Modelling of fluorescence imaging of quantal neurotransmitter release at single synapses

Dr Yulia Timofeeva
Department of Computer Science, Centre for Complexity Science and SBIDER, office MSB 5.26, y.timofeeva@warwick.ac.uk
Collaboration with Prof Kirill Volynski lab (Institute of Neurology, UCL)

Background. Synaptic release of neurotransmitters provides the basis for communication among neurons in the brain. When an action potential invades a presynaptic structure it triggers fast fusion of synaptic vesicles filled with neurotransmitters. Neurotransmitters quickly diffuse towards the postsynaptic neuron, where they bind to specific receptors and evoke further electrical and/or chemical signalling. Although the general molecular mechanism of transmitter release is well established, the precise regulation of vesicular release process at different synapses remains incompletely resolved. The main difficulty studying this regulation at the level of single synapses is that the majority of presynaptic boutons in the brain are very small, and as a result the experimental techniques are confronted with serious limitations. Very recently, a novel approach has been developed that allows experimentalists to directly image quantal vesicular release in single synapses with millisecond precision. It is based on the use of a fluorescence probe iGluSnFR "glutamate sniffer" that binds glutamate (major neurotransmitter in the brain) with high speed and affinity.

Project aim. The main aim of this project is to develop a predictive experimentally constrained model of glutamate release, its diffusion and binding to iGluSnFR in order to quantify dynamic changes of quantal neurotransmission during physiological patterns of neuronal activity. The project will involve collaboration with K. Volynski group in University College London, and the student will have an opportunity to take advantage of direct interaction with the experimental scientists.

Skills. The project will require good modelling skills and an interest in applying theoretical approaches to understanding biological data. Implementation can be performed using any programming language (for the student with strong programming skills), or alternatively it can be done in Virtual Cell (vcell.org, a comprehensive platform for modelling cell biological systems).

Extension to a PhD. This work can be extended to a PhD project under the collaborative project "Virtual presynaptic terminal" funded by the MRC. It will focus on developments of biologically constrained models of Ca^{2+} influx, buffered diffusion and neurotransmitter release using electrophysiological, optical, and pharmacological experimental data.