UNIVERSITÀ DI TRENTO

Fondazione The Microsoft Research - University of Trento Centre for Computational and Systems Biology (COSBI)

Borsa di studio/Scholarship

E	Mechanistic and Quantitative Systems Pharmacology Modelling for Complex Diseases
Project Code:	
CUP:	
Topic: Applied Mathematics, Systems Biology and Biomedical Modelling	
Project Manager: Federico Reali	
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Synthetic description of the activity and expected research outcome: Mathematical modelling is increasingly central to neuroscience and drug development, where disease mechanisms involve nonlinear dynamics, feedback regulation, multiple time scales, partial observability, and heterogeneous data. This PhD project aims to develop flexible mechanistic and quantitative systems pharmacology models that can be estimated from sparse data and reused within larger models of disease progression and therapeutic response. The candidate will work on deterministic and stochastic dynamical systems, compartmental and reaction-network models, sensitivity analysis, identifiability, uncertainty quantification, parameter estimation, and optimal experimental design, using tools such as MATLAB, R, Python, or Julia. The project will initially use a compartmentalized biochemical network relevant to neurodegeneration as a tractable test case, with possible applications to lysosomal biology, lipid metabolism, proteostasis, metabolic regulation, or neuroinflammatory signalling. The broader goal is to build reusable modelling components that integrate molecular measurements and biomarker readouts, support virtual experimentation, and help evaluate therapeutic strategies ranging from small molecules and biologics to emerging modalities such as RNA-based therapies and gene therapy.	
References	

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Kaddi, C., Reali, F., Marchetti, L., Niesner, B., Parolo, S., Simoni, G., Zaph, S., Tao, M., Abrams, R., van Rijn, Z., Leonard, J., Judith Peterschmitt, M., Puga, A. C., Mange, K., Barrett, J. S., Priami, C., Schuchman, E. H., & Azer, K. (2018). 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*, *123*(2), S73–S74. https://doi.org/10.1016/J.YMGME.2017.12.183

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Righetti, E., Marchetti, L., Domenici, E., & Reali, F. (2025). A mechanistic model of pure and lipidic α-synuclein aggregation for advancing Parkinson's therapies. *Communications Chemistry*, *8*(1), 186. https://doi.org/10.1038/s42004-025-01558-3

Marano, M., Zizzo, C., Cavallieri, F., Avenali, M., Schirinzi, T., Monfrini, E., Spagnolo, F., de Micco, R., Ramat, S., Malaguti, M. C., Reali, F., Cilia, …, & di Fonzo, A. (2026). Association between plasma glucosylsphingosine levels and dyskinesia burden in GBA1-related Parkinson's disease. *Neurobiology of Disease*, *219*, 107271. https://doi.org/10.1016/J.NBD.2026.107271

Ideal candidate (skills and competencies)

MSc in Applied Mathematics, Mathematical Biology, Physics, Computer Science, Bioinformatics, Quantitative Computational Biology or a related quantitative discipline.
Strong interest in dynamical systems, biochemical networks, parameter estimation, and biological modelling.
Programming skills in Matlab, R, Python, Julia, or related modelling tools.
No prior expertise needed (but appreciated) but curiosity for biomedical and pharmacological applications and willingness to work across mathematics, biology, pharmacology, and clinical data are essential.