BIOGRAPHICAL SKETCH

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NAME: Matthew Jordan McLeod

eRA COMMONS USER NAME (credential, e.g., agency login): mcleodmj

POSITION TITLE: Post-doctoral Fellowship - Physics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Waterloo, Waterloo Ontario, Canada	B.Sc	05/2014	Biomedical Sciences, Biology
University of Waterloo, Waterloo Ontario, Canada	M.Sc	08/2016	Protein Biochemistry
University of Waterloo, Waterloo Ontario, Canada	Ph.D	08/2020	Protein Biochemistry
Cornell University, Ithaca New York, U.S.A	PDF	Ongoing – Started 10/2021	Biophysics

A. Personal Statement

I am currently a postdoctoral fellow at Cornell University in the Physics department. I have recently completed my Ph.D and during my short academic career, I have begun to carve a niche of skills and research questions. I am an expert in protein biochemistry, specifically utilizing kinetics and structural (crystallography, SAXS) techniques to study proteins of interest. I have worked on my own research, creating research questions and implementing experiments to investigate these questions. I have also extensively collaborated with other research groups contributing experimental results and intellectual value. My current academic interests lie in investigating a previously uncharacterized enzyme class, pyrophosphate-dependent phosphoenolpyruvate carboxykinases (PEPCK) as well as studying functional/structural responses of enzymes to changing temperature. I have presented my scientific findings at national and international conferences (13 total) as well as guest lectures in various classroom (8). This research excellence is documented through my many publications at respected journals, being awarded the prestigious W.B. Pearson Medal for creative dissertation research, and securing national and local scholarships and funding for my graduate studies. During my graduate studies, I have mentored new members to the lab in writing, experiments, and scientific dissemination of results. Furthermore, I have begun an active teaching career. First, I have taught a first-year course for Science and Applied Health Science students at the University of Waterloo for three years. Second, I was a lab coordinator for first year international students in the department of Science. Finally, I have worked in various departments at the University of Waterloo in training graduate students and post-doctoral fellows how to teach in the University setting.

- Gao, XH., Li, L., Parisien, M., **Mcleod MJ.,** Wu, J., Bederman, I., Gao, Z., Krokowski, D., Chirieleison, SM., Diatchenko, L., Abbott, D., Yee, V., Hoppel, CL., Kibbey, RG., Holyoak, T., Willard, B., Arvan, P., Hatzoglou, M. "Discovery of a redox-thiol switch regulating cellular energy metabolism", BioRXiv (2019). ***Pre-print.***
- Johnson, TA., **Mcleod, MJ**., Holyoak, T. "Utilization of Substrate Intrinsic Binding Energy for Conformational Change and Catalytic Function in Phosphoenolpyruvate Carboxykinase." Biochemistry (2016).
- Balan, MD., **Mcleod, MJ.,** Lotosky, WR., Ghaly, M., Holyoak, T. "Inhibition and Allosteric Regulation of Monomeric Phosphoenolpyruvate Carboxykinase by 3-Mercaptopicolinic Acid", Biochemistry (2015).

B. Positions, Scientific Appointments, and Honors

2021	W.B Pearson Medal, University of Waterloo
2019-2020	Graduate Educational Developer
2018	Lab coordinator, Renison University College
2017	Margaret Etter Student Lecturer Award, American Crystallographic Association
2016-2018	Instructor, Faculty of Science and Applied Health Science, University of Waterloo
2014-current	Member, American Crystallographic Association

Scholarships/Fellowships

2019-2020	W.S. Rickert Graduate Student Fellowship – University of Waterloo ($20 000)
2016-2019	NSERC PGS – Graduate Scholarship ($63 000)
2016-2019	Presidents Graduate Scholarship ($20 000)

Research Funding Grants

2015	Catalyst Grant – Network for Aging Research – University of Waterloo ($10 000)

C. Contributions to Science

1. During my graduate schooling and now post-doctoral fellowship, I have used biochemical and structural techniques to study the biophysics of enzymes. Specifically, relating kinetic observations to specific structural features and changes that occur. The model enzyme that I have used is phosphoenolpyruvate carboxkyinase (PEPCK). This series of publications described specific dynamic motifs in PEPCK in order to understand the conformational changes required for PEPCK to turnover its substrate. Additionally, I investigated a new inhibitor of PEPCK that was based off upon previous molecules which combines multiple binding modes to create a more selective molecule. Most recently, I have used new methods in order to complete time-resolved crystal studies to further investigate PEPCKs catalytic cycle. My contributions to these works vary, whether through data analysis, sample preparation, kinetic analysis, structural studies, and or writing. In addition to these primary research articles, I have written and published a review on the *in vivo* and *in vitro* features of PEPCKs.

   - Clinger, JA., Moreau, DW., **McLeod, MJ.,** Holyoak, T., Thorne, RE. "Millisecond Mix-and-Quench Crystallography (MMQX) Enables Time-Resolved Studies of PEPCK with Remote Data Collection", IUCrJ (2021).
   - **McLeod, MJ.**, Holyoak, T. "Phosphoenolpyruvate Carboxykinases", Encyclopedia of Biochemistry 3rd Edition (2021).
   - **Mcleod, MJ.,** Krismanich, AP., Assoud, A., Dmitrienko, GI., Holyoak, T. "Characterization of 3-((carboxymethyl)thio)-picolinic acid – A novel inhibitor of phosphoenolpyruvate carboxykinase." Biochemistry (2019).
   - Cui DS, Broom A, **Mcleod, MJ**., Meiering EM, Holyoak, T. "Asymmetric Anchoring is Required for Efficient Ω-Loop Opening and Closing in Cytosolic Phosphoenolpyruvate Carboxykinase", Biochemistry (2017).

2. Much of my Ph.D dissertation work has not been published yet but will be in the coming months/year. The first study is an investigation on a new PEPCK class, one that is 50kDa larger and functionally/structural divergent, was characterized both structurally and kinetically, giving the most comprehensive analysis of this relatively under-studied enzyme. Second, I have studied the temperature dependencies of PEPCKs by studying a psychrophilic, mesophilic, and thermophilic PEPCK kinetically. Additionally, the psychrophilic variant was crystallized. Finally, I studied the inhibition of CTP synthase with various fluorinated compounds showing the atomic structural details, giving rationale to the wide range of potencies of these compounds. This project has recently been accepted and is currently being edited for publication. In these studies, I am the primary author as I completed all experiments, data analysis, and writing for these projects.

   To be published:
   - **McLeod, MJ**., Holyoak, T. "Biochemical, structural and kinetic characterization of PP_i-dependent phosphoenolpyruvate carboxykinase from Propionibacterium freudenreichii". PROTEINS: Structure, Function, and Bioinformatics. (2022). ***Under revision***.
   - **McLeod, MJ.**, Holyoak, T. "Kinetic and Structural Characterization of Temperature Variant Isozymes of PEPCK".
   - **McLeod, MJ.,** Tran, N., Gillis, TD., McCluskey GD., Bearne SL., Holyoak T. "Right binding of gemcitabine-5'-triphosphate is facilitated by the formation of a metal-nucleotide complex associated with the filament-competent conformation of *Escherichia coli* CTP synthase".