Forging physics-corrected deep-learning approaches and AI robotics for high performance drug discovery

Jung-Hsin Lin

[1]Biomedical Translation Research Center (BioTReC), [2]Research Center for Applied Science (RCAS), and [3]Institute of Biomedical Sciences (IBMS), Academia Sinica, Taipei, Taiwan, [4]School of Pharmacy, College of Medicine, National Taiwan University, Taipei, Taiwan, [5]College of Engineering Sciences, Chang Gung University, Chungli, Taiwan

Dr. Jung-Hsin Lin received his Ph.D. training at Institute für Festkörperfoschung, Forschungszentrum Jülich, Germany, under the supervision of Dr. Artur Baumgaertner, and he then worked as Bioinformatics Specialist at Howard Hughes Medical Institute, at University of California, San Diego, under the supervision of Prof. J. Andrew McCammon. He returned to Taiwan and started his independent career in 2003 as Assistant Professor at School of Pharmacy, College of Medicine, National Taiwan University. In 2004 he joined Institute of Biomedical Sciences, Academia Sinica as a Jointly-Appointed Research Fellow. In 2006 he was recruited to Research Center for Applied Sciences, Academia Sinica. He was the Chief Executive Officer of the Thematic Center for Biomedical Applications of Research Center for Applied Sciences (RCAS) between 2015 and 2020, and the Deputy Director of RCAS between 2019 and 2020. He is currently the Deputy Director of BioTReC, and also the Chief Executive Officer of the Thematic Center for Intelligence Medicine. He is the inventor of 16 patents for the new drugs discovered from his collaborative teams. Two series of drug candidates on neurodegenerative diseases and cancer treatment were exclusively licensed to the companies in Taiwan in 2015 and 2016, respectively. One small molecule drug for treating Alzheimer's disease is anticipated to enter the Phase I clinical trial at the Q1 of 2024. Since about six years ago, he established a lab to carry out protein expression, purification, several biophysical assessments, also X-ray crystallography and cryo-EM experiments for determining structures of membrane transporters and chemical sensory proteins, as well as NMR experiments for structure determination and dynamics characterization of structured proteins and intrinsically disordered proteins. In the past few years he also created automatic laboratory systems with well-controlled experimental environment and AI robotics for carrying out cell culture. virus titration assays, chemical synthesis, and drug testing.

Abstract

In this seminar I start with the progress of our small molecule drug for treating Alzheimer's disease, which is anticipated to enter the Phase I clinical trial at the Q1 of 2024. I will highlight some major research topics of my lab on the developments and applications of computational methodologies for design and discovery of new drugs, and for unravelling the molecular mechanisms of biological systems based on fundamental physical chemical principles, which are facilitated by biophysical

experiments, as well as molecular modelling and simulations. I will also describe an integrated virtual screening scheme established in our lab, which combines rapid docking and deep-learning-based scoring approaches, molecular dynamics simulations and adaptive umbrella sampling methods, enabling the screening of very large libraries of chemical compounds in a very efficient manner while preserving high accuracy. I will also give some examples that are quite challenging for AI-based structure prediction, and our recent efforts to address these difficult topics. Finally, I will talk about our recently established automatic laboratory systems with well-controlled experimental environment and AI robotics for carrying out cell culture. virus titration assays, chemical synthesis, and drug testing.