Numerous findings indicate that auditory nerve fibers (ANFs) of deaf cats are re-arranged with higher rates of electrical stimulation, given cochlear implants, undergo spike-rate adaptation and accommodation. A simulation study by Néguyen and Bruce (2009) reported that low-threshold potassium (LTK) and hyperpolarization-activated cyclic nucleotide-gated (HCN) channels are the determining components of this behavior, whereas standard Hodgkin-Huxley-type ANF models, containing fast and delayed-rectifier K+ channels only, cannot explain adaptation. To investigate the effect of rate-dependent modulation of multiple ion channels species on the neuronal response, we carry out a compartmental simulation study using the model of the rat ANF fiber. We base our simulation on the neuron morphology proposed by Woo et al. (2010) (and implement two versions of the model): A) just fast Na+ and delayed-rectifier K+ for all nodes of Fink et al. and B) with the addition of HCN channels (Yi et al., 2010) at the first peripheral node and on the nodes of Raven’s neighboring the soma. Our results indicate that simultaneous activation of peripheral nodes in model B exhibits a higher threshold current for action potential generation, shorter mean latency and smaller delays than for model A. This effect is observed even at peripherial nodes distant from the myelinated soma in model B that do not themselves have the HCN channel, whereas HCN channels have no effect in model A. In contrast, the statistics of action potential generation are identical between the two model versions for stimulation at central nodes of Raven’s. The properties of refractoriness, spike-rate adaptation, and accommodation for the two versions will be explored and discussed.

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1. INTRODUCTION

1.1 Recent studies have shown that electrically stimulated type I rat ANF displays behavior such as spike-rate adaptation and accommodation (Zheng et al., 2017).

1.2 Computational models of the ANF that are based on the Hodgkin-Huxley equations containing only fast Na+ and K+ channels do not quantitatively describe spike-rate adaptation and accommodation.

1.3 Yi et al. (2010) have experimentally found HCN channels in the first peripheral node (or terminus) and the nodes neighboring the soma in mouse spiral ganglion cells. HCN channels are known to co-localize with HCN channels.

1.4 A computational membrane model of the rat ANF incorporating Nav, K+ and HCN channel models shows that inclusion of HCN channels increases with the rate of electrical stimulation (Néguyen and Bruce, 2010).

1.5 We built a computational model of the rat ANF in an effort to better understand the phenomena observed during the location and populations of voltage-gated ion channel species (Nav, K+ and HCN) and the location and rate of electrical stimulation from a Cl-.

1.6 The morphology of the computational model is derived from Woo et al. (2010).

1.7 In order to simulate the activity of various ion channels species, we employ a stochastic characterization since the ensuing fluctuations about the threshold are considered important to users of cochlear implants (Brune et al., 1994a,b).

2. METHODS: Ion Channel Simulation

2.1 We stimulate the ANF with extracellular current injections. The stimulating electrode is a spherical monopole with radius 1 μm (Min et al., 2009). As a consequence, the current is zero if the cathode is at FE = 0 and the relative spread is RS = 0.5. Model B has a slightly lower threshold than model A.

2.2 Membrane potential is set to 0 mV at each node in order to produce a fixed resting potential of 0 mV.

2.3 Circuit Model

2.4 The circuit model is solved using a partial differential equation (PDE) and is computed with MATLAB.

3. RESULTS: Ion Channel Simulation

3.1 Channel kinetics obey continuous-time discrete-state Markov processes (Woo et al., 2000). HCN and (Néguyen and Bruce, 2008) are given by

\[
\begin{align*}
\text{Nav activation} & : h_{\text{Nav}} &= \frac{h_{\text{Nav}}}{\alpha_{\text{Nav}} - \beta_{\text{Nav}}} \\
\text{Nav inactivation} & : h_{\text{Nav}} &= \frac{h_{\text{Nav}}}{\alpha_{\text{Nav}} - \beta_{\text{Nav}}} \\
\text{K+ activation} & : n_{\text{K+}} &= \frac{n_{\text{K+}}}{\alpha_{\text{K+}} - \beta_{\text{K+}}} \\
\text{K+ inactivation} & : n_{\text{K+}} &= \frac{n_{\text{K+}}}{\alpha_{\text{K+}} - \beta_{\text{K+}}} \\
\text{HCN activation} & : m_{\text{HCN}} &= \frac{m_{\text{HCN}}}{\alpha_{\text{HCN}} - \beta_{\text{HCN}}} \\
\text{HCN inactivation} & : m_{\text{HCN}} &= \frac{m_{\text{HCN}}}{\alpha_{\text{HCN}} - \beta_{\text{HCN}}} \\
\end{align*}
\]

4. RESULTS: Ion Channel Simulation

4.1 Membrane potential is derived from the Nav, K+ and HCN channel models.

4.2 Time (ms)

4.3 Voltage (mV)

4.4 The membrane potential is set to 0 mV at each node in order to produce a fixed resting potential of 0 mV.

4.5 The site of stimulation is defined by the current source in the rat ANF model.

5. RESULTS: Ion Channel Simulation

5.1 The site of stimulation is defined by the current source in the rat ANF model.

5.2 The site of stimulation is defined by the current source in the rat ANF model.

5.3 The site of stimulation is defined by the current source in the rat ANF model.

5.4 Time (ms)

5.5 Voltage (mV)

5.6 The site of stimulation is defined by the current source in the rat ANF model.

6. RESULTS: Ion Channel Simulation

6.1 The site of stimulation is defined by the current source in the rat ANF model.

6.2 The site of stimulation is defined by the current source in the rat ANF model.

6.3 The site of stimulation is defined by the current source in the rat ANF model.

6.4 Time (ms)

6.5 Voltage (mV)

6.6 The site of stimulation is defined by the current source in the rat ANF model.

7. RESULTS: Ion Channel Simulation

7.1 The site of stimulation is defined by the current source in the rat ANF model.

7.2 The site of stimulation is defined by the current source in the rat ANF model.

7.3 The site of stimulation is defined by the current source in the rat ANF model.

7.4 Time (ms)

7.5 Voltage (mV)

7.6 The site of stimulation is defined by the current source in the rat ANF model.

8. RESULTS: Ion Channel Simulation

8.1 The site of stimulation is defined by the current source in the rat ANF model.

8.2 The site of stimulation is defined by the current source in the rat ANF model.

8.3 The site of stimulation is defined by the current source in the rat ANF model.

8.4 Time (ms)

8.5 Voltage (mV)

8.6 The site of stimulation is defined by the current source in the rat ANF model.

9. RESULTS: Ion Channel Simulation

9.1 The site of stimulation is defined by the current source in the rat ANF model.

9.2 The site of stimulation is defined by the current source in the rat ANF model.

9.3 The site of stimulation is defined by the current source in the rat ANF model.

9.4 Time (ms)

9.5 Voltage (mV)

9.6 The site of stimulation is defined by the current source in the rat ANF model.

10. RESULTS: Ion Channel Simulation

10.1 The site of stimulation is defined by the current source in the rat ANF model.

10.2 The site of stimulation is defined by the current source in the rat ANF model.

10.3 The site of stimulation is defined by the current source in the rat ANF model.

10.4 Time (ms)

10.5 Voltage (mV)

10.6 The site of stimulation is defined by the current source in the rat ANF model.

11. RESULTS: Ion Channel Simulation

11.1 The site of stimulation is defined by the current source in the rat ANF model.

11.2 The site of stimulation is defined by the current source in the rat ANF model.

11.3 The site of stimulation is defined by the current source in the rat ANF model.

11.4 Time (ms)

11.5 Voltage (mV)

11.6 The site of stimulation is defined by the current source in the rat ANF model.

12. RESULTS: Ion Channel Simulation

12.1 The site of stimulation is defined by the current source in the rat ANF model.

12.2 The site of stimulation is defined by the current source in the rat ANF model.

12.3 The site of stimulation is defined by the current source in the rat ANF model.

12.4 Time (ms)

12.5 Voltage (mV)

12.6 The site of stimulation is defined by the current source in the rat ANF model.