BOOK ABSTRACT

Fourth Workshop
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DSABNS 2013

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Plenary Talks

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Fouth Workshop Dynamical Systems Applied
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Rural origin of the propagation of dengue, an urban disease, in Southeast Asia

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ABSTRACT

Dengue is the most important arboviral disease worldwide and a major public health problem in tropical areas. Knowledge of spatial and temporal patterns in dengue transmission at a sub-national level is relevant for two main reasons: it can provide insights into the biological and ecological mechanisms that drive transmission, and it may facilitate predictions of the magnitude, timing and location of future dengue epidemics. For both of these purposes I analyze, with wavelet analysis, phase analysis and Granger causality, the spatial-temporal pattern of propagation of dengue epidemics in different countries in Southeast Asia.

The results reveal spatial heterogeneity in the propagation of the annual epidemic. Each year, epidemics are highly synchronous over a large geographic area at regional scale. In most of the cases, travelling waves emanate from a few rural areas and move towards the regional capital where epidemics occurred 13 months later than elsewhere. These results clearly refute the main paradigm of urban origin of dengue propagation; urban centres are thought to act as a reservoir of the virus from where it can spread to the rest of the country. These findings constitute a new starting point in the understanding of the processes driving dengue spread and can aid the targeting of vector-control interventions and the planning for dengue vaccine implementation.

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Linking PK-PD of anticancer drugs with proliferating cell population dynamic models

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ABSTRACT

With the aim to optimise combinations of anticancer drugs, I will present models of proliferating cell dynamics coupled via external control targets, representing different drug effects, with pharmacological models of a few number of drugs that are of classical use in the clinic of cancers.

Cell population dynamic models are either systems of age-structured PDEs for the division cycle in cell populations or integro-differential equations structured in a continuous phenotype representing evolution towards drug resistance.

Pharmacological models are ODEs describing the fate of drugs in living organisms. Numerical optimisation algorithms used to design optimal combined drug delivery schedules in cell populations or at the whole body level, under toxicity or drug resistance constraints, will then be sketched.

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Interactions between serotypes of dengue highlight epidemiological impact of cross-immunity

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ABSTRACT

The immunological interactions between serotypes of dengue are of central importance in understanding epidemiological dynamics and anticipating the impact of dengue vaccines. Using novel mechanistic models to represent different hypothesized immune interactions between serotypes, we analyzed time-series of serotype specific incidence from multiple locations. We found strong evidence that infection with dengue provides substantial short-term cross-protection against other serotypes (roughly 1-3 years). Using dynamical models, I show the dynamical impact of cross-protection and estimated seasonality in transmission of dengue.

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Evolution in the bacterial, archaeal, and jawed vertebrate immune systems

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ABSTRACT

The influenza virus has a high evolution rate, which makes designing the annual flu vaccine challenging. A mismatch between the strain in the vaccine and the strain infecting the public leads to a less effective vaccine and broader infection in the population. A precise measure of how different the immune system perceives the vaccine and virus to be enables a better design of the flu shot. I will discuss a method to predict vaccine efficacy that we have developed. Data show that this method is at least as predictive as, and sometimes more so than, animal model studies. Interestingly, the immune system typically recognizes the $H1N1$ strain of the flu to a greater degree than the $H3N2$ strain, leading to better flu shots for $H1N1$ than $H3N2$. The evolution rate of $H1N1$ is also greater than that of H3N2, presumably due to greater pressure on the virus to evolve.

Dengue virus (DENV) infections result in an estimated 50 to 100 million cases annually. Since DENV is comprised of four related serotypes, an ideal vaccine would provide the basis for a simultaneous and balanced attack against all four viral variants. I will describe a theory of the immune response to DENV vaccines. I will use this theory to explain limitations in the vaccine for dengue fever and to suggest a transport-inspired amelioration of these limitations.

Clustered regularly interspaced short palindromic repeats (CRISPR) in bacterial and archaeal DNA have recently been shown to be a new type of anti-viral immune system in these organisms. I will discuss the diversity of spacers in CRISPR under selective pressure. I will propose a population dynamics model that explains the biological observation that the leader-proximal end of CRISPR is more diversified and the leader-distal end of CRISPR is more conserved. I will show this result to be in agreement with recent experiments. The results show that the CRISPR spacer structure is influenced by and provides a record of the viral challenges that bacteria face.

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Metabolic dynamics: acceleration during the life cycle of an individual

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ABSTRACT

We analyse the effects of the symmetry of a two-strain compartmental dengue fever model. The model is an extension of the classical compartmental susceptible–infected–recovered (SIR) model where the exchange between the compartments is described by ordinary differential equations (ODE' s). Two-strains of the virus exist so that a primary infection with one strain and secondary infection by the other strain can occur. There is life-long immunity to the primary infection strain, temporary cross-immunity followed by life-long immunity to the other strain after the secondary infection. Susceptible individuals can become infected with two different infection rates depending from whom they are getting the infection (preliminarily or secondarily infected). In the previously studied models [1,2] the two stains are assumed to be identical with respect to their epidemiological functioning: that is the epidemiological process parameters of the two strains are equal. As a result the mathematical model possesses a mathematical symmetry property. In this talk we study a variant with epidemiological asymmetry between the two strains: the force of infection rates differ for both strains while all other epidemiological parameters are equal. Numerical bifurcation analysis and simulation techniques including Lyapunov exponent calculation will be used to study the long-term dynamical behaviour of the model. The basic reproduction number R_0 threshold will be related to the existence of a transcritical bifurcation. Parameter values used are after [1] which are realistic for dengue fever. For the single-strain system stable endemic equilibria exist and for the two-strain system endemic equilibria, periodic solutions and also chaotic behaviour.

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primary and secondary infections: complex dynamics and its implications for data analysis. Journal of Theoretical Biology, 289:181–196, 2011.

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Metabolic dynamics: acceleration during the life cycle of an individual

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ABSTRACT

The life cycle of a typical multicellular organism has an embryo phase, which does not eat, a juvenile, which does not allocate to reproduction and an adult. Quantitative knowledge of this life cycle is key to population and ecosystem dynamics. Modelling the cycle requires the notion of metabolic memory as state variable of the individual conceived as a dynamical system, since an embryo grows, but does not eat. An egg (or seed) is energetically isolated from its environment; foetal development is a variation on this scheme.

To my knowledge, the Dynamic Energy Budget (DEB) model is the only one that can capture this full cycle. It has been applied to data on a wide variety of aspects of energetics of over 200 animal species in the add_my_pet collection; its goodness of fit is typically very high. Although the amount of data varies a lot among species, all parameters could be estimated using the covariation method.

A first observation on the add_my_pet collection is that a single set of parameter values actually captures the full cycle for many species. So the parameter values remain constant over the stage transitions, despite impressive morphological changes. This is remarkable, because DEB theory is based on simple physical and chemical principles and not aimed to be descriptive.

A second observation is that particular taxonomic groups seem to accelerate their metabolism temporarily during the cycle. Such an observation is only possible after having an quantitative expectation for the cycle without acceleration. I will discuss the various acceleration patterns and mechanisms, and discuss how acceleration turns out to be linked to other features of the life cycle.

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A general intro to DEB theory:
http://www.bio.vu.nl/thb/research/bib/Kooy2012.pdf

Add_my_pet in the electronic DEB laboratory:
http://www.bio.vu.nl/thb/deb/deblab

Covariation method for parameter estimation:
http://www.bio.vu.nl/thb/research/bib/LikaKear2011.html

Metabolic acceleration:
http://www.bio.vu.nl/thb/research/bib/KooyPecq2011.html
http://www.bio.vu.nl/thb/research/bib/Kooy2012b.html

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Quantifying the Risk of Malaria from Prevalence Data

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ABSTRACT

This work proposes a general model for vector-borne infections that is flexible enough to comprise the dynamics of some known diseases transmitted by arthropods. From equilibrium analysis we determined the number of infected vectors as an explicit function of the models parameters and the prevalence of infection in the hosts. From the analysis it is also possible to derive the Basic Reproduction Number and the equilibrium force of infection as a function of those parameters and variables. From the force of infection we can conclude that, depending on the diseases structure and the models parameters, it is possible to estimate a risk quantifier for those diseases. The analysis is exemplified by the case of malaria.

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Metabolic dynamics: acceleration during the life cycle of an individual

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ABSTRACT

Dengue disease is caused by dengue virus that includes four serotypes antigenically distinct viruses belonging to the family Flaviviridae. The viruses are transmitted by the prolific urbanized mosquito vector, Aedes aegypti. Dengue has become a major international public health concern and one of the most important arthropod-borne diseases. The majority of symptomatic cases are classified as Dengue fever (DF), an acute viral infection characterized by fever, rash, headache, muscle and joint pain, and nausea. Occasionally, DF progresses to dengue hemorrhagic fever (DHF), a potentially life-threatening illness associated with vascular leakage, haemorrhage, and shock. Escalations in the number of outbreaks and people involved have and the 'population-at-risk' is increasing yearly. More than 3.5 billion people (approximately 55% of worlds population) are at risk of dengue infection, including asymptomatic infections, which potentially increase the risk for the individual to develop severe disease following subsequent. It is estimated that every year, there are 70-500 million dengue infections, generating 36 million cases of DF and 2.1 million cases of DHF, with more than 20,000 deaths per year. This prolific increase has been connected to societal changes such as population growth, increasing urbanization generating intense agglomeration leading to proliferation of synanthropic species. In addition, it has been suggested that rising temperatures and global climate change may lead to the expansion of the range of major mosquito vectors into new areas, extension of the transmission season in areas with currently circulating dengue virus and increase in the mosquito species vectorial capacity. Human migration and international travel provide a continued source of virus (and potentially mosquito vectors), feeding the potential for invasion and eventual colonisation.

Despite this rapidly developing public health disaster, our knowledge of dengue epidemiology is rudimentary, with focus primarily on clinical dengue. A significant investment in gathering community-based data is, however, required to understand dengue

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epidemiology. The incontrovertible fact is that it is impossible to develop appropriate intervention strategies if the epidemiology is not understood. Here I will outline the recent progress in developing the necessary tools, highlight several key unknowns and benefit from the largely theoretical audience to urge increased collaborative efforts between empiricists and theoreticians to prioritise data acquisition.

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Resolving the interplay between climate forcing, transmission, host immunity and intervention measures in dynamic approaches to infectious diseases

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ABSTRACT

The full quantification of the mechanisms accounting for the coupling of climate to the dynamics of infectious diseases is poorly served by the scarcity of long-term time-series. At present there are less than twenty long-term data sets for infectious diseases from which we can construct predictive models for regional disease outbreaks. Shorter spatio-temporal records exist where the high spatial resolution can provide alternative valuable information on disease dynamics (e.g., Chikungunya outbreaks of Reunin island, and the recent cholera epidemic in Haiti). One way to quantify the influence of climate variability on rates of transmission relates to the reproductive number of an infectious disease and consists of examining changes in infection with host age and then predicting how climate-driven changes in transmission affect this relationship. Related quantities that consider only part of the transmission cycle by focusing on the vector, such as vectorial capacity and the critical density threshold of vector populations, have also been used to produce risk maps as a function of climate change. However, the population dynamics of cholera, malaria and other key water-borne, and vector-transmitted pathogens have the potential to resonate with both annual and longer-term climate cycles to produce more complex patterns of long-term epidemic behaviour. It has been recognized that the propensity of disease dynamics to oscillate with the waxing and waning of herd immunity in the host population, can place significant constraints on the ability to detect potential climate signals in time series records for important tropical diseases. Innovations in quantitative approaches have been developed to retrospectively disentangle the effects of endogenous disease dynamics, for example, as the result of herd immunity, vs. exogenous drivers such as climate variability. Lessons learnt may not transfer in a simple way to the case of vector-borne infections, because of the more complex transmission cycle as well as the more complex nature of immunity acquisition and loss that is intimately related to the antigenic diversity of the parasite. I will illustrate how decoupling occurs between incidence and climate forcing in a model

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of malaria transmission that incorporates parasite diversity in the form of superinfection. or alternately how the coupling can facilitate strain dominance in historic cholera pandemics. The interaction of control efforts with climate variability should be of particular relevance when intervention measures are implemented in response to previous increases in incidence, for example for residual insecticide spraying in desert malaria in NW India. A clear need manifests to develop a new class of semi-mechanistic models with limited parameters to minimize confounding effects of over-parameterization. Current approaches tend either to include a myriad of parameters that cannot realistically be specified in ordinary differential equations systems, or conversely, use over-simplistic statistical methodologies that are at most extrapolated, and provide little expectation of success in the future for different environmental ranges.

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Disease Extinction as a Dynamical System: Stochastic controls from single to multistrain epidemics

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ABSTRACT

The eradication or fade-out of infectious diseases is a penultimate goal for improving public health. In order to promote and design control methods, such as vaccination and social group quarantine, one must predict how the disease spreads probabilistically. However, modeling the dynamics of an outbreak includes many complicating features, such as deterministic and stochastic chaotic-like behavior. Such complicated dynamics can enhance the probability of extinction. In large populations, although extinction is a rare event, extinction will eventually occur.

In this talk, we show that the most likely path to extinction possesses a maximal sensitivity to initial conditions which is similar to local measures of chaotic behavior, and may be quantified by computing finite time Lyapunov exponents. As a result, the extinction path emerges naturally from the underlying dynamical geometry and may be constructed explicitly. The theory will be applied to several stochastic epidemiological models ranging from single to multistrain epidemic outbreaks. In addition, we will show how the theory of stochastic control may be applied to enhance the extinction process in single strain models, but may be deficient in multistrain models such as the control of dengue fever.

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Modelling and model evaluation on empirical data in epidemiology: dynamic noise, chaos and predictability

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ABSTRACT

Modelling and model evaluation on empirical data in epidemiology: dynamic noise, chaos and predictability

We revisit the parameter estimation framework for population biological dynamical systems, including Bayesian approach and model selection in simple analytic examples. Then we develop the computational framework for application to more complex and more realistic models.

When it comes to complex models like multi-strain dynamics to describe the virus-host interaction in dengue fever, even most recently developed parameter estimation techniques, like maximum likelihood iterated filtering, come to their computational limits. The subtle interplay between possible chaotic dynamics and dynamical noise are investigated, and applications mainly to influenza and dengue fever are shown.

Implications for predictability in such complex scenarios are discussed. Even though large fluctuations prevent long term prediction in most cases, short term predictability can be achieved in noisy data.

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Population models of mathematical ecogenetics

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ABSTRACT

Demographic systems of genetically distinguished interacting populations are proposed and investigated.
These ecosystems can coexist at suitable stable equilibria or through persistent oscillations.
A suitably defined parameter, the "invasion number", can be identified, that when exceeding a threshold destabilizes these equilibria.

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Invited Talks

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Maps in the Brain: encoding spatial information in neuronal activity

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ABSTRACT

The nervous system is, without hesitation, one of the most complex structures known to man. Neurons, the key structural elements of the nervous system, are cells specialized in processing and storing information, and the biophysical mechanisms exploited by neurons to fulfill these tasks are often sophisticated and ingenious.

In this talk I will explore in detail one important problem in theoretical neuroscience: the encoding and processing of spatial information in the hippocampus, a brain region part of the limbic system with and important role in spatial memory/learning and navigation. It is known that when a rat or mouse moves around in an environment, neurons in its hippocampus become strongly active only at specific locations of the environment. Collectively, these space encoding neurons provide a cognitive map of the animals location. I will present recently published work by our group where we use detailed biophysical models of neuronal dynamics to better understand some of the key mechanisms related to spatial information encoding in the hippocampus.

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Models for population growth in a randomly varying environment and the stochastic calculus used

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ABSTRACT

Autonomous stochastic differential equations (SDE) are commonly used to model the growth of populations in randomly varying environments. However, depending on the stochastic calculus used, different results are obtained both quantitatively and qualitatively. This fact compromises the application of such models. In previous papers we have considered It and Stratonovich calculi and have shown that the apparent difference between their results was due to the fact that the deterministic part of the SDE, interpreted as the average growth rate, was indeed representing different types of averages under the two calculi. If one takes into account the difference between the two averages, the results obtained under the two calculi are completely coincidental. In reality, besides these two calculi, there is a whole continuum of stochastic calculi which can be parameterized by a continuous parameter varying between 0 (It calculus) and 1, where $\alpha = 1/2$ corresponds to the Stratonovich calculus. Here we study this much more general situation. We also show that, in a certain sense, the Stratonovich calculus is more "natural".

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An agent-based model driven by tropical rainfall to understand the spatio-temporal heterogeneity of a chikungunya outbreak

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ABSTRACT

Vector-borne diseases, such as dengue, malaria and chikungunya, are increasing across their traditional ranges and continuing to infiltrate new, previously unaffected, regions. The spatio-temporal evolution of these diseases is determined by the interaction of the host and vector, which is strongly dependent on local social structures and mobility patterns. We develop an agent-based model, in which each individual is explicitly represented and vector populations are linked to local host and precipitation estimates in a tropical setting. The model is implemented as a scale-free network. The spatio-temporal transmission of chikungunya fever is demonstrated on this network and the presence of asymptomatic silent spreaders within the population is investigated in the context of implementing travel restrictions during an outbreak. Preventing the movement of symptomatic individuals is found to be an insufficient mechanism to halt the spread of the disease, which can be readily carried to neighbouring nodes via subclinically infected individuals. Public health interventions should attempt to identify such asymptomatic infected individuals to help control the spread of a chikungunya epidemic.

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Fractional? Where?

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ABSTRACT

The term fractional emerged in recent years in connection with different signal processing theories and techniques, sometimes with no visible connection between them. However, most are based on Fractional Calculus. The works of Mandelbrot on Fractals, that led to a significant impact in several scientific areas and attracted, definitively, the attention to fractional objects . Presently, new topics are the object of active research such as, fractional Brownian motion, discrete-time fractional linear systems, fractional delay filltering, fractional splines and wavelets. Moreover its applications in modeling natural and man made systems has been increasing. Several examples will be used to illustrate this affirmation. A brief introduction to the Fractional Calculus will be presented.

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Dengue in Urban Settings, the Belo Horizonte Experience

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ABSTRACT

We consider the dengue occurrence in the City of Belo Horizonte over the last fifteen years. Approximately 200,000 cases registered from 1996 to 2012 were analyzed. The home address of individuals whose dengue case was notified was used as a proxy for exposure location. For determining possible outbreaks of disease and the specific patterns of dengue cases, spatial statistics used included Kernels estimation. The occurrence of waves of dengue outbreaks were correlated with climatic and vector presence data. Outbreaks had different durations and intensities; case clustering, thinned out both spatially and temporally. This experience may be useful for public health professionals responsible for fighting the disease, providing some tools for improving evaluation of interventions such as vector control and patient care, minimizing the collective and individual burden of the disease.

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Contributed Talks

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Descriptive and Predictive models of dengue epidemiology: an overview

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ABSTRACT

We present a set of nested models to be applied to dengue fever epidemiology. The models are extentions of the basic SIR epidemic model, which consists of a set of classes representing parts of the population to be susceptible, infected and recovered individuals. The notion of at least two recurrent infections is needed to describe differences between primary and secondary infections. The processes of infection are described in uniform mixing approximation and immunity to a particular strain is assumed to be lifelong. The demography of the host population is also included, assuming constant population size. We perform a qualitative study in order to show how much complexity we really need to add into epidemiological models to be able to describe the fluctuations observed in empirical dengue hemorrhagic fever incidence data.

Key words: duengue fever, temporary cross-immunity, epidemiological models, chaos, predictability

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On the exact measure of the disease spread in stochastic epidemic models

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ABSTRACT

The basic reproduction number, R_0, is probably the most important quantity in epidemiology. It is used to measure the transmission potential during the initial phase of an epidemic. In this talk, we are specifically concerned with the quantification of the spread of a disease modelled by a Markov chain. Due to the existence of repeated contacts taking place between a typical infective individual and other individuals already infected before, R_0 overestimates the average number of secondary infections. We present two alternative measures, namely, the exact reproduction number, R_{e0}, and the population transmission number, R_p, that overcome this difficulty and provide valuable insight. The applicability of R_{e0} and R_p to control the disease spread is also examined.

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Control strategies for a stochastic model of host-parasite interaction in a seasonal environment

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ABSTRACT

We examine a nonlinear stochastic model for the parasite load of a single host over a predetermined time interval. We use nonhomogeneous Poisson processes to model the acquisition of parasites, the parasite-induced host mortality, the natural (no parasite-induced) host mortality, and the reproduction and death of parasites within the host. Algebraic results are first obtained on the age-dependent distribution of the number of parasites infesting the host at an arbitrary time t. We define control strategies based on isolation and vaccination of the host at a certain age t_0. This means that the host is free living in a seasonal environment, and it is transferred to an uninfected area at age t_0. In the uninfected area, the host does not acquire new parasites, undergoes a treatment to decrease the parasite load, and varies in its susceptibility to natural and parasite-induced mortality. Then, we investigate how the host will develop immunity to the parasite infection! in terms of the vaccination instant t_0 and various control criteria, which are based on simple probabilistic principles. The resulting control strategies can be thought of as evasive strategies in the terminology of helminth control technologies.

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Dynamic Energy Budget Theory: an Axiomatic Theory for Metabolism

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ABSTRACT

In contrast to what have been frequent statements in the ecological literature, DEB theory has shown that it is possible to obtain a unified mathematical theory for biology, similar to physical theories. At the same time, DEB has attained this aim by establishing a theory which is compatible with physical constraints, again something which is frequently disregarded in biology, thus ensuring Edwards Wilsons aim of consilience between the sciences.

Building on the axiomatic formalisation of DEB theory (Sousa, T., T. Domingos, S. A. L. M. Kooijman, 2008, From empirical patterns to theory: A formal metabolic theory of life, Philosophical Transactions of the Royal Society of London B 363: 24532464), here we show that DEB theory can be built from 1) the fundamental thermodynamic constraints that all processes obey mass and energy conservation but lead to entropy production, 2) a physical assumption of quite general applicability, that local flows are proportional to differences in intensive variables (and, hence, total flows are proportional to surface areas), 3) a biological assumption, that cells are metabolically very similar, independently of the organism or its size, and, 4) in a systems theory type of approach, an application of Occams razor, in always choosing the simplest possible formulation of a mathematical theory (minimize the number of state variables; choose linear over non-linear functions; minim! ize the number of parameters).

Having condensed DEB theory in this compact definition, we then show how these fundamental assumptions lead to the strong and weak homeostasis principles, and then to partitionability of reserve dynamics and the reserve dynamics itself. With this, we obtain the von Bertallanfy growth curve and Kleibers rule, for intra- and inter-specific comparisons.

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Capturing the impact of climate on Dengue using stochastic dynamical systems

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ABSTRACT

This work explores the potential role of climate in the variability of the amplitude of Dengue epidemics in Southe-East Asia. We use a multi-strain dengue model to capture differences between primary and secondary infections [1], and estimate variations of the time-varying effective contact rate in time. Partly, this contact rate reflects the concentration of mosquitoes that are the vector of dengue transmission and are subject to the influence of climate. Its trajectory over time is estimated using stochastic dynamical systems, using a recent methodology developed in [3], and contrasted with climatic data. Exact inference is conducted using recent algorithms as iterated filtering [4] and the particle MCMC [2], as one of the first applications of the inference methods library of the Public Library of Models in epidemiology (www.plom.io).

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Stochastic parabolic partial differential equations and the brain cancer

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ABSTRACT

In this paper a stochastic mathematical model is presented that describes the concentration of tumor cells of the brain. The treatment of the brain cancer is interpreted as a stochastic control problem. Evolution of the disease is characterized by a stochastic parabolic partial differential equation that describes the growth of a tumor brain.
While bio medical research concentrates on the development of new drugs and experimental and clinical determinations of their treatment schedules, the analysis of mathematical models can assist in testing various treatment strategies and searching for optimal ones.
Using the considered mathematical model, we try to solve medical problems in brain caner by using some stochastic numerical methods.

Key words: Optimal control, tumor cells,brain cancer, stochastic parabolic partial differential equations.

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On a exponential decay of the solution for a stochastic coupled system of reaction-diffusion of non-local type

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ABSTRACT

In this talk we investigate the existence and uniqueness of teh strong solutions for a stochastic nonlinear parabolic coupled system of reaction-diffusion of nonlocal type with multiplicative white noise. We prove the existence and uniqueness of strong solutions by the classical Faedo-Galerkin method, It?? formula and some technical ideas. An important result on the exponential decay of solutions is presented.

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The role of seasonality in vector-borne disease dynamics

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ABSTRACT

Dengue fever is a vector-borne infection which is distributed by the tropical and sub-tropical areas of the world. It is one of the main reasons of illness and death in this region. The main vectors of this disease are two mosquito species of genus *Aedes* (*i.e. Aedes aegypti* and *Aedes albipictos*). In recent years the disease has spreading to north and it is now in the gates of the Europe, with some endemic cases in France and Croatia and also the recent outbreak in Madeira Island, which shows the importance of the study of the dengue in order to prevent the this continuous spreading.

We have modelled the disease from the simple SIS to the SIR and also the incorporation of the mosquito dynamics into the systems, in the SISUV and SIRUV.

The mosquitos species are sensitive to the temperature, so the populations present seasonal fluctuations, so we made the infection rate β (in SIS and SIR) or the total number of mosquitos M (in SISUV and SIRUV) seasonally forced, via a cos function. As $cos(\omega t) = \frac{1}{2}(e^{i\omega t} + e^{-i\omega t})$ we defined the seasonally forcing as $\beta(t) = \beta_0 + \varepsilon\beta_1(e^{i\omega t} + e^{-i\omega t})$ for models with only human dynamics and $M(t) = M_0 + \varepsilon M_1(e^{I\omega t} + e^{-i\omega t})$ in model with the mosquito dynamics included. With that seasonally forcing, each state variable is defined by its mean value plus some small perturbations with a specific amplitude and phase. So, using ansatz and Taylor's expansion, we calculated the general solution for each variable with seasonal forcing included and we found out the values of the amplitude and the phase given by the seasonal forcing. Moreover, we compared the results obtained in the SIR and SIRUV model and we concluded that we would obtain the same result by replacing β by $\frac{\vartheta}{\nu}\beta$ in SIR model.

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The diffusion approximation for template coexistence in protocells

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ABSTRACT

Compartmentalization of self-replicating molecules (templates) in protocells is a necessary step towards the evolution of modern cells. However, coexistence between distinct template types inside a protocell can be achieved only if there is a selective pressure favoring protocells with a mixed template composition. Here we study analytically a group selection model for the coexistence between two template types using the diffusion approximation of population genetics. The model combines competition at the template and protocell levels as well as genetic drift inside protocells. At the steady state, we find a continuous phase transition separating the coexistence and segregation regimes, with the order parameter vanishing linearly with the distance to the critical point. In addition, we derive explicit analytical expressions for the critical steady-state probability density of protocell compositions.

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Evolution of n-species Kimura/voter models towards criticality, a surrogate for general models of accidental pathogens

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ABSTRACT

In models for accidental pathogens, with the paradigmatic epidemiological system of bacterial meningitis, there was evolution towards states exhibiting critical fluctuations with power law behaviour observed [1]. This is a model with many possibly pathogenic strains essentially evolving independently to low pathogenicity. A first and previous study had shown that in the limit of vanishing pathogenicity there are critical fluctuations with power law distributions observed, already when only two strains interact [2]. This earlier version of a two strain model was very recently reinvestigated [3] and named as Stollenwerk-Jansen model (SJ). Muñoz et al. demonstrated that this two-strain model for accidental pathogens is in the universality class of the so-called voter model. Though this model clearly shows criticality, its control parameter, the pathogenicity, is not self-tuning towards criticality. However, the multi-strain version mentioned above [1] is well evolving towards criticality, as well as a spatially explicit version of this, shown in [4] p. 155. These models of multi-strain type including explicitly mutations of the pathogenicity can be called SJ-models of type II [5]. Since the original epidemiological model is of SIRYX-type, the evolution to zero pathogenicity is slow and perturbed by large population noise. In the present article we now show on the basis of the notion of the voter-model universality classes the evolution of n-voter models with mutaion towards criticality, now much less perturbed by population noise, hence demonstrating a clear mechanism of self-organized criticality in the sense of [6, 7]. The present results have wide implications for many diseases in which a large proportion of infections is asymptomatic, meaning that the system has already evolved towards an average low pathogenicity. This holds not only for the original paradigmatic case of bacterial meningitis, but was reecently also suggested for example for dengue fever (DENFREE project).

Key words: stochastic processes, master equation, self organized criticality, power laws, bacterial meningitis

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Evolutionary game theoretical model for hermaphrodite gender conflict

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ABSTRACT

For hermaphrodite species, it arises a fundamental and fascinating question: is a hermaphrodite simply splitting its time between maximizing its reproductive fitness as a female and maximizing its reproductive fitness as a male, or is evolutionary fitness as a hermaphrodite optimized by an entirely different, longer-term strategy? This leads us to an evolutionary analysis of these species. More precisely, we suggest evolutionary game theoretical models to investigate on the effect of cost of changing from one sex to the other, of gamete production and male-male competition on sex role of the hermaphrodite. By mathematical and numerical analysis of the models, conditions on stability of the equilibrium state and the asymptotic behavior of the solutions were obtained and interpreted.

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A Comparison of a bidimensional SDE and VARMA model for forecasting mortality rates

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ABSTRACT

To explain mortality trends in human population and to predict its behavior in the medium / long term, we consider a cross-sectional analysis over time and assume that there are random environmental fluctuations that may explain the variability of the phenomenon. We applied, to each series of crude death rates (CDR) of the Portuguese population, models of stochastic differential equations (SDE) and autoregressive and moving average models (ARMA) and noticed that there are similar patterns in the data (by age and sex). This suggests the application of multivariate models with a correlation structure.

Previously [1] we proposed a bi-dimensional stochastic Gompertz model (BSGM) with correlated Wiener processes by sex, for each considered age. Now we present a multiple time series analysis (starting with bivariated case and first order vector autoregressive compound: a VAR(1) model) and compare the performance of the two models, with respect to forecasting, using mortality data of the Portuguese population (1940 to 2009).

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Spread of infectious diseases in large geographical areas

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ABSTRACT

The spread of infectious diseases is driven by the interplay of two factors: mobility of individuals and transmissibility of the disease. Our research focuses on the study of disease spread in geographically detailed populations, in particular on the study of stochastic amplification. We study an SIR model with demography where disease transmission at a distance is mediated through human mobility. We describe human mobility using the radiation model recently introduced by Simini et al. [F. Simini et al., Nature, 484, 96100 (2012)], and report some of our preliminary results.

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Life Engine – Modeling the individual, the population and the ecosystem using a biological engine

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ABSTRACT

The Life Engine project is a partnership between Instituto Superior Tcnico and Biodroid, a videogame company. The project aims at building a software tool package for modeling organisms in an ecosystem, with the double purpose of being used by video game companies to enhance the realism of videogames and being used by the scientific community for simulation of organisms, populations and ecosystems. The Dynamic Energy Budget (DEB) theory is a theoretical framework that enables the modeling of the dynamics of an organism, including assimilation, growth, maintenance and reproduction through its entire life cycle. This makes it the most adequate for the purpose of this project. In most cases DEB users have applied the Standard DEB Model (SDM) to the organism they want to simulate. SDM uses one substrate and defines an organism using two state variables: reserve and structure, and it can also have maturity, a reproduction buffer and a product. The Life Engine simulator uses DEBlib which is a C++ library that aims at modeling any organism using a generalized DEB model. Several other features beyond the SDM are already included using policies, which allows for the user of DEBlib to choose between different forms of modeling a given feature. For example, ageing can be computed with a DEB policy that includes the usual state variables for acceleration and hazard, but the user can also choose a policy where one can introduce a survival probability function to use in the simulation. Other included features are: transition between life stages controlled by a policy with the usual maturity state variable or a policy dependent on time; several policies for reproduction, including sexual and asexual reproduction, and reproduction by division, egg or foetus; and some assimilation policies that include a functional response given by a fixed function and predation of an organism by another. This library is to be used coupled w! ith other software that simulates the environment, such as Life Engine. The Life Engine system includes the simulator but also a DEB parameter database. This database allows for the user to include DEB parameters of organisms with different numbers of reserves, structures or other DEB state variables. It also allows the definition of trophic relations

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and the building of ecosystems for subsequent simulations. In this talk we present the Life Engine system and results for individual organisms and populations in an individual-based modeling (IBM) approach using DEBlib. The simulations will be based on realistic scenarios and will also aim to present the different features of DEBlib.

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Stability and Hopf bifurcation for a cell population model with state-dependent delay

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ABSTRACT

We propose a mathematical model describing the dynamics of a hematopoietic stem cell population. The method of characteristics reduces the age-structured model to a system of differential equations with a state-dependent delay. A detailed stability analysis is performed. A sufficient condition for the global asymptotic stability of the trivial steady state is obtained using a Lyapunov??Razumikhin function. A unique positive steady state is shown to appear through a transcritical bifurcation of the trivial steady state. The analysis of the positive steady state behavior, through the study of a first order exponential polynomial characteristic equation, concludes the existence of a Hopf bifurcation and gives criteria for stability switches. A numerical analysis confirms the results and stresses the role of each parameter involved in the system on the stability of the positive steady state.

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Mathematical models of West Nile Virus infection

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ABSTRACT

In this talk we present a mathematical model for the time evolution of the West Nile Virus epidemic. We use field data to show the general behavior of the infection dynamics and the existence of an endemic state. We show the impact of the seasonal variations on the outbreaks from this endemic state. Finally, we show some results on the role of the coexistence of different species of birds and mosquitoes on the prevalence of the infection.

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Superdiffusion and epidemiological spreading

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ABSTRACT

We generalized Laplace operator to super-diffusion using fractional calculus. We found the explanation how we can get the integral representation of the fractional Laplace operator from Fourier representation. We explain how we can solve the diffusion equation numerically using Fourier tranform and how we can generalize this method to solve superdiffusion equation. We did simulations in one and two-dimensional cases. We applied super-diffusion to epidemiological models, in which spreading happens with high propability for large distance. We considered stochastic spatially extended epidemiological systems, especially stochastic SIS model on the lattice and we extend this model to the superdiffusive case. We used integral representation of fractional Laplace operator in the Riemann-Liouville sense for adjacency matrix transition probablilities of the infection rate. For an analogous stochastic version of free diffusion we compared stochastic simulation with analytic expressions.

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Dynamic Equilibria and Coexisting Absorbing States in Asymmetric Adaptive Voter Models

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ABSTRACT

We generalize the adaptive voter model of [1] to investigate the asymmetric competition of two opinions in a structured population. Allowing for a coevolution of network topology and node states similar to [2], coexisting consensus states as well as an active phase are observed and described. In a model variant additionally allowing for network fragmentation as a frozen phase, the fragmentation configurations are characterized.

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The role of seasonality and import in a minimalistic multi-strain dengue model capturing differences between primary and secondary infections

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ABSTRACT

Our study focuses on a seasonally forced model with temporary cross immunity and possible secondary infection, motivated by dengue fever epidemiology. The notion of at least two different strains is needed in a minimalistic model to describe differences between primary infections, often asymptomatic, and secondary infection, associated with the severe form of the disease. We extend the previously studied non-seasonal model by adding seasonal forcing, mimicking the vectorial dynamics, and a low import of infected individuals, which is realistic in the dynamics of dengue fever epidemics. A comparative study between three different scenarios (non-seasonal, low seasonal and high seasonal with a low import of infected individuals) is performed.

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Stochastic epidemic model for dengue fever

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ABSTRACT

We developed a Leslie-type matrix model for the deepsea lantern shark Etmopterus spinax that occurs in the NE Atlantic on or near the bottoms of the outer continental shelves and slopes. This species is regularly captured as bycatch and discarded in deep water commercial fisheries. Given the lack of knowledge on the impacts of fisheries on this poorly known species, a demographic analysis is carried out considering uncertainties in mortality estimates and other available life history parameters. We conduct a Monte Carlo simulation study taking into account different scenarios with associated stochastic errors in the parameters. If only natural mortality is considered, even after introducing uncertainties in all estimated parameters, the estimated population growth rate () suggests an increasing population. However, if fishing mortality from trawl fisheries is considered, the estimates of usually indicate declining populations. In the later cases, the uncertainties in th! e species reproductive cycle seem to be particularly relevant, as a two year reproductive cycle seems to point to a stable population, while a longer (three year cycle) probably results in a declining population. Our elasticity analysis shows that survivorship parameters are in generally more sensitive for the younger age classes. This seems to be a typical result for larger sized and longer lived elasmobranch species, but highlights the vulnerability of this deep sea Squaloid to increasing fishing mortality. Although this is a small sized species, it shows population dynamics patterns more typical of the larger sized and more vulnerable species.

Keywords: Bottom trawling, deepsea fisheries; demographic analysis, fishing mortality; Leslie matrices; life cycles.

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Study of a stochastic epidemic model with the BSDE approach

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ABSTRACT

The interest is focused on studying the number of cases of infection in a population of K computers using the block-structured state-dependent event (BSDE) approach. The BSDE approach provides the possibility of considering non-exponential models with correlated flows, but keeping tractable the dimensionality of the underlying Markov chain. The work is inspired in the study of the number of recovered and infected individuals in the SIS scalar stochastic epidemic models. It considers an extension of a flow of external infections as well as the possibility of dealing with batch infection taking place when the infection initiated at an individual computer is immediately propagated to other computers of the network.

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Evolution towards critical fluctuations in a system of accidental pathogens

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ABSTRACT

We investigate the by now so called SJ model [1] not only in its simples formulation as recently used, but an extended version, the SJ model version II. In this we find the system to evolve to low pathogenicity causing large critical fluctuations without tuning the control parameter, a self-organization of critcality

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The influence of the vector Aedes aegypti in dynamics of the epidemiology of dengue fever

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ABSTRACT

The epidemic modelling has been used to know the evolution of diseases over the time, and allow to test different parameters in order to predict what will happen with the changes of the ecosystem. The Dengue is a caused by four serotypes of an arboviral virus. Like in other epidemies , the transmission of Dengue between people needs an vector, in this case is mosquito, *Aedes aegypti*, which bite people and pass the virus. In recent years has been verified an expantion of the ecological niche of the mosquito *Aedes aegypti* caused by the global changes and the facility of travelling between countries. So their expansion increase the risk of the Dengue to infect a new area. The proposal of this work is to study an epidemic model (SIRUV) which include the influence of the vector in the evolution of the Dengue. The study of SIRUV model was based on finding the stationary states and to plot and compare the deterministic and the stochastic model.

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Study of a stochastic epidemic model with the BSDE approach

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ABSTRACT

Discrete time models are used in Ecology for describing the evolution of an age-structured population. Usually, they are considered from a deterministic viewpoint but, in practice, this is not very realistic. The statistical model we propose in this article is a reasonable model for the case in which the evolution of the population is described by means of a projection matrix. In this statistical model, fertility rates and survival rates are unknown parameters and they are estimated by using a Bayesian approach.

Usual Bayesian and data cloning methods (based on Bayesian methodology) are applied to real data from the population of the Steller sea lions located in the Alaska coast since 1978 to 2004. The estimates obtained from these methods show a good behavior when they are compared to the actual values.

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Optimal control of a tuberculosis model

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ABSTRACT

We propose and solve an optimal control problem applied to a tuberculosis model. We show that optimal control measures ensure a reduction on the fraction of infected individuals.

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Stochastic epidemic model for dengue fever

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ABSTRACT

A SISUV epidemic model describes the evolution of a vector-borne desease considering the interaction between the vector and the host population. In case of Dengue Fever the main vector that transmits the virus is the *Aedes*' family mosquitos and the main hosts are humans. A stochatistic simulation shows as a deterministic one, that the dynamics of the vector is completely slaved by the one of the human because of their substantially different life span.

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