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Mathematical and Computational Oncology

Third International Symposium, ISMCO 2021
Virtual Event, October 11–13, 2021
Proceedings

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Preface

It is with great pleasure that we welcome you to the proceedings of the 3rd International Symposium on Mathematical and Computational Oncology (ISMCO 2021), which was held virtually (October 11–13, 2021).

Despite significant advances in the understanding of the principal mechanisms leading to various cancer types, less progress has been made toward developing patient-specific treatments. Advanced mathematical and computational models could play a significant role in examining the most effective patient-specific therapies. The purpose of ISMCO is to provide a common interdisciplinary forum for mathematicians, scientists, engineers and clinical oncologists throughout the world to present and discuss their latest research findings, ideas, developments and applications in mathematical and computational oncology. In particular, ISMCO aspires to forge stronger relationships among researchers in a variety of disciplines, including mathematics, physical sciences, computer science, data science, engineering and oncology, with the goal of developing new insights into the pathogenesis and treatment of malignancies.

The program includes 6 keynote presentations, 6 oral sessions, 1 panel discussion, and 2 tutorials. ISMCO 2021 received 20 submissions, from which we accepted 16 submissions for oral presentation. This LNBI volume includes only the full and short papers accepted for presentation. All abstracts that were accepted for presentation appear in an online volume, which was published by Frontiers (a link is provided on the ISMCO website).

All submissions were reviewed with an emphasis on the potential to contribute to the state of the art in the field. Selection criteria included accuracy and originality of ideas, clarity and significance of results, and presentation quality. The review process was quite rigorous, involving at least three independent double-blind reviews, followed by several days of discussion. During the discussion period, we tried to correct anomalies and errors that might have existed in the initial reviews. Despite our efforts, we recognize that some papers worthy of inclusion may not be in the program. We offer our sincere apologies to authors whose contributions may have been overlooked.

Many contributed to the success of ISMCO 2021. First and foremost, we are grateful to the Steering, Organizing, and Program Committees; they strongly welcomed, supported, and promoted the organization of this new meeting. Second, we are deeply indebted to the keynote speakers who warmly accepted our invitation to talk at ISMCO 2021; their reputation in mathematical and computational oncology added significant value and excitement to the meeting. Next, we wish to thank the authors who submitted their work to ISMCO 2021 and the reviewers who helped us to evaluate the quality of the submissions. It was because of their contributions that we succeeded in putting together a high-quality technical program. Finally, we would like to express our appreciation to Springer, Frontiers and the International Society for Computational Biology (ISCB) for supporting ISMCO 2021.

We sincerely hope that despite the difficulties due to the pandemic, ISMCO 2021 offered participants opportunities for professional growth. We look forward to many more successful meetings in mathematical and computational oncology.

October 2021

George Bebis
Terry Gaasterland
Mamoru Kato
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Discussion Panel

Bringing Mathematical Methods to the Broader Oncology Community

Moderator

Deslattes Mays Anne	Science and Technology Consulting, LLC

Panelists

Soheil Meshinchi	Fred Hutchinson Cancer Center
Ching Lau	The Jackson Laboratory
Adam Resnick	The Children's Hospital of Philadelphia
Lincoln Stein	Ontario Institute for Cancer Research
Jinghui Zhang	St. Jude Children's Research Hospital

Tutorials

(1) Current methods and open challenges for structural modeling in cancer immunotherapy - 3rd Edition

Instructors:

Antunes Dinler	Rice University, USA
Fonseca Andre	University of Houston, USA
Hall-Swan Sarah	Rice University, USA
Lydia Kavraki	Rice University, USA
Rigo Mauricio	Pontifical Catholic University of Rio Grande do Sul, Brazil

(2) How can (experimental) data go on tumor growth models?

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Emanuelle A. Paixao	National Laboratory of Scientific Computing (LNCC), Brazil

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Meirav Zehavi	Ben-Gurion University, Israel
Alex Zelikovsky	Georgia State University, USA

Keynote Talks

Precision Oncology via the Tumor Transcriptome

Eytan Ruppin

CDSL, NCI, NIH, USA

Abstract. Precision oncology has made significant advances, mainly by targeting actionable mutations and fusion events involving cancer driver genes. Aiming to expand treatment opportunities, recent studies have begun to explore the utility of tumor transcriptome to guide patient treatment. I will introduce a new approach, termed SELECT, which harnesses genetic interactions to successfully predict patient response to cancer therapy from the tumor transcriptome. SELECT is tested on a broad collection of 35 published targeted and immunotherapy clinical trials from 10 different cancer types. It is predictive of patients' response in 80% of these clinical trials and in the recent multi-arm WINTHER trial. In summary, we report the first systematic, transcriptomics-based approach that is predictive across many targeted and immune therapies. The predictive signatures and the code are made publicly available for academic use, laying a basis for future prospective clinical studies. As time permits, I will provide a brief overview of MadHitter, a new approach for guiding precision cancer therapy based on single cell tumor transcriptomics.

Population Genomic Approaches for Molecular Biomarker Discovery in Clinical Oncology

Elli Papaemmanuil

Memorial Sloan Kettering Cancer Center, USA

Abstract. Recent characterization of the genes recurrently mutated in cancer have led to the routine implementation of tumor profiling at diagnosis with the expectation to diagnose and treat patients according to their unique molecular profile - the vision of precision medicine. However, development of molecularly guided clinical decision support tools warrants the delivery of evidence based, data driven, comprehensive models that extend beyond single markers. In my talk I will discuss critical considerations for biomarker characterization, statistical model development, and clinical decision support tool development for clinical adoption.

Speaker Bio-Sketch: Dr. Papaemmanuil got her BSc and MSci in Human Molecular Genetics with Honors at the University of Glasgow and her PhD in Human population genetics at the Institute of Cancer Research in London. She performed her postdoctoral studies at the Wellcome Trust Sanger Center and joined the University of Cambridge as faculty, prior to moving to the Memorial Sloan Kettering Cancer Center. Dr. Papaemmanuil has employed genome profiling methodologies to study the role of acquired mutations in cancer development and how these determine clinical phenotype and response to therapy. More recently she has established high-throughput laboratory profiling approaches and developed statistical modelling methodologies that integrate clinical and molecular parameters to inform patient tailored disease classification and clinical decision support (prognosis and treatment decisions). Her main research motivation is to develop research that helps translate recent cancer genome discoveries into clinical practice. Her current research spans, bioinformatic and algorithmic platform development, biomarker discovery and validation and experimental models of disease biology. Additionally, Dr. Papaemmanuil has a strong interest to understand the effects of treatment in disease progression and genetic drivers of treatment response. Dr. Papaemmanuil leads the Pediatrics Precision medicine initiative for MSK Kids, which sets out to evaluate, validate and deliver a clinical prototype for integrative whole genome and whole transcriptome sequencing analyses to understand mechanisms of disease biology and guide treatment strategies in pediatric cancers.

Three Problems in Mathematical Oncology

Paul K. Newton

Viterbi School of Engineering and Ellison Institute for Transformative Medicine,
University of Southern California, USA

Abstract. I will introduce three problems in mathematical oncology all of which involve nonlinear dynamics and control theory. First, I will describe our work using Markov chain models to forecast metastatic progression. The models treat progression as a (weighted) random walk on a directed graph whose nodes are tumor locations, with transition probabilities obtained through historical autopsy date (untreated progression) and longitudinal data (treated) from Memorial Sloan Kettering and MD Anderson Cancer Centers. Then, I will describe our models (both deterministic and stochastic) that use evolutionary game theory (replicator dynamics/Moran processes with prisoner's dilemma payoff matrix) to design multi-drug adaptive chemotherapy schedules to mitigate chemo-resistance by suppressing 'competitive release' of resistant cell populations. The models highlight the advantages of antagonistic drug interactions (over synergistic ones) in shaping the fitness landscape of co-evolving populations. Finally, I will describe our work on developing optimal control schedules (based on Pontryagin's maximum principle) that maximize cooperation for prisoner's dilemma replicator dynamical systems.

Towards Optimizing Therapy on a Patient Specific Basis via Imaging-Based Mathematical Modeling

Tom Yankeelov

Oden Institute for Computational Engineering and Sciences, Livestrong Cancer Institutes, Departments of Biomedical Engineering, Diagnostic Medicine, Oncology, The University of Texas at Austin, USA

Abstract. The ability to accurately predict the response of tumors to therapy, and then use this information to optimize treatment on an individual patient basis, would dramatically transform oncology. In an attempt to move in this direction, we have developed a clinical-mathematical framework that integrates quantitative magnetic resonance imaging (MRI) data into mechanism-based mathematical models to predict the response of locally advanced breast cancer to neoadjuvant therapy. We will present our recent efforts on this topic and then discuss how these methods can be extended to enable patient-specific simulations of treatment response to a range of therapeutic regimens, thereby providing a pathway for optimizing therapy on a patient-specific basis.

Barrett's Esophagus: Efficient Design of Multiscale Simulations for Surveillance And Treatment

Georg Luebeck

Fred Hutchinson Cancer Research Center, USA

Abstract. Barrett's Esophagus (BE), a metaplastic tissue alteration associated with gastroesophageal reflux, predisposes to esophageal adenocarcinoma (EAC). Endoscopic screening of patients with persistent symptomatic reflux aims to identify patients with BE at risk of progressing to cancer. Such patients are recommended to undergo follow-up examinations for dysplasia or small cancers in the earliest stages. This is useful because the prognosis for EAC detected at an early stage is dramatically better than for advanced stages that are mostly lethal. Thus, endoscopic surveillance of BE, in which multiple biopsies are routinely examined for preneoplastic changes and/or early neoplastic lesions, will increase patient survival compared with patients diagnosed with EAC without prior BE surveillance. However, over-diagnosis is a major concern because the annual rate of progression from BE to EAC is less than 1% overall but depends on age, gender, race/ethnicity, BE segment length, history of gastroesophageal reflux and other life-style factors. Multiscale models that include these factors have been developed but suffer computational bottlenecks and are technically demanding. In this talk I will discuss how mathematical insights and multitype branching process theory can be used to significantly speed up simulations to assess and evaluate various screening modalities in a large number of individuals.

Integrative Methods for Deciphering Cancer Networks

Mona Singh

Princeton University, USA

Abstract. Networks of molecular interactions underlie virtually all functions executed within a cell. Networks thus provide a powerful foundation within which to interpret a wide range of rapidly accumulating biological data. In this talk, I will present formulations and algorithms that leverage the structure and function of biological networks in order to analyze cancer genomes and discover cancer-relevant genes. This is a difficult task, as numerous somatic mutations are typically observed in each cancer genome, only a subset of which are cancer-relevant, and very few genes are found to be somatically mutated across large numbers of individuals. I will introduce a framework that can rapidly integrate multiple sources of information about molecular functionality in order to discover key interactions within a network that tend to be disrupted in cancers. Crucially, our approach is based on analytical calculations that obviate the need to perform time-prohibitive permutation-based significance tests. Next, I will describe algorithms that consider both prior and newly collected data within a network context in order to uncover cancer-relevant subnetworks. Overall, our work showcases the versatility and power of a network viewpoint in advancing biomedical discovery.

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