# DAVID W. KASTNER

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## Education

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|---|---|---|
| Ph.D. Bioengineering | Massachusetts Institute of Technology | *Current* |
| | GPA **5.0** | *MIT Spotlight* | |
| B.S. Biophysics | Brigham Young University, Provo, Utah | 2019 |
| | GPA **4.0** | Honors | *Summa Cum Laude, Valedictorian Speech* | |

## Research/Professional Experience

**Massachusetts Institute of Technology (MIT) –** *Cambridge, MA*          Sept 2020 – Current

**Co-Advisors**: Dr. Forest White and Dr. Heather J. Kulik
- Graduate student researching how non-covalent interactions drive substrate positioning
- Published 10+ peer-reviewed manuscripts on small molecule-protein binding
- Software lead developer: QuantumPDB, PyEF, QuantumAllostery, CADDKit, MolecuLearn

**Pfizer Pharmaceutical Internship –** *Cambridge, MA*          Sept 2023 – Sept 2024

**Machine Learning Computational Sciences (MLCS) Group**
- Developed ML and physics-based workflows for predicting molecular-glue degrader binding
- Extensive benchmarking of AF3, Boltz-1, DiffDock-L, RFAA, Chai-1, and Protenix
- 50+ billion molecule high-throughput virtual screen (HTVS) of molecular glue candidates

**Huntsman Cancer Institute (HCI) –** *Salt Lake City, UT*          Dec 2018 – Aug 2020

**Oncological Sciences Department**
- Full-time cancer computational and wet-lab biologist researching small cell lung cancer (SCLC)
- Gene expression bioinformatics and wet lab protocol optimization (IHC)

**National Institutes of Health (NIH) –** *Bethesda, MD*          Jul 2018 – Sept 2018

**Advisor**: Dr. Nico Tjandra
- Biophysics internship requiring electron microscopy, light scattering, NMR, circular dichroism

**Dana-Farber/Harvard Cancer Center (DFCI/HCC) –** *Boston, MA*          Apr 2018 – Jul 2018

**Advisor**: Dr. Haribabu Arthanari
- Biophysics internship requiring NMR, protein expression, biochemical pathway engineering

**Simmons Center for Cancer Research (SCCR) –** *Provo, UT*          May 2014 – Apr 2018

**Advisor**: Dr. Steven L. Castle
- Organic synthesis and computationally modelling (QM/MM) of anticancer peptides
- Engineered a potent anticancer peptide in collaboration with *Bristol-Myers Squibb* (BMS).

## Skills and Specializations

- Spanish (bilingual)
- Computational chemistry
- Computer-Aided Drug Discovery (CADD)
- Structure activity relationships (SAR)
- End-point free energy calculations
- MMGBSA/MMPBSA
- ADMET principles
- Molecular visualization expert
- Lead Python software developer (GitHub)
- Molecular dynamics (MD) simulations
- AMBER and OpenMM
- Quantum mechanical (QM) calculations
- Density functional theory (DFT)
- TeraChem and ORCA
- Hybrid QM/MM multiscale simulations
- High-performance Computing
- Linux, Bash, SLURM, SGE
- Machine Learning
- Enhanced sampling (Metadynamics/TPS)
- High-performance computing (HPC)
- Molecular docking (AutoDock, MOE)
- High-throughput virtual screening

## Continued Education and Certifications

Computational Chemistry School at Novartis Cambridge, MA
Fundamentals of Accelerated Computing with CUDA Python issued by NVIDIA
Fundamentals of Deep Learning issued by NVIDIA

## Fellowships

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| MIT Whitehead Fellowship | 2021 |
| Vice Chancellor's Inclusive Excellence Fellowship | 2020 |
| National Science Foundation Graduate Research Fellowship (NSF GRFP) | 2019 |
| Tolero Pharmaceuticals Fellowship | 2018 |
| Inspired Learning University Fellowship | 2018 |
| Simmons Center for Cancer Research Fellowship (SCCR) | 2017 |

## Prestigious Awards

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| Siebel Scholars Award | 2025 |
| ACS Chemical Computing Group (CCG) Research Excellence Award | 2024 |
| Cornell Colman Inclusive Leadership Award | 2021 |
| Alfred P. Sloan Exemplary Mentorship Award (UCEM) | 2019 |
| Elva Pedersen Jorgenson Scholarship | 2019 |
| Warren Rollins and Murdell Hull Scholarship | 2019 |
| National Hispanic Fund Scholarship (HSF) | 2018 |
| Lieutenant Governor's Community Service Award | 2018 |
| National President's Volunteer Service Award | 2018 |
| National Honor Society Phi Kappa Phi Outstanding Student Award | 2018 |
| Karl G. Maeser Scholarship | 2018 |
| University Undergraduate Research Award (URA) | 2018 |
| National Barry Goldwater Scholarship | 2017 |
| National American Chemical Society Scholars Award (ACS) | 2017 |
| Full-Ride Merit-Based Scholarship | 2017 |

## Front Cover Highlighted Publications  (Google Scholar) (ORCID) (GitHub)

**1. [Front Cover]** **Kastner, D.W.**; Nandy, A.; Mehmood, R.; Kulik, H.J. Mechanistic Insights into Substrate Positioning That Distinguishes Non-heme Fe(II)/a-Ketoglutarate-Dependent Halogenases and Hydroxylases. *ACS Catal.* **2023**, 13 (4), 2489-2501. DOI: 10.1021/acscatal.2c06241.

**2. [Front Cover]** Duan, C.; Nandy, A.; Terrones, G.G.; **Kastner, D.W.**; Kulik, H.J. Active Learning Exploration of Transition-Metal Complexes to Discover Method-Insensitive and Synthetically Accessible Chromophores. *JACS Au* **2023**, 3 (2), 391-401. DOI: 10.1021/jacsau.2c00547.

**3. [Front Cover]** Del Rio Flores, A.; **Kastner, D.W.**; Du, T.; Narayanamoorthy, M.; Shen, Y.; Cai, W.; Vennelakanti, V.; Zill, N.A.; Dell, L.B.; Zhai, R.; Kulik, J.H.; Zhang, W. Probing the Mechanism of Isonitrile Formation by a Non-Heme Iron(II)-Dependent Oxidase/Decarboxylase. *JACS* **2022**, 144 (13), 5893-5901. DOI: 10.1021/jacs.1c12891.

**4. [Front Cover]** Nazemi, A.; Steeves, A.H.; **Kastner, D.W.**; Kulik, H.J. Influence of the Greater Protein Environment on the Electrostatic Potential in Metalloenzyme Active Sites: The Case of Formate Dehydrogenase. *J. Phys. Chem. B* **2022**, 126 (22), 4069-4079. DOI: 10.1021/acs.jpcb.2c02260.

**5. [Front Cover]** Lo, C.L.L.; Joaquin, D.; Moyá, D.A.; Ramos, A.; **Kastner, D.W.**; White, S.A.; Christensen, B.L.; Naglich, J.G.; Degnen, W.J.; Castle, S.L. Synthesis and Evaluation of Potent Yaku'amide A Analogs. *Chem. Sci.* **2022**, 13, 1899-1905. DOI: 10.1039/D1SSC05992K.

## Other Peer-reviewed Publications

**6.** Keys, A.M.; **Kastner, D.W.**; Kiessling, L.L.; Kulik, H.J. The Energetic Landscape of CH-π Interactions in Protein-Carbohydrate Binding. *Chemical Science*. 2025, DOI: 10.1039/D4SC06246A.

**7.** Torrens-Spence, P.M.; Matos, O.J.; **Kastner, D.W.**; Li, T.; Glinkerman, M.C.; Sherk, J.; Wang, Y.; Kulik, H.J. Weng, J. Mechanistic Basis for the Emergence of EPS1 as a Catalyst in Plant Salicylic Acid Biosynthesis. *Nat. Commun*. **2024**. DOI: 10.1038/s41467-024-54437-1.

**8.** Del Rio Flores, A.; Zhai, R.; **Kastner, D.W.**; Seshadri, K.; Yang, S.; Matias, K.D.; Shen Y.; Cai, W.; Narayanamoorthy, M.; Do, N.B.; Xue, Z.; Marzooqi, D.A; Kulik, H.J.; Zhang, W. Enzymatic Synthesis of Azide by a Promiscuous N-nitrosylase. *Nature Chemistry*. **2024**. DOI: 10.1038/s41557-024-01646-2.

**9.** Kevlishvili, I.; Vakil, J.; **Kastner, D.W.**; Huang, X.; Craig, S.; Kulik, H. High-Throughput Discovery of Ferrocene Mechanophores with Enhanced Reactivity and Network Toughening. ChemRxiv. 2024. DOI: 10.26434/chemrxiv-2024-dsj2g.

**10. Kastner, D.W.**; Reinhardt, C.R.; Adamji, H.; Manetsch, M.; Roman-Leshkov, Y.; Kulik, H.J. Dynamic Charge Distribution as a Key Driver of Catalytic Reactivity in an Artificial Metalloenzyme. *ChemRxiv*. **2024**. DOI: 10.26434/chemrxiv-2024-xhlgh.

**11.** Edholm, F.; Nandy, A.; Reinhardt, C.R.; **Kastner, D.W.**; Kulik, H.J. Protein3D: Enabling analysis and extraction of metal-containing sites from the Protein Data Bank with molSimplify. *J. Comput. Chem.* 2023, 45 (6), 352-361. DOI: 10.1002/jcc.27242.

**12.** Kim, C.Y.; Mitchell, A.J.; **Kastner, D.W.**; Albright, C.E.; Michael, A.G.; Glinkerman, C.M.; Kulik, H.J.; Weng, J. Emergence of a protein exchange-based isomerization and lactonization mechanism in the plant coumarin synthase COSY. *Nat. Commun.* **2023**, 14 (597). DOI: 10.1038/s41467-023-36299-1.

**13.** Nandy, A.; Adamji, H.; **Kastner, D.W.**; Vennelakanti, V.; Nazemi, A.; Liu, M.; Kulik, H.J. Using Computational Chemistry to Reveal Nature's Blueprints for Single-Site Catalysis of C–H Activation. *ACS Catal.* **2022**, 12 (15), 9281-9306. DOI: 10.1021/acscatal.2c02096.

**14.** Nandy, A.; Terrones, G.; Arunachalam, N.; Duan, C.; Duan, C.; **Kastner, D.W.**; Kulik, H.J. MOFSimplify, Machine Learning Models with Extracted Stability Data of Three Thousand Metal-Organic Frameworks. *Nat. Sci. Data* **2022**, 9 (74). DOI: 10.1038/s41597-022-01181-0.

**15.** Olsen, R.R.; Ireland, A.S.; **Kastner, D.W.**; Groves, S.M.; Spainhower, K.B.; Pozo, K.; Kelenis, D.P.; Whitney, C.P.; Guthrie, M.R.; Wait, S.J.; Soltero, D.; Witt, B.L.; Quaranta, V.; Johnson, J.E.; Oliver, T.G. ASCL1 Represses a SOX9+ Neural Crest Stem-like State in Small Cell Lung Cancer. *Genes Dev.* **2021**, 37, 13-14. DOI: 10.1101/gad.348295.121.

**16.** Ireland, A.S.; Micinski, A.M.; **Kastner, D.W.**; Guo, B.; Wait, S.J.; Spainhower, K.B.; Conley, C.C.; Chen, O.S.; Guthrie, M.R.; Soltero, D.; Qiao, Y.; Huang, X.; Tarapcsak, S.; Devarakonda, S.; Chalishazar, M.D.; Gertz, J.; Moser, J.C.; Marth, G.; Puri, S.; Witt, B.L.; Spike, B.T.; Oliver, T.G. MYC Drives Temporal Evolution of Small Cell Lung Cancer Subtypes by Reprogramming Neuroendocrine Fate. *Cancer Cell* **2020**, *38* (1), 60-78. DOI: 10.1016/j.ccell.2020.05.001.

**17.** Joaquin, D.; Lee, M. A.; **Kastner, D. W.**; Singh, J.; Morrill, S. T.; Damstedt, G.; Castle, S. L. Impact of Dehydroamino Acids on the Structure and Stability of Incipient $3_{10}$-Helical Peptides. *J. Org. Chem.* **2020**, *3* (85), 1601-1613. DOI: 10.1021/acs.joc.9b02747.

**18.** Morris, D.L.; **Kastner, D.W.**; Johnson, S.; Strub, M.; He, Y.; Bleck, C.K.; Lee, D.; Tjandra, N.; Humanin induces conformational changes in the apoptosis regulator BAX and sequesters it into fibers, preventing mitochondrial outer-membrane permeabilization. *J. Biol. Chem.* **2019**, *50* (294), 19055-19065. DOI: 10.1074/jbc.ra119.0112977.

**19. Kastner, D.W.** Computational Modelling of Peptides Containing Non-Standard Amino Acids *Undergraduate Honors Thesis* **2019**. *ScholarsArchive*, 61. ISSN: 2572-4479.

**20. Kastner, D.W.** The Ultimate Triumph of Truth. *Brigham Young University Commencement*, **2019**. URL: speeches.byu.edu.

**21.** Ashraf, N.M., Krishnagopal, A., Hussain, A,. **Kastner, D.W.**, Sayed, A.M., Mol Y.K., Swaminathan. K., Zeeshan, N. Engineering of serine protease for improved thermostability and catalytic activity using rational design. *Int. J. Biol. Macromol.* **2018**, 126, 229-236. DOI: 10.1016/j.ijbiomac.2018.12.218.

**22.** Jalan, A.; **Kastner, D.W.**; Webber, K.G. I.; Smith, M.S.; Price, J.L.; Castle, S.L. Bulky dehydroamino acids enhance proteolytic stability and folding in β-hairpin peptides. *Org. Lett.* **2017**, *19* (19), 5190-5193. DOI: 10.1021/acs.orglett.7b02455.

**23.** Ashraf, N.M.; Imran, K.; **Kastner, D.W.**; Ikram, K.; Mushtaq, A.; Hussain, A.; Zeeshan, N. Potential involvement of mi-RNA 574-3p in progression of prostate cancer: A bioinformatic study. *Mol. Cell. Probes* **2017**, *36,* 21-28. DOI: 10.1016/j.mcp.2017.07.002.

## Submitted and In-Progress Publications

**24.** **Kastner, D.W.**; Kulik, H.J.; Zhang, Z. Evaluation of In-silico Structural Predictions of Glue-Induced Ternary Complexes with Generative Models. *In preparation*.

**25.** **Kastner, D.W.**; Clorice, R.R.; Kulik, H.J. Mechanistic Insights into the Reaction of the Non-Heme Iron Enzyme DMFase. *In preparation.*

**26.** **Kastner, D.W.**; Wilson, H.; Luo, W.; Clorice, R.R.; Kulik, H.J. QuantumPDB: Automatic generation of quantum mechanical cluster models for high-throughput screening of protein structures. *In preparation*.

**27.** Colin, Y.K.; **Kastner, D.W.**; Mitchell, J.A.; Gutierrez, M.A.; Yao, S.J.; Neumann, N.E.; Kulik, J.H.; Weng, J. Tracing the Stepwise Darwinian Evolution of a Plant Halogenase. *Science Advances*. **Submitted**.

## Oral and Poster Presentations

**1.** **Kastner, D.W.**; Clorice, R.; Adamji, H.; Manetsch, M.; Kulik, H.J. Mechanistic Insights from Electronic Properties in Artificial Mini-enzymes. *ACS Spring Conference Denver*, **2024**. DOI: 10.1021/scimeetings.4c10442.

**2.** **Kastner, D.W.**; Nandy, A.; Mehmood, R.; Kulik, H.J Substrate positioning in Non-heme Fe(II)/α-ketoglutarate-dependent halogenases and hydroxylases: A computational study. *Virtual Conference on Chemistry and its Applications (VCCA)*, **2023**. Video recording.

**3.** **Kastner, D.W.**; Jalan, A.; Castle, S. L. Conformational ensemble calculations of proteolytically stable β-hairpins containing bulky α,β-dehydroamino acids. *American Chemical Society 254th National Meeting*, Washington D.C., **2017**.

**4.** **Kastner, D.W.**; and Castle, Steven L., Progress toward synthetically simplified natural anticancer peptide (2018). *Library Undergraduate Poster Competition* **2018**, *5*. ISSN: 2572-4479

**5.** **Kastner, D.W.**; Castle, S. L. Computational predictions β-hairpins containing bulky dehydroamino acids. *Scholars Archive* **2017**, *4*. ISSN: 2572-4479

**6.** **Kastner, D.W.**; Lo, C. C. L.; Castle, S. L. Progress towards a synthetically simplified anticancer peptide. *Student Research Conference (SRC)*, Provo, **2018**.

**7.** **Kastner, D.W.**; Jalan, A.; Castle, S. L. QM/MM analysis of proteolytically stable β-hairpins. *Student Research Conference (SRC)*, Provo, **2017**.

**8.** **Kastner, D.W.**; Castle, S. L. ONIOM geometry optimization of bulky dehydroamino acids in β-hairpins. *IEEE Poster Session*, Provo, **2017**.

## Highlighted Coursework

### Massachusetts Institute of Technology

*Biological Engineering* • Fundamentals of Drug Development (20.201)                     Grade: A (5.0)

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| *Biological Engineering* • Research Experience in Biopharma (20.930) | Grade: A (5.0) |
| *Biological Engineering* • Protein Engineering (20.535) | Grade: A (5.0) |
| *Biological Engineering* • Analysis of Biological Networks (20.440) | Grade: A (5.0) |
| *Computer Science* • Modeling with Machine Learning: Algorithm to Apps (6.C51) | Grade: A (5.0) |
| *Chemical Engineering* • Machine Learning for Molecular Engineering (10.C51) | Grade: A (5.0) |
| *Chemical Engineering* • Computational Chemistry (10.637) | Grade: A (5.0) |

**Brigham Young University**

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|---|---|
| *Physiology* • Biophysics (PDBIO 568) | Grade: A (4.0) |
| *Physiology* • Advanced Physiology (PDBIO 362) | Grade: A (4.0) |
| *Biology* • Cell Biology (BIO 360) | Grade: A (4.0) |
| *Biology* • Computational Biology (BIO 362) | Grade: A (4.0) |
| *Chemistry* • Biophysical Chemistry (CHEM 468) | Grade: A (4.0) |
| *Chemistry* • Organic Chemistry (CHEM 351 & 352) | Grade: A (4.0) |
| *Chemistry* • Biochemistry (CHEM 481) | Grade: A (4.0) |
| *Physics* • Molecular Dynamics (PDBIO 550R) | Grade: A (4.0) |
| *Physics* • Electricity and Magnetism (PHSCS 220) | Grade: A (4.0) |
| *Physics* • Newtonian and Modern Physics (PHSCS 121 & 123) | Grade: A (4.0) |

## Teaching Experience

Instructor • *Biological Engineering* • 3D Scientific Rendering (20.S947)
Teaching Assistant • *Chemical Engineering* • Computational Chemistry (10.437)
Teaching Assistant • *Biological Engineering* • Principles of Molecular Bioengineering (20.420)
Teaching Assistant • *Cell Biology & Physiology* • Cell Biology (PDBIO 360)

## Current Societal and Honors Affiliations

Foundation for Science and Disability (FSD)
Society for Advancement of Chicanos/Hispanics & Native Americans in Science (SACNAS)
National Spanish Speaker Honor Society (SDP)
Hispanic Scholarship Fund (HSF)
American Chemical Society (ACS)
The Protein Society (TPS)
National Scientific Research Honor Society Sigma Xi

## Press

"The art of the enzyme" MIT News, **2024**.
"Computational model captures the elusive transition states of chemical reactions" *MIT News*, **2023**.
"Scientists use computational modeling to design "ultrastable" materials" *MIT News*, **2023**.
"Computational modeling guides development of new materials" *MIT News*, **2022**.
"The Ultimate Triumph of Truth" *BYU Speeches*, **2019**.
"Part of the search: Q&A with BYU Commencement Speaker" *BYU Honors Program News*, **2019**.
"A wonderful world to share joy, show love, create connections" *BYU News*, **2019.**
"Kastner chosen as commencement speaker at BYU" *Napa Valley Register*, **2019**.
"Rex Lee Run unites those affected and impacted by cancer" *Daily Herald*, **2018**.
"Kastner receives fellowship for cancer research" *Napa Valley Register*, **2018**.
"Napa's Kastner family creates artwork for new dealership" *Napa Valley Register*, **2016**.