Northern Regional Meeting of the London Mathematical Society
&
Workshop on Mathematics of Human Biology

Abstracts of Communications

Mathematics, Northumbria University
6th & 8th June 2012

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Complex dynamics of cellular transcriptional response: how do cells get on the fast lane?

Eytan Domany[a]

a. Department of Physics of Complex Systems, Weizmann Institute of Science, Rehovot, Israel.

The talk will start with a very basic introduction aimed at the non-expert.

In response to external stimuli, cells adjust their behavior to a changing environment - for example, they start to divide or migrate. In order to perform these actions, the protein content of the cell must change. To accomplish this, a cell must modify the levels at which the genes that code for these proteins are transcribed. These transcriptional responses to extracellular stimuli are regulated by tuning the rates of transcript production and degradation. I present here the results of a study aimed at deducing the dynamics of these two processes from measurements of the transcriptome, and to elucidate the operational strategy behind this dynamics.

By combining a simple theoretical model of transcription with simultaneous measurements of time-dependent precursor mRNA and mature mRNA abundances, we were able to infer unexpected complex stimulation-induced time-dependent transcript production and degradation. In particular, we found that production of many transcripts was characterized by a large dynamic range, which allowed these genes to exhibit an unexpectedly strong and brief pulse of production, thereby accelerating their induction. Surprisingly, we found that the widely used assumption of close correspondence between mRNA abundance and production profiles is incorrect: timing of mRNA maxima does not allow inference of the production pulse. Finally, we discovered that mRNA degradation is regulated in a precisely timed and transcript specific manner.

References

[1] Coupled pre-mRNA and mRNA dynamics unveil operational strategies underlying transcriptional responses to stimuli. Amit Zeisel, Wolfgang J Kostler, Natali Molotski et al (2011) Molecular Systems Biology 7: 529

A mathematical modeling study of neutrophil dynamics in response to chemotherapy and G-CSF

Michael Mackey[a]

a. McGill, Centre for Applied Mathematics in Bioscience and Medicine, Montreal, Canada.

We have used a mathematical model of the combined dynamics of the hematopoietic stem cells and the differentiated neutrophil progeny to examine the effects of periodic

chemotherapy in generating neutropenia, and the corresponding response of this system to granulocyte colony stimulating factor given to counteract the neutropenia. We find that there is a significant period of chemotherapy delivery that induces resonance in the system (at a period twice the average neutrophil lifespan from commitment to death) and a corresponding neutropenia, suggesting that myelosuppressive protocols should avoid this period to minimize hematopoietic damage. The response to G-CSF is highly variable. All of these results, seemingly mysterious initially, are easily understood through an analysis of the dynamical equations and have significant potential impact in clinical practice. I will discuss these results as well as extensions of this research currently underway.

Empirical approaches to the application of mathematical techniques in health technologies

H.T. Nguyen [a], **A.G. Shannon**[a]

a. Faculty of Engineering and Information Technology, University of Technology, Sydney, NSW 2007, Australia

Mathematical modeling of ageing is built in this paper around research and development activities in cooperation with pharmaceutical companies and hospitals. The interaction of *dirty data* with appropriate mathematical techniques is exemplified mainly with applications to health technologies in endocrinology and oncology. The emphasis is more on old techniques in new situations than on new techniques, though there are references to some novel approaches to modeling.

Workshop: Abstracts of Communications

Affine Reflection Groups for Tiling applications: Knot theory and Modeling of DNA Site-Specific Recombination

Mark Bodner[a]

a. Mind Research Institute, California, USA

DNA exists in a highly compact and tangled form in the nucleus of a cell. The packing, twisting, and topological constraints on the structure of DNA present problems in carrying out the functions and processes necessary for life such as transcription, replication, and recombination. However, the actions of enzymes that make these functions possible–topologically cutting, pasting, and passing strands of DNA through each other–cannot be directly observed, and must be deduced mathematically. In this talk, starting from tools developed for carrying out tilings of the real Euclidean plan, a correspondence between such tilings and knots will be elucidated. The resulting mathematical structure provides a framework within which is encompassed recent work utilizing knot theory for modeling the structure and function of genetic molecules. Particularly, the determination of the action of specific enzymes in altering the topology and geometry of DNA in site-specific recombination will be addressed within this mathematical framework.

Multiscale mathematical modelling of cancer growth and spread

Mark Chaplain[a]

a. Mathematics, University of Dundee, UK

Cancer growth is a complicated phenomenon involving many inter-related processes across a wide range of spatial and temporal scales, and as such presents the mathematical modeller with a correspondingly complex set of problems to solve. This talk will present multi-scale mathematical models for the growth and spread of cancer and will focus on three main scales of interest: the sub- cellular, cellular and macroscopic.

The sub-cellular scale refers to activities that take place within the cell or at the cell membrane, e.g. DNA synthesis, gene expression, cell cycle mechanisms, absorption of vital nutrients, activation or inactivation of receptors, transduction of chemical signals. The cellular scale refers to the main activities of the cells, e.g. statistical description of the progression and activation state of the cells, interactions among tumour cells and the other types of cells present in the body (such as endothelial cells, macrophages, lymphocytes), proliferative and destructive interactions, aggregation and disaggregation properties. The macroscopic scale refers to those phenomena which are typical of continuum systems, e.g. cell migration, diffusion and transport of nutrients and chemical factors, mechanical responses, interactions between different tissues, tissue remodelling.

The models themselves will range from systems of partial differential equations, to individual force- based models and hybrid discrete-continuum models.

Time series in physical and biological systems: listening to bubbles, quakes and heartbeats

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c. Instituto Nacional de Geriatría, México

d. Northumbria University, Newcastle, UK

Dynamical systems from different areas of knowledge can be studied within the theoretical framework of time series, where the system itself can be considered as a black box, that does not need to be manipulated, but only to be "listened" to. In this framework, non-correlated series (white noise) and strongly correlated series (such as periodic or quasiperiodic series) constitute extreme behaviors. Many dynamical systems auto-organize themselves in a state characterized by $1/f$ or flicker noise. $1/f$ noise is fractal and is a signature of criticality, it maximizes memoryand information content, signaling complex behavior. We explore the fractal properties of fluctuations in dynamical systems, using some of the available tools of time series analysis. Besides the traditional methods of power spectra in the Fourier domain, detrended fluctuation analysis (DFA) and autocorrelation functions, we apply the Empirical Mode Decomposition Method (EMD), which provides a natural and more effective way to analize the information underlying physical and physiological phenomena. We describe several applications, including a study of heart rate in a C-elegans model.

Viruses and Geometry - Where Symmetry meets Function

Reidun Twarock[a]

a. York Centre for Complex Systems Analysis, Mathematics and Biology University of York

Viruses display symmetry for reasons of genetic economy: By packaging their genomic material into protein containers (viral capsids) arranged with icosahedral symmetry, they maximize container volume while minimizing the portion of the genomic sequence needed to code for the capsid. From a mathematical point of view, this implies that techniques from group theory can be used to predict virus architecture. We show here that via an affine extension of the icosahedral group new information regarding structural constraints on virus architecture can be obtained, that reveal a previously unrecognised structural correlation between different viral components. We discuss the implications of such structural features for function, i.e. for how viruses form and infect their hosts. In particular, structural transitions of the viral capsids important for infection and the role of structure in the assembly of viral particles will be considered in detail.

Modeling the kinetics of physiological variables as a dynamical system

Maria Zakynthinaky[a]

a. Mathematics, ELKE-Technical University of Crete, Greece

This talk will present a model (Stirling et al., Bul. Math. Biol. 67 (5), 2005) of the underlying dynamics of the kinetics of a physiological variable s (where let s be the heart rate or the rate of change of Oxygen uptake) in response to movement. Assuming that s is a function of time t and intensity v, i.e. s=s(v,t) the model is given in the form of a set of nonlinear coupled vector fields for the second derivative of s with respect to time and the first derivative of v with respect to time. The model not only provides a perfect fir to raw physiological time series data (examples will be presented) but also has the power to estimate the time dependency of the physiological demand and also give predictions regarding the behavior of the physiological system under intensities for which no data exist (such as for example very high intensities). A physiological justification of the model will be presented and the results of a linear stability analysis of the model will also be discussed.

References

[1] Stirling et al., Bul. Math. Biol. 67 (5), 2005.

Title: Time-frequency analysis in biomedical data analysis

Hongmei Zhu[a]

a. Mathematics, Your University, Toronto, Canada

The aim of this talk is to present an overview of time-frequency analysis, i.e., techniques to unravel frequency and time information within a non-stationary signal whose frequency content varies over time. For such a signal, the traditional Fourier analysis of frequency loses its effectiveness and hence one needs to seek a way to capture the time-varying nature of the frequencies occurred in a signal. In this talk, we introduces the audience the highlights to the related theory and demonstrate its usefulness in biomedical applications.

Workshop on Mathematics of Human Biology and LMS Northern Regional Meeting; 6-8 June 2012

Programme	LMS Northern Regional Meeting Wednesday 6 June	Workshop Thursday 7 June	Workshop Friday 8 June
10 – 11		**Mark Bodner**	**Alejandro Frank**
Coffee Break 10 – 10:30			
11:30 – 12:30		**Reidun Twarock**	**Maria Zakynthinaki**
Lunch and Poster display 12:30 – 14:00			
14 – 15	**Michael Mackey**	**Mark Chaplain**	Open discussion motivations talks
15 – 16	**Anthony Shannon**	Open discussion motivations talks	Round table - Open discussion
Coffee Break 16 – 16:30			
16:30 – 17:30	**Eytan Domany**	Round table - Open discussion	**Hongmei Zhu**
	LMS Northern Regional Meeting Dinner (from 19:00)		

For your Notes

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