Biology + Computing = ??

A joint meeting of the CSE:SEABIS group and the ModAbs group
Sponsored by SICSA

Monday 21st May 2012
10.30 – 5.30
Cottrell Building 2X4/6, University of Stirling

09.45 -	Coffee and tea will be available on arrival
10.30 - 11.30	**Modelling protein trafficking: progress and challenges** Vashti Galpin, University of Edinburgh
11.30 - 12.30	Contributed talks - 15 mins each
	Modeling Flocking: A Synthetic Ethological Approach Andrew Taylor, Heriot-Watt University **Systems biology approach to in silico and in vitro modelling of drug sensitivity-resistance transition in PI3K/PTEN/AKT signalling in cancer** Alexey Goltsov, University of Abertay Dundee **Synthetic neural systems** Leslie Smith, University of Stirling **Epidemiology in the heart of informatics** Dalila Hamami, University of Algeria
12.30 – 13.30	lunch
13.30 – 14.30	**Computational Modeling, Analysis and Synthesis of Gene Regulatory Networks** Yaochu Jin, University of Surrey
14.30 – 15.15	Contributed talks - 15 mins each
	Biologically inspired Coupled Complex Networks Saray Shai, University of St Andrews **An Investigation of Cellular Intelligence and its Role in Artificial Intelligence** Claire Gerrard/ John McCall, The Robert Gordon University **Qualitative and Semi-quantitative Approaches to Systems Biology** Wei Pang, University of Aberdeen
15.15 – 15.45	coffee/tea
15.45 – 16.30	Contributed talks - 15 mins each
	Optimisation of Process Algebra Models Using Evolutionary Computing David Marco, University of Stirling **Relationship between AMH and follicle number throughout life** Tom Kelsey, University of St Andrews **A critical study of network models for neural networks** Gordon Govan, Heriot-Watt University
16.30 – 17.30	Group discussion on key difficulties and opportunities, e.g. modelling of multi-scale systems, biological design of complex systems (not just computational), abstraction level – do we really need to be realistic? difficulties (or joys!) of working in biology, different approaches to biological modelling, Exciting emerging possibilities from crossovers, and future collaboration plans.
17.30 -	adjourn to pub, followed by meal in local restaurant for those who wish to stay on.

Abstracts: Invited Talks

Modelling protein trafficking: progress and challenges
Vashti Galpin, University of Edinburgh
Experimental research has shown that the oncoprotein Src is trafficked in endosomes between different parts of the cell. What techniques can be applied to develop a useful model that will provide hypotheses for further experimentation? What are the challenges involved when there is a lack of quantitative experimental data? This presentation describes how process algebra approaches have been applied to this difficult problem which involves dynamic behaviour, spatial aspects, and populations of independent entities.

Computational Modeling, Analysis and Synthesis of Gene Regulatory Networks
Yaochu Jin, University of Surrey
Followed by a brief introduction to computational models of gene regulatory networks (GRN), this talk first presents our recent results on analysing and synthesising gene regulatory motifs, particularly from the robustness and evolvability perspective. We show that in a feedforward Boolean network, the trade-off between robustness and evolvability cannot be resolved. In contrast, this trade-off can be resolved in an ODE-based GRN model for cellular growth. In addition, we demonstrate that robust GRN motifs can emerge from in silico evolution without an explicit selection pressure on robustness. Our results also suggest that evolvability is evolvable without an explicit selection pressure. Finally, simple genetic motifs are coupled using an evolutionary algorithm to design more complex genetic dynamics. In the second part of the talk, two examples of GRN models are presented for solving engineering problems. In the example, a hierarchical GRN is employed to self-organise swarm robots for tracking and surrounding moving objectives. We show that the system does not reply on a centralised control and is able to construct shapes adaptive to the position of the objectives. In the second example, a multi-cellular growth model governed by a GRN is developed. This cell growth model has been used for designing lightweight structures and simulating morphological development.

Abstracts: Contributed Talks

Modeling Flocking: A Synthetic Ethological Approach

Andrew Taylor, Heriot-Watt University

Modeling Flocking: A Synthetic Ethological ApproachThis research presents a new approach to the study of biologically inspired agents within multi-agent systems, using the phenomena of sheep flocks as an example.Multi-agent systems within the natural world that have been modeled within software simulation and upon robotic platforms, these include the schooling of fish and the flocking of birds. There are several benefits to an animal partaking in flocking behaviour, including increases in foraging and hunting efficiency, and avoiding the effects of predation.Several approaches have been taken to the modeling of these type of systems including the 'Boids' model by Reynolds (1987) and the fish schooling simulation by Tu (1990). These models are rule-based systems which are inadequate to the task of validly reproducing flocking behaviour for three primary reasons a) they impose a global homogeneity of behaviour across all agents b) the ignore individual development within members of the flock or school and c) these models ignore the evolution of a population's behaviour over time. Two approaches however do address some or all of these problems these are 'Evolutionary Robotics' and 'BioLand'. Using techniques from these approaches this model a) produces a model that is a valid reproduction of sheep behaviour b) is implemented within simulation environment c) models small groups of agents engaged in predator prey interactions and examines their behavioral evolution over time. To validate this model we compare its behaviour with sheep flocks using a variety of metrics such as complexity plots, mean social distance and the aggregation metrics proposed by Garnier et al (2005).

Systems biology approach to in silico and in vitro modelling of drug sensitivity-resistance transition in PI3K/PTEN/AKT signalling in cancer

Alexey Goltsov, University of Abertay Dundee

Genome transformation of cancer cells leading to oncogene addiction of tumor is a basis of drug targeted anticancer therapy. Successful drug development in this direction explores this tumor addiction and aims to suppress oncogene activity. The main challenge of targeted therapy is due to de novo or required cancer resistance resulting mainly from additional gain-to-function mutations and aberrations in cancer genome causing repression of tumor suppressors and concomitant activation of other oncogenes. These mutual aberrations in cancer genome endow cancer cells with robustness to drug intervention. A systems biology approach was developed to study the efficacy of monoclonal antibody therapy (trastuzumab, pertuzumab) targeting HER2 receptor. Breast and ovarian cancer cells in 20-30% suffer addiction to HER2 expression, which elicits prosurvival and proliferation signalling through activation of RAS/MEK/ERK1/2 and PI3K/PTEN/AKTsignalling pathways. The integrated systems framework developed includes iterated in silico, in vivo experiments, and analysis in clinical cohorts, allowing cyclic generation and validation of hypotheses for mechanisms of drug sensitivity. The kinetic and dose response of pAKT and pERK1/2 signals to HER2 inhibitor was studied by manipulation of activities of the following receptors/proteins involved the signalling network: HER2, HER3, PTEN, PI3K, AKT, CK2, GSK3, PTPN13, and DUSPs. This technique permits us to model different perturbations in the PI3K/PTEN/AKT signalling network typical in cancer development, therapy, and drug resistance. Using this method we modelled the sensitive and resistant modes of behaviour in the signalling network, and observed the sensitivity-to-resistance transition from the combined inhibition of the receptors/proteins involved. Using sensitivity analysis of signalling network we elucidated the mechanisms underlying network sensitivity-to-resistance transition as a result of activating/repressing mutations and proposed the strategy to restore initial sensitivity by drug combinations.

Synthetic neural systems
Leslie Smith, University of Stirling
From modelling sensory processing to novel ideas in brain/machine interfacing to cyborgs, neural systems have provided a basis for applicable computing capabilities, and directions for novel research. I propose to briefly describe a set of related ideas based on my research, and to pose questions, but not to provide answers.

Epidemiology in the heart of informatics
Dalila Hamami, University of Algeria
Epidemiology is the study of patterns of health and illness and associated factors at the population level. It is a field that is greatly accredited with the determination of precise evidence based medicine and medical practices used in identifying risk factors for disease and is also used in the determination of optimal treatment approaches to clinical practice and preventive medicine. Epidemiologists rely on scientific disciplines such as Bio-informatics to better understand disease processes, obtain the current raw information available, store data and map disease patterns, to better understand proximate and distal risk factors that affect the spread of major diseases and facilitate to make decision. Currently we are being dogged by great challenges in health and the integration of modelising methods, simulation and data mining methodologies will greatly reduce the load taken in data collection and analysis and also validate results.

Biologically inspired Coupled Complex Networks
Saray Shai, University of St Andrews
In the past decade, complex networks have been proved to be a useful framework to study interconnected systems. Most real networks do not live in isolation, but often depend or interact with other networks, creating a system of coupled networks. Recently, the effect of non-random inter-network coupling has been examined, suggesting that positively correlated coupled networks (e.g. high-degree nodes in one network are coupled with high-degree nodes another)are more robust. While technological and social networks exhibit high positive correlation coefficient, it seems that coupled biological networks exhibit a closer to random one. Inspired from this observation, we claim that coupled nodes often share resources and these are limited. Using epidemic spreading over coupled networks, we demonstrate that for systems that must share resources, positive correlation can impede flow processes through contention, when compared to negative.

An Investigation of Cellular Intelligence and its Role in Artificial Intelligence
Claire Gerrard, The Robert Gordon University
The Artificial Reaction Network (ARN) is a bio-inspired connectionist paradigm based on the emerging field of Cellular Intelligence. It has properties in common with both AI and Systems Biology techniques including Artificial Neural Networks, Petri Nets, Random Boolean Networks and S-Systems. Rather than focus on micro-molecular detail, the ARN aims to elucidate emergent behaviour within a network of chemical reactions. Its biological basis was validated using real biochemical data, including simulation of the well characterized signalling network of E. coli chemotaxis. The adaptability of the ARN was later examined as a basis for development of novel AI techniques and applied to problems in optimisation, pattern recognition and robotic control.

Qualitative and Semi-quantitative Approaches to Systems Biology
Wei Pang, University of Aberdeen
Qualitative and semi-quantitative models are complementary representations to quantitative models. They can provide, at varying precision, a global picture of the behaviour of a system even when the model is incomplete. Although in molecular biology it is difficult to obtain sufficient time series data to perform numerical system identification it is still possible to utilise machine learning to identify qualitative models of such systems. We aim to employ

such qualitative approaches to (1) understand the dynamics of biological systems at qualitative and semi-quantitative levels and (2) provide guidance for quantitative modelling.

Optimisation of Process Algebra Models Using Evolutionary Computing
David Marco, University of Stirling
This paper presents initial results of applying a Genetic Programming (GP) approach to the evolution of process algebra models defined in Bio-PEPA. An incomplete model of a system is provided together with target behaviour. GP is then used to evolve new definitions that complete the model while ensuring a good fit to target data. Our results show that a set of effective models can be developed with this approach that can either be used directly or further refined using a modeller's domain knowledge. Such an approach can greatly reduce the time taken to develop new models, enabling a modeller to focus on the subtler modelling aspects of the problem domain. Although the work presented here concerns the modelling of biological systems, the approach is generally applicable to systems for which appropriate target behaviour can be captured and that can be formalised as a set of communicating processes.

Relationship between AMH and follicle number throughout life
Tom Kelsey, University of St Andrews
AMH is the best currently available marker of the number of small-growing follicles in the ovary. Recent advances in modelling allow us to compare rates of change in follicle recruitment and AMH levels in the blood. The resulting hypotheses are testable, leading to an increased understanding of human reproductive endocrinolgy and physiology.

A critical study of network models for neural networks
Gordon Govan, Heriot-Watt University
Network models have been shown to match the global topological features of some empirical networks.These models may even match the distribution of measurements throughout the network.But how do their dynamics compare to the network that they are modelling?We compare three networks models, the Erdos-Renyi, the Watts-Strogatz, and the Structured nodes model.We find networks from each model that are able to match some of the topological features of the C. elegans neural network.We observe the difference between their topological features and those of the C. elegans, before simulating the dynamics of the networks by running them as random recurrent neural networks.We find that none of the considered network models is able to closely match the C. elegans neural network for all measurements that we observed.