University of Mississippi

eGrove

2-21-2024

Computational Chemistry and Bioinformatics Research CORE (CCBRC)

Sushil K. Mishra
University of Mississippi

Priyanka Samantha
University of Mississippi

Mohamed E. Jahan
University of Mississippi

Robert J. Doerksen
University of Mississippi

Follow this and additional works at: https://egrove.olemiss.edu/pharm_annual_posters_2024

Recommended Citation

Computational Chemistry and Bioinformatics Research CORE (CCBRC)

Sushil K. Mishra[1], Priyanka Samanta[1], Mohamed E. Jahan[1], Robert J. Doerksen[1,2]

[1]Glycoscience Center of Research Excellence, Department of BioMolecular Sciences;
[2]Research Institute of Pharmaceutical Sciences, The University of Mississippi, University, MS, 38677-1848 USA

Glycoscience Center of Research Excellence
AT THE UNIVERSITY OF MISSISSIPPI

THE UNIVERSITY of MISSISSIPPI
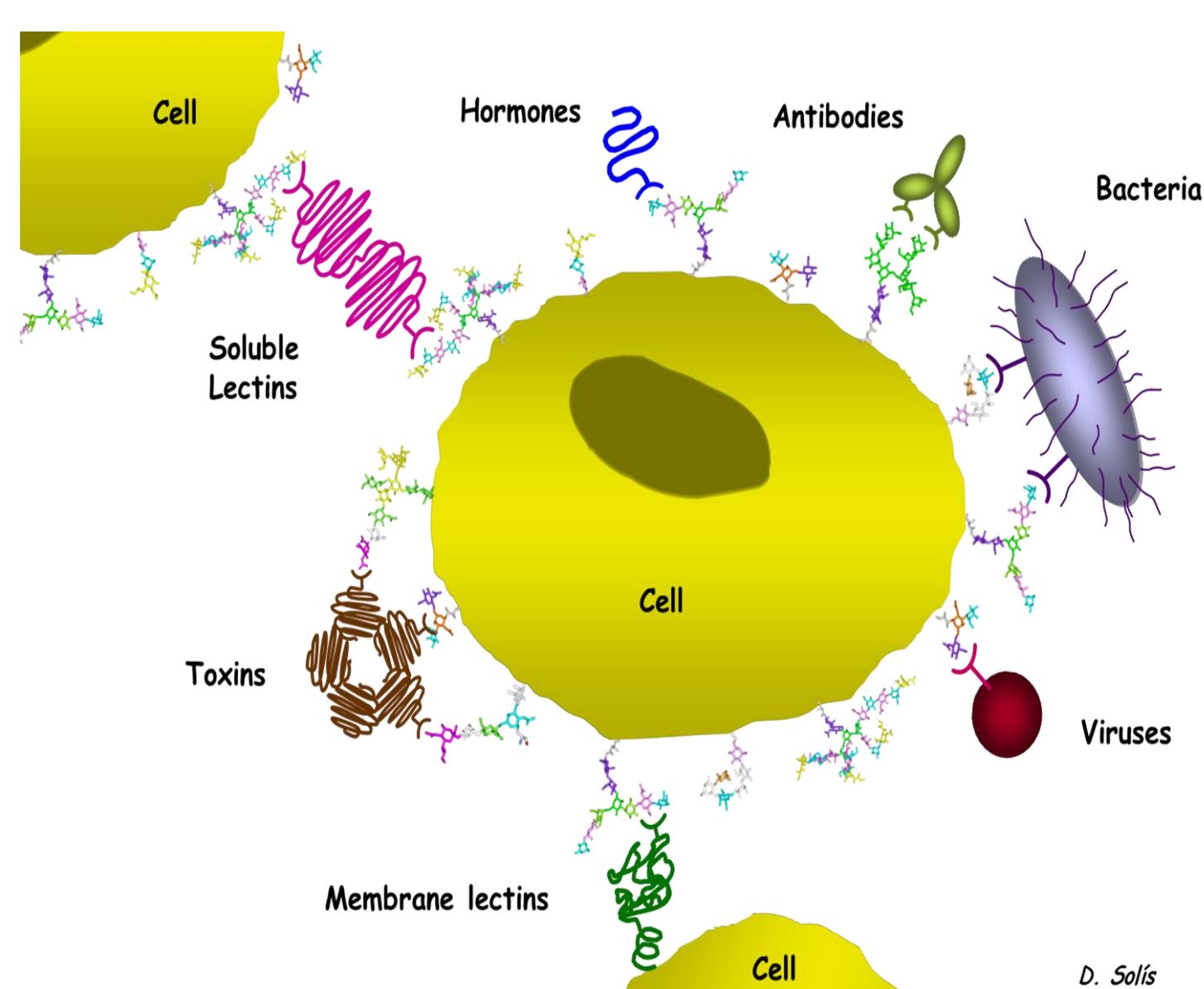DEPARTMENT OF BIOMOLECULAR SCIENCES

CCBRC

o Glycoscience Center of Research Excellence (CORE) is an NIH COBRE Phase 1 center in the Mid-South region of the USA focused on glycoscience research.

o The CCBRC, a core facility of GlyCORE, specializes in performing computational glycoscience research.

o The CCBRC provides training, access to hardware and software, and collaboration opportunities to support scientific problem-solving in the field of glycoscience.
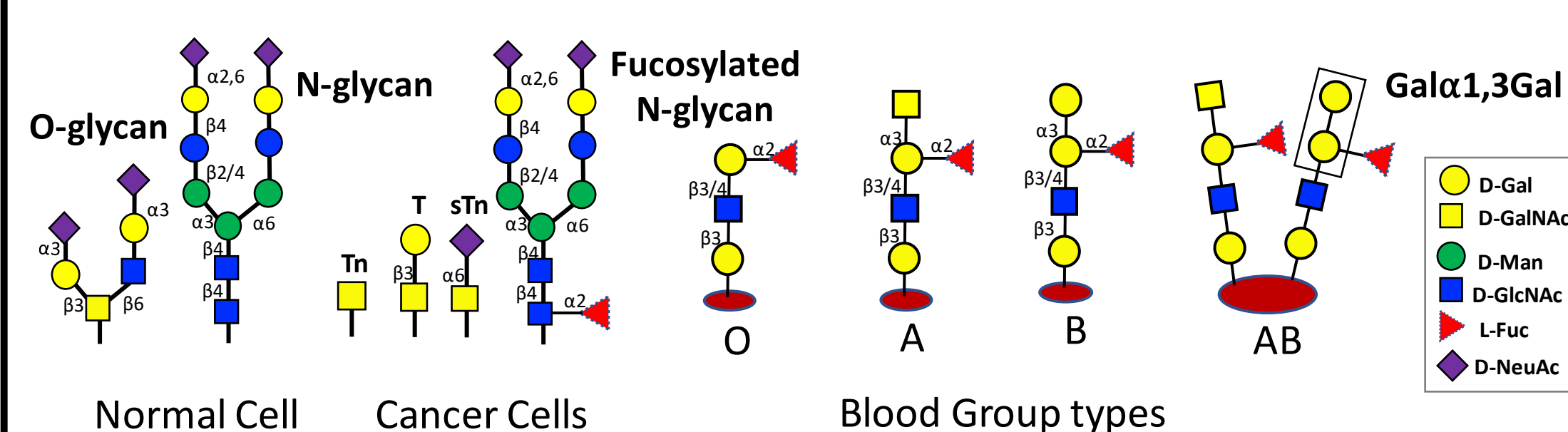
Why Glycoscience?

Protein–Glycan Interactions

o Glycosylation is a most common posttranslational modifications.

o Protein–glycan interactions are important for many biological processes, including molecular recognition, cell signaling, immune response, and cell–cell adhesion [1-2].

Protein–glycan interactions are key to numerous physiological and pathological processes (Fig[2])

o Cancer cells often have altered glycosylation patterns [3].

o Non-host glycans can trigger an immune response [4-6].

Glycoantigens and Glycomarkers

Normal Cell   Cancer Cells   Blood Group types

It is important to understand protein–glycan interactions and to design molecules that can recognize specific glycan patterns

Services

o Providing all sorts of computational support for GlyCORE RPLs.

o Research on computational glycosciences.

o Performing computations as part of service or collaboration.

o Consultation on glycoscience research.

o Providing access to high performance and GPU computing.

o Providing access to software for molecular modeling.

o Training and workshops on computational glycosciences.

CCBRC Personnel

Robert J Doerksen (CCBRC Director)
Sushil Mishra (CCBRC Manager)
Mohamed Jahan (Postdoc)
Priyanka Samanta (PhD Graduate)

CORE Facilities

Hardware:

o GAG: 8x A5000 GPUs, 384 GB memory, 42 TB storage

o GPU Cluster: 14x A6000 Ada GPUs, 1 TB memory, 60 TB storage

o High-end workstations: 2x RTX 3080 GPUs, 512 GB memory, 24 TB storage

o Workstations: 24 cores, 32 GB memory, RTX 3080/ TRX4000 GPUs

o Storage server: 80 TB of storage (6x 16 TB; RAID5)

GetForce 3080 (~ $400)   RTX A5000 (~ $2000)   NVIDIA A6000 Ada (~ $12,000)
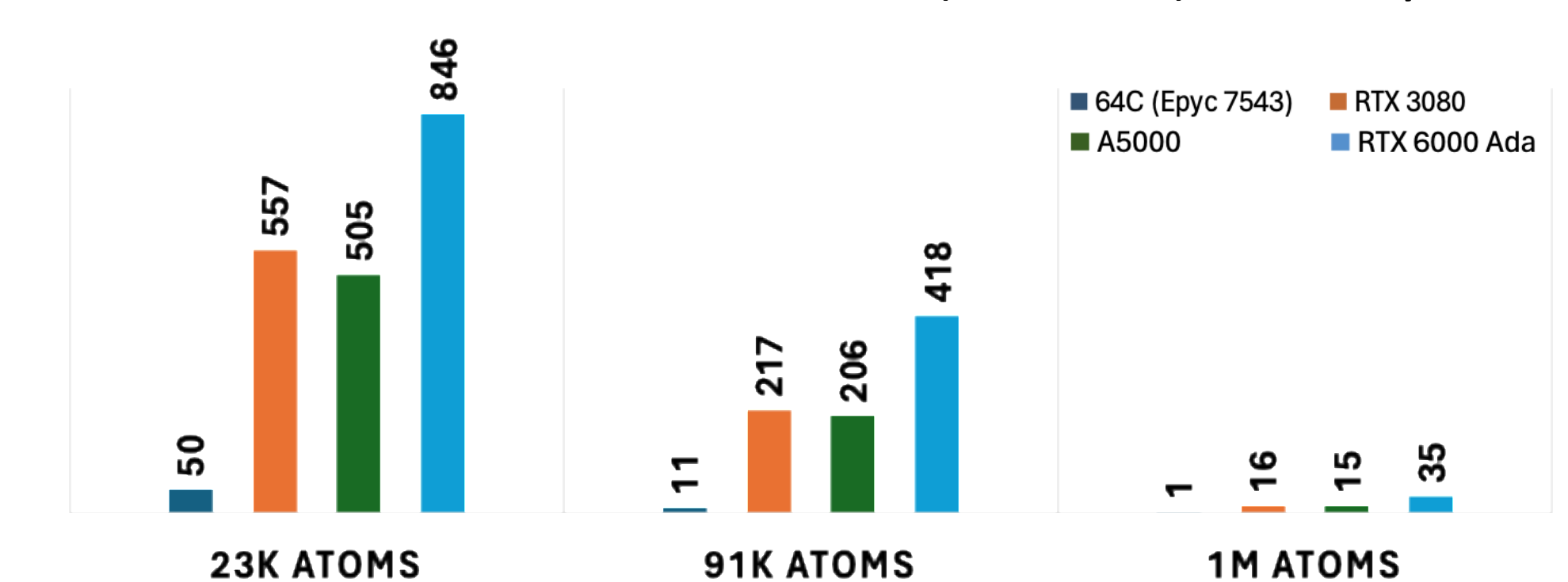
Licensed software:

o Schrödinger Drug Discovery Platform
o BioLuminate
o Desmond
o PyMol v.2

Other software:

o Molecular Dynamics: Amber22, NAMD, GROMACS, Desmond
o Docking: AutoDock Vina, Vina-Carb, GNINA, Glide,
o Structure Prediction: AlphaFold 2, MODELLER, ROSETTA
o Binding Energy Calculation: Sire, FESetup, Plumed
o Molecular Viewers: VMD, PyMol, Maestro, Chimera
o Sequencing: Guppy, Flye, PycoQC, Flitlong, racon, raven, porechop
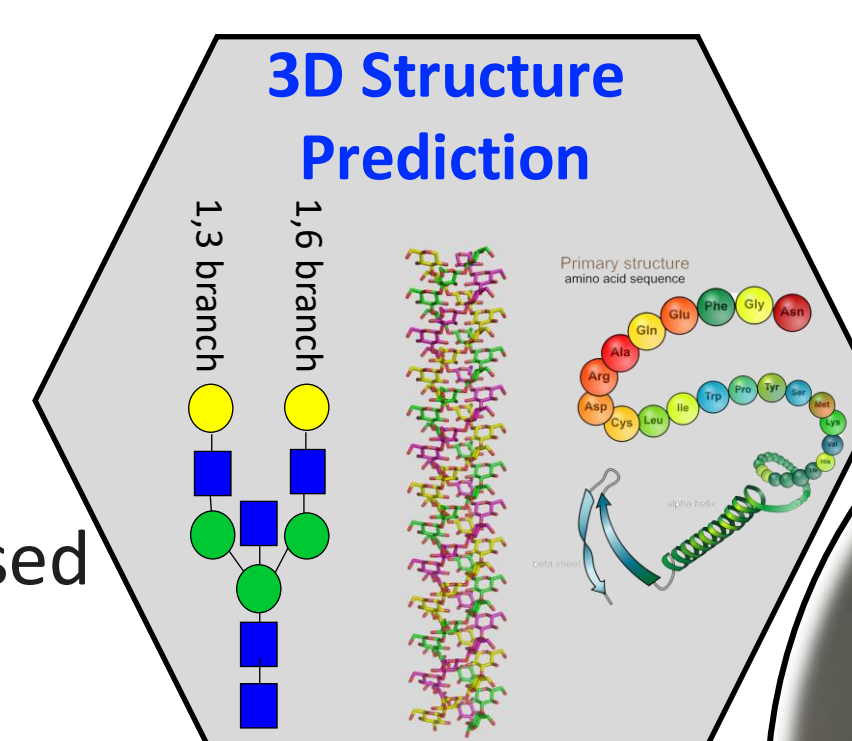o LC/MS Analysis: GlycoWorkbench, Glyconote

Computing Facility (March 2024)

Name	#Cores	Memory	GPUs	Storage
Front node	32	512 GB	Intel	48 TB
node1	64	512 GB	8x NVIDIA A6000 ADA	8 TB
node2	64	512 GB	6x NVIDIA A6000 ADA	8 TB
gag	48	384 GB	8x NVIDIA A500	42 TB
Fucose	64	512 GB	2x NVIDIA 3080	24 TB
Mannose	24	384 GB	2x NVIDIA 3080	36 TB
Glycocalyx	12	64 GB	-	80 TB
Total	308	2.8 TB	26 GPUs	246 TB

Amber22 MD Benchmarks (NPT; 2 fs) – ns/day

Legend: 64C (Epyc 7543), A5000, RTX 3080, RTX 6000 Ada

23K ATOMS: 50, 557, 505, 846
91K ATOMS: 11, 217, 206, 418
1M ATOMS: 1, 16, 15, 35

CORE Competencies

GPU Cluster
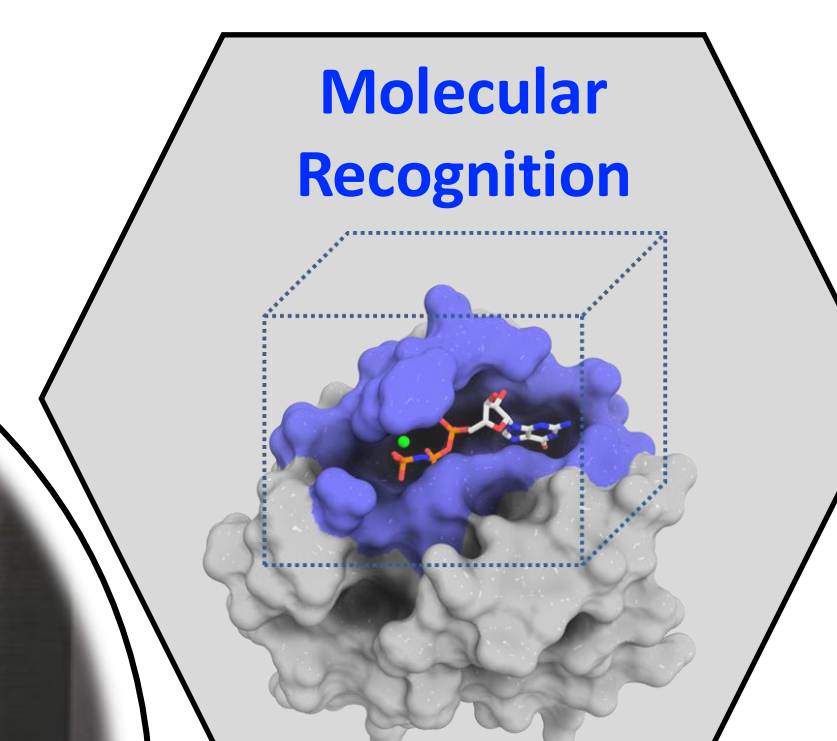
Structure Prediction
3D Structure Prediction
o Glycam-web
o Homology modeling
o ab Initio: Rosetta
o Machine learning based

Molecular Recognition

Docking
o Empirical
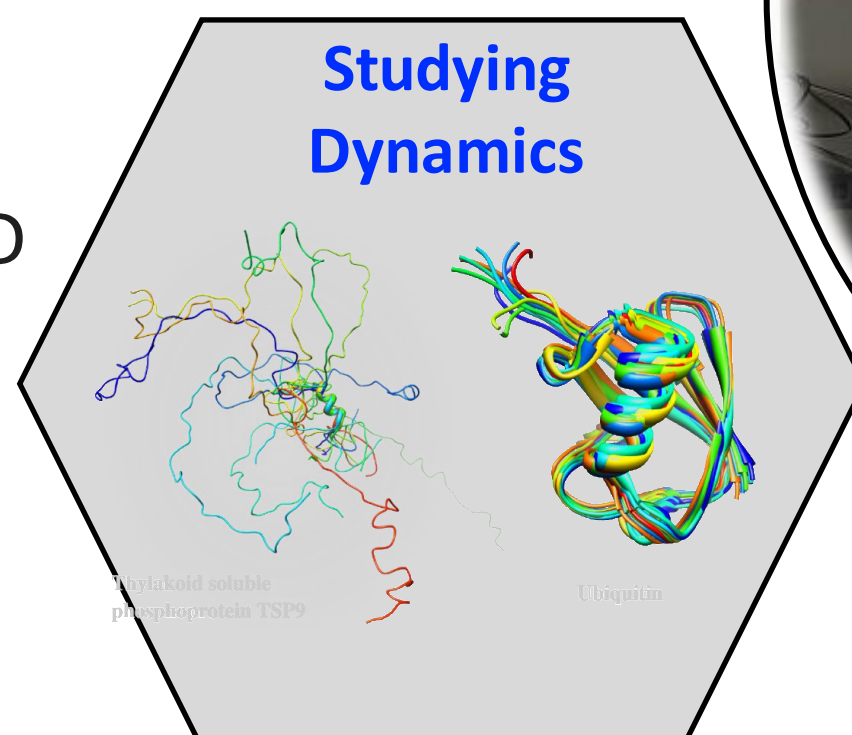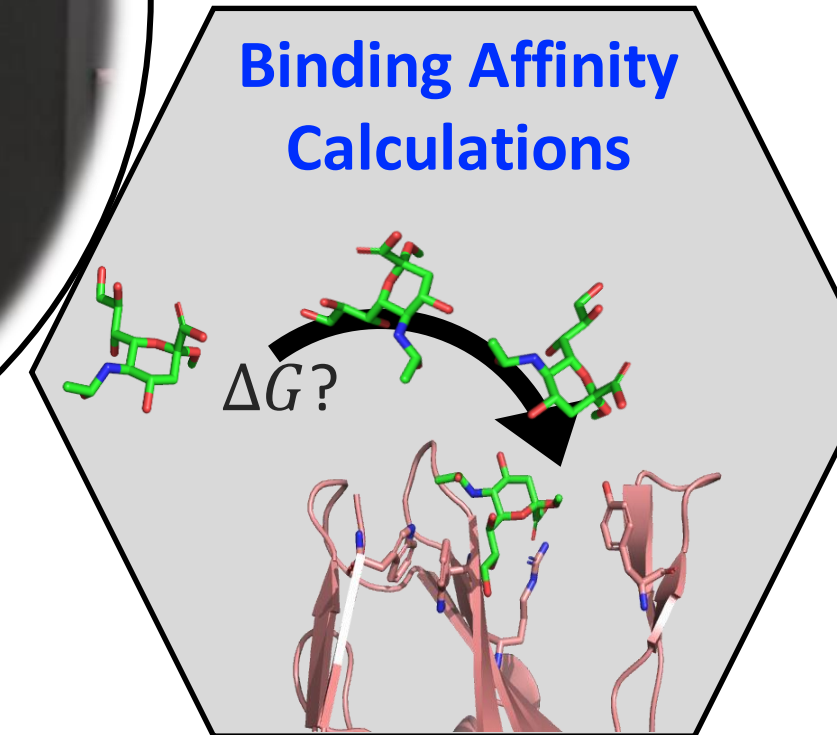o Machine-learning based
o Deep-learning based
o Protein–glycosaminoglycans

Molecular dynamics (MD)
Studying Dynamics
o Replica Exchange MD
o Umbrella sampling
o Steered MD
o Metadynamics

Binding Affinity Calculations
ΔG?

Binding-energy calculations
o Scoring functions
o End-point approaches
o Alchemical approaches
o Potential of Mean Force

Structure-Guided Drug Design

Identifying Hits → Hit to Lead → Lead Optimization

Some Recent Publications:

1. **Samanta P, Mishra SK, Doerksen RJ.** Docking and molecular dynamics simulations clarify binding sites for interactions of novel marine sulfated glycans with SARS-CoV-2 spike glycoprotein. *Molecules.* 2023, 28(17):6413
2. **Samanta P, Doerksen RJ.** Identifying FmlH lectin-binding small molecules for the prevention of Escherichia coli-induced urinary tract infections using hybrid fragment-based design and molecular docking. *Comput Biol Med.* 2023, 163:107072.
3. Maurya AK, Sharma P, **Samanta P**, Shami AA, Misra SK, Zhang F, Thara R, Kumar D, Shi D, Linhardt RJ, Sharp JS, **Doerksen RJ**, Tandon R, Pomin VH. Structure, anti-SARS-CoV-2, and anticoagulant effects of two sulfated galactans from the red alga Botryocladia occidentalis. *Int J Biol Macromol.* 2023, 238:124168.
4. Kim SB, Farrag M, Mishra SK, Misra SK, Sharp JS, Doerksen RJ, Pomin VH. Selective 2-desulfation of tetrasaccharide-repeating sulfated fucans during oligosaccharide production by mild acid hydrolysis. *Carbohydr Polym.* 2022, 301:120316.
5. Alkhodier RA, **Mishra SK, Doerksen RJ**, Colby DA. Comparison of Conformational Analyses of Naturally Occurring Flavonoid-O-Glycosides with Unnatural Flavonoid-CF2-Glycosides Using Molecular Modeling. *J Chem Inf Model.* 2023, 63(1):375–386.
6. Shofolawe-Bakare OT, de Mel JU, **Mishra SK**, Hossain M, Hamadani CM, Pride MC, Dasanayake GS, Monroe W, Roth EW, Tanner EEL, **Doerksen RJ**, Smith AE, Werfel TA. ROS-Responsive Glycopolymeric Nanoparticles for Enhanced Drug Delivery to Macrophages. *Macromol Biosci.* 2022, 12:e2200281.
7. Nagae M, Hirata T, Tateno H, **Mishra SK**, Manabe N, Osada N, Tokoro Y, Yamaguchi Y, **Doerksen RJ**, Shimizu T, Kizuka Y. Discovery of a lectin domain that regulates enzyme activity in mouse N-acetylglucosaminyltransferase-IVa (MGAT4A). *Commun Biol.* 2022, 5(1):1–11.
8. Vibhute AM, Tanaka HN, **Mishra SK**, Osuka RF, Nagae M, Yonekawa C, Korekane H, **Doerksen RJ**, Ando H, Kizuka Y. Structure-based design of UDP-GlcNAc analogs as candidate GnT-V inhibitors. *Biochim Biophys Acta Gen Subj.* 2022, 1866(6):130118.
9. Khaje NA, Eletsky A, Biehn SE, Mobley CK, Rogals MJ, Kim Y, **Mishra SK, Doerksen RJ**, Lindert S, Prestegard JH, Sharp JS. Validated determination of NRG1 Ig-like domain structure by mass spectrometry coupled with computational modeling. *Commun Biol.* 2022, 5(1):1–8.
10. Kim SB, Zoepfl M, **Samanta P**, Zhang F, Xia K, Thara R, Linhardt RJ, **Doerksen RJ**, McVoy MA, Pomin VH. Fractionation of sulfated galactan from the red alga Botryocladia occidentalis separates its anticoagulant and anti-SARS-CoV-2 properties. *J Biol Chem.* 2022, 298(5):101856.

References

[1] H. Us, N. Sharon, *Chem. Rev.* **98**, 637–674 (1998).
[2] D. Solis, N. V. Bovin, A. P. Davis, J. Jiménez-Barbero, et al., *Biochim. Biophys. Acta.* **1850**, 186–235 (2015).
[3] N. Taniguchi, Y. Kizuka, *Advances in Cancer Research*, (eds. Drake, R. R. & Ball, L. E.) **126**, 11–51 (Academic Press, 2015).
[4] C. Yu, K. Gao, L. Zhu, W. Wang, L. Wang, F. Zhang, C. et al., *Sci. Rep.* **6**, 20029 (2016).
[5] S. Cunningham, E. Starr, I. Shaw, J. Glavin, M. Kane, L. Joshi, *Anal. Chem.* **85**, 949–955 (2013).
[6] H. Clausen, S. Hakomori, *Vox Sang.* **56**, 1–20 (1989).

Acknowledgements

CCBRC Contact

Prof. Robert Doerksen, Core Director: rjd@olemiss.edu
Dr. Sushil Mishra, Core Manager: sushil@olemiss.edu
Follow us: X @UM_glycore   Instagram @um_glycore   Facebook @GlyCORE

SCAN ME