WPI CHEMISTRY & BIOCHEMISTRY



Department of Chemistry and Biochemistry
Worcester Polytechnic Institute

Wednesday, November 11th, 2026
12:00 PM
Gateway Park 1002

Dr. Mary Jo Ondrechen

Distinguished Professor of Chemistry and Chemical Biology
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"AI-enhanced physicochemical approaches to understand protein function"

Artificial Intelligence (AI) has accelerated advances in science in recent years with dramatic breakthroughs, including good-performing solutions to the ab initio protein folding problem. We developed a machine learning (ML) method Partial Order Optimum Likelihood (POOL), first reported in 2009, to predict the amino acids in a protein structure that are biochemically active in catalysis or ligand binding. POOL has been used to identify catalytically active residues and to establish how distal residues contribute to activity in enzymes. More recently, features from POOL are being used to address the question of how the amino acids in enzyme active sites gain their catalytic activity. For instance, the side chains of lysine, aspartate and glutamate are weak Brønsted acids and bases for the free amino acids in solution, yet inside the enzyme active site they can become strong acids, bases, and nucleophiles – Insights into how proteins affect this extraordinary increase in activity will be shared. POOL has been used to predict the function of protein structures of unknown function, using a local structure match at the site of biochemical activity, with subsequent experimental testing and verification. Our ML approach has also successfully predicted whether specific missense mutations impair catalysis in an enzyme. Disease-associated mutations in human ornithine transcarbamylase are featured.

Host: Dr. Aya Narunsky