Cold Spring Harbor Laboratory
Karel Svoboda, Ph.D.
Professor

December 29, 2003

Biocomplexity Faculty Search Committee
c/o Prof. Rob de Ruyter van Steveninck
Biocomplexity Institute
Indiana University
Swain Hall West 117
Bloomington IN, 47405-7105

Dear Committee Members,

I am writing in support of **Dr. Armen Stepanyants**, who is applying for an Assistant Professor position in your department. I have known Armen since 2000, when he arrived at Cold Spring Harbor Laboratory as a postdoctoral fellow in Professor Mitya Chklovskii's laboratory. We collaborate and share group meetings and I therefore know Armen and his work very well. Before I go into details, let me state that I am convinced that Armen is an *outstanding young theoretical neuroscientist.* He has strong analytical and computational abilities coupled with creativity and scholarship. I am confident that he will have a significant impact on brain research.

Although Armen has already had a distinguished career in theoretical and engineering physics, my high opinion of him is based on his subsequent work in neuroscience. Most of Armen's work on the brain has focused on principles of brain design and theoretical anatomy. His approach is as follows: He formulates a simple hypothesis and rigorously derives its implications, thereby generating experimentally testable predictions. Because of his scholarship and close relationship with experimental colleagues at CSHL and elsewhere he has an unusually detailed understanding of what constitutes a 'testable prediction' in neuroscience research, which helps to make his work biologically relevant. Because his analytical and computational skills his predictions are often non-trivial and surprising.

Let me illustrate with an example: Armen has tackled an old question whether local cortical connectivity (within individual dendritic and axonal arbors) is deterministic or random. To answer this question for particular cell types, Armen has developed a method based on anatomical reconstructions of overlapping dendritic and axonal arbors, data that are readily available from paired recordings in brain slices. Briefly, the algorithm involves shifting arbors with respect to each other randomly to ask how the pattern of actual synaptic connections compares to the expected number of connections by chance. The conclusion is that some cell types make random

HHMI, Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, New York 11724
Tel: 516/367-6878 Fax: 516/367-8866 Email: svoboda@cshl.org

connections while others make highly deterministic connections, demanding the presence of trophic factors acting on short length scales. I find this project impressive because it couples one type of data (reconstructions of dendritic and axonal arbors) to predictions about a completely distinct aspect of neuronal function (the presence of chemo-attractants acting over micrometers length scales).

Other ongoing projects pioneered by Armen have had quite an impact on my laboratory's thinking about cortical organization and plasticity. For example, Armen formulated the concept of a 'potential synapse', defined as a point of dendritic overlap where a synapse could form. He also devised computational methods to use this concept to construct circuit diagrams from reconstructions of dendritic and axonal arbors. Stimulated by his work we are performing paired recordings to generate a circuit diagram for barrel cortex. I have no doubt that once Armen's work becomes more widely known its impact will be huge.

Armen is a delightful colleague who likes to collaborate. He writes well and he knows how to get funded. He was recently awarded a K25 award from the NIH.

Please do not hesitate to contact me if you have additional specific questions.

Sincerely,

(Karel Svoboda)