

BINOD NEPAL, Ph.D.

Computational Chemist | Structure-Based & AI-Enabled Small-Molecule Drug Design

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PROFESSIONAL SUMMARY

Computational chemist (Ph.D., Chemistry) with 5+ years of embedded computational support of **small-molecule drug discovery from hit identification through late-stage lead optimization**, partnering with medicinal chemists, biologists, pharmacologists, and structural biologists across internal and multi-institution collaborations. Expert practitioner of **structure-based drug design: molecular docking, virtual screening, molecular dynamics, free energy perturbation (FEP+), homology and pharmacophore modeling, and quantum mechanics**, applied to challenging targets including **allosteric sites, protein-protein interfaces, ion-motive ATPases, GPCRs, and SLC transporters**. Combines physics-based methods with **cheminformatics and machine learning (CNN, GNN; PyTorch, scikit-learn, RDKit)** to analyze SAR, predict ADME/Tox properties, and prioritize compounds for synthesis. Track record of design hypotheses that shaped potency, selectivity, and resistance profiles of lead series, including allosteric antagonists at an **immunology**-relevant target. Publications in *Science*, *Nature Communications*, *PNAS*, *Journal of Medicinal Chemistry*, and *ACS Infectious Diseases*.

EDUCATION & POSTDOCTORAL TRAINING

Postdoctoral Research Fellow

2021 – Present

Drexel University College of Medicine • Philadelphia, PA

Advisor: Dr. Sandhya Kortagere

- Served as **computational lead** on small-molecule **antimalarial** programs targeting *Plasmodium falciparum* ATP4 and the cytochrome bc1 complex: built homology models from X-ray templates, ran **docking and virtual screening campaigns**, performed MD and **free-energy of binding calculations**, and delivered SAR hypotheses that guided medicinal chemistry through **late-stage lead optimization** of potency and resistance liabilities (*PNAS*, *ACS Infectious Diseases*).
- Worked within **multi-institution, multi-partner drug-discovery collaborations**, aligning computational priorities and timelines with external medicinal chemistry and biology teams and reporting results at regular project meetings.
- Identified and rationalized **allosteric antagonists of the aryl hydrocarbon receptor (AhR)**, an **immunology**-relevant target, using docking, MD, and **MD-driven binding-site and pocket analysis** (*Nature Communications*).
- Contributed structure-based design of a small-molecule modulator of influenza ribonucleoprotein complex assembly, a **protein-protein interaction** target (*Science*, 2025).
- Applied **cheminformatics and ML/AI (CNN, GNN)** to **SAR analysis and ADME/Tox prediction**; built Python/RDKit pipelines for compound library curation, clustering, and virtual-hit triage, integrating ML predictions with structure-based scores to prioritize designs.
- Characterized the **dopamine transporter (DAT, SLC6A3)** and dopamine D3 receptor (GPCR) with long-timescale MD and enhanced sampling to resolve conformational states, phosphorylation-dependent dynamics, and biased agonism for CNS design.

- Presented computational findings to **cross-functional project teams** and external audiences (Gordon Research Conference, ASPET, SfN); mentored graduate and undergraduate trainees in docking, MD, and cheminformatics workflows; supported target identification through RNA-seq analysis (GO/KEGG, WGCNA).

Postdoctoral Research Associate

2016 – 2021

Department of Chemistry and Biochemistry, The City College of New York • New York, NY

Advisor: Dr. Themis Lazaridis

- Developed **implicit-membrane models** for spherical and tubular membrane geometries and implemented them in the **CHARMM** molecular dynamics package—shipping working simulation software now used by the broader biophysics community.
- Ran large-scale MD of membrane proteins and peptides to characterize ESCRT-III (Snf7) and I-BAR membrane curvature mechanisms (both involving **protein-protein interfaces**), pore-forming antimicrobial peptides, bacterial toxins, and amyloid β -peptide (published in *Structure*, *Protein Science*, and *Biophysical Journal*).
- Managed hundreds of long-timescale trajectories on Linux/HPC clusters with systematic convergence analysis and free-energy computation; automated workflows in Python and Bash.

Ph.D. in Chemistry

2016

Utah State University • Logan, UT

Advisor: Dr. Steve Scheiner

Dissertation: Quantum-mechanical investigation of charge-assisted noncovalent interactions (hydrogen, halogen, and chalcogen bonding)—foundation for careful analysis of protein–ligand interaction networks and electrophile context.

M.S. in Chemistry

2008

Tribhuvan University • Kathmandu, Nepal

B.Sc. in Chemistry

2004

Amrit Science College, Tribhuvan University • Kathmandu, Nepal

AREAS OF EXPERTISE

- Structure-based drug design (SBDD): molecular docking, virtual screening, homology and pharmacophore modeling
- Molecular dynamics, enhanced sampling, and free energy perturbation (FEP+, alchemical methods) for lead optimization
- Allosteric and hard-to-drug binding-site identification (AhR, dopamine transporter, PfATP4)
- Protein–protein interaction modeling and interface analysis (influenza RNP complex, ESCRT-III, I-BAR)
- Cheminformatics: SAR analysis, compound clustering, library curation, and design triage (RDKit, Python)
- Machine learning / AI-driven drug design: CNN and GNN models for activity and ADME/Tox prediction
- Compound design for potency, selectivity, and pharmacokinetic optimization in collaboration with medicinal chemists
- Quantum mechanics of noncovalent interactions (hydrogen, halogen, chalcogen bonding) to inform ligand design
- Ligand-based design: QSAR and conformational analysis

- Use of X-ray, cryo-EM, and AlphaFold-derived structures to seed docking and modeling
- Clear reporting of computational results to technical and non-technical audiences
- Method development and implementation in MD software (CHARMM)
- Bioinformatics for target identification: RNA-seq, GO/KEGG enrichment, WGCNA

TECHNICAL SKILLS

Structure-Based Design	Schrödinger Suite (Maestro, Glide, FEP+), MOE (CCG), AutoDock/Vina, GOLD
Free-Energy & MD	GROMACS, AMBER, NAMD, CHARMM; FEP+ and alchemical free-energy calculations on HPC
Ligand-Based Design	Pharmacophore modeling, QSAR, conformational analysis, virtual screening
Chemoinformatics	RDKit, pandas, NumPy; SAR analysis and design prioritization in Python
Machine Learning	PyTorch, TensorFlow, scikit-learn; CNN and GNN for activity and ADMET prediction
Quantum Mechanics	Gaussian, GAMESS; high-level ab initio analysis of noncovalent interactions
Modeling & Visualization	PyMOL, VMD, Modeller, Maestro; homology and antibody modeling
Programming & Systems	Python, Bash, R, FORTRAN, C; Linux environments and HPC clusters
Bioinformatics	RNA-seq analysis, GO/KEGG enrichment, WGCNA

AWARDS & HONORS

- First Place, Poster Presentation (Postdoctoral Category) — Mid-Atlantic Pharmacology Society Annual Meeting, Philadelphia, PA (2023)
- Outstanding Postdoctoral Fellow Poster Award — Discovery Day, Drexel University College of Medicine, Philadelphia, PA (2023)
- Outstanding Graduate Student in Chemistry — Department of Chemistry and Biochemistry, Utah State University (2016)
- Doctoral Dissertation Enhancement Fund — Utah State University (2016)
- College of Science Graduate Student Travel Award — Utah State University (2016)
- Joseph Reuel Harris Graduate Scholarship — Utah State University (2014)
- Chhita Bahadur Tuladhar Gold Medal — Amrit Science College, Kathmandu, Nepal (2004)

PUBLICATIONS

27 peer-reviewed publications and 1 preprint; selected venues include *Science*, *Nature Communications*, *PNAS*, *Journal of Medicinal Chemistry*, *ACS Infectious Diseases*, and *Biophysical Journal*. Author name in **bold**.

- Pou, S.; Liebman, K. M.; Winter, R. W.; Nilsen, A.; Li, Y.; Lyche, I. N.; Riscoe, T. M.; Montgomery, J.; Gramelspacher, M. J.; Dodean, R. A.; Zakharov, L. N.; **Nepal, B.**; et al. Revisiting 2-substituted-4(1H)-quinolones for targeting the *Plasmodium falciparum* cytochrome bc1 complex. *Journal of Medicinal Chemistry* 2026, 69 (12), 14114–14139.
- Peng, R.; Xu, X.; **Nepal, B.**; Gong, Y.; Li, F.; Ferretti, M. B.; et al. Molecular basis of influenza ribonucleoprotein complex assembly and processive RNA synthesis. *Science* 2025, 388 (6748), eadq7597.
- Rachuri, S.; **Nepal, B.**; Shukla, A.; Ramanathan, A.; Morrissey, J. M.; Daly, T.; Mather, M. W.; Bergman, L. W.; Kortagere, S.; Vaidya, A. B. Mutational analysis of an antimalarial drug target, PfATP4. *PNAS* 2025, 122 (2), e2403689122.
- Das, S.; McCloskey, K.; **Nepal, B.**; Kortagere, S. EAAT2 activation regulates glutamate excitotoxicity and reduces impulsivity in a rodent model of Parkinson's disease. *Molecular Neurobiology* 2025, 62 (5), 5787–5803.
- Pou, S.; Winter, R. W.; Dodean, R. A.; Liebman, K.; Li, Y.; Mather, M. W.; **Nepal, B.**; et al. 3-Position biaryl endochin-like quinolones with enhanced antimalarial performance. *ACS Infectious Diseases* 2024, 10 (7), 2419–2442.
- **Nepal, B.**; Barnett, J.; Bearoff, F.; Kortagere, S. Biased signaling agonists promote distinct phosphorylation and conformational states of the dopamine D3 receptor. *International Journal of Molecular Sciences* 2024, 25 (19), 10470.
- Duffy, B. C.; King, K. M.; **Nepal, B.**; Nonnemacher, M. R.; Kortagere, S. Acute administration of HIV-1 Tat protein drives glutamatergic alterations in a rodent model of HIV-associated neurocognitive disorders. *Molecular Neurobiology* 2024, 61 (10), 8467–8480.
- Ondrová, K.; Zůvalová, I.; Vyhřídálová, B.; Krasulová, K.; Miková, E.; Vrzal, R.; Nádvorník, P.; **Nepal, B.**; Kortagere, S.; Kopečná, M.; et al. Monoterpenoid aryl hydrocarbon receptor allosteric antagonists protect against ultraviolet skin damage in female mice. *Nature Communications* 2023, 14 (1), 2728.
- **Nepal, B.**; Das, S.; Reith, M. E.; Kortagere, S. Overview of the structure and function of the dopamine transporter and its protein interactions. *Frontiers in Physiology* 2023, 14, 1150355.
- **Nepal, B.**; Sepehri, A.; Lazaridis, T. Mechanism of negative membrane curvature generation by I-BAR domains. *Structure* 2021, 29, 1440–1452.e4.
- Sepehri, A.; **Nepal, B.**; Lazaridis, T. Lipid interactions of an actinoporin pore-forming oligomer. *Biophysical Journal* 2021, 120, 1357–1366.
- Sepehri, A.; **Nepal, B.**; et al. Distinct modes of action of IAPP oligomers on membranes. *Journal of Chemical Information and Modeling* 2021, 61 (9), 4645–4655.
- **Nepal, B.**; Sepehri, A.; Lazaridis, T. Mechanisms of negative membrane curvature sensing and generation by ESCRT III subunit Snf7. *Protein Science* 2020, 29, 1473–1485.
- Rodnin, M. V.; Vasquez-Montes, V.; **Nepal, B.**; Ladokhin, A. S.; Lazaridis, T. Experimental and computational characterization of oxidized and reduced protegrin pores in lipid bilayers. *The Journal of Membrane Biology* 2020, 253, 287–298.
- **Nepal, B.**; Leveritt, J.; et al. Membrane curvature sensing by amphipathic helices: insights from implicit membrane modeling. *Biophysical Journal* 2018, 114 (9), 2128–2141.
- **Nepal, B.**; Scheiner, S. $\text{NX}\cdots\text{Y}$ halogen bonds: comparison with $\text{NH}\cdots\text{Y}$ H-bonds and $\text{CX}\cdots\text{Y}$ halogen bonds. *Physical Chemistry Chemical Physics* 2016, 18, 18015–18023.
- **Nepal, B.**; Scheiner, S. Enhancing the reduction potential of quinones via complex formation. *The Journal of Organic Chemistry* 2016, 81, 4316–4324.

- Fick, R. J.; Kroner, G. M.; **Nepal, B.**; Magnani, R.; Horowitz, S.; Houtz, R. L.; Scheiner, S.; Trievel, R. C. Sulfur-oxygen chalcogen bonding mediates AdoMet recognition in the lysine methyltransferase SET7/9. *ACS Chemical Biology* 2016, 11 (3), 748–754.
- **Nepal, B.**; Scheiner, S. Building a better halide receptor: optimum choice of spacer, binding unit, and halosubstitution. *ChemPhysChem* 2016, 17 (6), 836–844.
- **Nepal, B.**; Scheiner, S. Substituent effects on the binding of halides by neutral and dicationic bis(triazolium) receptors. *The Journal of Physical Chemistry A* 2015, 119 (52), 13064–13073.
- **Nepal, B.**; Scheiner, S. Microsolvation of anions by molecules forming $\text{CH}\cdots\text{X}^-$ hydrogen bonds. *Chemical Physics* 2015, 463, 137–144.
- **Nepal, B.**; Scheiner, S. Long-range behavior of noncovalent bonds: neutral and charged H-bonds, pnictogen, chalcogen, and halogen bonds. *Chemical Physics* 2015, 456, 34–40.
- **Nepal, B.**; Scheiner, S. Competitive halide binding by halogen versus hydrogen bonding: bis-triazole pyridinium. *Chemistry – A European Journal* 2015, 21 (38), 13330–13335.
- **Nepal, B.**; Scheiner, S. Anionic $\text{CH}\cdots\text{X}^-$ hydrogen bonds: origin of their strength, geometry, and other properties. *Chemistry – A European Journal* 2015, 21 (4), 1474–1481.
- **Nepal, B.**; Scheiner, S. Angular dependence of hydrogen bond energy in neutral and charged systems containing CH and NH proton donors. *Chemical Physics Letters* 2015, 630, 6–11.
- **Nepal, B.**; Scheiner, S. Effect of ionic charge on the $\text{CH}\cdots\pi$ hydrogen bond. *The Journal of Physical Chemistry A* 2014, 118 (40), 9575–9587.
- **Nepal, B.**; Das, S. Sustained water oxidation by a catalyst cage-isolated in a metal-organic framework. *Angewandte Chemie International Edition* 2013, 52 (28), 7224–7227.

Preprint

- Snyder, A. K.; Tedesco, F.; Kelsen, A.; Wehri, E.; **Nepal, B.**; et al. Identification of UCB-9721 as a potent inhibitor of MyoA, the essential class XIV myosin motor of apicomplexan parasites. *bioRxiv* 2026. doi:10.64898/2026.06.18.733251

SELECTED CONFERENCE PRESENTATIONS

- **Nepal, B.**; Das, S.; Kortagere, S. Conformational analysis of phosphorylated dopamine transporter and its interactions with dopamine D3 receptor. Mid-Atlantic Pharmacology Society Annual Meeting, Philadelphia, PA (2025).
- **Nepal, B.**; Das, S.; Xu, W.; Kortagere, S. Molecular characterization of the interactions between dopamine transporter and dopamine D3 receptor. Mid-Atlantic Pharmacology Society Annual Meeting, Philadelphia, PA (2024).
- **Nepal, B.**; Morrissey, J.; Zhang, Z.; Burrows, J.; Brand, S.; Fan, E.; Vaidya, A.; Kortagere, S. Structure-activity relationship and computational modeling of pyrazole amide core-based PfATP4 inhibitors. Gordon Research Conference, East Greenwich, RI (2024).
- **Nepal, B.**; Barnett, J.; Xu, W.; Bearoff, F.; Kortagere, S. Molecular mechanisms of agonist-dependent biased signaling of dopamine D3 receptors. Society for Neuroscience Annual Meeting, Washington, D.C. (2023).
- **Nepal, B.**; Barnett, J.; Xu, W.; Bearoff, F.; Kortagere, S. Molecular mechanisms of agonist-dependent biased signaling of dopamine D3 receptors. Mid-Atlantic Pharmacology Society Annual Meeting, Philadelphia, PA (2023).
- **Nepal, B.**; Morrissey, J.; Brand, S.; Vaidya, A.; Kortagere, S. Structural analysis of the interaction of pyrazole and benzimidazole core compounds with PfATP4. Annual ASPET Meeting, Philadelphia, PA (2022).

- **Nepal, B.;** Barnett, J.; Xu, W.; Bearoff, F.; Kortagere, S. Conformational analysis of agonist-dependent phosphorylation signatures of dopamine D3 receptor. Mid-Atlantic Pharmacology Society Annual Meeting, Philadelphia, PA (2022).
- **Nepal, B.;** Sepehri, A.; et al. Mechanisms of negative membrane curvature sensing and generation. 64th Annual Meeting of the Biophysical Society, San Diego, CA (2020).

TEACHING & MENTORSHIP

- Mentored graduate and undergraduate trainees in computational drug discovery methods (docking, MD, ML/AI) at Drexel University College of Medicine (2021–Present).
- Graduate Teaching Assistant, Utah State University (2011–2016) — General Chemistry Recitation and General Chemistry Laboratory I & II across multiple semesters.
- Lecturer in Chemistry, Trinity International College, Kathmandu, Nepal (2009–2011).
- Teacher of General Science, Shishu Milan Secondary School, Kathmandu, Nepal (2004–2005).

PROFESSIONAL REFERENCES

Available upon request.