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SPECIAL ISSUE ON MATHEMATICAL METHODS IN SYSTEMS BIOLOGY

The present Special Issue collects contributions from researchers in applied math and mathematical biology proposing new approaches to analyze complex biological systems. We first provide a rationale for the issue and then comment on the various contributions.

Rationale. Living organisms exhibit complex dynamical behaviors and systems and control theory has a great potential as a tool to describe and analyze them. Moreover, new directions such as systems and synthetic biology have, in their nature, the ideal features to be prone to such analysis. Classical approaches of differential equations, systems and control theory have been applied to a number of engineering research areas, thus they create an ideal platform to migrate its mathematical tools and expertise to other important areas including biology and biomedical research. To strengthen the link between biology and such theories it is vital to bring together researchers who have successfully bridged into other disciplines and applied tools to solve concrete applications.

Contributions. The issue is comprised of the following contributions.

- Title: Controlled Cellular Automata. Authors: Monique Chyba, Achilles Beros, Oleksandr Markovichenko.
- Title: Energy and implicit discretization of the Fokker-Planck and Keller-Segel type equations. Authors: Luis Neves De Almeida, Federica Bubba, Benoît Perthame, Camille Pouchol.
- Title: Optimal stopping for response-guided dosing. Author: Jakob Kotas.
- Title: A network model of immigration: Enclave formation vs. cultural integration. Authors: Yao-Li Chuang, Tom Chou, Maria D'Orsogna.
- Title: A case study of optimal input-output system with sampled-data control: Ding et al. force and fatigue muscular control model. Authors: Toufik Bakir, Bernard Bonnard, Jérémy Rouot.
- Title: Stability of Metabolic Networks via Linear-In-Flux-Expressions. Authors: Nathaniel J. Merrill, Zheming An, Sean T. McQuade, Federica Garin, Karim Azer, Ruth E. Abrams, Benedetto Piccoli.
- Title: On the Role of Tumor Heterogeneity for Optimal Cancer Chemotherapy. Authors: Urszula Ledzewicz, Heinz Schättler, Shuo Wang.
- Title: Steady distribution of the incremental model for bacteria proliferation. Authors: Pierre Gabriel, Hugo Martin.
- Title: The cardiac bidomain model and homogenization. Authors: Kenneth Hvistendahl Karlsen, Erik Grandelius.

The articles cover a wealth of mathematical approaches and applications to specific biological problems. The contribution by Chyba et al. introduces a new class of controlled Cellular Automata with application to fire spreading and morphogenesis and tumor growth. The article by De Almeida et al. develops new numerical

methods for the parabolic-elliptic Keller-Segel equation with sensitivity saturation. Kotas deals with optimal decisions based on patient conditions in response-guided dosing using stochastic dynamic programming. Chuang et al. develop an agent-based network model for integration of newcomers in communities. Bakir et al. paper uses optimal control and analyze the muscular force response to optimize electrical pulses. Merrill et al. deal with metabolic networks and the possible equilibria given a specific structure of linearity in the fluxes. Ledzevic et al. paper focuses on optimal chemotherapy protocols and immunotherapies in case of tumor heterogeneity. Gabriel and Martin consider a cell division model and provide tools to study the long time asymptotic behavior of the Cauchy problem. Finally, Karlsen and Grandelius study the bidomain model of cardiac electrophysiology and provide an homogenization result.

We wish NHM audience a pleasant and fruitful reading of the issue.

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