Graham Thomas Holt

www.grahamtholt.com

Education

Duke University
Sept. 2016 - Present — Ph.D. Candidate, Computational Biology & Bioinformatics
GPA: 3.9/4.0

Dartmouth College
June 2014 — B.A., Biomedical Engineering with Honors
Minor, Computer Science
GPA: 3.65/4.0 - Cum Laude

Research

Donald Lab, Duke University
Sept. 2016 - Present — Ph.D. Candidate, Durham, NC
Dr. Bruce R. Donald, Advisor

I develop provable algorithms to compute the partition function and energy landscape of a protein conformation ensemble. I apply these algorithms to design protein therapeutics and investigate the structural biology of peptide binding, antibiotic resistance, and antibody:antigen interactions.

GENIE Project, Howard Hughes Medical Institute
July 2014 - July 2016 — Research Technician, Ashburn, VA
Dr. Douglas Kim, Program Scientist; Dr. Eric Schreiter, Group Leader

Responsible for mutagenesis and high-throughput screening of genetically encoded calcium indicator (GECI) variants. Improved activity of CaMPARI, a novel calcium-dependent green to red photoconvertible fluorescent protein.

Higgs Lab, Geisel School of Medicine
Nov. 2010 - June 2014 — Undergraduate Researcher, Hanover, NH
Dr. Henry N. Higgs, Principal Investigator

My honors thesis, *Examination of the Bioengineering of Polarized Microstructures*, characterized the localization and behavior of a mammalian cytoskeleton regulatory protein, FMNL3. Research included limited alanine scanning of putative binding sites and fluorescence microscopy.

US Dept. of Energy, Lawrence Berkeley National Laboratory
Aug. - Dec. 2012 — Science Undergraduate Laboratory Intern, Berkeley, CA
Dr. Priscilla Cooper, Principal Investigator; Dr. Kelly Trego, Mentor

My independent project, *Transcriptional Regulation of XPG in the DNA Damage Response*, evaluated putative transcription factors of XPG, a double-stranded break DNA repair protein. I inhibited TFs in cultured human cells and evaluated the levels of XPG via qRT-PCR and Western blotting.

Awards and Fellowships

Teaching Assistant Award - Duke University Dept. of Computer Science, 2020
Poster Award - Duke University Dept. of Biochemistry, 2019
RECOMB Travel Fellowship Award - NSF, 2019
James B. Duke Fellowship - Duke University, 2016 - 2020
Tau Beta Pi Engineering Honors Society - Dartmouth College, 2014
Junior Research Scholarship - Dartmouth College, 2013
Sophomore Science Scholarship - Dartmouth College, 2012

Technical Skills

Algorithm Development, Java, Python, MATLAB, LaTeX, Unix, Protein Biochemistry, Automated Liquid Handling, Fluorescent Microscopy, Tissue Culture, PCR, SDS-PAGE

Publications

Lowegard, A. U., Frenkel, M. S., Holt, G. T., Jou, J. D., Ojewole, A. A. & Donald, B. R. Novel, provable algorithms for efficient ensemble-based computational protein design and their application to the redesign of the c-Raf-RBD:KRas protein-protein interface. *PLOS Computational Biology* **16** (ed Dunbrack, R. L.) e1007447. ISSN: 1553-7358 (June 2020).

Jou, J. D., Holt, G. T., Lowegard, A. U. & Donald, B. R. Minimization-Aware Recursive K*: A Novel, Provable Algorithm that Accelerates Ensemble-Based Protein Design and Provably Approximates the Energy Landscape. *Journal of Computational Biology* **27.** PMID: 31855059, 550–564. eprint: `https://doi.org/10.1089/cmb.2019.0315` (2020).

Holt, G. T., Jou, J. D., Gill, N. P., Lowegard, A. U., Martin, J. W., Madden, D. R., *et al.* Computational analysis of energy landscapes reveals dynamic features that contribute to binding of inhibitors to CFTR-associated ligand. *The Journal of Physical Chemistry B* **123,** 10441–10455. eprint: `https://doi.org/10.1021/acs.jpcb.9b07278` (2019).

Reeve, S. M., Si, D., Krucinska, J., Yan, Y., Viswanathan, K., Wang, S., *et al.* Toward Broad Spectrum Dihydrofolate Reductase Inhibitors Targeting Trimethoprim Resistant Enzymes Identified in Clinical Isolates of Methicillin Resistant Staphylococcus aureus. *ACS Infectious Diseases* **5.** PMID: 31565920, 1896–1906. eprint: `https://doi.org/10.1021/acsinfecdis.9b00222` (2019).

Moeyaert, B., Holt, G., Madangopal, R., Perez-Alvarez, A., Fearey, B. C., Trojanowski, N. F., *et al.* Improved methods for marking active neuron populations. *Nature Communications* **9,** 4440 (2018).

Hallen, M. A., Martin, J. W., Ojewole, A., Jou, J. D., Lowegard, A. U., Frenkel, M. S., *et al.* OSPREY 3.0: Open-source protein redesign for you, with powerful new features. *Journal of Computational Chemistry* **39,** 2494–2507. eprint: `https://onlinelibrary.wiley.com/doi/pdf/10.1002/jcc.25522` (2018).

de Juan-Sanz, J., Holt, G. T., Schreiter, E. R., de Juan, F., Kim, D. S. & Ryan, T. A. Axonal Endoplasmic Reticulum Ca2+ Content Controls Release Probability in CNS Nerve Terminals. *Neuron* **93,** 867–881.e6. ISSN: 0896-6273 (2017).

Dana, H. *et al.* Sensitive red protein calcium indicators for imaging neural activity. *eLife* **5** (ed Häusser, M.) e12727. ISSN: 2050-084X (Mar. 2016).

Henderson, M. J., Baldwin, H. A., Werley, C. A., Boccardo, S., Whitaker, L. R., Yan, X., *et al.* A Low Affinity GCaMP3 Variant (GCaMPer) for Imaging the Endoplasmic Reticulum Calcium Store. *PLOS ONE* **10,** 1–17 (Oct. 2015).