International Conference

Modelling Biological Evolution 2017:

Developing Novel Approaches

University of Leicester (UK), April 4- April 7, 2017

Sponsored by the London Mathematical Society and the University of Leicester

Organizer: **Andrew Morozov** (University of Leicester, UK)

Aims and Scope

Mathematical modelling is a powerful, efficient and ethically justifiable tool for exploring various aspects of biological evolution and adaptation in biosystems ranging from biomolecules to human societies. Currently, new mathematical and computational approaches are being rapidly developed to allow us to cope with the existing and newly emerging challenges. The aim of this meeting is to bring together a number of leading researchers who are constructing and/or implementing novel mathematical and computational approaches in modelling biological evolution based on game theory (including adaptive dynamics), optimisation, system complexity reduction, reinforcement learning, networks modelling, data mining, agent-based simulation and their combinations. Intensive debates are planned to discuss the universality of newly developed approaches to tackle various aspects of biological evolution, which might go well beyond the initial area of implementation of the suggested methods. This meeting will be as well an open forum for interaction between theoreticians and empirical biologists with the main goal to enhance interdisciplinary approaches and stimulate further advances in developing new mathematics to improve our undemanding of biological evolution and adaptation.

Organization & structure

Honorary Lecture:

Karl Sigmund (University of Vienna, Austria)

Plenary Speakers:

Alexander Gorban (University of Leicester, UK)

Robert Holt (University of Florida, USA)

Eva Kisdi (University of Helsinki, Finland)

Hanna Kokko (University of Zurich, Switzerland)

Philip Maini (University of Oxford, UK)

John McNamara (University of Bristol, UK)

Sylvie Méléard (Ecole Polytechnique, France)

Hans Metz (Leiden University, the Netherlands)

Kalle Parvinen (University of Turku, Finland)

Advisory Scientific Committee:

Mark Broom (City University London, UK)

Sergey Gavrilets (University of Tennessee, Knoxville, USA)

Alexander Gorban (Leicester, UK)

Yoh Iwasa (Kyushu University, Japan)

Olof Leimar (Stockholm University, Sweden)

Sebastien Lion (CEFE, Montpellier, France

Geza Meszena (Eotvos University , Budapest, Hungary)

Minus van Baalen (Université Pierre et Marie Curie, France)

Local organizing committee:

Halil I. Egilmez (University of Leicester, UK)

Oksana Gonchar (University of Leicester, UK)

Simran Sandhu (University of Leicester, UK)

Anna Zincenko (University of Leicester, UK)

Detailed Conference Program

Tuesday April 4th

Venue: Bennett Building, ground floor
8.20-9.00 **Registration**

9.00-10.50 **Introduction and plenary talks 1, 2**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
9.00-9.10 **Introduction and welcome address**
9.10-10.00 **Plenary talk 1**. **Hans Metz**. Evolutionary branching in the multivariate case
10.00-10.50 **Plenary talk 2**. **John McNamara.** Towards a richer evolutionary game theory.

10.50-11.20 Coffee break: Bennett Building, ground floor

11.20-13.00 **Contributed talks** (session 1)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
11.20-11.40 **Yoav Soen.** Darwinian selection induces lamarckian adaptation in a holobiont model
11.40-12.00. **Mark Broom.** Game theoretical modelling of a dynamically evolving network
12.00-12.20 **Anne Kandler.** Novelty, popularity, and emergent neutrality: Detecting transmission biases in population-level data.
12.20-12.40 **Michael Sieber.** Neutral model of microbiome composition
12.40-13.00. **John Norbury.** Defining a food web landscape for quantitative trait (QT) population modelling.

13.00-14.10 Lunch break

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
14.10-15.00 **Plenary talk 3**. **Eva Kisdi. Dispersal polymorphisms in stable habitats.**

15.05-16.05 **Contributed talks** (session 2)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
15.05-15.25 **Ludek Berec.** Density-dependent selection on mate search and evolution of Allee effects.
15.25-15.45. **Barbara Boldin.** Evolutionary suicide of pathogens.
15.45-16.05 **Matthew Adamson.** Identifying the sources of structural sensitivity in ecological models using partially specified models

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16.05-16.35 Coffee break: Bennett Building, ground floor

16.35-18.15 **Invited talks**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
16.35-17.00 **Tamas David-Barrett.** Fertility, kinship and the evolution of mass ideologies
17.00-17.25 **Vincent Jansen.** The evolution of sex-specific virulence in infectious diseases.
17.25-17.50 **Olof Leimar.** Genetic conflict with a basis in ecology.
17.50-18.15 **Richard A. Watson.** The learning principles of evolution by natural selection.

Time for rest and relaxation

Wednesday April 5th

9.00-10.40 **Plenary talks 4,5**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
9.00-9.50 **Plenary talk 4. Robert D. Holt.** Thoughts on the interplay of demographic stochasticity, fitness, and the niche concept.
9.50-10.40 **Plenary talk 5**. **Kalle Parvinen.** The effect of spatial heterogeneity on evolution in spatial models

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10.40-11.10 Coffee break: Bennett Building, ground floor

11.10-12.50 **Theme session 1:** Eco-evolutionary models

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
11.10-11.30 **Alex Best.** The impact of community interactions on host-parasite evolution.
11.30-11.50 **Farnoush Farahpour.** Eco-evolutionary dynamics in interaction space of competitive communities: How diversity emerges and persists.
11.50-12.10 **Charlotte de Vries**. Combining stage-classified demography and population genetics to study eco-evolutionary dynamics.
12.10-12.30 **Jan Olaf Mirko Härter.** Assembly rules and a minimal theory for invasion and extinction in food webs.
12.30-12.50 **Veronika Bernhauerova.** Evolution of mate-finding Allee effect in prey.

11.10-12.50 **Contributed talks** (session 3)

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)
11.10-11.30 **Jörgen Ripa.** Speciation cube trajectories cluster around three modes of parapatric speciation.
11.30-11.50 **Thomas Aubier.** Speciation along ecological gradients and the costs of choosiness.
11.50-12.10 **Richard J. Bingham.** RNA virus evolution via a quasi-species theory-based model reveals a novel drug target.
12.10-12.30 **Sophie Pénisson.** A genealogical model for the ancestor paradox
12.30-12.50 **Cornelia Metzig.** Phylogenies from dynamic networks.

12.50-14.00 Lunch break

14.00-15.40 **Minisyposium: Evolutionary dynamics under selections of multiple scales**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
14.00-14.25 **Xiang-Yi Li.** Softness of selection and the evolution of sex-biased dispersal.
14.25-14.50. **Piter Bijma.** The consequences of multilevel selection and interactions among kin: a quantitative genetic approach
14.50-15.15 **Yuriy Pichugin.** Fitness correlation as a new indicative metric of transition in Darwinian individuality.
15.15-15.40 **Florence Debarre.** Fidelity of parent-offspring transmission and the evolution of social behavior in structured populations.

14.00-15.40 **Theme session 2:** Modelling evolution of cooperation

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)
14.00-14.25. **Felix Geoffroy.** Partner choice and the evolution of mutually beneficial cooperation
14.25-14.50. **Johannes Müller (in the memory of Burkhard Hense)**. Do phages help to stabilize cooperative behavior of bacteria?
14.50-15.15 **Adam Kun.** Why animals cooperate? – The insensitivity of the Snowdrift Game to network dynamics
15.15-15.40 **Rebecca Hoyle.** Modelling social influence on cooperation: the public goods game on a multiplex network

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15.40-16.10 Coffee break: Bennett Building, ground floor

16.10-17.10 **Contributed talks** (session 4)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
16.10-16.30 **Gergely Boza.** The evolution and stability of reactive investment strategies.
16.30-16.50 **Patrick Doncaster.** Mitigation cannot be nature's sole answer to climate change.
16.50-17.10 **Khatri Bhavin.** Fisher's angular transformation and quantifying evolutionary dynamics from variant-frequency time series - a case of genetic flux not drift.

16.10-17.10 **Contributed talks** (session 5)

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)
16.10-16.30 **Ricardo Martinez-Garcia.** Lack of ecological and life-history context can create the illusion of social interactions.
16.30-16.50 **Omer Edhan.** Sex with no regrets.
16.50-17.10 **Alexander Lange.** A mathematical framework for predicting lifestyles of viral pathogens.

17.20-18.20 **Honorary Lecture**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)
17.20-18.20 **Karl Sigmund.** The prisoner's dilemma: partners and rivals

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18.20-20.00 **Poster session and wine reception**: Bennett Building, ground floor

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Time for rest and relaxation

Thursday April 6th

9.00-10.40 **Plenary talks 6,7**

Venue: Bennett Building, Bennett Building, Lecture Theatre 1 (BEN LT1)

9.00-9.50 **Plenary talk 6. Alexander Gorban.** Adaptation free energy: The third generation of models of physiological adaptation

9.50-10.40 **Plenary talk 7. Philip Maini.** Modelling collective cell movement.

10.40-11.10 Coffee break: Bennett Building, ground floor

11.10-12.50 **Minisyposium: Molecular evolution and fitness landscapes. Part I**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

11.10-11.35 **Ard Louis.** Genotype-phenotype maps: when does variation dominates over selection?

11.35-12.00. **Joshua L. Payne.** Exhaustively-enumerated genotype-phenotype maps in transcriptional regulation

12.00-12.25 **Roberto Alamino.** Modelling of the evolution of antimicrobial resistance with Statistical Physics.

12.25-12.50 **Marjon de Vos.** Breaking through evolutionary constraint by variable environments.

11.10-12.50 **Minisyposium: How does spatial structure influence cancer evolution? Part I**

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)

11.10-11.35 **Benjamin Werner.** Detecting truly clonal alterations from multi-region profiling of solid tumours

11.35-12.00. **Chay Paterson.** An exactly solvable, spatial model of mutation accumulation in cancer.

12.00-12.25 **Cindy Gidoin.** The use of range expansion framework to better understand the evolutionary dynamics of cancer

12.25-12.50. **Jill A. Gallaher**. Adaptive Therapy for Heterogeneous Cancer: exploiting space and trade-offs in drug scheduling.

12.50-14.10 Lunch break

14.10-16.10 **Contributes talks** (session 6)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

14.10-14.30. **Arturo Araujo.** Mathematical and computational modeling of tumor cell/bone microenvironment interactions.

14.30-14.50 **Jean Clairambault.** Why is evolution important in cancer and what mathematics should be used to treat cancer?

14.50-15.10 **Robert Noble.** Evolutionary ecology of senescence and cancer risk: from naked mole rats to modern humans.

15.10-15.30 **Johannes Müller.** The effect of fluctuating population size and seedbanks on evolution

15.30-15.50 **Ivan Tyukin.** High-dimensional brain: a blessing or a curse?

15.50-16.10 **Valeri Makarov.** Construction of compact cognitive maps for limb manipulation in dynamic situations

14.10-16.10 **Contributed talks** (session 7)

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)

14.10-14.30 **Michael Stich**. Replicator dynamics on an RNA fitness landscape

14.30-14.50 **Ramses Djidjou Demasse.** Steady state concentration for an evolutionary epidemic system.

14.50-15.10 **Louise Lassalle.** Evolution of medication strategies in the monarch butterflies.

15.10-15.30 **Andreas Weber.** Gene networks accelerate evolution by fitness landscape learning

15.30-15.50 **Charle Mullon** A kin selection perspective on multi-dimensional adaptive dynamics in subdivided populations

15.50-16.10 **Omri Tal.** A new perspective from information theory on properties of genetic sequences

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16.10-16.40 Coffee break: Bennett Building, ground floor

16.40-18.20 **Minisyposium: 'Molecular evolution and fitness landscapes. Part II'**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

16.40-17.05 **Jacobo Aguirre.** Towards a theory of competition in evolutionary systems modelled as complex networks.

17.05-17.30 **András G. Hubai.** The coexistence of independent genes is aided by multilevel selection, but only to a limited extent.

17.30-17.55 **Saúl Ares.** Gene regulatory networks that optimize the cost of performing a function: pattern formation in nitrogen-fixing cyanobacteria.

17. 55-18.20. **Sebastian Ahnert.** The organisation of biological information determines fundamental properties of genotype-phenotype maps

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16.40-18.20 **Minisyposium: How does spatial structure influence cancer evolution? Part II**

Venue: Bennett Building, Lecture Theatre 3 (BEN LT3)

16.40-17.05 **Ewa Szczurek.** Modeling metastasis formation and its bottleneck.

17.05-17.30 **Laura Hindersin**. Amplification and suppression of selection in cancer mutations through tissue structure.

17.30-17.55. **Artem Kaznatcheev.** Effective games and operationalizing spatial structure.

17. 55-18.20. **Philip Gerlee.** Spatial structure and the dynamics of growth factor production in solid tumours

Time for rest and relaxation

Friday April 7th

9.00-9.50 **Plenary talks 8,9**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

9.00-9.50 **Plenary talk 8. Hanna Kokko.** Bet-hedging in evolutionary theory.

9.50.10-10.40 **Plenary talk. Sylvie Méléard.** The effect of competition and horizontal inheritance on invasion, fixation and evolution.

10.40-11.10 Coffee break: Bennett Building, ground floor

11.10-12.50 **Contributed talks** (session 8)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

11.10-11.30. **Magnus Lindh** Evolving phenology of root and shoot allocation

11.30-11.50. **Alexandru Hening.** Stochastic population growth in spatially heterogeneous environments: The density-dependent case.

11.50-12.10. **Max Souza.** On the stochastic evolution of finite population

12.10-12.30. **Philipp Thomas.** Single-cell histories in growing populations: relating physiological variability to population growth

12.30-12.50. **Andrew Pomiankowski.** Sexual conflict over the inheritance of mitochondria

11.10-12.50 **Contributed talks** (session 9)

Venue: Bennett Building, Lecture Theatre 8, (BEN LT8)

11.10-11.30. **Oleg Kuzenkov.** Modelling dial vertical migration of zooplankton using variational principle.

11.30-11.50. **Galina Kuzenkova.** Mathematical modelling of natural selection processes using the dynamics of measure.

11.50-12.10. **Sybille Duehring.** Modelling the host-pathogen interactions of macrophages and *Candida albicans* using game theory and dynamic optimization.

12.10-12.30. **Lourdes Juan.** Space/time evolutionary stoichiometric model for the algae-daphnia ecosystem.

12.30-12.50. **Pietro Landi.** Evolution of the good colonizer syndrome of high self-fertilization and dispersal rates in a metapopulation: model predictions reconcile with Baker's law.

12.50-14.00 Lunch break

14.00-15.00 **Contributed talks** (session 10)

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

14.00-14.20 **Christopher Turkington.** The role of localised hypermutation in resistance of *Haemophilus influenzae* to bacteriophage predation

14.20-14.40 **Aurélien Velleret.** Quasi-stationary distributions for a model of populations adapting to a changing environment

14.40-15.00 **Jacob Johansson.** Birds, mistimed reproduction and evolutionary games in a warming world.

14.00-15.00 **Contributed talks** (session 11)

Venue: Bennett Building, Lecture Theatre 8, (BEN LT8)

14.00-14.20 **Jonas Wickman.** Determining selection across heterogeneous landscapes: a perturbation-based method and its application to modelling evolution in space.

14.20-14.40 **Charlotte Ferris.** Evolution of host defence in fluctuating environments

14.40-15.00 **Paula Vasconcelos** How organismal complexity affects evolutionary diversification

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15.10-15.15 **Closing address and end of meeting.**

Venue: Bennett Building, Lecture Theatre 1 (BEN LT1)

Honorary Lecture

&

Plenary Talks

(in alphabetic order)

Honorary Lecture:

Karl Sigmund, Institute of Mathematics, University of Vienna, Austria

The Prisoner's Dilemma: Partners and Rivals

Abstract

The Prisoner's Dilemma game, the working horse for studying social traps, has recently undergone a remarkable rejuvenation. New results allow to characterize partner strategies, competitive strategies and aligning strategies. If a player uses a partner strategy, both players can fairly share the social optimum; but a co-player preferring an unfair solution will be penalized by obtaining a reduced payoff. A player using a competitive strategy never obtains less than the co-player. A player using an aligning strategy unilaterally enforces a linear relation between the two players payoffs. These properties hold for all possible strategies of the co-player and thus cover a vast range of behavior. The new results will be embedded in an overview covering a wide field of theoretical and experimental results.

Alexander Gorban, Department of Mathematics, University of Leicester, UK

Adaptation free energy: The third generation of models of physiological adaptation

(joint work with Tatiana A. Tyukina[1])

Abstract

The concept of biological adaptation was closely connected to some mathematical and engineering ideas from the very beginning. Cannon's homeostasis is, in its essence, automatic stabilisation of the body: "whenever conditions are such as to affect the organism harmfully, factors appear within the organism itself that protect or restore its disturbed balance" [1]. Selye discovered the phases and limits of adaptation to harmful conditions [2]. His model of General Adaptation Syndrome (GAS) states that an event that threatens an organism's well-being leads to a three-stage bodily response: Alarm – Resistance – Exhaustion. He concluded from his experiments that the regulatory mechanisms need some "adaptation resource" (adaptability) and demonstrated that the adaptability decreases in the course of adaptation [3]. This adaptability is a hypothetical extensive variable. Selye proposed for this resource the term "adaptation energy". He distinguished the superficial adaptation energy (easily accessible) and deep energy (reserve [4]). Selye did not use mathematical formalism but formalisation of his phenomenological theory is straightforward and lead to verifiable predictions [4,5].

Careful analysis of Selye's experiment demonstrates a fundamental difference between the resource (adaptation energy) which is exhausting in GAS and adaptability studied in his work [3] about experimental evidence supporting the conception of "adaptation energy". In GAS, the adaptation resource is spending for continuous neutralisation of a harmful factor which affects the organism. In [3] it was demonstrated that the adaptability is spending for training: a rat was trained for resistance to one factor but lost the ability to train for resistance to another factor. First type of resource and reserve spending was analysed by us in [4,5]. The second type is the change of the resistivity landscape. The domain of values of the harmful factors, where the organism can survive, can be changed but cannot be extended to infinity. The volume of this domain can be extended but not for free, its extension requires adaptation energy. Logarithm of this volume is an entropy, and we can call it the "*adaptation entropy*".

Thus, analysis of Selye's experiments and physiological hypotheses lead us to the notion of adaptation entropy and, in combination with adaptation energy, to the "*adaptation free energy*".
In the talk we present the new family of dynamical models of physiological adaptation based on the notion of the adaptation free energy. This is a new class of the "top-down" thermodynamic models for physiology.

[1]Department of Mathematics, University of Leicester, UK

References

[1] Cannon W.B. The wisdom of the body. 1932. NY Norton. 1932.

[2] Selye H. A syndrome produced by diverse nocuous agents. Nature 138(3479) (1936), 32.

[3] Selye H. Experimental evidence supporting the conception of "adaptation energy". Am. J. Physiol. 1231(938), 758-765.

[4] Gorban A.N., Smirnova E.V., Tyukina T.A., Correlations, risk and crisis: From physiology to finance. Physica A 389(16) (2010), 193-217.

[5] Gorban A.N., Tyukina T.A., Smirnova E.V., Pokidysheva L.I., Evolution of adaptation mechanisms: adaptation energy, stress, and oscillating death. J. Theor. Biol. 405 (2016) 127- 139.

Robert D. Holt, Department of Biology, University of Florida, USA

Thoughts on the interplay of3 demographic stochasticity, fitness, and the niche concept

Abstract

G.E. Hutchinson's niche concept is an abstract mapping of one aspect of population dynamics (in particular a measure of absolute fitness) onto an environmental space. For continuously growing populations, the metric is traditionally assumed to be the intrinsic growth rate, r, at low densities (with units 1/time). But at small absolute numbers, extinctions can occur for populations with a positive intrinsic rate of growth because of demographic stochasticity. Another familiar fitness metric, R0 (the expected number of offspring produced per individual over their lifetime), arises when considering extinction risk. This alternative metric can influence the shapes of niche response surfaces. This talk will broadly aim at assaying the relevance of demographic stochasticity for concepts of both absolute and relative fitness in small populations, such as at range margins and in sink habitats, with an eye towards refinement of ecological niche concepts. These different fitness metrics also have implications for how we think about species' evolution, particularly in rapidly changing environments, and also arise in models of macroevolutionary dynamics.

Eva Kisdi, Department of Mathematics and Statistics, University of Helsinki, Finland

Dispersal polymorphisms in stable habitats

Abstract

Kin competition is well known to favour dispersal. In temporally stable habitats, kin competition is the most important factor thought to explain why dispersal evolves despite its associated costs. May dispersal evolution also lead to an evolutionarily stable polymorphism? This question has long ago been answered in the affirmative when dispersal is favoured by temporal fluctuations of the environment, but received, until recently, surprisingly little attention in temporally stable habitats where kin competition is the sole factor promoting dispersal. In this talk, I review several recent models that predict the evolution and coexistence of diverse dispersal strategies under the influence of kin competition, spatial heterogeneity such as variable patch size or variable patch connectivity, and life history trade-offs. These models generalize kin competition models of dispersal in simple and biologically relevant directions, explain dispersal polymorphisms economically, and are amenable to analysis using the methods of adaptive dynamics.

Hanna Kokko, Department of Evolutionary Biology and Environmental Studies, University of Zurich, Switzerland

Bet-hedging in evolutionary theory

(joint work with Xiang-Yi Li[1], and Nina Gerber[1])

Abstract

Bet-hedging in biology has been called a "seductive" explanation, meaning that it is often applied whenever organisms appear to benefit by diversifying their portfolio of actions or traits. The real definition of bet-hedging is more stringent: a bet-hedger enjoys an evolutionary long-term advantage because its traits predict that variance in fitness is reduced (a benefit) while arithmetic fitness falls below that of a baseline (a cost) - where the baseline is a non-bet-hedger. The baseline non-bet-hedger may or may not exist in reality; "bet-hedging occurs" is a statement that can only be made in a comparative sense (i.e. relative to another strategy). We discuss a few examples: (1) sexual reproduction can be thought of as bet-hedging, but this may apply more strongly against certain types of asexual reproduction than others. In simple models at least, it is difficult to explain sex purely based on bet-hedging benefits, simply because the expected cost of sex is too large. (2) Dispersal, which is costly (risky) but diversifies the fates of offspring, can be thought of as a bet-hedging strategy. Bet-hedging theory predicts that reducing variance through one route (e.g. dispersal in space, or dispersal 'in time' i.e. dormancy) should reduce selection to reduce it through another alternative (here sex can be thought to be 'dispersal in identity' as an allele ends up in new genetic backgrounds). Against this expectation it is curious to note a pattern in nature: facultatively sexual organisms often undergo sexual life cycles in conditions that also promote dispersal in time or space. I will ask whether we really can explain such positive correlations based on theory.

[1]University of Zurich, Switzerland

Philip Maini, Mathematical Institute, University of Oxford, UK

Modelling collective cell movement

Abstract

Collective cell movement is a phenomenon that occurs in normal development, wound healing and disease (such as cancer). In many cases, the ability of cell populations to move large distances coherently arises due to a structure of "leaders" and "followers" within the population. I will present two such examples: (i) angiogenesis -- this the process by which new blood vessels form in response to injury, or in response to a cancerous tumour's demand for more nutrient. We systematically derive a discrete cell-based model for the "snail-trail" phenomenon of blood vessel growth and show that this leads to a novel partial differential equation model. We compare and contrast this model with those in the literature. (ii) neural crest cell invasion – this is the process by which cells move to target locations within the embryo to begin construction of body parts. Through an interdisciplinary research project we show how a hybrid discrete-cell-based mathematical model, and an experimental model, combine to allow us to gain new insights into this phenomenon.

John McNamara, School of Mathematics, University of Bristol, UK

Towards a richer evolutionary game theory

Abstract

Evolutionary game theory predicts and explains what will evolve in populations in which there are conflicts of interest between population members. To do so biologists make mathematical models which capture essential aspects of the underlying biology. These necessarily simplify the world, but are often too simple; for example, leaving out essential features such as the variation between individuals within a population, and ignoring how individuals gain information and interact with others. Much work also assumes an idealised world in which both the ecology of an animal and its psychological mechanisms are ignored. I argue that to understand the natural world we need models of greater richness. To do so I present a series of models that illustrate that adding richness can radically change predictions.

Sylvie Méléard, Department of Applied Mathematics, Ecole Polytechnique, France

The effect of competition and horizontal inheritance on invasion, fixation and evolution

(joint work with S. Billiard, P. Collet, R. Ferrière and C.V. Tran)

Abstract

We propose a general eco-evolutionary stochastic model of population dynamics with clonal reproduction and mutations. The individuals compete for resources and exchange genes, as in the transfer of plasmids in bacteria. We study different asymptotics of this general birth and death process depending on demographic, ecological and horizontal transfer time-scales and on the population size. Firstly, we show how the dynamics of two types can be approximated by a nontrivial dynamical system when the population is large. The approximation is used to analyse the conditions for the invasion of a mutation under selection or its maintenance in a polymorphic state with the resident type. We also provide its probability of fixation and time to fixation. Next we consider a continuum of types. Under large population and rare mutations assumptions, we show that at the long mutation time scale, the population process is approximated by a jump process which describes the successive invasions of successful mutants. We explain how horizontal gene transfer can drastically affect the evolutionary outcomes and lead to evolutionary suicide.

Hans Metz, Institute of Biology Leiden, Leiden University, the Netherlands

Evolutionary branching in the multivariate case

Abstract

Over the last two decades evolutionary branching has emerged as a possible mathematical paradigm for explaining the origination of phenotypic diversity. Although branching is well understood for one-dimensional trait spaces, a similarly detailed understanding for higher dimensional trait spaces was still lacking. However, Stefan Geritz, Claus Rueffler and I recently arrived at some, surprising, first insights. In particular, we have shown that, as long as the evolutionary trajectory stays within the reign of the local quadratic approximation of the fitness function, any initial small scale polymorphism around an attracting invadable evolutionarily singular strategy (ess) will evolve towards a dimorphism. That is, if the trajectory does not pass the boundary of the domain of dimorphic coexistence and falls back to monomorphism (after which it moves again towards the singular strategy and from there on to a small scale polymorphism, etc.). The latter can only happen in dimensions 3 or higher. To reach these results we analyzed in some detail the behaviour of the solutions of the coupled Lande-equations purportedly satisfied by the phenotypic clusters of a quasi-n-morphism, and give a precise characterisation of the local geometry of the set D in trait space squared harbouring protected dimorphisms. Another matter is that in higher dimensional trait spaces an attracting invadable ess needs not connect to D. However, for the practically important subset of strongly attracting ess-es (i.e., ess-es that robustly locally attract the (quasi-)monomorphic evolutionary dynamics for all possible non-degenerate mutational (or genetic) covariance matrices) invadability implies that the ess connects to D, however without the guarantee that the polymorphic evolutionary trajectory will not revert to monomorphism still within the reign of the local quadratic approximation for the invasion fitnesses.

Kalle Parvinen[1,2]

The effect of spatial heterogeneity on evolution in spatial models

(Joint work with Hisashi Ohtsuki[1] and Joe Yuichiro Wakano[1])

Abstract

The Wright's island model consists of a large number of ecologically identical patches, in which a fixed number of adults produce offspring and die. Part of the offspring disperse. Those individuals surviving dispersal arrive randomly in any other patch. After dispersal, the n individuals to become adults are randomly chosen among the offspring present in each patch. In this model, classical results about the evolution of dispersal have been obtained [2]. We investigate an extension including spatial heterogeneity, so that patches can be of different quality. By investigating metapopulation fitness, we present analytical expressions for the selection gradient and conditions for convergence stability and evolutionary stability.

In the homogeneous model, evolutionary branching of dispersal is not possible [1]. We show that spatial heterogeneity selects against dispersal, but can promote evolutionary branching.

For a fecundity-affecting trait, Taylor's cancellation result holds in the homogeneous model: Not only singular strategies but also their convergence stability is identical to that in the corresponding well-mixed model. Homogeneous spatial structure also often inhibits evolutionary branching: Evolutionary branching never occurs when the dispersal rate is close to zero, and for a wide class of fecundity functions (including those determined by any pairwise game), evolutionary branching is impossible for any dispersal rate if branching does not occur in the corresponding well-mixed model [3]. In contrast, in a spatially heterogeneous model, evolutionary branching can happen for low dispersal rates, even when it does not happen when everybody disperses.

[1]Department of Evolutionary Studies of Biosystems, School of Advanced Sciences, SOKENDAI, Hayama, Kanagawa, Japan

[2]Department of Mathematics and Statistics, University of Turku, Finland

References

[1] E. Ajar. Analysis of disruptive selection in subdivided populations. BMC Evolutionary Biology, 3:22:1–12, 2003.

[2] W. D. Hamilton and R. M. May. Dispersal in stable habitats. Nature, 269:578–581, 1977.

[3] Kalle Parvinen, Hisashi Ohtsuki, and JoeWakano. The effect of fecundity derivatives on the condition of evolutionary branching in spatial models. J. Theor. Biol, 416:129, 143, 2017.

Contributed talks, minisymposia and invited talks

(in alphabetic order)

Matthew Adamson, Institute of Environmental Systems Research, School of Mathematics/Computer Science, University of Osnabruck, Germany

Identifying the sources of structural sensitivity in ecological models using partially specified models

(joint work with Andrew Morozov[1])

Abstract

Mathematical models in ecology and evolution are highly simplified representations of a complex underlying reality. For this reason, there is always a high degree of uncertainty with regards to the model specification, not just in terms of parameters, but also in the form taken by the model equations themselves. This uncertainty becomes critical for models in which the use of two different functions fitting the same dataset can yield substantially different model predictions - a property known as structural sensitivity. In this case, even if the model is purely deterministic, the uncertainty in the model functions carries through into uncertainty in our model predictions. The question of which model functions the model is most structurally sensitive to is vital, because it tells us which biological processes we need to understand better in order to improve the reliability of the model. Previously, we have introduced a method to detect and quantify the structural sensitivity of a model by representing it as a partially specified model: an ODE model in which unknown functions are represented not by a specific functional form, but by an entire data range and constraints of biological realism. In this talk, we shall show how this framework can be extended to compare the structural sensitivity of an ecological model to its various uncertain functions, in order to determine which of these functions acts as the main source of structural sensitivity in the system.

[1]Department of Mathematics, University of Leicester, UK

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Towards a theory of competition in evolutionary systems modeled as complex networks

Abstract

Competitive interactions represent one of the driving forces behind evolution and natural selection in biological, sociological and technological systems. For example, animals in an ecosystem may vie for food or mates; sensory stimuli may compete for limited neural resources in order to enter the focus of attention; web pages compete for absorbing the largest possible number of internauts... In summary, many of the complex systems that evolve in nature are based on competing in environments for limited resources, and a wide variety of them are modeled as networks. In addition, the environments in which these competitions take place are not always static. The biosphere is changing and faces continuous and often severe challenges. These affect systems that evolve at all levels, from the world of genomes to whole cities.

From this perspective, an open question of great interest is the understanding of the mechanisms and factors that induce competitors to succeed or fail in adapting to these time-depending conditions. In this talk, I will address:

(i) The possibility of establishing a general framework for analyzing processes in which different agents organized as networks compete for resources, either in constant or changing environments.

(ii) The actual usefulness of this theory in biological and biotechnological problems of real interest for society.

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Sebastian Ahnert[1,2]

The organisation of biological information determines fundamental properties of genotype-phenotype maps

Abstract

Biological information is stored in DNA, RNA and protein sequences, which can be understood as genotypes that are translated into phenotypes. The properties of genotype–phenotype (GP) maps have been studied in great detail for RNA secondary structure. These include a highly biased distribution of genotypes per phenotype, negative correlation of genotypic robustness and evolvability, positive correlation of phenotypic robustness and evolvability, shape-space covering, and a roughly logarithmic scaling of phenotypic robustness with phenotypic frequency. More recently similar properties have been discovered in other GP maps, suggesting that they may be fundamental to biological GP maps, in general, rather than specific to the RNA secondary structure map. We propose that the above properties arise from the fundamental organization of biological information into 'coding' and 'noncoding' sequences, in the broadest possible sense. To test our hypothesis we consider a highly simplified GP map that has genotypes with 'coding' and 'non-coding' parts. We term this the Fibonacci GP map, as it is equivalent to the Fibonacci code in information theory. Despite its simplicity the Fibonacci GP map exhibits all the above properties of much more complex and biologically realistic GP maps. These properties are therefore likely to be fundamental to many biological GP maps. We also discuss the implications of these genotype-phenotype maps to biological self-assembly, quantitative measurements of structural complexity, and protein quaternary structure.

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Roberto C. Alamino, Mathematics Department, Aston University, Birmingham, UK

Modelling of the evolution of antimicrobial resistance with statistical physics

Abstract

This work introduces a statistical physics lattice model for the study of **anti-microbial resistance** (AMR) emergence in a culture of cells in a Petri dish. Cells are modelled by **non-linear perceptrons**, which are very basic processing units capable of learning, interacting with local concentrations of anti-microbial drugs through a **fitness landscape** generated by three parameters:

* Minimum bactericidal concentration (MBC) of anti-microbial drug.
* Sensitivity to drug variations.
* Maximum death probability.

The microscopic dynamics of the model is probabilistic and out-of-equilibrium. We show that this model can reproduce qualitatively some observed features of AMR and be used to compare different multi-drug treatment protocols.

Arturo Araujo, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA

Mathematical and Computational Modeling of Tumor Cell/Bone Microenvironment Interactions

(joint work with Leah M. Cook[1], Conor Lynch[1] and David Basanta[1])

Abstract

Bone metastasis is common in prostate cancer progression and the ability to rapidly assess the efficacy of therapeutic strategies on this incurable disease is an urgent need. In bone, prostate cancer cells derive factors necessary for progression by manipulating bone forming osteoblasts and bone resorbing osteoclasts, resulting in areas of excessive osteogenesis and osteolysis, respectively. New targeted therapies present a dilemma since they can have differential effects on the various cell types in the tumorbone microenvironment. Pre-clinical in vivo models provide insights yet are limited in their capacity to interrogate simultaneous multicellular interactions occurring in the cancer-bone microenvironment. To tackle this, we propose integrating computational modeling with biological experimentation as a powerful, efficient and ethically justifiable tool for exploring key aspects of tumor evolution under different therapies.

For this, we developed a Hybrid-Discrete Cellular Automata model where the interactions between key cell types and their role on the evolutionary dynamics of the tumor microenvironment can be studied. The dialogue between the mathematical model and the biological experiments have expanded our understanding of the process of prostate to bone metastasis. Our model tackles evolutionary aspects of the disease that in vitro or in vivo studies cannot. The model emphasizes the roles that heterogeneity and selection can have on the temporal changes of the disease and gives insights on key experiments to carry out and suggest new ways of tackling the disease. Our in silico results predict that there therapies can impact prostate cancer cell viability directly but also by restricting nutrient availability and interfering with the differentiation and maturation of recruited microenvironmental cells. These results were validated in vivo with a model-enlightened minimization of the number of experiments needed, thus saving money, resources, time and mice. We demonstrate how this hybrid model can be used to predict the evolution of heterogeneous bone metastases in response to therapeutic targets.

Furthermore, we have adapted the model to accommodate for the inclusion of clinical data. With this we seek to find a mathematical optimization of standard of care therapy to delay the onset of resistance in advanced Prostate Cancer. This offers the tantalizing possibility of transforming this research into a new patient-specific assessment tool to help clinicians better determine intra-tumor heterogeneity, the evolution and selection of resistance and the complex interplay that the current standard of care could have on such tumors. This has allowed us to explore evolutionary-enlightened therapies that offer a readily available and viable alternative to conventional treatments. This advantage that mathematics can bring to the clinic can be key to extending the patient's quality of life, especially important when dealing with an incurable disease. Collectively, our results underscore the power of integrated biological and computational frameworks for defining temporal and evolutionary changes in the cancer-bone microenvironment in the context of applied therapeutics.

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Saúl Ares, GISC and Departamento de Matemáticas, Universidad Carlos III de Madrid, Spain

Gene regulatory networks that optimize the cost of performing a function: pattern formation in nitrogen-fixing cyanobacteria

(joint work with Katherine Gonzales-Moreno, Daniel Bravo-Candel, Javier Muñoz-García[1])

Abstract

Cyanobacteria produce an important fraction of oxygen on Earth and, together with archaea, fix atmospheric nitrogen used by all other organisms. Some types live in colonies with specialized cells that perform different functions. In particular, the genus *Anabaena* forms filaments in which some cells differentiate into a nitrogen fixing form called heterocyst, forming patterns to effectively provide nitrogen for the colony. We have recently presented a theory combining genetic, metabolic, and morphological aspects to understand this prokaryotic example of multicellularity. Our results quantitatively reproduced the appearance and dynamics of this pattern and we used them to learn how different aspects, like fixed-nitrogen diffusion, cell division, or stochasticity, affect it [1].

Here we present a bifurcation analysis of the different parameters of a simplified version of our theory. This simple version only models the appearance of nitrogen fixing cells, but not its maintenance after the initial pattern is formed. We have restricted our analysis to filaments of only two cells. HetR is a gene that acts as the master regulator of differentiation, activating its own expression and that of PatS. PatS is a protein whose product can diffuse along the filament of cells and inhibit differentiation. This inhibition works forming a complex with the activator that cannot bind to the regulatory regions of the DNA.

The pattern forming region, characterized by coexisting high and low concentration solutions, appears and disappears through subcritical pitchfork bifurcations where it coexists with homogeneous solutions, represented by intermediate stable concentrations. Strikingly, for all the parameters of the model, wild type values determined previously [1] are very close to a bifurcation point, always to the one with lower concentration of activator and inhibitor. This finding suggests that evolution may have tuned this pattern forming process to occur efficiently at a working point where the concentrations of proteins needed to attain a heterogeneous state are close to the minimal possible. This might be an example of a more general biological principle of *cost minimization*.

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Thomas Aubier, Centre for Evolutionary and Functional Ecology, CNRS & Université de Montpellier, Montpellier, France

Speciation along ecological gradients and the costs of choosiness

(joint work with Mathieu Joron[1])

Abstract

Recently, research on speciation has shifted from a focus on the geographical context of differentiation to a focus on the role of natural and sexual selection in reproductive isolation. Yet, the spatial context may be of prime importance in the feasibility of speciation, and indeed, species often replace each other spatially along environmental gradients. In fact, we still lack good theoretical predictions to understand the role of the spatial dimension of ecological changes in parapatric speciation. In particular, the effects of the costs of choosiness have been ignored so far.

Ecological speciation may fail if choosy females experience fitness costs. Notably, choosy females may remain unmated if they can assess only few mates in their lifetime. In parapatry, this effect may be especially strong because the relative proportion of the two taxa change across the ecological gradient, and females with uncommon phenotypes indeed risk remaining unmated if they are looking for a similar mate. Unfortunately, many theoretical models have used normalized mating probabilities so that all females eventually find a mate, which effectively ignores the effect of the costs of choosiness on the evolution of assortative mating.

Here, using a spatially-explicit individual-based model, we relax this hypothesis and allow females to fail finding a mate if they are too choosy. We model parapatric populations where disruptive natural selection leads to divergence in an ecological trait, and where assortative mating can evolve, limiting gene flow between incipient species. We show that the size of the transition zone (or hybrid zone) and the number of males each female may encounter have a major influence on the probability of speciation. Intriguingly, we show that speciation along ecological gradients is hindered not only when females may encounter very few males, but also when they may encounter many males. Moreover, while previous models have shown that speciation should be more likely along ecological gradients with intermediate steepness, we show that it is not always the case. We found that this depended on the ecology of mate finding: steep ecological gradients inhibit speciation if females may assess many males in their lifetime, but they facilitate speciation if females may assess only few males. Our predictions are explained by the direction of selection on the strength of mate choice of primarily affecting (maladapted) migrants dispersing through space.

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Density-dependent selection on mate search and evolution of Allee effects

(joint work with Andrew M. Kramer[1], Veronika Bernhauerová[2], John M. Drake [1])

Abstract

Sexually reproducing organisms require males and females to find each other. Increased difficulty of females finding mates as male density declines is the most frequently reported mechanism of Allee effects in animals. Evolving more effective mate search may alleviate Allee effects, but may depend on density regimes a population experiences. We develop an individual-based, eco-genetic model to study how mating systems and fitness trade-offs interact with changes in population density to drive evolution of the rate at which males or females search for mates. Since finite mate search rate triggers Allee effects in our model, we explore how these Allee effects respond to such evolution. We find density-dependent selection in most of scenarios, leading to search rates that result in lower Allee thresholds in populations kept at lower densities. This mainly occurs when fecundity costs are imposed on mate search, and provides an explanation for why Allee effects are often observed in anthropogenically rare species. Optimizing selection, with the attained trait value minimizing the Allee threshold independent of population density, depended on the trade-off between search and survival, combined with monogamy when females were searching. Other scenarios led to runaway selection on the mate search rate, including evolutionary suicide. Trade-offs involved in mate search may thus be crucial to determining how density influences the evolution of Allee effects.

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Evolution of mate-finding Allee effect in prey

(Joint work with Ludek Berec[1], and Barbara Boldin[2])

Abstract

We study, by means of adaptive dynamics, the evolution of the mate-finding Allee effect in a sex-structured prey population subject to predation by either generalist (without numerical response) or specialist predators (with numerical response). We consider the rate at which males search for females as evolving trait and assume this trait to affect the rate at which female prey are fertilized (a higher rate of search by male means greater chance for successful mating), and the rate at which male prey encounter predators and get consumed by them as they search for females (a higher rate of search by males means a greater risk for males to fall victims to predators). We show how various ecological conditions (handling time of the predators, refractory period of females after successful mating, etc.) affect evolution of the male search rate, and thus contribute to understanding how mate-finding Allee effects can be promoted or diminished in the prey population.

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[2] Department of Mathematics, Natural sciences and Information technologies University of Primorska, Slovenia

Alex Best, School of Mathematics and Statistics, University of Sheffield, UK

The impact of community interactions on host-parasite evolution

Abstract

There are key inter-dependencies between the co-evolution of hosts and parasites and community structure. The ecological community in which the host-parasite system is embedded drives selection, and evolution in turn feeds back to the ecological dynamics to shape community structure. However, for the most part both experimental and theoretical studies have studied host-parasite co-evolution in isolation. Only recently have researchers begun to directly study these complex eco-evolutionary feedbacks that are essential for us to predict and manage real-world infectious disease systems. In this talk I will give a general overview of recent theoretical and experimental work investigating how host and parasite evolution are impacted by community interactions, focussing on predation. I will show how some classic evolutionary predictions no longer hold when community interactions are present, and the importance of the ecological feedbacks generated to the outcomes.

Piter Bijma, Animal Breeding and Genomics Centre, Wageningen University and Research, The Netherlands

The consequences of multilevel selection and interactions among kin: a quantitative genetic approach

Abstract

Quantitative genetics (QG) is an empirically powerful approach for modelling and understanding response to selection, both in nature and agriculture. The traditional QG-model, however, ignores the social organisation of life. With social interactions, trait values and fitness may depend on genes in other individuals. Moreover, some traits cannot be attributed to single individuals, but are properties of groups or societies, such as the number of prey caught by a hunting pack. Social organisation may greatly affect heritable variation and response to selection, both in magnitude and direction. Moreover, response to selection in social traits critically depends on the level of selection and on relatedness between interacting individuals. Here I will present a recently developed quantitative genetic framework that integrates indirect genetic effects (IGE), multilevel selection and kin selection, both for fitness and trait values. Results show that, in the absence of IGE, response in trait values is affected only when multilevel selection acts on kin groups. With IGE, however, multilevel selection or relatedness alone may reverse the direction of response to selection. Remarkably, expressions for response are symmetric in relatedness and the degree of between-group selection. Both trait models and fitness models indicate that interactions with kin lead to utilization of heritable variation for increased fitness, suggesting that interaction with kin is an adaptive trait. The quantitative genetic framework also provides a definition of total heritable variation in a trait (or fitness), which reflects the potential of a population to respond to selection. An application to fitness shows that Fisher's fundamental theorem of natural selection and Hamilton's maximization of inclusive fitness are one and the same theorem about the direction of natural selection. Finally I will illustrate how IGE can be estimated using so-called animal models.

Barbara Boldin, Department of Mathematics, Natural sciences and Information technologies, University of Primorska, Slovenia

Evolutionary suicide of pathogens

(joint work with Eva Kisdi[1])

Abstract

Evolutionary suicide is a phenomenon in which adaptive evolution drives a viable population to extinction. Recently, Gyllenberg and Parvinen [2] showed that, within a certain class of deterministic models, a bifurcation leading to a discontinuous transition to extinction is a necessary condition for evolutionary suicide to occur. In this talk, we discuss evolutionary suicide of obligate pathogens in view of infection incidence and show that, for pathogens with frequency-dependent transmission, evolutionary suicide can occur through a gradual transition to extinction. We furthermore demonstrate that evolutionary suicide can occur by pathogens evolving higher or lower virulence. The talk is based on joint work with Éva Kisdi [1].

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Richard J. Bingham, Departments of Mathematics and Biology & York Centre for Complex Systems Analysis, University of York, United Kingdom

RNA virus evolution via a quasi-species theory-based model reveals a novel drug target

(joint work with Eric C. Dykeman[1], Peter G. Stockley[2], and Reidun Twarock[1])

Abstract

One of the most pressing problems for viral evolution is the rapid development of resistance to antiviral therapies. This is widely thought to predominantly result from the diversity of the 'cloud' of closely related mutant genomes that coexisting within a viral population. Termed a quasispecies, this model revolutionised the understanding of viruses and much subsequent theoretical work has been built upon these foundations. Many of these models, however lack a underpining in the biological detail and often use simplified fitness landscapes in order to remain analytically tractable. Here we present an assembly model based upon a dodecahedral model virus which undergoes packaging signal mediated assembly, whereby the viral RNA and coat protein co-assemble through molecular contacts of varying strength, a mechanism observed in many ssRNA viruses. The efficiency with which the viral genome can assemble into complete virions is considered as a measure of viral fitness, as this will have a direct effect upon the number of daughter virions produced. Repeated simulations of simplified genomes comprised of a chain of 'packinging signals' of differing strengths yield a complete, 12-dimensional fitness landscape. This landscape is then used in stochastic simulations to model the evolution of a progressing viral infection, considering both chronic and acute infections. We study the response of the infecting viral populations to different drug interventions, both conventional therapies and a new approach targeting the viral RNA itself to interrupt the RNA-protein contacts required for assembly. We find that in both infection types, targeting the viral RNA is the most effective treatment, due to the way it bias the inevitable evolution of therapy resistant strains. This suggests a new paradigm for the development of anti-viral drugs.

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Gergely Boza[1, 2]

The evolution and stability of reactive investment strategies.

Abstract

Cooperative investment behaviour has been studied widely both within and between species, traditionally focusing on discrete strategies with rigid investment levels. A growing amount of empirical evidence suggests, however, that numerous cooperative and mutualistic investments are conditional and context dependent. Building on these observations, our aim is to understand factors promoting the emergence and stability of cooperative behaviour, regarded as continuous investments performed by individuals with reactive strategies in a game-theoretical framework. For this we analyse the evolutionary dynamics for various interaction norms and for different interaction types. We demonstrate that reactivity, which defines the plasticity of investments in response to the partners' investment behaviour, can stabilize cooperation and offer a safeguard against exploitation. However, low reactivity can destabilize investment levels, as well as the unfavourable change of environmental conditions. We demonstrate that several factors, such as strategy diversity or spatial population structure, may offer efficient measures counteracting the decrease of investment levels. Our investigations shed light on yet unexplored aspects of diversity and dynamical complexity of cooperative interactions.

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[2]Department of Plant Systematics, Ecology, and Theoretical Biology, Eötvös University, Budapest Hungary.

Mark Broom, Department of Mathematics, City University of London, United Kingdom

Game theoretical modelling of a dynamically evolving network

(joint work with Chris Cannings[1])

Abstract

Animal (and human) populations contain a finite number of individuals with social and geographical relationships which evolve over time, at least in part dependent upon the actions of members of the population. These actions are often not random, but chosen strategically. Almost all previous work ignores at least one of these factors. In this talk we introduce a game-theoretical model of a population where the individuals have an optimal level of social engagement, and form or break social relationships strategically to obtain the correct level. This builds on previous work where individuals tried to optimise their number of connections by forming or breaking random links; the difference being that here we introduce a truly game-theoretic version where they can choose which specific links to form or break. This is more realistic and makes a significant difference to the model, one consequence of which is that the analysis is much more complicated. We discuss some general results and then focus on a particular example.

[1]School of Mathematics and Statistics, University of Sheffield, United Kingdom

Jean Clairambault, MAMBA team, INRIA Paris Research Centre & Jacques-Louis Lions Lab, UPMC, Paris

Why is evolution important in cancer and what mathematics should be used to treat cancer?

Abstract

In this talk, I will sum up works and results obtained in the past four years in our team, showing how the clinical question of drug resistance in cancer, our initial motivation to study continuous models of adaptive dynamics, leads naturally and more generally to consider the cancer disease itself from an evolutionary biology viewpoint, without which even apparently well-targeted therapies most often eventually fail. Among the challenging questions to mathematicians who tackle the task of understanding this disease and optimising its treatment are the representation of phenotypic heterogeneity of cancer cell populations and of their plasticity in response to anticancer drug insults. I will show how these representations can partly be taken into account in using optimal control methods, with the aim to implement them in the therapeutics of cancer.

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Tamas David-Barrett, Trinity College, University of Oxford, United Kingdom

Fertility, kinship and the evolution of mass ideologies

(joint work with Robin I.M. Dunbar[1])

Abstract

Traditional human societies are organised around kinship, and use kinship networks to generate large scale community projects. This is made possible by a combination of linguistic kin recognition, a uniquely human trait, which is mediated by the reliability of kin as collaborators. When effective fertility falls, this results in two simultaneous effects on social networks: there are fewer kin that can be relied on, and the limiting effect of the local kin-clustering becomes stronger. To capture this phenomenon, we used a model of kinship lineages to build populations with a range of fertility levels combined with a behavioural synchrony model to measure the efficiency of collective action generated on kin networks within populations. Our findings suggest that, whenever effective cooperation depends on kinship, falling fertility creates a crisis when it results in too few kin to join the community project. We conclude that, when societies transition to small effective kin networks, due to falling fertility, increased relative distance to kin due to urbanisation or high mortality due to war or epidemics, they will be able to remain socially cohesive only if they replace disappearing kin networks with quasi-kin alternatives based on membership of guilds or clubs.

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Florence Débarre, Centre Interdisciplinaire de Recherche en Biologie (CIRB), Collège de France, France

Fidelity of parent-offspring transmission and the evolution of social behavior in structured populations

Abstract

The theoretical investigation of how spatial structure affects the evolution of social behavior has mostly been done under the assumption that parent-offspring strategy transmission is perfect, i.e., for genetically transmitted traits, that mutation is very weak or absent. In this talk, we investigate the evolution of social behavior in structured populations under arbitrary mutation probabilities. We consider spatially structured populations of fixed size N, in which two types of individuals, A and B, corresponding to two types of social behavior, are competing. Under the assumption of small phenotypic differences (weak selection), we provide a formula for the expected frequency of type A individuals in the population, and deduce conditions for the long-term success of one strategy against another. We then illustrate this result with three common life-cycles (Wright-Fisher, Moran Birth-Death and Moran Death-Birth), and specific population structures. Qualitatively, we find that some life-cycles (Moran Birth-Death, Wright-Fisher -- when social interactions affect fecundities) prevent the evolution of altruistic behavior, confirming previous results obtained with perfect strategy transmission. Imperfect strategy transmission also alters the balance between the benefits and costs of staying next to one's kin, leading to surprising results in subdivided populations, in that higher emigration probabilities can be favourable to the evolution of altruistic strategies.

Marjon G. J. de Vos**,** Laboratory of Genetics, Wageningen University, The Netherlands

Breaking through evolutionary constraint by variable environments

(joint work with Alexandre Dawid[1], Vanda Sunderlikova[2] and Sander J. Tans[2])

Abstract

Evolution is constrained when mutational trajectories are trapped at suboptimal fitness peaks on the adaptive landscape, thereby causing evolutionary stasis. We show that these constraints can be overcome in an adaptive manner in variable environments. Cross-environmental tradeoffs, typically associated with evolutionary limitations, are an essential enabling component of this evolutionary mechanism. Our results underscore the importance of characterizing environmental dependencies of evolution and provide the clearest indication so far that environmental variability can accelerate evolution. Given that environmental variations and tradeoffs are ubiquitous, this evolutionary mechanism may be relevant to a wide range of genetically constrained phenotypes and major evolutionary transitions.

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Charlotte de Vries, University of Amsterdam, The Netherlands

Combining stage-classified demography and population genetics to study eco-evolutionary dynamics.

(joint work with Hal Caswell[1])

Abstract

The study of eco-evolutionary dynamics is based on the idea that ecological and evolutionary processes may operate on the same, or very similar, time scales. If they operate on similar time scales, feedbacks between ecological and evolutionary processes may have important consequences for both sides of the eco-evolutionary dividing line. We present a new framework which links simple Mendelian population genetics with matrix models for stage-classified demography to create a truly eco-evolutionary model. Any kind of ecological process can be included in the demographic component of the model: age- or stage-classified life histories of arbitrary complexity, linear or non-linear (density-dependent) dynamics, constant or time-varying (periodic or stochastic) environments. In the model, genotypes may differ in fertility, viability, or any other demographic process. The presence of fertility selection threatens the standard usage of genotype-specific population growth rates as measures of fitness. Mean growth rate does not always increase and heterozygote advantage in growth is not a sufficient condition for obtaining a protected polymorphism. We present conditions for obtaining a protected polymorphism in structured and unstructured population models.

[1]University of Amsterdam, The Netherlands

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Steady state concentration for an evolutionary epidemic system

(Joint work with Arnaud Ducrot[2], Frederic Fabre[1])

Abstract

In this talk, we construct a model to describe the evolutionary epidemiology of spore producing asexual plant pathogens in a homogeneous host population. The host population is subdivided into compartments (Susceptible or healthy host tissue (S), Infected tissue (i) and Airborne spores (A)). By considering the evolution in the space of the pathogen phenotypic values, we derive an integro-differential equation with nonlocal mutation terms. Next assuming that the mutation kernel depends on a small parameter $\epsilon > 0$ (the variance of the dispersion into the space of the pathogen phenotypic values), we investigate the concentration properties of the endemic steady state in the space of phenotypic values. Generally, by assuming that there is only one pathogen strain x^* which maximizes the *fitness function* (or the *basic reproduction number*) of the pathogen population, it's well known that x^* will be the strongest (or dominant) strain. However, the situation becomes more complicated to characterise the strongest strain when at least two pathogen strains maximize the fitness function. The results obtained in this note allow us to do so. Roughly speaking, in the context of this work, several Evolutionary Attractors (as defined in classical adaptive dynamics) may exist. However, in rather general situations, our results show that only one Evolutionary Attractor persists (called Globally Stable Evolutionary Attractor) when the populations are at equilibrium and when " is small enough. Our analysis strongly relies on a refined description of the spectral properties of some integral operator with a highly concentrated kernel.

Another interesting result is the *metastable behavior* of the evolutive model. More precisely, assume that there are two Evolutionary Attractors x_1 and x_2 such that x_1 is the Globally Stable Evolutionary Attractor (GSEA for short). Before the system concentrates around the GSEA x_1, it persists on the Evolutionary Attractor x_2 for a relatively long time interval, whose size depends on the parameter ϵ and diverges to $+\infty$ as $\epsilon \to 0$.

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Mitigation cannot be nature's sole answer to climate change

(Joint work with Tim Sluckin[2])

Abstract

Can wildlife mitigate global warming simply by tracking the climate envelope as it shifts poleward? Adverse climate change carries absolute fitness costs for individuals, which demand adaptation to the new conditions or else mitigation to avoid them. For example, a population might respond to climate warming by evolving adaptations or adopting behaviours that improve resilience to thermal stress or that increase the breadth of diet or of other niche axes. Alternatively, a poleward extension or shift to the geographic range of the population that keeps pace with climate warming would mitigate the selection pressure for adaptation. Mitigation has the capacity to cancel selection on adaptive responses altogether if everyone participates in it. Here we show that no matter how much less costly it might be to mitigate climate change than adapt to it, populations are unlikely to escape entirely from the need for an adaptive response, and cannot do so if mitigation has the character of a public good. We conclude that species cannot resolve climate warming simply by moving poleward, even when capacity exists for their populations to move and for new environments to accommodate them.

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Modelling the host-pathogen interactions of macrophages and *Candida albicans* using Game Theory and dynamic optimization

(Joint work with Jan Ewald[1], Sebastian Germerodt[1], Christoph Kaleta[2], Thomas Dandekar[3] and Stefan Schuster[1])

Abstract

The release of fungal cells subsequent to macrophage phagocytosis, called non-lytic expulsion, is reported for several fungal pathogens. On one side non-lytic expulsion may benefit the fungus in escaping the microbicidal environment of the phagosome. On the other side the macrophage could profit in terms of avoiding its own lysis and being able to undergo proliferation. To analyse the causes of non-lytic expulsion and the relevance of macrophage proliferation in the macrophage - C. albicans interactions, we employ Evolutionary Game Theory and dynamic optimisation in a sequential manner. We establish a game-theoretical model describing the non-lytic expulsion of C. albicans. Depending on the parameter values we find four different Nash equilibria and determine the influence of the systems state of the host upon the game. We further determine a parameter region, where the host response is robust against the fungal infections. We apply dynamic optimisation to analyse whether macrophage mitosis is relevant in the host-pathogen interaction of macrophages and C. albicans. For this, we study the population dynamics of the macrophage - C. albicans interactions and the corresponding optimal controls for the macrophages, indicating the best macrophage strategy of switching from proliferation to attacking fungal cells.

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Sex with no regret: how sexual reproduction uses a no regret learning algorithm for evolutionary advantage.

(joint work with Ziv Hellman[1], and Dana Sherill-Rofe[2])

Abstract

The question of 'why sex' has long been a puzzle. The randomness of recombination, which potentially produces low fitness progeny, contradicts notions of fitness landscape hill climbing. We use the concept of evolution as an algorithm for learning unpredictable environments to provide a possible answer. While sex and asex both implement similar machine learning no-regret algorithms in the context of random samples that are small relative to a vast genotype space, the algorithm of sex constitutes a more efficient goal-directed walk through this space. Simulations indicate this gives sex an evolutionary advantage, even in stable, unchanging environments. Asexual populations rapidly reach a fitness plateau, but the learning aspect of the no-regret algorithm most often eventually boosts the fitness of sexual populations past the maximal viability of corresponding asexual populations. In this light, the randomness of sexual recombination is not a hindrance but a crucial component of the 'sampling for learning' algorithm of sexual reproduction.

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Eco-evolutionary dynamics in interaction space of competitive communities: How diversity emerges and persists

(joint work with Mohammadkarim Saeedghalati[1] and Daniel Hoffmann[2])

Abstract

Eco-evolutionary dynamics are usually studied in 3 different levels: molecular, genetic or phenotypic level. In a higher level of "coarse-graining", interaction network of species could be considered as the subject of eco-evolutionary dynamics. This approach, despite its ability to shed light on very fundamental ambiguities in the field, has not gain enough attention in literature. Interaction networks of biological species are dynamic. Population of species (nodes) and interaction rates (edges) change continuously due to ecological and evolutionary forces and consequently network of species evolves due to frequency-dependent selection in order to be adapted to the external and internal constraints. In this study we introduced a stochastic eco-evolutionary model in interaction space in which species are competing for common resources and are subject to a life-history trade-off. We showed that trade-off is a determinant factor in diversity and also evolutionary process in interaction space of competing species has a tendency for enhancing intransitive relations.

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Evolution of host defence in fluctuating environments.

Abstract

Given rapidly changing environments, it is important for us to understand how the evolution of host defence and parasite infectivity respond to fluctuating environments. I will present results from a study of evolution of host resistance to parasitism when the host birth rate is time-dependent. I will show how the amplitude and period of seasonality affect the evolution of the host population, as well as other life-history traits, notably the recovery rate. I will discuss a special case where evolution can drive the population dynamics through a period-doubling bifurcation.

Jill Gallaher, Department of Integrated Mathematical Oncology, Moffitt Cancer Center, Tampa, FL, USA

Adaptive Therapy for Heterogeneous Cancer: exploiting space and trade-offs in drug scheduling

(joint work with Alexander R. A. Anderson[1])

Abstract

Over the past decade, there has been an explosion of new, targeted therapies for cancer. Yet for advanced disease, which is likely heterogeneous and disseminated, having a vast arsenal of treatment options does not always lead to sustained outcomes. Targeted treatments are too specific for heterogeneous tumors, and need to be used in combinations to target all cells to avoid recurrence. Cytotoxic treatments can attack a wide variety of proliferating cells, but are more taxing to the patient's health. Yet tumor cells are subject to selection from evolutionary pressures, and a difference in relative fitness will drive changes in clonal dominance. Despite the growing acknowledgement that heterogeneity is driving treatment failure, it is not often recognized that a successful treatment must be designed with the evolutionary response of the tumor in mind.

We investigate the role of spatial heterogeneity in the efficacy of adaptive therapy, an evolutionary-based treatment strategy that aims to balance cell kill with toxicity, by controlling the resistant population through competition with the sensitive population. The strategy aims to keep a constant tumor volume by adjusting the dose such that a shrinking tumor will receive a lower dose while a growing tumor will receive a higher dose. With an off-lattice agent-based model, we simulate the outcomes of different population mixes exposed to two general treatment strategies with an anti-proliferative drug: a continuous application given at the maximum tolerated dose or an adaptive strategy that incorporates dose-modulation and treatment vacations to sustain control of the tumor's sensitive and resistant cell populations. We assume that there is a trade-off between proliferation and drug sensitivity, so that the slower growing resistant cells get trapped in the interior of the tumor during growth and can hide from the drug during treatment. The more homogeneous, sensitive tumors are cured with continuous treatment, but even a few resistant cells in the mix will cause eventual recurrence. With the right scheduling parameters we can maintain a steady tumor size of these tumors with adaptive therapy, as long as there are sufficient sensitive cells to suppress resistant cell growth.

We explore two different scheduling parameters for the adaptive therapy strategy: one that emphasizes more dose modulation, and another that mostly relies on treatment vacations for maintenance. We find that they can both control the same tumor types, but with dose modulation, the average dose rate is significantly lower. Further, we find that cell migration and phenotypic drift disrupts the efficacy of adaptive therapy in general, but this can be partly preserved through a more vacation-oriented schedule. We also show how adaptive therapy can control multiple metastases with similar or dissimilar compositions.

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Félix Geoffroy, Institute of Evolutionary Sciences of Montpellier, France

Partner choice and the evolution of mutually beneficial cooperation

(joint work with Jean-Baptiste André[1], Nicolas Baumard[2])

Abstract

A growing number of experimental and theoretical studies show the importance of partner choice as a mechanism to promote the evolution of cooperation, especially in humans. Previous models in this field, however, have been mostly concerned with the mere existence of some cooperation at equilibrium. Here, we focus on the question of the precise amount invested into cooperation. Human beings express precise preferences regarding this *amount*, cooperating only to the extent that it increases the total welfare, and not more. Can partner choice explain the evolution of these preferences?

In a mathematical analysis, we first highlight an apparent paradox: partner choice leads to a *runaway* of the amount invested into cooperation, to the point where the cost of cooperation exactly cancels out its benefit. In other words, partner choice predicts that cooperation should have absolutely no benefit at ESS.

However, importing tools from economics to carefully solve search and matching models, we then show that, when individuals can *plastically* adapt their level of choosiness to their own quality, then likes end up interacting with likes (so called positive assortative matching), leading to the evolution of the most mutually profitable level of cooperation. By this means, we demonstrate that a biological market framework can account for the evolutionary origin of human preferences about the right amount to invest into cooperation.

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Spatial structure and the dynamics of growth factor production in solid tumours

(joint work with Philipp Altrock[1])

Abstract

Interactions between cancer subclones, and between cancer cells and the surrounding stroma are known to affect the outcome of the disease. For example, it has been shown that the production and release of diffusible substances such as growth factors can accelerate the growth rate of tumours. However, there is a cost related to growth factor production, which suggest a similarity to the classical public goods game. Typically, this problem has been addressed using the toolbox of evolutionary game theory, in particular the replicator equation that assumes a well-mixed population. We set out to investigate this problem using an explicitly spatial cell-based model, where cells are represented as discrete entities and the growth factor is described as a continous quantity subject to production, diffusion and decay. In the limit of infinitesimal cell size the model can be described by a set of coupled PDEs that capture the spatial and temporal dynamics of producer cells, non-producers and the growth factor. By analysing these PDEs we derive an explicit formula that shows that the benefit of producers increases with the group size and mean density, but decreases with the diffusion coefficient of the growth factor. This allows for a quantitative connection between populations dynamics and the physical parameters of the problem, which sheds new light on spatial aspect of tumour evolution.

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The use of range expansion framework to better understand the evolutionary dynamics of cancer

(joint work with Stephan Peischl[1] and Laurent Excoffier[2])

Abstract

Most of the studies focusing on range expansion discuss their results in the context of species' distribution change or invasive species in nature. However, we currently know that similar phenomena can occur during the growth of a tumor, which can be view as a population of abnormal cells expanding its range in the body of its host. For example, during a range expansion process, a mutation can surf in the wave front due to genetic drift and reach high frequency in the population. This phenomenon called "genetic surfing" is not restricted to new neutral mutations, but all variants present on the wave front can surf, including standing neutral variants, deleterious or beneficial mutations. Interestingly, when deleterious mutations occur more frequently than beneficial mutations, gene surfing can result in the accumulation of deleterious mutations at the wave front, a phenomenon which can cause a strong slowdown of the expansion process. In line with these results, recent studies reveal that neutral or deleterious mutations for cancer growth, called passengers, accumulate during tumor progression and that the phenotypes of cancerous cells from the core and from the leading edge of the tumor are different. It appears currently that the role of passengers on cancer dynamics and treatment outcomes has been underestimated. In this talk, my objective is to discuss the similarities between the range expansion process observed in experimental and theoretical studies and the development of solid tumors in order to identify the explicit consideration of spatial processes that could provide a better understanding of the evolutionary dynamics of cancer.

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Assembly rules and a minimal theory for invasion and extinction in food webs

(joint work with Namiko Mitarai[1], Kim Sneppen[1])

Abstract

A number of approaches have been taken to model the complexity of food web structure and stability. These range from structural models, describing the network of links that connect species in a community, models focused on linear stability analysis of an assumed steady state, to explicit numerical simulations of food web evolution or semi-analytical approaches.

We propose a minimal theory where the evolution of a food web can be determined analytically and the consequences of any species addition are computed exactly. Our theory hence gives insight into the impact of an invader on the resident community. Our theory is based on the standard generalized Lotka-Volterra equations, where basal species compete through resource depletion. The theory is "minimal", as each species only feeds on a single resource, either the basic nutrient source or another species – leading to a hierarchical, tree-like food web. We justify this assumption by (i) observed link strength distributions, which are found to be bimodal and skewed, hence showing few strong, and many very weak links; (ii) the gain in conceptual insight into food web evolution.

Specifically, our theory proves that at each invasion step there is one uniquely determined outcome: either the invader peacefully coexists with the residents and resources are re-distributed; the invader is eliminated; or one or several of the resident species are removed in a uniquely defined extinction cascade. At the end of either of these processes the resulting food web relaxes to a globally stable (and feasible) steady state.

Our theory is based in the "food web assembly rules", where each species can be seen as contributing to a non-overlapping consumer resource pair, either as a "free" consumer or a "controlled" resource. These assembly rules are ultimately based in a generalization of the competitive exclusion principle to Lotka-Volterra food webs with an arbitrary number of species.

The theory we present opens for analytical solutions of the persistence time as well as the extinction size distribution. We break down the essence of our theory in the conceptual "invasion extinction model" (IEM), which models a food web ecology by random number placed on a line. Extinctions are then determined by eliminating all species of smaller fitness.

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Stochastic population growth in spatially heterogeneous environments: the density-dependent case.

(joint work with Dang H. Nguyen[1], GerogeYin[1])

This work is devoted to studying the dynamics of a structured population that is subject to the combined effects of environmental stochasticity, competition for resources, spatio-temporal heterogeneity and dispersal. The population is spread throughout n patches whose population abundances are modeled as the solutions of a system of nonlinear stochastic differential equations living on $[0,\infty)^n$.We prove that r, the stochastic growth rate of the total population in the absence of competition, determines the long-term behaviour of the population. The parameter r can be expressed as the Lyapunov exponent of an associated linearized system of stochastic differential equations. Detailed analysis shows that if $r > 0$, the population abundances converge polynomially fast to a unique invariant probability measure on $(0;1)^n$, while when $r < 0$, the population abundances of the patches converge almost surely to 0 exponentially fast. This generalizes and extends the results of Evans et al (Journal of Mathematical Biology 2013) and proves one of their conjectures. Compared to recent developments, our model incorporates very general density-dependent growth rates and competition terms. Furthermore, we prove that persistence is robust to small, possibly density dependent, perturbations of the growth rates, dispersal matrix and covariance matrix of the environmental noise. We also show that the stochastic growth rate depends continuously on the coefficients. Another significant generalization of our work is allowing the environmental noise driving our system to be degenerate. This is relevant from a biological point of view since, for example, the environments of the different patches can be perfectly correlated. We show how one can adapt the nondegenerate results to the degenerate setting. As an example we fully analyze the two-patch case, $n = 2$, and show that the stochastic growth rate is a decreasing function of the dispersion rate. In particular, coupling two sink patches can never yield persistence, in contrast to the results from the non-degenerate setting treated by Evans et al. which show that sometimes coupling by dispersal can make the system persistent.

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Do phages help to stabilize cooperative behavior of bacteria?

(joint work with Alexander Klapproth[1,2], **Johannes Müller[2]**, Stefanie Spriewald[3], Nancy Obeng[3], Barbara Stecher[3])

Abstract

Evolutionary stability of cooperation as the release of public goods is not yet fully understood: non-contributing mutants (sometimes termed cheaters) can safe costs and thus should have a higher fitness than cooperators. One of the identified major stabilizing mechanisms is related to spatial structuring, as it can allow for a preferred assortment of public goods towards cooperative individuals. Whereas spatial heterogeneity obviously occurs in the bacterial colonies and biofilms, existence of cooperation in plankton is more challenging.

An over-proportionally high number of genes connected with public goods in bacteria are plasmid-coded. This led to the assumption that plasmid coding contributes to evolutionary stability of cooperation: plasmids with cooperative genes can re-infect via conjugation non-cooperative cells, which have lost their plasmid or the cooperative gene on their plasmid. However, it has been shown that this only shifted the problem of evolutionary stability from the level of cells to that of the plasmids: cooperative plasmids have lower fitness than non-cooperative.

Here, we will present a new regulation design for a public good related behavior in a system consisting of human pathogenic Salmonella enterica serovar Typhimurium strain SL1344 (S. Tm), a plasmid and a lysogenic phage (Nedialkova et al., 2015). S. Tm produces a bacteriotoxin colicin 1b (Col1b), which very effectively kills competitive species like E. coli. Generally, to release their colicins into the environment, producing cells have to lyse, which is controlled by a lyse gene. Like other colicins systems, in S. Tm both genes coding for colicin production and for immunity against self-lysis by Col1b are located on a plasmid. However, in contrast to colicin production in other species, lyse gene in in S. Tm is not coded by the same plasmid, but by an activated prophage.
We will analyze by a mathematical modelling approach the potential ecological and evolutionary advantage of this system. Specifically, we will analyze the hypothesis that due to different amplification strategies of plasmids and phages, phages may at least under some condition be more suitable to evolutionary.

[*]This talk will be given by Johannes Müller in the memory of Professor Burkhard A. Hense

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Amplification and suppression of selection in cancer mutations through tissue structure

(joint work with Arne Traulsen[1])

Abstract

A graph can represent a population structure by placing individuals or cells on the nodes of the graph and letting them interact or replace each other via the links. Compared to an unstructured population, a graph is called a suppressor of selection if it decreases the fixation probability of advantageous mutants and increases it for disadvantageous mutants (Lieberman et al., Nature 2005). The reverse is called an amplifier of selection, because it increases the effect of higher mutant fitness and decreases it for lower fitness. Based on this framework of evolutionary graph theory, we study the potential role of tissue organization in preventing cancer initiation. Amplification and suppression are defined as property of the graph in comparison to an unstructured population. This means that a graph that would prevent all kinds of mutations from spreading through the whole population would make a beneficial structure to maintain the integrity of a tissue. We show that this property highly depends on the specific details of the model. Moreover, the distribution of fitness effects of cancer mutations can determine which kind of tissue structure is optimal.

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Modelling social influence on cooperation: the public goods game on a multiplex network

(joint work with James M. Allen[1])

Abstract

We consider economic and social influences on the evolution of cooperative behaviour using a modified public goods game on a multiplex network as a model. We find that social influence leads to the persistence of initial cooperation strategies and so can promote the survival of highly cooperative strategies even when the economic reward for cooperation is relatively modest. This result holds for a range of social norms and for differing economic and social group structures

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The coexistence of independent genes is aided by multilevel selection, but only to a limited extent

(joint work with Ádám Kun[1,2])

Abstract

Inaccurate copying limits genome length. This, in turns, limits the emergence of more accurate replication -- a well-established puzzle of the origins of life. But as long as a molecule is copied more frequently than its mutants, it can afford to have some imperfect copies and still survive. The deciding factors are the proportion of perfect copies, and the selective superiority: the ratio of the replication rate of the original molecule to that of its mutants. And since the error-per-monomer rate (of e.g. RNA) cannot be arbitrarily low, there is an upper bound to the length of the molecule, and to the amount of information it can carry. This is a threshold attributable to error.

The amount of sustainable information can be increased by the coexistence of different molecules (genes). The competitive exclusion of genes, and the resulting information loss, can be overcome by compartmentalization and selection acting on the compartments (protocells). In an earlier study we have shown that in such systems the sustainable number of genes depends fundamentally on redundancy: the number of copies, per gene, inside the protocells. Here is also a threshold attributable to error. For the sake of clarity, we termed the former the *first* error threshold, and the latter the *second*.

Now, we will report on our investigation into the combination of these two phenomena. We assessed the survival, or loss, of the initial information of molecules inside a population of protocells, as a function of gene number (cf. diversity) and copy number (cf. redundancy). Selection acts on both the molecules and the protocells. The survival of information is impeded by (1) the inaccurate copying of genes, leading to loss-of-function mutants (cf. parasites), (2) the non-synchronous replication of genes, and (3) the genes' random assortment into daughter protocells upon division.

In our agent-based simulations, we found that the systems capable of sustaining all information, and those that are incapable, show clear separation in the gene number to copy number space: their boundary can be presented in the form of a phase diagram. The shape of the boundary is greatly influenced by the mutation rate and the selective superiority. The effect of the assortment load, however, was found to be negligible. The coexistence of two genes, which has been studied in previous package models, was achieved in almost all circumstances. Even 10 to 15 genes could have plausibly coexisted in such compartmentalized systems. But the coexistence of 60 to 100 genes, necessary for the first metabolisms, is apparently problematic in the absence of regulated copying. Accordingly, the appearance of advanced error correction, or regulation, must have preceded the emergence of the most primitive of metabolisms.

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The Evolution of Sex-specific Virulence in Infectious Diseases

(joint work with Francisco Ubeda[1])

Abstract

Fatality rates of infectious diseases are often higher in men than women. Although this difference is often attributed to a stronger immune response in women, we show that differences in the transmission routes that the sexes provide can result in evolution favouring pathogens with sex-specific virulence. Because women can transmit pathogens during pregnancy, birth or breast-feeding, pathogens adapt, evolving lower virulence in women. This can explain patterns in differences between the sexes for several diseases. In particular, this resolves the long-standing puzzle on progression from Human T-cell Lymphotropic Virus Type 1 (HTLV-1) infection to lethal Adult T-cell Leukaemia (ATL); a progression that is more likely in Japanese men than women, while it is equally likely in Caribbean women and men. We argue that breastfeeding, being more prolonged in Japan than in the Caribbean, may have driven the difference in virulence between the two populations. Our finding signifies the importance of investigating the differences in genetic expression profile of pathogens in males and females.

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Jacob Johansson[1,2]

Migratory birds, phenological mismatch and evolutionary games in a warming world

(joint work with Nadiah Kristensen[1], Jörgen Ripa[1], Isabel Smallegange[2,3] and Niclas Jonzén[1])

Abstract

Changes in the seasonal timing of biological events such as bird migration, flowering or insect emergence belong to the most well documented effects of global warming. These temporal shifts often differ among species and may alter or disrupt ecological interactions. The long-term consequences are unknown. Will species be able to adapt to the new conditions and maintain synchrony with necessary resources or will accelerating mismatches result in widespread population declines or even collapsing food webs?

I will present our game theoretic approach to study such questions. I will focus on migratory birds and the fact that their reproductive success in many cases depends on food which is available only during a short period in the spring. We specially consider game-like situations where success of an individual depends on how it times an action in relation to competitors. For example, arriving to breeding grounds before competitors often increases chances to obtain a high-quality territory.

As I will discuss, accounting for competitive timing games yield several surprising predictions - for example that a certain degree of reproductive mismatch might be expected from evolution, that genetic adaptation to track earlier resources may reduce population sizes and that in some cases it even makes sense to arrive later to breeding grounds even though resources appear earlier in the year. Game theory thus offers interesting and novel ways to interpret changes in nature's calendar and their evolutionary implications.

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Space/time evolutionary stoichiometric model for the algae-Daphnia ecosystem

(joint work with K. Long[1], C. Dissanayake[1,2], A. Peace[1])

Abstract

The development of ecological models that incorporate food quantity, as well as food quality has deepened our understandings of ecological dynamics. Models developed under the theory of Ecological Stoichiometry integrate Lotka-Volterra type models with stoichiometric constraints by considering chemical heterogeneity of the species. While current models track both energy (light) and nutrients across trophic levels, most neglect spatial dynamics. Harmful algal blooms block light from getting far beneath the surface and can result in severe ecological consequences. In order to begin investigation of these consequences mathematically requires a complex model that explicitly models the spatial dynamics of light, nutrients, and aquatic population densities. In this work we develop and analyze a stoichiometric model of the algae-Daphnia aquatic ecosystem using both time and spatial dynamics.

I. Loladze, Y. Kuang and J. J. Elser constructed a two-dimensional Lotka- Volterra type model using stoichiometric principles (the LKE model), which includes chemical heterogeneity of the first two trophic levels of a food chain, by assuming that both producer and grazer are composed of carbon and phosphorus. This model, however neglects spatial dynamics. Recently, C.Dissanayake spatially expanded the LKE model using lambert-beers law for light absorption to vary the light level with water depth. In this work, we extend the model further to include more realistic spatial light dynamics that depends on depth, as well as the population densities, for example algal self-shielding. In addition to the spatial distribution of light, the model incorporates spatial dynamics of dissolved phosphorus levels, which also depends on population densities. Model simulations and analysis lead to insights on algae and Daphnia population dynamics and how they are integrated with the spatial dynamics of nutrients and light.

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Novelty, popularity, and emergent neutrality: Detecting transmission biases in population-level data

Abstract

The concept of neutral evolution has been used fields as diverse as population genetics, ecology or cultural evolution. Here we apply an overlapping generation neutral model which originated in the ecological literature to cultural data. In particular, we focus on the progeny distribution and derive the first analytical representation under the hypothesis of neutrality. We show that it consists of two phases: a power law phase with a universally-applicable exponent of -3/2, followed by an exponential cut-off for variants with very large numbers of progeny in the time interval. Maximum likelihood estimations of the parameters of the neutral model then provide a direct way of evaluating the consistency between theory and observed data. We apply our approach to a data set of baby names from Australia registered over a 70-year period. We find that while neutrality provides a plausible description of the progeny distribution of abundant variant types, rare variant types deviate from neutrality. This indicates that analyses based on only the most popular variants, as is often the case in studies of cultural evolution, can provide misleading evidence for the neutral hypothesis. We further show that a kind of anti-novelty bias, where new variants are at a disadvantage by virtue of their novelty, is able to replicate more closely the complete progeny distribution of this data set.

Artem Kaznatcheev[1,2]

Effective games and operationalizing spatial structure

Abstract

A typical study of space in evolutionary game theory will start with a specification of how local interactions impact fitness -- the reductive game -- and then simulate that interaction over a graph (or other model of space) to show a surprising difference in dynamics between the spatial model and the inviscid mean-field. I will discuss a minimal example of this that spatializes the Go-vs-Grow game and shows that the edge effect of a static boundary (such as a blood vessel, organ capsule or basement membrane) allows a tumour without invasive phenotypes in the bulk to have a polyclonal boundary with invasive cells [1]. But how did we know that the local interactions were a Go-vs-Grow game? In general, we guess these games from intuitions acquired by looking at population level experiments. This looking can be formalized into an operational specification of an effective game [2,3]. I will show how we measure such an effective game in ALK+ non-small cell lung cancer [4], and that the presence or absence of treatment changes the qualitative type of game (and not just its quantitative details). However, this effective game collapses the reductive game and spatial structure into a single measurement. Thus, I advocate that we turn the typical space-in-EGT study on its head. Let's start from the measurement of an effective game and an operationalization of spatial structure [5] to then provide a method for inferring the reductive game.

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Fisher's angular transformation and quantifying evolutionary dynamics from variant-frequency time series - a case of genetic flux not drift.

Abstract

From Kimura's neutral theory of protein evolution to Hubbell's neutral theory of biodiversity, quantifying the relative importance of neutrality versus selection has long been a basic question in evolutionary biology and ecology. With deep sequencing technologies, this question is taking on a new form: given a time-series of the frequency of different variants in a population, what is the likelihood that the observation has arisen due to selection or neutrality? A main difficulty in solving the dynamics is that genetic drift has the property that the effective diffusion constant becomes smaller close to fixation or loss. Although a century ago Fisher developed an "angular" transformation to stretch space in such a way to remove the frequency dependence of diffusion, it has largely remained an intellectual curiosity, since the result is a complicated non-linear convective force, even in the neutral case. Here, we show that a heuristic Gaussian solution can be developed that gives accurate solutions for the asymptotic short-time dynamics for arbitrary evolutionary forces, including selection and unequal mutation rates between two alleles. We show that this calculation can be used to detect selection from time-series of allele frequencies. Further, we demonstrate that Fisher's transformation tells us something deep about the process of genetic drift, that although individual trajectories suffer no net bias towards fixation or loss, there is a net flux of diffusers towards the boundaries - the effective convective or drift force (in the conventional physics sense) in angular frequency describes precisely this flux of populations in normal frequency.

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Ádám Kun[1,2]

Why animals cooperate? – The insensitivity of the Snowdrift Game to network dynamics

(joint work with Adrienn Král[3])

Abstract

The default outcome of a situation depicted by the Prisoner's Dilemma is cheating. Cooperation, something which is rather widespread in Nature, is very hard to explain by this particular game. On the other hand, some level of cooperation can be easily achieved in the Snowdrift Game. The Snowdrift Game is such that mutual defection yields the lowest pay-off, and even being exploited it a better option. Territorial defense, predator vigilance and parental care are examples of situation to which the Snowdrift Game can apply [1].

Gregarious animals seldom interact randomly with each other. Moreover the interaction network changes over time, at least by the death and birth of group members. More often there is a dynamic on a much shorter time-scale. This dynamics negatively affects the level of cooperation that can be achieved in a Prisoner's Dilemma [2]. Albeit responsive, clever strategies that mitigate this effect [3].

We have investigated the fixation probability of cooperation on dynamic graphs in situation characterized by the Snowdrift Game. As expected, the fixation probabilities are higher compared to the Prisoner's Dilemma. On the other hand, network dynamics have very little effect on fixation probability. Nor clever strategies increase the level of cooperation. Animal cooperation can be widespread because it rests on a game situation which is insensitive to network dynamics that are dictated by other ecological considerations. Cooperation can robustly evolve in these situations without group dynamics hindering it.

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Modelling dial vertical migration of zooplankton using variational principle of selection.

(joint work with Andrew Morozov[1])

Abstract

Diel vertical migration (DVM) of zooplankton is a widespread phenomenon in both oceans and lakes, and is generally considered to be the largest synchronized movement of biomass on Earth. Most existing mathematical models of DVM are based on the assumption that animals would maximize a certain criterion such as the expected reproductive value, the venturous revenue, the ratio of energy gain/mortality, etc. The major shortcoming of this approach is that the resultant DVM may be strongly affected by a subjective choice of a particular optimization criterion. Here we implement another approach of finding optimal DVMs based on the variational principle of selection, where the optimal strategy should come directly from the underlying equations of population dynamics as a result of long term selection. The essence of the method is to derive the expression for the fitness function such that its highest value would correspond to the fittest strategy which will eventually outcompete the other strategies/traits. We show that the fitness function can found considering evolutionary dynamics of measures of behavioral strategies in infinite-dimensional functional space. Our approach is different from the classical adaptive dynamics methods and allow us to explore the evolutionary stability with respect to mutant strategies which are not necessarily close to the given strategy. As illustrative examples, we explore DVM patterns in models of zooplankton population dynamics with several developmental stages. Unlike previous studies, we consider not only the case of fixed density of zooplankton predators (fish) but also a more realistic case, where the amount of predators is a dynamical variable. We demonstrate different dependence of strategies for different development stages of zooplankton for variation of key parameters of the models (e.g. amount of food, predation level, cost of migration, etc). The results obtained through modelling are in general in good agreement with the empirical data from the ocean.

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Mathematical modelling of natural selection processes using the dynamics of measure.

(joint work with Andrew Morozov[2] and Oleg Kuzenkov[1])

Abstract

A major goal in modelling biological evolution is exploring selective advantages of species and obtaining mathematical expressions for their fitnesses. One of the most powerful approaches to modelling evolving biological systems is considering long term dynamics of distributions in the space of inherited units which can be described via dynamics of measure. This approach was first proposed by A. Gorban in 1985. Currently, modelling evolution often focuses on changes in density distributions of species densities in the parameter space of traits (e.g., G. Karev, A. Klimenko, etc.); however its connection with the underlying selection process is not trivial and presents a number of mathematical challenges. In particular, implementation of the measures dynamics approach in modeling is not straightforward for systems with a time lag.

This work presents ways to overcome the mentioned difficulties. The investigation is focused on modelling evolutionary selection based on differential equations for distributions (measures) in the space of hereditary traits. Unlike earlier publications on the topic, hereditary units are allowed to be elements of infinite dimensional functional space, for example, a continuous function of inherited behavior or a complex behavioral strategy of organisms. We firstly introduce the order of preference on the system of measurable subsets as result of long term selection by reflecting selective advantages of strategies. Then by applying a set of transformations to the initial equations (e.g. power, normalized and inverse transformations) we become able to quantify the introduced order of preference by computing generalized average per capita growth rate which can be considered as a generalized fitness function. Thus the evolutionary and invasive stable hereditary units can be found by finding via obtaining such generalized fitness function.In the case of inherited behavior, the fitness function allows to formulate the variational principle for searching the evolutionary stable strategy.

In the talk, a special attention will be paid to modelling evolutionary behavior in equations with a time lag for some classes of measures and densities. The expression of fitness function for these models will be derived. As illustrative examples, we will consider evolutionary behavior in some well-known models such as von Ferster population model with age/length structuring.

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Pietro Landi[1,2]

Evolution of the Good Colonizer Syndrome of high self-fertilization and dispersal rates in a metapopulation: model predictions reconcile with Baker's law

(joint work with James Rodger[1,3], Cang Hui[1,4])

Abstract

Baker's Law implies selection towards the Good Colonizer Syndrome (GCS) of high dispersal and self-fertilization (*selfing*) during colonization. This because high dispersal results in more propagules arriving in vacant habitats, and high selfing helps to overcome Allee effect of cross-fertilization in small populations. However, models of the evolution of dispersal and selfing emphasize a trade-off between the two traits, contradicting this idea.

We use an Adaptive Dynamics model of dispersal and selfing in a metapopulation with extinction and recolonization of patches through dispersal. Propagules disperse from and to all patches (suffering cost of dispersal and density-dependent competition). Fertilization happens through self-fertilization (suffering inbreeding depression) and out-crossing (suffering Allee effect).

The model predicts evolution of dispersal and selfing to any of the four possible combination of low and high dispersal and selfing. The final evolutionary syndrome depends on habitat and demographic parameters. At the ecological level, the meta-population displays three different scenarios: unconditional viability, unconditional extinction, and conditional viability, i.e., bi-stability between viability and extinction. The effect of each parameter on the final evolutionary syndrome is studied: increasing extinction rate and competition and decreasing inbreeding depression selects for the GCS and emphasize a positive correlation between dispersal and selfing, while cost of dispersal, out-crossing Allee effect, and fertility emphasize the trade-off between dispersal and selfing.

Evolution of both high dispersal and selfing (the Good Colonizer Syndrome) is selected when extinction rate and/or competition are high, e.g., in a disturbed environment with low resources. Climate change, habitat fragmentation, and exploitation could therefore select for the GCS. Weak inbreeding depression also intuitively selects for the GCS, making it easier for small founding populations to overcome out-crossing Allee effect. By contrast, cost of dispersal, out-crossing Allee effect and fertility emphasize the trade-off between dispersal and selfing. Our results reconcile model predictions with the biological principles of Baker's Law.

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Alexander Lange[1,2]

A mathematical framework for predicting lifestyles of viral pathogens

Abstract

Despite being similar in the way of functioning viral pathogens enjoy very different yet well-defined lifestyles. They are nomadic or sedentary, which manifests in acute and chronic infections. Transmission routes, infectiousness, antigenic variation and virulence define further pathogenic lifestyles, all depending on the host environment.

In order to persist pathogens must infect new hosts; the success determines their fitness. Infection happens with a certain likelihood during contact of hosts, where contact can also be mediated through vectors. Besides structural aspects of the contact network, three parameters are important here: the contact rate, the infectiousness during contact, and the immunity of susceptible hosts.

What can be concluded about the lifestyle of viral pathogens when maximizing their reproductive fitness? This is the biological question addressed in this talk. The answer extends the speaker's earlier results (Lange & Ferguson 2009, PLoS Comput Biol 5(10): e1000536) and makes explicit connection to other basic work on the evolution of pathogens (e.g., Grenfell et al 2004, Science 303: 327-332).

Mathematical models are investigated that encode intra- and inter-host dynamics in a minimalistic fashion while covering a broad spectrum of viral pathogens, including pathogens that cause childhood diseases, sexually transmitted- and u-like infections. The models involve differential equations, agent based simulation, networks, and probability.

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The evolution of medication strategies in Monarch butterflies

(joint work with Jacobus de Roode[2], André de Roos[1])

Abstract

Hosts have developed a number of strategies to fight infection, which is often classified in three different categories: avoidance, recovery or tolerance. The recovery strategies studied in evolution of host-parasite systems generally imply an immune response from the host. However, self-medication strategies do not require an immune response, but a behavioural one. Recently, it has been shown that self-medication strategies are more widespread than previously thought. And yet, self-medication strategies and the mechanisms behind their evolution are poorly understood so far, particularly in insects.

In our study we focus on the medication behaviour of the Monarch butterfly (*Danaus plexippus*) using plants (*Asclepias spp.*) with different toxicity levels to fight infection by its parasite (*Ophryocystis elektroscirrha*). We model the population with an age-structured model associated with an SI model. Unexpectedly, the most efficient strategy in the population is a preferencial behaviour from the infected individuals towards toxic plants whereas the healthy individuals randomly select their plants. These results hold for different virulence and toxicity scenarios. From these counter-intuitive results, we also discuss how the evolution of strategies in the monarch butterfly population is shaped using an adaptive dynamics framework.

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Genetic conflict with a basis in ecology

Abstract

Genetic conflicts occur when different genomic segments, or different alleles at a locus, differ in their evolutionary interests. This possibility has attracted much interest, most of it focused on conflicts with a basis in the properties of genetic transmission systems. Ecologically based genetic conflict is, however, a possibility that is less studied. In heterogeneous environments, genes can differ in their pathways of transmission to future generations, involving the kinds of environments they pass through. Genetic conflicts can then appear by favouring or suppressing these pathways, and such conflicts have a basis in ecology. A characteristic feature of these conflicts is that they are influenced by the degree of linkage between genes, where at least one locus is under strong disruptive selection between environments. The other genes can be modifiers of the effects at a focal polymorphic locus, or they can code for a reaction norm (plasticity) of the focal trait.

I will illustrate these effects of genetic linkage and genetic conflict in a two habitat model, with limited dispersal between habitats. I will show that so-called genomic islands of divergence can be seen as evolutionary outcomes of such conflicts, where tightly linked genes are responsible for local adaptation. These genes have a shared evolutionary interest in being successful in one habitat, possibly at the expense of success in other habitats. I also investigate how genetic conflict influences the importance of genetic local adaptation versus plasticity. I show that when genes for local adaptation are tightly linked to genes coding for plasticity, the slope of a reaction norm will be shallow, whereas for unlinked genes it will be steeper. The overall perspective I present is that the study of ecologically based genetic conflicts provides an understanding of the evolution of tightly linked clusters of genes, sometimes referred to as supergenes.

Xiang-Yi Li, Department of Evolutionary Biology and Environmental Studies, University of Zurich, Switzerland

Softness of selection and the evolution of sex-biased dispersal

(joint work with Marjo Saastamoinen[2], Hanna Kokko[1])

Abstract

"Soft selection" refers to the situation where the reproductive output of the local population is independent of the current fitness conditions of its members, and thus the detection of inferiority is only possible in the presence of superior types. Therefore soft selection has clear repercussions for local adaptation, as globally poorly performing genotypes can be "shielded" from selection if their fitness is locally evaluated in the relative absence of superior immigrants. In natural populations, selection on males is often both strong (only the most competitive males achieve significant success) and soft. The fecundity of females often directly determines the total numbers of offspring, and thus poorly adapted females can lead to population size decline and even the extinction of the local population. But if a local population consists of poorly adapted males, it only means that less impressive performance is required to achieve paternity among the locally produced offspring. Dispersal plays an important role in introducing immigrants, and thereby interacts with the softness of natural selection and coevolves with local adaptation. Although sex-biased dispersal is common in natural and there is already understanding of why it might evolve, sex-biased softness of selection is a concept largely absent from the models of dispersal and local adaptation. In this work we study the effect of different softness of selection on the evolution of sex-biased dispersal, under different intensities of sexual selection and under different mating systems.

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Magnus Lindh, Department of Biology, Lund University, Sweden

Evolving phenology of root and shoot allocation

Abstract

How to allocate growth during the lifetime is crucial for the survival, competition and reproduction of all organisms. For annual plants it is optimal to allocate first to vegetative growth and then switch immediately to reproductive growth, thereby maximizing size and taking advantage of the limited season. When the season length is uncertain the allocation switch is gradual instead. Under competition for resources, such as light, the reproduction time will instead be delayed to allow the plant to grow larger than the opponent. This highlights the importance of season length and competition for growth allocation.

To understand the phenology of competing annual plants we investigate size-structured populations. Typically size-structured populations have only one type of size such as the body mass of a fish or the mass of leaf of a tree. However, the type of competition can vary widely between different types of organs. While the shoot of a plant typically is involved in strongly asymmetric competition for light, the root is involved in a symmetric competition for water and nutrients. Light is a reliable resource, but water availability can be very uncertain. This motivates extending size-structured models to have more than one type of mass.

We devise a model to describe the phenology of annual plants and explore the evolution of size-structured populations with a root and a shoot.

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Genotype-phenotype maps: when does variation dominates over selection?

Abstract

Traditional evolutionary modelling has focused on the role of natural selection. Here I provide some explicit examples, including RNA secondary structure, protein quaternary structure and gene networks, where taking the full genotype-phenotype map into account shows that the arrival of variation can dominate over selection. This analysis may shed new light on Mayr's ultimate-proximate distinction in evolutionary biology.

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Construction of compact cognitive maps for limb manipulation in dynamic situations

(joint work with J.A. Villacorta-Atienza1, C. Calvo1, S. Lobov2)

Abstract

The fundamental bases of how our brain solves different tasks of the object manipulation remain largely unknown. Here we consider the problem of the limb movement in dynamic situations on an abstract cognitive level and propose a novel approach relying on: i) transformation of the problem from the limb workspace to the so-called hand-space, and ii) construction of a compact cognitive map (CCM) in the hand-space. The CCM provides a trajectory that can be followed by the limb, which ensures an efficient collision-free movement and target catching in the workspace. Our numerical simulations confirm the approach feasibility but also reveal the problem complexity. We then validate the CCM-based solutions in real-life scenarios. We show that a CCM-equipped humanoid robot can catch a fly ball in a similar way as a human subject does. Finally we discuss how the static nature of the CCMs enables learning and automation of sophisticated cognitive behaviors exhibited by humans.

This work was supported by the Spanish Ministry of Economy and Competitiveness under grant FIS2014-57090-P (theoretical development) and by the Russian Science Foundation under project 15–12–10018 (experimental verification in robot).

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Lack of ecological and life-history context can create the illusion of social interactions.

(joint work with Corina E. Tarnita[1])

Abstract

Research on social microbes often focuses on one fitness component (reproductive success within the social complex) undermining the effect of other stages of the life cycle and the role of the ecological context. This can lead to paradoxical results. The life cycle of the social amoeba *Dictyostelium discoideum* includes a multicellular stage in which not necessarily clonal amoebae aggregate upon starvation to form a possibly chimeric (genetically heterogeneous) fruiting body made of dead stalk cells and spores. Lab-measured spore contributions in these chimeras indicate a strong skew in the fraction of spores that belong to each genotype. This skew suggests a strong social antagonism that should result in low genotypic diversity, which is inconsistent with observations from nature.

Two studies have suggested that this inconsistency stems from the one-dimensional assessment of fitness (spore production) and that the solution lies in tradeoffs between multiple life-history traits [1], e.g.: number of spores versus viability; and spore-formation versus staying vegetative [2], [3]. I will present an ecologically-grounded, socially-neutral model (i.e. no social interactions between genotypes) for the life cycle of social amoebae to theoretically explore multiple non-social life-history traits and tradeoffs [4]. Experimental results regarding apparent social interactions within chimeric mixes can be qualitatively recapitulated under this neutral hypothesis, without needing to invoke social interactions. This allows for simple potential resolutions to the previously paradoxical results, but life-history tradeoffs alone do not resolve strain coexistence. I will finalize this presentation by proposing two ecological processes: spore dispersal among different patches [3] and seasonality within a single patch [5] as driving forces of diversity in *D. discoideum*.

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Phylogenies from dynamic networks

(joint work with Caroline Colijn[1])

Abstract

Human contact structures are an important determinant to understand pathogen evolution, since they limit the pathogen's opportunities for reproduction, and consequently shape pathogens' phylogenetic trees. These trees are therefore are not random trees; their specific characteristics vary. These characteristics include small substructures (cherries, pitchforks), measures of imbalance (Sackin index, Colless index) and other tree features. Whereas the existence of a link between contact networks and phylogenies seems obvious, the nature of the link is not yet well understood.

Previously, phylogenetic trees from transmitting pathogens have been simulated on static host contact networks of different topologies [4]. Studies with dynamic networks often use Erd¨os-Renyi (ER) random networks [8, 7]. However, data about contact networks (and on social networks in general) limits the applicability of ER networks: typically the observed shortest path length between people is much shorter than on ER-networks [9], real networks have slower decaying tails in the degree distribution [2, 6, 1] as well as positive assortiveness [5] and positive clustering coefficient [3].

Here, we use a novel dynamic contact network model exhibiting these realistic properties to simulate pathogen transmission and resulting pathogen phylogenetic trees. The network's skewed degree distribution can be derived theoretically. The model follows the general idea of preferential attachment like the Barabasi-Albert model [2], but whereas the BA model grows indefinitely, our network has stationary size, since it includes both entry and exit of people (and of partnerships).

We vary the rate at which people enter and exit the network, the average number of neighbours, and the extent of clustering. We compare pathogen phylogenetic trees to those from a dynamic ER-network with the same turnover and mean degree, and we compare dynamic to static networks. We find that trees from our dynamic networks have higher imbalance than trees from an ER network. However, clustering somewhat reduces this imbalance (measured in Sackin index, Colless index and average path length). In particular, higher entry and exit rates lead to higher imbalance in the phylogenetic tree. This highlights the importance of considering dynamics when modelling human contact networks, particularly where the network evolution is not negligibly slow compared to the timescale of the pathogen's transmission.

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The effect of fluctuating population size and seedbanks on evolution

(joint work with Lukas Heinrich, Aurélien Tellier[2], Daniel Živković[3])

Abstract

Seedbanks are well known to influence the time scale of evolution. In particular, the strength of genetic drift and selection are affected in a different way [1]. Standard models, based on the idea of the Wright-Fisher or the Moran model, assume a fixed population size for the above-ground population, and also a fixed size of the seedbank (either a finite number of seeds, or a deterministic seedbank of finite, constant seed density). However, a logistic model for the above-ground population, and a Poissonian distribution for the number of seeds could be considered to be more adequate for ecological models. This idea yields four models (combination of: above ground, fixed population size/logistic process; below ground, deterministic seed- bank/fluctuating number of seeds). These processes are analysed forward in time for a large population (diffusion limit) and weak selection. Using time scale analysis and dimension reduction, we obtain in all four cases a one-dimensional diffusive Moran model with weak selection. These results allow to study the effect of the additional noise due to fluctuations in the above and/or below ground population on genetic drift and selection.

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A kin selection perspective on multi-dimensional adaptive dynamics in subdivided populations

(joint work with Laurent Lehmann[1])

Abstract

Adaptive dynamics is a powerful toolbox to understand gradual phenotypic evolution through the invasion of rare mutants. In subdivided populations connected by limited dispersal, globally rare mutants may become locally common so that mutant invasion fitness depends on mutant-mutant interactions that may be difficult to track mathematically. A useful invasion fitness measure in this case is Rm, the total number of successful emigrants produced by a mutant lineage over its lifetime when the lineage was started in a single group. Even if Rm takes into account kin selection, which occurs whenever individuals that interact have a more recent common ancestor than random individuals, its effects are not straightforwardly apparent. Yet, an understanding of kin selection effects can be useful to understand the evolution of social traits, like cooperation, dispersal or sex ratio.

While kin selection effects on singular strategies (candidate ESSs) and their convergence stability (whether a mutant closer to a singular strategy than the resident invades) are well understood, they are much less so for the uninvadability of singular strategies (whether a mutant that arises in a resident at the singular strategy invades). Here, we use the theory of branching processes to derive an invasion fitness measure that reveals the effects of kin selection through the concept of relatedness. We use our fitness measure to derive the conditions for disruptive selection to occur on multiple co-evolving traits in terms of relatedness. We also explore the among-traits correlations that develop due to disruptive selection. We find that selection tends to favour a positive (negative) correlation between two traits, when the selective effect of one trait on relatedness is positively (negatively) correlated to the indirect fitness effects of the other trait.

We illustrate our results by studying the co-evolution of traits for which this matters: dispersal that decreases relatedness, and generosity that has positive indirect effects using Matrix games in the island model. Whereas a well-mixed population will stay monomorphic for a game strategy, here we find that when the strategy co-evolves with dispersal, selection is disruptive under a significant range of model parameters and leads to the emergence and maintenance of two broadly-defined social morphs: a sessile, generous morph; and a dispersive, self-serving morph. Overall, our results highlight the potential importance of population subdivision for evolutionary stability and shaping correlations among traits.

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Robert J Noble[1,2]

Evolutionary ecology of senescence and cancer risk: from naked mole rats to modern humans

(joint work with Stanton Braude[3] and Michael E Hochberg[1,4])

Abstract

Although evolutionary theory explains why metazoans are largely protected against negative fitness effects of cancers, high cancer incidence rates have been observed across diverse species. I will argue that most modern-day cancer is due to environments deviating from central tendencies of distributions that have prevailed during cancer resistance evolution. Otherwise, protection is generally imperfect but cancer risk almost never exceeds ~5%. I will support these claims with two case-study analyses. First, based on an empirically parameterized dynamical model, I will present estimates of cancer incidence in ancient humans, and subsequent changes related to lifestyle, lifespan and stature. Second, I will present a reassessment of an unusual mammal until recently thought to be virtually immune to cancer: the naked mole rat (NMR). Using a demographic model and previously unpublished field data, I will show that some ageing and disease – and cancer in particular – are to be expected in NMRs, consistent with recent case reports. The model – which exploits recently-developed matrix calculus methods extended for the first time to include caste structure – further shows how age-dependent extrinsic mortality is predicted to affect selection for senescence. The overarching framework provides a basis for understanding how environmental change impacts cancer risk, with potential implications for species ecology.

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Hochberg ME, Noble R (2017). A framework for how environment contributes to cancer risk. *Ecology Letters.* 20(2) 117-134; doi: 10.1111/ele.12726

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John Norbury, Mathematical Institute, University of Oxford, UK

Evolutionary population ecology defining a food web landscape for quantitative trait (QT) population modelling

(joint work with Roger Cropp[1])

Abstract

A quantitative trait is a measurable phenotype that depends on the cumulative actions of many genes and the environment. Traits typically vary slightly among individuals in a population to produce a continuous distribution of phenotypes. However, when investigating the eco-evolutionary dynamics of a population, this distribution of phenotypes is often approximated by its mean value. The nature of a population's interactions with other populations and non-living resources is determined by a set of parameter values that describe the population's average quantitative trait. The evolution of a population over ecological time scales may be represented by changes in the values of these quantitative trait parameters. These may represent subtle changes in the phenotype of the population that change the population's fitness but do not affect its trophic status or the structure of the food web within which it functions. For example, parameter variations that reflect increased foraging efficiency, reduced predator palatability, or the development of behavioural skills that lead to reduced predation rates or improved recruitment. However, quantitative trait parameters may also change sign, implying changes in trophic interactions and food web structure.

Evolutionary population ecology implies the existence of a smoothly connected space of parameters representing quantitative traits and a continuum of population interactions that enables a population to smoothly adapt to new trophic behaviours. Theoretical population/ecosystem ecology has historically lacked such a framework. The conceptual compass rose of population interactions derived from the simple two-population Lotka-Volterra model describes competition (-,-), predation (+,-), and mutualism (+,+) as the three pillars of population ecology, and recognises the transition states of commensalism (+,0) and amensalism (-,0). While the standard Lotka-Volterra conceptual framework has worked well for competition and predation, it has not provided useful answers for interactions such as mutualism and mixotrophy, which are now considered to dominate population interactions on land and amongst marine plankton respectively. Further, it has provided little insight into how populations can evolve different trophic interactions.

Here, we present a population modelling framework based on simple ecological axioms and show how it provides a rich landscape of trophic interactions within which eco-evolutionary models based on quantitative traits may smoothly navigate. The concept of finite resources is central to the framework, which implements rules such as local mass balance of direct population interactions, global mass balance of indirect population interactions and the constraints of limiting resources. Simple, intuitive rules are applied to each population to ensure ecological verisimilitude, and provide useful metrics to define the trophic status of each population based on the resources it utilises.

We show how within this framework populations may smoothly move between different trophic behaviours, identified by changes in sign of quantitative trait parameters. This provides a framework for populations to evolve from competition through mixotrophy to mutualism, and to create new trophic levels. We show these transitions for two interacting populations using simple state space diagrams with rotations, translations and bending of the zero isoclines of a single simple model. Finally, we demonstrate how additional populations may be included with minimal additional complexity.

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Chay Paterson, School of physics and astronomy, University of Edinburgh, UK

An exactly solvable, spatial model of mutation accumulation in cancer

Abstract

One of the hallmarks of cancer is the accumulation of driver mutations which increase the net reproductive rate of cancer cells and allow them to spread. This process has been studied in mathematical models of well mixed populations, and in computer simulations of three-dimensional spatial models. But the computational complexity of these more realistic, spatial models makes it difficult to simulate realistically large and clinically detectable solid tumours. Here we describe an exactly solvable mathematical model of a tumour featuring replication, mutation and local migration of cancer cells. The model predicts a quasi-exponential growth of large tumours, even if different fragments of the tumour grow sub-exponentially due to nutrient and space limitations. The model reproduces clinically observed tumour growth times using biologically plausible rates for cell birth, death, and migration rates. We also show that the expected number of accumulated driver mutations increases exponentially in time if the average fitness gain per driver is constant, and that it reaches a plateau if the gains decrease over time. We also discuss some novel insights into the behaviour of the model arrived at after our publication in December.

Joshua L. Payne, Institute of Evolutionary Biology and Environmental Studies, University of Zurich, Switzerland

Exhaustively-enumerated genotype-phenotype maps in transcriptional regulation

Abstract

Transcriptional regulatory circuits drive the development, physiology, and behavior of organisms across the tree of life. Their phenotypes are gene expression patterns –i.e., when, where, and to what extent the circuit's genes are expressed. These phenotypes can be mapped to genotypes that comprise the coding regions of the circuit's transcription factors, as well as the non-coding regulatory regions that bind these factors. Recent modeling efforts have produced exhaustively-enumerated genotype-phenotype maps for small regulatory circuits, which have provided new insights into the design constraints of such circuits and the extent to which circuit phenotypes can be inferred from circuit designs. At the same time, advances in high-throughput sequencing technologies have facilitated the construction of empirically-derived, exhaustively-enumerated genotype-phenotype maps for an important subcomponent of transcriptional regulatory circuits: transcription factor-DNA interactions. In this talk, I will discuss these recent advances and how they have helped us to better understand how transcriptional regulatory circuits evolve

Sophie Pénisson, Université Paris-Est Créteil, France

A genealogical model for the ancestor paradox

Abstract

Thinking naively, the structure of a person's ancestor tree is a binary tree, implying that this person has 2^n ancestors n generations back. Such an exponential growth conflicts however with the steadily decreasing size of the worldwide population back in time. This apparent paradox is explained by shared ancestors, referred to as pedigree collapse. Indeed, when family members such as cousins marry, lines of ancestors merge and the number of individuals on their ancestral tree decreases compared to the binary tree of reference. We propose a stochastic model of the pedigree collapse, in the form of a random directed acyclic graph. We study the probabilities for couples to be cousins of a given degree (with a possibility of being related at multiple degrees) and the probability for a graph of having the desired diamond shape of a collapsed pedigree.

Yuriy Pichugin, Department of Evolutionary Theory, Max Planck Institute for Evolutionary Biology, Germany

Fitness correlation as a new indicative metric of transition in Darwinian individuality

(joint work with Eric Libby[1], Paul B. Rainey[2])

Abstract

One of the most fascinating events in the course of the evolution of multicellularity is the transition in individuality, when the focus of selection shifts from the cells inside a group to the group itself. Currently, there is no robust criteria dedicated to detect such a process. Existing methods used for this task such as Price equation or contextual decomposition are prone to mistakes and examples of their errors are known. However, the transition in individuality is likely accompanied by the fitness decoupling - situation when the higher-level fitness of groups becomes independent from the lower-level fitness of cells. In this study we develop the numerical measure of the fitness coupling/decoupling state of a population - fitness correlation metric. We apply our metric to a model of population under weak multilevel selection. We found that there is a stationary regime, in which fitness (de)coupling state is independent on the initial state and determined by the configuration of fitness gradients in the space of traits. We found the class of such configurations promoting transition in individuality. Our findings help to understand under which conditions multicellularity evolved, and the developed metric can be used to test whether a given natural or experimental population undergoes the transition in individuality.

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Andrew Pomiankowski, Centre for Mathematics and Physics in the Life Sciences and Experimental Biology and Department of Genetics, Evolution and Environment, University College London, UK

Sexual conflict over the inheritance of mitochondria

(joint work with Arunas L. Radzvilavicius[1,2], Nick Lane[1])

Abstract

Mitochondria are predominantly inherited from the maternal gamete, even in unicellular organisms. Yet an extraordinary array of mechanisms enforce uniparental inheritance, which implies shifting selection pressures and multiple origins. We consider how this high turnover arises using an evolutionary model in which control of mitochondrial transmission occurs either during spermatogenesis (by paternal nuclear genes) or after fertilization (by maternal nuclear genes). The model treats paternal leakage as an evolvable trait. Our evolutionary analysis shows that maternal control consistently favours strict uniparental inheritance with complete exclusion of sperm mitochondria, whereas some degree of paternal leakage of mitochondria is an expected outcome under paternal control. Competition between these two forms of control is inevitable, and explains the repeated evolution of novel mechanisms (both in spermatogenesis and the fertilized egg) that restrict the transmission of paternal mitochondria, as well as the prevalence of paternal leakage and frequent heteroplasmy

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Jörgen Ripa, Department of Biology, Lund University, Lund, Sweden

Speciation cube trajectories cluster around three modes of parapatric speciation

Abstract

Driving biological diversity, speciation is a central evolutionary phenomenon of long-standing scientific interest. Speciation processes may involve mating differentiation, ecological differentiation, and spatial differentiation. Recognizing that alternative speciation modes differ in the temporal order, causal relation, and relative importance of these three dimensions, we show how speciation processes can be visualized as trajectories through the corresponding three-dimensional cube. We use the latter to analyze speciation dynamics in a two-patch eco-evolutionary model across a wide range of ecological and genetic conditions, reporting the following findings. (i) Speciation-cube trajectories cluster around three speciation modes. (ii) Increasing dispersal between patches causes these three modes of parapatric speciation to coalesce into a single mode of sympatric speciation. (iii) One of the three modes is characterized by a temporal peak in spatial differentiation, which increases at the beginning of the speciation process only to decrease again subsequently. (iv) The range of ecological conditions enabling speciation can be partitioned according to the three modes. (v) Our results are robust under a variety of changes in model structure and parameters. Underscoring the usefulness of speciation cubes for illustrating, comparing, and clustering speciation modes, our analyses elucidate how spatial segregation among incipient species can arise as an emergent property of speciation processes, instead of serving as their external driver.

Michael Sieber, Department of Evolutionary Theory, Max Planck Institute for Evolutionary Biology, Plön, Germany

Neutral Model of Microbiome Composition

Abstract

All animals and plants, from unicellular protists to mighty blue whales, are inhabited by diverse communities of microbial organisms. Those microbial lodgers form the microbiome of a host and they can have fundamental roles in host functioning. Understanding the processes that govern the assembly and maintenance of host-associated microbial communities are an important step towards understanding how different compositions of the microbiome affect host health and functioning. In particular, neutral models can help to disentangle the relative contributions of random processes (random birth, death and dispersal) vs. more deterministic selective processes. Divergence from the neutral null hypothesis can then point to microbes that may be positively or negatively selected for by the host. Here I will present results from the application of a neutral model to microbiome data from different host species and their respective environments, highlighting species-specific differences in the importance of random processes for the assembly of environmental and host-associated communities.

Yoav Soen, Department of Biomolecular Sciences, Weizmann Institute of Science, Rehovot 76100, Israel

Darwinian Selection Induces Lamarckian Adaptation in a Holobiont Model

(joint work with Osmanovic D[1], Kessler DA[1], Rabin Y[1,2])

Abstract

Current models of animal evolution focus on selection of individuals, ignoring the much faster selection of symbiotic bacteria. Here we take host-symbiont interactions into account by introducing a Population Genetics-like model of holobionts exposed to toxic stress. The stress can be alleviated by selection of resistant individuals (host and bacteria) and by secretion of a detoxification agent ("detox"). By defining a new measure, termed the '*Lamarckian*', we show that selection of resistant bacteria over one generation of hosts leads to stress-dependent increase in the tolerance of the hosts' offspring. This benefit is mediated by co-alleviation of toxic and physiologic stress. Prolonged exposure leads to further adaptation by 'group selection' of bacterial communities with higher detox per bacterium. These findings show that Lamarckian adaptation can arise via interactions between two levels of Darwinian selection within a holobiont system. The conclusions and modelling framework are applicable to diverse types of holobiont systems.

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Max O. Souza, Departamento de Matematica Aplicada, Universidade Federal Fluminense, Brazil

On the stochastic evolution of finite populations

Abstract

We will present systematic study of discrete Markov chains that are used to describe the evolution of a two-types population. Motivated by results valid for the well-known Moran (M) and Wright-Fisher (WF) processes, we define a very general class of Markov chains models which we term the Kimura class. It comprises the majority of the models used in population genetics, and we show that many well-known results valid for M and WF processes are still valid in this class. In this class, a mutant gene will be either fixed or eliminated, and we investigate when the fixation probability is increasing in the initial presence of mutants. We will show that an increasing fixation is equivalent to the process becoming strictly stochastically ordered in infinite time. In particular, under very mild assumptions the WF process might have non-monotonic fixation probabilities. As a by-product, we show that an increasing vector of fixation probabilities defines uniquely an M or WF process which realises it, and that any fixation probability with no state having trivial fixation can be realised by at least one WF process. If time allows, we show how the results can be extended to a subclass of processes that are suitable for describing time-inhomogeneous dynamics. This is joint work with F. A.C.C. Chalub.

Michael Stich, Mathematics, Aston University, Birmingham, UK

Replicator dynamics on an RNA fitness landscape

Abstract

The map from RNA sequence to secondary structure has been studied intensively as an example of a relatively simple, yet sufficiently complex genotype-phenotype map. Based on this map, fitness functions can be defined and the resulting evolution of a replicating population can be studied. We review some basic properties of such systems and consider some recent results with focus on recombination as way to create diversity within the evolving population. In particular, we consider two situations: first, a population constrained to a neutral network (sequences folding into the same secondary structure). The rules of recombination determine the topological properties of the network which are, however, different from those of a mutational neutral network. Second, we consider a population able to explore the whole sequence space and subjected to a more complicated fitness function.

Ewa Szczurek, Institute of Informatics, Faculty of Mathematics, Informatics and Mechanics, University of Warsaw, Poland

Modeling metastasis formation and its bottleneck

(joint work with Tyll Krüger[1], Barbara Klink[2] and Niko Beerenwinkel[3])

Abstract

Metastasis formation is a complex process in which cancer cells spread from their primary tumor of origin to distant organs where they initiate new tumors. However, only a tiny fraction of disseminating tumor cells succeeds in establishing a stable colony. There is evidence that while the early steps of this process, including release to the vascular system and infiltration of the secondary organ are efficient, the bottleneck is the initial expansion of the metastatic colony in the new environment. Here, we study this rate-limiting step of metastasis initiation in a quantitative fashion using a size-dependent branching process model. Our model adds to a systematic understanding of metastasis formation and may help defining medical intervention strategies.

We are able to compute the probability of metastatic colony survival and derive critical colony sizes under plausible initial growth assumptions. Using established models of primary tumor growth together with our metastasis initiation model, we further obtain the probability of metastatic invasion and expected patient survival given the tumor size. These models fit well to epidemiological data collected for fourteen cancers, were validated with independent datasets, and used to predict the impact of treatment delay and various treatment strategies on the risk of cancer death.

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Omri Tal, Max Planck Institute for Mathematics in the Sciences, Leipzig, Germany

A new perspective from information theory on properties of genetic sequences

(joint work with Tat Dat Tran[1], Jim Portegies[2])

Abstract

There has recently been growing interest at borrowing both concepts and technical results from information theory for analysis in the biosciences. Here we reveal deep conceptual and quantitative links between features of population genetic samples and a core information-theoretic property. In essence, long stretches of genetic variants may be captured as 'typical sequences' of a *nonstationary source* modelled on the source population. We introduce the concepts of typical genotypes, population entropy rate and mutual typicality, and their relation to the *asymptotic equipartition property*. The interplay of typical genotypes from differing populations and their geometric properties in high dimensional space will provide motivation for constructing simple typicality-based population assignment schemes. We will describe an analogy between a communication channel and an inferential channel, with 'noise' resulting from fuzzy population boundaries and allele frequency estimation, and where *inferential channel capacity* can be modelled on multilocus *informativeness*.

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[2]Eindhoven University of Technology, the Netherlands

Philipp Thomas, Department of Mathematics, Imperial College London, UK

Single-cell histories in growing populations: relating physiological variability to population growth

Abstract

Cell size and individual growth rates vary substantially across genetically identical cell populations. This variation cannot entirely be explained by asynchronous cell division cycles, but also needs to take into account the differences in the histories that cells experience during their lifespan. We describe a stochastic framework to characterise cell size histories in an exponentially growing population. We show that these histories differ from cells observed in isolation, such as observed in mother machines. Quantifying these historical fluctuations allows us to predict the population growth rate. We highlight that the maximum attainable population growth cannot exceed the rate at which an average cell grows, but the population doubles faster than an average cell doubles its size. We validate this prediction using recent single-cell data. The theory thus provides fundamental limits on population fitness in terms of individual cell properties.

Christopher J.R. Turkington[1,2], University of Leicester

The role of a hypermutable bacteriophage receptor on survival of *Haemophilus influenzae* to challenge by bacteriophage HP1c1

(joint work with Andrey Y. Morozov[3], Martha R.J. Clokie[2], and Christopher D. Bayliss[1])

Abstract

Bacterial populations must regularly contend with volatile environmental conditions to survive. As such, bacteria have evolved genetic mechanisms that provide a means of 'molecular bet-hedging', genetically pre-empting the population with contingencies for times of adversity. Phase variation, the stochastic, high frequency, reversible alteration in gene expression is one such mechanism that facilitates the constant generation of phenotypic variants within hypermutable regions of the bacterial chromosome termed 'contingency loci'. Such loci are believed to have arisen due to unpredictable oscillatory environmental selection pressures, such as the presence of the viral predator of prokaryotes, the bacteriophage. Here we show that localised hypermutation of one loci in *Haemophilus influenzae, lic2A*, may facilitate the control of the density and dissemination of bacteriophage through the bacterial populations. This evidence may signify that mechanisms of localised hypermutation do not only serve as a means of generating bacteriophage resistant cells that survive the viral attack, but can also provide a form of bacterial 'herd immunity' with the resistant members of the population acting as a barricade to reduce the viral load faced by the sensitive sub-population. We found experimentally, and through generation of a mathematical model that the population heterogeneity generated by phase variation could alter the survival probabilities of the bacteriophage population. Novel experimental protocol will be shown that facilitated modelling of bacteriophage expansion within these heterogeneous populations. Our results signify the likely key role mechanisms of localised hypermutation, such as phase variation, may play in dictating bacteriophage proliferation and generating the diversity in bacteriophage densities seen across nature. Moreover, our observations suggest that the requirement to face fluctuating viral predation pressures is likely a significant driver of evolution of such hypermutable contingency loci.

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High-dimensional brain: a blessing or a curse?

(joint work with Alexander. N. Gorban, Mathematics, University of Leicester)

Abstract

Human brain is arguably amongst the most sophisticated and enigmatic nature creations. Its processing power is unprecedented, and it contains massive number of neurons making its physical and mathematical description extremely high-dimensional and complicated. One of its mysterious puzzles is the well-known and documented phenomenon of Grandmother Cell [1,2]. A related phenomenon is the so-called Concept Cell that is believed to constitute a building block of declarative memory functions [3]. Some neurons respond unexpectedly selective to particular persons or objects. Not only brain is able to respond selectively to "rare" individual stimuli but also such selectivity can be learnt very rapidly from limited number of experiences [4]. The question is: Why small ensembles of neurons may deliver such a sophisticated functionality reliably? On the other hand, the need for the reliable responses to isolated stimuli with rapid learning capabilities is evident in the realm of artificial neuronal networks.

To date artificial neural networks (convolutional networks, deep learning networks, residual networks, cascades etc. [5]) are capable of solving visual recognition tasks with success rates similar to or exceeding that of human experts. Yet these networks are known to make "non-human" mistakes, and their training to recognize new stimuli takes significant amount of time. The problem is: How to correct these mistakes and learn new individual images from the first presentation? Answers to these puzzles can be found in the theory of measure concentration.

The theory of measure concentration is rooted in the Maxwell and Gibbs research in statistical physics but its mathematical development is boosted by recent research by Gromov, Talgrand and Milman [6]. These recent results give us proper framework for solving both groups of problems: biological and technical. Our novel stochastic separation theorems state that with high probability in high dimension and in an arbitrary set of random points any point can be separated by one formal neuron from the rest of the set. The efficiency of such separation drastically increases if one neuron is replaced with a small ensemble. In this ensemble, significant number of connections can be chosen at random. These additional ensembles are not only small but also sparse, with relatively small number of connections, and this finding conforms to biological discoveries [3,7]. These new theoretical results have been implemented in a technical system for visual object detection. It corrects "non-human" mistakes of pre-trained Convolutional Neural Networks [8].

Testing and validation results are provided. In the proposed paper we analyse and outline open biological and technical problems on reliable and fast learning of objects, present the mathematical solution for some of these problems in the manner accessible to broad readership of the journal, detail its implementation, and provide results of validation and testing.

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How organismal complexity affects evolutionary diversification

(joint work with Claus Rueffler[1])

Abstract

Evolutionary branching points are increasingly recognized as an important concept explaining the origin and maintenance of biological diversity. They arise in many mathematical models in which fitness is derived from explicit ecological scenarios accounting for frequency-dependent interactions. Existing theoretical results are mostly restricted to models assuming a single evolving quantitative trait. This is biologically very unrealistic. Organims are complex and consist of many co-evoling traits. If we are to understand the true significance of evolutionary branching points we have to increase the realism of our models. Here, we analyse under what circumstances a predator population feeding on two prey species experiences disruptive selection at an evolutionary branching point. In contrast to previous studies, we consider the simultaneous evolution of three traits involved in the feeding process. We find that (i) the critical trade-off curvature that separates alternative evolutionary outcomes depends on whether one considers traits evolving in concert or in isolation, (ii) traits that do not show branching when considered alone do so when they co-evolve, and (iii) with multidimensional trait spaces, whether or not branching occurs can depend on the mutational process. We conclude that accounting for organismal complexity has significant effects on the qualitative model predictions.

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Aurélien Velleret, Mathematics, Aix Marseille Université, France

Quasi-stationary distributions for a model of populations adapting to a changing environment

(joint work with M. Kopp[2] and E. Pardoux[1])

Abstract

In this presentation, I will investigate how the stochasticity in the emergence of new mutations affects the dynamics of adaptation in a population subject to long-term gradual environmental change. Unlike in classical adaptive dynamics, individual mutations will have non-infinitesimal effects that a conditioning (i.e., natural selection) can filter, and be sufficiently rare so that environmental change can lead to observable maladaptation. Due to this maladaptation, the population is expected to reduce in size, leading to increased extinction probability and a lack of diversity (since fewer mutations occur).

Following [1] and [2], we implement this model by means of a trait substitution process coupled to a a Feller logistic diffuusion for the size of the population :

$$(S)\begin{cases} X_t = x - vt + \int_{[0,t]\times\mathbb{R}\times\mathbb{R}_+} \omega 1_{\{u\le f(N_s)\times g(X_{s^-},\omega)\}} M(ds,d\omega,du) \\ N_t = z + \int_0^t \left(r(X_s)N_s - c_p(N_s)^2\right)ds + \sigma\int_0^t \sqrt{N_s}dB_s, \end{cases}$$

where N_t describes the size of the population and X_t the gap between its current phenotype and its optimal value given the environment that changes at speed v. With M a Poisson Point Process of intensity $ds\ v(d\omega)du$, the rate of appearance and fixation of new mutations of effect size ω is given by the measure $f(N_x)g(X_{s^-},\omega)v(d\omega)$. It is independent of the Brownian Motion B that governs N, and the maladaptation effect appears in the fact that the growth rate $r(x)$ is decreasing with$|x|$.

Since extinction of the population is almost sure, we will investigate the dynamics of the joint distribution of population state and size conditioned on survival. I intend to present some elements for the proof that this distribution converges with some exponential speed - independent of the initial condition - towards some unique quasi-stationary distribution (QSD), in the case where maladaptation is bounded (by extinction). This is especially non trivial because it combines a jump process for adaptation to a diffusive process for the size of the population. The method developed in [3] will be the keystone for this proof.

Let's just mention two parameters of great ecological relevance : the exponential rate of extinction λ_0 of the QSD and the exponential rate ς of convergence towards this QSD. Mainly, if $\varsigma >> \lambda_0$, convergence will usually occur before extinction, such that the inuence of the initial condition vanishes. In contrast, if $\varsigma << \lambda_0$, extinction will be quick and mainly depend on the initial condition.

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The learning principles of evolution by natural selection

Abstract

The equivalence between evolution by natural selection and simple mechanisms of reinforcement learning is well-recognised; but conventional evolutionary models suggest only very simple forms of learning. Specifically, the conventional model describes a Darwinian machine – i.e., heritable variation in reproductive success - that assumes fixed mechanisms of variation and selection operating on a fixed reproductive unit. This neglects significant extensions in current evolutionary theory. In fact, none of these mechanisms is fixed in nature. For example, the distribution of phenotypic variation changes over evolutionary time as a result of the evolution of development (evo-devo), the selective pressures on traits change as a result of the evolution of ecological interactions (evo-eco), and even the identity of the evolutionary unit changes as a result of the evolution of new reproductive strategies and new mechanisms of inheritance ('evo-ego'). Our recent work shows that when the evolution of such developmental, ecological and reproductive organisations is taken into account the model space (and therefore the type of inductive bias) that is implicit in natural evolution is much richer than previously realised. Specifically, natural evolution can learn how to evolve better with experience by acting on its own mechanisms of variation, selection and inheritance. This means that biological evolution is capable of rather more sophisticated types of learning, corresponding to well-known types of connectionist learning (including associative, unsupervised and deep learning). This finding helps to make sense of some hot topics in current evolutionary theory (e.g. the evolution of evolvability and evolutionary transitions in individuality) and suggests that the adaptive capabilities of natural evolution are significantly more advanced than the conventional concepts of incremental improvement via blind variation.

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Gene networks accelerate evolution by fitness landscape learning

(joint work with John Reinitz[1], Sergey Vakulenko[2], Dmitri Grigoriev[3])

Abstract

We consider evolution of a large population, where fitness of each organism is defined by many phenotypical traits. These traits result from expression of many genes. We propose a new model of gene regulation, where gene expression is controlled by a gene network with a threshold mechanism and there is a feedback between that threshold and gene expression. We show that this regulation is very powerful: depending on parameters we can obtain any functional connection between thresholds and genes. Un- der general assumptions on fitness we prove that such model organisms are capable, to some extent, to recognize the fitness landscape. That fitness landscape learning sharply reduces the number of mutations necessary for adaptation and thus accelerates of evolution. Moreover, this learning increases phenotype robustness with respect to mutations. However, this acceleration leads to an additional risk since learning procedure can produce errors. Finally evolution acceleration reminds races on a rugged highway: when you speed up, you have more chances to crash. These results explain recent experimental data on anticipation of environment changes by some organisms.

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Benjamin Werner, Institute of Cancer Research London, UK

Detecting truly clonal alterations from multi-region profiling of tumours

Abstract

Modern cancer therapies aim at targeting tumour-specific alterations, such as mutations or neo-antigens, and maximal treatment efficacy requires that targeted alterations are present in all tumour cells. Currently, treatment decisions are based on one or a few samples per tumour, creating uncertainty on whether alterations found in those samples are actually present in all tumour cells. The probability of classifying clonal versus sub-clonal alterations from multi-region profiling of tumours depends on the earliest phylogenetic branching event during tumour growth. By analysing 181 samples from 10 renal carcinoma and 11 colorectal cancers we demonstrate that the information gain from additional sampling falls onto a simple universal curve. We found that in colorectal cancers, 30% of alterations identified as clonal with one biopsy proved sub-clonal when 8 samples were considered. The probability to overestimate clonal alterations fell below 1% in 7/11 patients with 8 samples per tumour. In renal cell carcinoma, 8 samples reduced the list of clonal alterations by 40% with respect to a single biopsy. The probability to overestimate clonal alterations remained as high as 92% in 7/10 patients. Furthermore, treatment was associated with more unbalanced tumour phylogenetic trees, suggesting the need of denser sampling of tumours at relapse.

Jonas Wickman, Integrated Science Lab, Department of Mathematics and Mathematical Statistics, Umea University, Umea, Sweden

Determining selection across heterogeneous landscapes: a perturbation-based method and its application to modelling evolution in space

(joint work with Sebastian Diehl[2], Bernd Blasius[3], Christopher A. Klausmeier[4], Alexey B. Ryabov[3], Ake Brannstrom[1,5])

Abstract

Spatial structure can decisively influence the way evolutionary processes unfold. Several methods have thus far been used to study evolution in spatial systems, including population genetics, quantitative genetics, moment-closure approximations, and individual-based models. Here we extend the study of spatial evolutionary dynamics to eco-evolutionary models based on reaction diffusion equations and adaptive dynamics. Specifically, we derive expressions for the strength of directional and stabilizing/disruptive selection that apply in both continuous space and to metacommunities with symmetrical dispersal between patches. For directional selection on a quantitative trait, this yields a way to integrate local directional selection across space and determine whether the trait value will increase or decrease. The robustness of this prediction is validated against quantitative genetics. For stabilizing/disruptive selection, we show that spatial heterogeneity always contributes to disruptive selection and hence always promotes evolutionary branching. The expression for directional selection is numerically very efficient, and hence lends itself to simulation studies of evolutionary community assembly.

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Posters

Omar Alzeley (Mathematics, University of Leicester, UK). On superstatistics of stochastics process with application to biology.

Nurdan Cabukoglu (Mathematics, University of Leicester, UK). "Smart" diffusion in predator-prey models.

Cai Yuhua (Department of Mathematics and Statistics, University of Helsinki, Finland**).** Resident-invader dynamics of similar strategies in a random environment.

Diana-Patricia Danciu (Institute of Applied Mathematics, Heidelberg University, Germany). Mathematical modelling of stem cell dynamics in fish.

Ayabina Diepreye (Department of Mathematics, Imperial College London, UK**).** Detecting disruptive sites in tuberculosis genome.

Halil I. Egilmez (Department of Mathematics, University of Leicester, UK) Mathematical modelling of the seasonal bacterial dynamics mediated by a temperature-dependent phage.

Ruili Fan (Department of Mathematics and Statistics, University of Helsinki, Finland**)** Virulence management in the short-term and long-term based on a model with explicit within- and between-host dynamics.

Hu Yue (Department of Genetics, University of Leicester, UK) Finding the association between multiple markers for detecting epistasis in complex traits.

Daniel Nichol (University of Oxford / Institute of Cancer Research (ICR)**)** Collateral Sensitivity is Contingent on the Repeatability of Evolution.

Davide Palmigiani (Università di Roma - La Sapienza (RM, Italy)) A rare mutation model in a spatial heterogeneous enviroment.

Cordula Reisch (TU Braunschweig, Institut Computational Mathematics, Germany) Chemotactical effects in reaction-diffusion equations for inflammations.

Timothy Russell (Royal Holloway, University of London, UK). A Dynamical Systems Model of the Recombination Hotspot Paradox.

Mattias Siljestam (Department of Ecology and Genetics, Uppsala University). Highly polymorphic loci through allelic division of labour: a mathematical model of heterozygote advantage

Hanna ten Brink (Faculty of Science, University of Amsterdam) Evolution of metamorphosis in species that change their diet over ontogeny.

Yu Uchiumi (Department of Evolutionary Studies of Biosystems, SOKENDAI University, Japan) Evolution of vertical transmission through self-restrained cell division of symbionts.

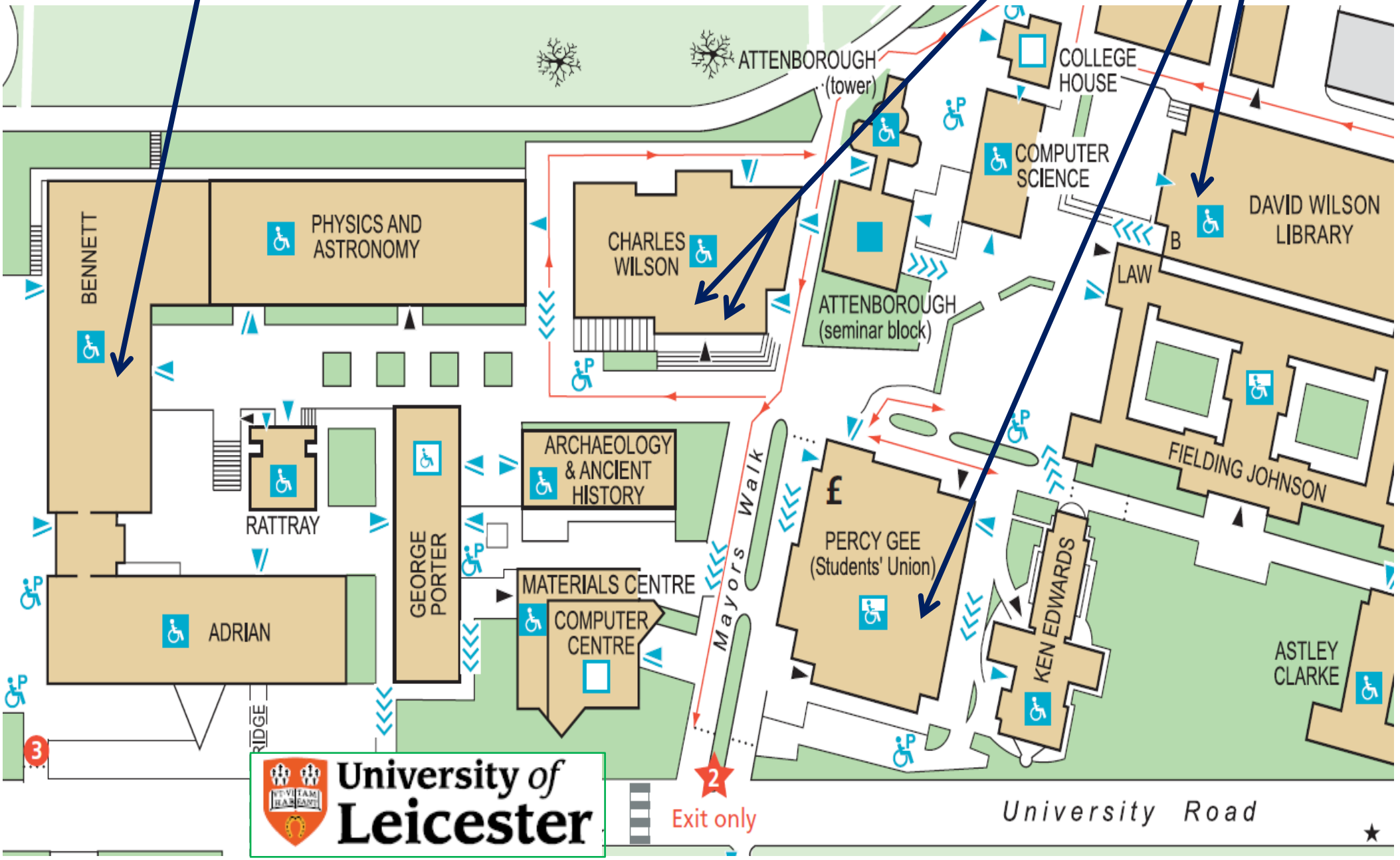
Vijay Kumar Shukla (Department of Mathematical Sciences, Indian Institute of Technology (BHU)). Transport of viscoelastic fluid through a diverging tube by peristaltic waves of varying amplitude: A mathematical model for hiatus hernia.

Christopher J.R. Turkington ([2]Department of Infection, Immunity, and Inflammation, University of Leicester**)** The role of a hypermutable bacteriophage receptor on survival of *Haemophilus influenzae* to challenge by bacteriophage HP1c1.

Main Campus Map

All talks are here! (Bennett)

Lunch suggestions!!!



Recommended places **to eat and drink** close to the conference site

Suggestions for lunch (on Campus)

Charles Wilson Building, ground floor: cafeteria Piazza (recommended) and the student canteen.

Charles Wilson Building, first floor: academic staff canteen (recommended)

Percy Gee Students' Union, Nineteen Twenty Three restaurant (recommended) and other cafeterias in the same building

The Library Building: cafeteria

Suggestions for dinner (off Campus)

Mumbai Inn (Indian food): the corner of London Road and De Montfort Street

Kayal (South Indian Restaurant: it is highly recommended!): in the beginning of Granby Street, near the train Station

La Tosca (Italian Restaurant), London Road, close to the Victoria Park (almost at the corner of London Road and Granville Road)

There is a really huge number and variety of restaurants and pubs in the city centre (and along London Road). You are encouraged to explore them by yourself!