

Advanced Model and Analysis of Activity in Neurons based on Liquid Junctions Induced in Cytoplasm

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Abstract: - When the inner (cytoplasm) potential grows up beyond zero potential (in the external liquid), positive ions cannot flow anymore into the cytoplasm. So effective knowledge of excitation was not provided by the conventional Hodgkin Huxley model. This paper first presents a model and analysis of a depletion layer formed at the boundary between positive and negative ($p - n$) zones. This paper then gives an advanced model of activity, which structure is composed of three zone separated by two junctions induced dynamically in cytoplasm for input stimulation. This paper then gives equivalent circuit of “activity” with input and surround passive circuit. This model are commonly applied to dual modes of excitation of positive and negative potential generations, and also applied to output signals with pulse and plateau for the first and the second messengers.

Key-Words: - Neuron, Activity, Electrophysical model, Zone and depletion layer, Liquid junction, Positive / Negative potentials, Pulse and plateau.

1 Introduction

A neuron operates as an oscillator (or signal generator) of pulse and plateau potentials. A group of neurons organizes a synchronous system by mutual injections of potentials among oscillators.

Variety of positive and negative ions are taken into ectoplasm in excitatory cells of neurons and unicellular animals in experiments by T. Kamada[1].

A neuron of *aplysia* generates positive pulse, positive pulse–plateau, and positive pulse–negative plateau with ionophoretically applied medicines in experiments by R.E. MacCaman, et al [2,3,4].

The relation between the potential polarities of pulse and plateau and the direction of motion were studied in unicellular organism by Y. Naito, R. Eckert, and K. Oami[5,6].

The authors have given electrophysical modelling and analysis of pulse generation by a neuron and synchronization by a neural group, and its application to estimate the time and the position in space of events by a neural groups[7,8,9,10,11].

In this paper, a novel model are given and analyzed as a negative model of activity as well as positive ones. This model is composed electrophysically based on the junction induced in cytoplasm responding to stimulus. This model covers whole functions of potential generation of pulse and plateau with positive and negative polarities.

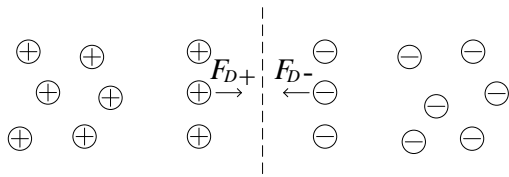
A junction induced in cytoplasm is usually observed between the cytoplasm and the liquid in glass tube electrode in experiment.

Pulse and plateau with negative potential polarities have been interpreted solely as inhibitory response for input stimulus.

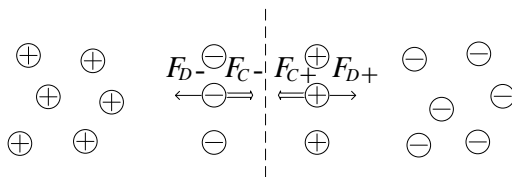
2 Liquid Junction

2.1 Formation of electrical zones and a depletion layer

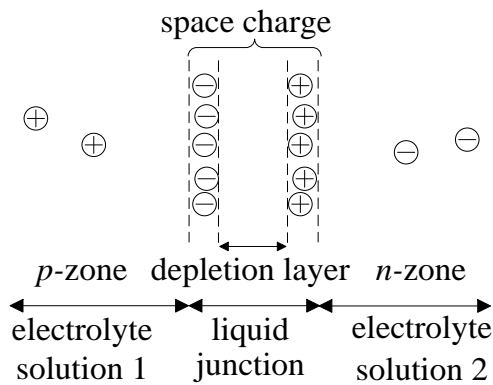
When electric charges are injected into a zone in electrical medium, charge density at the zone becomes higher and the other zone remains lower. It is assumed that quantity of injected charges is little and velocity of charges is low in the medium. Special phenomena are induced at a boundary between two zones as shown in Fig. 1.



Phase 1: Diffusion of charges by gradient of density F_D . Injected p-charges diffuse to n-zone, and n-charges diffuse to p-zone by the force of gradient of density F_D .



Phase 2: Balance of diffusion F_D and Coulomb's force F_C . Coulomb's force F_C (force by potential gradient) appears between diffused p- and n-ions. Directions of forces F_D and F_C are opposite. When they are balanced, diffusion is ceased.



Phase 3: Cease of diffusion and formation of;
 (a) p-zone and n-zone, and
 (b) space charges and depletion layer with depth d .

A pair of space charges appears at both sides of the boundary. Potential difference appears in the boundary. And electric charges are driven outside the boundary, and two zones and a depletion layer (liquid junction) formed at the boundary.

Fig. 1 Formation of zones and a depletion layer of a boundary.

2.2 Depth and capacity of depletion layer

The diffusion potential (liquid junction potential) V_D is defined as follows.

$$V_D = V_n(z_n) - V_p(-z_p)$$

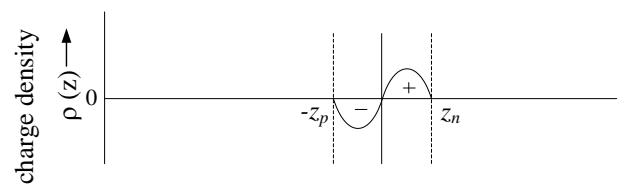
$$= \frac{q}{2\epsilon_e} (N_p z_p^2 + N_n z_n^2) \quad (1)$$

V_D is called as the height of potential wall for transmission of positive charge.

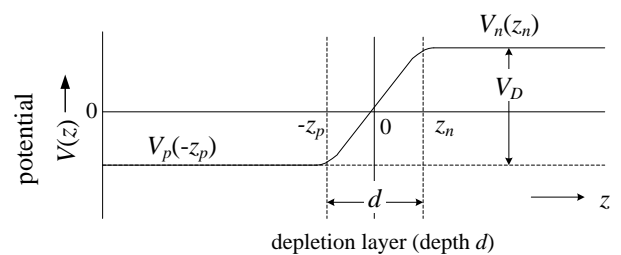
The depth of depletion layer is given as,

$$d = z_p + z_n$$

$$= \left(\frac{2\epsilon_e(N_p + N_n)}{qN_p N_n} V_D \right)^{\frac{1}{2}} \quad (2)$$



(a) Distribution of true electric charge density $\rho(z)$.



(b) Potentials V_p , V_n , and diffusion potential V_D .

Fig. 2 Distribution of true electric charge and diffusion potential of a boundary.

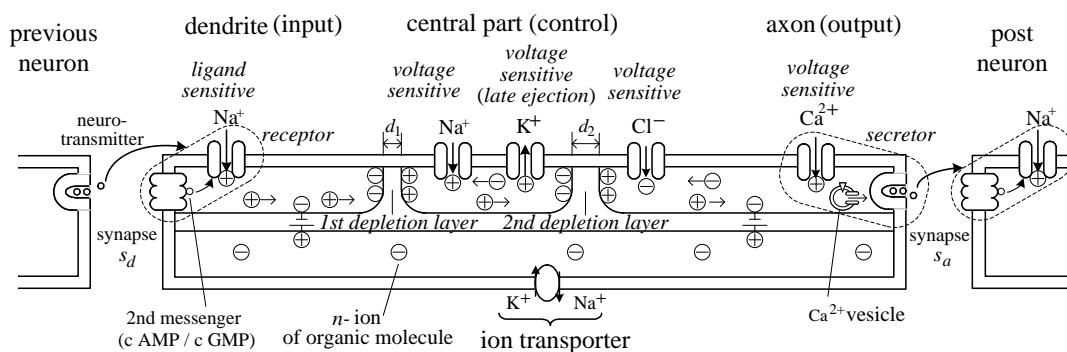


Fig. 3 Electro-physical modelling for positive potential generation. Na^+ channels at the dendrite are ligand-dependent. Na^+ channels at the central part are voltage dependent. Ejection of K^+ at the central part reduces pulse-width by rapid return to resting potential. Injection of Cl^- at the axon and its current flowing to the left contribute to current multiplication. $\text{Na}^+ - \text{K}^+$ transporter works as a battery.

3 Electro-physical Modelling for Positive Potential Generation

Electrophysical modelling of activity is essentially perceived as energy conversion from chemical to electrical energies. Or conversion from battery voltage and current to signals of pulse, plateau, or other waveforms. Based on the above concept, unknown models of neural activity are given from operational scheme of components of electrical devices and systems.

Actual semiconductor devices such as transistor are created with inhomogeneous three zones separated by two junctions induced in solid semiconductor.

In this study, modelling of active neurons is composed of three zones separated by two liquid junctions induced in cytoplasm of neuron. Liquid junction appears at the boundary between the cytoplasm of cell and liquid in glass electrodes in experiments, whenever test liquid is chosen as closer to the contents of cytoplasm.

3.1 Schematic diagram and electrophysical configuration

Electrophysical modelling of a neuron is shown in Fig. 3. The first messenger is received directly by Na^+ channels in receptor. The second messenger is received by a set of three proteins, and c-AMP is produced chemically[].

Na^+ , Na^+ and K^+ , and Cl^- are prepared at each zone. Input Na^+ channel injects Na^+ ions and the potential at the dendrite becomes high. This signal reaches the central part easily beyond lowered potential wall of the first depletion layer, and the potential becomes high. The potential at the central zone becomes higher by Na^+ injection, and later the potential becomes lower by ejection of K^+ ions. This operation yield a short time pulse waveform.

Na^+ ions reaches at the axon. Any way is not prepared to reduce the potential height of the wall at the second depletion layer, so the potential wall at the second depletion layer is kept high. Once positive charges (signal) enter into the axon, the signal energy is enhanced as the output of the neuron.

Cl^- ions are injected into the axon and flow to the left direction. Negative current to the left is equivalent to positive current to the right. This operation brings current multiplication to enhance activity of the neuron.

Ca^{2+} channels works for secretion of neurotransmitter to post neuron by exocytosis.

These ions distribute in thin layer under the membrane, because the quantity of total ions are very poor to fulfil whole cross section of cytoplasm. The other depletion layer is also induced between the thin current layer and the other cross-section in the cytoplasm.

3.2 Energy diagram of charges (ions)

Corresponding to Fig.3, energy vs position in z axis (energy diagram) is shown in Fig. 4.

The Fermi level is shown by a solid line for mean energy of positive (p -) and negative (n -) ions. Energy difference of p - and n -ions is estimated to be small in electrolyte.

The energy at the dendrite becomes high by injection of Na^+ ions (signal p -ions). By injection of p -ions at the central part, the energy becomes low corresponding to wall potential reduction. Early potential return to resting state by late ejection of K^+ at the central part yield a narrow pulse. This process is exhibited equivalently by the forward diode.

Carrier p -ions drift in the central part with flat potential. At the second boundary, potential wall is higher at the second depletion layer. A little charges pass over the potential wall with energy enhancing by thermal motion. The current multiplication is realized by additive negative current by Cl^- ions.

Pulse oscillation is made by a single neuron.

3.3 Equivalent circuit of essential activity

Corresponding to the energy diagram in Fig. 4, an equivalent circuit of activity is shown in Fig. 5 for positive potential generation.

Forward and reverse diodes n_d and n_a denote positive charge dynamics at the first and the second depletion layers respectively.

Points d , c , and a denote input (dendrite), control, and output (axon) ports. c_0 is a virtual point corresponding to average potential in the central part.

$\alpha \cdot i_d$ is the equivalent current source to drive the output load. α is current multiplication factor for i_d .

r_c is diffusion resistance at the central part.

Most of input current i_d reaches a . Current i_c is defined by components of input i_d and feedback of output current i_a .

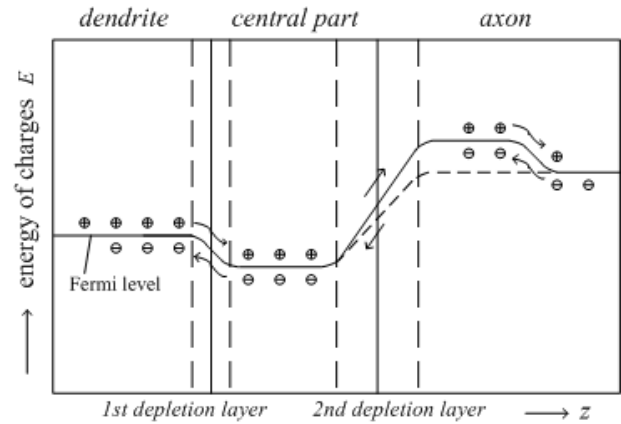


Fig. 4 Diagram of average energy (Fermi level) of positive and negative ions vs. positions along z -axis (longitudinal).

Energy is enhanced at the axon with current multiplication effect which is brought by negative charges injected through Cl^- channels. It is noted that solid and dotted lines correspond to Point Contact and Junction Transistors respectively [3, 6].

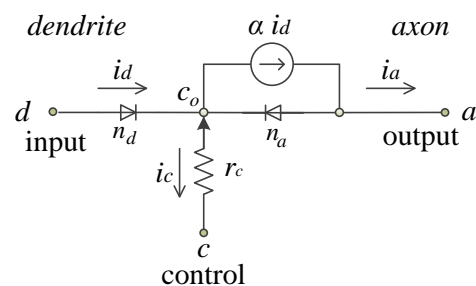


Fig. 5 Electrical modelling of essential activity of a neuron for positive potential generation.

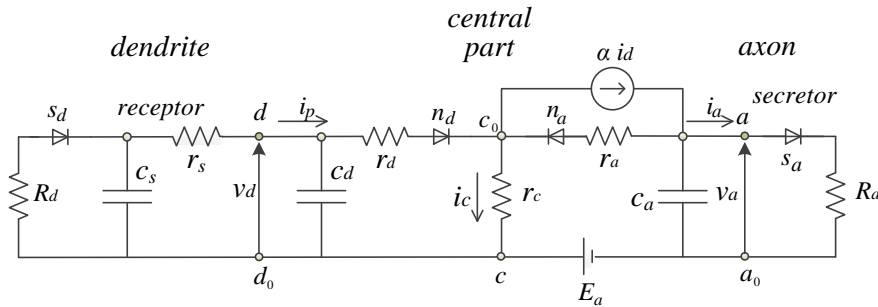


Fig.6 Equivalent circuit of a neuron for positive potential generation. Receptor is expressed by charge-discharge $c_s - r_s$ circuit.

4 Electrical Characteristic for Positive Potential Generation

4.1 Equivalent circuit of whole neuron

The whole equivalent circuit of a neuron is shown in Fig.6 for positive potential generation. Activity is given by a section between $d - d_0$ and $a - a_0$.

The capacities c_d and c_a are fundamentally defined by induced capacities at the first and the second depletion layers. Practically membrane capacity is added to them, but it is ignored in the analysis.

The equivalent circuit of input synapse and chemical process of receptor are shown by a voltage source and a charge-discharge $c_s - r_s$ circuit. This circuit defines the effects of the first-messenger-driven ion channels and the second-messenger (cAMP, cGMP, etc.)-driven ion channels.

The equivalent circuit of chemical process of secretor and output synapse are shown by the road resistance.

Impedances r_d and r_a of forward and reverse diodes n_d and n_a are low and high resistances respectively. Impedance ratio r_a / r_d is kept large enough to limit coupling of output to input circuits.

Input and output synapses s_d and s_a are shown as forward diodes for excitatory synapses (p -ions). Potential E_a is derived with an ion transporter (ion pump) in Fig. 3.

4.2 Characteristics as an amplifier

When reverse diode resistance $r_a \approx \infty$ approximately, closed loop gain G_v , open loop gain K , and feedback ratio β are given as follows.

$$G_v = \frac{v_a}{v_d} = \frac{\frac{\alpha R_a}{r_d + r_c}}{1 - \frac{\alpha R_a}{r_d + r_c} \cdot \frac{r_c}{R_a}} = \frac{K}{1 - K\beta} \quad (1)$$

$$K = \alpha \frac{R_a}{r_d + r_c} \quad (2)$$

$$\beta = \frac{r_c}{R_a} \quad (3)$$

where, v_d and v_a are input and output voltages of a neuron, G_v , K , β are closed loop gain, open loop gain, and inner feedback ratio of a neuron respectively. Oscillation condition is given by $K\beta \geq 1$.

In case that the axon has few Cl channels, $\alpha < 1$, $K\beta \ll 1$. Therefore a neuron operates as an amplifier with threshold for input signal with positive inner feedback.

Negative current flows to the left by injection of Cl^- charges.

The energy (power) gain G_E is given by;

$$G_E = G_v G_c \tag{4}$$

Where, G_c is current gain by sum of positive and negative currents flowing to the right.

Even if input stimulation could not exceed the threshold, a certain information is transmitted to the axon terminal and to the posit neurons. It is found in this paper that this effect is explained by amplification by a neuron.

4.3 Operational Characteristics as an oscillator

(1) Pulse oscillator

The neuron operates as a pulse oscillator to generate the output of potential waveforms when the product of open loop gain K and feedback ratio β exceeds 1.

This oscillator is composed of self-injection with inner feedback signal without external trigger.

$$T_1 = c_d \frac{r_c R_a}{r_c + R_a} \tag{5}$$

$$T_2 = c_a R_a \tag{6}$$

where, $R_d + r_d \gg r_c, r_a = \infty$
 are assumed for simplified analysis.

The period of oscillation T is given as the total time length as following;

$$T = T_1 + T_2 = C_d \frac{r_c R_a}{r_c + R_a} + C_a R_a \tag{7}$$

The mode of oscillation is astable. The stable point is only at the bottom.

The neuron operates as an astable mode tuned to external injection. Whenever, the phase and the period of original free running oscillator is fluctuating, the oscillator becomes stable by locking to the external signal as shown in Fig. 7.

Synchronization is established in a system with a group of neurons, and a stable timing clock is realized by total coupling among neurons.

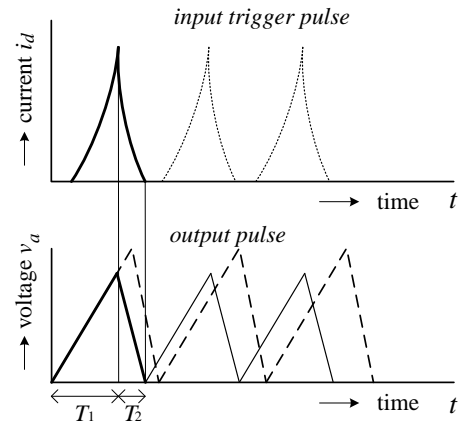


Fig.7 Output voltage waveform for positive potential generation. The dotted line is an original waveform. The solid line is synchronized waveform to the input trigger pulse.

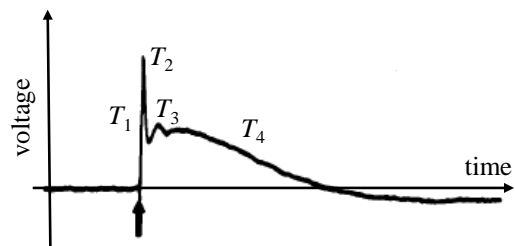


Fig. 8 Typical output voltage with positive pulse and plateau.

(2) Plateau oscillator

When the ion channel in the receptor is composed of a secondary messenger, the input signal is featured by a long holding time defined by discharge effects.

$$T_3 \approx c_s (r_s + r_c) + c_d \frac{r_c R_a}{r_c + R_a} \tag{8}$$

$$T_4 = c_a R_a \tag{9}$$

where, $r_a \ll r_c, c_d \ll c_s$

The period of oscillation T with pulse and plateau is given as the total time length as following (Fig. 8).

$$T = T_1 + T_2 + T_3 + T_4 \tag{10}$$

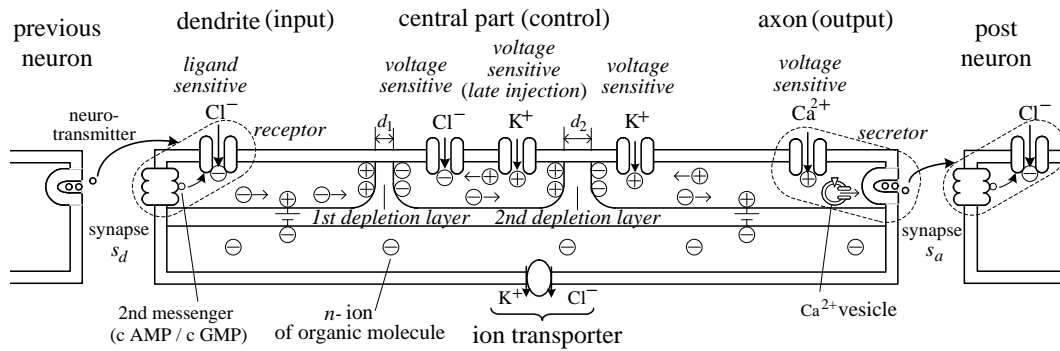


Fig. 9 Electro-physical modelling of an active neuron for negative potential generation. Cl⁻ channels at the dendrite is ligand-dependent. Cl⁻ channels at the central part are voltage dependent. K⁺ channels at the central part and at the axon contribute to reduction of pulse width and current multiplication respectively.

5 Characteristic of an Active Neuron for Negative Potential Generation

5.1 Equivalent circuit of whole neuron

Electro-physical modelling of a neuron for negative potential generation is given in Fig. 9.

Formation of zones and depletion layers in Fig. 9 is same to Fig. 3 except the kinds of ion channels. Ion channels for reception of signals from previous neurons are ligand-dependent Cl⁻ channels

Ion channels for reception of signals from previous neurons are ligand dependent Cl⁻ channels. Cl⁻ and K⁺ channels at the central part and at the axon are voltage dependent. Ca²⁺ channels are provided for secretion of neurotransmitters.

K⁺ and Cl⁻ transmitters operate to provide resting potential which works as a battery for neural circuit [17].

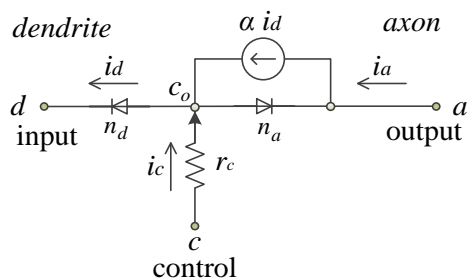


Fig. 10 Electrical modelling of activity of a neuron for negative potential generation.

5.2 Electrical Characteristics

Electrical modelling of the activity for negative potential generation is shown in Fig. 10. Input and output diodes n_d , n_a correspond to the first and the second depletion layers, which are shown as reverse and forward diodes respectively.

Equivalent circuit of an active neuron is shown in Fig. 11 for negative potential generation.

For negative potential generation, the waveform is just inverse of the waveform shown in Fig. 7 and 7.

It is summarized that modelling and analysis of electrical characteristics are common to neurons with positive and negative potential outputs except the direction of diodes and current flows in the equivalent circuit.

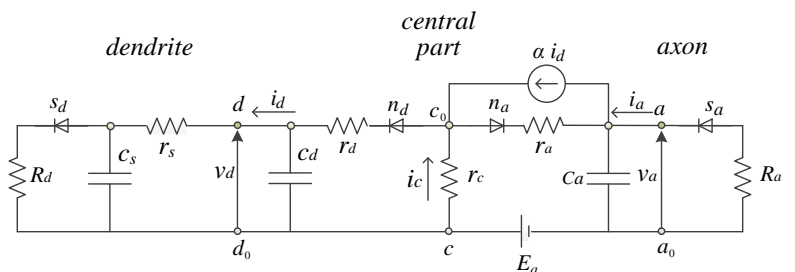


Fig. 11 Electrical modelling of an active neuron for negative potential generation.

6 Conclusion

Unified modelling of activity in neurons was given in this paper. By this modelling, typical potential output is positive pulse. And the variations in output potentials are negative pulse, positive and negative plateaus depending on ion channels in the receptor driven by the first and the second messengers. These output potentials depend on conditions of marine, limnetic, and physiological solutions in nature.

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