . Radial distances are (a) 53 μm and (b) 234 μm . Values of σ_e are given in $(\Omega \text{ m})^{-1}$

the fibre (ALBERS *et al.*, 1988a).

The ultimate effect of a variation in the conduction velocity is the result of these two opposite effects.

4.3 Intracellular volume fraction

The SFAP amplitude appears to be very sensitive to the value assigned to the intracellular volume fraction p (Fig. 5).

This sensitivity depends on the value of σ_e and the radial distance from the excited fibre, and is different for the two types of intracellular action potentials. At a distance of 234 μm (Fig. 5b) the sensitivity to p is smaller than closer to the fibre (Fig. 5a).

Another SFAP parameter which was studied in relation to changes in the intracellular volume fraction is the ratio between the amplitude V_1 of the first action potential phase and the top-to-top V_{tt} (Fig. 6), which is a well observable quantity in measured SFAPs. The ratio V_1/V_{tt} appears to be sensitive to the value of the intracellular volume fraction as well as to the action potential shape.

5 Discussion

Simulation results concerning the sensitivity to the conduction velocity (Fig. 4) show a variety of possible dependences of SFAP amplitudes on velocity. Amplitudes can be almost independent of velocity when membrane capacitance is high or radial distance is small (Figs. 4a and 4b). The other extreme approaches an inversely proportional dependence when capacitance is small, the source is fast (type I) and radial distance is large (Fig. 4b, upper curve). This latter dependence is almost in accordance with the simulation results of NANDEKAR and STÅLBERG (1983) in a homogeneous, noncapacitive, anisotropic volume conductor model. They obtained an inversely proportional dependence of SFAP amplitudes with conduction velocity. One should expect such an accordance because for smaller capacitances, faster sources and larger radial distances our microscopic nonhomogeneous capacitive model can be substituted more and more satisfactorily by the macroscopic, homogeneous and noncapacitive approach (ALBERS *et al.*, 1986; 1988a; 1988b).

Close to the fibre the amplitude of the first phase of the SFAP can equal that of the second phase (Fig. 6), i.e. the ratio V_1/V_{tt} is about 0.5. (It has to be emphasised that the ratio V_1/V_{tt} depends strongly on the applied source function. If, for example, the tripole model had been used (ROSENFALCK, 1969; GRIEP *et al.*, 1982), the amplitude of the first phase of the membrane current would always be

Fig. 6 Ratio between amplitude of the first phase of the action potential and the peak-to-peak amplitude as a function of the radial distance from the centre of the excited fibre, and for an intracellular volume fraction of 0.85 and 0.95. Broken lines: intracellular action potential I; solid lines: intracellular action potential II

smaller than that of the second phase). In published work on recorded SFAPs it is observed that V_1/V_{tt} has a maximum of about 0.3–0.4 (EKSTEDT, 1964; GATH and STÅLBERG, 1978). Our own experience is that V_1/V_{tt} ratios of about 0.5 are frequently observed in human SFEMG recordings. As well as recording distance, many other causes influence the ratio, such as the actual shape of the recording electrode, the filter settings used in a SFAP recording and the shape of the membrane current of the excited fibre.

In the sensitivity analysis presented in this paper the influence of one single parameter at a time was studied, under the condition that all other parameters were unchanged. In practice this condition will not easily be satisfied. For instance, it is unlikely that pathologies will influence only one property while leaving the remaining properties unaffected: for example KERR and SPERELAKIS (1983) reported differences between normal and dystrophic muscles of the mouse in the passive volume conductor properties as well as in the shape of the intracellular action potential. Therefore, changes in the SFAP amplitudes will most likely be the result of the change of several parameters.

The relationship between a SFAP parameter and a parameter concerning the source or the volume conductor is not unique. Fig. 6, for instance, illustrates that using intracellular action potential II instead of potential I has almost the same effect on the ratio V_1/V_{tt} as increasing the extracellular volume fraction from $p = 0.90$ to $p = 0.95$. Other examples can be observed in Fig. 3c and 5b. Therefore, the dependence of the SFAP on the large set of parameters incorporated in the microscopic model is not easy to analyse under experimental conditions. The similar effects of variations in different parameters suggest that a set of SFAP features should be used to describe the action potential shape.

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