Autumn 2021 Seminar Series

A Deep Generative Model for Molecule Optimization via One Fragment Modification

Abstract: Molecule optimization is a critical step in drug development to improve desired properties of drug candidates through chemical modification. We developed a novel deep generative model Modof over molecular graphs for molecule optimization. Modof modifies a given molecule through the prediction of a single site of disconnection at the molecule and the removal and/or addition of fragments at that site. A pipeline of multiple, identical Modof models is implemented into Modof-pipe to modify an input molecule at multiple disconnection sites. Here we show that Modof-pipe is able to retain major molecular scaffolds, allow controls over intermediate optimization steps and better constrain molecule similarities. Modof-pipe outperforms the state-of-the-art methods on benchmark datasets: without molecular similarity constraints, Modof-pipe achieves 81.2% improvement in octanol-water partition coefficient penalized by synthetic accessibility and ring size; and 51.2%, 25.6% and 9.2% improvement if the optimized molecules are at least 0.2, 0.4 and 0.6 similar to those before optimization, respectively. Modof-pipe is further enhanced into Modof-pipem to allow modifying one molecule to multiple optimized ones. Modof-pipem achieves additional performance improvement as at least 17.8% better than Modof-pipe.

About the Speaker: Dr. Xia Ning is a tenured Associate Professor in the Biomedical Informatics Department and Computer Science and Engineering Department, The Ohio State University. She co-directs the Computational Health and Life Sciences Community of Practice at the Translational Data Analytics Institute (TDAI) at OSU. Dr. Ning received her Ph.D. from University of Minnesota, Twin cities, in 2012. From 2012 to 2014, she worked as a research staff member at NEC Labs, America. From 2014 to 2018, she was an Assistant Professor in the Computer and Information Science Department, Indiana University – Purdue University Indianapolis. She joined OSU in July 2018. Ning's research is on Artificial Intelligence and Machine Learning with applications in Biomedicine. In specific, Ning's research focuses on developing scalable AI/ML models and computational methods to derive knowledge from heterogeneous Big Data via modeling, ranking, classification and prediction, etc., and ultimately to solve critical and high-impact problems. Specific research topics include information retrieval from electronic medical records, drug candidate prioritization for drug discovery, cancer drug selection for precision medicine, etc. Dr. Ning is a fellow of American Medical Informatics Association (AMIA).

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Friday, November 12th, 11:00am-12:00pm
Carmen Zoom