Mathematical Immunology
Mathématiques en Immunologie
(Org: **Beni Sahai** (Cadham Provincial Laboratory) and/et **Robert Smith** (Ottawa))

CATHERINE BEAUCHEMIN, Los Alamos National Laboratory, Los Alamos, NM, USA
Characterizing T Cell Movement within Lymph Nodes

The recent application of two-photon microscopy to the visualization of T cell movement has presented trajectories of individual T cells within lymphoid organs both in the presence and in the absence of antigen-loaded dendritic cells. Remarkably, even though T cells largely move along conduits of the fibroblastic reticular cell (FRC) network, they appear to execute random walks in lymphoid organs rather than chemotaxis. Here, we will present results from our analysis of experimental trajectories of T cells using computer simulations of idealized random walks. Comparisons of simulations with experimental data provide estimates of key parameters that characterize T cell motion in vivo. For example, we find that the distance moved before turning is about twice the distance between intersections in the FRC network, suggesting that at an intersection a T cell will turn onto a new fibre about 50% of the time. Finally, recent, more detailed models from other groups will also be discussed.

DANIEL COOMBS, Department of Mathematics, University of British Columbia, Vancouver, British Columbia, V6T 1Z2
Virus competition and evolution at multiple scales

Viruses compete and are subject to natural selection at multiple levels: within-cell, within-host and within-population (of hosts). We examine how viruses can optimally exploit their hosts and how this behaviour may influence the most successful strategy at the between-host, or epidemiological level. I will present a fairly general way to consistently combine models of disease process and disease spread with the goal of understanding the net selection pressure on a model virus. The method is illustrated using two popular models at the within- and between-host levels.

VITALY GANUSOV, Utrecht University, Padualaan 8, 3584CH Utrecht, The Netherlands
Modeling CD8 T cell dynamics following acute and chronic viral infections

Mathematical modeling is a re-emerging field of current immunology. I review some of our work in which we have used mathematical models to address interesting questions in immunology. First, I show how simple models can be used to quantify and compare the dynamics of T cell responses following acute and chronic viral infections. Second, I will demonstrate how one can use models to discriminate between different hypotheses on the generation of memory CD8 T cells following an acute infection. Finally, I discuss how models can be used to investigate validity of a verbal hypothesis on whether and how cross-reactivity of memory CD8 T cells influences the rate of loss of immunological memory.

BENI SAHAI, Cadham Provincial Laboratory, Winnipeg, Manitoba, R3C 0Y1
A Basis for Immunological Protection from Death Upon Pandemic Influenza Infection

While infection with interpandemic influenza virus strains threatens survival among the elderly and other immunocompromised individuals, the infection with pandemic viral strains frequently proves fatal among immunocompetent adults. Although a precise reason for this contrast is not fully understood, the cause of death in the latter case is attributed to a cytokine storm triggered by the pandemic strains.

However, it is important to note that while an unacceptably large numbers of individuals die, a large majority of infected individuals do survive during each pandemic. It is unclear how the latter escape or survive virus-induced cytokine storm.

Understanding the basis for their survival may aid in designing strategies that could minimize the impact of influenza pandemics. To explore an immunological basis for survival, we devised a multidimensional mathematical model that monitors the dynamics of interaction between influenza virus and uninfected and infected respiratory epithelial cells, in the presence of innate and virus-induced adaptive immunities. The results of our simulations indicate that the rate of death of infected epithelial cells can be a major determinant of the course of disease and survival after infection with a pandemic viral strain. This rate may be affected by innate immunity, MHC make up of the individual, and any preexisting adaptive immunity.

ROBERT SMITH, The University of Ottawa, 585 King Edward Ave
Predicting the potential impact of a cyctotoxic T-lymphocyte HIV vaccine: how often should you vaccinate and how strong should the vaccine be?

To stimulate the immune system's natural defences, a HIV vaccination program consisting of regular boosts of cytotoxic T-lymphocytes (CTLs) has been proposed. We develop a mathematical model to describe such a vaccination program, where the strength of the vaccine and the vaccination intervals are constant. We apply the theory of impulsive differential equations to show that the model has an orbitally asymptotically stable periodic orbit. We show that, on this orbit, it is possible to determine vaccine strength and vaccination intervals so that the number of infected $CD4^+$ T cells remains below a maximal threshold. We also show that the outcome is more sensitive to changes in the vaccine strength than the vaccination interval and illustrate the results with numerical simulations.

DOMINIK WODARZ, University of California Irvine, Dept. of Ecology and Evolution, 321 Steinhaus Hall, Irvine, CA 92697
HIV coinfection, immunity, and virus evolution in vivo

It is commonly thought that virus evolution in vivo can contribute to or correlate with the progression of HIV infection from the asymptomatic phase towards AIDS. The virus evolves towards immune escape, increased replication kinetics, and a higher degree of cell killing, leading to the depletion of the T helper cell population.

Mathematical models of in vivo HIV evolution have been useful in shaping our understanding of the disease process. However, the models considered so far assume that one cell can only harbor one virus particle. Recent data, however, indicate that one cell can be infected by more than one virus particle, a process called co-infection. I will discuss a mathematical model that studies the effect of co-infection on HIV evolution in vivo and on the process of disease progression. This gives rise to some counter-intuitive insights that find some support in experimental data. It also gives rise to a theory for why natural SIV infection does not progress to AIDS despite the presence of high virus loads and high virus diversity in some cases.