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Data and Computational Biology (DCB) Lab

**DATA &
COMPUTATIONAL
BIOLOGY**

# Alex Graudenzi
## Curriculum vitae
*(Update: July 22)*

## CURRENT POSITION(S)

♦ Tenure-track Researcher ("RTD-B"), Dept. of Informatics, Systems and Communications (DISCo), Univ. of Milan-Bicocca

♦ Co-head of the Data and Computational Biology Lab, Univ. of Milan-Bicocca. https://dcb.disco.unimib.it/

♦ Director of the Lake Como School of Advanced Studies on Cancer Development and Complexity. https://cdac2021.lakecomoschool.org/

♦ Member of the B4 Bicocca Bioinformatics, Biostatistics and Bioimaging Centre, Milan, Italy

## PREVIOUS POSITIONS

♦ 2018-2022: Tenured Researcher, Inst. of Molecular Bioimaging and Physiology, Consiglio Nazionale delle Ricerche (IBFM-CNR), Milan

♦ 2016-2018: Researcher ("RTD-A"), DISCo, Univ. of Milan-Bicocca

♦ 2015-2016: Researcher, IBFM-CNR. Project: "Bioinformatics and Systems Biology for the study of aging processes"

♦ 2011-2015: Researcher, DISCo, Univ. of Milan-Bicocca. Projects: "Retronet" and "Multiscale modeling, analysis and simulation of biological systems". Supervisors: M. Antoniotti, G. Mauri

♦ 2010-2011: Researcher, European Centre for Living Technology, University Ca' Foscari of Venice. Project: "Auto-catalytic cycles in models of systems of interacting polypeptide". Supervisors: R. Serra, I. Poli

♦ 2007-2010: Ph.D. in Multiscale Modeling, Computational Simulations and Characterization in Material and Life Sciences, Univ. of Modena and Reggio Emilia. Thesis: "Criticality and Perturbations in Boolean Models of Gene Regulatory Networks". Supervisors: R.Serra, M.C. Menziani

## PUBLICATION RECAP *(update Jul 22)*

♦ Indexed publications: 68 (Scopus), 38 either as first, last, or corresponding author

♦ Overall citations: 1272 (Scholar) 775 (Scopus)

♦ H-index: 19 (Scholar) 16 (Scopus)

♦ i-10 index: 36 (Scholar)


♦ Scopus: https://www.scopus.com/authid/detail.uri?authorId=25121540100

♦ Google scholar: https://scholar.google.com/citations?hl=it&user=FtHxbLIAAAAJ

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(MAIN) RESEARCH AREAS

- Computational methods for cancer and viral evolution
- Data science for health and medicine
- Multiscale modeling and simulation of biological systems
- Bioinformatics methods for multi-omics (single-cell) data analysis and integration
- Explainable AI and deep learning

PROJECTS

- 2021 – 2025: AIRC Investigator grant (IG): "ANAKIN" Advanced Nanotechnology to Assist Keeping the tumor microenvironment Involved in cancer Neutralization (PI: Miriam Colombo – Univ. of Milan-Bicocca).
  Role: collaborator (0.5 man/year 2024-2025).
- 2019 – 2024: My First AIRC Grant: "Integrating pharmacogenomic and pharmacometabolomic data towards personalized opioid therapies for cancer pain" (PI: Francesca Colombo - ITB-CNR).
  Role: collaborator.
- 2019 – 2022: Call HUB Resarch and Innovation, Regione Lombardia, POR FESR 2014-2020 project "INTERSLA" Innovation, new technological models and networks to treat ALS (PI: Giuseppe Lauria Pinter – IRCSS Istituto Neurologico "Carlo Besta").
  Role: co-responsible of WP4: Bioinformatics techniques for the analysis and integration of clinical big data (1140 hours).
- 2019 –2021: PON 2014 project "MOLIM ONCOBRAIN" Innovative methods of molecular imaging for the study of oncological and neurodegenerative diseases". Role: collaborator (770 hours).
- 2018 – 2023: CRUK/AIRC/AECC Accelerator Award "SCCEIC" Single-cell cancer evolution in the clinic (PI: Giovanni Tonon - IRCCS Ospedale San Raffaele.).
  Role: co-responsible of Programme 3: Bioinformatics analysis, single-cell data integration and evolutionary methods.
- 2016 –: ESFRI/MIUR project SysBioNet (Director: Lilia Alberghina – Univ. of Milan-Bicocca)
  Role: collaborator.
- 2015-2016: CNR Project "Aging: technological and molecular innovation for health improvement of aging people".
  Role: collaborator.
- 2011-2015: Regione Lombardia 2010 project "RetroNet" project through the ASTIL project (PI: Marco Antoniotti – Univ. of Milan-Bicocca)
  Role: WP-task team scientific leader.
- 2011-2015: Fondo Accordi Istituzionali 2009 project "NEDD" - Network Enabled Drug Design project (PI: Giancarlo Mauri – Univ. of Milan-Bicocca)
  Role: WP-task team scientific leader.

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- 2010-2011: Fondazione di Venezia project "DICE" - Designing Informative Combinatorial Experiments for Living Technology project (PI: Irene Poli – Univ. Ca' Foscari of Venice) Role: collaborator.
- 2007-2010: MIUR-FISR project "MITICA" (nr. 2982/Ric).
  Role: collaborator.

## PATENTS

- US Patent US11205519B2: "Methods, Computer-accessible Medium, and Systems to Model Disease Progression Using Biomedical Data from Multiple Patients".
  https://patents.google.com/patent/US11205519B2/en

## INDIVIDUAL FUNDINGS

- Individual senior contract with Univ. of Milan-Bicocca (5 years), within the AIRC/CRUK Accelerator Project "SCCEIC"
- Full financial support (3000€), MUR/FFABR initiative: "Annual funding for individual research activity"
- Recipient of a full financial support (2500€) with respect to the initiative: "H2020 ERC - Initiative for applicant profile strengthening. A project funded by Fondazione Cariplo and Regione Lombardia - 2017 Selection round".

## EDITORIAL ACTIVITY

- Editorial Board member of Cancer Informatics: https://journals.sagepub.com/home/cix
- Review Editorial Board member of Frontiers in Genetics (Computational Genomics) and Frontiers in Applied Mathematics and Statistics (Mathematical Biology): https://www.frontiersin.org/
- Guest editor of Natural Computing, Volume 13, Issue 3, Part1: doi:10.1007/s11047-014-9448-3
- Guest Editor of EPTCS 130, DOI: 10.4204/EPTCS.130
- Guest Editor of Workshop Proceedings of AixIA 2009. ISBN: 978-88-903581-1-1

## AWARDS

- National Scientific Habilitation for Associate Professor in Computer Science (area: 01/B1).
- Silver prize (200 US$) at the Cancer Genomics and Mathematical Data Analysis Symposium, 7-8 February 2018, Columbia University, US, for the poster: "Pipelines for Inferring Cancer Progression: Present & Future".
- Silver prize (5000€) at the SysBio– Centre of Systems Biology annual competition, for the article: PNAS USA 113 (28). doi:10.1073/pnas.1520213113.
- Silver prize (2000 US$) at the "Open Source Software World Challenge 2016" by The Ministry of Science, ICT and Future Planning of Korea. Project: "TRONCO-PiCnIc".
- DISCo 2014 – Best Interdisciplinary Journal Paper Award (500€) for the paper. PLoS ONE 9(10): e108358. doi:10.1371/journal.pone.0108358.

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VISITING

♦ 2019, Responsible lecturer: "Bayesian Learning and Bayesian classifiers", Master's degree Program in Data Science and Advanced Analytics. Universidade NOVA de Lisboa (Portugal).

♦ 2017, Visiting at the New York Genome Center (NYGC), New York (USA) (host: Marcin Imielinski)

♦ 2015, May, Catalan Institute of Oncology (ICO) in Barcelona (Spain) (host: prof. Victor Moreno)

♦ 2012, March and October, New York University (NYU), USA. Bioinformatics Laboratory, Courant Institute of Mathematical Sciences (host: prof. Bud Mishra).

♦ 2012, March and October, University of Toronto, Canada. Bader Lab, The Donnelly Centre for Cellular and Biomolecular Research (host: prof. Gary Bader).

SUPERVISION

♦ Postdocs: F. Angaroni (Univ. of Milan-Bicocca, at the Human Technopole, Milan, from Sept. 2022). Title: "Control Theory for Therapy Design".

♦ PhD students in Computer Science (University of Milan-Bicocca): L. Patruno (ongoing), F. Craighero (ongoing), D. Maspero (currently at the CNAG-CRG, Centre for Genomic Regulation, Barcelona).

♦ Research grants: E. Schiavon (IBFM-CNR). Title: "Development of deep and transfer learning methods for biomedical image analysis"; D. Maspero (IBFM-CNR). Title: "Development of computational strategies for the investigation of complex pathologies".

♦ Master's/bachelor's students in Computer Science, Biotechnology (Univ. of Milan-Bicocca): 25+ students

CHAIR

♦ Chair of Wivace 2013, Italian Workshop on Artificial Life and Evolutionary Computation, Milan, 1-2, July 2013.

TALKS

♦ Invited speaker at 6 international conferences/seminars

♦ Peer-reviewed contributions at 15+ international conferences

SCIENTIFIC COMMITTEES

♦ Member of the program and organizing committees of 25+ international conferences.

EVALUATION COMMITTEES

♦ Member of 10+ committees for individual research grants and scholarships

♦ Member of 5+ committees for master's and bachelor's graduation sessions

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## REVIEWING ACTIVITY

♦ Peer reviewer for international journals, books, and conferences, including Nature Communications, Nucleic Acids Research, PLoS Computational Biology, IEEE Transactions on Cybernetics, Bioinformatics, Neural Networks, BMC Bioinformatics, Neurocomputing, Journal of Computational Science, Natural Computing, IET Systems Biology, Frontiers in Biosciences, Journal of the Royal Society Interface, Computational and Mathematical Methods in Medicine, Helyos, etc.

♦ Member of the Register of Expert Peer Reviewers for Italian Scientific Evaluation – REPRISE (https://reprise.cineca.it/).

♦ Reviewer for the research quality assessment (ANVUR-VQR), period 2015-2019. Italian Ministry of Research and University.

## DIDACTICS

♦ Responsible lecturer for 10+ courses in bachelor's and master's degrees at the Univ. of Modena and Reggio Emilia and at the Univ. of Milan-Bicocca

♦ Responsible Lecturer at 1 II level master's degree in Methods and Data Analysis in Biomedical Research

## SOFTWARE DEVELOPMENT

♦ Google Summer of Code (GSoC) mentor (https://summerofcode.withgoogle.com) via National Resource for Network Biology – NRNB

♦ Co-author of the following software:

- J-SPACE: https://github.com/BIMIB-DISCo/J-Space.jl
- ENAD: https://github.com/BIMIB-DISCo/ENAD-experiments
- OG-SPACE: https://github.com/BIMIB-DISCo/OG-SPACE
- VirMutSig: https://github.com/BIMIB-DISCo/VirMutSig
- PMCE: https://github.com/BIMIB-DISCo/PMCE
- VERSO: https://www.bioconductor.org/packages/release/bioc/html/VERSO.html
- LACE: https://bioconductor.org/packages/release/bioc/html/LACE.html
- MaREA4Galaxy: https://galaxyproject.org/use/marea4galaxy/
- CyTRON/JS: https://bimib.disco.unimib.it/cytronjs/welcome
- CyTRON: http://apps.cytoscape.org/apps/cytron
- SpidermiR: https://www.bioconductor.org/packages/release/bioc/html/SpidermiR.html
- COGNAC: https://chaste.cs.ox.ac.uk/trac/wiki/PaperTutorials/CoGNaC
- CABERNET: http://bimib.disco.unimib.it/index.php/CABERNET
- TRONCO: http://www.bioconductor.org/packages/release/bioc/html/TRONCO.html
- GESTODIFFERENT: http://bimib.disco.unimib.it/index.php/Retronet

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OTHER

♦ 2022 -: Scientific responsible for the framework agreement between IBFM-CNR and Dept. of Informatics, Univ. of Milan-Bicocca. Title of the research project: " Bioinformatics methods to analyze and integrate omics data for the investigation of multi-factorial diseases".

♦ 2019: Member of the IBFM-CNR team for risk assessment, impact evaluation, implementation of security measures, especially with respect to the cybersecurity risk and in relation to the EU regulation 2016/679 (GDPR).

♦ 2018 -: Full member of BITS – Bioinformatics Italian Society, http://bioinformatics.it/

♦ 2018-: Full member of GRIN (Computer Science Group), http://www.grin-informatica.it/opencms/opencms/grin/

♦ 2018-2022: Member of INLAB - Innovation & Integration in Molecular Medicine Laboratory, IBFM-CNR.

♦ 2018: Full member of AIxIA https://aixia.it/

♦ 2018: Member of the CSAI – Complex Systems and Artificial Intelligence Centre, Univ. of Milano - Bicocca

♦ 2011-2020: Member of the BIMIB – Bioinformatics Milano-Bicocca lab

SELECTED PUBLICATIONS (25)

1. Ramazzotti, D., Angaroni, F., Maspero, D., Ascolani, G., Castiglioni, I., Piazza, R., Antoniotti, M., Graudenzi, A. (2022) Variant calling from scRNA-seq data allows the assessment of cellular identity in patient-derived cell lines. **NATURE COMMUNICATIONS**, 13 (1), art. no. 2718. doi: 10.1038/s41467-022-30230-w

2. Angaroni, F., Guidi, A., Ascolani, G., d'Onofrio, A., Antoniotti, M., Graudenzi, A. (2022) J-SPACE: a Julia package for the simulation of spatial models of cancer evolution and of sequencing experiments. **BMC BIOINFORMATICS**, 23 (1), art. no. 269. doi: 10.1186/s12859-022-04779-8

3. Mella, L., Lal, A., Angaroni, F., Maspero, D., Piazza, R., Sidow, A., Antoniotti, M., Graudenzi, A., Ramazzotti, D. (2022) SparseSignatures: An R package using LASSO-regularized non-negative matrix factorization to identify mutational signatures from human tumor samples. **STAR PROTOCOLS**, 3 (3), art. no. 101513. doi: 10.1016/j.xpro.2022.101513

4. Calabretta, E., Guidetti, A., Ricci, F., Di Trani, M., Monfrini, C., Magagnoli, M., Bramanti, S., Maspero, D., Morello, L., Merli, M., Di Rocco, A., Graudenzi, A., Derenzini, E., Antoniotti, M., Rossi, D., Corradini, P., Santoro, A., Carlo-Stella, C. (2022) Chemotherapy after PD-1 inhibitors in relapsed/refractory Hodgkin lymphoma: Outcomes and clonal evolution dynamics. **BRITISH JOURNAL OF HEMATOLOGY**, 198 (1), pp. 82-92. doi: 10.1111/bjh.18183

5. Ramazzotti, D., Maspero, D., Angaroni, F., Spinelli, S., Antoniotti, M., Piazza, R., Graudenzi, A. (2022) Early detection and improved genomic surveillance of SARS-CoV-2 variants from deep sequencing data. **ISCIENCE**, 25 (6), art. no. 104487. doi: 10.1016/j.isci.2022.104487

6. Angaroni F, Chen K, Damiani C, Caravagna G, Graudenzi A, Ramazzotti D (2022). PMCE: efficient inference of expressive models of cancer evolution with high prognostic power.

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**BIOINFORMATICS**, vol. 38, p. 754-762, ISSN: 1367-4803, doi: 10.1093/bioinformatics/btab717

7. Ramazzotti, Daniele, Angaroni, Fabrizio, Maspero, Davide, Ascolani, Gianluca, Castiglioni, Isabella, Piazza, Rocco, Antoniotti, Marco, Graudenzi, Alex (2022). LACE: Inference of cancer evolution models from longitudinal single-cell sequencing data. **JOURNAL OF COMPUTATIONAL SCIENCE**, vol. 58, 101523, ISSN: 1877-7503, doi: 10.1016/j.jocs.2021.101523

8. Ramazzotti, Daniele, Angaroni, Fabrizio, Maspero, Davide, Mauri, Mario, D'Aliberti, Deborah, Fontana, Diletta, Antoniotti, Marco, Elli, Elena Maria, Graudenzi, Alex, Piazza, Rocco (2022). Large-Scale Analysis of SARS-CoV-2 Synonymous Mutations Reveals the Adaptation to the Human Codon Usage During the Virus Evolution. **VIRUS EVOLUTION**, ISSN: 2057-1577, doi: 10.1093/ve/veac026

9. Graudenzi A., Maspero D., Angaroni F., Piazza R., Ramazzotti D. (2021). Mutational signatures and heterogeneous host response revealed via large-scale characterization of SARS-CoV-2 genomic diversity. **ISCIENCE**, vol. 24, 102116, ISSN: 2589-0042, doi: 10.1016/j.isci.2021.102116

10. Maspero, Davide, Angaroni, Fabrizio, Porro, Danilo, Piazza, Rocco, Graudenzi, Alex, Ramazzotti, Daniele (2021). VirMutSig: Discovery and assignment of viral mutational signatures from sequencing data. **STAR PROTOCOLS**, vol. 2, 100911, ISSN: 2666-1667, doi: 10.1016/j.xpro.2021.100911

11. Patruno, L, Maspero, D, Craighero, F, Angaroni, F, Antoniotti, M, Graudenzi, A (2021). A review of computational strategies for denoising and imputation of single-cell transcriptomic data. **BRIEFINGS IN BIOINFORMATICS**, vol. 22, bbaa222, ISSN: 1467-5463, doi: 10.1093/bib/bbaa222

12. Ramazzotti. , Daniele, Angaroni, Fabrizio, Maspero, Davide, Gambacorti-Passerini, Carlo, Antoniotti, Marco, Graudenzi, Alex, Piazza, Rocco (2021). VERSO: a comprehensive framework for the inference of robust phylogenies and the quantification of intra-host genomic diversity of viral samples. **PATTERNS**, vol. 2, 100212, ISSN: 2666-3899, doi: 10.1016/j.patter.2021.100212

13. Angaroni, Fabrizio, Graudenzi, Alex, Rossignolo, Marco, Maspero, Davide, Calarco, Tommaso, Piazza, Rocco, Montangero, Simone, Antoniotti, Marco (2020). An Optimal Control Framework for the Automated Design of Personalized Cancer Treatments. **FRONTIERS IN BIOENGINEERING AND BIOTECHNOLOGY**, vol. 8, 523, ISSN: 2296-4185, doi: 10.3389/fbioe.2020.00523

14. Damiani, C, Rovida, L, Maspero, D, Sala, I, Rosato, L, Di Filippo, M, Pescini, D, Graudenzi, A, Antoniotti, M, Mauri, G (2020). MaREA4Galaxy: metabolic reaction enrichment analysis and visualization of RNA-seq data using Galaxy. **COMPUTATIONAL AND STRUCTURAL BIOTECHNOLOGY JOURNAL**, vol. 18, p. 993-999, ISSN: 2001-0370, doi: 10.1016/j.csbj.2020.04.008

15. Damiani, C, Maspero, D, Di Filippo, M, Colombo, R, Pescini, D, Graudenzi, A, Westerhoff HV, Alberghina, L, Vanoni, M, Mauri, G (2019). Integration of single-cell RNA-seq data into

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population models to characterize cancer metabolism. **PLOS COMPUTATIONAL BIOLOGY**, vol. 15, e1006733, ISSN: 1553-7358, doi: 10.1371/journal.pcbi.1006733

16. Ramazzotti D, Graudenzi A, De Sano L, Antoniotti M, Caravagna G (2019). Learning mutational graphs of individual tumour evolution from single-cell and multi-region sequencing data. **BMC BIOINFORMATICS**, vol. 20, p. 1-13, ISSN: 1471-2105, doi: 10.1186/s12859-019-2795-4

17. Ramazzotti, Daniele, Nobile, Marco S., Antoniotti, Marco, Graudenzi, Alex (2019). Efficient computational strategies to learn the structure of probabilistic graphical models of cumulative phenomena. **JOURNAL OF COMPUTATIONAL SCIENCE**, vol. 30, p. 1-10, ISSN: 1877-7503, doi: 10.1016/j.jocs.2018.10.009

18. Graudenzi, A, Maspero,D, Di Filippo,M, Gnugnoli,M, Isella,C, Mauri,G, Medico,E, Antoniotti,M, Damiani,C (2018). Integration of transcriptomic data and metabolic networks in cancer samples reveals highly significant prognostic power. **JOURNAL OF BIOMEDICAL INFORMATICS**, vol. 87, p. 37-49, ISSN: 1532-0464, doi: 10.1016/j.jbi.2018.09.010

19. Caravagna, G, GRAUDENZI, ALEX, Ramazzotti, D, Sanz Pamplona, R, De Sano, L, MAURI, GIANCARLO, Moreno, V, ANTONIOTTI, MARCO, Mishra, B. (2016). Algorithmic methods to infer the evolutionary trajectories in cancer progression. **PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA**, vol. 113, p. E4025-E4034, ISSN: 1091-6490, doi: 10.1073/pnas.1520213113

20. De Sano, L, CARAVAGNA, GIULIO, RAMAZZOTTI, DANIELE, GRAUDENZI, ALEX, MAURI, GIANCARLO, Mishra, B, ANTONIOTTI, MARCO (2016). TRONCO: An R package for the inference of cancer progression models from heterogeneous genomic data. **BIOINFORMATICS**, vol. 32, p. 1911-1913, ISSN: 1367-4803, doi: 10.1093/bioinformatics/btw035

21. RAMAZZOTTI, DANIELE, CARAVAGNA, GIULIO, Olde Loohuis, L, GRAUDENZI, ALEX, Korsunsky, I, MAURI, GIANCARLO, ANTONIOTTI, MARCO, Mishra, B. (2015). CAPRI: Efficient Inference of Cancer Progression Models from Cross-sectional Data. **BIOINFORMATICS**, vol. 31, p. 3016-3026, ISSN: 1367-4803, doi: 10.1093/bioinformatics/btv296

22. GRAUDENZI, ALEX, CARAVAGNA, GIULIO, De Matteis, G, ANTONIOTTI, MARCO (2014). Investigating the relation between stochastic differentiation and homeostasis in intestinal crypts via multiscale modeling. **PLOS ONE**, vol. 9, e97272, ISSN: 1932-6203, doi: 10.1371/journal.pone.0097272

23. De Matteis, G, GRAUDENZI, ALEX, ANTONIOTTI, MARCO (2013). A review of spatial computational models for multi-cellular systems, with regard to intestinal crypts and colorectal cancer development. **JOURNAL OF MATHEMATICAL BIOLOGY**, vol. 66, p. 1409-1462, ISSN: 0303-6812, doi: 10.1007/s00285-012-0539-4

24. Graudenzi A, Serra R, Villani M, Damiani C, Colacci A, Kauffman S (2011). Dynamical properties of a Boolean model of gene regulatory network with memory. **JOURNAL OF COMPUTATIONAL BIOLOGY**, vol. 18, p. 1291-1303, ISSN: 1066-5277, doi: 10.1089/cmb.2010.0069

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25. Serra, R, Villani, M, Graudenzi, A, Kauffman, SA (2007). Why a simple model of genetic regulatory networks describes the distribution of avalanches in gene expression data. **JOURNAL OF THEORETICAL BIOLOGY**, vol. 246, p. 449-460, ISSN: 0022-5193, doi: 10.1016/j.jtbi.2007.01.012