Sensors and Actuators A 261 (2017) 252–260

Contents lists available at ScienceDirect

Sensors and Actuators A: Physical

journal homepage: www.elsevier.com/locate/sna

Non-invasive measurement of electrical conductivity of liquids in biocompatible polymeric lines for hemodialysis applications

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ARTICLE INFO

Article history:
Received 20 December 2016
Accepted 19 April 2017
Available online 11 May 2017

Keywords:
Conductivity
Constant-phase element
Hemodialysis
Impedance spectroscopy

ABSTRACT

A non-invasive impedimetric sensing system measuring electrical conductivity of liquids in hemodialysis machines for continuous monitoring applications is introduced. Starting from the typical architecture of the capacitively coupled contactless conductivity approach, we developed an easy-to-use impedance spectroscopy model based on the constant phase element to quantitatively measure the conductivity of liquids in polymeric lines. We also show the experimental setup to determine the parameters of such a model to better cope with the application constraints. We demonstrated that this approach could be used to design conductivity sensing systems to be fit into the typical dimensions of the standard instrumentation for hemodialysis. Experimental results on saline solutions and blood-mimicking fluid report estimated conductivities with root-mean-square error of ≃0.05 mS/cm, corresponding to about 0.5% of the full scale.

1. Introduction

The monitoring of the electrical properties of a material is an important process because such properties are related to its internal structure. For this reason, changes in conductivity or permittivity can be used to detect alterations in composition. Specifically, in fluids the electrical properties are connected to the nature and concentration of suspensions. In the simple case of a mix of water and electrolytes with sufficient dilution, conductivity is determined by the concentration of the individual ionic species, weighted by ionic mobility [1]. The possibility of using electrical conductivity to estimate biological parameters has also been largely explored in biomedical engineering and science, with many different target tissues, such as blood [2,3] and skin [4].

A particularly important biomedical application for conductivity monitoring is in the field of hemodialysis for chronic patients. Hemodialysis is a periodical blood purification treatment for patients with end-stage renal failure [5,6]. During the treatment, the blood of the patient is pumped into an extracorporeal circulation system and put in contact with a liquid solution, the *dialysate*, through a semi-permeable membrane. Contact with dialysate removes toxins and balances electrolytes through diffusion and convection [7].

In this context, conductivity is important as a surrogate for sodium concentration measurements. Knowledge of the trend of sodium concentration during the treatment is useful for clinical purposes, but implementing an on-machine system for repeated blood sampling and chemical analysis is complex and expensive. Since electrical conductivity of blood plasma is mainly determined by sodium concentration, with a nearly linear relationship, conductivity monitoring is a valid substitute for sodium measurements [8]. Unfortunately, direct conductivity measurements cannot be carried out because of complications in using traditional immersion electrodes in this particular context. The first complication is the contact of the electrodes with blood, which demands for the electrodes to be either disposable or sterilized after every use. The second complication is the lack of biocompatibility of metallic electrodes, which is required for in vivo measurements on patient blood.

Currently, the state-of-the-art method for plasmatic conductivity estimation during standard hemodialysis treatments is based on the theory originally developed by Polaschegg [9]. This is an indirect method that allows estimation of plasmatic conductivity by

Abbreviations: C4D, capacitively-coupled contactless conductivity detection; IS, impedance spectroscopy; LP, lumped parameters; CPE, constant phase element; R–C, resistance–capacitance; R-CPE, resistance-constant phase element; BMF, blood-mimicking fluid.

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http://dx.doi.org/10.1016/j.sna.2017.04.034
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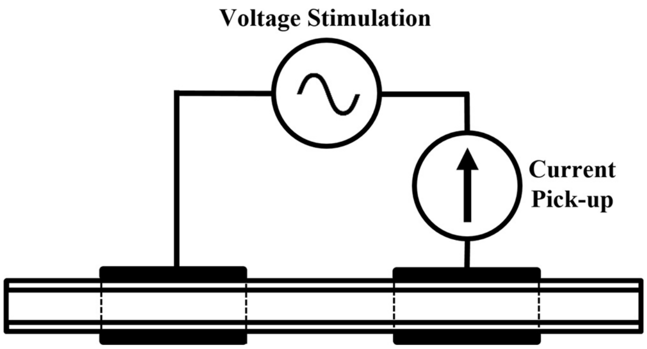

Fig. 1. C4D System. Schematic representation of the general setup for a C4D system in voltage-stimulation configuration.

applying conductivity steps to the dialysate fluid following a dynamic protocol. Briefly:

i) Conductivity steps are imposed on inlet dialysate by the hemodialysis machine, and conductivity is measured on both inlet and outlet dialysate.
ii) By use of a mathematical formulation, the measured conductivities of dialysate before and after its electrolyte exchange with blood can be employed to estimate plasmatic conductivity.

This method presents some disadvantages. The protocol, as currently implemented by modern machines, requires a measurement time of about 10 min and is repeated automatically every 30 min. Its accuracy is limited (typically in the order of 0.1 mS/cm in a 13–16 ms/cm full-scale measurement range) and, due to the conductivity steps, it also causes a temporary alteration of blood electrolytes content, so conceptually it can be somehow considered invasive.

The C4D (Capacitively-Coupled Contactless Conductivity Detection) is a technique employed in electrochemistry for the detection of transition of ionic species with different mobility values through an electrophoresis capillary exposed to a constant electric field [10–12]. It is one of the many measurement techniques proposed in the literature for the estimation of material properties in a fast and contactless way [13–16]. The basis of C4D is the capacitive coupling of an AC electrical signal between exterior and interior of the line containing the fluid. Two ring electrodes placed axially outside the line (Fig. 1) couple the signal to the fluid. The current finds a flowing pathway through the liquid, and the pick-up signal (current) amplitude is analyzed in conjunction with the stimulation signal (voltage). The relation between stimulation voltage and pick-up current can be analyzed to determine conductivity of the flowing liquid. The C4D technique has been applied to many different pharmaceutical and biological samples, as reported in [17–19]. Over the years, the role of the geometry of the measurement cell and of the operating parameters of the system (i.e. frequency) have been studied [20–24]. Recently, many evolutions in the electronics and measurement aspects of C4D have also been proposed, for example the use of the lock-in principle [25,26], phase-sensitive demodulation [27] or resonance sensing [28–32]. Contactless impedance cells with geometries similar to that of C4D cells have also been used for other purposes, like flow measurements [33].

The aim of this work is to explore the possibility of developing a contactless method to estimate the conductivity of liquids contained in biocompatible polymeric line for hemodialysis applications. This method would allow faster and more frequent measurements, in addition to being non-invasive and maintaining an accuracy equal or better than the traditional method.

The method we propose is loosely based on C4D regarding the topology of the measurement cell, but differs from such technique by using all the information available from impedance spectroscopy (IS, magnitude and phase of impedance at different frequencies) for conductivity estimation. In our case a quantitative estimation of the conductivity of the liquid is given, whereas traditional C4D is only used to monitor the time of passage of different ions during electrophoresis.

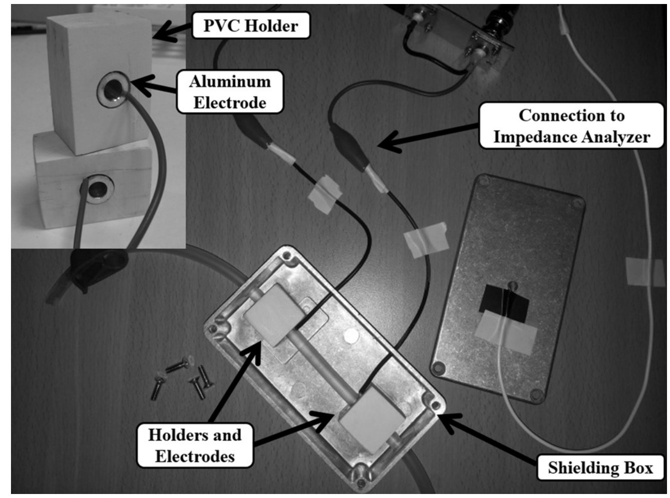

Fig. 2. Measurement Cell. Prototype of our C4D measurement cell with a biocompatible line. Inset: detail of the cylindrical electrodes enclosed in the PVC holders.

In the following sections, the development and testing of a contactless conductimetry cell for biomedical use will be described. The cell was first tested with hemodialysis biopolymeric line segments filled with saline solution, to validate the measurement principle with a simple fluid. Afterwards, it was tested with blood-mimicking fluid (BMF) to study the response of the system to a more complex fluid.

Impedance spectroscopy was used for experimental characterization of the cell and for measurements. A lumped-parameters (LP) electrical model of the cell was developed, and its performances were evaluated using experimental data as reference.

2. Methods

Our measurement cell was developed to scale the application of the C4D principle from the original electrophoresis capillaries to biocompatible lines with a diameter in the order of several millimeters. The device was implemented and tested by filling a polymeric line segment with liquid samples, first of saline solution and then of BMF. Each set of solutions was composed of samples with different conductivity values. A LP model of the electrical equivalent circuit of the cell was also developed. Characterization of the electrical properties of the biopolymer was also helpful in model development. The purpose of the LP model was dual: i) experimental data interpretation on a high abstraction level; ii) easy conductivity estimation.

2.1. Cell prototype

Our degrees of freedom in cell geometry design were partially limited by the intended purpose of use on-board of a dialysis machine, which puts an upper limit to cell size. The developed cell (Fig. 2) is composed of two cylindrical aluminum electrodes of length 20 mm and distance from each other of 70 mm (center-to-center), held by two PVC holders. The electrodes are round-shaped, 10 mm wide, with internal diameter of 6 mm.

Electrodes and holders are contained in an aluminum shielding box of approximately 115 mm × 60 mm × 30 mm, with two holes