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Sodium lactate solutions characterization using Electrochemical Impedance Spectroscopy

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Abstract—Lactate is an important metabolite in human body and, among possible medical applications, it can be used to monitor physical activity. Actually, its concentration represents a clear indication whether optimal training intensity is kept or if muscles are under anaerobic conditions. Routine procedures to measure lactate concentration during physical activity are represented by invasive measurements, which require blood sampling from the patient or the athlete. So, a great advantage would be derived by the possibility to monitor this analyte using non-invasive techniques. Considering the possibility to measure lactate in human sweat during sport activities, this paper presents the characterization of saline aqueous solutions containing sodium lactate by means of Electrochemical Impedance Spectroscopy (EIS). Measurements were performed using a two-electrode electrochemical cell and acquired spectra were analyzed also by means of equivalent electrical circuit (EEC) modeling. Results show an effect due to lactate concentration on solution impedance in the high-frequency region of spectrum, where a change in solution resistance is measured. At the same time, no changes in the measured capacitance were found. Future work will study the electrochemical behavior of lactate solutions also at higher frequencies to further investigate the possible use of EIS for lactate levels monitoring during sport activities.

Index Terms—Electrochemical Impedance Spectroscopy, Lactate, Non-invasive measurements

I. INTRODUCTION

Lactate is an important metabolite in human body and it is of great relevance in many physiological processes. Its concentration in blood and tissues is correlated to important diseases such as hypoxia, cardiogenic shocks or respiratory failures, but also to physical activity intensity [1]. Actually, lactate is the final product of tissue glucose metabolism in anaerobic conditions and by monitoring its levels it is possible to identify anaerobic thresholds for athletes [2]. So it is of great interest to find innovative methods to measure lactate concentration in body fluids in real time during physical exercise, perhaps integrating them in more complex

platforms able to provide additional information on the athlete performance [3].

Lactate concentration varies depending on the fluid in which it is measured. In blood, it ranges from 0.6 mM to 2.0 mM at rest, but it increases up to 20 mM or 30 mM during physical activity. If sweat is taken into account, lactate concentration varies from 4-25 mM at rest to 80-100 mM when intense physical activity is carried out [4]. Even if measuring lactate level in sweat would be more advantageous in terms of detection limits and needed measurement sensitivity, the so called 'gold standard' is represented by measurements performed collecting small blood samples, which are then analyzed using laboratory equipment such as Gas Chromatography (GC) and High Performance Liquid Chromatography (HPLC) [5], [6]. As a matter of fact, this procedure has huge drawbacks in terms of costs and of needed expertise to perform the measurements. Because of this, many studies addressed the topic of monitoring lactate concentration in body fluid aiming at developing enzymatic biosensors capable to assess athletes performance and identify their lactate threshold [7], [8]. They generally rely on amperometric techniques, based on the reaction of lactate with lactate oxidase, which leads to formation of pyruvate and hydrogen peroxide [9].

An additional possibility, not fully investigated yet, is represented by the lactate measure in human sweat by means of Electrochemical Impedance Spectroscopy (EIS). Actually, using this technique it would be possible to perform the measurement without any blood sampling, but just relying on two electrodes in contact with the skin. Apart from non-invasiveness, additional advantages coming from the use of EIS would be the limited amount of time needed to acquire the measurement, the possibility to develop wearable instrumentation and the limited overall cost for the equipment. To the best of Authors' knowledge, the first in-vivo studies

concerning the use of EIS for lactate monitoring in athletes were published on journals in 2017 [10]. In that paper the lactate threshold of professional rowers was assessed by bioimpedance measurements and the data were correlated to the results from the invasive ones. An equivalent electrical circuit was proposed to model the muscle and the interface between the electrode and the skin. In particular, it was shown that electrode capacitance variations could give a good estimation of the lactate threshold. Even though these early results from an in-vivo study look promising, a clear understanding of the mechanism responsible for this sensitivity has not been reached yet. Thus, additional benefits for the use of EIS in lactate monitoring could derive from in-vitro measurements, which allow researchers to face an experiment fully under control and without the variability due to biological aspects.

Considering the current lack of comprehensive scientific literature about lactate monitoring by means of EIS, the present work aims at characterizing saline solutions containing different concentrations of this analyte, with the final aim to investigate if it would be feasible to assess lactate concentration in in-vivo applications during sport activity. The paper is organized as follows: in Section II the experimental methodology is presented, describing the measurement setup, in Section III main results are reported, showing the effect of lactate concentration on impedance spectra, finally in Section IV conclusive remarks are summarized.

II. MATERIALS AND METHODS

Analyzed solutions were prepared adding different amounts of sodium L-lactate ($NaC_3H_5O_3$, purchased from Sigma-Aldrich) to deionized water containing 8.0 g/L of sodium chloride ($NaCl$, purchased from Sigma-Aldrich). Six sets of samples were produced, obtaining the following lactate concentrations: 0 mM, 1.0 mM, 5.0 mM, 20.0 mM, 40.0 mM, and 100.0 mM.

EIS measurements were performed at room temperature using an IVIUM-n-Stat potentiostat. A 10 mV sinusoidal signal was used, applied in the frequency range from 10^0 Hz to 10^5 Hz. 5 Points per frequency decade were acquired in each measurement; each solution sample was analyzed three times and the presented impedance spectra are the resulting average. Measurements were performed in a two-electrode configuration, using two pins from a female SMA jack (RND 205-00505) respectively as working and counter electrode, as described in [11]. The distance between the two pins was fixed and equal to 3.6 mm, so the measured solution resistance was not influenced by distance between the two electrodes. Using a two-electrode configuration has some limitations, such as the influence of electrode-solution interface in the measured impedance, but on the other hand it allows to conceive simple and low-cost solutions for the instrumentation in future applications [12].

Measurement error was computed as 'Type-A' uncertainty, using the formula:

$$U = \sqrt{\frac{\sum_{i=1}^N (x_i - x_{av})^2}{N - 1}} \quad (1)$$

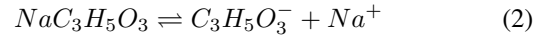
where N is the number of repetitions and x_{av} is the average value for that sample.

Impedance spectra were further analyzed using Equivalent Electrical Circuit (ECC) modeling, which was performed using the IviumSoft software (Release 4.982).

III. RESULTS AND DISCUSSION

Analyzed lactate concentrations were chosen to be significant in sport activity monitoring. 1 mM is a typical lactate concentration at rest and, if the physical exercise keeps in aerobic range, the value does not exceed 5 mM. During prolonged physical exercise, lactate concentration can increase up to the values of 20 mM and 40 mM, or even 100 mM.

Results from EIS measurements are reported in Fig. 1 as Bode diagrams. As can be seen, all solutions exhibit a resistive behavior at high frequency, namely close to 10^5 Hz, and a capacitive one in the central part of the investigated frequency range. Main differences among samples are evident in the impedance modulus in the frequency decade from 10^4 Hz to 10^5 Hz. Actually, higher is the lactate concentration, lower is the impedance value measured in this part of spectrum. This behavior is related to the fact that sodium lactate is an ionic compound, that, when dissolved in water, leads to the dissociation reaction:



and thus to an increase in solution conductivity due to higher concentration of charge carriers. Analyzing the spectrum region at lower frequencies, differences among samples are less evident. In particular, the only observed variation is in the phase values in the frequency decade from 1 Hz to 10 Hz, where samples containing 0 mM and 1.0 mM of lactate reach higher values. The Authors consider this phenomenon less relevant for the performed investigation, because it is related to the interface between the solution and the electrode and not strictly to the solution properties. Actually, a higher phase value in this part of the spectrum reflects a change toward a resistive behavior and thus a lower resistance to charge transfer. As the aim of the present study is to characterize the electrochemical behavior of the lactate solutions, this feature in the impedance spectra is considered less significant.

As a final remark, it is worth to notice that the slope of the impedance modulus as a function of frequency is almost constant for all samples. From graphical interpretation of Bode diagrams, this is related to the double layer capacitance, which results to be not affected by lactate concentration [13].

A. Equivalent Electrical Circuit

In order to analyze more in depth the electrochemical system under study, impedance spectra were modeled using EEC. Thanks to this technique, it is possible to derive the transfer function which fits best the experimental impedance

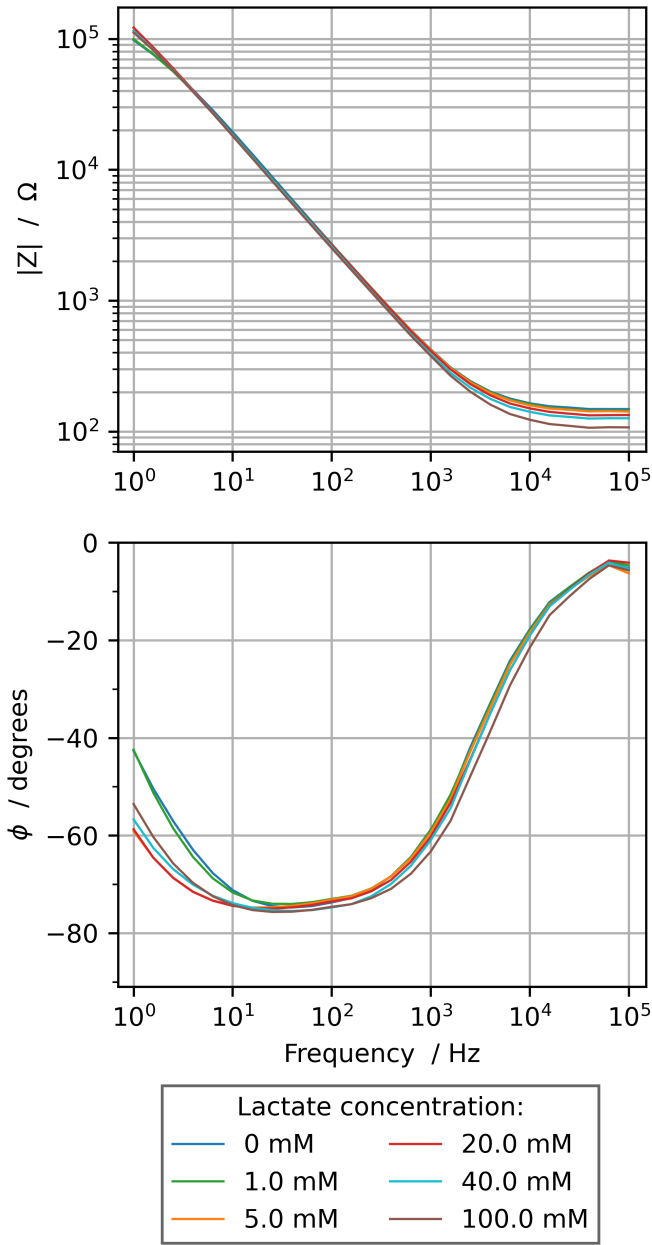


Fig. 1. Impedance spectra, presented as Bode diagrams, acquired analyzing different solutions containing 8 g/L of NaCl and an increasing concentration of lactate

spectra and thus derive appropriate values for the physical parameters that describe the investigated system.

All acquired spectra are characterized by a single time constant, as it is evident from the trend of the phase values. Thus a simplified Randle circuit was used for EEC, as shown in Fig. 2, which is composed of the following elements:

- solution resistance (R_s), which is represented by the impedance modulus at high frequency, where phase is close to zero;

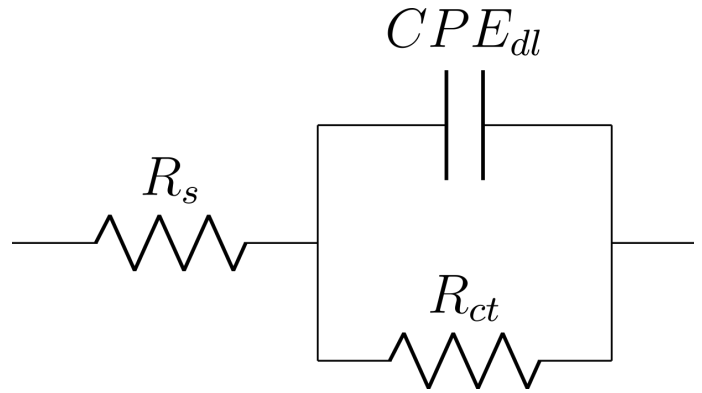


Fig. 2. Equivalent electrical circuit used for modeling the impedance spectra presented in Fig. 1.

- resistance to charge transfer (R_{ct}), corresponding to the solution impedance at low frequencies. This parameter models the electron transfer phenomena at the interface between the solution and the electrode;
- double layer capacitance (CPE_{dl}), to describe the capacitive phenomena occurring close to the electrode.

It is worth to notice that the double layer capacitance was modeled using a Constant Phase Element (CPE) instead of a pure capacitor. CPE is an element which is used to take into account non-idealities and time constant dispersion in real electrochemical systems [13]. Specifically, it improves fitting quality when impedance phase does not reach -90° and thus the system under study can not be described as a pure capacitor. CPE impedance is defined by the formula:

$$Z_{CPE} = \frac{1}{(j2\pi f)^n Q} \quad (3)$$

where Q is the CPE parameter, n is an exponent ranging from 0 to 1, and f is the frequency. When n is equal to 0, the CPE impedance describes a resistive behavior, while when n is equal to 1 the system is described by a pure capacitor; other values are characteristic of intermediate behavior [13].

Values obtained from EEC modeling for all parameters are listed in Table I. As can be seen, most significant variations as a function of lactate concentration are found for solution resistance values. This parameter goes from the value of 144.4Ω for the solution containing 8.0 g/L of sodium chloride to the value of 103.1Ω when 100 mmol/L are added to the solution. As shown in Fig. 3, the trend for solution resistance is linear as a function of lactate molar concentration and, in this compositional range, it can be described by the equation:

$$y = 140.8 - 0.39 \cdot x \quad (4)$$

where x represents the lactate concentration expressed in mM. In Fig. 3, measurement uncertainty is reported as vertical lines, but it is too small to be visible in the plot, as it is below 1Ω for all samples.

As discussed in the previous section, double layer capacitance is not affected by lactate concentration and it

TABLE I
PARAMETERS EXTRACTED FROM EQUIVALENT ELECTRICAL CIRCUIT MODELING

Lactate concentration (mM)	R_s (Ω)	R_{ct} (Ω)	$CPEdl$ ($\Omega^{-1} \cdot s^n$)	n_{CPE}
0.0	144.4	$1.8 \cdot 10^5$	$1.4 \cdot 10^{-6}$	0.86
1.0	141.4	$1.7 \cdot 10^5$	$1.5 \cdot 10^{-6}$	0.86
5.0	138.6	$4.0 \cdot 10^5$	$1.5 \cdot 10^{-6}$	0.86
20.0	130.3	$3.5 \cdot 10^5$	$1.4 \cdot 10^{-6}$	0.86
40.0	122.1	$3.2 \cdot 10^5$	$1.4 \cdot 10^{-6}$	0.86
100.0	103.1	$2.6 \cdot 10^5$	$1.4 \cdot 10^{-6}$	0.87

remains constant at about $1.4 \cdot 10^{-6}$ for all samples in the investigated compositional range. n parameter is constant for all lactate concentrations as well and it is equal to about 0.86. This value confirms the choice to use a CPE instead of a pure capacitor, even if it is still fairly close to unity.

The trend for resistance to charge transfer (R_{ct}) is reported in Fig. 4 as a function of lactate concentration. As it was mentioned during graphical interpretation of impedance spectra, solutions containing 0 mM and 1.0 mM of lactate exhibit a slightly lower value for this physical parameter. Apart from this variation, other samples present similar values for resistance to charge transfer.

Results from EEC show that, in the frequency range from 1 Hz to 10^5 Hz, sodium lactate affects solution impedance only in its conductivity. As a matter of fact, this measure can not be proposed as an analytical tool to detect lactate, because it would lack of chemical selectivity. On the other hand, if we take into account an application related to bioimpedance such as lactate threshold identification, additional considerations can be formulated. As reported by W. Gao and coauthors [14], human sweat during physical activity is a complex system, composed of different analytes which vary their

concentration depending on the exercise intensity. In particular, in that study a flexible sensors array was used to monitor concentration of lactate, glucose, sodium ions and potassium ions. During intense physical activity, lactate presents an increasing trend, characterized by a step-like rise when lactate threshold is reached. On the other hand, glucose concentration has a decreasing trend, due to energy consumption in muscles, as well as potassium ions. Sodium ions concentration increases in sweat during activity, and this trend can be related to dehydration phenomena. Excluding glucose [11], all other species have an effect on conductivity in the considered concentration range, so an overall monitoring of the athlete physical conditions may be realized by means of bioimpedance. Even if the chemical selectivity could not be achieved, the requirement to monitor effort intensity may be fulfilled. Because of this, additional in-vivo studies would be required in order to investigate this possibility, which would pave the way to a low-cost and non-invasive way to monitor athlete performance. Moreover, additional insights could be obtained assessing the electrochemical properties of solutions containing sweat metabolites in different frequency ranges.

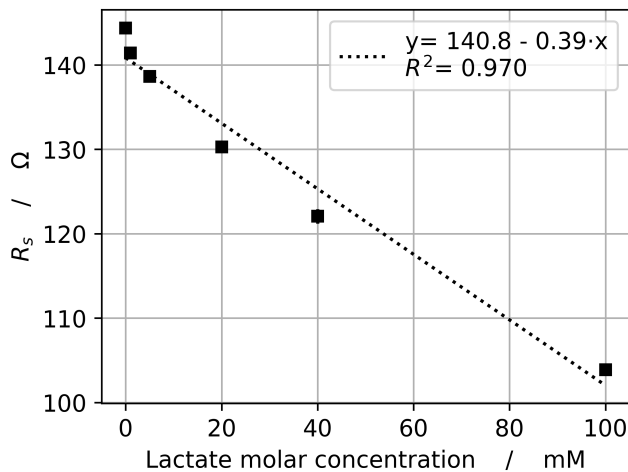


Fig. 3. Trend of solution resistance (R_s) as a function of lactate molar concentration.

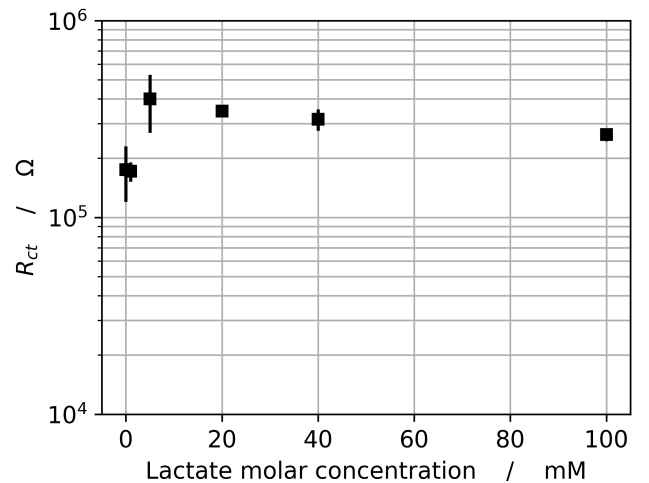


Fig. 4. Trend of resistance to charge transfer (R_{ct}) as a function of lactate molar concentration.

IV. CONCLUSIONS

The paper presented the characterization of sodium lactate solutions at physiological concentration by means of EIS, proposed here as a pre-study to then perform measurements in human sweat. The use of EEC allowed to derive a physical model for the system under study, providing the trend for all parameters as a function of solute concentration. Results showed that lactate concentration in saline solutions has a marked effect on solution resistance, due its ionic dissociation. No relevant effects were highlighted on resistance to charge transfer nor on double layer capacitance. As a matter of fact, the change in solution resistance does not allow to identify this specific compound, so the measure is not chemically selective for sodium lactate. At the same time, it may be exploited for those applications, such as sport activity monitoring, where chemical selectivity may be a less severe constraint and a simple indication related to electrolytes concentration is sufficient.

Future work will characterize by means of EIS the behavior of saline solutions containing lactate also in the frequency range above 1 MHz in order to investigate the applicability of this electrochemical technique for lactate monitoring in in-vivo applications, e.g. in human sweat during sport competitions. Moreover additional potential for future developments is represented by the use of chemometrics in order to process the acquired data and discriminate lactate levels [15], [16].

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