Applications of SPICE for Modeling Miniaturized Biomedical Sensor Systems

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Abstract—This paper proposes a model for a miniaturized signal conditioning system for biopotential and ion-selective electrode arrays. The system consists of three main components: sensors, interconnections, and signal conditioning chip. The model for this system is based on SPICE. Transmission-line based equivalent circuits are used to represent the sensors, lumped resistance–capacitance circuits describe the interconnections, and a model for the signal conditioning chip is extracted from its layout. Conclusion: A system for measurements of biopotentials and ionic activities can be miniaturized and optimized for cardiovascular applications based on the development of an integrated SPICE system model of its electrochemical, interconnection, and electronic components.

Index Terms—Biopotential, electrode, equivalent circuit, ion-selective, Kapton, SPICE, system model, transmission line.

I. INTRODUCTION

A N IMPLANTABLE, inductively powered biotelemetry system for short-term in vivo measurements of cardiac biopotentials and ionic activities is being developed through a joint effort by researchers at North Carolina State University, Stanford University, and NASA Ames Research Center (Fig. 1). This system will greatly enhance the performance and usability of existing flexible electrode arrays in cardiology. It will enable continuous monitoring of biopotentials and ionic activities over several days thereby providing data that is not obtainable with existing, cable-based electrodes. This data will accelerate the investigations of ischemic events leading to an increased understanding of cardiac arrhythmias.

Kapton-based microelectrode arrays are used by cardiologists because of their mechanical flexibility, which reduces tissue damage. Microelectronics technologies allow the fabrication of arrays with a large number of sensor sites. Electrochemical processes and thick-film technologies prepare the sensor sites for biopotential or ion-selective measurements. The current application of these arrays involves a large number of discrete amplifiers that are connected to the array via ribbon- and flat-cables. This setup results in interconnection problems, difficulties in handling, and does not permit long-term implantation of the arrays.

A miniaturization of this system is highly desired. The first step must demonstrate the possibility of miniaturizing the current system while maintaining, and possibly improving, its performance parameters. Since a reduction in size may lead to interactions between the system components that can not easily be predicted, a model is required that can take these interactions into consideration. Such a model must provide detailed descriptions of all components. It should allow variations of component parameters and show how these affect the overall system response.

The principal system components are the electrode array with biopotential and ion-selective recording sites including a reference electrode, the signal conditioning circuit implemented on a chip, and the interconnections between chip and electrode array (see Fig. 2). Since a model for the signal conditioning chip can easily be obtained through SPICE extraction, it is convenient to use SPICE as the basis for the complete system model. Electrodes are commonly modeled as equivalent circuits which makes them compatible with SPICE as well. Transmission-line based models accurately describe the behavior of electrochemical cells at low frequencies between dc and 500 Hz. Since this frequency range corresponds to the bandwidth of the proposed system, a detailed investigation of these models is relevant. SPICE circuit simulation can be applied to interconnection systems as well. Resistance—capacitance (RC) models, for example, can be derived from impedance measurements.

Besides proving the feasibility of miniaturization, this approach can also be used to investigate and refine the complete system by adjusting component parameters, e.g., site size, ion-selective membrane composition, performance of reference electrode, interconnection technology, and input impedance and small-signal behavior of input amplifiers. The simulation results, which are primarily the performance parameters of
the signal conditioning circuit, can serve as feedback in the design process. The noise behavior of the system can be determined by SPICE, as well as the noise contributions from each element. This permits the selection of an appropriate interconnection technology and CMOS fabrication process, for example. Crosstalk between two signal lines can be modeled as well. In addition, environmental parameters, e.g., temperature, can be included in the simulation. Finally, general relationships between parameters of the three main system components can be extracted from these simulations and can serve as a basis for future designs. Examples are the influence of site size on amplifier input impedance, the effect of ion-selective membrane composition on system accuracy, or performance specifications for a currently developed miniature reference electrode.

II. METHODS

A. Modeling of System Components

1) Sensor: Depending on the sensor type, this system can either measure biopotentials or ionic activities. In both cases the sensor is an electrochemical cell consisting of two electrodes and the tissue as the electrolyte. For biopotential measurements the electrodes simply consist of a suitable metal, typically gold or silver/silver chloride and measurements are made using bipolar or unipolar techniques. Ionic activities are measured with ion-selective electrodes, which always require a reference electrode that provides a constant, concentration independent potential. This reference electrode should be preferably close to the ion-selective (sensing) electrodes and small in size.

All of the electrodes mentioned above can be modeled with equivalent circuits. The biopotential gold electrode has the simplest model description. These electrodes establish a blocked interface between the gold layer and the tissue and can be represented with a single capacitor. It is the circuit equivalent for the double layer composed of ions and electrons that develops at the solution/metal interface. No dc current can be passed by this electrode since it is not possible for either ions or electrons to cross the interface. When current must pass through the site, Ag/AgCl electrodes are often used. They consist of a chloridized silver layer that allows Cl\(^-\) ions to join the AgCl and donate their electrons for conduction, and vice versa. Thus a dc current can flow if the solution contains Cl\(^-\) which is the case for most biological fluids. The equivalent circuit model for this electrode type is a capacitor in parallel with a resistor. The capacitor is again a representation of the double layer and the resistor characterizes the charge transfer between solution and AgCl layer.

Ion-selective electrodes consist of a membrane which is selective to only one ion of interest, typically K\(^+\), H\(^+\), or Ca\(^2+\). The membrane separates two solutions—the test solution (tissue) and an inner reference solution. A typical structure of an ion-selective microelectrode used in this system is shown in Fig. 3. A compartment for the inner reference solution is created by a hydrogel which is contacted on one side by the membrane and on the other side by a Ag/AgCl layer that provides the electrical contact to the inner reference solution. Several different layers and interfaces make up this structure and these lead to a more complicated model than for the biopotential electrode as shown in Fig. 4. The impedance of the Ag/AgCl layer can again be modeled by a parallel RC circuit. The membrane impedance varies according to different chemical processes that determine its value in various frequency regions. The process that determines the membrane impedance in the frequency range of biological signals (0.05–500 Hz) is diffusion and migration of charge carriers inside the membrane. It can accurately be modeled by a modified transmission line circuit, developed by Barker, Brumleve, and Buck [1] (the BBB circuit). Each charge carrier (ion) is represented by a resistor chain. The chains are connected to each other by capacitors.
(Nernst–Planck capacitors) which simulate the coupled motion of charge carriers at low frequencies. The membrane solution interfaces on each side of the membrane can be modeled like most interfaces with a double layer capacitor and a kinetic (activation) resistance. But since the surface processes of the ion-selective membranes used for this system are reversible, the kinetic resistances \( R_{\text{k}} \) can be replaced by a short. At higher frequencies, the resistor chains that model the charge transport in the membrane bulk generate a time constant with the “geometric”; capacitance of the membrane

\[
C_g = \varepsilon_r \varepsilon_0 \frac{A}{d}
\]

where
- \( \varepsilon_r \) relative permittivity of the plasticized PVC-matrix of the membrane;
- \( \varepsilon_0 \) dielectric constant;
- \( A \) membrane area;
- \( d \) membrane thickness.

\( C_g \) is formed by the two external space charge layers at the outside of the membrane with the membrane itself acting as a dielectric. It is modeled by the chain of capacitors \( C_p \) (Poisson capacitors) that run along the middle of the transmission line. The Nernst–Planck capacitors \( C_{+} \) and \( C_{-} \) act as shorts at these high frequencies and connect the resistors \( R_{+} \) and \( R_{-} \) in parallel to the Poisson capacitors \( C_p \). A detailed description of this model can be found in [2] and [3].

A common ion-selective microelectrode of the sensor system uses a potassium ion-selective membrane containing the ionophore valinomycin (val). The charged species in this membrane are valinomycin-bound potassium (Kval+) and negative sites [TPB, Tetrakis (4-chlorophenyl) borate] [4]. These have to be modeled as the two chains of the transmission line. Their concentrations and diffusion coefficients can be used to assign values for the BBB circuit model components [2]

\[
R_{+} = \frac{RT}{F^2 z_{+} c_{+}} \frac{d}{A N} = 141 \text{ k} \Omega
\]

\[
R_{-} = \frac{RT}{F^2 z_{-} c_{-}} \frac{d}{A N} = 141 \text{ k} \Omega
\]

\[
C_{+} = \frac{2 F^2 c_{+}}{RT} \frac{dA}{N} = 71 \text{nF}
\]

\[
C_{-} = \frac{2 F^2 c_{-}}{RT} \frac{dA}{N} = 71 \text{nF}
\]

where
- \( A \) membrane area (1.96E-3 cm²);
- \( d \) membrane thickness (0.01 cm);
- \( N \) number of differential elements that are used to model the transmission line (100);
- \( c_{+} \) concentration of Kval+ (10^{-7} mol cm^{-3});
- \( c_{-} \) concentration of TPB (10^{-7} mol cm^{-3});
- \( D_{+} \) diffusion coefficient of Kval+ (10^{-5} cm² s^{-1});
- \( D_{-} \) diffusion coefficient of TPB (10^{-5} cm² s^{-1}).

The Poisson capacitors \( C_p \) can be derived from the geometric capacitance \( C_g \) of the membrane which is the total capacitance of the Poisson capacitor string. Each \( C_p \) is, therefore, \( N \) times larger than \( C_g \)

\[
C_p = NC_g = N \frac{\varepsilon_r \varepsilon_0 A}{d} = 11.8 \text{ pF}
\]

where \( \varepsilon_r = 7, \varepsilon_0 = 8.854E-14 \text{ F cm}^{-1}, N = 100, A = 1.96E-3 \text{ cm}^2, \) and \( d = 0.01 \text{ cm}. \)

The reference electrode (for ion-selective electrode measurements) has a structure similar to an ion-selective electrode (Fig. 3). It also consists of a compartment containing an inner reference solution, but it is separated from the test solution by a tiny hole, the liquid junction, instead of a membrane. The tiny hole provides the electrical contact between test and inner reference solution while minimizing the mixing of these two solutions [5]. The diffusion of ions through this junction can be modeled by a conventional transmission line. The interface between inner reference solution and AgCl layer has the same circuit description as the one in the ion-selective microelectrode.

Values for \( R \) and \( C \) of this transmission line can be calculated as follows, these relations are similar to (2) and (3) and have been discussed in a previous paper [2]

\[
R = \frac{1}{2} \frac{RT}{F^2 z_{-} c_{-}} \frac{d}{A N} = 1.9 \Omega
\]

\[
C = \frac{1}{2} \frac{RT}{F^2 z_{-} c_{-}} \frac{dA}{N} = 9 \text{ pF}
\]

where the geometric (area \( A = \pi/4100^2 \mu m^2 \) and thickness \( d = 63.5 \mu m \)) and electrochemical parameters (diffusion coefficient \( D_{-} = 2E-5 \text{ cm}^2 \text{s}^{-1} \), concentration \( c_{-} = 3E-3 \text{ mol} \)
cm$^{-3}$) of the liquid junction of a micro reference electrode (developed by S. Ufer at the BMMSL [5]) were used.

Both ion-selective electrodes and their reference electrodes use a Ag/AgCl-layer to provide an unblocked, nonpolarizable interface for conduction between the inner reference solution (mostly KCl) and the metal electrode. These interfaces have been investigated and modeled in [6]. Their circuit equivalent is a parallel $RC$ circuit. Average values of $R$ and $C$ for 500-$\mu$m Ag/AgCl sites (ISE’s) were determined experimentally by using an HP model 4284A LCR meter: $R = 20 \, k\Omega$ and $C = 60 \, pF$. For reference electrodes in which the area of the Ag/AgCl layer is large (>5 mm$^2$), the resulting $R$ is very small (<1 k$\Omega$) and can usually be neglected in simulations.

2) Interconnections: Two types of interconnections have to be modeled: the gold conductor lines that connect the electrode sites with their corresponding bondpads (see Fig. 1) and the leads connecting the bondpads of the chip and electrode array with each other. The latter can be either wirebonds or flip-chip solder bumps. Fig. 5 shows a lumped circuit model for the interconnections as part of a complete system model for measurements of ionic activities. Mutual capacitance and inductance components are used to model crosstalk. $R_{\text{line}}$ and $R_{\text{lead}}$ are the ohmic resistances of the interconnect line or lead, and $C_{\text{line}}$ and $C_{\text{lead}}$ are the capacitances of the line or lead to ground. Inductances $L_{\text{line}}$ and $L_{\text{lead}}$ have an effect on the propagation delay of the signals. This quantity, however, is negligible here since the length of the interconnections is much smaller than the signal wavelength.

Typical values for lead inductances and capacitances can be found in [7]. They are listed in Table I for various lead types. The lead capacitance is split evenly between the two capacitors shown in Fig. 5. The values in Table I depend, of course, on the location of the ground plane/conductors and can only be taken as estimates.

The wirebond leads of the sensor system are comparable to the electrode array interconnect lines in terms of cross-sectional area and encapsulating dielectric medium. Since the inductance increases linearly with length, it is possible to estimate $L_{\text{line}}$ from $L_{\text{lead}}$. Since $L_{\text{lead}} \approx 2 \, nH$ (Table I) and a typical interconnect line is about ten times longer than the wirebond, the inductance $L_{\text{line}}$ is approximately 20 nH. A calculation of the line capacitance, however, is more difficult. It will most likely be smaller than the value given in Table I due to the lack of a ground plane. Therefore, it is assumed that a capacitance of 0.5 pF per lead and line represents a “worst case” scenario. The effect of this capacitance on the frequency response of the system is not negligible and will be discussed later.

The mutual capacitance $C_m$ between two parallel lines can be calculated for geometries typical in the electrode arrays fabricated at North Carolina State University, Raleigh. For a line length of 20 mm, a spacing of 25 $\mu$m, and a line thickness of 10 $\mu$m, the mutual capacitance is

$$C_{m, \text{line}} = \varepsilon_r \varepsilon_0 \frac{A}{d} = 0.25 \, pF$$  \hspace{1cm} (7)

where $\varepsilon_r = 3.5$ is the dielectric constant of polyimide, the insulating layer in which the gold lines are embedded. The mutual inductance between two parallel lines can be estimated by using the following equation (a circular interconnect line of radius $r$ is assumed for simplicity)

$$L_{m, \text{line}} = \frac{\mu_0}{2\pi} \ln \frac{d}{r} = 22 \, nH$$  \hspace{1cm} (8)

where $d$ is the distance between two lines; $l$ is the length of each line.

The mutual inductance $L_{m, \text{line}}$ is, therefore, comparable to the estimated line inductance $L_{\text{line}}$. The mutual capacitance and mutual inductance between two wirebonds is approximately $C_{m, \text{lead}} = 1 \, pF$ and $L_{m, \text{lead}} = 1 \, nH$ [7].

The ohmic resistance of the wirebond leads and interconnect lines can easily be calculated from their geometries and is <1 $\Omega$. Compared with the high input impedance of the MOSFET based input amplifier it is obvious that these resistances can be neglected in simulations of the sensor system.

3) Signal Conditioning Circuit: The signal conditioning circuit of the sensor system consists of several channel amplifiers, a multiplexer, sample-and-hold circuit, a successive approximation analog-to-digital converter, and an input–output register. The detailed description of the entire circuit is beyond the scope of this paper. Although it is possible to simulate the entire signal conditioning circuit, only the input amplifier needs to be included in simulations that are aimed at analyzing the interactions between the three main system components. Once the electrode signal is buffered, there are only negligible interactions.
between the following stages and the electrodes and interconnections.

B. Simulation Procedures

The BBB-transmission lines described above were modeled in SPICE with discrete components. The number of differential elements \( N = 100 \) was chosen by finding a compromise between simulation speed and accuracy.

To simulate the complete sensor system, all components are combined as shown in Fig. 5 for measurements of ionic activities. The recorded potential is modeled by an ac signal source that may contain a dc-offset component. The input amplifier is shown in a voltage follower configuration, a commonly used signal buffering technique.

III. RESULTS

Both biopotential and ion-selective sensor systems were modeled and simulated. Only the ion-selective case will be described here.

One goal was to determine system component interactions. Therefore, a simulation with ideal interconnections is performed first (sensor and amplifier only). The resulting amplifier frequency response of this case is shown in Fig. 6(a) (solid line). These simulations can be used to study the influence of sensor impedance on accuracy and bandwidth of the system. The gain deviation in the range of 0.05 Hz to 500 Hz caused by the sensors only is 0.006 dB. This value is within the required accuracy limit of 0.017 dB or 0.2%, which corresponds to an 0.5-bit error of an 8-bit system.

Next, the interconnections without their crosstalk components \( (C_m, L_m) \) are included (Fig. 6(a), dashed line). The transfer characteristic does not change significantly, the gain error even decreases in the frequency range of interest, and approaches zero near dc. The gain deviations caused by the ion-selective electrode and interconnections cancel each other out which is an interesting result that can be used for future optimizations of the system. Finally, the crosstalk components \( L_m \) and \( C_m \) are included, their effect can be seen in Fig. 6(a), dotted line. The high cutoff frequency now approaches 500 Hz, and a slight drop in gain can be observed.

IV. DISCUSSION

A. Analysis of System Parameters from Simulation Results

Sections II and III described the development of an equivalent circuit model for the sensor system. The model can now be used to study the influence of parameter variations on the system’s responses. The latter are the accuracy of the amplified signal, the frequency response of the amplifier, and the noise performance of the system. The most interesting system parameters for an ion-selective sensor system are the composition of the ion-selective membrane (concentration and diffusion coefficient of charge carriers), the composition of the reference electrode and the size of its liquid junction, and the operating temperature of the system.

1) Ion-Selective Membrane Composition: The membrane impedance is determined by the concentration and diffusion coefficients of its charge carriers [see (2) and (3)]. The charge carriers in the example described previously are Kval⁺ and negative sites. Their concentration can be varied which is reflected in the model by changing the values for \( C_m \), \( L_m \), \( K_{val} \) and \( C_m \) according to (2) and (3). Reducing the concentration of Kval⁺ for instance increases the impedance of the membrane. Likewise, changing the composition of the membrane (e.g., species with different diffusion coefficients) has the same effect. These parameters influence the accuracy of the system mainly in the region where the membrane impedance is governed by diffusion/migration of ions. The damping effect observed at these frequencies is due to the nonlinear Warburg impedance of the membrane.

First, the simulation result can be used to determine the maximum gain deviation in the frequency range of interest (0.05–500 Hz) for standard values of concentration and diffusion coefficient. This deviation is 0.006 dB. A comparison with the required system accuracy (0.017 dB) can then be used to determine the ion concentration and/or diffusion coefficient limits for this system using (2). This result can be conveniently expressed as a lower limit for the product of concentration and diffusion coefficient \( cD \)

\[
cD = \frac{1}{2} \frac{RT}{F^2 z^2 R_{+\text{max}}} d \frac{1}{A N} \tag{9}
\]

where \( R_{+\text{max}} \) is the value of \( R_+ \) at which the gain deviation is equal to 0.017 dB. \( R_{+\text{max}} \) was determined by simulations. For the electrode geometries used previously (diameter 500 µm, membrane thickness 100 µm) it is approximately 1.5 MΩ. Therefore, the \( cD \) product for Kval⁺ should not be less than
The $cD$ value for the negative site is not critical, since its diffusion coefficient is about ten times higher than the $K^{\text{val+}}$ concentration. A minimum amplifier input resistance can be determined for the membrane composition described above. The system was simulated for different values of $R_{\text{in}}$ and the gain deviation was recorded [see Fig. 6(b)]. The minimum amplifier input resistance corresponds to a gain deviation of $0.017 \text{ dB}$ and is $4.8 \text{ G}\Omega$.

2) Reference Electrode Composition and Size: The reference electrode can be treated similarly to the ion-selective electrode. But here the concentration of the inner reference solution (KCl) is so high that the lower limit of $cD$ will never be reached in real electrodes. However, it is possible to determine the smallest length to area ratio of the liquid junction (the opening that separates the inner reference solution from the test solution). This value is $145 \mu m^{-2}$, it was obtained by simulating the system at different values of $R$ (see Fig. 4, reference electrode). Larger ratios cause gain deviations greater than $0.017 \text{ dB}$. This ratio will not be reached even in miniaturized reference electrodes. The reference electrode has, therefore, negligible influence on the system’s accuracy.

3) Temperature: SPICE allows the simulation of the circuit model under different operating temperatures. The temperature of the system environment will be the body temperature of the animal. It is unlikely that the small power dissipation of the signal-conditioning chip (5 mW) will generate higher temperatures. Nevertheless, simulations under different operating temperatures ($37^\circ\text{C}$-$45^\circ\text{C}$) were performed, they yielded only minimal deviations in the frequency response of the system.

V. CONCLUSION

A SPICE system model for the proposed miniaturized cardiovascular sensor array has been developed based on equivalent circuits of its electrochemical, interconnection, and electronic elements. It was found fully suitable for analyzing issues of miniaturization. Values for the circuit components were assigned using measurements on real systems, analytical expressions, or estimates from other sources [4], [7]. The components were first simulated by themselves and then combined to simulate the system as a whole. This approach allowed investigations of the influence of each component on the system response as well as interactions between single components.

REFERENCES


Carsten Mundt (S’94–M’97) received the M.S. degree in electrical engineering from the Technical University of Dresden, Dresden, Germany. During the course of his study in Germany, he focused his research on thick-film technologies and investigated solder paste stencil printing in ultrafine pitch. He received the Ph.D. degree in electrical engineering with a minor in biomedical engineering from North Carolina State University, Raleigh, in 1997. His dissertation examined the design of a miniaturized signal conditioning system for Kapton-based biopotential and ion-selective electrode arrays.

He was a Visiting Scientist at North Carolina State University where he was involved in the fabrication and characterization of thin-film cardiovascular microelectrode arrays. Between 1994 and 1997, he was a Fellow of the NSF/Engineering Research Center for Emerging Cardiovascular Technologies at Duke University, Durham, NC. He presented his research at several conferences and published a series of journal papers with Dr. R. P. Buck on general equivalent circuits for electrochemical cells. Since 1997, Dr. Mundt has been working as a lead engineer with NASA’s Sensors 2000! Program. His work is focused on the development of biotelemetry and data acquisition systems for biosensors. He is also involved with the development and testing of a variety of chemical and biosensors. He currently manages the “Advanced Technology Development—Biosensors” program at NASA Ames and directs the associated chemistry and sensor labs.

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