Hungary-Serbia
IPA Cross-border Co-operation Programme

Good neighbours creating common future

University of Szeged - UNS Faculty of Science Novi Sad

Non-Standard Forms of Teaching Mathematics and Physics: HUSRB/1203/221/024

Interdisciplinary Conference on

Modeling in Life Sciences

November 3, 2014

Bolyai Institute, University of Szeged

organized by

Bolyai Institute, University of Szeged

in the framework of

IPA HUSRB/1203/221/024 project
“Non-Standard Forms of Teaching Mathematics and Physics:
Experimental and Modeling Approach”

The project is co-financed by the European Union

The Host Institution:

Bolyai Institute, University of Szeged

www.math.u-szeged.hu

Bolyai Institute – the mathematical institute of the University of Szeged – was founded in 1921 by the two world-famed professors of mathematical analysis, Frigyes Riesz and Alfréd Haar. Since then, the institute has become one of the most important centers for mathematics in Hungary, where several internationally renowned researchers have been working. More than 50 mathematicians – including four members of the Hungarian Academy of Sciences – work in the six departments: Algebra and Number Theory, Applied and Numerical Mathematics, Analysis, Geometry, Set Theory and Mathematical Logic, and Stochastics. The institute has a mathematical library with about 50000 volumes. The distinguished international journal Acta Scientiarum Mathematicarum founded by Riesz and Haar, and several mathematical textbooks are published by the institute.

The IPA HUSRB/1203/221/024 project:

Non-Standard Forms of Teaching Mathematics and Physics: Experimental and Modeling Approach

www.model.u-szeged.hu

Continuing the traditional cooperation on modern methods of teaching Mathematics and Sciences between the University of Szeged and the University of Novi Sad, this project focuses ont he application of mobile tools, experimental and modeling approach in teaching. Open lecturing days, international compact courses, the traditional interdisciplinary Szeged – Novi Sad school, several conferences are organized. We continue the tradition of “Meet the Prof” lectures at schools. We develop several electronic teaching materials in Physics and Mathematics. To promote the computer-aided experiments in Physics classes, Edaq530 tools are manufactured and will be installed in several schools of our cross-border region. Participation in our events and the availability of our developments is free. Details can be found on the project web site.

Program

9:00 **Registration**

9:40 *Gergely Röst*: **Opening**

9:45 *Jane Heffernan*: **The effects of mass media in epidemics**

10:30 *Miklós Gyuranecz*: **Epidemiological investigations of Q fever and tularemia in Hungary**

11:00 Coffee break

11:20 *Tamás Ferenci:* **Modeling the time series of infectious diseases and its applications**

11:45 *Gábor Boross:* **Do negative epistatic interactions constrain stochasticity and evolution of gene expression?**

12:10 *Vladimir Francisti*: **Mathematical modeling of drug concentration**

12:35 **Poster session** & Lunch break

13:15 *Kyeongah Nah*: **Malaria dynamics with long incubation period in hosts**

13:40 *Branislava Rakić*: **Extraction methods and operational conditions on antioxidant activity of basil**

14:05 *Gergely Röst*: **Ebola – what does the math say?**

14:30 *Seyed M. Moghadas*: **Impact of geographic and demographic variables on disease outcomes and interventions**

15:15 Coffee break

15:25 *István Scheuring*: **How to feed your bacteria?**

16:00 *János Karsai*: **Teaching mathematics for students in life sciences**

16:25 *János Karsai:* **Closing remarks**

Posters

Eliza Bánhegyi: **Visual introduction to modeling systems with delay**

Ábel Garab: **Global stability of some second order difference equations**

Viktória Herczeg: **A dynamic introduction to fractional calculus**

Branislava Rakić: **Determination of antioxidant activity of sweet basil using different in vitro methods**

Zsolt Vizi: **Visual introduction to bifurcations**

Talks

Do negative epistatic interactions constrain stochasticity and evolution of gene expression?

Gábor Boross, Csaba Pál, Balázs Papp

Synthetic and Systems Biology Unit, Biological Research Centre of the
Hungarian Academy of Sciences, Szeged, Hungary

The phenotypic effects of mutations frequently depend on the presence of other mutations in the genome. Recent systematic studies generated a comprehensive map of such genetic (epistatic) interactions between null mutations in yeast (*Saccharomyces cerevisiae*). These works have revealed that a small fraction of genes (‘hubs’) have a very large number of epistatic interaction partners. It was recently proposed that negative genetic interactions might constrain the stochasticity of gene expression. We test this theory by analysing existing data on yeast genetic interactions and expression variation and by using kinetic modeling of the yeast glycolysis metabolic pathway.

Modeling the time series of infectious diseases and its applications

Tamás Ferenci

Óbuda University, Budapest, Hungary

Classical models of infectious diseases such as the SIR model are instructive because they provide a 'mechanistic' modeling of the dynamics of the disease. It is, however, practically hard to estimate the involved parameters from a sample (i.e. from routinely collected surveillance data) as – among other factors – they usually do not include information on the number of susceptibles. This problem gives rise to another approach, where the underlying mechanism is disregarded, and the aim is simply to provide the best possible model of the time series of the number of new cases, including information on the time of the observation, describing seasonality and secular trends (parameter-driven models) and perhaps on past observations as well (observation-driven models). These are typically formulated within a regression framework, such as generalized linear models. I will introduce the foundations of such time series models, and illustrate them on real-life surveillance data. As a practical application of such models, I will touch the topic of prospective outbreak detection (which sometimes involves the mixing of the two approaches).

Mathematical modeling of drug concentration

Vladimir Francisti

Department of Mathematics and Informatics, Faculty of Sciences,
University of Novi Sad, Novi Sad, Serbia

Mathematical modeling process is applied to the following problems:

1. Determine the quantity of a certain drug that the patient is supposed to receive at once in order to achieve the optimal concentration in the bloodstream.
2. Determine the quantity of certain drug that the patient is supposed to receive continuously (through infusion) in order to achieve the optimal concentration in the bloodstream.

The obtained mathematical models are

1. a homogeneous system
2. a nonhomogeneous system

of differential equations, where the variables correspond to the quantity of drug in the bloodstream and the tissue, respectively for the real problems.

The solutions of these systems determine the quantity of the drug that the patient is supposed to receive in order to achieve the optimal concentration in bloodstream.

Epidemiological investigations of Q fever and tularemia in Hungary

Miklós Gyuranecz

Institute for Veterinary Medical Research, Centre for Agricultural Research,
Hungarian Academy of Sciences, Budapest, Hungary

In the first part of my presentation I would like to talk about the epidemiological investigation of the Q fever outbreak that occurred in Hungary during the spring and summer of 2013. During the epidemic seventy human cases were confirmed by analysing their serum and blood samples with micro-immunofluorescence test and real-time polymerase chain reaction (PCR). The source of infection was a sheep flock (450 ewes) where 44.6% (25/56) seropositivity was detected by enzyme-linked immunosorbent assay while *Coxiella burnetii* DNA was detected in 20% (4/20) of individual's milk and 65.1% (41/65) of manure samples by real-time PCR. The multispacer sequence typing examination of *C. burnetii* DNAs detected in one human sample and two manure samples from the sheep flock revealed sequence type (ST) 18. The multi-locus variable number tandem repeat analysis pattern of the sheep and human strains were also almost identical, 4/5-9-3-3-0-5 (Ms23-Ms24-Ms27-Ms28-Ms33-Ms34). It is hypothesised that dried manure and maternal fluid contaminated with *C. burnetii* was dispersed by the wind from the sheep farm towards the local inhabitants. The manure was eliminated in June and the farm was disinfected in July. The outbreak ended by the end of July, 2013.

In the second part of my presentation I would like to talk about a study in which we analyzed the dynamics of the tularemia – wildlife – human system. The study area included 3 counties in Hungary and the analyzed data (Spearman's rank correlation) represented 25 years. A 2-3 year cycling was characteristic for the analyzed data. The number of human tularemia cases showed significant correlation with the *F. tularensis* specific seroprevalence of European brown hares and with the population density of common voles. A significant negative correlation was observed between seroprevalence and population density of hares. Significant correlation was found between the cumulative precipitation between May to July and the number of human tularemia cases in 2 of the 3 counties. It is hypothesized that hares and ticks are the reservoirs during inter-epizootic periods, but during the cyclic peaks of high vole population densities; aggression, cannibalism and contamination of the environment through body discharges facilitate *F. tularensis* intra- and interspecific transmission including spillover to hares, eventually expanding local outbreaks to epizootic proportions. It is suspected that higher precipitation in summer effects increased tick activity and *F. tularensis* transmission. Finally it can be concluded that higher numbers of infection sources in the environment result in elevated numbers of human cases.

The studies in part were supported by the Lendület (Momentum) program (LP2012-22) of the Hungarian Academy of Sciences.

The effects of mass media in epidemics

Jane Heffernan

Department of Mathematics and Statistics, York University, Toronto, Canada

Reports on the number of infections and disease in mass media can influence social behaviour during an infectious disease outbreak/epidemic. However, individuals can also become desensitized to this information over time. We have developed a mathematical model which incorporates both mass media induced changes in social behaviour, and desensitization to media reports. Model results show that key epidemic measurements depend on the rates of change in social behaviour and desensitization. Results also show a similar epidemic curve to that observed during the H1N1 pandemic.

Teaching mathematics for students in life sciences

János Karsai

Bolyai Institute, University of Szeged, Szeged, Hungary

Deductive or experimental reasoning, most benefit with less effort, deep theories needed but no time for deep study. These are some problems of teaching mathematics in life sciences, and they hardly can be resolved. Based on the long teaching pharmacy, biology and medical students, we give a summary of the experiences, and deal with professional, didactic as well as psychological aspects. We present our way of teaching, in which the computer-aided and manual, real experiments and complex modeling approach are of central role. We show many dynamic demonstrations in different topics, used regularly in our courses.

Impact of geographic and demographic variables on disease outcomes and interventions

Seyed M. Moghadas

Agent-Based Modelling Laboratory, York University, Toronto, Canada

In Canada, differential outcomes of the 2009 influenza H1N1 pandemic (H1N1pdm09) in remote and isolated communities raised several important questions for public health. We aimed to address two policy and program delivery questions, namely: (i) the effect of geographic location of residence and access to healthcare on disease outcomes (including hospitalization) during the first wave; (ii) the effect of ethnicity and on-reserve residency on pandemic vaccination during the second wave. We hypothesized that ethnicity and place of residence influenced the outcomes and odds of vaccination. To test these hypotheses, we obtained pandemic databases for the entire province of Manitoba, Canada, and used regression analysis to address these questions. We discuss the findings and place them in the context of public health policy and practice. Our results highlight the importance of demographic and geographical variables in developing population-specific intervention strategies for protecting high-risk groups.

Malaria dynamics with long incubation period in hosts

Kyeongah Nah

Bolyai Institute, University of Szeged, Szeged, Hungary

The incubation period of malaria can vary depending on the species of parasite or the geographic regions. In particular, in endemic areas of temperate climate (for example in Korea), the incubation period of *Plasmodium vivax* shows bimodal distribution of short and long term incubation periods. Assuming fixed length for the long term incubation period (DDE) gives a distribution that is much closer to the empirical distribution in the most common probability metrics, than the exponentially distributed long term incubation period (ODE).

In this talk, we compare two transmission models for *P. vivax* malaria, where we model the long term incubation period using ordinary differential equations or delay differential equations. We identify the basic reproduction number R_0 and show that it is a threshold parameter for the global dynamics of the model. For the DDE model, the global analysis is performed using persistence theory and Lyapunov functionals. We show that, while the qualitative behaviors of the two models are similar, the ODE model overestimates the basic reproduction number and also the level of endemicity, compared to the DDE model. By calculating R_0, we can see that long incubation time is not beneficial to the parasite in a constant environment, thus its presence is connected to the seasonal mosquito activity in Korea. In contrast to the autonomous case, when we incorporate seasonality into our model equations, the interplay of the time delay and the periodicity results that in some situations the DDE model predicts higher prevalence of malaria. The periodic DDE model is also superior to periodic ODE in capturing the qualitative properties of the observed Korean malaria time series, while its mathematical analysis is rather challenging.

Extraction methods and operational conditions on antioxidant activity of basil extract (*Ocimum basilicum* L.)

Branislava Rakić[1]*, Nevena Grujić-Letić*[2]*, Svetlana Goločorbin-Kon*[2]*,*
Momir Mikov[2]*, Aleksandar Rašković*[2]

[1]Faculty of Pharmacy, European University, Novi Sad, Serbia
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Basil (*Ocimum basilicum* L.) is widely used spice and therapeutic plant due to its contents of vitamins, mineral elements and phenolic compounds. It represents a rich source of natural antioxidants and other active compounds and is mostly used in a treatment of inflammatory diseases, headaches, respiratory infections, flu and cough. The objective of this study is to evaluate the influence of different extraction techniques and operational conditions on antioxidant activity and phenolic/flavonoid content of basil extracts.

88 obtained extracts were analysed. The extraction with concentrated methanol (95%, v/v), varying concentrations of ethanol (30, 40, 50, 60, 96%, v/v) and water was performed during different periods of time (10 and 30 minutes, 24, 48 and 72 hours). Antioxidant activity was tested by spectrophotometric method using DPPH (2,2-diphenyl-1-picrylhydrazyl) radical. Total phenolic and flavonoid content were determined by spectrophotometric methods and expressed as mg of gallic acid equivalents on g of dry extract (mg GAE/g SE) and mg of quercetin equivalents on g of dry extract (mg KE/g SE), respectively.

The extraction yield ranged 1,25-31,22 g of dry extract on 100 g of drug. IC50 values (the concentration of analysed sample that is required for 50% inhibition of DPPH radical) varied from 0,03-20,99 µg/ml. Total phenolic content ranged 2,81-191,5 mg GAE/g SE, and flavonoid content from 0,11-35,04 mg KE/g SE.

The results showed that analysed extracts had significant antioxidant activity. Extracts with the strongest antioxidant capacity were obtained by ethanol (96%, v/v) maceration during 10 minutes and water during 48 hours. This work was supported by the Provincial Secretariat for Science and Technological Development of Vojvodina (grant number 114-451-2056/2011-01) and The Ministry of Science and Technological Development, Republic of Serbia (grant number OI 172058).

Ebola – what does the math say?

Gergely Röst

Bolyai Institute, University of Szeged, Szeged, Hungary

The unprecedented Ebola epidemic in West Africa and the recent cases in Europe and US received huge media attention. Researchers around the globe are trying to construct mathematical and computational models to understand the transmission dynamics of the disease and to project what we can expect in the future. In this talk we give an overview of the actual worldwide Ebola situation. We summarize the methodologies and the results of previous and current modeling efforts, discuss their predictions and the implications for possible control strategies.

How to feed your bacteria?

<u>István Scheuring</u>[1], Gergely Boza[2] and Douglas W. Yu[3,4]

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Chinese Academy of Sciences, Kunming, Yunnan, China
[4]School of Biological Sciences, University of East Anglia, Norwich, Norfolk, United Kingdom

There is great interest in explaining how beneficial microbiomes are assembled. Antibiotic-producing microbiomes are arguably the most abundant class of beneficial microbiome in nature, having been found on corals, arthropods, molluscs, vertebrates and plant rhizospheres. An exemplar is the attine ants, which cultivate a fungus for food and host a cuticular microbiome that releases antibiotics to defend the fungus from parasites. One explanation posits long-term vertical transmission of Pseudonocardia bacteria, which (somehow) evolve new compounds in arms-race fashion against parasites. Alternatively, attines (somehow) selectively recruit multiple, non-coevolved actinobacterial genera from the soil, enabling a ‘multi-drug’ strategy against parasites. We reconcile the explanations by showing that when hosts fuel interference competition by providing abundant resources, the interference competition favours the recruitment of antibiotic-producing (and - resistant) bacteria. This partner-choice mechanism is more effective when at least one actinobacterial symbiont is vertically transmitted or has a high immigration rate, as in disease-suppressive soils. We arrive to these conclusions by studying a strategic model and set of individual based models of complex microbiota.

Posters

Visual introduction to modeling systems with delay

Eliza Bánhegyi, *János Karsai*

Bolyai Institute, University of Szeged, Szeged, Hungary

Delays can appear in many phenomena in the Nature, and hence delay systems appear in many fields of Sciences. Their mathematical theory is quite new. Since understanding needs deep mathematics, hence only advanced courses deal with delay systems in mathematical curricula. On the other hand, undergraduate math and even science students should have a first impression of delay systems.

In our talk, we consider the didactic problems of teaching delay systems to students without or partly having the required knowledge. We present a short easy-to-understand visual way of introducing delay systems with the help of series of dynamic demonstrations developed in Mathematica. The basic concepts, properties, the difference between systems without and with delay are treated via elementary examples. We also give applications appearing in engineering and sciences.

The interactive demonstrations will be available on our website www.model.u-szeged.hu.

Global stability of some second order difference equations

Ábel Garab, Ferenc Bartha, Tibor Krisztin

Bolyai Institute, University of Szeged, Szeged, Hungary

Consider the second order difference equation

$$x_{k+1} = x_k e^{a - x_{k-d}}$$

where α is a positive parameter and *d* is a nonnegative integer. The case *d* = 0 was introduced by W. E. Ricker in 1954. For the delayed version $d \geq 1$ of the equation S. Levin and R. May conjectured in 1976 that local stability of the nontrivial equilibrium implies its global stability. Based on rigorous, computer-aided calculations and analytical tools, we prove the conjecture for $d = 1$. We also apply our method to give necessary and sufficient conditions for the global stability of the trivial equilibrium of the difference equation $x_{k+1} = mx_k + a \tanh x_{k-1}$, where m and α are real parameters. Joint work with Ferenc Bartha and Tibor Krisztin.

This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP 4.2.4. A/2-11-1-2012-0001 'National Excellence Program'.

A dynamic introduction to fractional calculus

Viktória Herczeg[1]*, János Karsai*[1]*, Djurdjica Takači*[2]

[1]University of Szeged, Szeged, Hungary
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Fractional calculus, i.e., calculus of derivatives and integrals of fractional order are getting more and more important in applications, in particular in oscillation theory, biology, etc. However these notions are not part of any standard university curricula, mainly due to the deep mathematical theories needed. In our talk, we will present a series of dynamic demonstrations developed in *Mathematica* and *Geogebra*. We give an interactive introduction to different definitions, properties of "diffintegrals" by simple examples to both math and applied students. The interactive demonstrations will be available on our website www.model.u-szeged.hu.

Determination of antioxidant activity of sweet basil using different in vitro methods

Branislava Rakić

Faculty of Pharmacy, European University, Novi Sad, Serbia

See abstract of talk.

Visual introduction to bifurcations

Zsolt Vizi, *János Karsai*

Bolyai Institute, University of Szeged, Szeged, Hungary

Investigating the dependence on parameters is essential in studying dynamical systems. In particular, the bifurcation theory is getting more and more important in most fields of engineering and sciences. Nevertheless, these theories are hardly included in standard university curricula.

We will give an intuitive introduction with the help of dynamic demonstrations developed in Mathematica. We consider elementary examples of both difference and differential equations presenting different types of bifurcation. During the whole treatment, we keep in mind the real didactic "contradiction" that the students do not or only partly have the required knowledge.

The interactive demonstrations will be available on our website www.model.u-szeged.hu.

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Announcement

Szeged Novi Sad Winter School on Non-Standard Forms of Teaching Mathematics and Physics: Experimental and Modeling Approach

Szeged: January 30 – February 1, 2015
Novi Sad: February 6 – 8, 2015

A summary

A very important basis of intellectual and economic development is the improvement of creativity, problem solving abilities and applicable scientific knowledge. An essential element of them is the effective use of computational tools and methods both in research and at any level of teaching. Within the new – third – IPA program supported by the European Union, we develop joint educational programmes at the University of Szeged and the University of Novi Sad. Two intensive schools are being organized in winter of 2015, both in Szeged and Novi Sad (3 days, 24 teaching hours in each). The schools in Szeged and Novi Sad are independent, but they will complement each other. It is possible to register for only one of them, but we recommend taking part on both.

Programme of the schools

The courses will concern interesting topics, modeling problems and tools in Mathematics and Physics, applications in several areas of sciences in such a way that it will be enjoyable for everyone. The participants will learn some parts of the following fields: signal processing and computer-aided measuring techniques; mobile tools and dynamic modelling in teaching Math; computer-aided study of physical, and biological-chemical models, geometrical structures. For participating teachers, we emphasize the didactic aspects of these techniques. The courses will be held in computer rooms. The participants will study the topics via practical examples.

Who are welcome?

We welcome PhD students, researchers, high school teachers and students from our neighbourhood on any side of the borders who work in mathematics, physics or other sciences. Talented undergraduate students may also apply with the recommendation of their supervisors.

Conditions

Participation is free, registration is required; participants will receive course materials. We have limited possibilities to support accommodation in student hostels. Participants from the other side of the border and participants invited by their results on competitions are of high priority. Travel costs are covered by the participants. We ask the participants to give a seminar at their workplaces or schools for their colleagues and/or students from the subjects they studied on the courses. A report should be prepared from this presentation, illustrated with photos, which will appear on the website of the project.

Language

Szeged: Hungarian and English, Novi Sad: Serbian and English.

Information

www.model.u-szeged.hu (event calendar)

Conference on Modeling in Life Sciences

November 3, 2014

Bolyai Lecture Hall, Bolyai Institute, 1 Aradi vértanúk Square, Szeged, Hungary

Organized by the Bolyai Institute, University of Szeged in the framework of the IPA HUSRB/1203/221/024 project "Non-Standard Forms of Teaching Mathematics and Physics: Experimental and Modeling Approach".

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