Lift-Off Fellowship report: Robustness analysis of the carbon and nitrogen co-metabolism model of *Mucor mucedo*

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An emerging important area of the life sciences is systems biology, which involves understanding the integrated behavior of large numbers of components interacting via non-linear reaction terms. A centrally important problem in this area is an understanding of the co-metabolism of protein and carbohydrate, as it has been clearly demonstrated that the ratio of these metabolites in diet is a major determinant of obesity and related chronic disease [1]. In this regard, the first systems biology model for the co-metabolism of carbon and nitrogen in colonies of the fungus *Mucor mucedo* has been developed by Lui *et al.* [2]. Fungi have been chosen for this study because of their capacity to grow in conditions of extreme nitrogen deficiency relative to carbon, which makes them unique among other kingdoms. Furthermore, they have relatively simple network. In [2], periodic rhythms of biomass production in the colonies of these fungi under various nutrient regimes have been tested, and oscillatory behaviour, which is an important characteristic of a regulatory network, has been observed.

Oscillations are an important diagnostic of underlying dynamical processes. The key properties of a dynamical state are characterised by experiment. For understanding the oscillatory behaviour, the dynamic characteristics of the interactive components and their collective behaviours of the system need to be investigated. According to previous studies of the dynamics of complex systems, oscillatory behaviour can result from self-organising feedbacks (see, for example, [3]). In this regard, theoretical approaches play an important role in analysis of these behaviours. The maintenance of specific patterns of oscillation and its relation to the robustness of a system is a matter of ongoing research. In this research project, theoretical analysis of the robustness of the model developed by Liu *et al.* [2] has been accomplished.

Robustness is defined as the persistence of system functions in the presence of environmental perturbation. It should be considered in the analysis and validation of a biological model, since it is an important characteristic of living systems. In particular, if a model turns out to lack robustness under the potential perturbations, it should be investigated whether the lack of robustness is due to the cellular functions or uncertainty or incompletion of the model. An approach that examines the parametric sensitivities, i.e. the sensitivity of the behaviour with respect to changes in the model parameters, has been considered for robustness analysis of biochemical network model by many researchers (see, for example, [4], [5]).

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Metabolic Control Analysis (MCA), which presents a local sensitivity measure, has been applied to many systems as a common approach to parametric sensitivity. By this analysis, the range of variations of the model parameters values in which the metabolic oscillations of the system can still be obtained are determined.

We have considered a parametric sensitivity approach in the analysis of the co-metabolism of protein and carbohydrate model by Liu *et al.* [2]. As a result, the parameters of the model which produce the largest sensitivities have been identified. Furthermore, the largest change that can be made in each parameter of the model without losing the oscillations in biomass production have been computed. The results are currently being written up for publication.

References

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Nahid completed her master and bachelor degrees in applied mathematics in Iran. She was a mathematics lecturer in Iran from 2006 to 2009. In 2009, she received University President's Scholarships (UPS) from the University of South Australia to start a PhD in applied mathematics. She completed this degree in 2013 followed by receiving a Lift-off Fellowship award from the Australian Mathematical Society. The award was granted to accomplish research on the robustness analysis of a system biology model at the Charles Perkins Centre in the University of Sydney. This fellowship gave her a wonderful opportunity to work with Professor John Crawford and his research group. Moreover, it resulted in receiving a postdoctoral research associate position at the Charles Perkins Centre on the Alzheimer's disease.