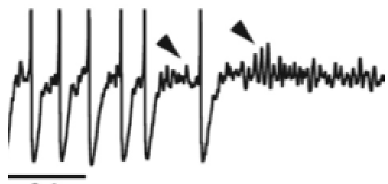
Network of motoneurons with mixed-mode oscillatory dynamics

Yulia Timofeeva (Centre for Complexity Science, office D2.12)
E-mail: y.timofeeva@warwick.ac.uk
Reserved for Arturo Leos-Zamorategui



Experimental studies demonstrate that neurons of different types can support the so-called mixed-mode oscillations (MMOs), where MMOs refer to a dynamical regime where high-frequency oscillations of small amplitude alternate with low-frequency oscillations of large amplitude (i.e., the spikes). For example, spinal motoneurons of anesthetised mice display MMOs characterised by subthreshold oscillations at high frequency (100 -150 Hz) that precede the firing of a full blown spike. In this regime, the discharge is very irregular, starts at frequencies as low as 2-3 Hz and increases with the applied current up to 40-70 Hz. Recently we demonstrated that MMOs in mouse motoneurons are not related to the sub-thershold resonance, one of the mechanisms that explains the MMOs in a number of neuronal types. We showed that high-frequency oscillations are due to the fast currents involved in spike generation and that MMOs require a low membrane excitability, most likely due to a slow inactivation of the sodium current. Our study revealed a new role for the afterhyperpolarization (AHP) current that sets the membrane excitability level by counteracting the slow inactivation of the sodium current and allows or precludes the appearance of MMOs. To study this phenomenon at the single-cell level we recently proposed a three dimensional model which includes the sodium, potassium, leak and AHP currents. This model nicely captures the MMO dynamics as well as regular spiking observed in real motoneurons.

The main goal of this project is to investigate the dynamics of motoneurons at the network level. We are particularly interested in focusing on the regime of MMOs. Both coupling, via electrical and chemical synapses, will be considered. These two types of coupling operate at different time scales and are expected to affect network outputs. Numerically obtained data will be analysed for gaining a better understanding of the role of MMOs in obtaining synchronous or other dynamic patterns that may arise. By reducing the single cell model to a minimal model that can support the MMOs, we might be able to get better mathematical insight into the observed phenomena. The outcome of the project will be of interest to theoretical/computational and experimental neuroscientists alike.

Some relevant publications:

1. C Iglesias, C Meunier, M Manuel, Y Timofeeva, N Delestree, D Zytnicki (2011) Mixed mode oscillations in mouse spinal motoneurons arise from a low excitability state *J Neurosci* Vol 31(15).

2. L Rela, L Szczupak (2002) Coactivation of Motoneurons Regulated by a Network Combining Electrical and Chemical Synapses, *J Neurosci*, Vol 23 (2).

3. M Brns, T J Kaper, H G Rotstein (2008) Introduction to Focus Issue: Mixed Mode Oscillations: Experiment, Computation, and Analysis, *Chaos* Vol 18.