DAHLIA WEISS

334 N Claremont Street
San Mateo, CA 94401 USA

dahlia.weiss at gmail.com
http://www.rationaldrugdesign.org
https://www.linkedin.com/in/dahliaweiss/

CURRENT POSITION

Director, Computational Chemistry — 2024-
Septerna, South San Francisco, CA

EDUCATION

Ph.D. — Structural Biology / Chemistry — 2009
Department of Chemistry, Stanford University, USA
Advisor: Professor Michael Levitt, Computational Structural Biology

Joint B.S. *Magna cum laude* — Chemistry and Biology — 2001
Department of Chemistry and Department of Biology, Tel Aviv University, Israel

PUBLICATIONS AND PATENTS

1. WO2021168197 Bifunctional degraders of interleukin-1 receptor-associated kinases and therapeutic use thereof (2021)
2. WO2020081450 Bifunctional compounds for degrading btk via ubiquitin proteosome pathway (2020)
3. WO2021021761 Urea, amide, and substituted heteroaryl compounds for cbl-b inhibition (2021)
4. WO2020210508 3-substituted piperidine compounds for cbl-b inhibition, and use of a cbl-b inhibitor in combination with a cancer vaccine and/or oncolytic virus (2020)
5. WO2020236654 Cyano cyclobutyl compounds for cbl-b inhibition and uses thereof (2020)
6. WO2020264398 Substituted benzyl-triazole compounds for cbl-b inhibition, and further uses thereof (2020)
7. **DR Weiss**, JL Baylon, ED Evans, A Paiva, G Everlof, J Cutrone, F Broccatelli; *Balanced Permeability Index: a multi-parameter index for improved in-vitro permeability,* ACS Medicinal Chemistry Letters 15 (4) 457–462 (2024)
8. S Hollingsworth, et al, DR Weiss, V Shanmugasundaram; *The Rise of Targeting Chimeras (TACs): Next-Generation Medicines that Preempt Cellular Events*, Medicinal Chemistry Research 32, 1294–1314 (2023)
9. **DR Weiss**, A Bortolato,Y Sun,X Cai, C Lai, S Guo, L Shi, V Shanmugasundaram; *On Ternary Complex Stability in Protein Degradation: In-silico molecular glue binding affinity calculations* Journal of Chemical Information and Modeling, 63 (8) 2382–2392 (2023)
10. **DR Weiss**, J Karpiak, XP Huang, MF Sassanno, J Lyu, BL Roth, BK Shoichet; *Selectivity Challenges in Docking Screens for GPCR Targets and Antitargets* Journal of Medicinal Chemistry 61 (15), 6830-6845 (2018)
11. M Korczynska, MJ Clark, C Valant, J Xu, E Von Moo, S Albold, DR Weiss, et al, RK Sunahara; *Structure-based discovery of selective positive allosteric modulators of antagonists for the M2 muscarinic acetylcholine receptor* Proceedings of the National Academy of Sciences 115 (10) E2419-E2428 (2018)
12. **DR Weiss**, A Bortolato, B Tehan, JS Mason; *GPCR-Bench: A Benchmarking Set and Practitioners' Guide for G Protein-Coupled Receptor Docking* Journal of Chemical Information and Modeling 56 (4),642-651 (2016)
13. A Bortolato, F Deflorian, DR Weiss, JS Mason; *Decoding the Role of Water Dynamics in Ligand–Protein Unbinding: CRF1R as a Test Case* Journal of Chemical Information and Modeling 55 (9), 1857-1866 (2015)
14. KA Bennet, AS Doré, JA Christopher, DR Weiss, FH Marshall; *Structures of mGluRs shed light on the challenges of drug development of allosteric modulators* Current Opinion in Pharmacology 20:1–7 (2015)
15. DA Silva, DR Weiss, FD Avila; LT Da, M Levitt, D Wang; X Huang; *Millisecond dynamics of RNA polymerase II translocation at atomic resolution* Proceedings of the National Academy of Sciences 111 (21) : 7665-7670 (2014)
16. **DR Weiss,** P Koehl; *Morphing Methods to Visualize Coarse-Grained Protein Dynamics* Protein Dynamics : 271-282 (2014)
17. RG Coleman, TS Sterling, DR Weiss; *SAMPL4 & DOCK3. 7: lessons for automated docking procedures* Journal of Computer-Aided Molecular Design : 41883 (2014)
18. **DR Weiss***, SK Ahn*, MF Sassano, A Kleist, X Zhu, R Strachan, BL Roth, RJ Lefkowitz, BK Shoichet; *Conformation Guides Molecular Efficacy in Docking Screens of Activated β-2 Adrenergic G Protein Coupled Receptor* ACS chemical biology (8) : 1018-1026 (2013)
19. AC Kruse*, **DR Weiss***, M Rossi, J Hu, K Hu, K Eitel, P Gmeiner, J Wess, BK Kobilka, BK Shoichet; *Muscarinic Receptors as Model Targets and Antitargets for Structure-Based Ligand Discovery* Molecular pharmacology (84) : 528-540 (2013)
20. JS Mason*, A Bortolato*, **DR Weiss***, F Deflorian, B Tehan, FH Marshall; *High end GPCR design: crafted ligand design and druggability analysis using protein structure, lipophilic hotspots and explicit water networks* In Silico Pharmacology (1) : 23 (2013)
21. MM Mysinger*, **DR Weiss***, JJ Ziarek*, S Gravel; AK Doak, J Karpiak, N Heveker, BK Shoichet, BF Volkman; *Structure-based ligand discovery for the protein–protein interface of chemokine receptor CXCR4* Proceedings of the National Academy of Sciences (109) : 5517-5522 (2012)
22. JK Bray, DR Weiss, M Levitt; *Optimized Torsion-Angle Normal Modes Reproduce Conformational Changes More Accurately Than Cartesian Modes* Biophysical journal (101) : 2966 (2011)
23. X Huang, D Wang, DR Weiss, DA Bushnell, RD Kornberg, M Levitt; *RNA polymerase II trigger loop residues stabilize and position the incoming nucleotide triphosphate in transcription* Proceedings of the National Academy of Sciences (107) : 15745-15750 (2010)

24. **DR Weiss**, M Levitt; *Can morphing methods predict intermediate structures?* Journal of molecular biology (385) : 665-674 (2009)

25. **DR Weiss**, TM Raschke, M Levitt; *How hydrophobic buckminsterfullerene affects surrounding water structure* The Journal of Physical Chemistry B (112) : 2981-2990 (2008)

*equal contributors

PAST RESEARCH POSITIONS

Associate Director, Molecular Structure and Design 2023-2024
Senior Principal Scientist, Molecular Structure and Design 2020-2023
Bristol-Myers-Squibb, Redwood City, CA
In this role, I championed a predictive mindset, emphasizing Structure Based Design and the utilization of predictive Machine Learning models to guide all synthetic decisions throughout the design-make-test-analyze cycle. I demonstrated meaningful difference in the progression of new chemical matter for the benefit of patients. I recruited, trained, and led a group of three computational scientists at the Redwood City site. Additionally, I formed and guided a matrix organization devoted to advancing predictive modelling in targeted protein degradation, and in that capacity, initiated an academic collaboration to study ternary complex prediction.

Senior Scientist, Modelling group leader, Nurix Inc, San Francisco, USA 2015-2020
E2 conjugating enzymes and E3 ligases control protein stability and protein fate through the Ubiquitin Proteasome System (UPS). Small molecule enhancers and inhibitors of E2 and E3 enzymes provide an innovative path to regulate key actors in cell fate through modulation of the UPS. I am leading the predictive design of bifunctional molecules for targeted protein degradation, applying protein-protein docking and prediction of ternary complex formation, and advanced ADME prediction for Beyond Ro5 space.

Senior Scientist, Computer Aided Drug Design, Heptares Therapeutics Limited, UK 2013-2015
G-protein coupled receptors (GPCRs), are the largest superfamily of proteins in the human body and are the targets of >30% of all marketed drugs. At Heptares Therapeutics, I applied computer aided drug design to challenging GPCR targets as part of the drug discovery team. I led the development of new computational methods for use of water structure in docking and lead optimization, MD simulation, Free Energy Perturbation in GPCRs and prediction of drug binding kinetics.

Post-doctoral research, Shoichet lab, Pharmaceutical Chemistry, University of California, San Francisco, USA 2009-2013
I applied virtual screening and GPCR homology modeling for the discovery of new chemical matter for GPCR targets, including the rational design of selectivity for receptor subtypes and ligand efficacy.

Visiting scholar, INRIA, French National Institute for Research in Computer Science and Control, France 2008
Geometries of waters at protein-protein interfaces in the dynamic setting
I applied computational geometry techniques to study the interaction and dynamics of water in the protein-protein interface.

Ph.D. Studies, Levitt Lab, Department of Chemistry, Stanford University, USA 2003-2009
Coarse graining of protein dynamics
Protein dynamics important to biological function often happen on a time scale that is unattainable through detailed simulation methods such as molecular dynamics (MD). We developed a novel interpolation method to study transitions between known crystal structures that does not extrapolate motion linearly and can therefore move around high energy barriers. The interpolation method I developed was used in several methods as a starting point for long-time-scale simulation.
Simulated behavior of nanoscale hydrophobic solutes in water
Using MD simulation, we studied details of the water structure surrounding a single molecule of Buckminsterfullerene (C_{60}). We showed ordering of water in both the first and second hydration shell, and an increase of hydrogen bonding within shells, with important implications for nanomaterials.

M.S. Studies, Department of Biochemistry, Tel Aviv University, Israel 2001-2003
The Anti-Codon Nuclease active site
We used multiple sequence alignment and secondary structure predictions to study a t-RNA nuclease with anti-HIV potential. Predicted mutations were experimentally shown to alter cleavage patterns, with possible therapeutic applications.

B.S. Studies, Department of Biotechnology, Tel Aviv University, Israel 2000-2001
Kinetics of self-assembly in amyloidal fibrils: Biophysical studies
We used biophysical measurements (CD and ELISA) to characterize the kinetics of self-assembly in amyloid fibrils.

AWARDS AND HONORS

NIH NRSA for Individual Postdoctoral Fellows, F32 GM093580-01, UCSF 2009-2012

SimBios, NIH Center for Biomedical Computation, Full fellowship, Stanford 2007-2009
SimBios is an NIH funded center, awarding up to 3 full doctoral fellowships each year.

Program in Mathematics and Molecular Biology, Full fellowship, Stanford 2006-2007

Wise Scholarship for Masters Studies, Full fellowship, Tel Aviv University 2001-2003

Magna cum laude, B.S. Studies, Chemistry and Biology 2001

TALKS AND WORKSHOPS (SELECTION)

Gordon Research Conference Computer Aided Drug Design, Mount Snow, Vermont, USA “"Cereblon dynamics, ternary complex stability and CELMoD optimization" July 2023

American Chemical Society National Meeting, Chicago, USA “Structure based drug design for prediction of molecular glue degradation potency” August 2022

American Chemical Society National Meeting, San Diego, USA “Computational Modelling Workflow to Characterize the Structure of Bi-functional Degrader-Protein-Protein Ternary Complex” August 2019

American Chemical Society National Meeting, San Francisco, USA “GPCR drug-binding kinetics: Insights from explicit water network modeling” August 2014