Gregory W. Kyro

Biophysical Chemistry PhD Student at Yale University
Fellow of the National Science Foundation
Founder & President of the Yale University Chapter of the Biophysical Society

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Summary

I am a Chemistry PhD student at Yale and Fellow of the National Science Foundation. My research pertains to the development and application of machine learning methods for drug discovery.

I created HAC-Net, the current state-of-the-art machine learning model for predicting protein-ligand binding affinity. I open-sourced all of the code, created a Python package and notebook with a corresponding demo video, and published a paper so that the broader scientific community can easily utilize this tool. Although recently developed, the model was already reported to contribute to the identification of a potential antivirulence drug for drug-resistant staphylococcal infections. Shortly after, I created ChemSpaceAL, which is the first active learning methodology for fine-tuning a molecular generative model toward a specified protein target, and is particularly applicable to the creation of protein target-specific molecular libraries for virtual screening in drug discovery. Recently, I created CardioGenAI, a machine learning-based framework for re-engineering both developmental and marketed drugs for reduced cardiotoxicity while preserving their pharmacological activity. The framework incorporates novel state-of-the-art discriminative models for predicting hERG, Nav1.5 and Cav1.2 channel activity, which can also serve independently as effective components of an early-stage virtual screening pipeline. Additionally, I developed a method for describing intraprotein information transfer as the propagation of electrostatic couplings throughout a secondary structure element-based network, which has led to valuable insights into the allosteric mechanisms of multiple important biological systems such as CRISPR-Cas9, imidazole glycerol phosphate synthase, and D-dopachrome tautomerase. Moreover, I contributed to the development of quantum computing-based methods for studying small molecules, and have developed software for PROTACs screening at a world-renowned scientific software company.

I have published numerous papers in top-tier academic journals, presented my work at several conferences, created multiple Python packages, established various collaborations with labs around the world, and founded a Biophysical Society chapter at Yale. For these reasons, I have received multiple highly prestigious awards and appeared in Yale News multiple times.

Education

Yale University *05/23 – 05/26*
PhD in Computational Biophysical Chemistry
Advisor: Prof. Victor S. Batista

Yale University *09/21 – 05/23*
MS in Computational Biophysical Chemistry
Grade Average: Honors

SUNY Binghamton *09/16 – 05/21*
BS in Chemistry, Minors in Biology & Mathematics
Major GPA: 4.0

Recent Projects

- Generative AI framework for re-engineering cardiotoxic drug candidates *In Progress*
- AI-based method for mutation-based protein optimization *In Progress*
- AI-based method for predicting protein conformations from NMR spectra *In Progress*
- Active learning methodology for protein-specific drug generation *Finished 12/23*
- Graph neural network for protein-protein interface classification *Finished 08/23*
- Quantum convolutional neural network for image classification *Finished 05/23*
- Deep learning model for protein-ligand binding affinity prediction *Finished 04/23*
- Mathematical toolkit for describing allostery from MD simulations *Finished 03/23*
- Statistical method for describing information transfer in proteins *Finished 02/23*

Selected Awards, Scholarships, & Honors

- *Graduate Research Fellowship* | National Science Foundation *03/23*
- *Conference Travel Fund* | Yale University *02/23*
- *Award No. 5T32GM008283-35* | National Institutes of Health *09/22*
- *Biophysical Training Grant* | National Institutes of Health *08/21*
- *Stanley K. Madan Award in Inorganic Chemistry* | SUNY Binghamton *05/21*
- *Honors Thesis in Chemistry* | SUNY Binghamton *05/21*
- *Summer Scholars Program Award* | SUNY Binghamton *06/21*
- *SUNY Binghamton Undergraduate Research Award for Spring 2020* | SUNY Binghamton *01/20*
- *SUNY Binghamton Undergraduate Research Award for Fall 2019* | SUNY Binghamton *09/19*
- *Research Conference Travel Fund* | SUNY Binghamton *03/19*
- *SUNY Binghamton Undergraduate Research Award for Spring 2019* | SUNY Binghamton *01/19*
- *SUNY Binghamton Undergraduate Research Award for Fall 2018* | SUNY Binghamton *09/18*
- *SUNY Binghamton Undergraduate Research Award for Spring 2018* | SUNY Binghamton *01/18*
- *SUNY Binghamton Undergraduate Research Award for Fall 2017* | SUNY Binghamton *09/17*

Publications

[11] **Kyro, GW**; Morgunov, A ; Brent, RI; Batista, VS. "ChemSpaceAL: An Efficient Active Learning Methodology Applied to Protein-Specific Molecular Generation". *Journal of Chemical Information and Modeling* **2024**, 64, 3, 653-665. DOI: 10.1021/acs.jcim.3c01456

[10] **Kyro, GW**; Brent, RI; Batista, VS. "HAC-Net: A Hybrid Attention-Based Convolutional Neural Network for Highly Accurate Protein-Ligand Binding Affinity Prediction". *Journal of Chemical Information and Modeling* **2023**, 63, 7, 1947-1960. DOI: 10.1021/acs.jcim.3c00251

[9] Maschietto, F; Allen, B; **Kyro, GW**; Batista, VS. "MDiGest: A Python Package for Describing Allostery from Molecular Dynamics Simulations". *Journal of Chemical Physics* **2023**, 158, 215103. DOI: 10.1063/5.0140453

[8] Smaldone, AM; **Kyro, GW**; Batista, VS. "Quantum Convolutional Neural Networks for Multi-Channel Supervised Learning". *Quantum Machine Intelligence* **2023**, 5, 41. DOI: 10.1007/s42484-023-00130-3

[7] Yang, KR; **Kyro, GW**; Batista, VS. "The Landscape of Computational Approaches for Artificial Photosynthesis". *Nature Computational Science* **2023**, 3, 504-513. DOI: 10.1038/s43588-023-00450-1

[6] Chen, E; Widjaja, V; **Kyro, GW**; Allen, B; Das, P; Bhandari, V; Lolis, EJ; Batista, VS; Lisi, GP. "Mapping N- to C-terminal Allosteric Coupling Through Disruption of the Putative CD74 Activation Site in D-Dopachrome Tautomerase". *Journal of Biological Chemistry* **2023**, 299, 6, 104729. DOI: 10.1016/j.jbc.2023.104729

[5] Maschietto, F; Morzan, U; Tofoleanu, F; Gheereart, A; Chaudhuri, A; **Kyro, GW**; Nekrasov, P; Brooks, B; Loria, JP; Rivalta, I; Batista, VS. "Turning Up the Heat Mimics Allosteric Signaling in Imidazole-Glycerol Phosphate Synthase". *Nature Communications* **2023**, 14, 2239. DOI: 10.1038/s41467-023-37956-1

[4] Maschietto, F; **Kyro, GW**; Allen, B; Batista, VS. "Electrostatic Networks for Characterization of Allosteric Pathways in Cas9 Apo, RNA- and DNA-Bound Forms". *Biophysical Journal* **2023**, 122 (3). DOI: 10.1016/j.bpj.2022.11.389

[3] Wang, J; Arantes, PR; Ahsan, M; Sinha, S; **Kyro, GW**; Maschietto, F; Allen, B; Skeens, E; Lisi, GP; Batista, VS; Palermo, G. "Twisting and Swiveling Domain Motions in Cas9 to Recognize Target DNA Duplexes, Make Double-Strand Breaks, and Release Cleaved Duplexes". *Frontiers in Molecular Biosciences* **2023**, 9. DOI: 10.3389/fmolb.2022.1072733

[2] Wang, J; Skeens, E; Arantes, P; Maschietto, F; Allen, B; **Kyro, GW**; Lisi, GP; Palermo, G; Batista, VS. "Structural Basis for Reduced Dynamics of Three Engineered HNH Endonuclease Lys-to-Ala Mutants for the Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR)-Associated 9 (CRISPR/Cas9) Enzyme". *Biochemistry* **2022**, 61 (9), 785-794. DOI: 10.1021/acs.biochem.2c00127

[1] **Kyro, GW**; Lees, AJ. "Photophysics of Rhenium(I) Polypyridyl-Based Complexes and Their Employment as Highly Sensitive Anion Sensors" **2021**. DOI: 10.13140/RG.2.2.29980.56962

Presentations

[13] **Kyro, GW** et al. "CardioGenAI: A Machine Learning-Based Framework for Re-Engineering Drugs for Reduced Cardiotoxicity" in Proceedings of the 19th Annual Drug Discovery Chemistry Conference (2024).

[12] **Kyro, GW** et al. "ChemSpaceAL: An Efficient Active Learning Methodology Applied to Protein-Specific Molecular Generation" in Abstracts of the 2024 Annual Biophysical Society Meeting (2024).

[11] **Kyro, GW**. "Development of Machine Learning and Statistical Methods for Modulating Protein Function with Small Molecules" in the NIH x Yale Biophysics Seminar (2023).

[10] **Kyro, GW** et al. "HAC-Net: A Hybrid Attention-Based Convolutional Neural Network for Highly Accurate Protein-Ligand Binding Affinity Prediction" in Abstracts of the 2023 Annual Biophysical Society Meeting (2023).

[9] Maschietto, F; **Kyro, GW** et al. "Electrostatic Networks for Characterization of Allosteric Pathways: Allosteric Paths in Cas9 Apo, DNA- and RNA-Bound Forms" in Abstracts of the 2023 Annual Biophysical Society Meeting (2023).

[8] Allen, BC; Maschietto, F; **Kyro, GW** et al. "MDiGest: a Comprehensive Toolkit for Detection of Allosteric Communication from Molecular Dynamics Simulations of Biochemical Systems" in Abstracts of the 2023 Annual Biophysical Society Meeting (2023).

[7] **Kyro, GW** et al. "Photophysics of Binuclear Rhenium (I) Tricarbonyl Complexes and Their Employment as Anion Sensors Through Charge-Mediated Hydrogen Bonding" in Abstracts of Papers of the 261st ACS National Meeting & Exposition (2021).

[6] **Kyro, GW** et al. "Variable Anion Recognition Sites in Phosphorescent Rhenium (I) Polypyridyl-Based Sensors" in Abstracts of Papers of the 259th ACS National Meeting & Exposition (2020).

[5] **Kyro, GW** et al. "Photophysics of Polypyridyl-Based Rhenium (I) Complexes and Their Employment as Highly Sensitive Anion Sensors" in Oral Presentations of the 3rd SUNY Binghamton University Conference in Chemistry Research (2020).

[4] **Kyro, GW** et al. "Highly Sensitive Rhenium (I) Sensors for Anions Through Amide Hydrogen Bonding" in Poster Presentations of the Proceedings of the Undergraduate Research Center at Binghamton University (2020).

[3] **Kyro, GW** et al. "Amide Protons as Binding Groups in a Polypyridyl-Based Rhenium (I) Anion Sensor" in Abstracts of Papers of the 257th ACS National Meeting & Exposition (2019).

[2] **Kyro, GW** et al. "Excited-State Properties of Rhenium (I)-Based Anion Sensors" in Poster Presentations of the 2nd Binghamton University Conference in Chemistry Research (2019).

[1] **Kyro, GW** et al. "Organometallic Complexes as Anion Sensors: a Highly Sensitive Rhenium (I) Complex for Cyanide and Halide Anions" in Poster Presentations of the 1st Binghamton University Conference in Chemistry Research (2018).

Research Experience

Laboratory of Prof. Victor S. Batista, Yale University *11/21 – Present*

National Science Foundation Graduate Research Fellow

- Designed multiple state-of-the-art deep learning models and methodologies for applications in drug discovery, and revealed functional insights of many important biological systems by developing and applying graph-based statistical methods for studying biomolecular dynamics

OpenEye Scientific, Cadence Design Systems *05/23 – 08/23*

Scientific Software Developer Intern

- Led the development of a cutting-edge supervised deep learning model for classification of protein-protein interaction interfaces, thus contributing to the company's virtual screening pipeline for PROTACs

PreScouter, National Aeronautics and Space Administration (NASA) *06/21 – 09/21*

Global Scholar

- Reported on cutting-edge advancements to which NASA should allocate attention by researching energy storage, privacy-preserving network (i.e., blockchain), image detection, aerial surveillance, and aerodynamic levitation technologies

Laboratory of Prof. Alistair J. Lees, SUNY Binghamton *08/17 – 06/21*

Undergraduate Researcher

- Progressed the scientific community's understanding of excited-state mechanisms of binuclear rhenium(I)-based organometallic systems by employing a combination of computational (quantum chemistry calculations) and experimental (NMR, UV-Vis, fluorescence, and IR spectroscopies) techniques

Professional & Leadership Experience

- *Founder & President* | Yale University Chapter of the Biophysical Society *01/24 – Present*
- *Scientific Reviewer* | Journal of Chemical Theory and Computation *10/22 – Present*
- *Biophysics Research Seminar Organizer* | Yale University *08/22 – Present*
- *Scientific Blog Writer* | Biophysical Society *02/23 – Present*
- *Tutor* | Transformation Tutoring *12/21 – 12/22*
- *Research Ambassador* | Undergraduate Research Center at SUNY Binghamton *8/19 – 06/21*
- *Network and Computer Systems Intern* | Rapid Access Communications Inc. *11/19 – 02/20*

Teaching Experience

- *Teaching Fellow* | Matrix Methods in Quantum Mechanics | Yale University *10/23 – 12/23*
- *Teaching Fellow* | Machine Learning & Quantum Computing | Yale University *03/23 – 06/23*
- *Teaching Assistant* | Inorganic Chemistry Fall 2020 | SUNY Binghamton *09/20 – 12/20*
- *Teaching Assistant* | Chemical Principles I Fall 2020 | SUNY Binghamton *09/20 – 12/20*
- *Teaching Assistant* | Inorganic Chemistry Fall 2019 | SUNY Binghamton *09/19 – 12/19*
- *Teaching Assistant* | Chemical Principles II Spring 2019 | SUNY Binghamton *01/19 – 05/19*
- *Teaching Assistant* | Introduction to Chemistry Fall 2017 | SUNY Binghamton *09/17 – 12/17*

Technical Skills

- **Deep Learning Architectures:** transformers, GANs, autoencoders, RNNs, LSTMs, GRUs, CNNs, GNNs, LLMs and more
- **Machine Learning Architectures:** linear regression, logistic regression, decision trees, random forests, SVMs, gradient boosting machines, and more
- **Machine Learning Techniques:** active learning, reinforcement learning, transfer learning, feature engineering, dimensionality reduction, regularization, hyperparameter optimization, ensemble methods, cross-validation, clustering, data preprocessing and more
- **Cheminformatics:** molecular property prediction, molecular interaction analysis, molecular modeling, virtual screening, ligand-based drug design, structure-based drug design, Molecular Dynamics simulation analysis, molecular feature representations, QSAR modeling, molecular similarity analysis, conformational analysis, protein visualization, molecular mechanical calculations, quantum chemistry calculations, and more
- **Data Analysis:** statistical and mathematical modeling, time series analysis, visualization, network analysis, optimization techniques, and more
- **Quantum Computing:** quantum machine learning, quantum circuit construction, quantum algorithms, and more

Foundational Skills

- **Problem Solving & Critical Thinking:** first-principles reasoning, creativity skills, optimization, and more
- **Leadership & Project Management:** idea generation, time management, multitasking, strategic thinking, mentorship, and more
- **Communication & Collaboration:** public speaking, technical writing, interpersonal skills, and more
- **Adaptability & Continuous Learning:** dynamic, curious, growth mindset, and more

Professional Development

Massachusetts Institute of Technology, edX

- Machine Learning With Python *06/22*
- Biochemistry: Biomolecules, Methods & Mechanisms *05/22*
- Computational Thinking Using Python *07/21*

Harvard University, edX

- Principles of Biochemistry *05/22*
- Using Python for Research *07/21*

Selected Coursework

Yale University

Machine Learning & Computational Modeling:	Machine Learning & Quantum Computing, Computational Chemistry
Quantum Physics & Statistics:	Advanced Quantum Mechanics, Statistical Mechanics I and II, Quantum Mechanics I and II
Biophysics:	Biochemical Rates & Mechanisms I and II, Quantitative Biochemical Imaging, Biophysical Optical Spectroscopy

SUNY Binghamton

Quantum Systems & Chemical Dynamics:	Quantum Chemistry, Physical Chemistry, Molecular Photochemistry
Molecular Biophysics & Biochemistry:	Biophysical Chemistry, Molecular Biology, Molecular Genetics
Chemistry Principles:	Intermediate Inorganic Chemistry, Chemical Principles I and II, Transition Metal Chemistry, Organic Chemistry I and II, Analytical Chemistry
Mathematical, Physical & Data Science Principles:	Infinite Series, Integration Techniques & Application, Integral Calculus, Differential Calculus, General Physics I and II, Biostatistics
Biological Systems:	Organismal Biology, Evolutionary Biology, Human Biology & Health

Professional Memberships

- American Chemical Society
- Biophysical Society
- OpenLabs at Yale

Software Repositories

[6] **Kyro, GW**; Morgunov, A ; Brent, RI (**2023**). ChemSpaceAL (v1.0.3) [Source code]. GitHub. URL: github.com/gregory-kyro/ChemSpaceAL

[5] **Kyro, GW**; Brent, RI (**2023**). HAC-Net (v1.4.2) [Source code]. GitHub. URL: github.com/gregory-kyro/HAC-Net

[4] Maschietto, F; Allen, B; **Kyro, GW**. (**2023**). mdigest [Source code]. GitHub. URL: github.com/fmaschietto/mdigest

[3] Smaldone, AM; **Kyro, GW**. (**2023**). QCNN-Multi-Channel-Supervised-Learning [Source code]. GitHub. URL: github.com/anthonysmaldone/QCNN-Multi-Channel-Supervised-Learning

[2] **Kyro, GW**. (**2022**). molecular_dynamics_analyses [Source code]. GitHub. URL: github.com/gregory-kyro/molecular_dynamics_analyses

[1] **Kyro, GW**. (**2022**). eigenvector_centrality [Source code]. GitHub. URL: github.com/gregory-kyro/eigenvector_centrality

Media Coverage

- Featured in *Yale Alumni Magazine* for insights on computational biochemistry research, November 2023 issue: https://yalealumnimagazine.org/articles/5744-conversations-with-first-years
- Featured in *Yale News* for becoming a National Science Foundation fellow: https://chem.yale.edu/news/meet-yale-chemistry-nsf-fellows-recipients-esteemed-research-fellowship
- Featured in the *Biophysical Society Blog* for sharing biophysics content at the 2023 BPS Annual Meeting: https://www.biophysics.org/blog/meet-the-2023-annual-meeting-guest-bloggers

Selected Volunteer Activities

- *Scientific Speaker* | Yale Pathways to Science *12/23 – Present*
- *Outreach Volunteer* | American Chemical Society *06/19 – 06/20*
- *Medical Volunteer* | Long Island Jewish Medical Center *06/17 – 01/19*
- *Patient Care Volunteer* | Ronalds McDonald House Charities *06/17 – 12/18*
- *Gift of Sight Volunteer* | Luxottica *05/16 – 08/16*
- *Special Education Volunteer* | Merillon Little League Baseball *06/15 – 08/15*

Additional Achievements

- Scored a perfect 28/28 in the New York State School Music Association guitar competition at level 4 when I was 8 years old
- Have done a high-intensity workout at least once every day since 2010 (no exceptions)
- 2944 chess puzzle rating on chess.com (99.9^{th} percentile)
- Five-sport athlete in high school (baseball, wrestling, basketball, track, football)

References

- Victor S. Batista: victor.batista@yale.edu, (203) 432-6672
- Alistair J. Lees: alees@binghamton.edu, (607) 777-2362
- John Swierk: jswierk@binghamton.edu, (607) 777-2013
- J Patrick Loria: patrick.loria@yale.edu, (203) 436-2518
- Christof Grewer: cgrewer@binghamton.edu, (607) 777-3250