FP7-PEOPLE-IRG 239429 NLAMATHMODELS

Nonlinear Analysis in Mathematical Models: Heat Damage, Stability of Nonlinear Waves and Spectral-Scattering Problems

Final Report October 21, 2009 - October 20, 2013

Summary

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NLAMATHMODELS is a Marie Curie International Reintegration Grant for Dr. Richard Kollár, supporting his return to Comenius University in Bratislava, Slovakia, after more than ten years of research experience in the United States. The main goal of the proposed projects that represent very different types of problems appearing in applied nonlinear science, is to extend understanding of various biological and mathematical phenomena. Specifically, the particular projects of Dr. Kollár research are

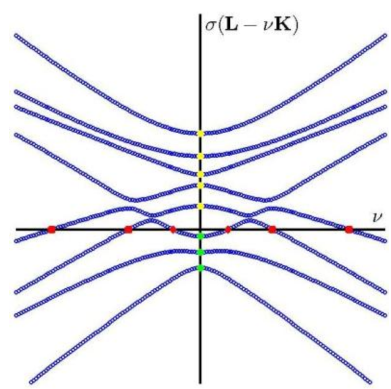
1. Non-selfadjoint spectral problems
2. Stability of nonlinear waves
3. Mathematical modeling of heat damage to cells

with an emphasis on unification aspects of desired results. In addition, the specific goal of the project proposal is to build a new collaboration with experimental researchers from Comenius University. Besides other areas the goal resulted into an intensive work on the project

4. Mathematical modeling of alternative telomere length maintenance.

Finally, the project should help to establish an applied mathematics research group at Comenius University and to introduce students of the hosting department to interdisciplinary research.

The main focus of Dr. Kollár work lies in the areas of Non-selfadjoint spectral problems and Stability of nonlinear waves where Dr. Kollár and his collaborators developed new methods, theory, and efficient algorithms to study spectral problems, and particularly Krein signature, Evans function, and Hamiltonian-Hopf bifurcations. The highlight is a an introduction of the concept of the graphical Krein signature that provides an elegant and efficient way to prove new theory and to reprove important theoretical results while removing unnecessary technical assumptions. Moreover, it visualizes a connection between the Krein signature and the Evans function, and thus it solves an important open problem. The results show various unification aspects in areas of nonlinear waves and matrix analysis.



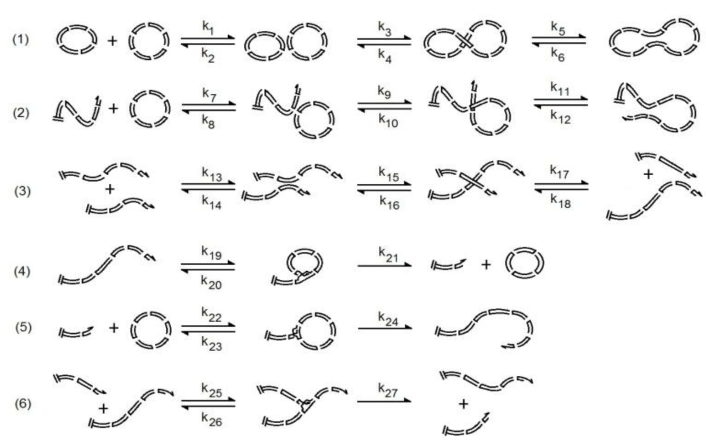
In the area of math biology Dr. Kollár studies heat damage to human skin and telomere length maintenance in yeast. In the case of heat damage the new model explains observations in old experiments with repeated skin exposure to heat that were not captured by existing models. The new characterization of the local damage of the skin cells may improve both safety measures in heat damage precautions and a control of the hyperthermia medical therapies. In the problem of telomere length maintenance the results of Dr. Kollár point out how important it is to include realistic biophysics in the model that is often ignored in mathematical modeling. Furthermore, the model of telomere length maintenance in telomerase-free environment may elucidate the process of cell aging or evolutionary advantage of cancer cells and it may serve as a general prototype of a dynamics of a mixture of flexible linear and circular polymers interacting through recombination.

All problems studied by Dr. Kollár demonstrate a common feature - an importance to look back at older problems and to approach them with new methods. This point of view helps to discover hidden connections and generalizations.

Stability of vortices in axially symmetric Bose-Einstein condensates is studied in (Kollár & Pego, AMRX 2012). Although the results on stability were known in physics literature some years ago, this is the first attempt to perform a rigorous analysis of the problem. Beside a detailed mathematical analysis of the particular applied problem the work contains the first results on perturbation theory of Krein signature of finite systems of eigenvalues. Theoretical aspects of spectral problems are studied in (Kollár, SJAM 2011) along with an application from hydrodynamic stability. Dr. Kollár’s analytic approach to self-adjoint eigenvalue pencils is based on graphical Krein signature, an algebraic quantity related to stability under a system's perturbation. It allows to obtain new very elegant and simple proofs of existence of a sequence of eigenvalues converging to zero for a wide class of eigenvalue pencils and an eigenvalue count for quadratic Hermitian matrix pencils.

In (Kollár & Miller, 2014) Dr. Kollár laid down the theoretical background of the graphical Krein signature that significantly generalizes and extends the theory in various fields of mathematics: stability of nonlinear waves, linear algebra of matrix pencils, functional analysis of operator pencils, and bifurcation theory in dynamical systems. Among various results obtained are a construction of rigorous foundations for the theory, the extension of the concept of Krein signature to non-polynomial operator/matrix pencils, and the theory of Evans-Krein function that extends Evans function and enables a direct calculation of Krein signature. The new technique also provides simple unified graphical proofs of index theorems. These general results may have a significant impact on the whole field of stability of nonlinear waves as they address its fundamental techniques and theorems. Dr. Kollár also investigated applications of the newly developed theory to Hamiltonian-Hopf bifurcations. In (Kollár & Miller, in preparation) he studies common but non-generic situations in which collisions of eigenvalues of opposite Krein signature (appearing in investigations of linear stability of Hamiltonian systems) do not lead to bifurcations and thus eigenvalues stay restricted to the imaginary axis indicating stability of an equilibrium of the underlying Hamiltonian system. He identified a new mechanism that prevents such bifurcations and identified classes of problems where it applies. Index theorems for polynomial matrix pencils were studied by Dr. Kollár and his student (Kollár & Bosák, 2014). New stability criteria were derived for finite-dimensional systems where stability is inferred from partial information on matrix coefficients. The work provides for the first time a detailed survey of existing literature on the subject that covers the theory developed within distinct fields (matrix eigenvalue pencils, gyroscopic stabilization, Sturm-Liouville theory, stability of nonlinear waves) and points out important connections emphasizing the unification aspects.

Dr. Kollár established a successful local collaboration with the group of Prof. Nosek (Biochemistry) and Prof. Tomáška (Genetics) and Dr. Bodova (IST Austria) on a project of Modeling of alternative telomere length maintenance. They developed a mathematical model based on detailed biophysics of interactions of telomeres, non-coding repetitive sequences at ends of DNA strands. In (Kollár, Bodová, Nosek & Tomáška, 2013) a full biophysical model of telomere length maintenance is derived in the absence of enzyme telomerase, a set up observed also in telomerase deficient cancer cell lines. The mathematical formulation of the dynamics of the system on a short time scale is reduced to an infinite system of coagulation-fragmentation equations and its exact solutions show a good agreement with experimental data. The derived equations offer a number of challenges for theoretical research in mathematics. The theoretical aspects of the problem were studied with Prof. Carr (Herriot-Watt) and produced interesting theoretical results. The approach of Dr. Kollár illuminates the role of biophysics in regulation of telomere length, a factor often completely omitted in modeling. Additional research of the group with Prof. Pego (Carnegie Mellon) includes a derivation of the model on a long time scale that involves shortening of telomeres due to the end-replication problem (responsible for cell aging) and cell duplication.



Dr. Kollár also worked on a problem of mathematical modeling of heat damage to cells. The commonly used theory of damage integral originating in 1940's fails to explain some of the experimental data, and thus more understanding of the process of damage is sought. Dr. Kollár proposed a novel model of heat damage to a single cell (Kollár & Pietrangelo, in preparation) and together with his student (R. Brestensky, Master thesis, 2012) visualizes numerically heat and blood flow in the affected skin area. A connection of the computer model with mathematical model of heat damage to skin is planned in the near future. It will enable precise description of the local heat damage and matching it to the traditionally observed measure of heat damage, the extent or a color of a burn.

Other ongoing applied projects of Dr. Kollár include rigorous analysis of the quasi-state approximation in various chemical systems and an investigation of regulation of apoptosis under simultaneous invasion by Trichinella Spiralis (with Prof. Bábala (Pathology)). Master level students of Dr. Kollár participate on both projects.

Over the duration of the project Dr. Kollár supervised 14 Master and Bachelor theses on various topics in applied and theoretical mathematics. Dr. Kollár's outreach activities also include redesign of multiple courses at his department and the Department of Natural Sciences with focus shifted to applications. As a part of the preparation Dr. Kollár wrote a chapter for the textbook on Genomics (Kollár, 2013). He also gave presentations to high school students, and prepared Slovak team for the International Mathematical Olympiad. Dr. Kollár has also successfully established small focused group at his department consisting of faculty, graduate and undergraduate students meeting weekly to discuss a particular topic. He also maintains active collaboration with researchers in the U.S.A., has built new connections with colleagues from Austria, Germany, Greece, Sweden, Switzerland, and United Kingdom, and presented results of his research at the high quality international conferences and seminars over the world.