Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

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BSc Hons (University of Victoria, 2013)
Diploma Applied Chemistry and Biotechnology (Camosun College, 2011)

“Development and Application of Structural Prediction Methods for Flexible Protein-Ligand Interactions”

Department of Chemistry

Tuesday, July 28, 2020
1:00 P.M.
Remote Defence

Supervisory Committee:
Dr. Irina Paci, Department of Chemistry, University of Victoria (Supervisor)
Dr. Fraser Hof, Department of Chemistry, UVic (Member)
Dr. Dennis Hore, Department of Chemistry, University of Victoria (Member)
Dr. Patrick Nahirney, Division of Medical Sciences, UVic (Outside Member)

External Examiner:
Dr. Stacey Wetmore, Department of Chemistry and Biochemistry, University of Lethbridge

Chair of Oral Examination:
Dr. Michelle Wiebe, Department of Curriculum and Instruction, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract
This dissertation presents a collection of biological simulations and predictions in collaboration with experiment to support and elucidate the trends observed in various protein-ligand systems. Within the model systems, there is strong focus on the support for development of peptidomimetic inhibitors for post-translational reader proteins (CBX proteins). The systems studied throughout this document each present their own unique challenges but fall under the general theme of protein flexibility and the difficulties of sampling such systems. As part of this work, methodological advances were made to address the challenges of structural prediction on flexible proteins and ultimately form the method Selective Ligand-Induced Conformational Ensemble (SLICE). The development, validation, and future directions of the SLICE method are also discussed. Ultimately, the collaborative efforts presented in this dissertation bring forward a greater understanding of the drug design challenges on the CBX proteins as well a new methodology in the field of structure-based drug design.