

## CHRISTIAN L. MÜLLER, PHD

PROJECT LEADER IN  
COMPUTATIONAL STATISTICS  
CENTER FOR COMPUTATIONAL BIOLOGY  
FLATIRON INSTITUTE

## SIMONS FOUNDATION

162 5<sup>TH</sup> AVENUE, 7<sup>TH</sup> FLOOR  
NEW YORK, NY 10010  
EMAIL: [cmueller@flatironinstitute.org](mailto:cmueller@flatironinstitute.org)  
OFFICE: +1-646-603-3716

### Education

- 2006–2011 PhD studies (**Dr. sc. (ETH)**), Institute for Computational Science and Institute of Theoretical Computer Science, **ETH Zürich**, Switzerland, and **Swiss Institute of Bioinformatics**
- 2005–2006 Studies at the **University of Tübingen**, Germany  
(**Diploma Computer Science**), Major:  
Bioinformatics, Certificate: Literature and Poetry
- 2003–2004 Studies at **Uppsala Universitet**, Sweden  
(**M.Sc. Computer Science**) Major: Computational Science
- 1999–2002 Studies at the **University of Tübingen**, Germany  
(**Pre-diploma (B.Sc. equiv.) Computer Science** (Bioinformatics))

### Academic employment

- In 2018 (summer) Visiting Faculty, Max-Planck/TU Dresden Center for Systems Biology, Dresden, Germany
- Since 2016 Project Leader (tenured) in Computational Statistics, **Flatiron Institute**, Simons Foundation, New York, USA
- 2014–2016 Research Scientist, **Simons Center for Data Analysis (SCDA)**, Simons Foundation, and, CS & Biology, NYU, New York, USA
- 2012–2014 Postdoctoral researcher, Center for Genomics and Systems Biology and Courant Institute for Mathematical Sciences, **New York University**, USA, Mentor: Dr. Richard Bonneau
- 2011–2012 Postdoctoral researcher, Institute of Theoretical Computer Science, **ETH Zürich**, Switzerland, and **Swiss Institute of Bioinformatics**, Mentor: Dr. Ivo F. Sbalzarini

## Current research interests

**Statistics and Optimization:** High-dimensional statistics, robust and concomitant regression, graphical model inference, proximal algorithms, stochastic global optimization, oracle-based volume computation, bio-inspired computation

**Computational Biology:** Statistical analysis of microbiome sequencing data, microbial ecological network inference, robustness quantification of biological systems, inference of protein-protein interactions, ecological and co-evolutionary models of (ocean) microbial ecosystems

## Selected key publications

### Statistics and Optimization

P.L. Combettes, **C. L. Müller**. Perspective Functions: Proximal Algorithms and Applications in High-dimensional Statistics, *J. Math. Anal. Appl.*, 2018.

J. Asmus, **C.L. Müller**<sup>#</sup>, and I. F. Sbalzarini<sup>#</sup>.  $L_p$ -Adaptation: Simultaneous Design Centering and Robustness Estimation of Electronic and Biological Systems, *Sci. Rep.*, 7, 2017.

J. Bien, I. Gaynanova, J. Lederer, and **C. L. Müller**. Non-convex global optimization and false discovery rate control for the TREX, *J. Comp. Graph. Stats.*, 2017.

J. Lederer, **C. L Müller**. Don't fall for tuning parameters: Tuning-free variable selection in high dimensions with the TREX. *Proc. AAAI*, 2015.

### Computational Biology

L. Tipton\*, **C.L. Müller**\*, Z. D. Kurtz, A. Morris, L. Huang, E. Kleerup, R. Bonneau, E. Ghedin, Fungi Stabilize Connectivity in Lung and Skin Microbial Ecosystems. *To appear: Microbiome*, 2018

K. Drew, **C.L. Müller**<sup>#</sup>, R. Bonneau, E. Marcotte. Identifying direct contacts between protein complex subunits from their conditional dependence in proteomics datasets. *PLOS Comp. Biol.*, 2017.

V. E Ruiz, ..., **C. L. Müller**, ..., M. J. Blaser. A single early-in-life antibiotic course has long-lasting effects on microbial network topology and host immunity. *Nature Communications* 8, 2017.

Z. D. Kurtz\*, **C. L. Müller**\*, E. R. Miraldi\*, D. R. Littman, M. J. Blaser and R. A. Bonneau. Sparse and compositionally robust inference of microbial ecological networks. *PLOS Comp. Biol.*, 2015.

(\* joint first author, <sup>#</sup>corresponding author)

## Preprints/Under review

P.L. Combettes, **C. L. Müller**. Proximal Analysis for Penalized Concomitant M-estimators, 2017.

J. Bien, I. Gaynanova, J. Lederer, and **C. L. Müller**. Prediction Error Bounds for Linear Regression with the TREX. Revised manuscript under review, TEST, <https://arxiv.org/abs/1801.01394>, 2017.

**C. L. Müller**, R. Bonneau, Z. D. Kurtz. Generalized Stability Approach for Regularized Graphical Models. <https://arxiv.org/abs/1605.07072>, 2016.

## Peer-reviewed publications

### 2018

[1] L. Tipton\*, **C.L. Müller\***, Z. D. Kurtz, A. Morris, L. Huang, E. Kleerup, R. Bonneau, E. Ghedin, Fungi Stabilize Connectivity in Lung and Skin Microbial Ecosystems. *To appear: Microbiome, 2018*

### 2017

[2] K. Drew, **C.L. Müller#**, R. Bonneau, E. Marcotte. Identifying direct contacts between protein complex subunits from their conditional dependence in proteomics datasets. *PLOS Comp. Biol.*, 2017.

[3] T. Äijö, **C.L. Müller**, R. Bonneau. Temporal probabilistic modeling of bacterial compositions derived from 16S rRNA sequencing. *Bioinformatics*, 2017.

[4] V. E Ruiz, T. Battaglia, Z. D. Kurtz, L. Bijmens, A. Ou, I. Engstrand, X. Zheng, T. Iizumi, B. J. Mullins, **C. L. Müller**, K. Cadwell, R. Bonneau, G. I. Perez-Perez, M. J. Blaser. A single early-in-life antibiotic course has long-lasting effects on microbial network topology and host immunity. *Nature Comms* 8, 2017.

[5] J. Asmus, **C.L. Müller#**, and I. F. Sbalzarini. Lp-Adaptation: Simultaneous Design Centering and Robustness Estimation of Electronic and Biological Systems, *Sci. Rep.*, 7, 2017.

[6] J. Bien, I. Gaynanova, J. Lederer, and **C. L. Müller**. Non-convex global optimization and false discovery rate control for the TREX, *J. Comp. Graph. Stats.*, 2017.

[7] P.L. Combettes, **C. L. Müller**. Perspective Functions: Proximal Algorithms and Applications in High-dimensional Statistics, *J. Math. Anal. Appl.*, 2018.

### 2016 and prior

[8] K. Y. Lam, Z.M. Westrick, **C. L. Müller**, L. Christiaen, and R. Bonneau. Fused regression for multi-source network inference. *PLOS Comp. Biol.*, 2016.

[9] D. Mahana, Z. D. Kurtz, N. A. Bokulich, C. M. Trent, T. Battaglia, J. Chung, **C. L. Müller**, H. Li, R. Bonneau, and M. J. Blaser. Antibiotic perturbation of the murine gut microbiome enhances the adiposity, insulin resistance, and liver disease associated with high-fat diet. *Genome Medicine* 2016

[10] R. Raviram, P. P. Rocha, **C. L Müller**, E. R. Miraldi, Y. Fu, E. Swanzey, S. Badri, C. Proudhon, V. Snetkova, R. Bonneau, J. Skok. 4C-ker: A method to reproducibly identify genome-wide interactions captured by 4C-Seq experiments. *PLOS Comp. Biol.*, 2016.

[11] E. H. Baugh, R. Simmons-Edler, **C. L. Müller**, R. F. Alford, N. Volfovksy, A.E. Lash, and R. Bonneau. Robust Classification of Protein Variation Using Structural Modeling and Large-Scale Data Integration. *Nucleic Acids Research.*, 2016.

[12] Steven M. Hill et al. Inferring causal molecular networks: empirical assessment through a community-based effort. *Nature methods*, **13**, 310–318, 2016.

[13] S. U. Stich, **C. L. Müller**, and B. Gärtner. Variable Metric Random Pursuit. *Math. Prog. A*, 156 (1-2), 549-579, 2016.

[14] A. Plessis, C. Hafemeister, O. Wilkins, Z. J. Gonzaga, R. S. Meyer, I. Pires, **C. L. Müller**, E. M. Septiningsih, R. Bonneau, M. Purugganan. Multiple abiotic stimuli are integrated in the regulation of

rice gene expression under field conditions. *eLIFE*, 2015.

[15] Z. D. Kurtz\*, **C. L. Müller\***, E. R. Miraldi\*, D. R. Littman, M. J. Blaser and R. A. Bonneau. Sparse and compositionally robust inference of microbial ecological networks. *PLOS Comp. Biol.*, 2015.

[16] J. Lederer\*, **C. L. Müller \***. Don't fall for tuning parameters: Tuning-free variable selection in high dimensions with the TREX. *Proc. AAAI*, 2015.

[17] **C. L. Müller**. Stochastic methods for single objective global optimization. In: *AAIA Computational Intelligence in Aerospace Sciences*, 63-112, 2014.

[18] K. Tchourine\*, C. S. Poultney\*, L. Wang\*, G. M. Silva, S. Manohar, **C. L. Mueller**, Richard Bonneau, and Christine Vogel. One third of dynamic protein expression profiles can be predicted by a simple rate equation. *Mol. BioSyst.*, 10, 2850-2862, 2014.

[19] S. Billerbeck, B. Calles, **C. L. Müller**, V. de Lorenzo, S. Panke. Towards functional orthogonalisation of protein complexes: individualization of GroEL monomers leads to distinct quasi-homogeneous single rings. *ChemBioChem*14(17):2310R21, 2013.

[20] S. U. Stich, **C. L. Müller**, and B. Gärtner. Optimization of convex functions with Random Pursuit. *SIAM J. Optim.* 23(2):1284-1309, 2013.

[21] **C. L. Müller** and I.F. Sbalzarini. Energy landscapes of atomic clusters as black box optimization benchmarks. *Evol. Compt.*, 20(4):543-573 2012.

[22] S.U. Stich and **C.L. Müller**. On spectral invariance or randomized Hessian and covariance matrix adaption schemes. *Parallel Problem Solving from Nature (PPSN)*, 2012.

[23] **C. L. Müller\***, R. Ramaswamy\*, I.F. Sbalzarini. Global parameter identification in stochastic reaction networks from single trajectories. *Adv. Exp. Med. Biol.* 736:477-98, 2012.

[24] **C. L. Müller** and I. F. Sbalzarini. Gaussian Adaptation for robust design centering. In Proc. Evolutionary and deterministic methods for design, optimization, and control (*EuroGen*), 2011.

[25] **C. L. Müller** and I. F. Sbalzarini. Global characterization of the CEC 2005 fitness landscapes using fitness-distance analysis. *EvoApplications, Lecture Notes in Computer Science*, 2011.

[26] **C. L. Müller** and I. F. Sbalzarini. A conjecture about an upper bound of the RMSD between linear chains. In *Proc. 27th European Workshop on Computational Geometry (EuroCG)*, 2011.

[27] **C. L. Müller**. Exploring the common concepts of adaptive MCMC and Covariance Matrix Adaptation scheme. In: *Theory of Evolutionary Algorithms, Dagstuhl Seminar Proceedings 10361*, Leibniz-Center for Informatics, 2010.

[28] **C. L. Müller** and I. F. Sbalzarini. Gaussian Adaptation as a unifying framework for black-box optimization and adaptive Monte Carlo sampling. In *Proc. IEEE CEC*, 2010.

[29] **C. L. Müller** and I. F. Sbalzarini. Gaussian Adaptation revisited – an entropic view on covariance matrix adaptation. *EvoApplications, Lecture Notes in Computer Science* 2010.

[30] **C. L. Müller** and I. F. Sbalzarini. A tunable real-world multi-funnel benchmark problem for evolutionary optimization (and why parallel island models might remedy the failure of CMA-ES on it). In *Proc. Intl. Conf. Evolutionary Computation (ICEC)*, 2009.

[31] **C. L. Müller**, B. Baumgartner, G. Ofenbeck, B. Schrader, and I. F. Sbalzarini. pCMALib: a parallel FORTRAN 90 library for the evolution strategy with covariance matrix adaptation. In *Proc. ACM Genetic and Evolutionary Computation Conference (GECCO '09)*, 2009.

[32] **C. L. Müller**, B. Baumgartner, and I. F. Sbalzarini. Particle swarm CMA evolution strategy for the optimization of multi-funnel landscapes. In *Proc. IEEE CEC*, 2009.

[33] **C. L. Müller**, I.F. Sbalzarini, W.F. van Gunsteren, B. Zagrovic, and P.H. Hünenberger. In the eye of the beholder: Inhomogeneous distribution of high resolution shapes within the random walk ensemble. *J.Chem.Phys.*,130(21):214904, 2009.

[34] A. Tusek, **C. L. Müller**, J. Supper, A. Zell, Z. Kurtanjek, and I. F. Sbalzarini. Systems biology markup language: Case study of T-cell signal transduction network. In *Proc. IEEE of the 29th International Conference on Information Technology Interfaces (ITIO7)*, 2007.

[35] R. Dölling, H. Mielenz, and **C. L. Müller**. Efficient Simulation of Automotive Multi- Physical Systems by Optimization with Evolutionary Algorithms, In *Proc. IASTED Applied Simulation and Modeling Conference (AMS)*, 2007.

## Technical reports

F. Cázáls, C. Robert, A. Roth, and **C. L. Müller**, Towards Morse Theory for Point Cloud Data. preprint <https://hal.inria.fr/hal-00848753>, 2013.

S. U. Stich, **C. L. Müller**, and B. Gärtner. Matrix-valued Iterative Random Projections, ETH Zürich, 2013.

**C. L. Müller**. Finding maximizing Euclidean TSP tours for the Häme-Hyytiä-Hakula conjecture, MOSAIC technical report, Department of Computer Science, ETH Zürich, April 2011.

**C. L. Müller**, G. Ofenbeck, B. Baumgartner, and I. F. Sbalzarini. pCMALib – Manual for version 1.0, MOSAIC technical report, Department of Computer Science, ETH Zürich, May 2010.

**C. L. Müller**. Benchmark runs of pCMALib on Nehalem and Shanghai nodes. MOSAIC technical report, Department of Computer Science, ETH Zürich, April 2009.

## Theses

**C. L. Müller**. Black-box Landscapes: Characterization, Optimization, Sampling and Application to Geometric Configuration Problems. PhD thesis, Department of Computer Science, ETH Zürich, 2010/2011. **Thesis Committee: Ivo F. Sbalzarini, Bojan Zagrovic, Philippe Hünenberger, Nikolaus Hansen, Emo Welzl**

**C. L. Müller**. Parameter Sensitivity Analysis in Behavioral and Analog Circuit Simulations of Neuro-Fuzzy Models. Diploma thesis, Robert Bosch GmbH and Department of Information and Cognitive Sciences, University of Tübingen, 2006. **Thesis Committee: Wolfgang Rosenstiel, Hanspeter A. Mallot, Rolando Doelling**

**C. L. Müller**. die erde dreht sich zu laut – gedichte von der schwedischen oberfläche. Poem collection/Certificate thesis, Studio Literatur und Theater, University of Tübingen, 2005. **Thesis Committee: Dagmar Leupold, Hans Raab**

**C. L. Müller**. High order accurate numerical solution of the linearized Euler equations for sound propagation in the atmosphere. Master's thesis, Department of Computer Science, Uppsala University, 2004. **Thesis Committee: Bernhard Müller, Tom Smedsaas**

# Academic Supervising, Mentoring and Services

## Principal supervision of (graduate) students/postdocs

### Postdocs

Aditya Mishra, since 2017, Flatiron Institute, (PhD in Statistics, 2017 from UConn)

### PhD theses

Josh Fass (ongoing since 2016, with Dr. John Chodera, MSKCC)

Josefine Asmus (completed 2017, with Dr. Ivo F. Sbalzarini, MPI-CBG/TU Dresden)

Sebastian Stich (completed 2014, with Dr. Bernd Gärtner, ETH Zürich)

### Master/diploma theses (2006-2012, ETH Zürich)

Ana Tusek, Benedikt Baumgartner, Christian Fiegl, Georg Ofenbeck, Markus König, Daniel Zünd, (supervised by Dr. Ivo F. Sbalzarini), Thomas Lampart (supervised by Dr. Peter Widmayer)

### Bachelor/semester theses (2006-2010, ETH Zürich)

Johannes Lederer, Yannick Misteli, Patrick Plattner (supervised by Dr. Ivo F. Sbalzarini)

## Mentoring of graduate students

Zachary Kurtz (completed 2016, with Dr. Richard Bonneau, Dr. Martin Blaser, NYU)

Evan Baugh (completed 2016, with Dr. Richard Bonneau, NYU)

## Workshop organization

“ASA Statistical Learning and Data Science conference”, Local organizing committee, New York, June, 2018.

“Operator Splitting in Data Analysis”, SAMSI workshop, Research Triangle, NC, March, 2018.

“Third Workshop on **Statistical and Algorithmic Challenges in Microbiome Data Analysis**”, held jointly by the Flatiron Institute and the MIT Center for Microbiome Informatics and Therapeutics, Simons Foundation, New York, March, 2018.

“Second Workshop on **Statistical and Algorithmic Challenges in Microbiome Data Analysis**”, held jointly by the Flatiron Institute and the MIT Center for Microbiome Informatics and Therapeutics, Broad Institute, Cambridge, Feb 16-17, 2017.

“First Workshop on **Statistical and Algorithmic Challenges in Microbiome Data Analysis**”, held jointly by the Simons Center for Data Analysis and the MIT Center for Microbiome Informatics and Therapeutics, New York City, Feb 25-27, 2016.

Minisymposium “**Computational Geometric Learning** – Exploring geometric structure in high dimensions”, at the 28<sup>th</sup> Symposium on Computational Geometry (SoCG), 2012.

## Scientific reviewing service/program committee

NIPS, SIAM J. Optimization, SIAM ALENEX (Algorithm Engineering and Experiments), PLOS ONE, ACM GECCO (Theory track), Evo\* (Numerical optimization track), PPSN (Parallel Problem Solving from Nature), Bioinformatics, PLOS Computational Biology, Genome Biology, Microbiome

## Grants and Scholarships

- 2017 – 2022      **Co-Investigator** Simons Collaboration on computational bio-geochemical modeling of marine ecosystems (SC CBIOMES)
- 2010 – 2013      **Co-PI** of the **EU FP7-ICT grant** on *Computational Geometric Learning*  
FET-Open grant number: 255827, EU contribution of 2.4M€, coordinated by Joachim Giesen, Friedrich-Schiller University, Jena, Germany
- 1999 – 2005      **Full study stipend of the Bavarian state** (Bay. Stipendium für Besonders Begabte / Bavarian excellence program for gifted students, less than 1% acceptance rate among all Bavarian senior high school students per year)

## Teaching experience

- Since 2016      Summer Faculty, STAMPS ([Strategies and Techniques for Analyzing Microbial Population Structures](#)), Marine Biological Laboratory, Woods Hole, MA
- Since 2015      Math for America (MfA) Lecturer: “Networks in Science”, Course for math/biology teachers in New York City
- 2013-2014      Guest lectures for NYU Center for Genomics and Systems Biology (undergraduate courses on bioinformatics, data analysis, and network inference)
- 2007 – 2011      Teaching assistant for summer schools on **Biological image processing** and **Computational Biology** at ETH Zürich and MedILS, (Prof. I.F. Sbalzarini, ETH Zürich)
- 2007 – 2010      Main teaching assistant for "Spatiotemporal Modeling and Simulation" (Prof. I.F. Sbalzarini, ETH Zürich)
- 2000 – 2006      Teaching assistant for "Modeling and Simulation" (Prof. G. Gonnet, ETH Zürich), "Mathematics for biologists" (Prof. K.P. Haderler, University of Tübingen)

## Collaborations/Collaborative Research Stays

- Since 2015      Dr. Patrick Combettes, Math Department, NC State, **Proximal algorithms for high-dimensional statistics**
- Since 2013      Dr. Jacob Bien, Stats Department, University of Southern California, **High-dimensional statistics, time series analysis**
- Dr. Johannes Lederer, Statistics Department, University of Washington, Seattle, USA, **High-dimensional statistics**
- Dr. Martin Blaser, New York School of Medicine, USA, **Analysis of**



## microbiome data

- Nov 2011 Dr. Thomas J. Fuchs, Caltech, USA, **Approximate Bayesian Computation in Vision**
- Sept 2011 Dr. Frederic Cazals, INRIA Sophia-Antipolis, Sophia-Antipolis, France, **Computational topological analysis of sampled landscapes**
- April 2011 Dr. Bojan Zagrovic, Max F. Perutz Laboratories and University of Vienna, Vienna, Austria, **Conformation space analysis of chain molecules**

## Selected Recent Invited Talks

- May 2017 Computational Seminar @ **Max Planck/TU Dresden Center for Systems Biology**, Germany: *Inference and analysis of microbial association networks across ecosystems*
- Feb 2017 Computational Seminar @ **Pacific Northwest National Lab**, USA: *Inference and analysis of microbial association networks across ecosystems*
- May 2016 Computational Biology Seminar @ **Rutgers University**, USA: *Large-scale Inference and Topological Analysis of Microbial Interaction Networks*
- Nov 2015 Data Science @LHC workshop, **CERN**, Switzerland: *High-dimensional model selection and estimation* (workshop covered in *Nature* 528, 18–19, Dec 2015)
- Oct 2015 Metagenomics seminar, **New York Genome Center**, USA: *Large-scale Inference and Topological Analysis of Microbial Interaction Networks*
- Oct 2015 Math Department Seminar, **Dartmouth College**: *High-dimensional sparse linear regression: Models, Algorithms, and Applications in Microbial Ecology*
- Sept 2015 Multi-Omics for Microbiomes Conference, **Pacific Northwest National Lab**, Tri-Cities, USA: *The Structure of Microbial Interaction Networks*
- July 2014 Theoretical Computer Science *Mittagsseminar*, **ETH Zurich**, Switzerland: *Sparse model estimation and selection with the LASSO and the TREX in systems biology applications*
- May 2014 Statistics Seminar, **Cornell University**, Ithaca, USA: *Inference of Microbial Ecological Interaction Networks with SPIEC-EASI*



## Academic references

**Prof. Dr. Patrick Combettes**

Distinguished Professor of Data-driven Science  
Department of Mathematics  
North Carolina State University  
Website: <http://www4.ncsu.edu/~pcombet/>  
Email: [plc@math.ncsu.edu](mailto:plc@math.ncsu.edu)

**Reference for:** Proximal algorithms, convex optimization, statistical modeling

**Prof. Dr. Jacob Bien**

Assistant Professor of Data Sciences and Operations  
Marshall School of Business, USC  
Website: <https://www.marshall.usc.edu/personnel/jacob-bien>  
Email: [jbien@usc.edu](mailto:jbien@usc.edu)

**Reference for:** High-dimensional statistics, convex optimization, time series analysis

**Prof. Dr. Ivo F. Sbalzarini**

Chair of Scientific Computing for Systems Biology, TU Dresden  
MOSAIC Group, Center for Systems Biology Dresden,  
Max Planck Institute of Molecular Cell Biology  
Website: <http://mosaic.mpi-cbg.de>  
Email: [ivos@mpi-cbg.de](mailto:ivos@mpi-cbg.de)

**Reference for:** Numerical analysis, stochastic optimization, MCMC, image processing, spatio-temporal modeling, energy and fitness landscapes

**Prof. Dr. Leslie Greengard**

Courant Institute for Mathematical Sciences, New York University  
Director Flatiron Institute, Simons Foundation  
Website: <http://www.math.nyu.edu/faculty/greengar/>  
Email: [greengard@cims.nyu.edu](mailto:greengard@cims.nyu.edu)

**Reference for:** General information about my role at the Flatiron Institute