Libertas Academica
FREEDOM TO RESEARCH

Computer Simulation, Visualization, and Image Processing of Cancer Data and Processes

- **David Johnson**
  Senior Research Associate, Oxford e-Research Centre, University of Oxford, Oxford, UK.
- **James Osborne**
  Lecturer in Applied Mathematics, School of Mathematics and Statistics, University of Melbourne, Melbourne, Australia.
- **Zhihui Wang**
  Associate Professor, Department of NanoMedicine and BioMedical Engineering, University of Texas Medical School at Houston, Houston, TX, USA.
- **Kostas Marias**
  Principal Researcher and Head, Computational Biomedicine Laboratory, Institute of Computer Science of the Foundation for Research and Technology Hellas (ICS-FORTH), Heraklion, Greece.

Supplement Aims and Scope

Cancer Informatics represents a hybrid discipline encompassing the fields of oncology, computer science, bioinformatics, statistics, computational biology, genomics, proteomics, metabolomics, pharmacology, and quantitative epidemiology. The common bond or challenge that unifies the various disciplines is the need to bring order to the massive amounts of data generated by researchers and clinicians attempting to find the underlying causes and effective means of treating cancer.

The future cancer informatician will need to be well-versed in each of these fields and have the appropriate background to leverage the computational, clinical, and basic science resources necessary to understand their data and separate signal from noise. Knowledge of and the communication among these specialty disciplines, acting in unison, will be the key to success as we strive to find answers underlying the complex and often puzzling diseases known as cancer.

Articles should focus on computer simulation, visualization, and image processing of cancer data and processes and may include:

- Multi-dimensional Simulation Models of Tumor Response
- Simulating Tumor Growth Dynamics
- Spatio-Temporal Simulation Models
- Parametric Validation of Simulation Models
- Simulation of Dynamic Phenomena in Cancer using Highly Specialized Algorithms
- Hyper-High Performance and Biocomplexity Systems Modeling of Cancer
- Robust Feature Selection
- Spectra Analysis
- Generic Visualization Tools
- Array-Comparative Genomic Hybridization Visualization
- Meta-Data Imaging
- Equivalent Cross-Relaxation Imaging
- Mathematical Modeling and Image Enhancement of MRI Cancer Data
- Rapid Imaging Analysis of PET Cancer Scans

Computer simulation of cancer data and processes *in silico* is vital to making progress in cancer research. While there have been many advances in systems biology, statistical methods, data science and machine learning on both basic and clinical biomedical research levels, mathematical modeling and computer simulation of cancer still play an important role in developing computer-aided diagnosis and in the optimization of clinical tools.[1,2] The proliferation of data generated from high-throughput molecular profiling and physiological imaging offers great opportunities for development of personalized approaches to diagnosing disease and guiding and optimizing clinical decision-making.

This supplement solicited papers on all aspects of computer simulation, visualization and image processing of cancer data and processes which are all essential elements for an integrated cancer predictive medicine environment. What is

clear from the composition of contributions is that computer simulation and mathematical modeling have been used as a tool for understanding cancer processes, revealing a clear trend towards developing predictive models of cancer progression as well as computer-simulation of candidate treatments. In particular, the contributions included in this supplement highlight the breadth of computer-based cancer research that is happening worldwide, with representations from research and innovators participating in national research programs (Mumenthaler et al), international research collaborations, in particular through the European Commission (Marias et al, Graf et al, Stamatakos et al, Sakkalis et al and Buffa et al), industry (Ogilvie et al), and open-source initiatives (Osborne et al and Rubinacci et al). These cover varying aspects of simulation of cancer data and processes, from tissue homeostasis and carcinogenesis utilizing the general-purpose multiscale simulation package Chaste[3] (Cancer, Heart and Soft Tissue Environment) to personalized and clinical application of simulations using oncosimulators.[4–7] We summarize in brief each of the supplement contributions here:

In "The Standardized Histogram Shift of T2 Magnetic Resonance Image (MRI) Signal Intensities of Nephroblastoma Does Not Predict Histopathological Diagnostic Information", Müller et al present a study on histogram comparisons of T2-MRI before and after preoperative chemotherapy for nephroblastoma (Wilms' tumor). They go on to question how these comparisons correlate with the histology of the tumor.

Roniotis et al present a novel modelling framework for predicting the temporal evolution of tumor vascularity based on the initialization of the cancer cell populations and vasculature from image-derived parameters in their paper, "A Proposed Paradigm Shift in Initializing Cancer Predictive Models with DCE-MRI Based PK Parameters: A Feasibility Study".

In "The Impact of Microenvironmental Heterogeneity on the Evolution of Drug Resistance in Cancer Cells", Mumenthaler et al present a study that integrates experiments with computational modeling in order to understand the relationships between selection pressures imposed by the microenvironment (eg, oxygen, glucose, and drug levels) and the rate of tumor growth and the penetrance of drug resistance in non-small cell lung cancer. They found that tumor growth and response to therapy were both closely regulated by microenvironmental conditions, highlighting the importance of accounting for the tumor microenvironment when developing optimal treatment strategies.

In "*In Silico* Neuro-Oncology: Brownian Motion-Based Mathematical Treatment as a Potential Platform for Modeling the Infiltration of Glioma Cells into Normal Brain Tissue", Antonopoulos and Stamatakos present a novel modelling framework for predicting the temporal evolution of tumor vascularity. The framework is based on the initialization of the cancer cell populations and vasculature from image-derived parameters.

"Assessing Treatment Response Through Generalized Pharmacokinetic Modeling of DCE-MRI Data", by Kontopodis et al, compares the predictive value of two DCE-MRI pharmacokinetic models in a cohort of cancer patients. They also present a novel method for segmenting the tumor area into subregions according to their vascular heterogeneity characteristics, which increases the predictive value of the image biomarkers.

Rubinacci et al's paper, "CoGNaC: A Chaste Plugin for the Multiscale Simulation of Gene Regulatory Networks Driving the Spatial Dynamics of Tissues and Cancer", concerns the use of noisy random Boolean networks to represent gene regulatory networks. Moreover, the paper embeds these networks within a multicellular representation of the colorectal crypt and investigates the progression to colorectal cancer.

In "The Importance of Neighborhood Scheme Selection in Agent-based Tumor Growth Modeling", Tzedakis et al refer to a hybrid tumor model on a 2D square lattice. The paper examines how Neumann vs. Moore neighborhood schemes affect tumor growth and morphology.

Ogilvie et al describe a mechanistic approach to predictive in silico modeling of cancer and patient responses to drug treatment in their paper, "Predictive Modeling of Drug Treatment in the Area of Personalized Medicine". They go on to describe how they developed the ModCell™ systems biology modeling platform to build virtual patient models in oncology.

Finally in Osborne's paper on a "Multiscale Model of Colorectal Cancer Using the Cellular Potts Framework", the author presents an open source implementation of the Cellular Potts modeling framework. The paper details how one can model the interactions of populations of cells with different mechanical properties, for example representing groups of mutant cells. This model is used to investigate how the position size and shape of cells are effected in the early stages of colorectal cancer.

Going forward, clinical validation of cancer models and simulations are key to clinical translation of computer-based predictive tools. Validation and translation of such research can, at the very least in a pre-competitive environment, be driven by open science initiatives.[8] Open science initiatives seek to make published research more transparent and accessible to all, where published research should be fully reproducible with adequately comprehensive supplementary material alongside the publication. We are already witnessing the emergence of *data descriptor* publications and *data journals*,[9,10] as well as *executable papers*,[11] that encourage sharing of data for reproducibility of results and for re-running *in silico* experiments alongside published works. This transparency and reproducibility is something that hopefully becomes commonplace in all areas of science, including in cancer research and innovation.

REFERENCES

1. Deisboeck TS, Wang Z, Macklin P, and Cristini V. Multiscale cancer modeling. *Annual Review of Biomedical Engineering.* 2011;13:127–55
2. Di Ventura B, Lemerle C, Michalodimitrakis K, Serrano L. From in vivo to in silico biology and back. *Nature.* 2006;443:527–33.
3. Mirams GR, Arthurs CJ, Bernabeu MO, et al. Chaste: An open source C++ library for computational physiology and biology. *PLoS Comput. Biol.* 2013;9(3): e1002970.
4. Stamatakos GS, Dionysiou DD, Graf NM, et al. The "Oncosimulator": a multilevel, clinically oriented simulation system of tumor growth and organism response to therapeutic schemes. Towards the clinical evaluation of in silico oncology. *Conf Proc IEEE Eng Med Biol Soc.* 2007;2007:6629–32.
5. Stamatakos G, Dionysiou D, Lunzer A, et al. The technologically integrated oncosimulator: combining multiscale cancer modeling with information technology in the in silico oncology context. *IEEE J Biomed Health Inform.* 2014 May;18(3):840–54. doi: 10.1109/JBHI.2013.2284276. Epub 2013 Oct 2.
6. Stamatakos GS, Kolokotroni E, Dionysiou D, et al. In silico oncology: exploiting clinical studies to clinically adapt and validate multiscale oncosimulators. *Conf Proc IEEE Eng Med Biol Soc.* 2013;2013:5545–9. doi: 10.1109/EMBC.2013.6610806.
7. Marias K, Sakkalis V, Roniotis A, et al. Clinically Oriented Translational Cancer Multilevel Modeling: The ContraCancrum Project. In: Dössel O, Schlegel WC, eds. *World Congress on Medical Physics and Biomedical Engineering, September 7–12, 2009, Munich, Germany.* Berlin: Springer Heidelberg Berlin; 2009:2124–7.
8. Molloy JC. The Open Knowledge Foundation: Open Data Means Better Science. *PLoS Biol.* 2011 Dec;9(12):e1001195.
9. More bang for your byte. *Scientific Data.* 2014;1:Article number: 140010 (2014) doi:10.1038/sdata.2014.10.
10. Goodman L, Edmunds SC, Basford AT. Large and linked in scientific publishing. *GigaScience.* 2012;1:1. doi:10.1186/2047-217X-1-1.
11. Koers H, Gabriel A, Capone R. Executable papers in computer science go live on ScienceDirect [blog post]. Munich: Elsevier; 2013. Available at: https://www.elsevier.com/connect/executable-papers-in-computer-science-go-live-on-sciencedirect.

Lead Guest Editor **Dr David Johnson**

Dr David Johnson is a Senior Research Associate at the University of Oxford's e-Research Centre. He completed his PhD at the University of Reading and has previously worked at Imperial College London where he was a founding member of the Data Science Institute, and in the Department of Computer Science at Oxford University. He now works primarily in developing data standards and data management infrastructure for the life sciences. Dr Johnson is the author or co-author of 30 published papers and has presented at 11 conferences, and serves on the technical programme committees of a number of international conferences including the *International Conference on Computational Science* series.

david.johnson@oerc.ox.ac.uk
http://www.oerc.ox.ac.uk/people/david-johnson

Guest Editors

JAMES OSBORNE

Dr James Osborne is a Lecturer in Applied Mathematics at the University of Melbourne. He completed his DPhil in Computational Biology at the University of Oxford in 2009 and has previously worked as an Associate Director of the Life Sciences Interface Doctoral Training Centre at and as a Senior Researcher in the Computational Biology Group, both at the University of Oxford. Prior to moving to Melbourne he was a Visiting Scientist at Microsoft Research Cambridge's Computational Science Laboratory. He now works primarily in the development of robust mathematical and numerical methods for multiscale multicellular modeling in systems biology, with specific applications in colorectal cancer and development. Dr Osborne is the author or co-author of over 25 published papers and has presented at over 20 conferences and workshops on four continents.

jmosborne@unimelb.edu.au
http://www.jmosborne.com

ZHIHUI WANG

Dr Zhihui Wang is an Associate Professor at the University of Texas Medical School at Houston. He completed his PhD at Niigata University, Japan, and has previously worked at Harvard Medical School, Massachusetts General Hospital, and the University of New Mexico. He now works primarily in developing, calibrating, and validating multiscale models (across multiple biological scales) using discrete, continuum, and hybrid techniques and biophysical drug transport models for predicting cancer treatment outcome. Dr Wang is the author or co-author of over 30 published papers and has presented at over 20 conferences, and holds an editorial appointment at Frontiers in Physiology.

zhihui.wang@uth.tmc.edu
https://med.uth.edu/nbme/faculty/zhihui-bill-wang/

KOSTAS MARIAS

Dr Kostas Marias is Principal Researcher at the Computational Biomedicine Laboratory at the Institute of Computer Science of the Foundation for Research and Technology Hellas (ICS-FORTH) and Head of the Computational Biomedicine Laboratory at ICS-FORTH. He completed his PhD at the University College London Medical School and has previously worked at the University of Oxford and the University of Crete. He now works primarily in medical image processing and modelling for personalized medicine. Dr Marias is the author or co-author of more than 30 published journal papers and has presented at 80 conferences, and serves on the technical programme committees of a number of international conferences.

kmarias@ics.forth.gr
https://www.ics.forth.gr/cbml/index_main.php?l=e&c=547

SUPPLEMENT TITLE: Computer Simulation, Visualization, and Image Processing of Cancer Data and Processes

CITATION: Johnson et al. Computer Simulation, Visualization, and Image Processing of Cancer Data and Processes. *Cancer Informatics* 2015:14(S4) 105–108 doi: 10.4137/CIN.S37982

ACADEMIC EDITOR: J. T. Efird, Editor in Chief

TYPE: Editorial

FUNDING: ZW acknowledges funding support from the National Science Foundation (NSF) Grant DMS-1562068, the National Institutes of Health (NIH) Grant 1U01CA196403, and The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM) at The University of Texas Health Science Center at Houston. The authors confirm that the funder had no influence over the content of the article, or selection of this journal.

COMPETING INTERESTS: Authors disclose no potential conflicts of interest.

CORRESPONDENCE: david.johnson@oerc.ox.ac.uk

All editorial decisions were made by the independent academic editor. All authors have provided signed confirmation of their compliance with ethical and legal obligations including (but not limited to) use of any copyrighted material, compliance with ICMJE authorship and competing interests disclosure guidelines.