Evoked membrane potential change in rat optic nerve fiber: Computer simulation

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Abstract: Objective The optic nerve is a key component regarding research on visual prosthesis. Previous pharmacological and electrical studies has pinned down the main features of the mechanisms underlying the nerve impulse in the rat optic nerve, and this work proposed a mathematical model to simulate these phenomena. **Methods** The main active nodal channels: fast Na^+ , persistent Na^+ , slow K^+ and a fast repolarizing K^+ (A-current) were added on a double layer representation of the axon. A simplified representation of K^+ accumulation and clearance in the vicinity of the Ranvier node was integrated in this model. **Results** The model was able to generate the following features. In the presence of 4-aminopyridine (4-AP), spike duration increased and a depolarizing afterpotential (DAP) appeared. In the presence of 4-AP and tetraethylammonium (TEA), the DAP was followed by a hyperpolarizing afterpotential (AHP) and the amplitude of this AHP increased with the frequency of the stimulation. In normal conditions (no drugs): DAP and AHP were absent after a single action potential (AP) and a short train of AP; there was a relative refractoriness in amplitude lasting for 30 ms after an AP; an early AHP was revealed by a continuous depolarizing current; and there was a partial spike adaptation for a long current step stimulus. **Conclusion** The model successfully reproduced previous experiments results including long-lasting stimulation experiment, which is known to modify nerve physiological parameter values and is a key issue for visual prosthesis research.

Keywords: rat; optic nerve; model; channels; potassium homeostasis

1 Introduction

As a relatively accessible part in central nervous system (CNS), many researches aiming at CNS have focused on rat optic nerve (RON) understanding thus provided a great deal of data. Because of its interest in vision research, particularly in vision prosthesis, a model reproducing the main phenomenon underlying action potential (AP) in these myelinated fibers is needed. Moreover, an insight on stimulation threshold is a key point for optic nerve selective stimulation hoping for artificial vision. Therefore, this rat optic nerve model focuses on post-spike recovery.

Due to the thin diameter of RON fibers, extensive channel dynamics studies cannot be conducted, thus many data are obtained by compound action potential (CAP) recordings coupled with pharmacological studies. The main channel blockers are 4-aminopyridine (4-AP) and tetraethylammonium (TEA) for K^+ channels, and tetrodotoxin (TTX) for Na^+ channels.

Based on RON experiment results^[1,2], the rough mechanism of AP generation in RON is widely believed to be as follows. The AP depolarization is due to fast Na^+ channels, and the repolarization is due to a 4-AP-sensitive K^+ current similar to the A-current found in other experiments^[3,4]. In the presence of 4-AP, AP is broadened (approximately doubled), then followed by a depolarizing afterpotential (DAP) (dozens of milliseconds) and a late, TEA-sensitive, hyperpolarizing afterpotential (AHP) (several hundreds of milliseconds). Because of the qualitative use of drugs and measure of CAP instead of AP in previous cited data acqui-

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sition protocol, those time duration data can only be seen as qualitative. The DAP present in mammalian motor axons was suggested to be due to a TTX-sensitive persistent, noninactivating Na^+ current and a passive discharge of the internodal axolemma^[5,6]. The AHP was attributed to a slow K^+ current^[5].

Moreover, the repolarization of an AP leads to K^+ expulsion in the extracellular space (ECS), which have a significant influence on membrane excitability, like conduction failure^[7]. Because of the relatively low baseline of extracellular potassium concentration $[\text{K}^+]_{\text{out}}$ in the RON, the limited volume of ECS and the important role of A-current, the significant of extracellular potassium concentration $[\text{K}^+]_{\text{out}}$ increase in the vicinity of the node must be expected and the resulting effect on the K^+ currents driving force ($V-E_{\text{K}^+}$) must be considered. Unfortunately, experiments give access to average $[\text{K}^+]_{\text{out}}$ but not to transient concentrations near the node^[8]. To compensate for this lack of data, the present study had to make simple hypothesis on $[\text{K}^+]_{\text{out}}$ variations and channel dynamics to explore the influence of extracellular potassium concentration change. The simulation results are consistent with the electrical records from RON which had never been reproduced by model simulation, namely: no DAP and AHP following a single AP and a short train of AP, a relative refractoriness in AP amplitude lasting for 30 ms, existence of an early AHP revealed by a depolarizing current^[1,2], and spike accommodation that can be overcome by large stimulation step^[9].

2 Materials and methods

2.1 Cable model Although the present model mainly focuses on membrane dynamics, a compartmental double layer cable model was used for two reasons. First is to include the influence of demonstrated passive components on DAP^[5], for which myelin sheath cannot be modelised as an electrical insulator. Second is to provide flexibility for future improvement of the model, especially in the case that the model is linked to an imaging system of the nerve giving geometric details. The ten segments between two successive nodes representing myelin attachment (MYSA), paranode main segment (FLUT), and internode segment (STIN) (Fig. 1) are the same as in a previous study^[5]. The geometric and electrical parameters are from various RON measurements (Tab. 1, Tab. 2). As the myelin sheath is not considered as a perfect insulator, and no sodium channels are modelised under the myelin sheath (in the reality there are a few), there is an attenuation of the AP shape between

two contiguous nodes (more than ten percent of the AP amplitude), and the AP is then re-amplified at the following node by the Na^+ channels. All the figures in this paper are made with the potential value at a node.

2.2 Ion channels At each node, four non-linear (see equations in appendix) and one leakage ionic currents were considered. Fast Na^+ , persistent Na^+ , slow K^+ and leakage currents are derived from a previous study on afterpotentials^[5].

Fig. 1 Multi-compartment double cable model^[5]. Between one node and the middle of the internodal section there is one paranodal myelin attachment segments (MYSA), one paranodal main segments (FLUT), and 3 internodal segments (STIN). Between two nodes there are ten compartments. The nodal membrane dynamics included fast (Na_f) and persistent (Na_p) sodium, slow potassium (K^+), persistent A-current (A_p) and linear leakage (L_p) conductances in parallel with the nodal capacitance (C_n). The internodal segments were represented by a double cable structure of linear conductances with an explicit representation of the myelin sheath (G_m in parallel with C_m) and the internodal axolemma.

Tab. 1 Model geometric parameters

Parameter	Value
Number of myelin lamella ^a	8
Node length ^b	0.72 μm
Node radius ^c	0.2 μm
MYSA length ^{a,d}	1.25 μm
MYSA radius ^c	0.2 μm
MYSA periaxonal space width ^e	0.002 μm
FLUT length	10 μm
FLUT radius ^c	0.4 μm
FLUT periaxonal space width ^e	0.004 μm
STIN length	175 μm
STIN radius ^c	0.4 μm
STIN periaxonal space width ^e	0.004 μm
Node-node separation	198.2 μm

for references see ^a[38], ^b[12], ^c[39], ^d[40], ^e[5].

Tab. 2 Model electrical parameters

Parameter	Value
Nodal capacitance ^a	2 $\mu\text{F}/\text{cm}^2$
Internodal capacitance ^a	2 $\mu\text{F}/\text{cm}^2$
Myelin capacitance ^a	0.1 $\mu\text{F}/\text{cm}^2$
Axoplasmic resistivity ^a	70 $\Omega\cdot\text{cm}$
Periaxonal resistivity ^a	70 $\Omega\cdot\text{cm}$
Myelin conductance ^{a,c}	1 ms/cm^2
MYSa conductance	1.15 ms/cm^2
FLUT conductance ^a	0.1 ms/cm^2
STIN conductance ^a	0.1 ms/cm^2
Maximum fast Na^+ conductance	297 ms/cm^2
Maximum slow K^+ conductance	40 ms/cm^2
Maximum persistent Na^+ conductance	1.41 ms/cm^2
Maximum persistent A-current conductance	446 ms/cm^2
Nodal leakage conductance	2 ms/cm^2
Na^+ Nernst potential ^b	46.6 mV
Resting K^+ Nernst potential ^b	-98.6 mV
Leakage reversal potential ^a	-90 mV
Resting potential ^a	-80 mV

^afor references see [5], ^b[28], ^cPer lamella membrane (2 membranes per lamella).

The last active component is an A-current, a rapidly activating, and usually rapidly inactivating, K^+ current, which will be described in detail later in this paper, as well as the slow K^+ . Due to the absence of quantitative data on the juxta-paranodal fast K^+ channels and their obscure role in healthy, adult and axons^[10,11], these channels were neglected. The grand variety of K^+ channels in the RON^[12-14] and CNS^[15] was not reproduced, as well as the non-selective cationic current H-current^[19], which is activated only by large hyperpolarization.

Fig. 2 Strength-duration curve computed for the complete model. The rheobase value was 0.73 mA/cm^2 .

2.3 Simulation procedure The stimulus was delivered as a current injection in the node localized at the middle of 21 nodes. Conditioning current (depolarizing or polarizing) could be applied at the boundaries, permitting to artificially change (increase or decrease) the resting trans-membrane potential. Equations system was closed with Neumann boundary conditions, and was solved using backward Euler implicit integration scheme^[16] with an integration time step of 0.005-0.05 ms in Matlab software. The resulting model has threshold values (Fig. 2) consistent with anterior study^[17].

3 Results

3.1 Extracellular potassium The numerous mechanisms about K^+ regulation following the AP in the CNS can be categorized as either K^+ uptake or K^+ spatial buffering^[18-20]. A model for the RON has been proposed^[8], in which the activity-dependent K^+ increase is handled mainly by the Na^+/K^+ exchanging ATPase pump of both glia and axons. It proposes that the glial uptake stops the $[\text{K}^+]_{\text{out}}$ increase at a ceiling level during the stimulation and establishes the initial, rapid fall in $[\text{K}^+]_{\text{out}}$ at the end of the stimulation. The axonal uptake dominates during the later, slower period of post-stimulus recovery of K^+ . But these mechanisms are based on mean values, rather slow (some seconds), and overlook the diffusion issue. Then what about the $[\text{K}^+]_{\text{out}}$ at the node, near the ion channels?

We therefore chose to make the following hypothesis: a single AP will cause an increase of approximately 3 mmol/L (3.24 mmol/L, leading to $E_{\text{K}^+} = -80$ mV) in the nodal area, the remaining expelled K^+ being diluted in the rest of the ECS. Moreover, only the K^+ expelled by the persistent A-current is responsible for $[\text{K}^+]_{\text{out}}$ increase. In this way there will be no DAP or AHP after an AP because the two potentials E_{K^+} and E_{Rest} will be identical, which will make the three currents i.e. A-current, leakage current and slow K^+ current work together to impose a -80-mV transmembrane potential.

The K^+ expelled by the following AP(s) will be mainly reversed and diluted in the rest of the ECS and trapped via glial uptake in order to keep the potassium concentration $[\text{K}^+]_{\text{out}}$ between the nodal area and the rest of the ECS at a value near 3 mmol/L. This 3 mmol/L difference can be interpreted as a diffusion obstacle caused by the recess at the node and the thin ECS volume.

From the second AP, each AP will lead to a small increase in $[\text{K}^+]_{\text{out}}$ (Fig. 3), whose value is fixed to +0.02 mmol/L in order to reach a +2 mmol/L peak for a 1-s, 100-Hz

Fig. 3 $[K^+]_{out}$ homeostasis model in the nodal area. At resting state, $[K^+]_{out}$ in the ECS was at its baseline value, 3 mmol/L. In this model, the first AP will lead to $[K^+]_{out}$ increasing 3 mmol/L in the nodal area. K^+ expelled by the persistent A-current during the following AP(s) will mainly be diluted in the ECS. K^+ recuperation is attributed to axonal Na^+-K^+ ATPase pump activity.

stimulation in the ECS^[8], i.e. $[K^+]_{out} = \text{baseline} + 2 \text{ mmol/L}$ for the ECS and $[K^+]_{out} = \text{baseline} + (3+2) \text{ mmol/L}$ for the nodal area. In this model, the recovery near the node is only due to the axonal Na^+-K^+ exchanging ATPase pump activity and the time constant τ_{axonal} for clearance is fixed to one second, leading to the equation

$$[K^+]_{out}(t + \delta t) = ([K^+]_{out}(t) - [K^+]_{out}^{Rest}) \times \exp\left(-\frac{\delta t}{\tau_{axonal}}\right) \quad (1)$$

It should be noted that the persistent A-current channels remains opened during a long time ("persistent"), but the K^+ expelled by the persistent A-current in the repolarization following an AP is a brief process. This is because once the transmembrane potential value is near E_K^+ value, the current of this channel can be negligible. Consequently, for the calculations, each $[K^+]_{out}$ augmentation is performed instantaneously when the persistent A-current value goes past $0.5 \times 10^{-7} \text{ mA}$ per node (that is one fifth of its maximum during a full grown AP).

3.2 Slow potassium The TEA-sensitive channel is believed responsible for AHP^[1,2] and spike accommodation^[9]. Consequently the slow K^+ channel was chosen very closed to the one used by a previous study to reproduce AHP and spike accommodation^[5]. Gating kinetics were modified to match RON time constants as well as to overcome the spike accommodation for a large stimulation step (Fig. 4). Usually the TEA-sensitive current is responsible for an activity dependent AHP following a stimuli train^[21], but in the case of RON, this property is only true in the presence of 4-AP. In the absence of 4-AP there is no TEA-sensitive DAP^[2], even for stimuli train longer than 1 s^[22]. In our model, due to $[K^+]_{out}$ increase, E_{K^+} and E_{Rest} had a similar value after the

Fig. 4 Model response to a depolarizing step, consistent with experimental data^[9]. A long duration suprathreshold current step stimuli resulted in spike accommodation for low intensity stimuli: one AP was generated near rheobase (bold line), and two for higher intensity (thin line). For strong stimuli the accommodation was overcome (dashed line).

AP, which prevents from any AHP by nullifying the driving force of K^+ channels. In the presence of 4-AP the persistent A-current was blocked, so there was no $[K^+]_{out}$ modification. Therefore the slow K^+ channel was not shut down and we obtained an AHP (Fig. 5B) that was activity dependent^[2] (Fig. 6).

3.3 A-current According to previous experiments^[1,2], the 4-AP-sensitive current should participate in axonal repolarization, which can be seen as a fast process. But it should also be responsible for an early AHP of a few dozen of milliseconds duration revealed by a prior depolarization and reversed by a prior hyperpolarization, which can be seen as a slow process. Moreover, intra-axonal recordings^[1] have pinned down a relative refractoriness on the amplitude of a second spike lasting for 30 ms. It should be noted that this early AHP and this relative refractoriness have the same time constant.

Therefore the 4-AP-sensitive current was modeled with three activating gates and one deactivating gate^[23,24] in order to have a fast activation to permit a fast repolarization (Fig. 5A). But the deactivating rate constant of the activating gate had to be considerably slowed down in order to obtained a persistent A-current reproducing the relative refractoriness (Fig. 7). Due to $[K^+]_{out}$ accumulation, E_{K^+} and E_{Rest} have a similar value ($= -80 \text{ mV}$) after the AP. If there is a depolarizing current injected during the whole stimulation, the resting potential will be artificially raised ($E_{Rest} \geq -80 \text{ mV}$). Therefore its value is superior to the potassium potential after the AP (-80 mV). This leads to an early AHP

Fig. 5 Response to a mono-stimulation. A: 4-AP influence. Response of the complete model with (continuous line) and without (dashed line) the persistent A-current. B: DAP in the presence of 4-AP, i.e. absence of the persistent A-current; the DAP is followed by an AHP in presence of both 4-AP and TEA, i.e. absence of the persistent A-current and the slow K⁺. Action potentials are truncated.

Fig. 6 Membrane potential response to a 100-Hz, 100-ms duration suprathreshold stimuli train, with (bold line) and without (thin line) the persistent A-current. Phenomenon reproduced for the first time: in normal conditions there is no AHP. In presence of 4-AP there is an activity dependent AHP. Its amplitude can be compared to Fig. 5B. Action potentials are truncated. Simulation matched well with experimental recordings^[2].

Fig. 8 Phenomenon reproduced for the first time: early, TEA-insensitive AHP revealed by conditioning depolarizing current (thin line) and reversed by hyperpolarization current (dashed line), matching well experimental recordings^[2]. All the responses were recentered on E_{rest} , action potentials are truncated. The conditioning depolarizing current must not be applied too early before the stimulation to prevent an hyperactivation of the slow K⁺.

Fig. 7 Phenomenon reproduced for the first time: relative amplitude refractoriness. Two identical successive stimuli were delivered to the model and generated two AP. The ratio of the amplitude of the second spike to the first spike is plotted against the inter-stimulus interval. Simulation matched well with experimental recordings^[1].

Fig. 9 Model characteristics: threshold change after a first AP. A suprathreshold 1-ms conditioning stimulus was followed by a 1-ms test stimulus. Response from the complete model (bold line), without the persistent A-current (dashed line) and without both the persistent A-current and the slow K⁺ (thin line).

because now $E_{K^+} \leq E_{Rest}$. Hyperpolarizing current artificially decreases the resting potential ($E_{Rest} \leq -80$ mV), therefore $E_{K^+} \geq E_{Rest}$ after the AP, which will reverse the AHP (Fig. 8).

In the presence of 4-AP, i.e. blockage of the persistent A-current, there was an increase of the firing rate response to the depolarizing step. This is coherent with the supposed delaying role of the A-current of other mammalian neurons^[25]. And it is the opposite of the A-current in salamander retinal ganglion cells^[4], where 4-AP decreases spike frequency. In the presence of both 4-AP and TEA, i.e. no active K^+ channels, the model was not far from instability during the repolarization of an AP, which limits the value chosen for the persistent Na^+ maximum conductance. The great post-spike threshold decrease (Fig. 9) is coherent with the spontaneous repetitive firing observed in many RON fibers^[1].

4 Discussion

The present simulation study can be seen as a continuation of a previous work on mammalian nerve fibers afterpotentials^[5] adapted to the RON. This model was completed by the addition of a persistent A-current and a simple $[K^+]_{out}$ variation model to match RON characteristics. Previously some modeling work was done on optic nerve^[26], and recently a model for mammalian optic nerve mainly based on RON data has been proposed^[17]. It could generate many AP characteristics, but is unable to reproduce some key RON features in normal conditions (absence of drugs). Therefore to explain the early AHP and the relative refractoriness, our model proposes a persistent A-current coupled with $[K^+]_{out}$ variations modelisation. The absence of DAP and AHP after short trains of AP was achieved with $[K^+]_{out}$ variations, and the activation of the slow K^+ current was kept near E_{Rest} to reproduce spike accommodation.

It has been suggested that axonal Na^+-K^+ exchanging ATPase pump activity is only linked to intra-axonal $[Na^+]_{in}$ ^[8]. Because of a higher baseline and a bigger intra-axonal volume, $[Na^+]_{in}$ relative variations are inferior to $[K^+]_{out}$ relative variations. We consequently considered that the electrogenic contribution of the Na^+-K^+ ATPase pump responsible for the AHP following long stimuli train^[22] had no significant role during mono stimulation or short stimuli train. Therefore it was not modeled and the Na^+-K^+ ATPase pump contribution to resting axonal potential, estimated at 7 mV^[27], was tacitly included in E_{Rest} ^[28]. However, for long stimuli train, $[Na^+]_{in}$ variations may not be negligible. In our model, the persistent A-current strongly maintain the membrane

potential around E_{Rest} after an AP, which is consistent with the spontaneous repetitive firing observed in many RON fibers in the presence of 4-AP^[1].

Although a double cable layer gives a geometric representation of the fiber, this model is far from the complex reality. However it would be pointless to ameliorate this inherent flaw before working on the two limitations of this model: channels and ions. First, the relatively low number of channels are considered, especially in the internodal segment. Second, other ions like Cl^- and Ca^{2+} ^[29] are totally ignored, as well as Na^+ homeostasis. Therefore our model, which also as a simple K^+ homeostasis modelisation, cannot compare with what have been done in other fields like cardiac ventricular action potential^[30]. However it should be reminded that RON fibers are almost impossible to be studied separately.

Nonetheless we were able to reproduce all the experimental data available on the RON concerning short stimuli train. Therefore, in the absence of new data that could be acquired through more recent techniques^[31], other hypothesis would not have brought significant interest and would have been too speculative. This can be explained by thoughts on the CAP. Indeed, the sole consideration of volume conductor effect is not enough to reproduce conduction velocity distribution in sciatic nerve^[32], therefore because of numerous factors like fiber torsion, diameter inhomogeneity along one axon, among axons, and among optic nerve regions^[33], CAP interpretation cannot be too precise. Consequently it has to be expected that many interesting features about RON fibers are still to be discovered. For example, due to the absence of intra-axonal recordings for long stimuli train, existence and characteristics of propagation failures^[25] are unknown.

In the perspective of visual stimulation, if there is no technical progress allowing extensive study of RON single axon, modeling the whole nerve activity might be a non-invasive solution allowing the CAP interpretation. Considering very long stimuli train, the AHP linked to Na^+-K^+ exchanging ATPase pump hyperactivity^[22] could also be modeled by CAP interpretation, which allows an insight on pump activity and $[Na^+]_{in}$ variations. Therefore the next step in RON modeling should be a whole nerve modeling. In this way it could be linked with studies on electrodes^[34]. As RON fibers are very different, the use of medical imaging is required. Finally, to increase the accuracy of such a model, ECS swelling due to expelled K^+ ^[19] and ephaptic coupling

between myelinated nerve fibers^[35,36] must be modeled.

5 Appendix

Following the Hodgkin-Huxley theory^[37], the general form of the ionic current density is

$$I_X = g_X \times \mu^m \times \nu^n \times (V_m - E_X) \quad (2)$$

where g_X is the maximum conductance density for the ion X channel (ms/cm); μ is the activating (resp. inactivating) gate variable, ranging from 0 to 1; m (resp. n) is the number of gate(s) μ (resp. ν) in the channel; V_m denotes the membrane potential and E_X the Nernst potential of the ion X . The time and voltage dependence for the gating variable μ (or ν) is

$$\frac{d\mu}{dt} = \alpha(V_m) \times (1 - \mu) - \beta(V_m) \times \mu \quad (3)$$

The activation and inactivation parameters expressions at 22 °C are given below. Fast Na^+ current

$$I_{\text{Na}^+} = g_{\text{Na}^+} \times m^3 \times h \times (V_m - E_{\text{Na}^+}) \quad (4)$$

$$\alpha_m = \frac{5.65 \times (V_m + 20.4)}{1 - e^{-(V_m + 20.4)/10.3}}, \quad \beta_m = \frac{-0.2612 \times (V_m + 25.7)}{1 - e^{(V_m + 25.7)/9.16}}$$

$$\alpha_h = \frac{-0.0876 \times (V_m + 102)}{1 - e^{(V_m + 20.4)/11}}, \quad \beta_h = \frac{3.2478}{1 + e^{-(V_m + 19.8)/13.4}}$$

Persistent Na^+ current

$$I_{\text{Na}^+} = g_{\text{Na}^+} \times p^3 \times (V_m - E_{\text{Na}^+}) \quad (5)$$

$$\alpha_p = \frac{0.0342 \times (V_m + 27)}{1 - e^{-(V_m + 27)}}, \quad \beta_p = \frac{-0.000571 \times (V_m + 34)}{1 - e^{(V_m + 34)/10}}$$

Slow K^+ current

$$I_{\text{K}^+} = g_{\text{K}^+} \times s \times (V_m - E_{\text{K}^+}) \quad (6)$$

$$\alpha_h = \frac{0.0064}{1 + e^{-(V_m + 77.5)/0.5}}, \quad \beta_h = \frac{0.0154}{1 + e^{-(V_m + 102.5)}}$$

persistent A-current

$$I_A = g_A \times a^3 \times b \times (V_m - E_{\text{K}^+}) \quad (7)$$

$$\alpha_a = \frac{0.1134 \times (V_m + 40)}{1 - e^{-(V_m + 40)/5}}, \quad \beta_a = 0.0088 \times e^{-(V_m + 36.5)/18.4}$$

$$\alpha_b = 0.152 \times e^{-(V_m + 60)/20}, \quad \beta_b = \frac{2.28}{1 + e^{-(V_m + 30)/10}}$$

Leakage current

$$I_{\text{Leak}} = g_{\text{Leak}} \times (V_m - E_{\text{Leak}}) \quad (8)$$

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计算机模拟的大鼠视神经动作电位变化

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摘要: **目的** 目前已有的神经模型大多基于 Hodgkin-Huxley 理论, 并且只考虑主要离子通道的影响。尽管主要离子通道如快速钠离子通道、快速钾离子通道和渗漏通道能够解释动作电位的产生和传递, 但不足以解释动作电位的阈值差异和长期刺激的影响。而这些正是视觉假体需要考虑的问题。目前尚没有满意的视神经模型, 因此本研究根据现有的各种视神经实验数据, 对大鼠视神经 (rat optic nerve, RON) 进行建模。**方法** 在建模过程中考虑了小离子通道、轴突的空间特征、细胞外液的钾离子浓度变化。考虑到实验数据的易获性, 使用大鼠神经作为模型; 髓鞘的结构用双层电缆来明确模拟; 提出一个新的“持续时间”A-current, 并且与动力学特性被改进的其他常用离子通道一起用于模拟中; 钾离子的累积和清除也采用一种新的方法来模拟。系统中大量的公式用 Matlab 编写的程序代码解决。**结果** 在系统中重现了以下的特点: 当存在 4-氨基吡啶 (4-aminopyridine, 4-AP) 药物时, 动作电位持续时间增加; 超极化后电位 (hyperpolarizing afterpotential, AHP) 随着去极化后电位 (depolarizing afterpotential, DAP) 出现; 动作电位频率和四乙胺 (tetraethylammonium, TEA) 药物会影响超极化后电位的敏感性。在没有药物的时候模型仍重现了以下的特点: 一个单一的动作电位和一个短序列的动作电位后没有出现去极化后和超极化后电位; 动作电位的振幅回复时间持续 30 ms; 去极化电流会显示早期超极化后电位的出现以及动作电位的适应性。**结论** 该模型成功地模拟了大鼠实验结果, 包括会影响静息参数的长时间刺激实验, 是视觉假体研究的重要课题。

关键词: 大鼠; 视神经; 模型; 离子通道; 钾稳态