Günay et al. BMC Neuroscience 2010, 11(Suppl 1):P147
http://www.biomedcentral.com/1471-2202/11/S1/P147

BMC Neuroscience

POSTER PRESENTATION Open Access

Modeling Drosophila motoneurons to examine the functional effect of Na channel splice variants

Cengiz Günay[1*], Logesh Dharmar[1], Fred Sieling[1], Richard Marley[2], Wei-Hsiang Lin[2], Richard A Baines[2], Astrid A Prinz[1]

From Nineteenth Annual Computational Neuroscience Meeting: CNS*2010
San Antonio, TX, USA. 24-30 July 2010

Neurons have diverse electrophysiological characteristics controlled by voltage-gated ion channels. It is not known how much of the diversity of neuronal activity is caused by differential channel gene expression as opposed to alternate splicing of these genes.

The contribution of alternate splicing to neural activity and therefore neuronal function can be addressed more easily in invertebrates because of their smaller genome. Specifically, the fruitfly *Drosophila melanogaster* represents a very powerful molecular genetic model system that has been instrumental for our understanding of early development of the nervous system. Recently in *Drosophila*, several voltage-gated sodium channel (DmNav) splice variants have been identified [1,2].

Splice variants can be expressed in the oocytes of the South African clawed frog *Xenopus Laevis*. The expression of these channels in *Xenopus* oocytes allows the electrophysiological characterization and the construction of computational ion channel models. If these models are built with sufficient detail, the functional effect of the splice variants on neuronal activity can be analyzed.

To achieve this, we build a novel computational model of the *Drosophila* motoneuron. As a first step, we show that repetitive firing in response to current injections can be achieved in a minimal model neuron that includes a well-characterized fast inactivating sodium (DmNav10) channel, and slow (non-inactivating delayed rectifier) and fast (A-type, inactivating) potassium channels. To build this model, we combined potassium channel data recorded from 3rd instar *Drosophila* larvae motoneurons and sodium channel data recorded from *Xenopus* oocytes. In the oocytes, recordings contain artifacts of an endogenous calcium-dependent chloride, Ca(Cl), channel [3] and a space clamp problem. The space clamp is caused by the oocytes' large size, which is required for sufficient expression of DmNav splice variants. We address this problem with a spatial model of leak and Ca(Cl) currents in the oocyte (with a similar approach to [4]).

Drosophila motoneurons also have a calcium channels and calcium-dependent potassium (BK and SK) channels. Morphological localization of various channels makes modeling a challenge. In summary, we present solutions to several obstacles in modeling fast kinetics of DmNav channels and also putting them together in a full model of a *Drosophila* motoneuron.

Acknowledgments
Career Award at the Scientific Interface (CASI) from the Burroughs Wellcome Fund awarded to AAP.

Author details
[1]Dept. Biology, Emory University, Atlanta, Georgia 30322, USA. [2]Life Sciences, University of Manchester, Manchester M13 9PT, UK.

Published: 20 July 2010

References

1. O'Donnell Olson R, Liu Z, Nomura Y, Song W, Dong K: **Molecular and functional characterization of voltage-gated sodium channel variants from Drosophila melanogaster.** *Insect Biochem Mol Biol* 2008, **38**:604-610.
2. Lin W-H, Wright DE, Muraro NI, Baines RA: **Alternative splicing in the voltage-gated sodium channel DmNa(v) regulates activation, inactivation, and persistent current.** *J. Neurophysiol* 2009, **102(3)**:1994-2006.
3. Barish ME: **A transient calcium-dependent chloride current in the immature Xenopus oocyte.** *J Physiol* 1983, **342**:309-325.
4. Cox SJ: **Direct correction of non-space-clamped currents via Cole's theorem.** *J. Neurosci. Methods* 2008, **169(2)**:366-373.

doi:10.1186/1471-2202-11-S1-P147
Cite this article as: Günay *et al.*: Modeling Drosophila motoneurons to examine the functional effect of Na channel splice variants. *BMC Neuroscience* 2010 **11**(Suppl 1):P147.

* Correspondence: cgunay@emory.edu
[1]Dept. Biology, Emory University, Atlanta, Georgia 30322, USA