How Mathematics Illuminates Biology

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ORGANIZERS: Marta Tyran-Kamińska (*University of Silesia, PL)*, Michael C. Mackey (*McGill University, CA)*

Friday, July 6, 10:45–12:45, Medium Hall B

TALKS:

Fabien Crauste (*Université Claude Bernard Lyon, FR*), **Fighting the infection: analysis of a model of the CD8 T-cell immune response**

Wilhelm Huisinga (*University of Potsdam, DE*), **Intregrating cell-level kinetics into pharmacokinetic models to predict the effect of anti-HIV drugs in vivo**

Mirosław Lachowicz (*University of Warsaw, PL*), **A mesoscopic model of DNA denaturation**

Ryszard Rudnicki (*Polish Academy of Sciences & University of Silesia, PL*), **Piecewise deterministic processes in biological models**

Fighting the infection: analysis of a model of the CD8 T-cell immune response

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When confronted to an infection by a pathogen (virus, bacteria,etc.), the organism triggers an immune response. In particular, in human as well as most of living beings, a specific response, targeting the pathogen-specific antigen, can expand. Two main specific responses are observed, based respectively on B cells (humoral response) and T cells (cellular response). Apart from fighting the infection, the aim of specific responses is to generate memory cells, which will be able, when confronted for a second time to the antigen, to react faster and stronger. Hence, they participate to a better defense of the organism. We will consider a model of the T-CD8 immune response, describing activation of CD8 T cells, a subclass of T cells exhibiting cytotoxic abilities, and generation of memory CD8 T cells. These mechanisms are particularly important for vaccine design, and getting a better information on the development of the CD8 T cell response is a major issue for vaccine designers. The model will consist in a system of age-structured partial differential equations coupled with ordinary differential equations, describing evolution of CD8 T cell counts (with the description of different types of CD8 T cells: naive cells, effector cells, memory cells) and of pathogen count. The analysis of the model (existence and stability of steady states) will show that under certain conditions the pathogen can be eliminated and memory cells generated. Then, by confronting the model to experimental data, values of key parameters of the model will be estimated, and the relevance of the model for the understanding of cellular mechanisms involved in the CD8 T cell response will be discussed.

Intregrating cell-level kinetics into pharmacokinetic models to predict the effect of anti-HIV drugs in vivo

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A key step in the infection cycle of the human immunodeficiency virus type 1 (HIV-1) is the reverse transcription from the RNA to the DNA viral code, which is then integrated into the human cellular DNA. One important drug class in anti-HIV therapy, the so-called reverse transcriptase inhibitors, aims at inhibiting this process via competitive or allosteric binding. In this talk we demonstrate, how mathematical modeling provides the bridge between cell- based in vitro data and in vivo drug pharmacokinetic data to predict the inhibitory effect of reverse transcriptase inhibitors in vivo. The approach is illustrated for the drug zidovudine. A stochastic Markov chain-based model of reverse transcription is used to predict the effect of the drug. The slow-down of reverse transcription is quantified in terms of the increase in expected time to completion of reverse transcription. Model-based predictions not only allow for reproducing experimental pharmacokinetic data for various dosing regimes, but also allow for understanding why increasing doses will eventually lead to decreased efficacy, coming along with an increase in toxicity.

A mesoscopic model of DNA denaturation

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We propose a model that may describe some aspects of deoxyribonucleic acid (DNA) de- naturation process at the mesoscopic level. DNA denaturation is the process of separation of the two strands due to breaking of the hydrogen bonds. Such a breaking may occur under some condition like higher temperature. DNA thermal denaturation is called DNA *melting*. Various processes important for func- tioning of DNA as well as technological processes proceed through separation of the DNA strands.

Piecewise deterministic processes in biological models

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In my talk I am going to present two biological phenomena modelled by means of piecewise- deterministic processes: gene expression and blood cell dynamics. We study stochastic semigroups corresponding to these processes. The main result is asymptotic stability of the involved semigroups in the set of densities. The strategy of the proof of this result is as follows. First we show that the transition function of the related stochastic process has a kernel (integral) part. Then we find a set E on which the density of the kernel part of the transition function is positive. Next we show that the set E is a stochastic attractor. Then we apply results concerning asymptotic behavior of partially integral stochastic semigroups. We show that the semigroup satisfies the "Foguel alternative", i.e. it is either asymptotically stable or "sweeping". If the attractor E is a compact set then the semigroup is asymptotically stable.