

# CURRICULUM VITAE



## General Information

Name ***Tiziana Sanavia***  
Birth 26/04/1984 a Dolo (Venezia), Italiana  
e-mail [tiziana.sanavia@unito.it](mailto:tiziana.sanavia@unito.it)  
website <http://compbio.hms.harvard.edu/people/tiziana-sanavia>

## Current Position

From February 2020 **Assistant Professor**  
Institution Department of Medical Sciences, **University of Torino (Italy)**  
Research Activity Inferential statistics and Machine (deep) Learning for clinical and biomedical approaches, using 'omics' sequencing data (WGS/WES, RNA-seq, miRNA and Methylation seq.)

## Education

March, 23<sup>th</sup> 2012 **Ph.D. in Bioengineering**  
Institution Department of Information Engineering, **University of Padova (Italy)**  
Thesis Biomarker lists stability in genomic studies: analysis and improvement by prior biological knowledge integration into the learning process (Supervisor: Prof. Barbara Di Camillo)  
July, 8<sup>th</sup> 2008 **Master's Degree in Bioengineering**  
Institution Department of Information Engineering, **University of Padova (Italy)**  
Thesis Function-based discovery of temporal gene expression patterns in endothelial cells stimulated with insulin. (Supervisor: Prof. Barbara Di Camillo) Graduation: 110/110 cum laude  
July, 27<sup>th</sup> 2006 **Bachelor's Degree in Information Technologies Engineering**  
Institution Department of Information Engineering, **University of Padova (Italy)**  
Thesis Compartmental models: identification and parameter estimation. (Advisor: Prof. Claudio Cobelli, Co-advisor: Prof. Chiara Dalla Man) Graduation: 105/110

## Research Experiences

April 2016 – December 2019 **Senior Research Fellow** on analyses of whole-genome/exome data (mutations, CNVs and structural variants) from cancer and neurological diseases. (Supervisor: Prof. Peter J Park)  
Institution Department of Biomedical Informatics, **Harvard Medical School (USA)**  
January 2014 - December 2015 **Senior Post-doctoral Fellow** on research project "Integrative epigenomic and genomic computational methods for high-throughput sequencing data" (P.I. Tiziana Sanavia PhD)  
Institution Department of Information Engineering, **University of Padova (Italy)**  
January 2012 - December 2013 **Junior Post-doctoral Fellow** on research project "Robust biomarker selection from genomic high-throughput data: integration of biological prior information in classification algorithm" (P.I. Prof. Barbara Di Camillo)  
Institution Department of Information Engineering, **University of Padova (Italy)**  
April 2012 - March 2013 **Visiting scientist** on research projects related machine learning methods applied to Next Generation Sequencing time series data. (Supervisor: Prof. Christian J. Stoeckert Jr.)  
Institution Perelman School of Medicine at **University of Pennsylvania (Philadelphia, USA)**  
October 2008 - December 2008 **Scholarship** on research project "Systems Biology approaches to infer gene regulation from gene and protein time-series expression data" (Supervisor: Prof. Barbara Di Camillo)  
Institution Department of Information Engineering, **University of Padova (Italy)**

## Bibliometric indicators

**Scientific Research Articles** (in international peer-reviewed journals): 28  
**Proceedings** to conferences: 37 (one book chapter)  
**Citations:** 721 (Scopus); 1310 (Google Scholar)  
**h-index:** 11 (Scopus); 13 (Google Scholar)  
**i10-index:** 12 (Scopus); 16 (Google Scholar)  
**ORCID ID:** 0000-0003-3288-0631; **ResearcherID:** F-9446-2015; **Scopus Author ID:** 36731487500  
**Referee activity:** 38 reviews in international journals and 4 in international conferences  
**Publons:** <https://publons.com/researcher/1678031/tiziana-sanavia/peer-review/>

## Participation to research projects and consortia

### *European projects/consortia*

**H2020-EU.3.1.5 (101017549)** GenoMed4ALL - Genomics and Personalized Medicine for all through Artificial Intelligence in Haematological Diseases (P.I. Prof. Federico Álvarez García; Prof. Santiago Zazo Bello, Universidad Politécnica de Madrid) **Role: Participant contact**

**H2020-EU.3.1.4.2 (101017598)** Brainteaser - BRinging Artificial INTelligence home for a better cAre of amyotrophic lateral sclerosis and multiple SclERosis (P.I. Prof. Maria Fernanda Cabrera, Universidad Politécnica de Madrid) **Role: Participant contact**

**H2020-EU.3.1.5 (101016775)** Intervene - INTERnational consortium for integratiVE GeNomics PrEdiction (P.I. Prof. Samuli Ripatti; Prof. Andrea Ganna, University of Helsinki) **Role: Team Member**

### *US projects/consortia*

**NIMH-NIH 2015/2020 (5U01MH106883)** Somatic Mosaicism and Autism Spectrum Disorder (P.I. Prof. Christopher Walsh, Boston Children's Hospital; Prof. Peter J. Park, Harvard Medical School) **Role: Collaborator**

**NIMH-NHGRI 2014/2019 (1P50MH106933)** Neuropsychiatric Genome-Scale and RDOC Individualized Domains (P.I. Prof. Isaac S. Kohane, Harvard Medical School) **Role: Collaborator**

**NICHD-NHGRI 2013/2018 (5U19HD077671)** Genome sequence-based screening for childhood risk/newborn illness (P.I. Prof. Robert C. Green, Brigham and Women's Hospital) **Role: Collaborator**

**NIDDK-NIH 2005/2015 (2R01DK065949)** Pancreatic Beta cell development and functional maintenance (P.I. Prof. Gu Guoqiang, Vanderbilt Univ.; affiliated to Beta Cell Biology Consortium) **Role: Collaborator**

Participation to the international annual competitions **DREAM Challenges** and published as member of the DREAM consortium in the following years:

- 2010 – Systems Genetics Challenge (won honourable mention for best performer):  
<https://www.synapse.org/#!Synapse:syn2820440/wiki/71024>
- 2011 – FlowCAP2 Molecular Classification of Acute Myeloid Leukemia Challenge:  
<https://www.synapse.org/#!Synapse:syn2887788/wiki/72178>
- 2013 – HPN-DREAM Breast Cancer Network Inference Challenge:  
<https://www.synapse.org/#!Synapse:syn1720047/wiki/55342>
- 2014 – Acute Myeloid Leukemia Outcome Prediction Challenge:  
<https://www.synapse.org/#!Synapse:syn2455683/wiki/64007>

### *Italian projects/consortia*

**National research projects (PRIN) 2017:** Integrative tools for defining the molecular basis of the diseases: computational and experimental methods for protein variant interpretation (P.I. Prof. Piero Fariselli, University of Torino) **Role: Collaborator**

**Research Fundings from University of Padova 2014 (CPDA148778)** An integrative analysis of DNA methylation and RNA-Seq in canine Diffuse Large B-Cell Lymphoma (P.I. Prof. Luca Aresu, Dept. of Comparative biomedicine and food science, University of Padova) **Role: Collaborator**

**Research Fundings from University of Padova 2010 (CPDA101217)** Models of RNA sequencing data variability for quantitative transcriptomics (P.I. Prof. Barbara Di Camillo, Dept. of Information Engineering, University of Padova) **Role: Collaborator**

**Research Fundings from University of Padova 2009/2010** Methods for the integration of background knowledge in kernel-based learning algorithms for the robust identification of biomarkers in genomics (P.I. Prof. Fabio Aioli, Dept. of Mathematics, University of Padova) **Role: Collaborator**

<b>Grants and Awards</b>	<p><b>CARIPARO Foundation – Research projects of Excellence 2007/2008</b> Inference of transcriptional regulatory pathways from integrative analysis of gene and protein data (P.I. Prof. Gianna Toffolo, Dept. of Information Engineering, University of Padova) <u>Role: Collaborator</u></p> <p><b>National research projects (PRIN) 2006/2007</b> Dynamic models of gene and protein expression in endothelial progenitor cells in evolution of diabetes (P.I. Prof. Gianna Toffolo, Dept. of Information Engineering, University of Padova) <u>Role: Collaborator</u></p> <p><b>Personal Grant for a 2-year senior post-doctoral fellowship as independent researcher</b> from University of Padova, Italy. January 2014-December 2015.</p> <p><b>Grant for an oral presentation at 11<sup>th</sup> Annual Meeting of the Bioinformatics Italian Society</b> Rome, Italy, 2014.</p> <p><b>Study Abroad Scholarship</b>, awarded by “Fondazione Aldo Gini”. Padova, Italy, 2013.</p> <p><b>Honourable Mention for Best Performer (fourth place) in DREAM5</b> (Dialogue for Reverse Engineering Assessments and Methods), Systems Genetics Challenge, Columbia University, New York, USA, 2010.</p> <p><b>National Award for Best Master Thesis in Bioengineering</b>. Bressanone, Italy, 2008.</p>
<b>Seminars and talks</b>	<p>CME (Continuing Medical Education) “Approaches in NGS and ‘omics’ analyses for study and diagnosis of human/mendelian diseases”. <b>Machine Learning for clinical genomics</b>. Oct 29<sup>th</sup> 2021.</p> <p><b>Function-based discovery of temporal patterns in beta cell development</b>. Genetics Research Talks. Jan 11<sup>th</sup> 2013, Perelman School of Medicine at <u>University of Pennsylvania</u> (USA).</p> <p>9<sup>th</sup> course of methodology and applied research: Trends in molecular and cellular biology. <b>Quantitative analysis of high-throughput gene expression data</b>. <u>Padova University</u>, Dec 16<sup>th</sup> 2009.</p>
<b>Teaching</b>	<p>Assistant Professor Course “<b>Data Mining: Statistical Modeling and Learning from Data</b>” for Master’s students in Physics of Complex Systems, <u>University of Torino</u>, Academic Years 2020-2021 and 2021-2022: frontal lessons and preparation of laboratories.</p> <p>Course “<b>Machine Learning for Medical Physics</b>” for students at the graduate School in Medical Physics, <u>University of Torino</u>, Academic Year 2020-2021: frontal lesson.</p> <p>Course “<b>Statistical Inference and Machine Learning</b>” for students in the PhD Programme in Complex Systems for Life Sciences, <u>University of Torino</u>, Academic Year 2019-2020: on-line lessons.</p> <p>Adjunct professor Course “<b>Bioengineering for genomics</b>” for Master’s students in Bioengineering, <u>University of Padova</u>, Academic Year 2014-2015: frontal lessons and preparation of laboratories.</p> <p>Teaching assistant <b>BMI 713 - Computing Skills for Biomedical Sciences</b> (Prof. Nils Gehlenborg), Bioinformatics and Integrative Genomics PhD (BIG) program, Fall 2017, Dept. of Biomedical Informatics, <u>Harvard Medical School</u>: frontal lessons and preparation of laboratories.</p> <p><b>BMI 715 - Computational Statistics for Biomedical Sciences</b> (Prof. Peter J Park), Bioinformatics and Integrative Genomics PhD (BIG) program, Fall 2017, Dept. of Biomedical Informatics, <u>Harvard Medical School</u>: frontal lessons and preparation of laboratories.</p> <p><b>Quantitative Methods Bootcamp</b> for Master’s and PhD students (Prof. Nils Gehlenborg and Peter Kharchenko), August 2016, Dept. of Biomedical Informatics, <u>Harvard Medical School</u>.</p> <p>Course “<b>Analysis of biological signals</b>” (Prof. Gianna Toffolo) for Master’s students in Bioengineering, <u>University of Padova</u>, Academic Year 2009-2010: preparation of laboratories and frontal lessons.</p> <p>Course “<b>Bioengineering for genomics</b>” (Prof. Barbara Di Camillo) for Master’s students in Bioengineering, <u>University of Padova</u>, Academic Year 2009-2010: preparation of laboratories and frontal lessons.</p> <p>Co-Advisor and mentoring activity <b>Diane Zhang</b>, <u>Copy Number Variations and their impact on gene expression in liver</u>, Summer Internship, <u>Harvard Medical School</u>, 2017. Work published in <a href="http://cjsjournal.org/2018-cusj">http://cjsjournal.org/2018-cusj</a></p> <p><b>Aler Crepaldi</b>, <u>Integration of functional annotations in the classification of gene expression data</u>, Master's degree thesis, <u>University of Padova</u>, Academic Year 2010-2011</p> <p><b>Roberta Mazzucco</b>, <u>Gene expression correlation analysis for robust biomarker selection</u>, Master's degree thesis, <u>University of Padova</u>, Academic Year 2010-2011</p>

## Editorial and Referee Activity

**Editor** for *Frontiers in Molecular Biosciences* on the Research Topic “Computational and Experimental Protein Variant Interpretation in the Era of Precision Medicine”

**Reviewer Editor** for *Frontiers in Artificial Intelligence* and *Frontiers in Big Data* (section Medicine and Public Health)

### Reviewer:

- *Conferences*: **CIBB 2021 Scientific Committee** (17<sup>th</sup> IEEE International Conference on Computational Intelligence Methods for Bioinformatics and Biostatistics); **CIBCB 2019 Scientific Committee** (16<sup>th</sup> IEEE International Conference on Computational Intelligence in Bioinformatics and Computational Biology)
- *Journals*: **BMC Bioinformatics** (2022), **Bioinformatics** (2019-2021), **Liver International** (2021), **Genes** (2021), **Peer J Computer Science** (2021), **The American Journal of Pathology** (2019), **IEEE/ACM Transactions on Computational Biology and Bioinformatics** (2018), **PLoS ONE** (2017), **Journal of Biomedical Informatics** (2016-2021), **IEEE Journal of Biomedical and Health Informatics** (2021), **Frontiers in Artificial Intelligence** (2021), **Biophysica** (2021), **PLoS Computational Biology** (2021), **Frontiers in Cell and Developmental Biology** (2020), **RMD Open** (2020), **Applied Sciences** (2020), **Cancers** (2020)

## Memberships

**EACR** (European Association for Cancer Research)  
**AAAS** (American Association for the Advancement of Science)  
**ISCB** (International Society for Computational Biology)  
**BITS** (Bioinformatics Italian Society)

## Languages

**Italian** (Mother tongue)  
**English** (Professional working proficiency, GRE in 2008, FCE in 2003)  
**French** (Elementary proficiency)

## Software

[S1] Benevenuto S, Pancotti C, Fariselli P, Birolo G, **SANAVIA T** (2021) **ACDC-NN: a deep learning predictor of protein stability change upon mutation**. Python library: <https://pypi.org/project/acdc-nn/> Github: <https://github.com/compbio-med-unito/acdc-nn>

[S2] **SANAVIA T**, Finotello F, Di Camillo B (2015) **FunPat: Function-based Pattern analysis on RNA-seq time series**. R package: <http://sysbiobig.dei.unipd.it/?q=node/79#FunPat>

[S3] **SANAVIA T**, Di Camillo B (2014) **Snail: Supervised Network-based Algorithm for Integrative Learning**. Python code: <https://www.synapse.org/#!Synapse:syn2700016/wiki/>

[S4] Carlon A, Di Camillo B, Finotello F, Giarretta A, Manfrini M, Sambo F, **SANAVIA T**, Toffolo G, Trifoglio E [alphabetical order] (2014) **Local and global optimization of sparse ODE systems based on goodness of fit**. MATLAB code: <https://www.synapse.org/#!Synapse:syn2343026/wiki/62102>

[S5] Collaboration on Python library **FastsemSim** <https://sites.google.com/site/fastsemsim/>

## Programming skills

*Operative systems*: **Windows, Mac OS, Linux**

*Programming Languages* **R** (Expert), **MATLAB** (Expert), **Python** (Advanced), **Bash** (Advanced), **Perl** (Intermediate), **Java** (Intermediate), **SQL** (Intermediate), **Pascal** (Intermediate)

*Software tools*: Main **Bioconductor/CRAN packages** for analysis of **microarray e RNA-seq data**, e.g. **edgeR**, **DESeq2**, **limma**, **affy**, **AgiMicroRna** (Expert); **Alignment tools**: **BWA**, **Bowtie**, **STAR**, **RUM**, **RSEM** (Advanced); **DNA-seq tools**: **GATK** (Intermediate), **callers per Copy Number and Structural Variants in whole-genome/exome data** (Advanced); **Bisulfite-seq tools**: **Bismark**, **methylKit** (Advanced); **Chip-Seq tools**: **MACS**, **Homer** (Intermediate)

## Publications

### Peer-reviewed journal papers

Nature Methods (2)  
Oncotarget (2)  
Genes (2)  
Science (1)  
Developmental Cell (1)  
Journal of Hepatology (1)  
Scientific Reports (1)  
Brief Bioinform (1)  
PLoS Comput Biol (1)  
BMC Genomics (1)

[J1] Nicolè L\*, **SANAVIA T\***, Cappellesso R, Maffeis V, Kawahara A, Naito Y, Yano H, Guzzardo V, Radu CM, Orvieto E, Cillo U, Simioni P, Guido M, Zanus G, Akiba J, Fassina A. **Immunogenicity of Necroptosis in Hepatocellular Carcinoma**. Accepted at Journal of Immunotherapy in Cancer.

[J2] Pancotti C, Benevenuto S, Birolo G, Alberini V, Repetto V, **SANAVIA T**, Capriotti E, Fariselli P (2022) **Predicting protein stability changes upon single-point mutation: a thorough comparison of the available tools on a new dataset**. Briefings in Bioinformatics, doi:10.1093/bib/bbab555.

[J3] Zenone M, Zocchi L, Moccia C, Passerini SG, **SANAVIA T**, Fariselli P, Broganelli P, Ribero S, Maule M, Quaglino P (2021) **Digital dermoscopy monitoring of melanocytic lesions: Two novel calculators combining static and dynamic features to identify melanoma**. Journal of the European Academy of Dermatology and Venereology, doi:10.1111/jdv.17852.

BMC Bioinformatics (1)  
Liver Int (1)  
Front Cell Dev Biol.(1)  
Front Mol Biosci (1)  
Cells (1)  
J Phys D: Appl Phys (1)  
IJC Heart Vasc (1)  
JITC (1)  
CSBJ (1)  
JEADV (1)  
SCBM (1)  
IJBM (1)  
PLoS ONE (3)

\* co-first authorship  
+ corresponding

[J4] Anastasiadou E, Messina E, **SANAVIA T**, Labruna V, Ceccarelli S, Megiorni F, Gerini G, Pontecorvi P, Camero S, Perniola G, Venneri MA, Trivedi P, Lenzi A, Marchese C (2021) **Calcineurin Gamma Catalytic Subunit PPP3CC Inhibition by miR-200c-3p Affects Apoptosis in Epithelial Ovarian Cancer**. *Genes*, 12(9):1400.

[J5] Younes R, Caviglia GP, Govaere O, Rosso C, Armandi A, **SANAVIA T**, Pennisi G, Liguori A, Francione P, Gallegoduran R, Ampuero J, GarciaBlanco MJ, Aller R, Tiniakos D, Burt A, David E, Vecchio FM, Maggioni M, Cabibi D, Pareja MJ, Zaki MY, Grieco A, Fracanzani AL, Valenti L, Miele L, Fariselli P, Petta S, RomeroGomez M, Anstee QM, Bugianesi E (2021) **Long-term Outcomes and Predictive Ability of Simple Non-Invasive Scoring Systems in Patients with Non-Alcoholic Fatty Liver Disease**. *Journal of Hepatology*, 75(4):786-794.

[J6] Pancotti C, Benevenuta S, Repetto V, Birolo G, Capriotti E, **SANAVIA T**<sup>+</sup>, Fariselli P (2021) **A Deep-Learning Sequence-Based Method to Predict Protein Stability Changes upon Genetic Variations**. *Genes*, 12(6):911.

[J7] **SANAVIA T**<sup>+</sup>, Huang C, Manduchi E, Xu Y, Dadi P, Potter La, Jacobson DA, Di Camillo B, Magnuson MA, Stoeckert CJ, Gu G. **Temporal transcriptome analysis reveals dynamic gene expression patterns driving  $\beta$ -cell maturation**. *Frontiers in Cell and Developmental Biology*, 9:796.

[J8] Benevenuta S, Pancotti C, Fariselli P, Birolo G, **SANAVIA T** (2021) **An antisymmetric neural network to predict free energy changes in protein variants**. *J. Phys. D: Appl. Phys.*, 54(24):245403.

[J9] Anastasiadou E, Messina E, **SANAVIA T**, Mundo L, Farinella F, Lazzi S, Megiorni F, Ceccarelli S, Pontecorvi P, Marampon F, Di Gioia CRT, Perniola G, Panici PB, Leoncini L, Trivedi P, Lenzi A, Marchese C (2021) **MiR-200c-3p contrasts PD-L1 induction by combinatorial therapies and slows proliferation in epithelial ovarian cancer through downregulation of c-myc and  $\beta$ -catenin**. *Cells*, 10(3):519.

[J10] Birolo G, Benevenuta S, Fariselli P, Capriotti E, Giorgio E, **SANAVIA T** (2021) **Protein stability perturbation contributes to the loss of function in haploinsufficient genes**. *Front Mol Biosci.*, 8:10.

[J11] Ferretto S, Giuliani I, **SANAVIA T**, Bottio T, Fraiese AP, Gambino A, Tarzia V, Toscano G, Iliceto S, Gerosa G, Leoni L (2021) **Atrial fibrillation after orthotopic heart transplantation: Pathophysiology and clinical impact**. *IJC Heart & Vasculature* 32, 100710.

[J12] **SANAVIA T**, Birolo G, Montanucci L, Turina P, Capriotti E, Fariselli P (2020) **Limitations and challenges in protein stability prediction upon genome variations: towards future applications in precision medicine**. *Computational and Structural Biotechnology Journal*, 18:1968-1979.

[J13] Marioni G, Nicolè L, Cappellesso R, Marchese-Ragona R, Fasanaro E, Di Carlo R, La Torre FB, Nardello E, **SANAVIA T**, Ottaviano G, Fassina A (2019)  **$\beta$ -Arrestin-1 expression and epithelial-to-mesenchymal transition in laryngeal carcinoma**. *Int J Biol Markers*, 34(1):33-40.

[J14] Huang C, Walker EM, Dadi PK, Hu R, Xu Y, Zhang W, **SANAVIA T**, Mun J, Liu J, Nair GG, Tan HYA, Wang S, Magnuson MA, Stoeckert CJ Jr, Hebrok M, Gannon M, Han W, Stein R, Jacobson DA, Gu G (2018) **Synaptotagmin 4 Regulates Pancreatic  $\beta$  Cell Maturation by Modulating the Ca<sup>2+</sup> Sensitivity of Insulin Secretion Vesicles**. *Dev Cell*, 45(3):347-361.

[J15] Nicolè L\*, Cappellesso R\*, **SANAVIA T**, Guzzardo V, Fassina A (2018) **Mir-21 over-expression and Programmed Cell Death 4 down-regulation features malignant pleural mesothelioma**. *Oncotarget*, 9(25): 17300–17308.

[J16] Ferraresso S, Aricò A, **SANAVIA T**, Ros S, Milan M, Cascione L, Comazzi S, Martini V, Giantin M, Di Camillo B, Mazzariol S, Giannuzzi D, Marconato L, Aresu L (2017) **DNA methylation profiling reveals common signatures of tumorigenesis and defines epigenetic prognostic subtypes of canine Diffuse Large B-cell Lymphoma**. *Sci Rep.*, 7(1):11591.

[J17] McConnell MJ, Moran JV, Abyzov A, Akbarian S, Bae T, Cortes-Ciriano I, Erwin JA, Fasching L, Flasch DA, Freed D, Ganz J, Jaffe AE, Kwan KY, Kwon M, Lodato MA, Mills RE, Paquola ACM, Rodin RE, Rosenbluh C, Sestan N, Sherman MA, Shin JH, Song S, Straub RE, Thorpe J, Weinberger DR, Urban AE, Zhou B, Gage FH, Lehner T, Senthil G, Walsh CA, Chess A, Courchesne E, Gleeson JG, Kidd JM, Park PJ, Pevsner J, Vaccarino FM, Brain Somatic Mosaicism Network (**SANAVIA T** within BSM Consortium) (2017) **Intersection of diverse neuronal genomes and neuropsychiatric disease: The Brain Somatic Mosaicism Network**. *Science*, 356(6336):eaal1641.

[J18] Nicolè L\*, **SANAVIA T**\*, Veronese N, Cappellesso R, Luchini C, Dabrilli P, Fassina A (2017) **Oncofetal gene SALL4 and prognosis in cancer: a systematic review with meta-analysis**. *Oncotarget*, 8(14):22968-22979.

- [J19] Noren DP, Long BL, Norel R, Rhissorakrai K, Hess K, Hu CW, Bisberg AJ, Schultz A, Engquist E, Liu L, Lin X, Chen GM, Xie H, Hunter GA, Boutros PC, Stepanov O, DREAM 9 AML-OPC Consortium (**SANAVIA T** Within The DREAM Consortium), Norman T, Friend SH, Stolovitzky G, Kornblau S, Qutub AA (2016) **A Crowdsourcing Approach to Developing and Assessing Prediction Algorithms for AML Prognosis**. *PLoS Comput Biol.*, 12(6):e1004890.
- [J20] Hill SM, Heiser LM, Cokelear T, Unger M, Carlin D, Zhang Y, Sokolov A, Paull E, Wong CK, Graim K, Bivol A, Wang H, Zhu F, Afsari B, Danilova LV, Favorov AV, Lee W, Taylor D, HPN-DREAM Consortium (**SANAVIA T** Within The DREAM Consortium), Mills GB, Gray JW, Kellen M, Norman T, Friend S, Fertig EJ, Guan Y, Song M, Stuart J, Koepl H, Spellman PT, Stolovitzky G, Saez-Rodriguez J, Mukherjee S (2016) **Inferring causal molecular networks: empirical assessment through a community-based effort**. *Nature Methods*, 13(4):310-8.
- [J21] **SANAVIA T**, Finotello F, Di Camillo B (2015) **FunPat: function-based pattern analysis on RNA-seq time series data**. *BMC Genomics*, 16 Suppl 6:S2.
- [J22] Sinigaglia A, Lavezzo E, Trevisan M, **SANAVIA T**, Di Camillo B, Peta E, Scarpa M, Castagliuolo I, Guido M, Sarcognato S, Cappellesso R, Fassina A, Cardin R, Farinati F, Palu' G, Barzon L (2015) **Changes in microRNA expression during disease progression in patients with chronic viral hepatitis**. *Liver Int.*, 35(4):1324-33.
- [J23] Zycinski G, Barla A, Squillario M, **SANAVIA T**, Di Camillo B, Verri A (2013) **Knowledge Driven Variable Selection (KDVS) - a new approach to enrichment analysis of gene signatures obtained from high-throughput data**. *Source Code for Biology and Medicine* 8:2.
- [J24] Aghaeepour N, Finak G, the FlowCAP Consortium, the DREAM Consortium (**SANAVIA T** within the DREAM consortium), Hoos H, Mosmann TR, Gottardo R, Brinkman RR, Scheuermann RH (2013). **Critical Assessment of Automated Flow-Cytometry Analysis Techniques**. *Nat Meth*, 10(3):228-38.
- [J25] **SANAVIA T**, Aiolfi F, Da San Martino G, Bisognin A, Di Camillo B (2012) **Improving biomarker list stability by integration of biological knowledge in the learning process**. *BMC Bioinformatics* 13 Suppl 4:S22.
- [J26] Di Camillo B, **SANAVIA T**, Martini M, Jurman G, Sambo F, Barla A, Squillario M, Furlanello C, Toffolo G, Cobelli C (2012) **Effect of size and heterogeneity of samples on biomarker discovery: synthetic and real data assessment**. *PLoS ONE* 7(3):e32200.
- [J27] Di Camillo B, Irving BA, Schimke J, **SANAVIA T**, Toffolo G, Cobelli C, Nair Ks (2012) **Function-based discovery of significant transcriptional temporal patterns in insulin stimulated muscle cells**. *PLoS ONE* 7(3):e32391.
- [J28] Di Camillo B, **SANAVIA T**, Iori E, Bronte E, Roncaglia E, Maran A, Avogaro A, Toffolo G, Cobelli C (2010) **The Transcriptional Response in Human Umbilical Vein Endothelial Cells Exposed to Insulin: a Dynamic Gene Expression Approach**. *PLoS ONE* 5(12):e14390.
- Submitted or in preparation
- [J29] Sherman MA\*, **SANAVIA T\***, Kwon M, Barton A, Vizthum C, Walsh CA, Park PJ. **Patterns of PCR amplification artifacts in high-throughput sequencing and its impact in variant discovery**. In preparation.
- [J30] Xi R\*, **SANAVIA T\***, Ceyhan-Birsoy O, Lebo MS, Rehm HL, Green RC, Beggs A, Park PJ. **Improving copy number variations in whole-exome sequencing data using Bayesian information criterion**. In preparation.
- Book chapters
- [B1] Sambo F, **SANAVIA T**, Di Camillo B (2013) **Integration of Genetic Variation as External Perturbation to Reverse Engineer Regulatory Networks from Gene Expression Data**. In: De La Fuente A (ed). *Gene Network Inference*. Springer Berlin Heidelberg, pp. 107-118.
- International Conference Proceedings
- [C1] **SANAVIA T\***, Nicolè L\*, Cappellesso R, Fariselli P, Dei Tos AP, Fassina A. **Pan-cancer evaluation of the association between immune cell infiltration and Necroptosis activity**. 27<sup>th</sup> Congress of the European Association for Cancer Research, Virtual Congress. June 9<sup>th</sup>-12<sup>th</sup> 2021.
- [C2] Nicolè L, Sarcognato S, Cappellesso R, **SANAVIA T**, Luchini C, Mescoli C, Capelli P, Fassina A, Guido M. **Diagnostic accuracy of an immunohistochemical panel to distinguish intrahepatic cholangiocarcinoma from bile duct adenoma**. 31<sup>st</sup> European Congress of Pathology, Sep 7<sup>th</sup>-11<sup>th</sup> 2019, Nice, France. Published in *Virchows Arch*, 475-S220.
- [C3] Nicolè L\*, **SANAVIA T\***, Cappellesso R, Fassina A. **Transcriptomics landscape of Necroptosis genes is associated with Dendritic cells infiltration: a pan-cancer study of 5,451 primary solid tumors**. 32<sup>nd</sup> European Macrophage & Dendritic Cell Society, Sep 27<sup>th</sup>-29<sup>th</sup> 2018, Verona, Italy.

- [C4] Nicolè L\*, **SANAVIA T**\*, Cappellesso R, Maffeis V, Radu CM, Guzzardo V, Maria G, Zanus G, Fassina A. **Evaluation of necroptosis related genes RIPK1, RIPK3 and MLKL-p immunogenicity in hepatocellular carcinoma.** 30<sup>th</sup> European Congress of Pathology, Sep 8<sup>th</sup>-12<sup>th</sup> 2018, Bilbao, Spain.
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- [C6] **SANAVIA T**, Finotello F, Di Camillo B. **FunPat: a function-based pattern analysis pipeline for RNA-seq time-series data.** BITS 2014, Feb 26<sup>th</sup>-28<sup>th</sup> 2014, Rome, Italy. ORAL PRESENTATION
- [C7] Mina M, **SANAVIA T**. **FastSemSim: fast and easy evaluation of semantic similarity measures on biomedical ontologies.** BITS 2014, Feb 26<sup>th</sup>-28<sup>th</sup> 2014, Rome, Italy.
- [C8] Sinigaglia A, Lavezzo E, **SANAVIA T**, Di Camillo B, Scarpa M, Castagliuolo I, Farinati F, Palu G, Barzon L. **MicroRNA expression signatures in chronic viral hepatitis progression.** European congress of virology, Sep 11<sup>th</sup>-14<sup>th</sup> 2013, Lyon, France.
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- [C12] Fontana P, **SANAVIA T**, Facchinetti A, Lavezzo E, Falda M, Cavalieri D, Di Camillo B, Toppo S. **Can we go beyond sequence similarity to predict protein function?** Critical Assessment of Function Annotations (CAFA). Jul 14<sup>th</sup> 2012, Long Beach - California (USA).
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- [C15] **SANAVIA T**, Aiolfi F, Da San Martino G, Bisognin A, Di Camillo B. **Improving biomarker list stability by integration of biological knowledge in the learning process.** 19<sup>th</sup> International Conference on Intelligent Systems for Molecular Biology (ISMB) & 10<sup>th</sup> European Conference on Computational Biology (ECCB). Jul 15<sup>th</sup>-19<sup>th</sup> 2011, Wien, Austria.
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- [C17] **SANAVIA T**, Aiolfi F, Da San Martino G, Bisognin A, Di Camillo B. **Stable Feature Selection for Biomarker Discovery: Use of Biological Information.** BITS Annual Meeting 2011, Jun 20<sup>th</sup>-22<sup>nd</sup> 2011, Pisa, Italy. ORAL PRESENTATION
- [C18] Facchinetti A, **SANAVIA T**, Di Camillo B, Lavezzo E, Fontana P, Toppo S. **A Method to Reveal and Handle Heterogeneities and Inconsistencies in Gene Ontology Annotation.** BITS Annual Meeting 2011, Jun 20<sup>th</sup>-22<sup>nd</sup> 2011, Pisa, Italy.
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- [C22] **SANAVIA T**, Barla A, Di Camillo B, Mosci S, Toffolo G. **Function-based analysis of microarray data via l1-l2 regularization**. 17<sup>th</sup> International Conference on Intelligent Systems for Molecular Biology (ISMB) & 8<sup>th</sup> European Conference on Computational Biology (ECCB). Jun 27<sup>th</sup> – Jul 2<sup>nd</sup> 2009 Stockholm, Sweden.
- [C23] **SANAVIA T**, Di Camillo B, Iori E, Maran A, Bronte E, Avogaro A, Toffolo G, Cobelli C. **Function-based discovery of characteristic temporal expression profiles in endothelial cells stimulated with insulin**. 11<sup>th</sup> International Meeting of Microarray and Gene Expression Data Society (MGED). Sep 1<sup>st</sup>-4<sup>th</sup> 2008, Riva del Garda (TN), Italy.
- US Conference Proceedings**
- [C24] **SANAVIA T**, Kwon M, Sherman MA, Barton A, Rodin R, Walsh C, Park PJ. **Impact of Library-specific Artifacts on Single Nucleotide Variant Analysis in Whole-genome Sequencing Data**. MidAtlantic Bioinformatics Conference, Oct 10<sup>th</sup> 2017, Philadelphia PA, USA.
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- [C26] Sherman MA\*, **SANAVIA T\***, Kwon M, Rodin R, Walsh C, Park PJ. **Impact of PCR Amplification during Library Preparation on Variant Discovery in Whole Genome Sequencing**. 10<sup>th</sup> Annual Program in Quantitative Genomics (PQG) Conference “Whole Genome Sequencing Analysis: Comprehensive Capture of Genetic Variants”, Nov 3<sup>rd</sup>-4<sup>th</sup> 2016, Boston MA, USA.
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- [C27] Eran A, **SANAVIA T**, Wang J, Kwon D, Park PJ, Kohane IS, Perlis R (2018) **Multidimensional profiling of treatment response in schizophrenia**. Centers of Excellence in Genomic Science (CEGS) 16<sup>th</sup> Annual Grantee Meeting 2018, University of Chicago, USA.
- [C28] **SANAVIA T**, Kwon M, Wang J, Eran A, Cai T, Park PJ, Kohane IS, Perlis R. **Whole genome sequencing and transcriptome profiling in neuropsychiatric diseases**. Centers of Excellence in Genomic Science (CEGS) 15<sup>th</sup> Annual Grantee Meeting. Oct 2<sup>nd</sup>-3<sup>rd</sup> 2017, Bell Harbor International Conference Center, Seattle WA, USA. ORAL PRESENTATION
- [C29] **SANAVIA T**, Wang J, Kwon D, Park PJ, Kohane IS, Perlis R. **Copy number and single nucleotide variants in neuropsychiatric diseases: a cross-disorder whole-genome sequencing study**. Centers of Excellence in Genomic Science (CEGS) 14<sup>th</sup> Annual Grantee Meeting. October 2016, Stanford University, Palo Alto CA, USA. ORAL PRESENTATION
- [C30] Manduchi E, Greenfest-Allen E, Potter LA, **SANAVIA T**, Huang C, Choi E, Osipovich A, Cartailier JP, Gu G, Stoeckert CJ, Magnuson MA (2013) **Whole transcriptome profiling of beta cell development in the mouse**. Beta Cell Biology Consortium 2013 Investigator Retreat, May 2013, Reston VA, USA.
- Italian Conference Proceedings**
- [C31] Franz L, Ottaviano G, Nicolè L, Marchese-Ragona R, Fasanaro E, di Carlo R, Biagio La Torre F, Nardello E, **SANAVIA T**, Fassina A, Marioni G (2019) **L'espressione di  $\beta$ -arrestina-1 e la transizione epitelio-mesenchimale nel carcinoma laringeo**. CVI Congresso Nazionale della Società Italiana di Otorinolaringoiatria e Chirurgia Cervico-facciale, Rimini, Italy.
- [C32] Nicolè L\*, **SANAVIA T\***, Cappellesso R, Fassina A. **Transcriptomics landscape of Necroptosis genes is associated with Dendritic cells infiltration: a pan-cancer study of 5,451 primary solid tumors**. Congresso Annuale di Anatomia Patologica (SIAPEC-IAP), Oct 18<sup>th</sup>-20<sup>th</sup> 2018, Bari, Italy.
- [C33] Nicolè L\*, **SANAVIA T\***, Maffei V, Cappellesso R, Salizzato K, Pegoraro M, Zorzi S, Guzzardo V, Maria G, Zanusi G, Fassina A. **Immunogenic role of Necrosis-inducing complex RIPK1-RIPK3-MLKL-P in Hepatocellular Carcinoma**. Congresso Annuale di Anatomia Patologica (SIAPEC-IAP), Oct 12<sup>th</sup>-14<sup>th</sup> 2017, Naples, Italy.
- [C34] **SANAVIA T**, Finotello F, Di Camillo B. **FunPat: a function-based pattern analysis framework for RNA-seq time-series data**. IV Congresso Gruppo Nazionale di Bioingegneria (GNB). Jul 25<sup>th</sup>-27<sup>th</sup> 2014, Pavia, Italy.
- [C35] Trevisan M, **SANAVIA T**, Albonetti C, Lavezzo E, Di Camillo B, Sinigaglia A, Toppo S, Toffolo G, Cobelli C, Palù G, Barzon L. **Human cytomegalovirus microRNAs target prediction by dynamic expression analysis**. III Congresso Gruppo Nazionale di Bioingegneria (GNB). Jun 26<sup>th</sup>-29<sup>th</sup> 2012, Rome, Italy.

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[C36] Di Camillo B, Martini M, **SANAVIA T**, Cobelli C, Toffolo G (2010) **In silico assessment of effect of size and heterogeneity of samples on biomarker discovery**. II Congresso Nazionale di Bioingegneria (GNB). Jul 8<sup>th</sup>-10<sup>th</sup> 2010, Turin, Italy.

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[C32] Nicolè L\*, **SANAVIA T**\*, Cappellesso R, Fassina A. **Transcriptomics landscape of Necroptosis genes is associated with Dendritic cells infiltration: a pan-cancer study of 5,451 primary solid tumors**. Congresso Annuale di Anatomia Patologica (SIAPEC-IAP), Oct 18<sup>th</sup>-20<sup>th</sup> 2018, Bari, Italy.

[C33] Nicolè L\*, **SANAVIA T**\*, Maffei V, Cappellesso R, Salizzato K, Pegoraro M, Zorzi S, Guzzardo V, Maria G, Zanusi G, Fassina A. **Immunogenic role of Necrosis-inducing complex RIPK1-RIPK3-MLKL-P in Hepatocellular Carcinoma**. Congresso Annuale di Anatomia Patologica (SIAPEC-IAP), Oct 12<sup>th</sup>-14<sup>th</sup> 2017, Naples, Italy.

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**High-impact publication acknowledgements**

Clayton HW, Osipovich AB, Stancill JS, Schneider JD, Vianna PG, Shanks CM, Yuan W, Gu G, Manduchi E, Stoeckert CJ Jr, Magnuson MA (2016) **Pancreatic Inflammation Redirects Acinar to  $\beta$  Cell Reprogramming**. Cell Reports, 17(8):2028-2041. [Personal contribution in quality check and preprocessing (PCA, cluster analysis) of RNAseq data]

**Research activity**

Aim of the research is the robust identification, mainly from high-throughput (both microarray and Next-Generation Sequencing) data, of genes, genomic variants, proteins, biological functions and related regulatory mechanisms characterizing different phenotypes (i.e. observable physiological or pathological traits) or specific temporal genetic patterns, which is a fundamental step for early diagnosis and treatment. In particular:

**1. Function-based discovery of significant transcriptional temporal patterns**

A method was developed to characterize temporal patterns from gene expression data. Using functional annotations from genomic databases, the algorithm searches the main temporal patterns in classes of functionally related genes by expectation-maximization and weighted least squares. From 2012, applications to RNA sequencing data have been investigated focusing on the development and maturation of pancreatic beta cells, in collaboration with the **Perelman School of Medicine at University of Pennsylvania (CBIL-Stoeckert Lab)** and the Center for Stem Cell Biology at **Vanderbilt University (Magnuson Lab)**. An R package for the analysis of RNA-seq time series expression data is available [S2]. Other collaborations on dynamic models on host-virus interactions and on the role of SigE in Mycobacterium gene regulatory network are open with the **Dept. of Molecular Medicine at University of Padova**. Scientific contributions: 6 papers with a preliminary analysis [J28], the method and its application to microarray [J27] and RNA-seq [J7, J14, J21] data; 6 contributions to international [C6,C9,C23], Italian [C34-35] and US [C30] conferences.

**2. Protein stability prediction upon genome variations and effects of heterogeneities in protein functional annotations**

Protein stability predictions are becoming essential in medicine to develop novel immunotherapeutic agents and for drug discovery. Despite the large number of computational approaches for predicting the protein stability upon mutation, there are still critical unsolved problems: 1) limited and unbalanced number of thermodynamic measurements for proteins provided by current databases; 2) large intrinsic variability of  $\Delta\Delta G$  values due to different experimental conditions; 3) biases in the development of predictive methods caused by ignoring the anti-symmetry of  $\Delta\Delta G$  between mutant and native protein forms; 4) over-

optimistic prediction performance, due to sequence similarity between proteins used in training and test datasets. Novel deep learning-based tools have been developed in order to address these issues, focused on preserving the antisymmetric physical properties [S1].

In addition, most of the current protein functions are derived by computational prediction based on functional annotations from public databases such as Gene Ontology (GO). However, these predictions are known to be heterogeneous and sometimes inconsistent. A method combining semantic similarity measures in GO annotations and sequence similarity between proteins was developed, able to identify outliers in clusters of proteins characterizing patterns across GO functional annotations. Semantic similarity metrics were also further explored in a collaboration supporting the development of a dedicated Python library [S5].

*Scientific contributions:* 2 papers assessing current methods to predict protein stability upon mutations [J2,J12] and 2 papers on tools for reproducible predictions through deep learning [J6,J8], 1 paper investigating the relationship between protein stability and haploinsufficiency [J10] and 6 contributions to international conferences [C7, C11-12, C16, C18, C20].

### **3. Assessment and Integration of prior information in supervised machine learning**

Investigation of how high dimensionality in high-throughput data and within-class variability of mRNA measurements affect the classification performance and biomarker discovery was performed on simulated and real datasets. Two integrative approaches were developed investigating the effects of different types of prior knowledge from genomic databases in supervised classification methods. In the first, biological databases on gene functions (e.g. Gene Ontology) and protein-protein interactions were considered to define functional groups of genes/proteins, using a set of classifiers depending by these functional groups. The second approach codifies the biological information into similarity matrices, which are integrated into kernel functions to be used in the learning process. These methods have proven an increasing stability in biomarker discovery and an improved biological interpretability of the results.

*Scientific contributions:* 2 papers [J23, J25] of the two integrative approaches and 3 papers on the assessment of classification methods in gene [J26] and protein [J19] expression data and in high-throughput data from flow-cytometry techniques [J24]; 8 contributions to international [C10, C13-15, C17, C21-22] and Italian conferences [C36].

### **4. Reproducibility of whole-genome/exome sequencing data analyses**

Most of sequencing techniques are affected by artifacts induced by PCR amplification during the library preparation and the extent to which it impacts the identification of genomic variants (e.g. mutations, copy number variants) remains uncharacterized. By comparing whole-genome sequencing (WGS) with and without PCR, the effects on copy number variant (CNV) and single nucleotide variant (SNV) detection were investigated, identifying specific patterns in SNV/CNV profiles characterizing the PCR-induced bias. Whole-exome sequencing (WES) interrogates the coding portion (<3%) of the genome, but at higher coverage than comparably priced WGS. However, the required capture step for WES is limited by the design of capture oligonucleotides (only 70-80% of efficiency, mainly due to the high GC content of exonic sequences). A novel copy number variation caller for WES data was investigated within the **Park Lab (Harvard Medical School)** to normalize the read depth using a model able to estimate the probe efficiency and improve the sensitivity in the identification of CNVs. *Scientific contributions:* 2 manuscripts in preparation [J29-30], 3 contributions to US conferences [C24-26].

### **5. Systems genetics approaches to describe complex genetic traits**

Modelling genetic variations as randomized, multifactorial perturbations of the gene expression profiles of each individual as the system response to a specific set of perturbations. A first integrative reverse-engineering approach was developed, which exploits both genetic and expression data to infer cause-effect relationships between genes.

*Scientific contributions:* 1 book chapter [B1], a contribution to an international conference [C19] (honorable mention awarded in DREAM challenges), 1 paper [J20] as part of DREAM consortium on an empirical assessment of causal network learning from human cancer data and in-silico data from a nonlinear dynamical model of signaling.

### **6. Identification of novel biomarkers in complex diseases**

The rate-limiting step for large-scale genomic investigation in clinical populations is how phenotyping. Most of the diseases show complex phenotypes and the primary cell types of

interest are difficult to access directly, making challenging the identification of the main biomarkers involved in each disease. The following studies were performed:

- Define a genome-wide model integrating genomic variants and/or transcriptomic signatures from WGS/RNA-seq to clinically-characterize neuropsychiatric patients. (P.I. **Isaac Kohane, Harvard Medical School; Roy Perlis, Massachusetts General Hospital**); Scientific contributions: 3 contributions to US meetings [C27-29], 1 paper in preparation and 1 paper [J17] as part of a related consortium investigating brain somatic mutations.
- Investigate copy number and structural variants from a panel of different congenital disorders in order to assess the clinical relevance in integrating exome sequencing into the care of newborns (BabySeq project, P.I. **Robert C. Green, Brigham and Women's Hospital; Alan H. Beggs, Boston Children's Hospital**) Scientific contributions: 1 paper in preparation [J30] on a tool for CNV detection.
- Apply novel statistical/machine-learning pipelines in order to improve both cross-sectional and longitudinal analysis in the clinical characterization of cohorts of patients. Specifically:
  - 1) increase the predictive ability of simple non-invasive scoring systems in NAFLD patients (**University of Torino, Prof. Elisabetta Bugianesi**) and the detection of long-term outcomes in MDS patients (**Humanitas, Prof. Matteo Giovanni Della Porta, Genomed4all consortium**);
  - 2) improve dermoscopic prediction models for the diagnosis of cutaneous melanoma (**University of Torino, Prof. Pietro Quaglino**);
  - 3) assess the clinical impact of atrial fibrillation after orthotopic heart transplantation (**University of Padova, Prof. Loira Leoni**)  
Scientific contributions: 3 papers [J3,J5,J11]
- Characterize complex combinations of molecular events driving the deregulation of signaling pathways and accumulation of genetic alterations in cancer, in relation with the tumor microenvironment and shifting the immune response towards tumor tolerance. In particular:
  - 1) miRNA-mRNA biomarkers across several cancer types and the immunogenicity of necroptosis signaling pathway in hepatocellular carcinoma (**Dept. of Medicine at University of Padova, Prof. Ambrogio Fassina**);
  - 2) prediction of miRNA/mRNA expression variations in ovarian cancer under different anti-tumoral therapies (**University La Sapienza at Rome, PhD Eleni Anastasiadou**);
  - 3) differential analysis and clustering of methylation profiles in canine diffuse large B cell lymphoma (**Dept. of Comparative biomedicine at University of Padova, Prof. Luca Aresu**);
  - 4) differential analysis of gene expression of B cells in Waldenstrom's Macroglobulinemia (**Niguarda Hospital in Milan, Dr. Alessandra Trojani**)  
Scientific contributions: 8 papers [J1,J4,J9,J13,J15-16,J18,J22]; 9 contributions to international [C1-5,C8] and Italian conferences [C31-33].

Torino, February 16<sup>th</sup> 2022

Tiziana Sanavia