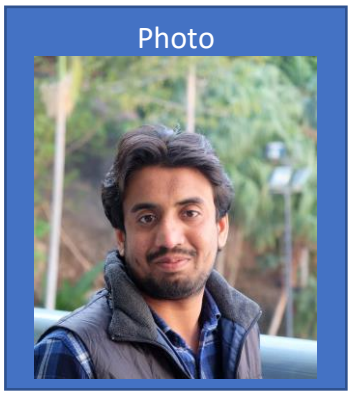
PhD Oral Defense

Date: **8 January 2021 (Friday)** **Time:** **2:30pm**

Thesis Title

Analyze, Visualize, and Predict Lung Cancer Drug Resistance Based on Molecular Dynamics Simulation and Machine Learning



Mr. Rizwan (Supervisor: Prof. Hong Yan)

Abstract

Lung cancer is a leading cause of cancer deaths worldwide, resulting in the loss of millions of lives each year. The mutation in the epidermal growth factor receptor (EGFR) is a pathogenic factor in lung cancer development. EGFR tyrosine kinase inhibitors (TKIs), such as Gefitinib/Erlotinib, have been developed to treat lung cancer patients. Interventions using these inhibitors have produced encouraging early outcomes, but the long-term efficacy appears limited with the emergence of drug resistance following one or more secondary mutations, such as L858R-T790M.

This thesis used molecular dynamics (MD) simulations and machine learning-based methods to study EGFR-mutated drug resistance. In our first contribution, we used time series model to estimate the parameters of a molecular dynamics trajectory. Our second work uses normal modes and complex network theory to find correlated motions and highly communicating residues. Our third contribution presents a systematic protein-drug interactions visualization method for drug resistance analysis, and our final contribution is related to predicting the drug response using machine learning classifiers.

This thesis has developed computational methods to analyze, visualize, and predict the drug-resistance and drug-response for lung cancer patients. These studies will lead to a better understanding of the molecular mechanisms contributing to drug resistance. The proposed methods can also be applied to other types of cancer or related disease and can improve the drug discovery pipeline.