Christopher Mathy, PhD - Postdoctoral Scholar

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Protein scientist and systems biologist using genome-wide screens to engineer protein function in diverse cellular contexts.

- Protein biochemistry and biophysics, deep mutational scanning, synthetic biology, mitochondrial engineering
- Large-scale analysis of interaction networks and omics data, protein modeling in Rosetta, protein language models

EDUCATION AND TRAINING

Postdoctoral Scholar, Dept. of Genetics Stanford University 10/2022 - Present Protein engineering using transfer learning on genetic interaction maps, advised by Lars Steinmetz, PhD

PhD in Bioengineering UC San Francisco and UC Berkeley 2022

Systems biology of allosteric GTPase mutations, advised by Tanja Kortemme, PhD

BS in Bioengineering, with honors Stanford University 2016

Engineering the NK1 Fragment of the Human Hepatocyte Growth Factor for Dual Use as a Potent Agonist and a

Gene Therapy Delivery Vehicle, advised by Jennifer Cochran, PhD

PUBLICATIONS

Peer-reviewed:

- 1. Mathy CJP, Mishra P, Flynn JM, Perica T, Mavor D, Bolon DNA, Kortemme T. (2023). A complete allosteric map of a GTPase switch in its native network. *Cell Systems*. https://doi.org/10.1016/j.cels.2023.01.003
- 2. Perica T*, Mathy CJP*, Xu J, Jang GM, Zhang Y, Kaake R, Ollikainen N, Braberg H, Swaney DL, Lambright DG, Kelly MJS, Krogan NJ, & Kortemme T. (2021). Systems-level effects of allosteric perturbations to a model molecular switch. *Nature*, 599, 152–157. * denotes equal contribution.
- 3. Baker JJ, Mathy CJP, Schaletzky J. (2021) A proposed workflow for proactive virus surveillance and prediction of variants for vaccine design. *PLOS Computational Biology*, 17(12), e1009624.
- 4. Bouhaddou M, Memon D, Meyer B et al. [including Mathy CJP] (2020). The Global Phosphorylation Landscape of SARS-CoV-2 Infection. *Cell*, 182(3), 685–712.e19.
- 5. Gordon DE, Jang GM, Bouhaddou M et al. [including Mathy CJP] (2020). A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature*, 583(7816), 459–468.

Under review:

Mathy CJP, Kortemme T. (2023). Emerging maps of allosteric regulation in cellular networks. *Current Opinion in Structural Biology*. (Invited review).

Additional works:

Mathy CJP (2016). Engineering the NK1 Fragment of the Human Hepatocyte Growth Factor for Dual Use as a Potent Agonist and a Gene Therapy Delivery Vehicle. *Stanford Digital Repository*. Senior Undergraduate Thesis, http://purl.stanford.edu/kw533qg7356

AWARDS

2022	Best Poster Award, 36th Annual Symposium of the Protein Society, High-Throughput Protein Science track. (\$250)
2022	Bioengineering Service and DEIB Awards - for service to the graduate program and contributions to diversity, equity, inclusion, and belonging. (\$1500)
2018 - 2021	Byers Family Discovery Fellow, UC San Francisco. (\$6000)
2019	Best Poster Award, Quantitative Biosciences Consortium Retreat, UC San Francisco.
2016	Top 10 team nationwide, NIBIB/VentureWell Design by Biomedical Undergraduate Teams Challenge.

INVITED TALKS

As Postdoctoral Scholar:

2023-03-06 Mapping allosteric perturbations from structure to cellular networks in a central GTPase switch. Synthetic Biology and Cell Engineering Meeting. UCSF.

As PhD student:

- 2021-11-11 Integrating biophysics and high-throughput systems biology to uncover new models of GTPase switch function. Special Guest Speaker, Pathology Advanced Translational Research Unit (PATRU). Emory University School of Medicine Department of Pathology and Laboratory Medicine.
- 2021-08-09 Conformational switching constrains the mutational tolerance of novel allosteric sites in the GTPase Gsp1. *Annual RosettaCon Protein Design Conference*. RosettaCommons, virtual conference.
- 2021-04-07 Integrating biophysics and systems biology to uncover new models of GTPase switch function. 19th Annual National Graduate Student Symposium. St. Jude Children's Research Hospital, Memphis, TN.
- 2020-01-28 Integrating biophysics and systems biology to understand mutations of the GTPase Ran/Gsp1. *Signaling Across Scales Symposium*. Quantitative Biosciences Institute, UC San Francisco.
- 2018-10-27 Mapping molecular properties of Gsp1 point mutants to cellular phenotype. *Bioengineering Retreat*. UC Berkeley UC San Francisco Graduate Group in Bioengineering.

POSTER PRESENTATIONS

As PhD student:

- 2022-07-07 Mathy CJP, Mishra P, Flynn JM, Perica T, Mavor D, Bolon DN, Kortemme T. Complete mutational mapping of a GTPase switch in vivo reveals novel allosteric regulation. 36th Annual Symposium of the Protein Society. Awarded Best Poster
- 2021-10-14 Mathy CJP, Mavor D, Flynn JM, Perica T, Mishra P, Kelly MJS, Kortemme T, Bolon DN. Conformational switching constrains the mutational tolerance of novel allosteric sites in the GTPase Gsp1. UC Berkeley UC San Francisco Bioengineering Retreat.
- 2019-10-05 Mathy CJP, Perica T, Xu J, Zhang Y, Ollikainen N, Jang G, Kaake R, Swaney D, Kelly MJS, Krogan NJ, Kortemme T. Allosteric coupling between interfaces and the nucleotide binding site of the small GTPase Gsp1 influences cellular processes. Quantitative Biosciences Consortium, UCSF. Received Best Poster Award
- 2019-06-02 Mathy CJP, Perica T, Zhang Y, Ollikainen N, Xu J, Jang G, Kaake R, Swaney D, Kelly MJS, Krogan NJ, Kortemme T. Targeted mutational perturbations of the small GTPase Ran reveal how pleiotropy is encoded in a model molecular switch. *Protein Science* (Vol. 28, pp. 200-201). Annual Protein Society Meeting.
- 2018-08-09 Mathy CJP, Perica T, Zhang Y, & Kortemme T. Biophysical analysis to map molecular properties of Gsp1 point mutations to their cellular scale phenotypes. Annual RosettaCon Protein Design Conference.
- 2018-02-21 Mathy CJP, Perica T, & Kortemme T. Mapping of molecular-level perturbations to systems-level phenotypes in Gsp1/Ran, a highly conserved protein switch. Biophysical Society Annual Meeting.
- 2017-10-07 Mathy CJP, Perica T, & Kortemme T. Mathematical modeling of Gsp1, a protein switch, to map mutations to phenotypic perturbations. UC Berkeley UC San Francisco Bioengineering Retreat.

As undergraduate:

- 2016-05-24 Mathy CJP, Engineering the NK1 Fragment of the Human Hepatocyte Growth Factor for Dual-Use as a Potent Agonist and a Gene Therapy Delivery Vehicle. Stanford Bioengineering Honors Poster Fair.
- 2016-04-07 Baisiwala S, <u>Mathy CJP</u>, Moahi K, & Malavé C. Gel-Aid, Redefining Wound Packing: An Absorbent Removable Hydrogel. Stanford Tau Beta Pi + IEEE Engineering Showcase.
- 2015-10-24 Mathy CJP, Lim S, & Cochran JR. Internalization Study of the NK1 Fragment of the Human Hepatocyte Growth Factor. Symposium of Undergraduate Research and Public Service at Stanford University.
- 2013-08-29 <u>Mathy CJP</u>, Lim S, & Cochran JR. Development of Reporter Cell Assay for Engineering Human Hepatocyte Growth Factor. Summer Research Experience for Undergraduates Poster Fair at Stanford University

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2021	Teaching Assistant, UCSF Biophysics 219: Computational Protein Design. Prepared exercises on computational protein modeling in Rosetta. Led a project group which successfully predicted the binding affinities of mutations in the SARS-CoV-2 Spike protein with the ACE2 receptor using $\Delta\Delta G$ calculations in Rosetta. Prepared lectures for first year UCSF graduate students, including the topic of protein design for therapeutic applications.
2018	Certificate, Science Teaching Effectiveness Program for Upcoming Professors (STEP-UP) workshop, UC San Francisco. 16-hour program on evidence-based teaching strategies that support student-centered learning in the college classroom, with an emphasis on supporting diverse learners.
2016 2014 - 2016	Teaching assistant, BIOE 131: Ethics in Bioengineering, Stanford University. Personal tutor for middle- and high-school aged students in the San Francisco Bay Area.
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SERVICE & OUTREACH

2021 - 2022	Co-President, UC Berkeley - UCSF Graduate Group in Bioengineering Association of Students. Non-voting member of the graduate program Executive Committee, advocating for student issues.
2020 - 2022	Admissions Committee, UC Berkeley - UCSF Graduate Group in Bioengineering Association of Students. Performed holistic admissions review for 70 applicants to the graduate program alongside faculty and 9 other PhD students.
2020 - 2021	Specialist, Rapid Reviews COVID-19 (MIT Press). Screened and pitched preprints for review and publication at Rapid Reviews COVID-19, an open-access overlay journal based at UC Berkeley.
2018 - 2019	Volunteer Educator, UCSF Science & Health Education Partnership. Taught scientific lessons in collaboration with teachers at local area elementary schools.
2017 - 2019	Retreat Committee, UC Berkeley - UCSF Graduate Group in Bioengineering Association of Students. Organized two annual scientific meetings with over 150 attendees.
2017 - 2019	Recruitment Committee, UC Berkeley - UCSF Graduate Group in Bioengineering Association of Students. Organized two annual visits for over 50 PhD program applicants.
2018	UCSF Center for Community Engagement Research Committee. Strategic planning and grant application review for partnerships between UCSF and community organizations.
2017	Volunteer Educator, Bay Area Scientists in Schools. Taught scientific lessons in collaboration with teachers at local area elementary schools.

MENTORSHIP

2022	Jon Zhang, UCSF Biophysics PhD Student. Mentored in GTPase protein production and biochemistry.
2019	Wilson Nieves Vasquez, UCSF Biophysics PhD Student. Supervised for 10-week rotation project using hydrogen-deuterium exchange to study the differences in GTPase conformations.
2019	Maru Jaime Garza, UCSF Biophysics PhD Student. Supervised for 10-week rotation project using 1-D ³¹ P-NMR to study the effect of partner binding on GTPase conformations.
2019	Christina Stephens, UCSF Biophysics PhD Student. Supervised for 10-week rotation project using computational protein modeling to examine how mutations impact GTPase conformational dynamics.