



Name and surname

**FEDERICO REALI, PHD**

Current location

**TRENTO (TN), ITALY**

Telephone

E-mail

Nationality

Italian

Date of birth

## ABOUT ME

I am a senior scientist and group leader with expertise in biological modeling, statistical analysis, and model-informed drug development across preclinical and clinical phases. My background spans statistics, stochastic processes, numerical modeling, optimization, and machine learning. I lead a team in quantitative systems pharmacology, designing in-silico pipelines that integrate mechanistic models, pharmacometrics, and AI-based approaches to support early-stage research, regulatory strategy, and clinical development. I collaborate with pharmaceutical companies, non-profits, and academic institutions on projects addressing global health priorities. My current interests focus on advancing predictive and translational modeling at the intersection of systems pharmacology, artificial intelligence, and emerging technologies such as digital twins and organs-on-chip.

## WORK EXPERIENCE

Dec 2024 - Present

### Quantitative Systems Pharmacology (QSP) Group Leader

*Fondazione The Microsoft Research - University of Trento Centre for Computational Systems Biology (COSBI), Italy.*

- Provide strategic and scientific leadership for a multidisciplinary team focused on quantitative systems pharmacology and model-informed drug development across multiple therapeutic areas.
- Oversee modeling activities supporting preclinical and clinical development, including dose/regimen optimization, PK/PD analysis, and preparation of regulatory documentation.
- Supervise the design and execution of integrated in-silico pipelines that combine modeling, machine learning, and physicochemical descriptors to support early-phase candidate selection.
- Guide the development and dissemination of interactive web-based simulation tools that enable collaborators to apply model-informed strategies in real-time decision-making.
- Coordinate collaborations with pharmaceutical companies, global non-profit organizations, and academic partners, with a focus on infectious diseases (tuberculosis), neurodegenerative disorders (Parkinson's), and rare genetic conditions (lysosomal storage disorders).
- Initiate new scientific collaborations and industrial partnerships; define research objectives, draft project plans, contribute to grant proposals, and support the development and negotiation of research agreements and contracts.
- Contribute to COSBI's strategic roadmap by participating in executive meetings, defining research priorities, and shaping long-term organizational goals.
- Lead the preparation of technical reports and peer-reviewed publications; support engagement with regulatory stakeholders where applicable.
- Mentor postdoctoral researchers, PhD students, and master's students in applied and research-oriented projects.

Jan 2022-Dec 2024

### Senior Modeling Scientist and Project Leader

*Fondazione The Microsoft Research - University of Trento Centre for Computational Systems Biology (COSBI), Italy.*

- Led the design and implementation of in-silico modeling pipelines for anti-tuberculosis drug development, supporting Gates MRI and global TB consortia.
- Applied PBPK, PK/PD, and machine learning models to optimize dose selection and inform early-stage decision-making using.
- Drove the development of QSP models to investigate molecular targets in neurodegenerative and rare diseases (Parkinson's and Gaucher).
- Managed scientific collaborations, contributed to regulatory documents, and developed interactive tools to promote model-informed strategies.
- Supervised academic trainees and contributed to COSBI's strategic research agenda.

Jan 2017-Jan 2022	<b>Postdoctoral Researcher</b> <i>Fondazione The Microsoft Research - University of Trento Centre for Computational Systems Biology (COSBI), Italy.</i> <ul style="list-style-type: none"> <li>Collaborated with large- and mid-size pharmaceutical industries and non-profit organizations on quantitative systems pharmacology projects for infective, metabolic, and rare genetic diseases. <ul style="list-style-type: none"> <li>Integrate systems biology and pharmacokinetics/dynamics models to support the preclinical and clinical drug development of new compounds (e.g., Matlab, R).</li> <li>Generate and analyze virtual populations of patients and digital twins to support the clinical development of new drugs.</li> <li>Support the development of a model-based pipeline for data-driven phenotype clustering and stratifications.</li> <li>Develop an integrated cross-disease modeling platform for a family of rare genetic diseases.</li> </ul> </li> <li>Implemented models, analyzed, and visualized data using Matlab, R, Python and C.</li> <li>Contributed to the refinement of algorithms for simulation, optimization, and sensitivity analysis.</li> <li>Supervised and guided, bachelor, master, and PhD students.</li> </ul>
May 2023-Present	<b>Young Investigator</b> <i>UNITE4TB (part of IMI AMR Accelerator)</i> Collaborate with other early career researchers in the field of tuberculosis and work on TB-related initiatives with senior researchers and clinicians in the field.
Jan 2016-Apr 2016	<b>Visiting Researcher</b> <i>Sanofi – Aventis Deutschland GmbH, Frankfurt am Main, Germany</i> Mathematical modeling for understanding diabetes and identify new drug targets by combining transcriptomic analysis (R) and dynamical modelling (Matlab).
<b>EDUCATION AND TRAINING</b>	
2013- 2017	<b>Doctoral school in Mathematics</b> Università degli Studi di Trento, Italy Systems biology and applied mathematics: modeling for biological systems (EQF 8) Dynamical models for diabetes: insights into insulin resistance and type 1 diabetes Note: with laude
2010-2013	<b>Master's degree in Mathematics</b> Università degli Studi di Perugia, Italy Faculty of Mathematical, Physical and Natural Sciences General mathematics (EQF 7) Final score: 110/110 with laude
2007-2010	<b>Bachelor's degree in Applied Mathematics</b> Università degli Studi di Perugia, Italy Faculty of Mathematical, Physical and Natural Sciences Applied Mathematics: Information Theory, Codes and Cryptography (EQF 6) Final score 110/110 with laude
<b>TEACHING ACTIVITIES</b>	
2012-Present	Teaching experience across various academic programs offered at the University of Trento. In recent roles, I instructed Mathematical Modeling and Simulation for the master's program in Quantitative and Computational Biology and Advanced Topics in Biomathematics (Systems Biology and Pharmacometrics) for the master's program in Applied Mathematics. Furthermore, I delivered instruction in Statistical Learning (Biostatistics) within the Data Science master's program. My teaching responsibilities also span a broad spectrum of subjects, including probability, statistics, R and Matlab laboratories, and applied mathematics to bachelor and master's students. During my career, I have also guided bachelor and master's student during internships and thesis projects.
<b>PROFESSIONAL ASSOCIATIONS</b>	
MEMBER	<b>ISOP</b> – International society of pharmacometrics <b>SIOoC</b> – Italian society of organ-on-chip <b>GNCS</b> – National group for scientific computing of INdAM

## EDITORIAL ACTIVITIES

GUEST EDITOR

### Frontiers in Systems Biology

Research topic: Use of Quantitative Systems Pharmacology Pipelines to Bridge in Vitro and in Vivo Results in Drug Discovery

REVIEWER

Frontiers in Systems Biology, Frontiers in Pharmacology, NPJ Scientific Reports, Computational and Structural Biotechnology Journal, ACOP Conference

## ORGANIZING COMMITTEE

**11th Conference on Dynamical Systems Applied to Biology and Natural Sciences DSABNS 2020**, University of Trento, Trento (TN), Italy

## PERSONAL SKILLS

### - COMPETENCES

MOTHER TONGUE

Italian

OTHER LANGUAGE

English: C1 - TOEFL iBT Test: 101/120

OTHER LANGUAGE

German: A1

### PUBLICATIONS

1. Marchetti\* L, Reali\* F, Dauriz M, Brangani C, Boselli L, Ceradini G, Bonora E, Bonadonna RC and Priami C, A Novel Insulin/Glucose Model after a Mixed-Meal Test in Patients with Type 1 Diabetes on Insulin Pump Therapy, *Scientific Reports*, v. 6, (2016), p. 36029, DOI: <http://doi.org/10.1038/srep36029>
2. Reali\* F, Morine\* MJ, Kahramanoğlu\* O, Raichur S, Schneider HS, Crowther D and Priami C, Mechanistic interplay between ceramide and insulin resistance, *Scientific Reports*, v 7, (2017), p. 41231, DOI: [doi.org/10.1038/srep41231](http://doi.org/10.1038/srep41231)
3. Reali F, Priami C and Marchetti L, Optimization algorithms for computational systems biology, *Frontiers In Applied Mathematics And Statistics*, v. 3, (2017).DOI: [10.3389/fams.2017.00006](http://doi.org/10.3389/fams.2017.00006)
4. Kaddi C, Reali F, et al, Integrated quantitative systems pharmacology (QSP) model of lysosomal diseases provides an innovative computational platform to support research and therapeutic development for the sphingolipidoses, *Molecular Genetics and Metabolism*, Volume 123, Issue 2, February 2018, Pages S2-S6, New York, USA: Elsevier, 2018, p. S73-S74. - (MOLECULAR GENETICS AND METABOLISM; 2). Proceedings of: WORLD Symposium 2018, San Diego, California, USA, 5-9 February 2018. DOI: <http://doi.org/10.1016/j.ymgme.2017.12.183>
5. Vo Hong T, Marchetti L, Reali F and Priami C, Incorporating extrinsic noise into the stochastic simulation of biochemical reactions: A comparison of approaches, *THE JOURNAL OF CHEMICAL PHYSICS*, v. 148, n. 6 (2018), p. 064111. DOI: [doi.org/10.1063/1.5016338](http://doi.org/10.1063/1.5016338)
6. Simoni G, Reali F, Priami C and Marchetti L, Stochastic simulation algorithms for computational systems biology: exact, approximate and hybrid methods, *WIREs Systems Biology and Medicine*, e1459 (2019). DOI: [doi.org/10.1002/wsbm.1459](http://doi.org/10.1002/wsbm.1459).
7. Reali F, Simoni G, Domenici E and Marchetti L, An Extended Dynamical Model of  $\alpha$ -Synuclein Metabolism, Proceedings of the 11th International Conference Dynamical Systems Applied To Biology and Natural Sciences, Trento, Italy, 4-7 February 2020, p. 151-152, ISBN 978-989-98750-7-4
8. Abrams R, Kaddi C, Tao M, Leiser R, Simoni G, Reali F, Tolsma J, Jasper P, van Rijn Z, Li J, Niesner B, Barrett J, Peterschmitt M, Marchetti L, Azer K, Neves-Zaph S, A quantitative systems pharmacology model of Gaucher disease provides insight into the response to substrate reduction therapy with eliglustat, *CPT: Pharmacometrics & Systems, Pharmacology*, v. 9, n. 7 (2020), p. 374-383. DOI: <https://doi.org/10.1002/psp4.12506>
9. Simoni G, Kaddi C, Tao M, Reali F, Tomasoni D, Priami C, Azer K, Neves-Zaph S and Marchetti L, A robust computational pipeline for model-based and data-driven phenotype clustering, *Bioinformatics*, v. 37, n. 9 (2021), p1269–1277, DOI: [10.1093/bioinformatics/btaa948](http://doi.org/10.1093/bioinformatics/btaa948)
10. Fochesato A, Simoni G, Reali F, Giordano G, Domenici E, Marchetti L, A Retrospective Analysis of the COVID-19 Pandemic Evolution in Italy, *Biology*, 10(4), 311 (2021); DOI: <https://doi.org/10.3390/biology10040311>
11. Tomasoni D, Paris A, Giampiccolo S, Reali F, Simoni G, Marchetti L, Kaddi C, Zaph S, Priami C, Azer K, and Lomabrdo R, QSPcc reduces bottlenecks in computational model simulations, *Communications Biology*, 4, 1022 (2021), DOI: <https://doi.org/10.1038/s42003-021-02553-9>
12. Righetti E, Antonello A, Marchetti L, Domenici E and Reali F, Mechanistic models of  $\alpha$ -synuclein homeostasis for Parkinson's disease: A blueprint for therapeutic intervention,

*Frontiers in Applied Mathematics and Statistics*, 8:1060489 (2022), DOI: [10.3389/fams.2022.1060489](https://doi.org/10.3389/fams.2022.1060489)

13. Reali F, Csikász-Nagy A and Selvaggio G, Editorial: Use of quantitative systems pharmacology pipelines to bridge in vitro and in vivo results in drug discovery, *Frontiers in Systems Biology*, 3:1291610 (2023) DOI: <https://doi.org/10.3389/fsysb.2023.1291610>
14. Reali\* F, Fochesato\* A, Kaddi C, et al., A minimal PBPK model to accelerate preclinical development of drugs against tuberculosis, *Frontiers in Pharmacology*, 14:1272091 (2024), DOI: [10.3389/fphar.2023.1272091](https://doi.org/10.3389/fphar.2023.1272091)
15. Giampiccolo S, Reali F, Fochesato A, Iacca G, Marchetti L, Robust parameter estimation and identifiability analysis with hybrid neural ordinary differential equations in computational biology. *npj Syst Biol Appl* 10, 139 (2024). DOI: <https://doi.org/10.1038/s41540-024-00460-3>
16. Visintainer R, Fochesato A, Boaretti D, Giampiccolo S, Watson S, Levi M, Reali F, Marchetti L, stormTB: A web-based simulator of a murine minimal-PBPK model for anti-tuberculosis treatments, *Front. Pharmacol.* 15:1462193. DOI: [10.3389/fphar.2024.1462193](https://doi.org/10.3389/fphar.2024.1462193).
17. Righetti E, Marchetti L, Domenici E and Reali F, A mechanistic model of pure and lipid-mediated  $\alpha$ -synuclein aggregation for advancing Parkinson's disease therapies, *Nat Commun Chem* 8, 186 (2025). DOI: <https://doi.org/10.1038/s42004-025-01558-3>
18. Sips F, Virgolin M, Pasculli G, Reali F, et al, Transforming Pediatric Rare Disease Drug Development: Enhancing Clinical Trials and Regulatory Evidence with Virtual Patients, *submitted*

\*: equal contribution.

#### SELECTED TALKS, CONFERENCES, AND WORKSHOPS

3-6 June 2025	<b>Population Approach Group Europe meeting 2025</b> , Thessaloniki, Greece
1-4 April 2025	<b>AD/PD Conference 2025</b> , Vienna, Austria. Poster
14-16 Ju 2024	<b>Population Approach Group Europe meeting 2024</b> , Rome, Italy
14-16 May 2024	<b>10° Congresso della Società LIMPE-DISMOV</b> , Milan, Italy. Talk
19-20 Oct 2023	<b>Workshop BUILDing a Digital Twin 2023</b> , CNR, Rome, Italy. Talk: Digital twins and virtual populations: applications in Quantitative Systems Pharmacology
27-30 Jun 2023	<b>Population Approach Group Europe meeting 2023</b> , A Coruña, Spain. Poster
4-5 May 2023	<b>Primo convegno Società italiana organ-on-chip</b> , CNR, Rome, Italy
30 Oct-03 Nov 2022	<b>ACOP13: American conference on pharmacometrics</b> , Colorado, USA. Poster
28-31 Aug 2022	<b>Foundations of Systems Biology in Engineering (FOSBE 2022)</b> , Cambridge, USA
28 Jun-01 Jul 2022	<b>Population Approach Group Europe meeting 2022</b> , Ljubljana, Slovenia Talk: PBPK/PD modeling and machine learning approaches to support the development of new drugs and regimens against tuberculosis <a href="https://youtu.be/Vudti7evLT4?t=3370">youtu.be/Vudti7evLT4?t=3370</a>
20-22 Apr 2022	<b>Quantitative Systems Pharmacology Conference 2022</b> , Leiden, Netherlands. Poster
09-11 Nov 2021	<b>ACOP12: American conference on pharmacometrics</b> , Online event. Poster
16-20 Aug 2020	<b>ISOP - Virtual Quantitative Systems Pharmacology Week 2020</b> , Online event Talk: Integrated modeling platform of lysosomal storage disorders provides an innovative computational platform to support research and therapeutic development for the sphingolipidoses
04-07 Feb 2020	<b>11th Conference DSABNS 2020</b> , University of Trento, Italy Talk: An extended dynamical model of $\alpha$ -synuclein metabolism
08-11 Oct 2018	<b>Math for Biomedicine</b> , Accademia dei Lincei and CNR, Rome (RM), Italy Talk: Integrated modeling platform for Lysosomal Storage Disorders
06-12 Aug 2017	<b>18th International Conference on Systems Biology (ICSB 2017)</b> , Virginia Tech, USA, Talk and Poster: Mechanistic interplay between sphingolipids and insulin resistance
26-28 Jun 2017	<b>Workshop "Modeling and computational approaches to Biology and Medicine"</b> , University "La Sapienza", Rome, Italy, Talk: Mechanistic interplay between ceramide and insulin resistance

TRENTO, 21/07/25  
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