Proceedings of IEEE Asia Pacific Conference on Circuits and Systems '96
November 18 ~21, 1996, Seoul, Korea

Semi-State Description of Potassium and Sodium Channels in Hair-Cell-Type Circuits

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Abstract

Hair cells act as neural interfaces of sound signals and, therefore, circuit representations are important to signal processing systems based upon characteristics of the ear. Here a nonlinear bidirectional model of a hair-cell is presented. Also developed are a canonical semi-state description for its Potassium and Sodium channels, and circuits suitable for a transistorized hardware implementation.

Introduction

Circuits which mimic the behavior of the cochlea are useful for determining properties of the ear from stimulated acoustic emissions, as well as for the design of ear-type systems [1, 2]. The presence of nonlinearities and active behavior in the cochlea is supported by experimental data that show discrepancies between basilar membrane and neural tuning. Two major categories of sources of cochlear nonlinearity have been suggested in the literature [3, 4]. The first category finds its origins in the bounds on the motion of the basilar membrane and the cochlear fluids, and the second one resides in the mechano-electrical transduction process that occurs in the hair cells: mechanical resonance of the stereociliary-tectorial structure and limits on the amplitude of electrical resonance of the hair cell membrane. Experimental evidence has shown that this process, besides being an active one, is bidirectional and nonlinear [3, 4]. It is believed that the bidirectional process of the hair cells is the physical basis for a variety of phenomena observed in mammals, including Kemp echoes and spontaneous acoustic emissions [1, 2].

The cochlea lattice model developed in [5, 6] is passive and linear. But since experimental evidence shows that Kemp echo phenomena [7] are active and nonlinear, it is important to incorporate nonlinearities and active behavior into the full model. Toward this we assume that the nonlinearities and the active behavior are due to the hair cells and, therefore, propose a nonlinear active bidirectional model of a hair cell, based on that of Weiss and Leong [9, 8] and Secker, Searle, and Wilson [10]. We then convert the equations describing the activities of the Potassium and Sodium channels to a canonical semi-state form from which we develop circuits appropriate for future VLSI implementation.

Hair-Cell-Type Circuits

The proposed active and nonlinear hair-cell model (Figure 1), following from that of Weiss and Leong, is based on the mechano-electrical behavior of the hair cells and embodies two parts: an electrical part and a mechanical part. The electrical part models the electrical activities of the hair cell, namely the opening and closing of Potassium and Sodium channels, and transduction channels, specific to the hair cells, that regulate the fluctuations of the membrane voltage, through the control of ion transport into the cell, and via which neural signals, encoding acoustical information, are transmitted to the brain. These channels are modeled by the nonlinear conductances $G(\theta)$ and $G_{sh}(V_p)$ which we convert to current and voltage controlled nonlinear current sources for simulation purposes. As indicated in Figure 1, θ is the charge across C_M and V_p the voltage across C_p. The slow process of the opening and closing of potassium channels is symbolically represented by the series path R_pC_p. The hair cell membrane is represented by the nonideal capacitor C and its leakage resistance R and resting voltage V_c.

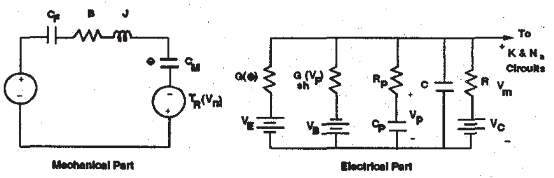

Figure 1: The electrical equivalent nonlinear bidirectional model of a hair cell.

The mechanical part of the hair cell concerns mainly the movement of the bundle and its bidi-

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rectional coupling with the body of the cell. The hair bundle is modeled by a second order mechanical system with an inertia J, a viscous drag B, and a compliance C_M, and the electro-mechanical feedback by a torque controlled by the membrane potential V_m. The mechanical system is then converted to an electrical equivalent circuit consisting of an RLC circuit and a nonlinear voltage controlled voltage source $T_R(V_m)$ which mimics the electro-mechanical feedback. The stimulus is a torque applied to the hair bundle and is represented here by a voltage source T_F. In their experiment, Howard and Hudspeth [4] used a thin flexible glass fiber to drive the hair bundle. This fiber is represented by a capacitor C_F, to account for its compliance.

Semi-State Equations and Circuits for Hair-Cell Model

The canonical semi-state representation takes the form of the equations

$$E\frac{dx}{dt} = A(x,t) + Bu \qquad (1)$$

$$y = Cx \qquad (2)$$

where u, x, y are the input, semistate, and output vectors, B, C, E constant matrices (with E possibly singular), and $A(.,.)$ a possibly nonlinear function. These are very useful for VLSI design using current mode circuits. Consequently, we obtain such a representation for the nonlinear hair cell-type structures considered here and represented by Figure 1 with the addition of the refinements of Figure 2 to include ion channels as mentioned below.

In the hair cell model of Figure 1 the slow process of the opening and closing of Potassium and Sodium channels is modeled by allowing the effective conductances of these channels to vary according to laws determined by Hartline [11] and given below as equations (3) and (4)

$$G_i = \frac{G_M}{1+\exp[-(V_m(t)-V_{oi})/\mu_i]} \quad i = Na, K \qquad (3)$$

where G_M, V_{oi} and μ_i are constants associated with the basic sodium, $i = Na$, or potassium, $i = K$, channels. Physically, G_M is the maximum conductance, reached when all channels are open, V_{oi} a half-activation voltage and μ_i the channel characteristic voltage. In addition to the characterization in terms of voltage dependent conductances, there is the slow opening and closing of these channels which are modeled by the following differential equations due to Hartline [11].

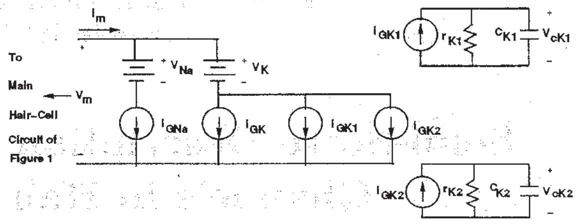

Figure 2: Equivalent circuit for the hair cell Potassium and Sodium channels semistate equations

$$\tau_{Ki}\frac{dG_{Ki}}{dt} = \frac{G_{MKi}}{1+\exp[-(V_m(t)-V_{oi})/\mu_i]} - G_{Ki} \qquad (4)$$

for $i = 1, 2$ and where τ_{K1} and τ_{K2} are the slow and fast time constants for these two channels.

To lead to transistorized hardware implementations for the hair cell model, we interpret these laws in terms of a basic circuit (Figure 2) for which canonical semi-state equations are derived below, following a treatment in [12, 13]. With Figure 2 in hand, we set the semistate vector as

$$x = [V_{cK1}, V_{cK2}, i_{GNa}, i_{GK}, i_{GK2}, i_{GK2}, V_m, i_m]^T \qquad (5)$$

and describe the dynamics by

$$\begin{bmatrix} \tau_{K1} & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \tau_{K2} & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \end{bmatrix} \dot{x} =$$

$$\begin{bmatrix} -1 & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & -1 & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & -1 & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & -1 & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & -1 & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & -1 & \cdot & \cdot \\ \cdot & \cdot & 1 & 1 & 1 & 1 & \cdot & -1 \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & A_v & A_i \end{bmatrix} x+$$

$$\begin{bmatrix} G_{K1}(x_7) \\ G_{K2}(x_7) \\ G_{Na}(x_7)[x_7 - V_{Na}] \\ G_K(x_7)[x_7 - V_K] \\ x_1(x_7 - V_K) \\ x_2(x_7 - V_K) \\ 0 \\ 0 \end{bmatrix} + Bu \qquad (6)$$

Here the .'s inside the matrices represent 0 and the A_v and A_i depend on the choice of the input. Also, for compactness we have defined for (6)

$$G_j(V_m) = \frac{G_{MKj}}{1 + exp[-(V_m(t) - V_{0j})/\mu_j]} \qquad (7)$$

for $j = Na, K, K_1, K_2$ and where $V_{oK1} = V_{oK2} = V_{oK}$. $G_j(V_m)$ represents the current i_j for a 1Ω resistance r_j. Next we determine the matrices B and C for the two cases (admittance or impedance basis) below.

Case 1: $u = V_m, y = i_m$. By inspection we get

$$\begin{aligned} B &= [0,0,0,0,0,0,1,0]^T, \quad A_v = -1 \\ C &= [0,0,0,0,0,0,0,1], \quad A_i = 0 \end{aligned} \qquad (8)$$

Case 2: $u = i_m, y = V_m$. In this case

$$\begin{aligned} B &= [0,0,0,0,0,0,0,1]^T, \quad A_v = 0 \\ C &= [0,0,0,0,0,0,1,0], \quad A_i = -1 \end{aligned} \qquad (9)$$

Simulation and Results

To test the circuit models we perform a Spice simulation of the nonlinear bidirectional circuit of Figure 1 incorporating those of Figure 2 to include Potassium and Sodium channels, with the circuit components being estimated from experimental data [1]. Because the mechanical part of the model is converted from recti-linear to rotational, on the one hand, and from mechanical to electrical, on the other hand, the resulting circuit is scaled down to bring the values of capacitances C_F and C_M to reasonable values. Also, the initial conditions across the capacitors are set up so that the resting potential of the cell is -61 mv. We excite the circuit with a voltage pulse of magnitude 4.8 mv and width 25 ms, simulating the torque T_F, and measure the membrane potential V_m and the voltage V_{CM} across C_M. The latter is proportional to θ which represents the deflection of the stereocilia of the hair-cell. As shown in Figures 3 and 4, the results obtained reproduce the waveforms recorded by Howard and Hudspeth in their shape and order of magnitude.

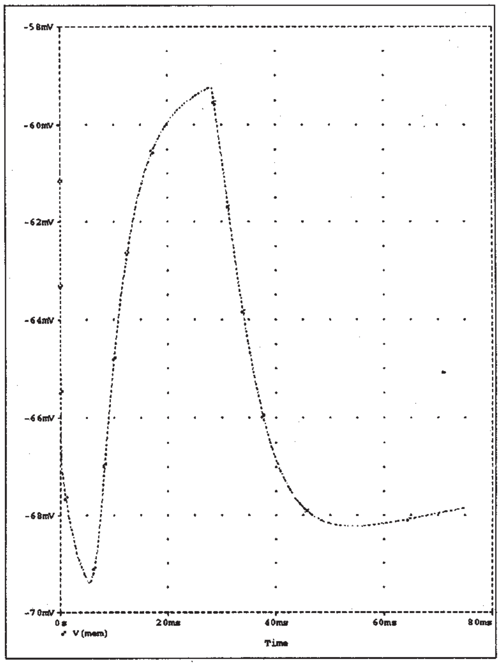

Figure 3: The hair-cell membrane potential V_m

Discussion

In this paper we have presented a nonlinear bidirectional hair-cell circuit and developed a set of canonical semi-state equations and circuits for its Potassium and Sodium channels. Although a large number of other sets can be used, the ones developed are of special interest since they should lead to transistor circuit realizations of the hair-cell-type circuits.

The semi-state equations derived present a number of difficulties for realization in terms of electronic hardware largely due to the fact that the equations include differential equations for conductance rather than for voltage and current. Consequently, a transfer of the equations into voltage and current ones was needed and that was carried out by numerically converting the conductances into voltages and then realizing the resulting currents via voltage controlled current sources (VCCS). It is in this direction that

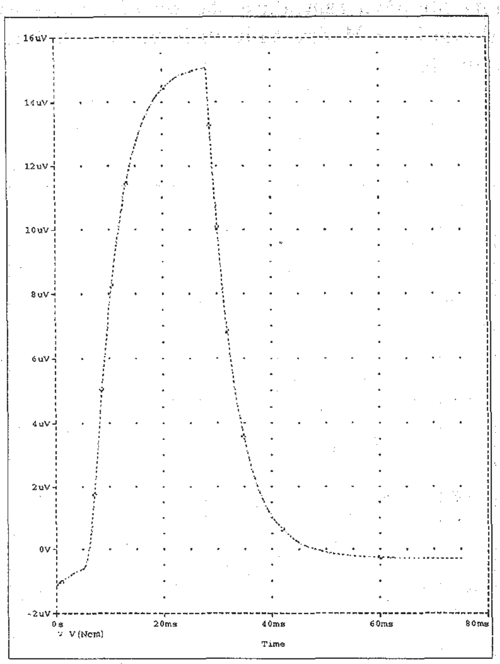

Figure 4: The voltage V_{CM} across the capacitor C_M.

our equations have evolved. The best way to make a VCCS is usually to use a differential amplifier with a current mirror [14]. When BJTs are used this leads to an hyperbolic tangent gain function whereas when MOS transistors are used the result is a square root function, both of which can closely approximate the nonlinearities of (3) and (4).

State variable types of equations work with inputs and outputs while the equations of hair cells are somewhat like resistors in that sometimes voltage is an input and sometimes current is an input, a property which one might call "non-orientedness." To reflect this non-orientedness of the hair cell we developed two sets of canonical semi-state equations which will be useful for ear-type systems incorporating hair-cell types of behaviors.

Acknowledgements

The research of L. Sellami is partly supported by the Naval Academy Research Council.

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