**PROJECT SUMMARY**

**Proposal Overview:**

The goal of this proposal is to study the role of synaptic ensheathment (the tightness of wrapping of the synapse by astrocytes) in regulating the spiking activity of the neuronal network. It is now known that synaptic ensheathment properties vary considerably between brain areas and in some disease conditions. However, what role that might play in regulating the brain activity is unknown. This is the question we set out to investigate.

We will use multiscale computational and mathematical analysis to address this question at different spatial and temporal scales. Specifically, we will approach this question in three distinct project components. The project components I and II will uncover the specific relationship between the degree of ensheathment and the properties of individual synapse. In project component III, we will consider a two-layer excitatory-inhibitory network, with each synapse endowed with its ensheathment parameter, and thus its own synaptic properties. We will then will ask how the distribution of the ensheathment parameter in the network relates to its firing rate and synchronization properties. The approaches that we choose to employ are quite general, and it will make the results relevant to other networks and experimental situations as well.

**Intellectual merit:**

While astrocytes are as numerous as neurons in the mammalian brain, there is relatively little known about specifics of their interaction with neurons. Expected findings from this work will contribute widely to understanding of the complex interactions between the two major brain cell types. Further, synaptic ensheathment is ubiquitous in the brain, but it is not ordinarily included in models as a property of network structure. Thus, this study explores a novel aspect of a more general problem of structure-function relationship, and will be of great interest to wide computational neuroscience community.

Based on our smaller scaled studies (components I and II), we will derive a network-level way to include synaptic ensheathment. Maximizing the ease of implementation and minimizing computing costs, we will provide a straightforward way to include the degree of synaptic ensheathment among the properties of an idealized synapse, often used in spiking neuronal networks.

We also propose to develop new mathematical tools such as: extension of a method for parameter sensitivity analysis to quantify specific roles of individual parameters in controlling the system behavior; significant extensions of diffusion with recharging receptors theory; and extension of network activity coherence measures to include synaptic ensheathment.

**Broader impact:**

The proposed activity will enhance and expand the interdisciplinary and educational opportunities on multiple levels, from high school students to the PIs colleagues.

The PI teaches mathematical biology courses at all possible levels and to diverse audiences including mathematicians, biologists, engineers, and pre-medical students. As the Director of Undergraduate Studies in her department she is involved in all aspects of the undergraduate education and research advancement. Results of the project will be presented at national and international conferences and workshops. The resulting software will be made publicly available through ModelDB and on the PI’s website.

Graduate students recruited for this project will be involved in all phases, and will also be able to participate in active community of mathematical biologists at the University of Utah, including participation in courses, tutorials, journal clubs, seminars and workshops (including those activities funded by Mathematical Biology NSF RTG program).

In her outreach activities, Borisyuk gives lectures at local high schools, participates in K-12 teacher training in interdisciplinary thinking. She has also been the leader and organizer of the Math Circle for elementary students for the past 4 years. She has been teaching and mentoring students in the ACCESS program – a summer program for women entering university with STEM interests. She will continue these enagagements.