Computer Modeling of the Neuronal Activity Described with the Simplified Hodgkin-Huxley System of Differential Equations

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Abstract: – A simplified Hodgkin - Huxley system of two nonlinear ordinary differential equation of the first order is considered. It describes an applied problem of a neuronal activation. A new local piecewise-constant approximation in solution of the inverse problem for recuperation of the non linear coefficients of this system is used and compared with the traditional rational expression by functions of the exponential type. The corresponding numerical algorithms are constructed and carried out as programs in the MatLab system for computing modeling of synthetic examples. The quality of algorithms is demonstrated on the numerical experiments.

Key-words: – Differential equations, Inverse problems, Neuronal activation, Computer modeling.

1 A simplified Hodgkin-Huxley system
The Hodgkin-Huxley system of equation (see [1] and also [2, pp. 50-52]) is presented in the form:

\[
C_m \frac{dV}{dt} = I_{apl} - m^3 h \overline{g}_{Na} (V - V_{Na}) - n^4 \overline{g}_{K} (V - V_{K}) - \overline{g}_{L} (V - V_{L}),
\]

\[
\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m,
\]

\[
\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n,
\]

\[
\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h,
\]

and can be regarded as describing the variations of membrane potential and ion conductance, which occurs at fixed point an the axon, in the terms of the potential function \(V(t)\), activation variables \(m, n\) and variable of inactivation \(h\), \(0 \leq m, n, h \leq 1\).

Here \(C_m\) is the capacitance of membrane, \(V_{Na}, V_{K}\) are potentials of the balance of sodium Na, potassium K, correspondently, \(V_{L}\) is the potential of the filtration balance; \(\overline{g}_{Na}, \overline{g}_{K}, \overline{g}_{L}\) are conductivities of sodium, potassium and of filtration correspondently; \(I_{apl}\) is control current.

Coefficients \(\alpha_m, \beta_m, \alpha_n, \beta_n, \alpha_h, \beta_h\) in traditional approach can be expressed [1] by functions depending of potential \(V\):

\[
\alpha_m(V) = \frac{0.1(V + 25)}{\exp[(V + 25)] - 1},
\]

\[
\beta_m(V) = 4\exp\left[\frac{V}{18}\right],
\]

\[
\alpha_n(V) = \frac{0.01(V + 10)}{\exp[0.1(V + 10)] - 1},
\]

\[
\beta_n(V) = 0.125\exp\left[\frac{V}{80}\right],
\]

\[
\alpha_h(V) = 0.07\exp\left[\frac{V}{20}\right],
\]

\[
\beta_h(V) = \frac{1}{\exp[0.1(V + 30)]}.
\]
The system (1) - (4) was constructed under the hypothesis that the potential of the membrane is uniform along the axon.

Defining:
\[
\tau_m = \frac{1}{\alpha_m + \beta_m}, \quad m_{st} = \frac{\alpha_m}{\alpha_m + \beta_m},
\]
\[
\tau_n = \frac{1}{\alpha_n + \beta_n}, \quad n_{st} = \frac{\alpha_n}{\alpha_n + \beta_n},
\]
\[
\tau_h = \frac{1}{\alpha_h + \beta_h}, \quad h_{st} = \frac{\alpha_h}{\alpha_h + \beta_h},
\]
we can transform expressions (2), (3), (4) to
\[
\tau_m \frac{dm}{dt} + m = m_{st}, \quad (11)
\]
\[
\tau_n \frac{dn}{dt} + n = n_{st}, \quad (12)
\]
\[
\tau_h \frac{dh}{dt} + h = h_{st}. \quad (13)
\]

The variable \( \tau_m(V) \) is very little in comparing with \( \tau_n(V) \) and \( \tau_h(V) \) for every value of \( V \), that give us possibility to use the Tikhonov theorem of the little parameter to eliminate equation (11) and use in reduction of the equation (1) the relation \( m = m_{st} \).

We will use also presented in [3], [4] the experimental relation \( n + h \approx c_0 \), where \( c_0 \approx 0.85 \), to eliminate (13).

So, we can consider here a case of the simplified model system:
\[
C_m \frac{dV}{dt} = I_{api} - m_{st} \frac{g_{Na}}{3} (0.85 - n)(V - V_{Na}) - n \frac{g_K}{4} (V - V_K) - g_I (V - V_L),
\]
\[
\tau_n \frac{dn}{dt} + n = n_{st}, \quad (15)
\]

By adjusting the experimental data with the first-order Boltzmann function in [3] it was obtained the formula
\[
m_{st} = 0.22 + \frac{0.78}{1 + \exp(-(V + 16.32)/10.02)}
\]
for steady-state activation \( m_{st} \) in nonlinear dependence of the potential \( V \).

## 2 Local Method for Inverse Problem

For the formulation of the proposing method and constructing simpler algorithm the second equation (15) of the system we will use again in the form (3).

The direct problem for system (14), (3) consists in its solution for given functions \( \alpha_n, \beta_n \) and values \( V_0, n_0 \) according to the Cauchy conditions \( V(0) = V_0, \ n(0) = n_0 \).

The inverse problem consists in recuperation of coefficients \( \alpha_n, \beta_n \), using data obtained by voltage clam experiments. The traditional empirical approximations are presented by formulas (7), (8).

The input data of the voltage clam experiments can be considered as \( N \) measured values \( V_i = V(t_i) \) of the potential function on the greed \( \{t_i\}, i=1,...,N \), of the time variable. The proposing approximations \( \tilde{\alpha}_n, \tilde{\beta}_n \) for functions \( \alpha_n, \beta_n \) are presented by piecewise-constant expansions with unknown coefficients \( \{a_i\} \):
\[
\tilde{\alpha}_n(V) = \sum_{i=1}^{N-1} a_i s_i(V), \quad (16)
\]
\[
\tilde{\beta}_n(V) = \sum_{i=1}^{N-1} a_{i,N-1} s_i(V). \quad (17)
\]

Here piecewise-constant basic functions \( s_i(V) \) are constructed on the auxiliary greed \( \{\tilde{V}_i\}, i=1,...,N \) such that
\[
\min_i \{V_i\} = \tilde{V}_1 \leq \tilde{V}_2 \leq ... \leq \tilde{V}_{N_i} = \max_i \{V_i\}.
\]

The proposing method for the reconstruction of the coefficients \( \{a_i\} \) consists in the next parts:

1) to calculate the approximation for the derivative \( dV/dt \) in the points \( \{t_i\} \) by divided differences;
2) to calculate the approximate values \( n_i \) for \( n(t_i) \) from the equation (14);

3) to calculate the approximation \( n'_i \) for the derivative \( dn/dt \) in the points \( t_i \) by divided differences;

4) to calculate for every index \( i=1,\ldots,N-1 \) the coefficients \( a_i, a_{i+M} \) as the solution of the local collocation scheme

\[
\begin{align*}
n'_i &= (1-n_i)a_i - n_{i+1}a_{i+1}, \\
n'_{i+1} &= (1-n_{i+1})a_i - n_{i+2}a_{i+2}. 
\end{align*}
\]

(18)

(19)

Solution of system of linear algebraic equations (18), (19) exists and is unique if approximate values \( n_i \) of function \( n(t) \) are not constant. Really, the determinant of the matrix \( A \) of the considered system is equal to

\[
\det(A) = -(1-n_i)n_{i+1} + n_i(1-n_{i+1}),
\]

(20)

that justified our conclusion.

Proposed method gives us really the explicit solution of the inverse problem, and therefore it is simpler in the numerical realization than traditional schemes, which require solution of some non linear equations.

3 Computing Modelling and Numerical Experiments

We realized proposed method as algorithm and software in MatLab system. To simulate the input data we have constructed numerically solutions \( \bar{V}(t) \) and \( \bar{n}(t) \) of system (14), (3) with traditional empirical approximations (7), (8), using the MatLab function \texttt{ode45} for the initial data \( V_0 = -11 \) mV, \( n_0 = 0.9 \), the capacitance of membrane \( C_m = 1 \) micro

\( \text{Farad/cm}^2, V_{Na} = -120 \) mV; \( V_K = -14 \) mV; \( V_L = -22 \) mV; \( \bar{g}_{Na} = 90 \) mho/cm\(^2\); \( \bar{g}_K = 36 \) mho/cm\(^2\); \( \bar{g}_L = 0.3 \) mho/cm\(^2\); \( I_{apl} = 120 \) mA.

In Fig. 1 left and right correspondently we present graphics of functions \( \bar{V}(t) \), \( \bar{n}(t) \). On Fig. 2 for \( N=15 \) and on Fig. 4 for \( N=10 \) the first graphic presents with the solid line and stars correspondently coefficients \( \alpha_n \) and \( \beta_n \); on the second graphic of these figures the coefficients \( \bar{\alpha}_n, \bar{\beta}_n \) are presented.

![Fig. 1. Solutions \( \bar{V}(t), \bar{n}(t) \)](image1)

![Fig. 2. Coefficients \( \alpha_n, \beta_n \) and \( \bar{\alpha}_n, \bar{\beta}_n \) for \( N=15 \).](image2)

![Fig. 3. Solutions \( \bar{V}(t), \bar{n}(t) \) of direct problem with recuperated coefficients \( \bar{\alpha}_n, \bar{\beta}_n \) for \( N=15 \).](image3)
Computing modeling on synthetic examples demonstrate that recuperated by the proposed method coefficients $\tilde{\alpha}_n, \tilde{\beta}_n$ are not close to initial $\alpha_n, \beta_n$. Nevertheless, it appears a satisfactory approximation for solution of the direct problem.

Developed method can be applied also for another mathematical models constructed on the base of the Hodgkin – Huxley ideas. For example, in the mathematical model of the dynamics of the general ion current in hair cell [5], or in the modified Hodgkin – Huxley models of activation of the primary neuron of vestibular apparatus [6].

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Referentes: