Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

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BSc (Dalhousie University, 2012)

“Na+ Channels Enhance Low Contrast Signalling in the Superior-Coding Direction-Selective Circuit”

Department of Biology (Neuroscience)

Tuesday, March 27, 2018
12:30 P.M.
Halpern Centre
Room 108

Supervisory Committee:
Dr. John Taylor, Department of Biology, University of Victoria (Supervisor)
Dr. Raad Nashmi, Department of Biology, UVic (Member)
Dr. Craig Brown, Division of Medical Sciences, UVic (Outside Member)

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Dr. Peter Lukasiewicz, Department of Ophthalmology & Visual Sciences, Washington University
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Chair of Oral Examination:
Dr. Serhy Yekelchyk, Department of Germanic and Slavic Studies, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract

Light entering the eye is transformed by the retina into electrical signals. Extensive processing takes place in the retina before these signals are transmitted to the brain. Beginning in the outer retina, light-evoked electrical signals are distributed into parallel pathways specialized for different visual tasks, such as dark vs. bright ambient light, the onset or offset of light, and the direction of stimulus motion. Pathway diversity is a consequence of cell type diversity, differential cell connectivity, synapse organization, receptor expression, or any combination thereof. Cell connectivity itself can be accomplished through excitatory or inhibitory chemical synapses, or electrical coupling via gap junctions. Gap junctions are further specialized based on the expression of different connexin subunit isoforms. In aggregate, this diversity gives rise to ganglion cells with highly specialized functions, including ON and/or OFF responses, contrast-tuning and direction-selectivity (DS).

The directionally-selective circuit, a circuit specialized for the encoding of stimulus motion, makes use of many of these circuit specializations. Bipolar cells provide highly-sensitive glutamatergic input to amacrine cells and DS ganglion cells (DSGCs) in this circuit, while amacrine cells provide cholinergic and directionally-tuned GABAergic input to DSGCs. One population of DSGCs also transmit signals laterally to one another via gap junctions. Thus numerous specializations in bipolar cells, amacrine cells and ganglion cells endow DSGCs with their unique encoding abilities.

In Chapters 2 and 3 of this dissertation, I focus on the encoding of neuronal correlations between gap junction coupled DSGCs. I first characterize electrical coupling of DSGCs through the identification of the molecular composition of DSGC gap junctions (Chapter 2). Physiological and immunohistochemical methods allowed me to demonstrate an important role for connexin 36 subunits in DSGC electrical coupling. Next (Chapter 3), I investigate the sub-cellular mechanisms underlying neuronal correlations between electrically coupled DSGCs. Using paired recordings, I show that chemical input (from bipolar cells and amacrine cells), electrical input (from gap junctions), and Na+ channel activity in DSGC dendrites underlie the generation of
correlated spiking activity. While a common feature of electrically coupled networks, the mechanisms underlying correlations were previously unclear.

In Chapter 4, I focus on the mechanisms within the DS circuit which endow these neurons with impressive sensitivity to stimulus contrast. Using physiological and pharmacological methods I first assess the relative contrast sensitivity of ganglion cells and starburst amacrine cells (SACs) in the DS circuit. The sensitivity of DSGC and SAC excitatory currents to antagonists of Na+ channels suggests an important role for these channels in amplifying weak inputs. This role is later attributed to the differential expression of voltage-gated Na+ channels in specific bipolar cell populations.

In aggregate, this dissertation describes several novel circuit mechanisms within the well-studied DS circuit. I also provide specific roles for such specializations in visual coding.