COST ACTION TD1409 “Mathematics in Industry Network”

Short-Term Scientific Mission: REPORT

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Host: Mathematical Institute, University of Oxford (Prof. Philip K. Maini)

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The STSM was particularly successful and beneficial for my career as I had the chance to develop my research in collaboration with world-leading researchers at the University of Oxford, attend the British Applied Mathematics Colloquium, as well as get guidance on further developing industrial and applied mathematics in Cyprus.

A) Progressing with my research: Through this STSM, I was given the opportunity to work intensively with Prof. Philip Maini (FRS), Director of the Wolfson Centre for Mathematical Biology, Mathematical Institute, Oxford, and world-leading expert in mathematical biology. In this research we study calcium signaling, an important and interesting research area to mathematicians, medical researchers, and pharmaceutical companies. Calcium is ubiquitous in a living organism, and plays a key role in many crucial processes such as in embryogenesis, cardiac function, and brain function. There are many interesting open problems, and this inevitably leads to interesting models and mathematics. A summary of our main results up to now is found below. Note that I will present these results at the **European Consortium for Mathematics in Industry conference**, in June 2016. (co-authors: Prof. S. Jon Chapman, Prof. Philip Maini)

Main results of the research

Title: Mathematical modeling of calcium signaling taking into account mechanical effects

Most of the calcium in the body is stored in the bones. The rest is stored elsewhere, and calcium signalling is one of the most important mechanisms of information propagation in the body. Yet, many questions are still open and mathematical modelling can help answer them; several models of calcium signalling have been proposed, see for example [1].

In this work, we initially consider the mathematical model by Atri et al. [2]. When we omit calcium diffusion, this model is a system of two nonlinear ODEs for the calcium concentration, and the fraction of IP_3 receptors that have not been inactivated by the calcium. We analyse in detail the bifurcations that arise in this model as the IP_3 concentration, the *bifurcation parameter*, is increased. The system exhibits relaxation oscillations for a finite range of the bifurcation parameter. Calcium oscillations are thought to control a wide variety of cellular processes, and are often organised into intracellular and intercellular calcium waves. To further study the relaxation oscillations that arise, we exploit a separation of timescales and we develop an appropriate asymptotic analysis [3].

Furthermore, motivated by experimental evidence that cells release calcium when mechanically stimulated and that, in turn, calcium release affects the mechanical behaviour of tissue, we propose an extension of the 2D system to a 3D ODE system. The third variable models the dilatation of tissue, and we also introduce a mechanical stimulus that induces calcium release. We now have two bifurcation parameters; the IP_3 concentration, as previously, and the strength of the mechanical stimulus, and we study the system and the bifurcations that arise. We investigate in detail the interplay of the

mechanical and the chemical effects; we find that as the strength of the mechanical stimulus increases, the IP_3parameter range for which oscillations emerge decreases until oscillations eventually vanish at a critical value of the mechanical stimulus. Furthermore, we again exploit a separation of timescales and we study the nonlinear 3D system asymptotically.

References

[1] J.P. Keener, J. Sneyd, Mathematical physiology, Vol. 1., Springer, New York, 1998.

[2] A. Atri, J. Amundson, D. Clapham, J. Sneyd, A single-pool model for intracellular calcium oscillations and waves in the Xenopus laevis oocyte, Biophysical Journal, 65(4), pp. 1727-1739, 1993.

[3] J. Grasman, Asymptotic methods for relaxation oscillations and applications, Vol. 63, Springer Science and Business Media, 2012.

B) BAMC and paper presentation: I have presented a research paper at the British Applied Mathematics Colloquium that took place at the Mathematical Institute in Oxford, 5-8 April 2016. The conference attracted nearly 400 delegates and it was a great opportunity to listen to some great talks, as well as meet and network with researchers in diverse sub-fields of industrial and applied mathematics.

The research I have presented is the solution to an industrial problem that was suggested to Oxford by Thales Underwater Systems. This problem is resolving Left-Right Ambiguity Resolution in Towed Array Sonar. The work is co-authored with Dr David Allwright (Senior Mathematician at the Smith Institute for Industrial Mathematics and Systems Engineering, UK), and it has been submitted to the European Journal of Applied Mathematics in September 2015.

C) Study Group with Industry and other industrial maths intiatives in Cyprus: I received guidance from Dr Hilary Ockendon, Prof. John Ockendon, and Dr David Allwright on how to organise and run a Study Group with Industry in Cyprus (last quarter of 2016). I also had a very fruitful meeting with Dr Joanna Jordan, Chair of MI-NET, when she was visiting Oxford on 08/04/16.

Furthermore, I met with Dr Kathryn Gillow, Director of the MSc in Mathematical Modelling and Scientific Computing at Oxford. We obtained information about the Oxford MSc, and good practices in connection with a recent proposal we have submitted at my home institution for launching an MSc course in Industrial and Applied Mathematics. This MSc course, if approved, will be another step in developing industrial and applied mathematics in Cyprus.

Outcomes and next steps:

1) Presented an industrial problem at the British Applied Mathematics Colloquium
2) I will present my research on calcium modeling at ECMI16 in June 2016
3) Submission of a research article to a high-impact, peer-reviewed journal in the next three months
4) Continuing research on calcium modeling

Overall, this STSM provided me with much needed funds in order to progress my research in collaboration with world-leading researchers, network with applied mathematicians from all over the world, and receive guidance on my quest to develop industrial and applied mathematics in Cyprus.