DESCRIPTION OF THE RESULTS:

(A) In the fifth grant period we planned:

(1) This year was a 'no-cost extension' thus any purchase of equipment was not planned.

(2) This was a 'no-cost extension' period, thus experiments were not planned for this year. However, we continued with all the experimental work we started in previous years. The section below will describe results of this experimental work and pinpoints realized and potential publications.

(2a) In one line of research we study how Cx36 mediated lateral signal flow across the coupled ganglion cell array affects the ganglion cell spike output towards the brain. Among many aspects that can be altered when this lateral signaling occurs we focused first on the altered temporal features of ganglion cell spike bursts evoked by light stimuli. However, various measures to determine such temporal signal features were inconsistent in the literature. Therefore, we generated a simple tool by which decay of spike bursts can easily be determined and utilized to characterize ganglion cell light evoked activity. Data of this work resulted a research paper (Ganczer et al. 2017; PlosONE). Equipped with the new tool we examined ganglion cell light responses and studied how temporal characteristics including response transiency and delay are altered as a result of changing stimulus parameters (intensity changes, spectral changes) or by the pharmacological blockade of specific retinal signaling pathways. This line of work so far resulted in three poster abstracts, two of which were presented at the FENS 2017 regional meeting (Pécs, 2017 September 20-23) and a third one at ERM 2017 (Paris, 2017 October 5-7). Results of this work will soon be submitted in a form of two manuscripts (Tengölics et al. and Ganczer et al.; see below).

(2b) In the past years we extended our investigations to the human retina. We described the Cx36 expression of human retinal bipolar cells and collected data were made public in a form of a research article (Kántor et al. 2017; Brain Structure and Function). We continue the experimental work with human retinal samples and collect data to describe the Cx36 plaque distribution over the dendritic arbors of human retinal ganglion cells in the near future.

(2c) As a part of the original grant proposal we studied the Cx36 plaque distribution in retinas on many mammalian species to perform a multiple species comparison. Our results show that besides the conservative overall Cx36 distribution across various mammalian species, there are subtle differences in both plexiform layers. The collected results have been analyzed and the now form the core of a manuscript (Kovács-Öller et al. 2017; Frontiers in Cellular Neuroscience).

(2d) One of our specific aims was to identify the microRNA sequences that potentially alter Cx36 protein expression. In addition we planned to examine if the levels of identified microRNAs as well as the Cx36 mRNA construct is significantly altered as a result of dark- (36 hours dark rearing) or light-adaptation (36 hours light rearing). We identified 2 microRNA sequences (mir152 and mir320) that are endogenously expressed in the rat retina and they both exhibit nucleotide sequences that are complementary with the Cx36 mRNA transcript UTR region. We performed the adaptation treatments in mice and collected retinal tissues for PCR measurements. We found that the level of Cx36 mRNA somewhat decreased during dark adaptation but the amount of the two microRNAs were not changed significantly. However, corresponding WB analyses were inconsistent with no clear adaptation induced change in the expression level of the Cx36 protein. We think that this is due to the fact that Cx36 comprises many different gap junctions each of whose expression levels may be altered differently during dark- or light-adaptation (some are down- others are upregulated). Therefore we plan to perform flow-cytometric experiments to measure Cx36 expression levels in neuron populations

separated based on specific markers (photoreceptors – opsin, ganglion cells – Thy1, amacrine cells – GAD65 etc.). We will start the flow cytometric experiments this fall.

(2e) As a part of our ongoing investigation to determine the various functions Cx36 gap junctions may play for vision we investigate the changes of OFF alpha ganglion cell signaling as a result of a blockade of ganglion cell gap junctions. In this study we found that OFF alpha cells may perform various encoding strategies (single cell- or population coding) depending on the conductance of their gap junctions. In this scheme OFF alpha cell gap junctions serve as switches between two encoding operation modes. Results of this project have been presented at the ERM 2017 meeting (Balogh et al.; Paris, October 5-7) and soon a corresponding manuscript will be submitted for publication.

(B) Accepted articles:

Ganczer A, Balogh M, Albert L, Debertin G, Kovács-Öller T, ***Völgyi B.*** *(2017) Transiency of retinal ganglion cell action potential responses determined by PSTH time constant. PLoS One. 2017 Sep 12;12(9):e0183436. doi: 10.1371/journal.pone.0183436. eCollection 2017.*

Kovács-Öller T, Debertin G, Balogh M, Ganczer A, Orbán J, Nyitrai M, Balogh L, Kántor O, ***Völgyi B.*** *(2017) Connexin36 Expression in the Mammalian Retina: A Multiple-Species Comparison. Front Cell Neurosci. 2017 Mar 9;11:65. doi: 10.3389/fncel.2017.00065. eCollection 2017.*

Kántor O, Varga A, Nitschke R, Naumann A, Énzsöly A, Lukáts Á, Szabó A, Németh J, ***Völgyi B.*** *(2017) Bipolar cell gap junctions serve major signaling pathways in the human retina. Brain Struct Funct. 2017 Aug;222(6):2603-2624. doi: 10.1007/s00429-016-1360-4. Epub 2017 Jan 10.*

(C) Articles under preparation:

Ádám Tengölics, Alma Ganczer, Márton Balogh, ***Béla Völgyi.*** *Retinal Ganglion Cells Responses Impose a Postdictive Processing of Visual Signals on the Brain.*

Alma Ganczer, Márton Balogh, ***Béla Völgyi.*** *Temporal response features of retinal ganglion cells are determined in the inner retina.*

Márton Balogh, Gerrit Hilgen, László Albert, Evelyne Sernagor, ***Béla Völgyi.*** *Ganglion Cell Electrical Synapses Serve as Switches between Independent and Population Coding Operation Modes in the Mouse Retina.*

(D) Paper and Poster presentations:

Ádám Tengölics, Alma Ganczer, Márton Balogh, ***Béla Völgyi.*** *Retinal Ganglion Cells Responses Impose a Postdictive Processing of Visual Signals on the Brain. FENS Pécs, 2017 September 20-23. P1-435.*

Ganczer A, Balogh M, ***Völgyi B.*** *Temporal Response Features of Retinal Ganglion Cells are Mostly Determined in the Inner Retina. FENS Pécs, 2017 September 20-23. P1-411.*

Debertin G, Kántor O, Kovács-Öller T, Balogh L, Szabó-Meleg E, Orbán J, Nyitrai M, ***Völgyi B.*** *Three Main Strategies Utilized by Tyrosine Hydroxylase Positive Amacrine Cells to Target Postsynaptic Neuronal Partners in the Mammalian Retina. FENS Pécs, 2017 September 20-23. P1-406.*

Béla Völgyi. *Electrical Synapses of the Mammalian Retina Serve to Fine-tune the Ganglion Cell Output Signal. FENS Pécs, 2017 September 20-23. Paper presentation in the symposium of 'Retinal neurochemistry and information processing'.*

Alma Ganczer, Márton Balogh, ***Béla Völgyi.*** *Temporal response features of retinal ganglion cells are determined in the inner retina. ERM Paris 2017 October 5-7.*

Márton Balogh, Gerrit Hilgen, László Albert, Evelyne Sernagor, ***Béla Völgyi.*** *Ganglion Cell Electrical Synapses Serve as Switches between Independent and Population Coding Operation Modes in the Mouse Retina. ERM Paris 2017 October 5-7.*

Gábor Debertin, Orsolya Kántor, György Sétáló Jr, Edina Szabó-Meleg, Miklós Nyitrai, Gábor Szabó, Ferenc Erdélyi, ***Béla Völgyi.*** *Parvalbumin-GFP Mice can be Utilized to Perform Type Specific Connexin36 Dendritic Arbor Mapping of Large Field Ganglion Cells. ERM Paris 2017 October 5-7.*