

*X-ray Crystallography and Automated
Biological Calorimetry Facilities Newsletter
Spring 2023*

Highlights

- NIH funded Beckman Optima Multiwavelength Analytical Ultracentrifuge (AUC) installed in room 8, Althouse Lab
- [Dr. Kevin Namitz](#), AUC specialist joins facility
- [Dr. Neela Yennawar](#) successful in procuring seven NIH and NSF grants in 2021-22. [Eighteen publications](#) output from the facility. Hurray!

For further information on X-ray crystallography, bio-SAXS, MW-AUC, SEC-MALS, ITC, DSC, CD & DLS contact director Drs. Neela Yennawar, nhy1@psu.edu 814-863-9387, Hemant Yennawar, hpy1@psu.edu 814-865-8383, Kevin Namitz, ken5223@psu.edu or research technician, Ms. Julia Fecko jaf48@psu.edu 814-865-8068.

Automated Biological Calorimetry

<http://www.huck.psu.edu/facilities/calorimetry-up>

X-ray Crystallography

<https://www.huck.psu.edu/core-facilities/x-ray-crystallography-facility>

Installation of the Optima Multiwavelength Analytical Ultracentrifuge (AUC)



AUC is a versatile, high throughput, and rigorous technology available for determining the hydrodynamic shape, size, molar mass, and binding thermodynamics of any macromolecule and its complexes. Multi-wavelength analytical ultracentrifugation is a recent development made

possible by highly sensitive optical systems. It extends the basic hydrodynamic information content of AUC to add the spectral domain, and provides simultaneous scans of up to twenty wavelengths. A wide range of new applications for studying biomolecular interactions, via their characteristic wavelength absorbance is now possible.

Parameters measured

- Sedimentation coefficient
- Diffusion coefficient
- Frictional coefficient
- Molar Mass estimates for each species
- Thermodynamics of binding interactions

Demonstration of oligomerization and interaction between macromolecules, through a concentration series and isotherm analysis of the species. This can be used to determine **binding kinetics including Kd values**.

Stay tuned for the Optima-AUC workshop to be held this summer by Prof. Borries Demeler

In this workshop Ultrascan software pioneer Prof. Demeler from the university of Lethbridge, will illustrate the power of MW-AUC where the benefit of the added spectral dimension to the hydrodynamic provides critical information that is impossible to resolve with traditional AUC methods.



Facility welcomes Dr. Kevin Namitz

Dr. Namitz graduated from Dr. Michael Cosgrove's lab at SUNY Upstate Medical University (Syracuse, NY), where he used SV-AUC extensively to characterize the thermodynamics of the Mixed Lineage Leukemia 1 (MLL1) histone H3 lysine 4 (H3K4) methyltransferase complex. He also performed both SV- and SE-AUC to look at binding and oligomerization kinetics for multiple protein and protein/DNA complexes during that time^{a-c}.



- a. Namitz, K. E. W., Tan, S., and Cosgrove, M. S. (2023) Hierarchical assembly of the MLL1 core complex regulates H3K4 methylation and is dependent on temperature and component concentration. *J Biol Chem*, 102874.
- b. Namitz, K. E. W., Zheng, T., Canning, A. J., Alicea-Velazquez, N. L., Castaneda, C. A., Cosgrove, M. S., and Hanes, S. D. (2021) Structure analysis suggests Ess1 isomerizes the carboxy-terminal domain of RNA polymerase II via a bivalent anchoring mechanism. *Commun Biol* 4, 398.
- c. Karchin, J. M., Ha, J. H., Namitz, K. E., Cosgrove, M. S., and Loh, S. N. (2017) Small Molecule-Induced Domain Swapping as a Mechanism for Controlling Protein Function and Assembly. *Sci Rep* 7, 44388.
10. Yoon J, Hou Y, Knoepfel AM, Yang D, Ye T, Zheng L, Yennawar N, Sanghadasa M, Priya S, Wang K. Bio-inspired strategies for next-generation perovskite solar mobile power sources. *Chem Soc Rev*. 2021 Nov 29;50(23):12915-12984.
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Recent co-authored publications

1. Vishweshwaraiah YL, Hnath B, Rackley B, Wang J, Gontu A, Chandler M, Afonin KA, Kuchipudi SV, Christensen N, Yennawar NH, Dokholyan NV. Adaptation-proof SARS-CoV-2 vaccine design. *Adv Funct Mater*. 2022 Dec 2;32(49):2206055.
2. Yeager C, Carter G, Gohara DW, Yennawar NH, Enemark EJ, Arnold JJ, Cameron CE. Enteroviral 2C protein is an RNA-stimulated ATPase and uses a two-step mechanism for binding to RNA and ATP. *Nucleic Acids Res*. 2022 Nov 11;50(20):11775-11798.
3. Uppuluri R, Hwang S, Maheshwari S, Zhao P, Gray JL, Rosas AS, Yennawar HP, Fan X, Janik MJ, Mallouk TE. Stabilization of Dinuclear Rhodium and Iridium Clusters on Layered Titanate and Niobate Supports. *Inorg Chem*. 2022 Nov 9.
4. Sieg JP, McKinley LN, Huot MJ, Yennawar NH, Bevilacqua PC. The Metabolome Weakens RNA Thermodynamic Stability and Strengthens RNA Chemical Stability. *Biochemistry*. 2022 Nov 15;61(22):2579-2591.
5. Xu Y, Zu R, Yennawar NH, Gopalan V, Hickey RJ. CocrySTALLINE Polymer Films Exhibiting Second-Order Nonlinear Optical Properties. *ACS Macro Lett*. 2021 Oct 19;10(10):1216-1222.
6. Yennawar HP, Sigmon A. Crystal structure of racemic (<i>R</i>,<i>S</i>,<i>E</i>)-2-(4-hydroxy-phen-yl)-4-(2-phenyl-hydrazin-1-yl-iden)chromane-5,7-diol ethanol monosolvate. *Acta Crystallogr E Crystallogr Commun*. 2022 Mar 1;78(Pt 4):346-348.
7. Yennawar HP, Medica JJ, Silverberg LJ. Synthesis and crystal structure of racemic (<i>R</i>,<i>R</i>*)-2,2'-(1,4-phenyl-ene)bis-(3-phenyl-2,3,5,6-tetra-hydro-4<i>H</i>-1,3-thia-zin-4-one). *Acta Crystallogr E Crystallogr Commun*. 2021 Nov 9;77(Pt 12):1263-1266.
8. Patterson DC, Liu Y, Das S, Yennawar NH, Armache JP, Kincaid JR, Weinert EE. Heme-Edge Residues Modulate Signal Transduction within a Bifunctional Homo-Dimeric Sensor Protein. *Biochemistry*. 2021 Dec 14;60(49):3801-3812.
9. Silverberg LJ, Mal TK, Pacheco CN, Povelones ML, Malfara MF, Lagalante AF, Olsen MA, Yennawar HP, Sobhi HF, Baney KR, Bozeman RL, Eroh CS, Fleming MJ, Garcia TL, Gregory CL, Hahn JE, Hatter AM, Johns LL, Klinger TL, Li JJ, Menig AJ, Muench GC, Ramirez ME, Reilly J, Sacco N, Sheidy AM, Stoner MM, Thompson EN, Yazdani SF. T3P-Promoted Synthesis of a Series of 2-Aryl-3-phenyl-2,3-dihydro-4<i>H</i>-pyrido[3,2-*e</i>][1,3]thiazin-4-ones and Their Activity against the Kinetoplastid Parasite <i>Trypanosoma brucei</i>. *Molecules*. 2021 Oct 9;26(20):6099.*

Facility Acknowledgements

15. Jennifer Park, Michael B. Cleary, Danyang Li. (2022) A genetically encoded fluorescent sensor for manganese(II), engineered from lanmodulin *PNAS*, Edited by Alison Butler, University of California Santa Barbara, Santa Barbara, CA; December 12, 2022 119 (51) e2212723119.
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18. Walker J.A., Wu Y., Potter J.R., Weinert E.E., (2020) π -Helix controls activity of oxygen-sensing diguanylate cyclases. *Biosci Rep*, Feb 2020,40(2): BSR2019360.

Successful grants by Dr. Neela Yennawar (2021-22)

1. *X-ray instrumentation upgrade for single crystal diffraction and solution small angle scattering - NIH 1S10OD028589-01*, Yennawar (PI)
2. *Wyatt SEC-MALS system - NIH 1 S10 OD030490-01*, Yennawar (PI)
3. *Molecular modeling workshop for PA K-12 teachers - NIH 1 R25 GM137390-01*, Yennawar (co-PI), PI Hill (Department of Education, PSU).
4. *Beckman Optima Multi Wavelength Analytical Ultracentrifuge- NIH S10OD032215-01*, Yennawar (PI).
5. *Enteroviral 2C protein as a therapeutic target - NIH 1R01 AI169462-01*, Yennawar (co-PI), PI Cameron (UNC).
6. *CAREER: The nature of interdomain coupling in the farnesoid X receptor, National Science Foundation Grant MCB-2144679*, Yennawar (senior personnel), PI Okafor (BMB, PSU).
7. *SemiSynBio-III: Novel Memory Devices for High-Density Data Storage and In-Memory Computing Based on Integrated Synthetic DNA-Semiconductors National Science Foundation Grant 2227484*, Yennawar (co-PI), PI Jha (UCincinnati).