Workshop on Analysis and Quantification of Noisy Effects in Biological Systems

Sponsor: **School of Mathematics and Statistics,**
Huazhong University of Science and Technology (HUST)
Wuhan, China

Time: **June 17 – 20, 2016**

Location: **Room 702 Science and Technology Building South,**
School of Mathematics and Statistics, HUST

主办单位：华中科技大学数学与统计学院

时间： 2016 年 6 月 17 – 20

地点： 华中科技大学数学与统计学院 科技楼 南楼 702

Co-organizers: **Xiaoying Han** (Auburn University, USA)
Peter E. Kloeden (HUST)
Fuke Wu (HUST)

Speakers

1. **Yusuke Asai** (Hokkaido University, Japan)
2. **Peter Bates** (Michigan State University, USA)
3. **Janet Best** (Ohio State University, USA)
4. **Peter Chesson** (University of Arizona, USA)
5. **Peter Hinow** (University of Wisconsin at Milwaukee, USA)
6. **Jinzhi Lei** (Tsinghua University, China)
7. **Ji Li** (HUST, China)
8. **Xiaoyue Li** (Northeastern Normal University, China)
9. **Zhenxin Liu** (Dalian University of Technology, China)
10. **Qing Nie** (University of California at Irvine, USA)
11. **Hong Qian** (University of Washington, USA)
12. **Stefanie Sonner** (University of Graz, Austria)
13. **Tianhai Tian** (Monash University, Australia)
14. **Jonathan Touboul** (Collège de France & Inria, France)
15. **Jianhong Wu** (York University, Canada)
16. **Ming Yi** (Huazhong Agricultural University, China)
17. **George Yin** (Wayne State University, USA)
18. **Qimin Zhang** (Ningxia University, China)
19. **Xue Zhang** (Northeastern University, China)
20. **Zhenzhong Zhang** (Donghua University, China)
21. **Yayun Zheng** (HUST, China)

Schedule

June 17, 2016 Friday		
Time	**Speaker**	**Title**
9:20 -- 9:30		Welcome Ceremony
9:30 -- 10:30	Qing Nie	Stochastic Dynamics and Robustness in Cell Signaling and Embryonic Development
10:30 -- 11:00		**Tea Break**
11:00 -- 12:00	Jonathan Touboul	TBA
12:15 -- 13:45		**Lunch: Buffet at Lu Yuan Restaurant**
14:00 -- 15:00	Stefanie Sonner	Nonlocal SDE-PDE Systems with Applications in the Modeling of Tumor Growth
15:00 -- 15:30	Ji Li	Chaotic Behavior in a Square Wave Bursting Model and Non-autonomous Perturbation
15:30 -- 16:00	Yayun Zheng	Transitions in a Genetic Transcriptional Regulatory System under Lévy Motion
18:00		**Dinner at Lu Yuan Restaurant**

June 18, 2016 Saturday		
Time	**Speaker**	**Title**
8:20 -- 8:30	Jun Wu	Welcome by the Head of School of Mathematics and Statistics, HUST
8:30 -- 9:30	George Yin	Quantifying Effects of Noise in Two Stochastic Models
9:30 -- 10:30	Tianhai Tian	Simplified Stochastic Models for Molecular Process of Multi-Step Reactions
10:30 -- 11:00		**Tea Break**
11:00 -- 11:30	Jinzhi Lei	Epigenetic State Transition in Stem Cell Regeneration
11:30 -- 12:00	Zhenxin Liu	Recurrent Solutions for Stochastic Differential Equations
12:15 -- 13:45		**Lunch: Buffet at Lu Yuan Restaurant**
14:00 -- 15:00	Peter Chesson	Environmental Fluctuations Are Not Noise in Ecology

15:00 -- 16:00	Hong Qian	Mathematical Models and A Theory of Biological Population Dynamics: From Cells to Ecology, Small and Large Systems
16:00 -- 16:30		**Tea Break**
16:30 -- 17:00	Xiaoyue Li	Switching Diffusion Logistic Models Involving Singularly Perturbed Markov Chains: Weak Convergence and Stochastic Permanence
17:00 -- 17:30	Ming Yi	Mathematical Modeling and Dynamical Analysis of Biological Network
18:00		**Dinner at Lu Yuan Restaurant**

June 19, 2016 Sunday

Time	**Speaker**	**Title**
8:30 -- 9:30	Jianhong Wu	Structured Population Models for Vector-Borne Infection Dynamics under Varying Environmental Conditions
9:30 -- 10:30	Peter Bates	TBA
10:30 -- 11:00		**Tea Break**
11:00 -- 11:30	Xue Zhang	Oscillation, Fluctuation Intensity and Optimal Harvesting of a Bio-Economic Model in a Complex Habitat
11:30 -- 12:00	Qining Zhang	Stability Analysis of Genetic Regulatory Network Models with Time-Vaying Delays and Reaction-Diffusion Driven by Markovian and Fractional Brownian Motion
12:15-13:45		**Lunch: Buffet at Lu Yuan Restaurant**
14:00 -- 15:00	Janet Best	TBA
15:00 -- 16:00	Peter Hinow	Ergodicity and Loss of Capacity for a Family of Concave Random Maps
16:00 -- 16:30		**Tea Break**
16:30 -- 16:00	Zhenzhong Zhang	Ergodicity for Stochastic Differential Equations Driven by Alpha-Stable Processes with Markov Switching
17:00 -- 17:30	Yusuke Asai	Numerical Methods of Random Ordinary Differential Equations and Parameter Estimation in Biology
18:00		**Dinner at Lu Yuan Restaurant**

June 20, 2016 Monday

9:00 -- 12:00 Tour at Buddhist Monastery (归元寺) and the Yangtze River

Abstracts

Numerical Methods of Random Ordinary Differential Equations and Parameter Estimation in Biology

Yusuke Asai, Department of Hygiene, Graduate School of Medicine, Hokkaido University, Japan

TBA

TBA

Peter Bates, Department of Mathematics, Michigan State University, USA

TBA

TBA

Janet Best, Department of Mathematics, Ohio State University, USA

TBA

Environmental Fluctuations Are Not Noise in Ecology

Peter Chesson, Department of Ecology, University of Arizona, USA and National Chung Hsing University, Taiwan

Variation in the physical environment is a feature of nature. Many scientific disciplines, however, focus on equilibria to define the properties to be expected of a system, and often treat environmental fluctuations as noise that disrupts or obscures equilibria. In ecology, temporal environmental fluctuations have often been thought of as providing a challenge that organisms face. On the other hand, spatial variation has often been regarded as providing opportunities for organisms—there is a place for every species to exist. I show that adaptations of organisms to temporal fluctuations allow them to take advantage of favorable times without suffering too greatly from unfavorable times. This means that temporal fluctuations can have roles similar to spatial variation by providing times sufficient to sustain many species. Far from being noise, these temporal fluctuations are required to explain the fundamental structure of a system, which is ill served by standard equilibrium ideas. Models demonstrating these outcomes can be viewed within the framework of nonautonomous dynamics, which provides concepts able to replace the traditional equilibrium notion with stable environmentally-dependent trajectories suitable also for a world of nonstationary environment change, which arguably the world is and has always been.

Ergodicity and Loss of Capacity for a Family of Concave Random Maps

Peter Hinow, University of Wisconsin at Milwaukee, USA

Random fluctuations of an environment are common in ecological and economical settings. We consider a family of concave maps on the unit interval, $f_\lambda(x) = x(1 + \lambda - x)$ that model a self-limiting growth behavior. The maps are parametrized by an independent, identically distributed random variable λ with values in the unit interval. We show the existence of a unique invariant ergodic measure of the resulting random dynamical system for arbitrary parameter distributions supported on certain subintervals of [0; 1]. Moreover, there is an attenuation of the mean of the state variable compared to the constant environment with the averaged parameter. We also provide an example of a family of just two maps such that the invariant probability measure is supported on a Cantor set.

This work has been supported by the grant "Collaborative Research: Predicting the Release Kinetics of Matrix Tablets" (DMS 1016214 and DMS 1016136) of the National Science Foundation of the United States of America.

Epigenetic state transition in stem cell regeneration

Zhijin Lei, Tsinghua University, China

Epigenetic state transition is an important stochastic events in cell cycling, and is important for stem cell regeneration. In this talk, I will introduce biological background of epigenetic state transition, and mathematical modeling of stem cell regeneration in terms of epigenetic state transition.

Chaotic Behavior in a Square Wave Bursting Model and Non-autonomous Perturbation

Ji Li, HUST, China

I will first describe the square wave bursting model, explaining why a smale horseshoe exists, which is the typical reason for the existence of chaotic switching of spike numbers. I will then unfold the model with a 2D non-autonomous ODE system, and explain possible mechanism for the chaotic behavior.

Switching Diffusion Logistic Models Involving Singularly Perturbed Markov Chains: Weak Convergence and Stochastic Permanence

Xiaoyue Li, Northeastern Normal University, China

Focusing on stochastic dynamics involve continuous states as well as discrete events, this talk focuses on stochastic logistic model with regime switching modulated by a singular Markov chain involving a small parameter. This Markov chain undergoes weak and strong interactions, where the small parameter is used to reflect rapid rate of regime switching among each state class. Two-time-scale formulation is used to reduce the complexity. We obtain weak convergence of the underlying system so that the limit has much simpler structure. Then we utilize the structure of limit system as a bridge, to invest stochastic permanence of original system driving by a singular Markov chain with a large number of states. Sufficient conditions for stochastic permanence are obtained. A couple of examples and numerical simulations are given to illustrate our results.

Recurrent Solutions for Stochastic Differential Equations

Zhenxin Liu, Dalian University of Technology, China

Recurrent dynamics (periodic, almost periodic, almost automorphic, Birkhoff recurrent, Poisson stable motions etc) play important roles in study of differential equations and dynamical systems. In this talk, we will report works on recurrent solutions for stochastic differential equations.

Stochastic Dynamics and Robustness in Cell Signaling and Embryonic Development

Qing Nie, Departments of Mathematics, Developmental and Cell Biology, and Biomedical Engineering, Center for Mathematical and Computational Biology Center for Complex Biological Systems, University of California Irvine

Noises and stochastic effects usually exist in every biological system due to many intrinsic and extrinsic factors. In this talk, I will discuss strategies and principles for noise attenuation and robustness to genetic or/and environmental perturbations in cell signaling and embryonic development. In one case, I will introduce a critical quantity that dictates capability of attenuating temporal noises in feedback systems. In another case, I will show that noise in signal transduction actually enables reduction of stochastic effects to play a beneficial role for better spatial embryonic patterns. In addition, I will present several new experimental data in yeast cells and zebrafish embryos that support our modeling and computational predictions.

Mathematical models and a theory of biological population dynamics: From cells to ecology, small and large systems

Qian Hong, Department of Applied Mathematics, University of Washington, USA

Complex dynamics of interacting populations of intrinsically stochastic individuals can be mathematically represented by a discrete-state, continuous-time Markov jump process. T. G. Kurtz's theorem establishes a relation between this stochastic process, in the limit of V tending infinity, and the traditional dynamical systems based on ODEs. We apply this theory to several problems in current cell biology in terms of the biochemical constituents, and illustrate the emergent notions of epigenetic phenotypes and their switching, and relation to the classical idea of phase transition. The mathematical origin of the latter in non-uniform convergence when time goes to infinity with respect to the parameter V is discussed, and a large deviations result based on WKB ansatz will be presented. We suggest some open questions and a set of computational issues as well.

Nonlocal SDE-PDE Systems with Applications in the Modeling of Tumor Growth

Stefanie Sonner, Karl-Franzens-Universität Graz, Austria

In nonlocal SDEs the sample paths of a solution can depend on the other sample paths. A special case is when coefficient functions contain expectation values of the solutions. The existence and uniqueness of solutions of such nonlocal scalar SDEs was established by Kloeden & Lorenz. Motivated by multi-scale models for acid-mediated tumor invasion, where stochastic effects are taken into account in subcellular processes, and where this intracellular dynamics is connected to the behavior of substrates and cells on the macro level, coupled systems of SDEs and PDEs were considered in Kloeden, Sonner & Surulescu.

We present results for the existence and uniqueness of solutions for general local and nonlocal SDE-PDE systems and discuss conditions ensuring their non-negativity and boundedness. As an application a micro-macro model for the proton dynamics in cancer cells is considered. If microscopic effects are averaged out on the upper scale, the reaction functions in the PDE contain expectation values of the SDE solution.

References:
[1] P. E. Kloeden and T. Lorenz, Stochastic differential equations with nonlocal sample dependence, *Stochastic Analysis and Applications*, **28** (2010), 937--945.
[2] P.E. Kloeden, S. Sonner and C. Surulescu, A nonlocal sample dependence SDE-PDE system modeling proton dynamics in a tumor, *Discrete Cont. Dyn. Syst. Ser. B*, to appear (2016).
[3] S. Sonner C. Surulescu and P.E. Kloeden, Stochastic micro-macro models for acid mediated tumor invasion, *YRS 2016 Proc.*, Fraunhofer Verlag (2016), 137--142.

Simplified Stochastic Models for Molecular Process of Multi-Step Reactions

Tianhai Tian, Monash University, Australia

Many molecular processes include detailed multi-step chemical reactions. Examples of such processes include gene transcription, translation, molecule degradation and metabolic synthesis process. For simplicity, these multi-step reactions are currently modelled by a single step reaction or chemical reaction with time delay. However, numerical results suggest that these simplified models cannot describe multi-step process accurately. In this work we will discuss two methods for modelling multi-step reactions. The first approach is the two-variable model by introducing the concept of length for indicating the position of molecules in multi-step reactions. The second method employs the state-dependent time delay, in which the value of time delay is determined by the system state.

TBA

Jonathan Touboul, Collège de France & Inria, France

TBA

Structured Population Models for Vector-borne Infection Dynamics under Varying Environmental Conditions

Jianhong Wu, York University, Canada

We review some fundamental frameworks and approaches to derive structured population models with varying developmental or spatial transition delays. We discuss how existing theories can be adapted to the need of qualitative analysis of the models incorporating climate changes, and we illustrate the usefulness of these mathematical adaptations in addressing some important public health issues such as avian influenza spread and vector-borne disease infection dynamics.

Mathematical Modeling and Dynamical Analysis for Biological Network

Ming Yi, College of Sciences, Huazhong Agricultural University

We will first give a simple introduction about mathematical modeling and dynamical analysis of biological network. Then two examples are further presented, including (i) the fluctuation and noise propagation in gene regulation motifs and (ii) the accuracy of cell fate decision under stochastic noise. Our results show that the structure of biological network plays a crucial role on the dynamics and function.

Quantifying Effects of Noise in Two Stochastic Models

George Yin, Department of Mathematics, Wayne State University, Detroit, MI 48202

In this talk, we reveal the noise effects of two stochastic models. The first one is concerned with a SIR epidemic model, whereas the second one deals with safeguarding biodiversity using protection zones. For the first model, we give sufficient conditions that are close to necessary for the permanence, develop ergodicity of the underlying system, and prove the transition probabilities converge in total variation norm to the invariant measure together with a precise characterization of the support of the invariant measure. For the second model, we answer the question how large a protection zone should be so that the species in both the protection sub-region and natural environment are able to survive. We do this by providing sufficient conditions that are sharp and close to necessary for permanence and extinction. Convergence to the invariant distribution in total variation norm and rates of convergence are also obtained.

Stability Analysis of Genetic Regulatory Network Models with Time-Varying Delays and Reaction-Diffusion Driven by Markovian and Fractional Brownian motion

Qining Zhang, Ningxia University, China

This paper conducts a stability analysis for comprehensive genetic regulatory network (GRN) models of mRNA and protein, which consider diffusion-reaction processes with fractional Brownian motion (fBm), Markovian jump, and time-varying delay. By constructing a new Lyapunov-Krasovskii functional and using Wirtinger's inequality and stochastic stability theory, the delay-dependent asymptotic stability criteria are derived in terms of linear matrix inequalities to achieve the global asymptotic stability in the mean square sense of the considered genetic regulatory networks. It is shown that the sufficient condition of asymptotic stability can be obtained as feasibility of linear matrix inequality (LMI) for the GRN models. Finally, an example is given to illustrate the effectiveness of the theoretical results.

Oscillation, Fluctuation Intensity and Optimal Harvesting of a Bio-economic Model in a Complex Habitat

Xue Zhang, Northeastern University, China

We investigate the effects of habitat complexity and multi-time delays on dynamics of a bio-economic predator-prey model. The differential-algebraic system theory is applied to transform the bio-economic model into a normal form, so that the local stability and existence of periodic solutions can be examined by varying the delays and the habitat complexity parameter. The direction of Hopf bifurcation and the stability of bifurcated periodic solutions are investigated. We discuss the effect of fluctuating environment on

dynamical behavior of a corresponding stochastic delayed-differential-algebraic system and derive expressions for intensities of population fluctuations. The model is also used to study the optimal harvesting strategy in order to maximize economic profit while sustaining the ecosystem.

Ergodicity for Stochastic Differential Equations Driven by alpha-Stable Processes with Markov Switching

Zhenzhong Zhang, Donghua University, China

In this talk, we first consider some criteria for ergodicity of stochastic differential equations driven by symmetric alpha-stable processes with Markov switching. Then convergence rates of some transition semi-groups to their invariant measures are discussed. Finally, several examples are presented to illustrate our results.

Transitions in a Genetic Transcriptional Regulatory System under Lévy Motion

Yayun Zheng, HUST, China

Based on the stochastic differential equation model of a single genetic regulatory system, we examine the dynamical effects of noisy fluctuations from the synthesis reaction, on the evolution of the transcription factor activator in terms of its concentration. The fluctuations can be modeled by Brownian motion and α-stable Lévy motion, respectively. Two deterministic quantities, the mean first exit time (MFET) and the first escape probability (FEP), are used to investigate the transition from the low to high concentration states. A shorter MFET or higher FEP in the low concentration region is in favour of transition. We have observed that higher noise intensities and larger jumps of the L\'evy motion reduce the MFET. The Lévy motion activates a transition from the low concentration region to the non-adjacent high concentration region, while Brownian motion cannot induce this phenomenon. There are optimal proportions of Gaussian and non-Gaussian noises, which maximise the quantities MFET and FEP for each concentration, when the total sum of noise intensities are kept constant. As the weaker stability indicates the higher probability for transition, a new geometric concept was introduced to quantify the basin stability of the low concentration region, which is characterised by the escaping behaviours.

Important Information

Workshop Contacts: Fuke Wu (Phone: +86-13657299548, Email: wufuke@hust.edu.cn)
Xiaoying Han (Phone: +86-18689869930, Email: xzh0003@auburn.edu)

Lodging: HUST International Academic Exchange Center, Building No. 8
(华中科技大学学术交流中心 8 号楼)

Meals: Lu Yuan Restaurant (绿园餐厅) June 17 – 20 breakfast starting from 7am, group lunch at 12:15 and group dinner at 18:00.

Documents required for reimbursements:

1. Copy of passport including first page, pages with visa, entry and departure stamps at Chinese custom. Please remember to bring your passport with you during the workshop; we will make the copies for you on site. You can scan and email your departure stamps to Xiaoying Han at xzh0003@auburn.edu or Fuke Wu at wufuke@hust.edu.cn after the trips are finished.

2. Brief Curriculum Vitae.

3. Receipts of flights and/or other transportations along with credit (or debit) card statements showing the payments of the expenses.

4. Boarding passes of all lags including incoming and return trips. You can scan and email your boarding passes for return trips to Xiaoying Han at xzh0003@auburn.edu or Fuke Wu at wufuke@hust.edu.cn after the trips are finished.

* *Please note that this is mandatory for all speakers; failing to provide all boarding passes will result in unsuccessful reimbursements.*

5. Chinese Bank account information (account number, account name, bank name, bank address) if you want your reimbursements to be direct deposited into your bank in China. Unfortunately we do not provide wire transfer to foreign banks; those who do not have a bank in China will get cash in RMB. Our assistants can help with the exchange at local banks if you need. Appointments have to be made at least 2 days in advance.

Directions to HUST:

（1）乘高铁到武汉站：可乘 513 路公交车（首车 06:30-末车 17:30）到珞喻路关山口下（华中科技大学南大门）。从武汉站乘出租车到华中科技大学南大门价位在 40 元人民币左右。
（2）乘火车到武昌站：可乘 593、510、518 路公交车到珞喻路关山口下（华中科技大学南大门）（车程约 50 分钟左右）。从武昌站乘出租车到华中科技大学价位在 30 元人民币左右。
（3）乘火车到汉口站：可乘坐 703 路公交车在珞喻路关山口下（华中科技大学南大门），从汉口站乘出租车到华中科技大学价位在 70 元人民币左右。或是坐地铁二号线到达光谷广场，再打的或步行到达华中科技大学
（4）乘飞机到武汉天河机场：乘坐机场大巴武昌线（武汉天河机场-傅家坡长途客运站）， 到傅家坡长途客运站下车，在傅家坡长途汽车站可乘 593、510、518、703、536 路公交车到省中医院站下车站过马路（华中科技大学南三门进直行 500 米苹果体验店左拐 50 米即到六号楼）下车（车程约 40 分钟左右）；或直接从付家坡长途汽车站出发坐出租车，约 30 元左右。

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