Dr. Fabian Fröhlich

Professional Address :
Institute for Computational Biomedicine
Im Neuenheimer Feld 130.3
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Education & Research Activity

web	**Visiting Fellow at University Hospital Heidelberg, Heidelberg, DE** Research Group: Systems Biomedicine, Institute for Computational Biomedicine Focus: Structure based modeling, data-driven models of heterogeneity, automated model formulation PI: Julio Saez-Rodriguez, PhD	since 2022
web	**Postdoctoral Fellow at Harvard Medical School, Boston, MA, USA** Research Group: Laboratory of Systems Pharmacology, Harvard Institute for Therapeutic Science Focus: Adaptive resistance in melanoma, model interpretability, protein-structure based modeling PI: Peter Sorger, PhD	since 2018
web	**PhD Candidate at the Helmholtz Zentrum München, Munich, Germany** Research Group: Data-Driven Computational Modeling, Institute for Computational Biology Focus: Scalable simulation and estimation for ODE models, efficient description of cell-to-cell variability Thesis: Scalable Methods for Parameter Estimation in Systems Biology (Defense Date: 29.03.2018) Degree Granting Institution: Technische Universität München PI: Prof. Dr. Jan Hasenauer	2013-2018
web	**Graduate School Quantitative Biosciences Munich (QBM), Munich, Germany** Course Work: Monthly lecture series and journal clubs with external speakers, monthly life sciences primer Workshops: Scientific Writing, Grant Writing, Presentation Skills, Poster Design	2013-2018
web	**Master of Science at the Technische Universität München, Munich, Germany** Principal Subject: Mathematics in Bioscience Focus: Parameter inference, biophysics, numerical methods Thesis: Approximation and Analysis of Probability Densities using Radial Basis Functions Thesis Advisor: Prof. Dr. Jan Hasenauer	2011-2013
web	**Bachelor of Science at the Technische Universität München, Munich, Germany** Principal Subject: Mathematics Secondary Subject: Physics Focus: Mathematical modeling, image processing, dynamical systems Thesis: Modelling and Analysis of DDEs for Hysteresis in Bacterial Quorum Sensing Thesis Advisor: Prof. Dr. Christina Kuttler	2008-2011

Awards & Fellowships

web	**MTZ®-Award for Medical Systems Biology 2020 (PhD Thesis)**	2020
web	**3-year Long-Term Fellowship from the Human Frontier Science Program (HFSP)**	2019-present
	3-year PhD fellowship from the German Research Foundation (DFG)	2013-2016
web	**International Genetically Engineered Machine Competition (iGEM)** Best Wiki (overgraduate division, worldwide)	2014
web	**International Genetically Engineered Machine Competition (iGEM)** 1st Runner Up (undergraduate, Europe; second best of 27 international teams) 1st Runner Up (undergraduate, worldwide; second best of 112 international teams) Best Environment Project (undergraduate, Europe + worldwide), Best Wiki (undergraduate, Europe)	2013

Teaching & Mentoring Experience

	Mentor of Graduate Student during Summer Internship Student: Javiera Cortes	2022
web	**Dana-Farber/Harvard Cancer Center – Harvard Medical School Mentor Training** Courses: Assessing, Understanding and Maintaining Effective Communication; Designing Short Term Research Projects; Equity, Inclusion and Navigating Research Culture	2019
	Mentor of PhD Candidate Student: Paul Stapor	2016-2018
web	**Foundation Level Certificate of Teaching in Higher Education (60 hours)** Courses: Designing and Conducting Examinations, Fostering Students Self-Directed Learning, Principles of Professional Teaching in Higher Education, Presentation Techniques, Role as Lecturer	2014-2018
	Teaching Assistant at the Technische Universität München Lectures: Statistical Inference for Dynamical Systems, Parameter Estimation for Dynamic Biological Systems I, Parameter Estimation for Dynamic Biological Systems II Responsibility: Lectures (substitute) and tutorials, conception and grading of exercises and examinations	2015-2017

	Co-Supervisior Master's Thesis **Student:** Laura Fink **Thesis:** Model selection in deterministic models of mRNA transfection	2015

Presentations (invited, oral)

13	**Maximum likelihood estimation and profile likelihoods** Workshop on Statistical Inference for Dynamical Systems, Berlin, DE	2022
12	**Mechanistic Models for Data-Driven Drug Sensitivity Prediction** Francis Crick Institute, London, UK	2022
11	**A Mechanistic Model of MAPK Signaling Reveals how Allostery and Rewiring Contribute to Drug Resistance** Pfizer Systems Modeling & Simulation Network Webinar, Virtual (US)	2022
10	**Dynamic Models for Data-Driven Drug Sensitivity Prediction** Department of Protein Science, KTH Royal Institute of Technology, Virtual (SE)	2022
9	**Kinetic Models for Data-Driven Drug Sensitivity Prediction** Faculty of Science, Stockholm University, Virtual (SE)	2022
8	**Mechanistic Models for Individualized Prediction of Resistance to Targeted Anti-Cancer Drugs** VIB Cancer Biology Lecture Series, VIB-KU Leuven Center for Cancer Biology, BE	2021
7	**Mechanistic Models for Personalized Drug Sensitivity Prediction** LySiM status seminar (MTZAward Ceremony), Virtual (DE)	2021
6	**Causal Deconvolution of a Mechanistic Model of EGFR and ERK Signaling explains Adaptive and Genetic Resistance in Melanoma** Novartis Institutes for Biomedical Research, Virtual (US)	2020
5	**In search of insight: Understanding large mechanistic models** Timmer Group, University of Freiburg, DE	2019
4	**In search of insight: Understanding large kinetic models** BioQuant, Heidelberg, DE	2019
3	**Unraveling Complexity in Large Kinetic Models** Department of Computational and Systems Biology, University of Pittsburgh, US	2019
2	**Efficient Parameterization of Large-Scale Mechanistic Models Enables Drug Response Prediction for Cancer Cell Lines** Instituto de Investigacións Mariñas, Consejo Superior de Investigaciones Científicas, ES	2017
1	**Accounting for Variability in Cell Populations** BioQuant, Heidelberg, DE	2015

Presentations (contributed, oral)

21	**A Mechanistic model of EGFR and ERK signaling reveals how allostery and rewiring contribute to drug resistance** ICSB 2022, Berlin, DE	2022
20	**A Mechanistic Model of EGFR and ERK Signaling Reveals how Allostery and Rewiring Contribute to RAF and MEK Inhibitor Resistance** ECMTB 2022, Heidelberg, DE	2022
19	**Scalable Calibration of Large Cancer Related Signaling Pathway Models in HPC Environments** ECCB 2022, Simulating Cellular Behaviours Workshop, Virtual	2022
18	**Fides: Reliable Trust-Region Optimization for Parameter Estimation of Ordinary Differential Equation Models** COMBINE 2021, Virtual	2021
17	**Causal Deconvolution of a Thermodynamic Model of MAPK Signaling explains Adaptive and Genetic Resistance to Targeted Drugs in BRAF-mutant Cancers** INCOME2021 Conference and Hackathon, Virtual	2021
16	**Causal Deconvolution of a Mechanistic Model of EGFR and ERK Signaling Explains Adaptive and Genetic Resistance in Melanoma** Computational Approaches for Cancer Workshop, Virtual	2020
15	**A thermodynamic Model of EGFR and ERK Signaling explains Adaptive and Genetic Resistance in Melanoma** COMBINE 2020, Virtual	2020
14	**Making Sense of Large Kinetic Models** Intelligent Systems for Molecular Biology (ISMB), Basel, CH	2019
13	**Simulation and Sensitivity Analysis for Large Kinetic Models in AMICI** COMBINE 2019, Heidelberg, DE	2019
12	**Hierarchical Modularization of Rule-Based Modeling Enables Construction of Complex Mechanistic Models** CSHL Meeting: Cellular Dynamics & Models, Cold Spring Harbor, US	2019

11	**Large-Scale Mechanistic Modeling Enables Robust Prediction of Cancer Cell Drug Response** Intelligent Systems for Molecular Biology (ISMB), Prague, CZ	2017
10	**Large-Dcale Mechanistic Modeling Rnables Robust Prediction of Cancer Cell Drug Response** Interdisciplinary Signalling Workshop (ISW), Visegrad, HU	2017
9	**Large-scale Modeling of Cancer Signaling: Mechanistic Modeling Meets Big Data** 2016 International Conference on Systems Biology (ICSB), Barcelona, ES	2016
8	**AMICI: An ODE Simulation Framework for Sensitivity Analysis of Large-scale Models** COMBINE 2016, Newcastle, UK	2016
7	**Think Adjoint – Methods Facilitating Parameter Estimation for Genome-scale Mechanistic Dynamic Models** 6th Conference on Systems Biology of Mammalian Cells (SBMC), Munich, DE	2016
6	**Parameter Estimation for Genome-Scale Mechanistic Models** Workshop e:Med PG "Informatics & Modelling", Heidelberg, DE	2015
5	**Parameter Estimation for Heterogeneous Populations** Numerical Methods for Optimal Control and Inverse Problems (OCIP 2015), Munich, DE	2015
4	**Parameter Estimation for the System Size Expansion** 9th European Conference on Mathematical and Theoretical Biology (ECMTB), Gothenburg, SE	2014
3	**Radial Basis Function Approximation of Bayesian Parameter Posterior Densities for Uncertainty Analysis** 12th Conference on Computational Methods in Systems Biology (CMSB), Manchester, UK	2014
2	**Uncertainty Analysis for Non-Identifiable Dynamical Systems: Profile Likelihoods, Bootstrapping and More** 12th Conference on Computational Methods in Systems Biology (CMSB), Manchester, UK	2014
1	**Uncertainty Analysis for Dynamical Systems using Radial Basis Functions** Numerical Methods for Optimal Control and Inverse Problems (OCIP 2014), Munich, DE	2014

Publications

25	**Fröhlich, F.***; Gerosa, L.*; Muhlich, J.; Sorger, P. K.; **Mechanistic model of MAPK signaling reveals how drug resistance arises from allostery and rewiring.** *bioRxiv*	2022
24	**Fröhlich, F.#**; Sorger, P.K.#; **Fides: Reliable optimization for parameter estimation of ordinary differential equation models.** *Accepted for publication in PLoS Comp. Bio.*	.
23	Shaikh, B.; Smith, L.P.; Vasilescu, D.; Marupilla, G.; Wilson, M.; Agmon, E.; Agnew, H.; Andrews, S.S.; Anwar, A.; Beber, M.E.; Bergmann, F.T.; Brooks, D.; Brusch, L.; Calzone, L.; Choi, K.; Cooper, J.; Detloff, J.; Drawert, B.; Dumontier, M.; Ermentrout, M.G; Faeder, J.R.; Freiburger, A.P.; **Fröhlich, F.**; Funahashi, A.; Garny, A.; Gennari, J.H.; Gleeson, P.; Goelzer, A.; Haiman, Z.; Hellerstein, J.L.; Hoops, S.; Ison, J.C.; Jahn, D.; Jakubowski, H.V.; Jordan, R.; Kalaš, M.; König, M.; Liebermeister, W.; Mandal, S.; McDougal, R.; J Medley, K.; Mendes, P.; Müller, R.; Myers, C.J.; Naldi, A.; Nguyen, T.V.; Nickerson, D.P.; Olivier, B.G.; Patoliya, D.; Paulevé, L.; Petzold, L.R.; Priya, A.; Rampadarath, A.K.; Rohwer, J.M.; Saglam, A.S.; Singh, D.; Sinha, A.; Snoep, J.; Sorby, H.; Spangler, R.; Starruß, J.; Thomas, P.J.; David Niekerk, V.; Weindl, D.; Zhang, F.; Zhukova, A.; Goldberg, A.P.; Blinov, M.L.; Sauro, H.M.; Moraru, I.I.; Karr, J.R.; **BioSimulators: a central registry of simulation engines and services for recommending specific tools.** *Nucleic Acids Research 50(1): W108-W114*	2022
22	Villaverde, A.F.; Pathirana, D.; **Fröhlich, F.**; Hasenauer, J.; Banga J.R.; **A protocol for dynamic model calibration.** *Brief. Bioinformatics 23(1), 1-19*	2022
21	Schmucker, R.; Farina, G.; Faeder, J.; **Fröhlich, F.**; Saglam, A.S.; Sandholm, T.; **Combination treatment optimization using a pan-cancer pathway model.** *PLoS Comp. Bio. 17(12): e1009689*	2021
20	**Fröhlich, F.#**; Weindl, D.; Schälte, Y.; Pathirana, D.; Paszkowski; Ł., Lines; G. T.; Stapor, P.; Hasenauer, J.#; **AMICI: High-performance sensitivity analysis for large ordinary differential equation models.** *Bioinformatics 37(20), 3676-3677*	2021
19	Schmiester, L.; Schälte, Y.; Bergmann, F.T.; Camba, T.; Dudkin, E.; Egert, J.; **Fröhlich, F.**; Fuhrmann, L.; Hauber, A.L.; Kemmer, S.; Lakrisenko, P.; Loos, C.; Merkt, S.; Pathirana, D.; Raimúndez, E.; Refisch, L; Rosenblatt, M.; Städter, P.; Wang, D.; Wieland, F.G.; Banga, J.R.; Timmer, J.; Villaverde, A.F.; Sahle, S.; Kreutz,C.; Hasenauer, J; Weindl, D.; **PEtab – interoperable specification of parameter estimation problems in systems biology.** *PLoS Comp. Bio. 17(1): e1008646*	2021
18	Gerosa, L.; Chidley, C.; Fröhlich, F.; Sanchez, G.; Lim, S.K., Muhlich, J., Chen, J.Y.; Baker, G.J.; Schapiro, D.; Shi, T.; Yi, L.; Nicora, C.D.; Claas, A.; Lauffenburger, D.A.; Qian, W.J.; Wiley, H.S.; Sorger, P.K.; **Sporadic ERK pulses drive non-genetic resistance in drug-adapted BRAFV600E melanoma cells.** *Cell Systems 11*(5), 478-494	2020
17	Schmiester, L.; Schälte, Y.; Fröhlich, F.; Hasenauer, J.; Weindl, D.; **Efficient parameterization of large-scale dynamic models based on relative measurements.** *Bioinformatics 36(2), 594-602*	2020

16	Fröhlich, F.; Loos, C.; Hasenauer, J.; **Scalable Inference of Ordinary Differential Equation Models of Biochemical Processes.** *Gene Regulatory Networks, 385-422*	2019
15	Villaverde, A.F.; Fröhlich, F.; Weindl, D.; Hasenauer, J.; Banga J.R.; **Benchmarking Optimization Methods for Parameter Estimation in Large Kinetic Models.** *Bioinformatics 35(5), 830-838*	2019
14	Fröhlich, F.*; Reiser, A.*; Fink, L.; Woschee, D.; Ligon, T.; Theis, F.J.; Rädler, J.; Hasenauer, J.; **Multi-Experiment Nonlinear Mixed Effect Modeling of Single-Cell Translation Kinetics after Transfection.** *npj Syst. Biol. Appl. 5(1), 1*	2018
13	Fröhlich, F.*; Kessler, T.*; Weindl, D.; Shadrin, S.; Schmiester, L.; Hache, H.; Muradyan, A.; Schuette, M.; Lim, J.H.; Heinig, M.; Theis, F.J.; Lehrach, H.; Wierling, C.; Lange, B.; Hasenauer, J.; **Efficient Parameter Estimation enables the Prediction of Drug Response using a Mechanistic Pan-Cancer Pathway Model.** *Cell Systems 7(6), 567-579*	2018
12	Stapor, P.; Fröhlich, F.; Hasenauer, J.; **Optimization and profile calculation of ODE models using second order adjoint sensitivity analysis.** *Bioinformatics 34(13), i151-159*	2018
11	Loos, C.; Möller, K.; Fröhlich, F.; Hucho, T.; Hasenauer, J.; **A Hierarchical, Data-Driven Approach to Modeling Single-Cell Populations Predicts Latent Causes of Cell-To-Cell Variability.** *Cell Systems, 6(5), 593-603. e13*	2018
10	Ligon, T.; Fröhlich, F.; Chis, O.; Banga, J.; Balsa-Canto, E.; Hasenauer, J.; **GenSSI 2.0: Multi-experiment structural identifiability analysis of SBML models.** *Bioinformatics 34(8), 1421-1423*	2018
9	Stapor, P.; Weindl, D.; Ballnus, B.; Hug, S.; Loos, C.; Fiedler, A.; Krause, S.; Hroß, S.; Fröhlich, F.; Hasenauer, J.; **PESTO: Parameter EStimation TOolbox.** *Bioinformatics 34(4), 705-707*	2018
8	Fröhlich, F.; Kaltenbacher, B.; Theis, F.J.; Hasenauer, J.; **Scalable parameter estimation for genome-scale biochemical reaction networks.** *PLoS Comp. Bio. 13(1): e1005331.*	2017
7	Fröhlich, F.; Theis, F.J.; Rädler, J.O.; Hasenauer, J.; **Parameter estimation for dynamical Systems with discrete events and logical operations.** *Bioinformatics 33(7), 1049-1056.*	2017
6	Fröhlich, F.; Thomas, P.; Kazeroonian, A.; Theis, F.J.; Grima, R.; Hasenauer, J.; **Inference for stochastic chemical kinetics using moment equations and system size expansion.** *PLoS Comp. Bio. 12(7): e1005030.*	2016
5	Kazeroonian, A.; Fröhlich, F.; Raue, A.; Theis, F.J.; Hasenauer, J.; **CERENA: ChEmical REaction Network Analyzer – A toolbox for the simulation and analysis of stochastic chemical kinetics**. *PLoS ONE 11: e0146732.*	2016
4	Fröhlich, F.; Hross, S.; Theis, F.J.; Hasenauer, J.; **Radial basis function approximation of bayesaian parameter posterior densities for uncertainty analysis.** *Lecture Notes Comp. Sci. 8859, 73-85.*	2014
3	Fröhlich, F.; Theis, F.J.; Hasenauer, J.; **Uncertainty analysis for non-Identifiable dynamical systems: profile likelihoods, bootstraping and more.** *Lecture Notes Comp. Sci. 8859, 61-72.*	2014
2	Morath, V.; Truong, D.J.J.; Albrecht, F.; Polte, I.; Ciccone, R.A.; Funke, L.F.; Reichart, L.; Wolf, C.G.; Brunner, A.D.; Fischer, K.; Schneider, P.C.; Brüggenthies, J.B.; Fröhlich, F.; Wiedemann, G.; Reski, R.; Skerra, A.; **Design and characterization of a modular membrane protein anchor to functionalize the moss *Physcomitrella patens* with extracellular catalytic and/or binding activities.** *ACS Synth. Biol. 3, 990-994.*	2014
1	Bongini, M.; Fornasier, M.; Fröhlich, F.; Haghverdi, L.; **Sparse control of force field dynamics.** *International Conference on NETwork Games, COntrol and OPtimization, 195-200.*	2014

Software

web	**AMICI –** Advanced MATLAB Interface for CVODES and IDAS (lead developer)
web	**Fides** – Reliable Trust Region Optimization in Python (lead developer)
web	**MEMOIR** – MATLAB toolbox for Mixed Effect Model InfeRence (lead developer)
web	**pyPESTO –** Parameter EStimation Toolbox (developer)
web	**PEtab** – Data Format for Parameter Estimation Problems (developer)
web	**CERENA** – ChEmical REaction Network Analyzer (developer)
web	**GenSSI** – Generating Series for testing Structural Identifiability (developer)

Service & Leadership

Reviewer for Cell Systems, eLife, PLoS Computational Biology, Bioinformatics, Complexity, BMC Systems Biology, IEEE Access, IEEE/ACM Transactions on Computational Biology and Bioinformatics, Journal of the Royal Society Interface, Journal of the Royal Society Proceedings A

Grant Referee for the **Marsden Fund**	
Program Committe Member for **CMSB2016**, **ISMB2018**, **ISBM2019**, **ISMB2020**, **ISMB2021**, **ISMB2022**	
Elected member of the editorial board for the **PEtab** format	2021-2023
Judge for the **international Genetically Engineered Machine (iGEM)** competition	2018-2019
Student representative in the **Life Sciences Graduate Network**	2016-2018
Student representative in the **QBM Graduate School** managing board	2014-2018