

## Subseries of Lecture Notes in Computer Science

### Series Editors

Sorin Istrail

*Brown University, Providence, RI, USA*

Pavel Pevzner

*University of California, San Diego, CA, USA*

Michael Waterman

*University of Southern California, Los Angeles, CA, USA*

### Editorial Board Members

Søren Brunak

*Technical University of Denmark, Kongens Lyngby, Denmark*

Mikhail S. Gelfand

*IITP, Research and Training Center on Bioinformatics, Moscow, Russia*

Thomas Lengauer

*Max Planck Institute for Informatics, Saarbrücken, Germany*

Satoru Miyano

*University of Tokyo, Tokyo, Japan*

Eugene Myers

*Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany*

Marie-France Sagot

*Université Lyon 1, Villeurbanne, France*

David Sankoff

*University of Ottawa, Ottawa, Canada*

Ron Shamir

*Tel Aviv University, Ramat Aviv, Tel Aviv, Israel*

Terry Speed

*Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia*

Martin Vingron

*Max Planck Institute for Molecular Genetics, Berlin, Germany*

W. Eric Wong

*University of Texas at Dallas, Richardson, TX, USA*


More information about this subseries at <http://www.springer.com/series/5381>

Paolo Cazzaniga · Daniela Besozzi ·  
Ivan Merelli · Luca Manzoni (Eds.)

# Computational Intelligence Methods for Bioinformatics and Biostatistics

16th International Meeting, CIBB 2019  
Bergamo, Italy, September 4–6, 2019  
Revised Selected Papers

*Editors*

Paolo Cazzaniga   
University of Bergamo  
Bergamo, Italy

Ivan Merelli   
National Research Council  
Segrate, Italy

Daniela Besozzi   
University of Milano-Bicocca  
Milan, Italy

Luca Manzoni   
Università degli Studi di Trieste  
Trieste, Italy

ISSN 0302-9743

ISSN 1611-3349 (electronic)

Lecture Notes in Bioinformatics

ISBN 978-3-030-63060-7

ISBN 978-3-030-63061-4 (eBook)

<https://doi.org/10.1007/978-3-030-63061-4>

LNCS Sublibrary: SL8 – Bioinformatics

© Springer Nature Switzerland AG 2020

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

# Preface

This volume contains the revised selected papers of the 16th edition of the international conference on Computational Intelligence Methods for Bioinformatics and Biostatistics (CIBB 2019), which provides a multidisciplinary forum for the scientific community interested in the advancements and future perspectives in bioinformatics and biostatistics.

Following its tradition and roots, CIBB 2019 brought together researchers with different background – from mathematics to computer science, from materials science to medicine and biology – interested in the application of computational intelligence methods for the solution of open problems in bioinformatics, biostatistics, systems biology, synthetic biology, and medical informatics. At CIBB 2019, current trends and future opportunities at the edge of computer and life sciences, as well as their impact on innovative medicine, were presented. Both theoretical and experimental biologists and computer scientists discussed novel challenges, and started multidisciplinary collaborations with the aim of combining theory with practice.

The conference program included only oral presentations, among which cutting-edge plenary keynote lectures were given by four prominent speakers: Malu Calle Rosingana (University of Vic - Central University of Catalonia, Spain), Ana Cvejic (Wellcome Trust Sanger Institute, UK), Uzay Kaymak (Eindhoven University of Technology, The Netherlands), and Marco Masseroli (Politecnico di Milano, Italy). The conference program was organized with a main conference track, including papers dealing with heterogeneous open problems at the forefront of current research, and four special sessions on specific themes: Modeling and Simulation Methods for Computational Biology and Systems Medicine, Machine Learning in Healthcare Informatics and Medical Biology, Algebraic and Computational Methods for the Study of RNA Behaviour, and Intelligence Methods for Molecular Characterization and Dynamics in Translational Medicine.

The conference was held at the Department of Human and Social Sciences, University of Bergamo, Italy, during September 4–6, 2019, thanks to the synergistic effort of the Organizing, Program, and Steering Committees, and to the support of the Department of Informatics, Systems and Communication, University of Milano-Bicocca, Italy, and the Institute of Biomedical Technologies of the National Research Council, Italy. The conference was attended by more than 90 participants from Europe, Asia, USA, Central and South America.

A total of 55 contributions were submitted for consideration to CIBB 2019 and, after a round of reviews handled by the members of the Program Committee, 47 papers were accepted for an oral presentation. After the conference, the authors of selected papers were invited to submit an extended version of their manuscript, and the accepted papers are collected in this volume. The volume is divided into five major sections: Computational Intelligence Methods for Bioinformatics and Biostatistics (i.e., the main conference track), Algebraic and Computational Methods for the Study of RNA

Behaviour, Intelligence Methods for Molecular Characterization and Dynamics in Translational Medicine, Machine Learning in Healthcare Informatics and Medical Biology, and Modeling and Simulation Methods for Computational Biology and Systems Medicine.

The editors warmly thank the Program Committee, the invited speakers, the authors of the papers, the reviewers, and all the participants for their contributions to the success of CIBB 2019.

October 2020

Paolo Cazzaniga  
Daniela Besozzi  
Ivan Merelli  
Luca Manzoni

# Organization

## Conference Co-chairs

Paolo Cazzaniga	University of Bergamo, Italy
Daniela Besozzi	University of Milano-Bicocca, Italy
Ivan Merelli	CNR, Italy

## Publicity Chairs

Stefano Beretta	University of Milano-Bicocca, Italy
Simone Spolaor	University of Milano-Bicocca, Italy

## Technical Chair

Angela Serra	University of Tampere, Finland
--------------	--------------------------------

## Proceedings Chair

Luca Manzoni	University of Trieste, Italy
--------------	------------------------------

## Local Organizers

Riccardo Dondi	University of Bergamo, Italy
Stefano Beretta	University of Milano-Bicocca, Italy
Marco S. Nobile	Eindhoven University of Technology, The Netherlands
Dario Pescini	University of Milano-Bicocca, Italy
Simone Spolaor	University of Milano-Bicocca, Italy

## Steering Committee

Pierre Baldi	University of California, Irvine, USA
Elia Biganzoli	University of Milan, Italy
Clelia Di Serio	Università Vita-Salute San Raffaele, Italy
Alexandru Floares	Oncological Institute Cluj-Napoca, Romania
Jon Garibaldi	University of Nottingham, UK
Nikola Kasabov	Auckland University of Technology, New Zealand
Francesco Masulli	University of Genova, Italy, and Temple University, USA
Leif Peterson	TMHRI, USA
Roberto Tagliaferri	University of Salerno, Italy

## Program Committee

Antonino Abbruzzo	University of Palermo, Italy
Claudio Angione	Teesside University, UK
Sansanee Auephanwiriyakul	Chiang Mai University, Thailand
Marco Beccuti	University of Torino, Italy
Gilles Bernot	University of Nice Sophia Antipolis, France
Andrea Bracciali	University of Stirling, UK
Giulio Caravagna	Institute of Cancer Research, UK
Mauro Castelli	Universidade NOVA de Lisboa, Portugal
Davide Chicco	Peter Munk Cardiac Centre, Canada
Angelo Ciaramella	Pathenope University of Naples, Italy
Chiara Damiani	University of Milano-Bicocca, Italy
Mohammed El-Kebir	University of Illinois at Urbana-Champaign, USA
Marco Frasca	University of Milan, Italy
Christoph M. Friedrich	Dortmund University of Applied Sciences and Arts, Germany
Enrico Formenti	University of Nice Sophia Antipolis, France
Filippo Geraci	Institute for Informatics and Telematics, CNR, Italy
Yair Goldberg	University of Haifa, Israel
Alex Graudenz	Institute of Molecular Bioimaging and Physiology, CNR, Italy
Marco Grzegorzczak	Groningen University, The Netherlands
Anne-Christin Hauschild	Philipps-Universität Marburg, Germany
Sean Holden	University of Cambridge, UK
Giuseppe Jurman	Fondazione Bruno Kessler, Italy
Johannes Köster	University of Duisburg-Essen, Germany
Giosuè Lo Bosco	University of Palermo, Italy
Hassan Mahmoud	University of Genova, Italy
Anna Marabotti	University of Salerno, Italy
Elena Marchiori	Radboud University, The Netherlands
Tobias Marschall	Saarland University, Max Planck Institute for Informatics, Germany
Giancarlo Mauri	University of Milano-Bicocca, Italy
Mickael Mendez	University of Toronto, Canada
Emanuela Merelli	University of Camerino, Italy
Luciano Milanesi	Institute of Biomedical Technologies, CNR, Italy
Bud Mishra	New York University, USA
Marianna Pensky	University of Central Florida, USA
Joao Ribeiro Pinto	Instituto de Engenharia de Sistemas e Computadores Tecnologia e Ciencia, Portugal
Paulo Ribeiro	Universidade NOVA de Lisboa, Portugal
Davide Rizzo	Cornell University, USA
Riccardo Rizzo	Institute for High Performance Computing and Networking, CNR, Italy
Paolo Romano	Ospedale Policlinico San Martino, Italy



Stefano Rovetta	University of Genova, Italy
Antonino Staiano	Parthenope University of Naples, Italy
Filippo Utro	IBM, USA
Maria Grazia Valsecchi	University of Milano-Bicocca, Italy
Alfredo Vellido	Universitat Politècnica de Catalunya, Spain
Blaz Zupan	University of Ljubljana, Slovenia

## **Special Session Organizers**

### **Modeling and Simulation Methods for Computational Biology and Systems Medicine**

Rosalba Giugno	University of Verona, Italy
Marco Beccuti	University of Turin, Italy
Marzio Pennisi	University of Catania, Italy
Pietro Liò	University of Cambridge, UK
Marco S. Nobile	Eindhoven University of Technology, The Netherlands

### **Machine Learning in Healthcare Informatics and Medical Biology**

Davide Chicco	Peter Munk Cardiac Centre, Canada
Anne-Christin Hauschild	Philipps-Universität Marburg, Germany
Mickael Mendez	University of Toronto, Canada
Giuseppe Jurman	Fondazione Bruno Kessler, Italy
Joao Ribeiro Pinto	Instituto de Engenharia de Sistemas e Computadores Tecnologia e Ciencia, Portugal

### **Algebraic and Computational Methods for the Study of RNA Behaviour**

Emanuela Merelli	University of Camerino, Italy
Stefano Maestri	University of Camerino, Italy
Michela Quadrini	University of Camerino, Italy

### **Intelligence Methods for Molecular Characterization and Dynamics in Translational Medicine**

Andrea Calabria	San Raffaele Telethon Institute for Gene Therapy, Italy
-----------------	---

# Contents

## Computational Intelligence Methods for Bioinformatics and Biostatistics

A Smartphone-Based Clinical Decision Support System for Tremor Assessment . . . . .	3
<i>Guillaume Zamora, Caro Fuchs, Aurélie Degeneffe, Pieter Kubben, and Uzay Kaymak</i>	
cyTRON and cyTRON/JS: Two Cytoscape-Based Applications for the Inference of Cancer Evolution Models. . . . .	13
<i>Lucrezia Patrino, Edoardo Galimberti, Daniele Ramazzotti, Giulio Caravagna, Luca De Sano, Marco Antoniotti, and Alex Graudenzi</i>	
Effective Use of Evolutionary Computation to Parameterise an Epidemiological Model . . . . .	19
<i>Ryan Mitchell, David Cairns, Dalila Hamami, Kevin Pollock, and Carron Shankland</i>	
Extending Knowledge on Genomic Data and Metadata of Cancer by Exploiting Taxonomy-Based Relaxed Queries on Domain-Specific Ontologies. . . . .	33
<i>Eleonora Cappelli, Emanuel Weitschek, and Fabio Cumbo</i>	
GAN-Based Multiple Adjacent Brain MRI Slice Reconstruction for Unsupervised Alzheimer's Disease Diagnosis . . . . .	44
<i>Changhee Han, Leonardo Rundo, Kohei Murao, Zoltán Ádám Milacski, Kazuki Umemoto, Evis Sala, Hideki Nakayama, and Shin'ichi Satoh</i>	
Improving the Fusion of Outbreak Detection Methods with Supervised Learning. . . . .	55
<i>Moritz Kulessa, Eneldo Loza Mencía, and Johannes Fürnkranz</i>	
Learning Cancer Drug Sensitivities in Large-Scale Screens from Multi-omics Data with Local Low-Rank Structure . . . . .	67
<i>The Tien Mai, Leiv Rønneberg, Zhi Zhao, Manuela Zucknick, and Jukka Corander</i>	
Mass Spectra Interpretation and the Interest of SpecFit for Identifying Uncommon Modifications . . . . .	80
<i>Guillaume Fertin, Matthieu David, Hélène Rogniaux, and Dominique Tessier</i>	

<b>MSAX: Multivariate Symbolic Aggregate Approximation for Time Series Classification . . . . .</b>	<b>90</b>
<i>Manuel Anacleto, Susana Vinga, and Alexandra M. Carvalho</i>	
<b>NeoHiC: A Web Application for the Analysis of Hi-C Data . . . . .</b>	<b>98</b>
<i>Daniele D’Agostino, Pietro Liò, Marco Aldinucci, and Ivan Merelli</i>	
<b>Random Sample Consensus for the Robust Identification of Outliers in Cancer Data . . . . .</b>	<b>108</b>
<i>André Verissimo, Marta B. Lopes, Eunice Carrasquinha, and Susana Vinga</i>	
<b>Solving Equations on Discrete Dynamical Systems . . . . .</b>	<b>119</b>
<i>Alberto Dennunzio, Enrico Formenti, Luciano Margara, Valentin Montmirail, and Sara Riva</i>	
<b>SW+: On Accelerating Smith-Waterman Execution of GATK HaplotypeCaller . . . . .</b>	<b>133</b>
<i>Meysam Roodi and Andreas Moshovos</i>	
<b>Algebraic and Computational Methods for the Study of RNA Behaviour</b>	
<b>Algebraic Characterisation of Non-coding RNA . . . . .</b>	<b>145</b>
<i>Stefano Maestri and Emanuela Merelli</i>	
<b>Bi-alignments as Models of Incongruent Evolution of RNA Sequence and Secondary Structure. . . . .</b>	<b>159</b>
<i>Maria Waldl, Sebastian Will, Michael T. Wolfinger, Ivo L. Hofacker, and Peter F. Stadler</i>	
<b>Label Core for Understanding RNA Structure. . . . .</b>	<b>171</b>
<i>Michela Quadrini, Emanuela Merelli, and Riccardo Piergallini</i>	
<b>Modification of Valiant’s Parsing Algorithm for the String-Searching Problem . . . . .</b>	<b>180</b>
<i>Yuliya Susanina, Anna Yaveyn, and Semyon Grigorev</i>	
<b>On Secondary Structure Analysis by Using Formal Grammars and Artificial Neural Networks . . . . .</b>	<b>193</b>
<i>Polina Lunina and Semyon Grigorev</i>	

## **Intelligence Methods for Molecular Characterization and Dynamics in Translational Medicine**

Integration of Single-Cell RNA-Sequencing Data into Flux Balance Cellular Automata . . . . .	207
<i>Davide Maspero, Marzia Di Filippo, Fabrizio Angaroni, Dario Pescini, Giancarlo Mauri, Marco Vanoni, Alex Graudenzi, and Chiara Damiani</i>	

## **Machine Learning in Healthcare Informatics and Medical Biology**

Characterizing Bipolar Disorder-Associated Single Nucleotide Polymorphisms in a Large British Cohort Using Association Rules . . . . .	219
<i>Alberto Pinheira, Rodrigo Dias, Camila Nascimento, and Inês Dutra</i>	
Evaluating Deep Semi-supervised Learning for Whole-Transcriptome Breast Cancer Subtyping . . . . .	232
<i>Silvia Cascianelli, Francisco Cristovao, Arif Canakoglu, Mark Carman, Luca Nanni, Pietro Pinoli, and Marco Masseroli</i>	
Learning Weighted Association Rules in Human Phenotype Ontology . . . . .	245
<i>Giuseppe Agapito, Mario Cannataro, Pietro H. Guzzi, and Marianna Milano</i>	
Network Modeling and Analysis of Normal and Cancer Gene Expression Data . . . . .	257
<i>Gaia Ceddia, Sara Pidò, and Marco Masseroli</i>	
Regularization Techniques in Radiomics: A Case Study on the Prediction of pCR in Breast Tumours and the Axilla . . . . .	271
<i>Eunice Carrasquinha, João Santinha, Alexander Mongolin, Maria Lisitskiya, Joana Ribeiro, Fátima Cardoso, Celso Matos, Leonardo Vanneschi, and Nickolas Papanikolaou</i>	

## **Modeling and Simulation Methods for Computational Biology and Systems Medicine**

In Silico Evaluation of Daclizumab and Vitamin D Effects in Multiple Sclerosis Using Agent Based Models. . . . .	285
<i>Marzio Pennisi, Giulia Russo, Giuseppe Sgroi, Giuseppe Alessandro Parasiliti Palumbo, and Francesco Pappalardo</i>	
Multiple Sclerosis Disease: A Computational Approach for Investigating Its Drug Interactions . . . . .	299
<i>Simone Pernice, Marco Beccuti, Greta Romano, Marzio Pennisi, Alessandro Maglione, Santina Cutrupi, Francesco Pappalardo, Lorenzo Capra, Giuliana Franceschinis, Massimiliano De Piero, Gianfranco Balbo, Francesca Cordero, and Raffaele Calogero</i>	

<b>Observability of Bacterial Growth Models in Bubble Column Bioreactors . . .</b>	<b>309</b>
<i>Paola Lecca and Angela Re</i>	
<b>On the Simulation and Automatic Parametrization of Metabolic Networks Through Electronic Design Automation . . . . .</b>	<b>323</b>
<i>Nicola Bombieri, Antonio Mastrandrea, Silvia Scaffeo, Simone Caligola, Franco Fummi, Carlo Laudanna, Gabriela Constantin, and Rosalba Giugno</i>	
<b>Deep Clustering for Metagenomics . . . . .</b>	<b>335</b>
<i>Isis Bonet, Alejandro Pena, Christian Lochmuller, Alejandro Patino, and Mario Gongora</i>	
<b>Author Index . . . . .</b>	<b>349</b>