Resting membrane potential of skeletal muscle calculated from plasma and muscle electrolyte and water contents

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INTRODUCTION

Among the fundamental properties of living cells is the ability to maintain a normal transcellular gradient of electrolytes. This requires the consumption of energy for transport of Na⁺ out of the cell, resulting in a high extra- to intra-cellular concentration gradient for Na⁺, while K⁺, in contrast, has a concentration gradient in the opposite direction. An electrical potential difference is thereby generated across the cell membrane. The resting membrane potential (RMP) in mammalian skeletal muscle is about −90 mV [1–5] and is essentially the consequence of the K⁺ concentration ratio existing across the sarcolemmal membrane, the permeability of K⁺ being about 100-fold higher than that of Na⁺. It has also been demonstrated that Cl⁻ is passively distributed across the sarcolemmal membrane and that its distribution can be predicted according to Nernst's equation, if the RMP is known [6]. In earlier studies, RMP in muscle has been determined by introducing a Ling type of microelectrode into the muscle cell and directly measuring the potential difference. This method has been used in several experimental studies and has also been used in a few studies in humans, in whom the electrode was introduced by the percutaneous technique [1, 2]. The technique is elaborate and time-consuming, and has been used in only a few clinical studies. From the results of such studies and experimental data it is evident that RMP is a sensitive index of metabolic derangement, low RMP having been found in sick patients with severe chronic illnesses and high RMP in clinical and experimental K⁺ depletion.

In this paper, we present an indirect method for calculating RMP in muscle across the sarcolemmal membrane from water and electrolytes determined in plasma and muscle specimens and combining two equations, the Goldman equation modified by Hodgkin and Horowitz [7], which expresses the relation between extra- and intra-cellular Na⁺ and K⁺ concentration and RMP, and the Nernst equation, which independently expresses the relation between extra- and intra-cellular Cl⁻ concentration and RMP [6]. This method of calculation has been

1. A method is described that enables the calculation of resting membrane potential from the electrolyte and water contents in blood plasma and in a sample of human muscle tissue obtained by the percutaneous needle-biopsy technique. In this calculation, the previously described equations for calculating resting membrane potential via the intra- and extra-cellular distribution of chloride were combined with the equation utilizing potassium distribution over the cell membrane.

2. The method of calculation was applied to 60 healthy subjects divided into three groups aged 19–40, 41–60 and 61–85 years. The calculated resting membrane potential in the subjects as a whole was −88.4 mV (SD 1.35; n = 60). A lower value was observed in the group aged 61–85 years (−87.7 mV, SD 1.0; n = 12) than in the group aged 19–40 years (−88.6 mV; SD 1.4; n = 32). No difference was observed between female and male subjects.

3. The RMP calculated with the present method in 60 healthy subjects was also compared with previously published values in healthy subjects, measured by the Clarke electrode method, and with values calculated from electrolyte and water distribution measured by isotope-dilution techniques. The results obtained in healthy subjects with different techniques were very similar. Data were analysed from earlier published studies in experimental animals in which resting membrane potential ranged from −91 to −65 mV. The resting membrane potential calculated from electrolytes in plasma and muscle showed a very good agreement with resting membrane potential recorded directly.

Key words: electrolytes, intracellular concentrations, muscle, resting membrane potential, water distribution.
Abbreviations: DPH, diphenylhydantoin; FFS, fat-free solids; HD, haemodialysis; H₂Oₑ, extracellular water content; H₂Oᵢ, intracellular water content; H₂Oₜ, total water content in muscle; Kₑ, muscle content of potassium; Naₑ, muscle content of sodium; Clₑ, muscle content of chloride; Kᵢ, intracellular potassium concentration; Naᵢ, intracellular sodium concentration; Clᵢ, intracellular chloride concentration. [Kₑ], [Naₑ], [Clₑ], plasma concentrations of potassium, sodium and chloride. [Kᵢ], [Naᵢ], [Clᵢ], extracellular concentrations of potassium, sodium and chloride; NEPH, nephrectomy; RMP, resting membrane potential.
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applied to two previously published studies of muscle electrolytes in men from our laboratory [8, 10], and also to three animal studies, published by other groups [3, 4, 12]. The animal studies contained both measured values of electrolyte and water in plasma and muscle and RMP measured with electrodes, and by water distribution estimated by the isotope-dilution technique. Calculated and directly measured RMP could thus be compared.

MATERIALS AND METHODS
From Forsberg et al. [8], with the addition of data from ten more subjects

Sixty healthy subjects (28 women and 32 men) took part in the investigation. Their age ranged from 19 to 85 years. All had normal body weight in relation to height (body mass index range 19–25.1 kg/m²). The subjects in the age group 19–60 years (48 subjects) were all hospital staff, but two of the remaining 12 subjects aged 61–85 years were retired healthy subjects and ten were patients admitted to hospital for minor surgery, i.e., inguinal hernia (nine subjects) or varicose veins (one subject). All subjects were in normal physical condition, without intensive training programme or abnormal inactivity. The surgical patients were admitted to hospital on the day of surgery and were not physically disabled by the disorders. Blood samples obtained before the investigation showed normal ranges for haemoglobin, blood cell content and electrolyte concentrations, as well as for plasma proteins and plasma enzyme activities. All subjects volunteered to participate in the study, which was approved by the Ethics Committee of Karolinska Institute.

Needle-biopsy samples weighing 50–100 mg were obtained from the lateral portion of the quadriceps femoris muscle by needle biopsy, as described by Bergström et al. [9]. The samples were dissected free from blood and visible connective tissue, weighed repeatedly for extrapolation of the wet weight to time zero, frozen in liquid nitrogen and freeze-dried after storage for a maximum period of 3 days at −70°C. The freeze-dried samples were weighed, fat-extracted in petroleum ether for 60 min, dried at room temperature and re-weighed. The weight was fat-free solids referred to as (FFS). The sample was powdered in an agate mortar and freed from flakes of visible connective tissue. The powder was divided into portions, approximately 2.5 mg for the analyses of electrolytes, and the rest for other analyses (total creatine, DNA, RNA, alkali-soluble proteins and amino acids). The electrolyte samples were dried at 80°C for 30 min. This procedure reduced the weight by 4–6%.

Na⁺ and K⁺ were extracted with 100 μl of HNO₃ (1 mol/l) per mg of muscle powder, ultra-sonicated for 15 min, left overnight, and then mixed and centrifuged. A portion (100 μl) of the supernatant was diluted with 1.0 ml of HNO₃ (1 mol/l) and 9.0 ml of an ionization and compensation solution [1.25 mmol/l CaCO₃, 12.4 μmol/l Fe(NO₃)₃, 0.5 mmol/l H₂SO₄, 5.9 mmol/l H₃PO₄] and analysed in an Atomic Absorption Photometer (IL 751) against standard solutions [9]. Cl⁻ content was analysed in the same supernatant with electrometric titration against silver nitrate using a Radiometer pH-meter 62 [9].

From Bergström and Fridén [10]

Ten healthy subjects, aged 24–35 years, were examined by means of needle biopsies taken from the quadriceps femoris muscle before administration of hydrochlorothiazide and amiloride. Venous blood was collected from a cubital vein at the time of biopsy, care being taken to avoid errors due to sampling and handling of the samples [11]. The subjects were not on a controlled diet and their water and salt intakes were not restricted. The muscle biopsies were performed between 08.00 and 10.00 hours after an overnight fast.

Muscle and blood samples were analysed as described in [10]. These results were used in our calculation of RMP.

From Williams et al. [3, 4]

All experiments were performed on male Sprague–Dawley rats weighing 110–150 g. Body temperature during the experiment was maintained at 36–37°C. Each rat received ouabain (10 mg/kg body weight) 1 h before killing, and diphenylhydantoïn (DPH; 40 mg/kg) at 40, 20 and 8 h and a final injection 2 h before killing. A comparable amount of control solution was given to control rats. In the nephrectomy (NEPH) experiment, rats were bilaterally nephrectomized 1 or 24 h before killing. All animals received [³H]inulin and the 1 h inulin space was used as a measure of the extracellular space for calculating the intracellular water and the electrolyte concentrations. RMP was recorded with a micro-electrode in the anterior gracilis muscle 10 min before killing. The indifferent electrode was a silver wire inserted into the peritoneal cavity of the rat.

Rats were then exsanguinated via the terminal aorta, and this was followed by collection of samples from the gracilis muscle for radioactivity and electrolyte determinations. The plasma and muscle water and electrolyte contents were used in our calculations of RMP.

From Guisado et al. [12]

Studies were performed on five separate groups of adult dogs. All but the control animals were made acutely uraemic by bilateral uretal ligation.

Skeletal muscle biopsies (vastus lateralis muscle) were obtained after a period of equilibrium of 1–2 h.
in control and uraemic animals and at the end of haemodialysis (HD) in all other dogs. The animal groups consisted of six normal dogs, five dogs with uraemia of 3.5 days' duration, eight uraemic dogs that were rapidly dialysed with standard dialysate solutions and two additional groups treated with HD, where the dialysate was modified to maintain a constant plasma osmolality during dialysis by addition of either glycerol (four dogs) or mannitol (eight dogs), at concentrations of 50–75 mmol/l.

Na\(^+\), K\(^+\) and water contents were determined in plasma and dry muscle tissue. Extracellular space (H\(_2\)O\(_e\)) was determined by intravenous administration of 200 \(\mu\)Ci of \(^{33}\)S\(_{O}{_4}^-\), calculated by evaluating the distribution of \(^{33}\)S\(_{O}{_4}^-\) in muscle tissue relative to plasma dialysate. RMP was determined from intra- and extra-cellular concentrations of K\(^+\) and Na\(^+\) assuming a permeability constant for sodium of 0.01.

In the calculation of RMP, from plasma and muscle water and electrolyte contents presented in [3], [4] and [12], we used the mean values in each experimental series, since no individual values were given.

**Calculations**

According to current literature, there are two ways [6, 7] to calculate the RMP:

\[
\text{RMP} = \frac{R \times T}{F} \ln \left( \frac{[\text{Cl}]_i}{[\text{Cl}]_e} \right) \tag{1}
\]

and

\[
\text{RMP} = \frac{R \times T}{F} \ln \left( \frac{[\text{K}]_e + 0.01 \times [\text{Na}]_e}{[\text{K}]_i} \right) \tag{2}
\]

Intracellular concentrations of Cl\(^-\) and K\(^+\) have been expressed by Cunningham et al. [2] as follows:

\[
[\text{Cl}]_i = \frac{[\text{Cl}]_m - [\text{Cl}]_e \times \text{H}_2\text{O}_e}{\text{H}_2\text{O}_i}
\]

\[
[\text{K}]_i = \frac{\text{K}_m - [\text{K}]_e \times \text{H}_2\text{O}_e}{\text{H}_2\text{O}_i}
\]

where H\(_2\)O\(_e\) = H\(_2\)O\(_m\)−H\(_2\)O\(_i\)

The equations for [Cl] and [K] can be expressed as:

\[
[\text{Cl}] = \frac{[\text{Cl}]_m - [\text{Cl}]_e \times (\text{H}_2\text{O}_m - \text{H}_2\text{O}_i)}{\text{H}_2\text{O}_i}
\]

\[
[\text{K}] = \frac{\text{K}_m - [\text{K}]_e \times (\text{H}_2\text{O}_m - \text{H}_2\text{O}_i)}{\text{H}_2\text{O}_i}
\]

The two expressions (1 and 2) denoting the RMP give the equation:

\[
\frac{[\text{Cl}]_i}{[\text{Cl}]_e} = [\text{K}]_e + 0.01 \times [\text{Na}]_e
\]

With the expression denoting [Cl] and [K] (both unknown values) in the equation above gives:

\[
\frac{[\text{Cl}]_m - [\text{Cl}]_e \times (\text{H}_2\text{O}_m - \text{H}_2\text{O}_i)}{[\text{Cl}]_e \times \text{H}_2\text{O}_i} = \frac{\text{H}_2\text{O}_i \times ([\text{K}]_e + 0.01 \times [\text{Na}]_e)}{\text{K}_m - [\text{K}]_e \times (\text{H}_2\text{O}_m - \text{H}_2\text{O}_i)}
\]

In this equation, all values are measured values, except H\(_2\)O\(_i\):

\[
\text{H}_2\text{O}_i = -\frac{B}{2A} \pm \sqrt{\left(\frac{B}{2A}\right)^2 - \frac{C}{A}}
\]

where:

\[
A = 0.01 \times [\text{Na}]_e \times [\text{Cl}]_e
\]

\[
B = 2 \times [\text{K}]_e \times [\text{Cl}]_e \times \text{H}_2\text{O}_m - \text{K}_m \times [\text{Cl}]_e - [\text{Cl}]_m \times [\text{K}]_e
\]

\[
C = \text{H}_2\text{O}_m \times ([\text{Cl}]_m \times [\text{K}]_e + \text{K}_m \times [\text{Cl}]_e - [\text{K}]_e \times [\text{Cl}]_e - \text{H}_2\text{O}_m) - \text{K}_m \times [\text{Cl}]_m
\]

There are two solutions to this equation of the second degree, but only one is correct if the intracellular water is not to exceed the total muscle water:

\[
\text{H}_2\text{O}_i = -\frac{B}{2A} \mp \sqrt{\left(\frac{B}{2A}\right)^2 - \frac{C}{A}}
\]

RMP can be calculated when the intracellular content H\(_2\)O\(_i\) is known, which also gives the [Cl]\(_i\), [Na] and [K]\(_i\).

With measured values of blood plasma concentrations of electrolytes and electrolyte and water content in muscle from the five refs. [8], [10], [3], [4] and [12], one can calculate RMP.

The extracellular Cl\(^-\) concentration was calculated from the plasma concentration, which was corrected for protein content and Donnan equilibrium (0.96),

\[
[\text{Cl}]_e = [\text{Cl}]_p / 0.96 \times [\text{H}_2\text{O}]_p
\]

\[
[\text{H}_2\text{O}]_p = 0.984 - 0.000718 \times \text{[total protein]}_p \ (g/l)\ [13]
\]

where [H\(_2\)O\(_p\)] is the plasma water.

Interstitial concentrations of potassium and sodium, [K]\(_e\) and [Na]\(_e\), are assumed to be the same as the plasma values [14].

**Grouping of the material and statistical methods**

Data are given as means with SD and the number of subjects [mean (SD; n)], and are calculated for the whole experimental group or for groups divided according to age. Group I comprised 32 subjects,
aged 19–40 years, with a mean age of 27.9 years, group II contained 16 subjects aged 41–60 years of age, with a mean age of 49.3 years, and group III contained 12 subjects aged 61–85 years, with a mean age of 71.1 years.

The subjects were also divided into women \((n = 28)\), with a mean age of 39.5 years, and men \((n = 32)\), with a mean age of 44.6 years.

Statistical calculations of RMP (Table 2) were based on one-way analyses of variance (ANOVA). Differences were determined at the 95% level of confidence, and \(P < 0.05\) was considered significant.

**RESULTS**

Electrolytes and RMP in normal subjects (Table 1)

Electrolyte content related to FFS, content of electrolytes in plasma, water content and distribution and intracellular concentrations of electrolytes, mean values and SDs, from females and males aged 19–85 years from the present study and recalculated values from ten healthy subjects from Bergström and Fridén [10] are presented. In our earlier paper [8], there were 50 subjects aged 19–85 years. We have analysed samples from ten more healthy subjects, seven of them in the groups aged more than 41 years.

The calculated RMP values, \(-88.4\) mV (SD 1.4; \(n = 60\)) and \(-88.8\) mV (SD 1.9; \(n = 10\)), differed very little from the predicted value of \(-87.2\) mV used in [8] and [10]. The calculated intracellular electrolytes were therefore nearly the same as in [8] and [10].

RMP with different age and gender (Table 2)

RMP, mean values, SDs and numbers, calculated with the present formula in the different age and sex groups are presented. Marginal decreases in RMP were found with advancing age, but there were no differences between female and male subjects.

Considering a 95% confidence interval, age group III (61–85 years) showed a significantly lower RMP than age group I (19–40 years).

Experimentally varied RMP in rat (Fig. 1)

Membrane potentials measured in rats with electrodes *in vivo*, by Williams et al. [3, 4], compared with RMP calculated with the formulae from this study are presented. The first study from [3], consisted of seven controls and seven ouabain-treated rats. In the second study from ref. [4], there were five control rats, six treated with DPH, six with ouabain and five with DPH and ouabain. The third study from [4] consisted of six rats analysed 1 h after NEPH and six rats analysed 24 h after NEPH. The mean value of RMP from different treatments varied between \(-91\) and \(-65\) mV, measured with electrodes, and between \(-92\) and \(-67\) mV, calculated with the present method.

Experimentally varied RMP in dogs (Fig. 2)

Calculated membrane potentials from isotope measurements of water distribution in normal dogs [12] are compared with RMP, calculated by the present formula, using blood plasma and muscle values from [12]. In this study there were six normal dogs, five uremic dogs, eight dogs treated with HD, four dogs treated with HD and glycerol and eight dogs treated with HD and mannitol.

The mean value of RMP from different treatments varied between \(-85.7\) and \(-71.4\) mV, calculated from isotope-measured H2O2, and between \(-88.2\) and \(-72.2\) mV, calculated by the present method.

**DISCUSSION**

After many years of muscle sampling using percutaneous biopsy, this now established method permits tissue to be obtained for determinations of water, electrolytes and various metabolites in humans under different experimental and clinical conditions. One difficulty in such studies is distinguishing precisely between the intracellular and extracellular parts of a substance which is present both in the extracellular and intracellular fluids, since the analysis of a muscle specimen gives only the total

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**Table 1. Muscle and plasma electrolytes and water, and calculated water distribution and RMP.** The muscle electrolyte and water contents are referred to FFS.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total water (kg FFS)</th>
<th>Cl(^{-}) (mmol/kg FFS)</th>
<th>Na(^{+}) (mmol/kg FFS)</th>
<th>K(^{+}) (mmol/kg FFS)</th>
<th>Cl(^{-}) (mmol/l)</th>
<th>Na(^{+}) (mmol/l)</th>
<th>K(^{+}) (mmol/l)</th>
<th>Protein (g/l)</th>
<th>H2O2 (l/kg FFS)</th>
<th>H2O2 (l/kg FFS)</th>
<th>[K(^{+})] (mmol/1 H2O2)</th>
<th>[Na(^{+})] (mmol/1 H2O2)</th>
<th>[Cl(^{-})] (mmol/1 H2O2)</th>
<th>RMP (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19–40</td>
<td>3.33</td>
<td>61.1</td>
<td>87.9</td>
<td>442</td>
<td>106</td>
<td>140</td>
<td>4.1</td>
<td>71</td>
<td>2.93</td>
<td>0.41</td>
<td>151</td>
<td>10.4</td>
<td>4.34</td>
<td>-88.4</td>
</tr>
<tr>
<td>41–60</td>
<td>3.37</td>
<td>60.3</td>
<td>93.2</td>
<td>467</td>
<td>104</td>
<td>143</td>
<td>4.1</td>
<td>75</td>
<td>2.96</td>
<td>0.41</td>
<td>157</td>
<td>11.8</td>
<td>4.21</td>
<td>-88.8</td>
</tr>
<tr>
<td>61–85</td>
<td>3.37</td>
<td>11.9</td>
<td>15.2</td>
<td>9</td>
<td>104</td>
<td>143</td>
<td>4.1</td>
<td>75</td>
<td>2.96</td>
<td>0.41</td>
<td>157</td>
<td>11.8</td>
<td>4.21</td>
<td>-88.8</td>
</tr>
</tbody>
</table>

From Forsberg et al. [8] \((n = 60)\)

Mean 42 3.33 61.1 87.9 442 106 140 4.1 71 2.93 0.41 151 10.4 4.34 -88.4

SD 10 0.12 16.6 18.1 14 5 2 0.2 4 0.11 0.15 5 3.2 0.26 1.4

From Bergström and Fridén [10] \((n = 10)\)

Mean 29 3.37 60.3 93.2 467 104 143 4.1 75 2.96 0.41 157 11.8 4.21 -88.8

SD 5 0.12 11.9 15.2 9 2 1 0.3 5 0.09 0.10 4 2.1 0.24 1.9
amount, while muscle tissue, in addition to the myocytes, contains an extracellular phase (interstitial fluid plus connective tissue). Cl⁻ has a high extracellular concentration gradient (about 26:1) provided that RMP is normal, implying that most of the Cl⁻ content in muscle is extracellular. Based on determinations of Cl⁻ in muscle and plasma (extracellular fluid), an estimate of the extracellular water content can be obtained, assuming RMP, and the Cl⁻ distribution, to be normal. The intracellular water content can then be calculated from the total water content and the intracellular concentration can be calculated for any substance determined both in plasma and in muscle. However, it is obvious that under conditions when RMP is low this method will yield erroneous values.

To establish the normal variation of RMP, we used previously published muscle and plasma water and electrolyte data from two studies in healthy subjects, in which we assumed RMP to be −87.2 mV, i.e., the average value obtained by the microelectrode method in healthy subjects, as reported earlier [1]. The studies consisted of 60 subjects, ranging in age from 19 to 85 years, in which the average RMP was −88.4 mV (SD 1.35) with a significant decrease in RMP with age between the oldest and the youngest groups: 19–40 years, −88.6 mV (SD 1.4; n = 32), 41–60 years, −88.4 mV (SD 1.3; n = 16) and 61–85 years, −87.7 mV (SD 1.0; n = 12). No significant variation could be attributed to gender (Table 2).

In a further study of 10 subjects, aged 28.7 years (SD 4.7 years), we found by our indirect method that the mean RMP was −88.85 mV with an SD of less than ±2 mV, the mean value being in close agreement with the assumed value based on data from the literature. Since the average normal muscle RMP calculated by our indirect method is in close agreement with the values −87.2, −88.8 and −89 mV published in [1], [2] and [15], using other methods and showing only a small interindividual variation (Table 3), we feel confident that, under normal conditions in the resting state, an approximation of RMP as −88 mV in the calculation of the Cl⁻ distribution, intracellular concentrations of electrolytes and other compounds seems to be appropriate.

Table 2. RMP calculated with the present formula in the different age and sex groups. Statistical significance: *P<0.05 compared with group I.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (years)</th>
<th>RMP (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (19–40 years)</td>
<td>27.9</td>
<td>−88.6 (SD 1.4; n = 32)</td>
</tr>
<tr>
<td>II (41–60 years)</td>
<td>49.3</td>
<td>−88.4 (SD 1.3; n = 16)</td>
</tr>
<tr>
<td>III (61–85 years)</td>
<td>71.7</td>
<td>−87.7 (SD 1.0; n = 12)*</td>
</tr>
<tr>
<td>Female</td>
<td>39.5</td>
<td>−88.7 (SD 1.0; n = 28)</td>
</tr>
<tr>
<td>Male</td>
<td>44.6</td>
<td>−88.1 (SD 1.5; n = 32)</td>
</tr>
</tbody>
</table>

Table 3. Comparison between RMP in healthy human subjects using different methods.

<table>
<thead>
<tr>
<th>Method</th>
<th>Reference</th>
<th>Age (years)</th>
<th>RMP (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With electrodes, micropuncture technique</td>
<td>Bolte et al. [1]</td>
<td>28.9</td>
<td>−87.2 (SD 1.4; n = 19)</td>
</tr>
<tr>
<td>With electrodes, micropuncture technique</td>
<td>Cunningham et al. [2]</td>
<td>28.9</td>
<td>−88.8 (SD 1.3; n = 26)</td>
</tr>
<tr>
<td>Water shift with isotope-dilution technique</td>
<td>Sjögard et al. [15]</td>
<td>Young males</td>
<td>−89.0 (range 88–92; n = 6)</td>
</tr>
<tr>
<td>Calculated with present formula</td>
<td>Values from Bergström and Frörén [10]</td>
<td>28.7±4.7 (SD)</td>
<td>−88.9 (SD 1.3; n = 10)</td>
</tr>
<tr>
<td>Calculated with present formula</td>
<td>Values from present study</td>
<td>42.2±18.2 (SD)</td>
<td>−88.4 (SD 1.4; n = 60)</td>
</tr>
</tbody>
</table>

Fig. 1. Comparison between RMP calculated with the present method and RMP measured with electrodes, in rats without and with different treatments, by Williams et al. [3, 4]
Under pathological conditions when RMP is reduced, it is desirable to have an accurate value for RMP in the calculation of intracellular concentrations, instead of using a hypothetical RMP. This is now possible using our new method, without having to measure RMP directly with an electrode or use a complicated isotope-dilution method. Comparisons between the RMP calculated from electrolyte measurements and measurements with the Clarke electrode in rats and from isotope-dilution methods in dogs are presented in Figs. 1 and 2. The RMP varied in the animal experiments using ouabain, DPH and NEPH treatments. Evidently, accurate measurements of RMP can be obtained with the described method, which would be of interest for understanding the pathophysiology in various conditions associated with electrolyte abnormalities, energy depletion, intoxications and muscle fatigue. We expect that our method of measuring RMP, which we now apply to earlier muscle biopsy studies performed under pathological conditions, will be used extensively in the future to obtain more precise information regarding the impact of cell membrane transport, extracellular distribution of various substances and intermediary metabolism for muscle cell integrity and function.

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