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Proposal of a New Mechanism for the Directional Propagation of the Action Potential Using a Mimicking System

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Supporting Information

The comparison of the present liquid-membrane cell system with a typical nerve cell

In the present study, the authors investigate a potential-conduction phenomenon by dividing a nerve cell into three domains (potential-sending site, potential-receiving site (I) and potential-receiving site (II)). The potential-sending site, potential-receiving site (I) and potential-receiving site (II) correspond to the domain indicating the action potential at the synapse, the domain except the potential-sending site at the synapse and the domain including the axon and the synaptic terminal, respectively, as shown in Fig. SI1. Usually, K^+ channels exist in the overall membrane surface of the nerve cell and a small part of K^+ channels always opens. At the synapse of the nerve cell, there are many channel-type receptors which mainly transport Na^+ from the outside to the inside. When the channel-type receptor combines with the transmitter, the channel opens for about 10 ms. By opening many Na^+ channels at a certain domain of the synapse, the membrane potential becomes to change from the resting potential to the action potential. This area is treated as the potential-sending site. The authors consider that the area except for the potential-sending site at

the synapse is determined as the potential-receiving site (I) and that the axon and the presynaptic terminal are provided as the potential-receiving site (II). In the area of the potential-receiving site (I), there are many K^+ channels and channel-type receptors (Na^+ channels). On the other hand, a lot of delayed K^+ channels and voltage-gated Na^+ channels existed in the area of the potential-receiving site (II). In the potential-sending site of the present model system, the RP cell indicating the resting potential and the AP cell indicating the action potential were placed. Namely, the RP and AP cells corresponded to the K^+ channels and the channel-type receptors (Na^+ channels), respectively. The Rec1' and Rec2' cells in the potential-receiving site (I) expressed the resting potential. Here, the Rec1' and Rec2' cells imitated the K^+ channels at the synapse. If the membrane potential exceeds the threshold, the channel-type receptors (Na^+ channels) cannot open. Therefore, only the Rec1' and Rec2' cells were set in the potential-receiving site (I). In the potential-receiving site (II), the Rec1 and Rec2 cells showed the resting potential and the V-ap1 and V-ap2 cells did

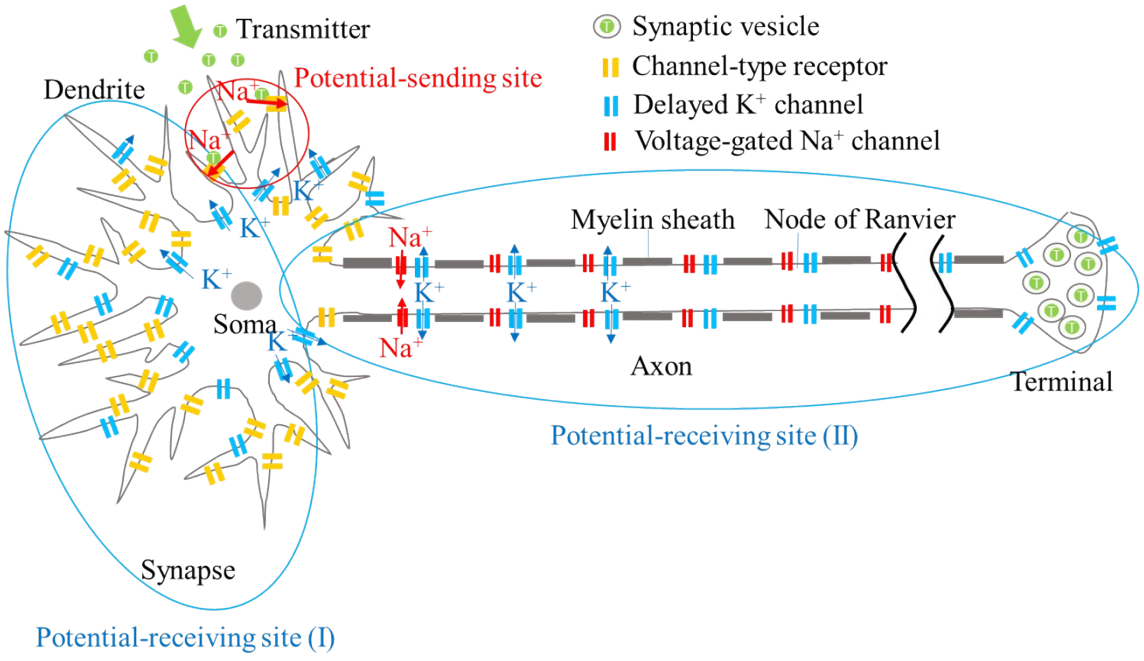

Fig. SI1 A typical nerve cell and the distribution of (delayed-)K^+ channels, channel-type receptors

(Na^+ channels) and voltage-gated Na^+ channels

the action potential. The V-ap1 and V-ap2 cells mimicked the voltage-gated Na^+ channels and the Rec1 and Rec2 cells did the K^+ channels in the axon and the presynaptic terminal.

The propagation of the action potential

The membrane potential ($E_{W2\text{-}W1}$) is defined as the potential difference between the inner aqueous phase (W1) and the outer aqueous phase (W2). Here, W2 is usually regarded as the reference side. Therefore, the resting potential caused by the transport of K^+ is a negative potential and the action potential depending on the Na^+ channels indicates a positive potential, as shown in Fig. 3. The direction of the electric current in the conventional electrophysiology is opposite with that determined in the electrochemistry. Therefore, the current due to the transport of K^+ or Na^+ from W1 (intracellular) to W2 (extracellular) shows a positive current and that due to the transport of K^+ or Na^+ from W2 (extracellular) to W1 (intracellular) does a negative current in the present work based on the electrochemical determination, as expressed in Figs. 2(B) and 4(B). On the other hand, black curves in Fig. 3 are represented by the handling of the conventional electrophysiology. Accordingly, the direction of the electric current of this figure reverses by the electrochemical notation, and gray curves are drawn according to the electrochemical expression. Figure SI2 shows the time-courses of the membrane current and membrane potential at a certain node of Ranvier based on the electrophysiological concept. When only K^+ can penetrate the cell membrane, the resting potential (about –80 mV) is settled by the ratio of the concentration of K^+ in the inner cell to that in the outer cell, as indicated in Fig. 3. If a lot of voltage-gated channels open at the potential-sending site, the $E_{W1\text{-}W2}$ at the potential-sending site shifts in the positive direction and the positive current due to the transport of Na^+ from W2 to W1 flows (the negative

current by the electrochemical notation). Then, the $E_{W1\text{-}W2}$ at the adjacent potential-receiving site begin to shift in the positive direction with the small positive current due to the transport of K^+ from W1 to W2. When the $E_{W1\text{-}W2}$ at the adjacent potential-receiving site exceeds the threshold, the voltage-gated Na^+ channels begin to open and the membrane potential sharply varies to the action potential. The membrane current caused by the sum of the transport of K^+ from W1 to W2 (the positive current) and that of Na^+ from W2 to W1 (the negative current) indicates the negative current at this time. Since the open-lives of the voltage-gated Na^+ channels are very short (about 1 ms) and the number of the opening K^+ channels increases, the membrane current changes from the negative value to the positive value. In the conventional electrophysiology, the positive current of the certain node of Ranvier flows first, and then the negative current is observed, as shown in Fig. SI2(A). During the electric conduction, the membrane potential is always more positive than the resting potential. Accordingly, it is thought that K^+ transports from the inside to the outside after the closing Na^+ channels and that $E_{W2\text{-}W1}$ gradually goes back to the resting potential, as represented in Fig. SI2(B). The authors consider that the lack of the consideration on the dynamic properties of the ion transport across the membrane creates the hyperpolarization in the cable theory. Since the delayed K^+ channels and the voltage-gated Na^+ channels coexist at the same node of Ranvier, the solution resistance among these channels is negligibly small. If the membrane potential across the Na^+ channel is different from that across the K^+ channel as regarded in the electrophysiological concept, the waste of energy seems to be too large.

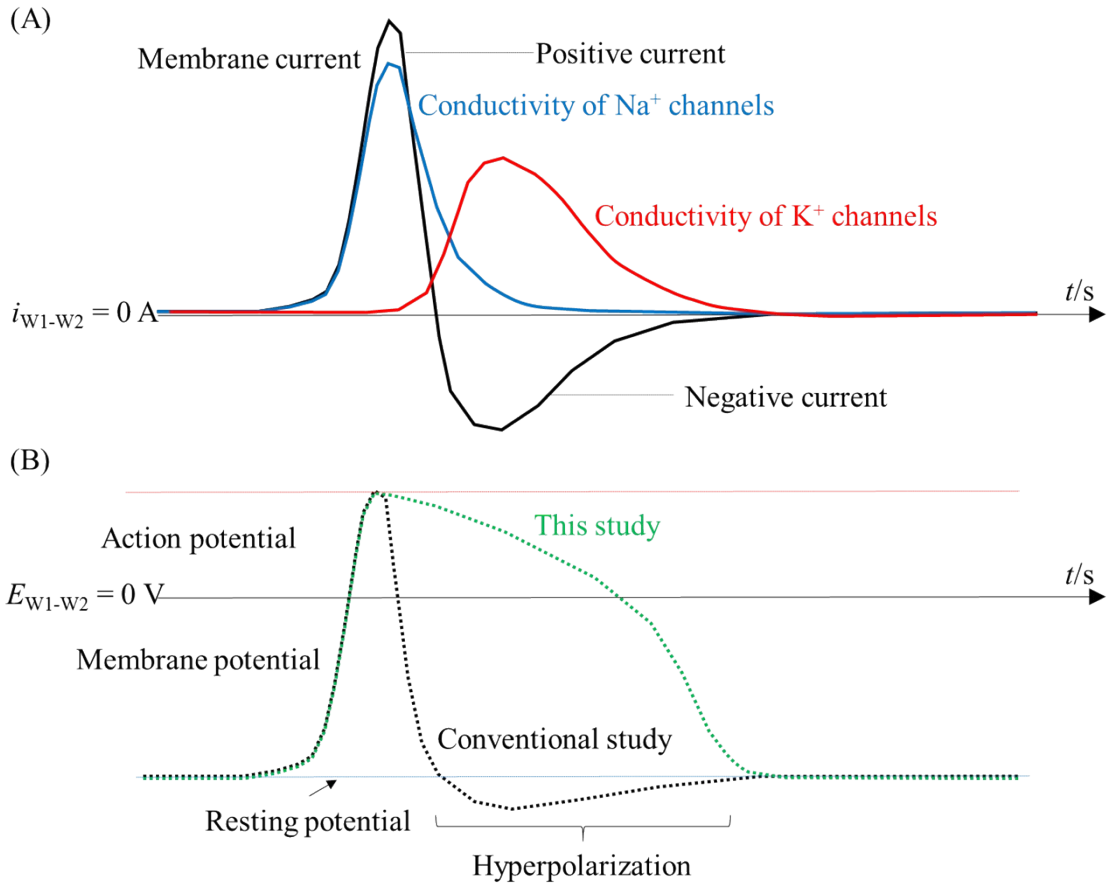

Fig. SI2 Time- courses of the membrane current concluding conductivities of K^+ and Na^+ channels (A) and the membrane potential (B) at the given area on the axon