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Implementation of a Fast Reconfigurable Array for Tissue Impedance Characterization

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Abstract—**Various tissue properties have been used in the past and present as metrics which can serve to discriminate healthy from diseased tissue. Electromagnetic absorption (of x-rays and optical signals), scattering of near-infrared light, and electrical impedance are a few such parameters. In order to serve as discriminants for diseased (e.g., neoplastic) tissue, the characteristics of these tissues must first be precisely determined. In this paper, we consider the electrical impedance properties of tissues and cell aggregates, and present the design of a reconfigurable electrode array which is capable of providing a well-defined electromagnetic interface to the tissue under study, for characterization in the 0.01-30 MHz range. The configuration of array elements may be easily changed under digital control, allowing for various electromagnetic field configurations to be applied to the tissue under study. The array is designed to interface to four-point as well as two-point impedance instrumentation, and may be used for two-dimensional bioimaging systems based on electrical impedances. The design may be scaled to higher frequencies and smaller dimensions, allowing for studies of electrical properties at the cellular level.**

I. Introduction

AN UNDERSTANDING of the electrical properties of living cells, cellular aggregates and tissues has been of great interest since the beginning of the last century [1, 2]. Indeed, it is precisely the unique electromagnetic, chemical and physical properties of tissues which make possible various imaging modalities, including x-radiographic imaging, magnetic resonance imaging and near-infrared diffuse optical tomography. As imaging exploration extends into new regions of the electromagnetic spectrum, it is essential to develop a thorough understanding of tissue characteristics across a wide range of frequencies. The determination of the electrical properties of tissues requires a well-defined electromagnetic interface with tissue. The availability of a suitable interface can also facilitate direct electrical measurements using conventional 4-point impedance and vector network analyzers. Although such instrumentation is widely utilized in electronic circuit and device characterization, the application of these tools to the characterization of living tissue is less widely used. This is due in part to the difficulty of finding a suitable interface which can link sophisticated test and measurement instrumentation to living tissue.

In order to address this need, we have designed a digitally-configurable array which serves as an electrode interface to living tissue. In this paper, we describe the design and implementation of a prototype 16-element electrode array which allows for impedance measurements of living tissue over a 30 MHz bandwidth. Our approach differs from an inter-digitated electrode array in both design (i.e. coaxial vs. finger-type geometry) and application (i.e., bulk tissue vs. superficial/surface measurement) [3]. The array makes use of monolithic high-speed video switches which allow for simple configuration of the array. Control of the array configuration is accomplished via USB interface to a laptop computer, using a LabVIEW graphical user interface. While our primary objective in this work is the demonstration of the array for characterization of tissue properties, a configurable electrode array can be more generally used in tissue imaging applications based on differing electrical properties of healthy and diseased tissue.

II. Instrumentation Design and Implementation

The architecture of the configurable array is shown in Figure 1. The heart of the measurement system is an Agilent 4294A Precision Impedance Analyzer which is capable of accurate impedance measurements over the frequency range 40 Hz to 110 MHz. For greater accuracy, the analyzer employs a four-point measurement technique. (This is reflected in Figure 1, in which the abbreviations HC, HP, LC and LP, refer to **h**igh-side **c**urrent and **p**otential measurement ports, and **l**ow-side **c**urrent and **p**otential ports, respectively.)

A switching network consisting of high-speed monolithic CMOS video switches is used to dynamically connect individual elements of a 4x4 electrode array to the impedance analyzer. The analog switches used in this application are Analog Devices *ADG1234* quad CMOS single-pole, double-throw (SPDT) switches. These devices feature very low capacitance and a wide 3-dB bandwidth of 900 MHz, more than adequate for the 30 MHz range of the 4294A impedance analyzer. A laptop computer is used to control the switching network using a digital USB interface

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(National Instruments USB 6008 I/O Module), along with a 4-to-16 demultiplexer which controls the ADG1234 switches. LabVIEW control software provides the graphical user interface to allow for simple array configuration. The array design and switching network will now be described in greater detail.

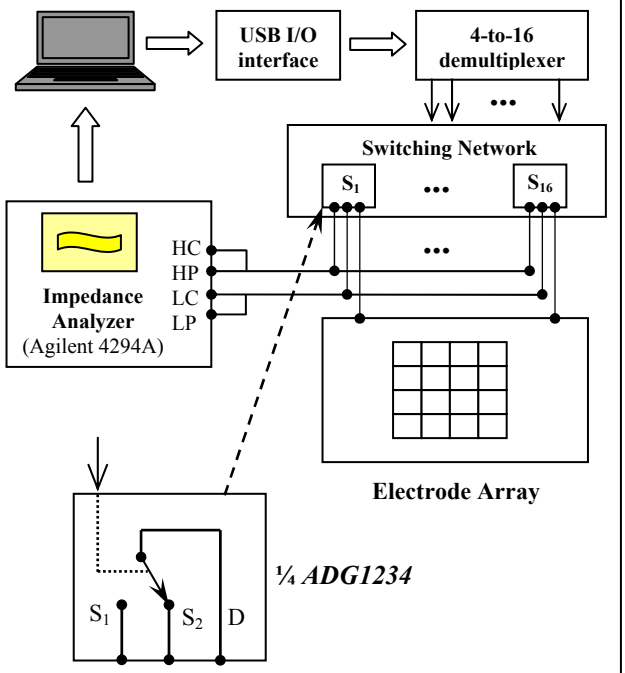


Fig. 1. Block Diagram of Array Architecture.
(See text for a description of the significance of the symbols.)

A. Array Design

Figure 2 illustrates the prototype 16-element array which is realized as a square 4 x 4 matrix. The array was fabricated on 1.6-mm thick FR-4 epoxy-glass laminate using conventional printed-circuit layout and fabrication processes (expresspcb.com). The array electrodes were subsequently electroplated with platinum. Several iterations of the array design were attempted; for the first iteration the monolithic CMOS switches were attached to the same substrate as the array itself. Figure 2 illustrates the front and back circuit patterning for the double-sided array board, connection from the front to back was accomplished using plated via-holes as part of the board fabrication process.

The Analog Devices ADG1234 switches are used to configure the array by connecting one of the sixteen electrodes to the high-side current and potential ports of the impedance analyzer. The remaining fifteen electrodes, as well as the surrounding ground shield, are connected to the low-side current and potential ports of the impedance analyzer, serving as a virtual ground. In this manner, current injected into a single (high-side) electrode distributes to the surrounding low-potential electrodes and outer shield. This is analogous to an open-ended coaxial probe which was initially designed for noninvasive tissue measurements in the radio-frequency range [4]. In the present implementation, the probe can be electronically repositioned on the surface of a tissue sample by appropriate choice of inner electrode (i.e., high-side array electrode).

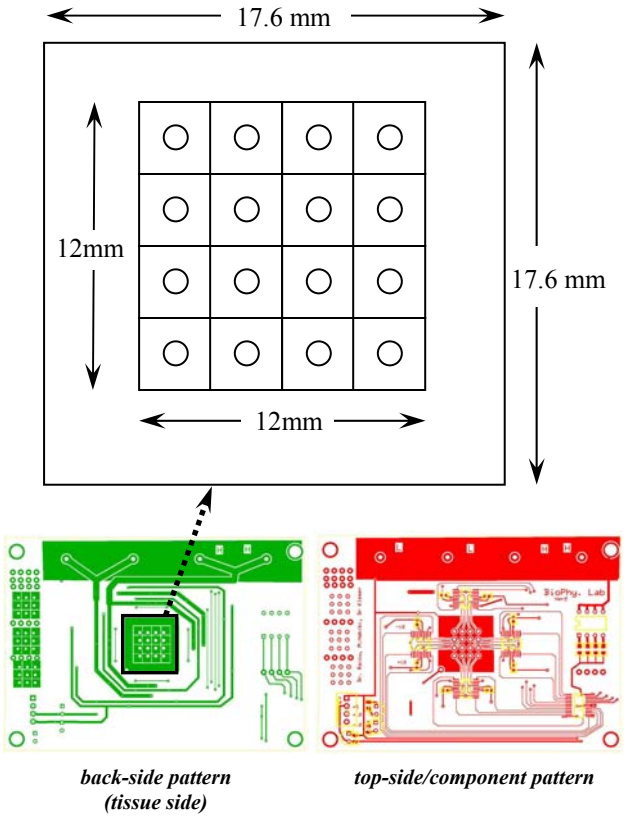
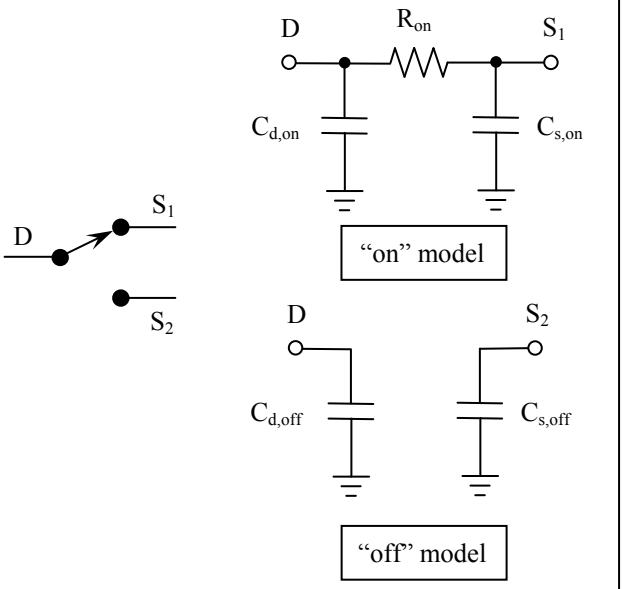


Fig. 2. Array Design and Layout.

B. Array Configuration Using High-speed Video Switches

As previously mentioned, Analog Devices ADG1234 high-speed monolithic CMOS switching arrays were used to facilitate signal routing, allowing for simple reconfiguration of the 16-element electrode array. The switches feature a wide bandwidth of 900 MHz, thus will remain suitable as we extend the frequency range of our characterization equipment. There are a number of considerations in the choice of monolithic switch for a characterization system, which primarily relate to the parasitic elements associated with the switches. For the present work, three monolithic switch options were considered, Analog Devices ADG1234, 1434 and 734. Figure 3 presents small-signal equivalent circuit models for the switches, along with parameter values provided by the manufacturer [5].

It is evident from the table in Figure 3 that there is a tradeoff between series resistance and parasitic capacitance; optimal



	ADG1234	*ADG1434*	*ADG734*
R_{on} (ohms)	120	4	2.5
3dB BW (MHz)	900	200	160
$C_{s,off}$ (pF)	1.5	12	11
$C_{d,off}$ (pF)	1.6	22	11
$C_{d,on}$,$C_{s,on}$ (pF)	3.5	72	34

Fig. 3. Equivalent Circuit Model of Monolithic CMOS Switches Used for Signal Routing.

design of the system thus depends on careful choice of parasitic resistance and capacitances. For the three integrated circuits considered in Figure 3, the "on" resistance magnitudes and parasitic capacitances tend to be inversely related. For the present design, lower parasitic capacitances associated with the instrumentation are preferred in order to obtain greater accuracy in final measurements of tissue parameters. The "on" resistances are relatively uniform across individual switch devices, permitting accurate measurement results after system calibration (or de-embedding analysis). After these careful design considerations, the monolithic CMOS SPDT switch *ADG1234* was used [5]; this integrated circuit incorporates 4 switches, further simplifying the printed circuit layout.

C. Impedance Measurement Hardware

An Agilent 4294A Precision Impedance Analyzer is used to measure tissue impedance using a standard four-point approach, in which current is sourced through an unknown sample via two ports (HC and LC), while the unknown voltage is separately measured via two different ports (HP and LP). Figure 4 shows the complete measurement system in which the measurement array is connected to the analyzer through standard 50-ohm coaxial cables.

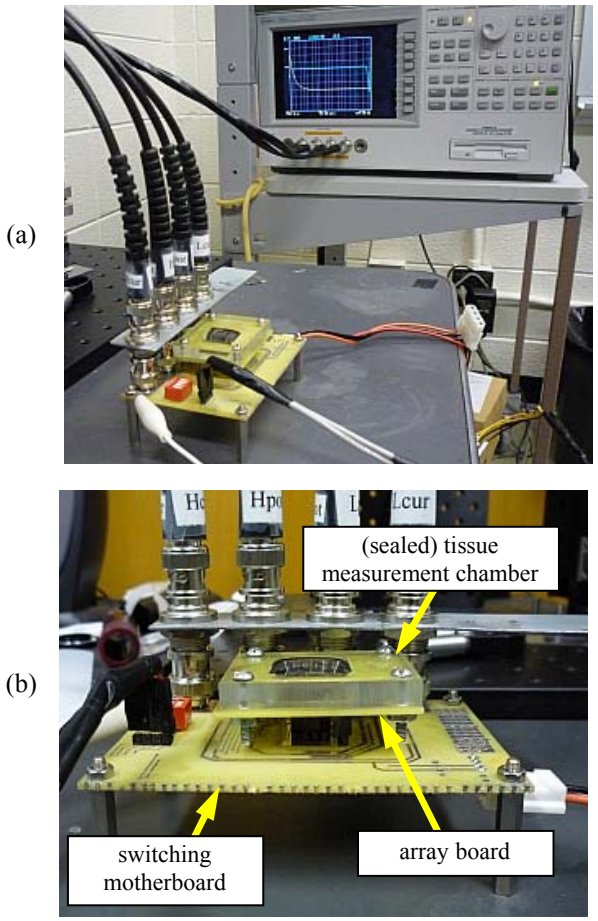


Fig. 4. Impedance Measurement System. (a) Complete System; (b) Close-up View of Array

For the system shown in Figure 4, the array has been replaced with a second-generation design in which the array proper is fabricated as a separate board, attached to a motherboard which supports the current switching circuitry. This design allows for the construction of a distinct, sealed measurement chamber, and facilitates the platinum electroplating process of the electrode array alone. In addition, the coaxial connections may be easily separated from the motherboard for simple calibration.

III. Calibration and Measurements

An important aspect of system performance regards the calibration scheme used to correct for errors in the system cabling, cable adaptor (Agilent 16048G), switching network and electrodes. The Agilent cable adaptor was first calibrated using the procedure recommended by Agilent [6]. Further calibration to a reference plane at the point of the array electrode was accomplished using an open-circuited line, a short-circuited line, and a surface mount resistor with nominal resistance of 100 ohms. These known standards

were connected from the array electrode under consideration to virtual ground, and calibration procedures recommended by Agilent for the 4294A Impedance Analyzer were used.

In order to determine permittivity and conductivity, a value for the geometrical constant, k_{cell}, is required. Values for this constant are determined using various known concentrations of sodium chloride (NaCl) in deionized water solution, along with the known dielectric properties of these saline solutions, available in the literature [7], [8]. Figure 5 shows the relative permittivity (ε_{rel}) and conductivity (σ) obtained after this calibration for four concentrations of NaCl solutions (not used in the determination of the cell constant): 25 millimolar (mM), 50 mM, 75 mM and 100 mM.

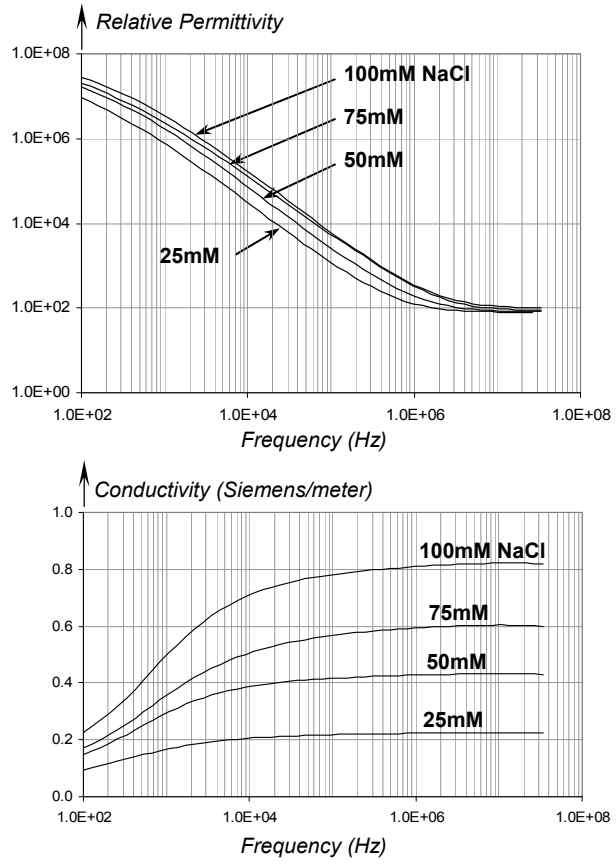


Fig. 5. Measurement of Relative Permittivity and Conductivity for Saline Solutions

A problematic artifact which appears with impedance measurement systems is electrode polarization (EP); this artifact occurs at low frequencies and is related to the build-up of charge at the interface between electrode and electrolyte (or tissue under measurement). The present work takes advantage of the fact that the EP artifact problem is well-known, along with techniques for compensation [2], [9]. EP effects can be corrected for the present system of electrodes using methods described in [9]. The effect of EP and can be seen in Fig 5, which shows an increase in permittivity as frequency decreases below 1 MHz. Although the effect of EP is diminished in a four-electrode system, other anomalies (e.g., high frequency distortion and inaccurate cell constant) may affect the measurements [10].

IV. Conclusions

Use of electromagnetic radiation for study and examination of human tissue has a long and interesting history, dating to early work in X-radiography. There is increasing interest in using lower frequency waves in the RF, microwave and millimeter-wave ranges for tissue characterization, imaging and diagnosis of pathology. In the present work, we demonstrate the implementation of a fast, reconfigurable electrode array which is suitable for tissue measurements and characterization. The instrumentation makes use of high-speed, broad-bandwidth, low-capacitance monolithic switches which allow for versatile reconfiguration of the electrode array. Future research will make use of the hardware for characterization of biological tissue.

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