

MARCH 3RD: MODELING IN BIOMATHEMATICS

Dr. Carlos Castillo Chavez, *Arizona State University*

Disease Transmission Dynamics in the Context of Rotavirus and Pneumonia Reported Infectious Data.

Efforts to evaluate the potential impact of vaccines in disease dynamics at the population level have led to questions tied in to the implementation of dynamical models, in response to available data. The use of Inverse problem techniques in disease specific contexts often generates new insights and conclusions. The recent implementation of two classes of rotavirus' vaccines, recent advances in efforts to generate effective pneumococcal vaccines and continuous efforts to understand the impact of cross-immunity on influenza dynamics provide the background for this presentation.

Souvik Bhattacharya, *University of Florida*

Density dependant predator prey model.

We consider a Lotka Volterra type predator prey model with size structure in prey. The prey birth and death rates are taken to be density -dependent. We find that the model has a unique extinction equilibrium which is l.a.s if the prey reproduction number is less than one and unstable otherwise. In addition we establish that the model can have multiple prey-only equilibria which have alternating stabilities if the predator reproduction is smaller than one and prey rate does not depend on size. Further we find that the model can have multiple predator-prey coexistence which may have alternating stabilities.

Brian J. Coburn, *University of Miami*

Multi-species Influenza Models with Recombination.

Avian influenza strains have been proven to be highly virulent in human populations, killing approximately 70 percent of infected individuals. Although the virus is able to spread across species from birds to humans, some strains, such as H5N1, have not been observed to spread from human-to-human. Pigs are capable of infection by both avian and human stains and seem to be likely candidates as intermediate hosts for co-infection of the

inter-species strains. A co-infected pig potentially acts as a "mixing vessel" and could produce a new strain as a result of a recombination process. Humans could be immunologically naive to these new strains, hence making them super-strains.

In this talk, I will introduce an interacting host system (IHS) for such a process that is formulated as a classical susceptible-infectious-susceptible (SIS) model with recombination. The model is used to give a new perspective for the trade-off hypothesis for disease virulence, by analyzing the behavior of a highly virulent super-strain. I will give permanence conditions for a number of the subsystems of the IHS in terms of basic reproductive numbers of independent strains. I will also show simulations of several relevant scenarios showing complicated dynamics and connections with epidemic forecasting.

Shurong Fang, *Michigan Technological University*

Incorporating multiple traits in genome-wide scans to find novel risk loci for rheumatoid arthritis.

An association study on a complex disease usually collects information on multiple traits. For example, there are one binary trait and two continuous traits in the rheumatoid arthritis dataset: RA status, AntiCCP and IgM. To incorporate multiple traits, we suggest a set of SNP-level F statistics by the concept of multiple-correlation to measure the genetic association between multiple phenotypic and SNP-specific genotypic scores and obtain their null distributions. To capture risk loci, we propose a combined genome-wide scheme to integrate multiple genome-wide one- and two-stage scans based on single, double and triple traits. Applying this scheme to the RA dataset, we successfully validate the genes which have been identified to be responsible for rheumatoid arthritis in the literature and detect more novel risk loci for follow-up studies. Each of the 22 autosomes is found to harbour susceptible genetic regions for rheumatoid arthritis.

Dr. Sergei Pilyugin, *University of Florida*

The Chemostat: What did we learn since 1950?

The mathematical study of the chemostat has begun after a formal description of this laboratory device was published by Novick and Szilard in 1950. Over the decades, the theory of chemostats, and more generally, of continuous microbial cultures has provided microbial ecologists with many useful insights and presented mathematicians with numerous questions to think about. In this talk, I will describe the general state of affairs in

the field, present some of the celebrated mathematical results, and discuss some open problems.

Kiranmoy Das, *Pennsylvania State University*

Parametric and nonparametric approaches to detect the QTL responsible for human growth in functional mapping framework with missing data.

In most of the medical or biological experiments, statisticians have to work with missing data. Several methods have been proposed yet to deal with missing observations in the data set. Here, we present a dynamic statistical model for explaining genetic pattern of growth based on individual genes that regulate human growth at different ages. Even when we have more than 50% missing observations, we incorporate mathematical equations into a framework for functional mapping aimed at identifying QTLs for the dynamic changes of this apparently simple but actually complex trait. Both, parametric and non parametric methods are implemented here to study the pattern of growth. We used "Legendre Polynomials" in the non parametric case to get the possible best pattern of human growth. The mathematical parameters are estimated by EM algorithm based maximum likelihood method. Our model provides a set of testable, biologically meaningful statistical hypotheses. Computer simulation was used to examine the statistical behavior of the proposed model.

Joseph Lucchetti, *University of Florida*.

An avian influenza model and its fit to human avian influenza cases.

Low Pathogenic Avian Influenza (LPAI) virus, which circulates in wild bird populations in mostly benign form, is suspected to have mutated into a highly pathogenic (HPAI) strain after transmission to the domestic birds. HPAI has recently garnered worldwide attention because of the "spillover" infection of this strain from domestic birds to humans - primarily those in poultry industry - causing significant human fatality and thus creating potentially favorable conditions for another flu pandemic. We use an ordinary differential equation model to describe this complex dynamics of the HPAI virus, which epidemiologically links a number of species in a multi-species community. We include the wild bird population as a periodic source feeding infection to the coupled domestic bird-human system. We also account for mutation between the low and high pathogenic strains. Finally, we fit our model to the actual number of avian flu cases obtained from WHO, and estimate the relevant reproduction numbers.

Juan B. Gutierrez, *Florida State University*

Contention of Mating Agents Using Trojan Chromosomes.

We present a strategy for contention and/or eradication of biological agents capable of mating, i.e. *mating agents*, whose spread can be modeled as a diffusion process. If intervention in the form of contention measures is introduced into the system, the questions that we will try to answer are: What are the conditions that guarantee success of contention measures against mating agents? What analytical test could we conduct in advance to predict the success or failure of contention measures? Particularly, we will study the use of Trojan chromosomes as a contention measure. The problem's complexity grows with the fact that geographic domains do not necessarily correspond to geometric domains of biological activity; we propose the use of diffusivity maps based upon a Karhunen-Loève transform of ecological features, in order to account for variable diffusivity in ecological domains at meso, topo and microscales.

Swati Debroy, *University of Florida*

Evaluating Treatment of Hepatitis C for Hemolytic Anemia Management.

The combination therapy of antiviral peg-interferon and ribavirin has evolved as one of the better treatments for Hepatitis-C. In spite of its success in controlling Hepatitis-C infection, it has also been associated with treatment related adverse side-effects. The most common among them is hemolytic anemia causing dose reduction or therapy cessation. The presence this side-effect leads to trade-off between continuing the treatment and exasperating the side-effects versus decreasing dosage to relieve severe side-effects allowing the disease to progress. A drug epoietin is often administered to stimulate the production of RBC in the bone marrow. We use mathematical models to study the effect of combination therapy in light of anemia. In order to achieve this we introduce RBC concentration and drug amount in the usual immunological virus infection model. Analysis of this model provides a quantification of the drug amount that is tolerable by the body without succumbing to hemolytic anemia. This also provides an estimate of the increment in RBC production necessary to sustain the entire period of treatment without encountering anemia.