Mathematical Modeling of the Informative Process in the Biosensor of Angular Acceleration

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Abstract: - In this work we present a mathematical model of the informative process of the biosensor of angular acceleration (vestibular system in the inner ear). The functional and numerical parameters of the model have been identified by physiological and morphological experiments in the inner ear of amphibians and mammals. The model developed is a compartmental-type model in which we considered all the stages of the sensory activation process in the biosensor of angular acceleration. We performed a comparative analysis between our model and the mathematical model of Fernandez and Goldberg (1971), in which they described the change of the firing frequency of primary afferent neurons in response to the angular acceleration of the head about the vertical axis. The comparative analysis of both models indicates that our model more appropriately reproduce the fast responses of the vestibular system than Fernandez and Goldberg model; in addition, the parameters used in our model have physiological meaning.

Key-Words: - Mechanical stimulus, hair cell, primary neuron, vestibular mechanoreceptor, afferent impulses

1 Introduction

In 1971 Fernandez and Goldberg [1, 2, 3] proposed a mathematical model that describes the changes in the firing frequency of the primary afferent neurons of the horizontal semicircular canal in response to a mechanical stimulus as trapezoidal-shape changes of angular velocity when the head turns around the vertical axis. This model was applied with modifications in the analysis of the role of acceleration biosensors [4,5,6,7] and for the development of prototypes of vestibular prosthesis [8].

Since 2001, a group of mathematicians and physiologists from Lomonosov University of Moscow and the Autonomous University of Puebla, Mexico, began a collaboration for the development of comprehensive mathematical model of informative processes in the biosensors of the vestibular system [9, 10, 11, 12, 13, 14]. Based on these publications, in this work we present a mathematical model of the biosensor of angular acceleration when the head turns counterclockwise around a vertical axis z.

In Fig. 1 it is shown a functional scheme of th information output in the biosensor of angular acceleration in response to a short stimulus (a few seconds) that arises when an active or a passive movement of the head occurs in the horizontal plane; therefore, the input is the angular acceleration \( \dot{\omega}_z(t) \). The scheme has two input blocks describing the dynamics of the cupula-endolymphatic system (CES) [14] of the horizontal semicircular canals. Assuming that the dynamics of displacements \( x_L, x_R \) in the left and right semicircular canals coincide with the dynamics of CES, it constitutes the input for two vestibular mechanoreceptors forming a string of hair cells and primary afferent neurons. The vestibular mechanoreceptors transform the mechanical stimulus in a change of the membrane potentials \( V_{IL}, V_{IR} \) of the hair cells in both left and right semicircular canals, and this is the primary output from this block. Subsequently, in the following blocks of the model scheme, this output produces the synaptic transmission and the firing of the primary afferent neurons. The scheme has two output signals that form the primary input to the oculomotor muscles that controls the eye movement in the horizontal plane.

2 Mathematical Model Formulation

In the following paragraphs we describe briefly the mathematical model corresponding to the functional scheme explained above. For simplification we consider only the top row of the functional scheme (Fig. 1) which corresponds to the left horizontal semicircular canal.

The mathematical model of the dynamics of the CES is presented as the equation of Steinhausen of order
two (1) where $\varphi$ is the angular displacement of the cupula, $\tau_1, \tau_2$ are time constants ($\tau_2 \ll \tau_1$), and $\omega$ is the angular acceleration. To move to the next block we used the proportion $x = \varphi r$, where $r$ is the length of the cilia bundle, $x$ is the displacement ($\mu$m) of the cilia bundle tip. This displacement produces the transduction current $I_{Tr}$. The equations (2), (3), (4), (5) describe the dynamics of the membrane potential $V_1$ and the total ionic current $I_T$ produced by the mechanical stimulus $x$. The variables $m, h_1, h_2$ are physiological parameters that correspond to the parameters of activation and inactivation $[10]$.

The block corresponding to the synaptic transmission is represented by the algebraic model shown in (6), obtained from experimental data reported by Keen and Hudspeth, 2006. The graph corresponding to (6) is shown in Fig. 2.

![Fig. 1. Scheme of the vestibular mechanoreceptor compartments considered in the angular acceleration sensor model](image1)

The equations (7), (8), (9) describe the secondary output (from the afferent neurons) with change in the frequency of autooscillations produced by sodium ($I_{Na}$) and potassium ($I_K$) currents. The variables of the output block are: $V_2$ is the membrane potential at the first node of Ranvier; $n, h_K$ are the parameters of activation and inactivation for the potassium current. The steady state, when the mechanic stimulus is absent ($\omega = 0$), is shown in Fig. 3 with the parameters $I_T, V_1, I_{syn}, V_2$. Noteworthy, the basal frequency of discharge of the neuron in resting condition is $V_0 = 55$ Hz.

In the presence of angular accelerations ($\omega(t) \neq 0$), the change of firing frequency $\Delta V(t) = V(t) - V_0$ provide the output information of the biosensor. The functional and numerical parameters are in $[11,13]$.

$$\varphi + \frac{1}{\tau_2} \varphi + \frac{1}{\tau_1} \varphi \tau_2 = \omega,$$  
\(1\)

$$C_m \frac{dV_1}{dt} = -I_{Tr} - I_T - I_{L1},$$  
\(2\)

$$I_{Tr} = g_{Tr}(x)(V_1 - E_{Tr}),$$

$$g_{Tr} = g_{Tr} p(x), \quad p(x) = \frac{1}{1 + \exp\left(-\frac{x - x_0}{s_1}\right)}, \quad x = r \varphi;$$

$$I_T = g_T m^3(h_1 + h_2)(V_1 - E_T),$$

$$I_{L1} = g_{L1} V_1,$$

$$\frac{dm}{dt} = \left(\frac{m_{SL}(V_1) - m}{\tau_m(V_1)}\right)Q_{Io}, \quad (3)$$

![Fig. 2. Relationship between hair cell voltage and synaptic current in the afferent neuron. Data were taken from the work of Keen and Huspeth, 2006, display a sigmoidal dependence.](image2)
Fig. 3. Process of the biosensor in angular acceleration when $\omega = 0$. In A) total ionic current $I_T$, B) synaptic current $I_{syn}$, C) membrane potential $V_1$ in hair cells, D) membrane potential $V_2$ in afferent neuron.

\[ \frac{dh_1}{dt} = \left( \frac{q_s h_{ST}(V_1) - h_1}{\tau_{h_1}(V_1)} \right) Q_{10}, \]

\[ \frac{dh_2}{dt} = \left( \frac{q_s h_{ST}(V_1) - h_2}{\tau_{h_2}(V_1)} \right) Q_{10}, \]

\[ I_{syn}(V_1) = \frac{59.6962}{1 + \exp\left(\frac{-(V_1 + 40.6031)}{4.5979}\right)}, \]

\[ C_{m2} \frac{dV_2}{dt} = I_{syn}(V_1) - I_{Na} - I_K - I_{L2}, \]

\[ I_{Na} = g_{Na}(m_s(V_2))^3(C(V_2) - n)(V_2 - V_{Na}), \]

\[ I_K = g_K h_s(V_2 - V_K), \]

\[ I_{L2} = g_{L2}(V_2 - V_L), \]

\[ \frac{dn}{dt} = \left( \frac{n_s(V_2) - n}{\tau_n(V_2)} \right) Q_{10}, \]

\[ \frac{dh_K}{dt} = \left( \frac{h_{Ks}(V_2) - h_K}{\tau_{h_K}(V_2)} \right) Q_{10}. \]

### 2.1 Other models

The mathematical model of the change in the firing frequency of afferent neurons in response to a mechanical stimulus proposed by Fernandez and Goldberg [1], is commonly presented as a transfer function [2, 3, 4]:

\[ H(s) = k \frac{\tau_d s}{\left(1 + \tau_d s\right)\left(1 + \tau_i s\right)\left(1 + \tau_s s\right)} \]

where $\tau_1, \tau_2$ are time constants derived from the model of Steinhausen and describing the dynamics of the cupula of semicircular canals of the vestibular system and coincides with the equation described in (1); the time constants correspond to another part of the transference function shown in the expression (10), $k = k_0 \frac{\tau_1 \tau_2}{\tau_1 + \tau_2}$ Where $\tau_1 = 5.7\,\text{s}$ $\tau_2 = 0.003\,\text{s}$ $\tau_d = 80\,\text{s}$ and $\tau_i = 0.049\,\text{s}$ ($\text{s} = \text{segundos}$).

The coefficient $k$, as described by Fernandez and Goldberg [2], does not have physiological sense and was elected according to the experimental results with the purpose of having a qualitative coincidence. As standard stimulus (10) they chose the trapezoidal change of the angular velocity when the duration of the constant acceleration was $10 - 40$ seconds.

Our model (1)-(9) was tested for stimuli analog to those used by Fernandez and Goldberg, and also shorter duration stimuli than that of the constant accelerations (0.1 - 0.2 seconds), that is why we are going to talk about long and short stimuli. For long stimulus (Fig. 4) we present the experimental results of Goldberg and Fernandez, 1971 [1] (Fig. 5) and the function of both models (1)-(9) and (10) (with value
of $k_0 = 70)$. The change of the frequency as the average value of the output of the first model was calculated for each second and is presented in Fig. 6 and 7; the same is shown in Fig. 8 for the model (10). If results in Figs. 6, 7, 8 are compared a qualitative coincidence between the experimental results and the results obtained by both models can be shown.

Fig. 4. Long stimulus used to test the model.

Fig. 5. Response (experimental) to velocity trapezoids before an acceleration magnitude 7.5 deg/s$^2$.

Fig. 6. Response of the model (1)-(9) to a long stimulus (corresponding to the left semicircular canal).

Fig. 7. Response of the model (1)-(9) to a long stimulus (corresponding to the right semicircular canal).

Fig. 8. Response of the model (10) to a long stimulus.

2.2 Comparison with other models

With the assumptions adopted in the development of some of the blocks of the model (1)-(9) and described in [9-14], our model is intended for reproduction of the informative process when $\dot{\omega}(t) \neq 0$ in an interval of 0.2 seconds; for this reason it is interesting to compare the reactions of the two models considered (1)-(9) and (10) in the presence of a trapezoidal stimulus with intervals of acceleration with duration of 0.2 seconds (Fig. 9). The dynamics of the reaction of the model (1)-(9) to this stimulus is presented in Fig. 9 ($r=60 \mu m$) with the temperature factor $Q_{10} = \left( \frac{21}{10} \right)$. The change on the firing frequency 20Hz in the presence of a steady acceleration $30^\circ/\sec^2$ can lead to the contraction of the oculomotor muscles producing a movement of the eyes of $3^\circ$ to the opposite side of the head movement. Fig. 10 shows the changes of $\Delta \nu(t)$ in the model (10) for different values of the coefficient $k$.

The model that we have developed (1)-(9) has a more appropriate response to fast stimuli than
model (10). In addition, no change is required in the model (1)-(9) to get responses at other stimulus time durations, but to have a qualitative coincidence with experimental results using the model (10) it is necessary to seek a multiplier $k$ for other stimulus durations.

3 Conclusion
The interest in obtaining mathematical models of the processes taking place in the biosensors of the vestibular system is linked to the development of different prototypes of vestibular prostheses [8]. That is why it is needed to define the general criteria for the mathematical modeling of inertial biosensor. The mechanical stimulus produced by the action of the inertial forces is transformed into the biomechanic part of the sensor. For this reason, mathematical models must present a description of the dynamics of the biomechanic section. In relation to the model output it should be noted that they have to generate the coordinated contraction of some muscles and the relaxation of the antagonistic ones in order to produce a stable and coordinated movement of eye globes.

Fig. 9. Response of the model (1)-(9), in A) short stimulus, B) corresponding to the left semicircular canal, C) corresponding to the right semicircular canal.

Fig. 10. Response of the model (10) to a short stimulus, in A) $k_0=175$, B) $k_0=701$. 
Thus the number of outputs of any biosensor of the vestibular system must be even.

The model (1)-(9) has the possibility to generate the output in three different forms: a) in the absence of a nerve impulse -autooscillations- in the afferent neuron; b) in the presence of an impulse; c) in the presence of packages of impulses with variable frequency. This possibility can be represented in this model when there is a shift of the intersection point of zeroclines

\[
\frac{dV}{dt} = 0 \quad \text{and} \quad \frac{dn}{dt} = 0.
\]

The last aspect to note about our model is its capability to react to short stimuli of 20-40 ms, at this time the firing frequency should increase at least to 10-20 Hz. The illustration of this rule is shown in the Figure 9.

We conclude that the model presented adequately reproduce the response of the vestibular biosensor to mechanical stimuli with various advantages in relation to previously develop models.

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References: