One-Day IOP meeting
Complexity and Nonlinear Phenomena in Biological Systems
20 May 2010, University of Bath

Abstracts

Raymond Goldstein (DAMTP, Cambridge)
Synchronisation of Eukaryotic Flagella

Flagella, among the most highly conserved structures in eukaryotes, are responsible for such tasks as fluid transport, motility and phototaxis, establishment of embryonic left-right asymmetry, and intercellular communication, and are thought to have played a key role in the development of multicellularity. These tasks are usually performed by the coordinated action of groups of flagella (from pairs to thousands), which display various types of spatio-temporal organization. The origin and quantitative characterization of flagellar synchronization has remained an important open problem, involving interplay between intracellular biochemistry and interflagellar mechanical/hydrodynamic coupling. In this talk I will describe our recent experimental studies of the synchronization dynamics of the two flagella of the green alga Chlamydomonas. We have found the first quantitative evidence for flow-induced synchronization, and further discovered that this organism exhibits stochastic transitions between synchrony and asynchrony, producing a eukaryotic version of the run-and-tumble locomotion of bacteria. The dynamics are consistent with a stochastic version of the Adler equation, which can be used to infer the changing intrinsic beat frequencies of the two flagella.

Mike Swift (Nottingham)
The collective dynamics of spheres in oscillatory fluid flows.

We describe a range of non-linear phenomena which occur when a collection of dense rigid spheres on a surface is subjected to horizontal oscillatory fluid flows. Pairs of equal-sized spheres are found to align perpendicular to the direction of oscillation with a well-defined gap between them. Similarly, multiple particles form chains aligned across the direction of vibration. Two unequal sized spheres are found to migrate at a constant velocity, also across the direction of vibration. The mechanisms responsible for these effects can be traced to the streaming flows induced by the motion of the solid spheres relative to the fluid. The possible relevance to swimming micro-organisms will be discussed.

Alexander Gorban (Leicester)
Asymptotic analysis of microRNA action on the protein translation process

We developed a method for asymptotic analysis of chemical reaction networks and used this method for analysis of protein translation regulated by small non-coding microRNAs. It remains unclear what mechanisms of microRNA action on protein translation are the most dominant: moreover, many experimental reports deliver controversal messages on what is the concrete mechanism actually observed in the experiment. Nissan and Parker have recently demonstrated that it might be impossible to distinguish alternative biological hypotheses using the steady state data on the rate of protein synthesis. In contrary, we show that dynamical data allow to discriminate some of the mechanisms of microRNA action. We demonstrate this using the same models.

The effect of microRNA action is measurable and observable only if it affects the dominant system (generalization of the limiting step notion for complex networks) of the protein translation machinery. The dominant system can vary in different experimental conditions that can partially explain the existing controversy of some of the experimental data.

Our analysis of the transient protein translation dynamics shows that it gives enough information to verify or reject a hypothesis about a particular molecular mechanism of microRNA action on protein translation. For multiscale systems only that action of microRNA is distinguishable which affects the parameters of dominant system (critical parameters), or changes the dominant system itself. Dominant systems generalize and further develop the old and very popular idea of limiting step.

Algorithms for identifying dominant systems in multiscale kinetic models are straightforward but not trivial and depend only on the ordering of the model parameters but not on their concrete values. Asymptotic approach to kinetic models allows to put in order diverse experimental observations in complex situations when many alternative hypotheses co-exist.

Zinovyev A., Morozova N., Nonne N., Barillot E., Harel-Bellan A., and Gorban A.: Dynamical modeling of microRNA action on the protein translation process. BMC Systems Biology, 4(1) (2010)

Sandra Chapman (Warwick)
A Fundamental Basis for Macroecological Patterns

Macroecological patterns, specifically how biodiversity, abundance and metabolic rate depend on the availability of resource, and on each other, are some of the most prominent but least understood features of how life is organized. We obtain a fundamental expression that constrains an ecosystem in dynamic balance. This expression yields Wright's rule and the species-area relationship. It also suggests the latitudinal gradient rule. If allometric scaling with body mass is present, it constrains the scaling exponents of the metabolic theory. We show how controlled comparisons across ecosystems can be made and identify the observable parameter controlling diversity and abundance of ecosystems. Our results explain the ubiquity of macroecological patterns, and suggest that counterexamples indicate ecosystems not in dynamic balance that are on the point of, or are already showing, rapid change in diversity or abundance.

Robert Endres (Imperial)
How one cell eats another: experiments and modelling elucidate early signalling events and biophysical requirements for uptake

Phagocytosis is the fundamental cellular process by which eukaryotic cells bind and engulf particles by their cell membrane, involving cell-surface recognition receptors, signaling and remodeling of the actin cytoskeleton. Despite the signaling complexity, phagocytosis also depends strongly on biophysical parameters. Noticeably, successive ligand-receptor binding in a zipper-like fashion appears necessary for guiding membrane around the particle. However, the conceptual zipper mechanism was never tested regarding its biophysical requirements. Here, we propose a minimal biophysical model in which thermal membrane fluctuations are rectified by receptor-induced actin polymerization, effectively reinforcing ligand-receptor bonds. Using finite-element simulations, we surprisingly find that even without actin polymerization, engulfment proceeds in a large parameter regime, albeit more slowly and with highly variable phagocytic cups. We experimentally test these predictions using fibroblasts, transfected with the immunoreceptor FcγRIIa for engulfment of immunoglobulin G-opsonized particles. Specifically, we compare cells with and without functional actin dynamics by reconstructing phagocytic cups from fluorescence imaging data. This confirms our predictions and shows that phagocytosis even works without active signaling pathways, rendering this ancient process highly robust.

Rainer Klages (QMUL)
Anomalous dynamics of cell migration

Cell movement, for example, during embryogenesis or tumor metastasis, is a complex dynamical process resulting from an intricate interplay of multiple components of the cellular migration machinery. At first sight, the paths of migrating cells resemble those of thermally driven Brownian particles. However, cell migration is an active biological process putting a characterization in terms of normal Brownian motioninto question. By analyzing the trajectories of two different types of wild-type and mutated epithelial (transformed Madin-Darby canine kidney) kidney cells, we show experimentally that anomalous dynamics [1] characterizes cell migration. A superdiffusive increase of the mean squared displacement, non-Gaussian spatial probability distributions, and power-law decays of the velocity autocorrelations are the basis for this interpretation. Almost all results can be explained with a fractional Klein-Kramers equation allowing the quantitative classification of cell migration by a few parameters [2].

[1] R. Klages, G.Radons, I.M.Sokolov (Eds.), Anomalous transport (Wiley-VCH, Weinheim, 2008)
[2] P.Dieterich, R.Klages, R.Preuss, A.Schwab, PNAS {\bf 105}, 459 (2008).

Christel Kamp (PEI)
Co-evolution of epidemic spread and transmission network topology

The spread of infectious agents is still a major threat to public health despite considerable efforts in epidemic control. Mathematical and computational models can help to understand the emergence of epidemic patterns that may differ largely depending on the pathogen, its routes of transmission and host population. Recent approaches have specifically focussed on the transmission network that represents infectious contacts among hosts: its structure and dynamics has strong influence on the speed and width of epidemic expansion. However, the transmission network is not a static support for the epidemic process but is in turn also shaped by epidemics: demographic change may occur naturally or due to excess death of infected hosts. Also various degrees of mixing between susceptible and infected hosts may arise during an epidemic. This co-evolutionary process can be studied for transmission networks with arbitrary degree distributions using a recently developed mathematical framework [1]. The method based on a set of partial differential equations will be briefly introduced and applied to synthetic populations to demonstrate its use and range of predictions.
Finally, we use the method to study HIV epidemics in synthetic populations with varying numbers of

concurrent partners. This allows for conclusions under which conditions new infections dominate which are either derived from primarily or latently infected individuals. The current findings encourage to fit the model with more realistic empirical data to improve our understanding of epidemics and their control.

[1] C. Kamp, Untangling the interplay between epidemic spreading and transmission network dynamic, under review, preprint available at http://arxiv.org/abs/0912.4189 (2009)

Matthew Turner (Warwick)
Fibre-like protein aggregates in disease and their interaction with cell membranes

Linear protein aggregates are associated with diseases like Alzheimer's, Huntington's and sickle cell. We first present experimental studies of the fibre-like aggregates that appear in sickle cell disease. We then discuss predictive models that describe how these fibres form, their mechanical properties, how they depolymerise and how they grow while interacting with ``soft'' fluid membranes, such as the plasma membrane of the red blood cell. We discuss the rich physics of these systems and how this reveals both unexpected complexity and nonlinear dynamics.

Joanna Bryson (Bath)
Determinants of the size of social species' culture

Since the late 1990s there has been a steady increase of field and experimental evidence that many species utllise social learning as source of behaviour. What determines the extent to which a species relies on socially acquired behaviour (culture) rather than that provided by genetic inheritance or purely individual learning? Previous researchers (e.g. Boyd & Richerson) have focused on a tradeoff between risk to the individual vs. the age of information. However, if we think of the individual learning of behaviour as a search, then theoretical computer science tells us that a concurrent search should be much more productive if the answers can be shared. Further, contemporary theoretical biology tells us that selection for altruistic sharing should be possible due to inclusive fitness. In this talk I will review evidence from agent-based simulations for several other dynamics, including
- ecological & life history tradeoffs determining size of culture (Cace & Bryson 2007; Bryson, Bilovich & Cace submitted)
- evidence of individual adjustment in cognitive investment based on apparent fitness to ecological context (Richards & Bryson 2009)
- selection on the content of culture itself (Kirby 1999; Bryson 2010).

Mario Nicodemi (Warwick)
A symmetry breaking model for X chromosome inactivation

In humans, female cells silence one of their two X chromosomes, which is randomly selected, to equalize X products with respect to males (having just one X). Such a process, named X Chromosome Inactivation (XCI), is crucial to survival and is related to serious genetic diseases. The mechanism, though, whereby cells count their X's and randomly choose the one to inactivate is one of the most mysterious aspects in X biology. We proposed a Statistical Mechanics model of XCI where a molecular complex, a 'blocking factor' (BF), can protect from inactivation the X chromosome whom it binds to. The BF is present in a single copy in the nucleus so just one X per cell, randomly selected, can be protected, as the second X is inactivated by default under the action of its Xist gene. A crucial step in the model was to explain how the molecular complex is self-assembled and why only one is formed, out of many diffusible molecules. We showed this is the result of a thermodynamics phase transition which spontaneously breaks the symmetry between the X's. As more recent experiments have indeed discovered complexing and binding molecules regulating XCI, the mechanism that directs the two chromosomes to opposite fates appears to be clarified. In a broader perspective, at least 10% of our genes has a behavior similar to the X's, i.e., out of two alleles one is randomly selected and inactivated, with important and poorly understood examples ranging from the immune system to our olfactory apparatus. The new stochastic regulatory mechanism we propose can be a key to those cases as well.

Paddy Royall (Bristol)
Colloidal dispersions: complexity from simplicity

It is hard to imagine anything simpler than an assembly of spheres. Like many biological systems, colloidal dispersions are suspended in a fluid medium, which imparts hydrodynamic couplings between the particles. Here we consider the case of micron-sized spheres sedimenting across a slit. We show that the behaviour of

this system is profoundly influenced by the initial conditions. The 1D time-evolution of a quasi-uniform initial condition is well captured by a dynamical density function theory, which accounts for hydrodynamics only a mean-field like manner [1]. Conversely, starting from a non-uniform condition, complex patterns emerge in a phenomenon quantitatively similar to the Rayleigh-Taylor instability in immiscible fluids [1,2]

[1] Royall CP, Dzubiella J, Schmidt M and van Blaaderen A, Phys. Rev. Lett, 98, 188304 (2007).

[2] Wysocki A, Royall CP, Winkler R, Gompper G, Tanaka H, van Blaaderen A and Loewen H, Soft Matter 5, 1340 (2009).

The meeting is organized by the Nonlinear and Complex Physics Group of the Institute of Physics.

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