Kenichiro Takaba

RESEARCH INTEREST

Drug design, Molecular dynamics simulation, Fragment molecular orbital method, Reinforcement learning, Active learning, Transfer learning, Deep neural networks

EDUCATION

- **2016-2020:** Ph.D. in Physics, The University of Tokyo, Japan
  Edge expansion parallel cascade selection molecular dynamics simulation (eePaCS-MD) for investigating protein dynamics

- **2010-2012:** M.S. in Physics, The University of Tokyo, Japan
  Theoretical study of the protonation states of H^+-PPase using molecular dynamics simulations

- **2006-2010:** B.S. in Engineering Science, University of Tsukuba, Japan

WORK EXPERIENCE

2012-Present: Computational chemist, Asahi Kasei Pharma Corporation
- Engaged with multiple structure-based and ligand-based drug discovery projects such as kinases and nuclear receptors
- Infrastructure development of computational tools for medicinal chemists such as automated docking simulations, QSAR/QSPR predictions and *de-novo* compound design
- Development of web services

2020-Present: Visiting scientist, Memorial Sloan Kettering Cancer Center
- Development of open-source software for computer-aided drug discovery

TECHNICAL EXPERIENCE

- Expertise with biomolecular simulations, cheminformatics, and machine learning for drug discovery
- Expertise in using computational tools such as Maestro and MOE
- Experience with Python programming language and Unix shell scripts
- Experience with open-source software packages such as RDKit, OpenMM, Perses, and machine learning frameworks such as Scikit-learn and Pytorch
- Experience with flask and SQLAlchemy to develop web services
- Exposure to GitHub (Gitea) for inhouse code sharing and development

SELECTED RECENT PUBLICATIONS

Preprints

- *arXiv:2307.07085* (2023)
  Espaloma-0.3.0: Machine-learned molecular mechanics force field for the simulation of protein-ligand systems and beyond
  Kenichiro Takaba, Kenichiro Takaba, Iván Pulido, Mike Henry, Hugo MacDermott-Opeskin, John D. Chodera, Yuanqing Wang

  Development of self-consistent molecular mechanics force field in an end-to-end differentiable manner directly from quantum chemical calculations using a machine learning framework (Espaloma). This paper extends the original Espaloma method by incorporating energy and force fitting, as well as L2 regularization to torsion and improper torsion force constants, effectively reducing the model variance. The resulting force field, espaloma-0.3.0, can achieve accurate protein-ligand binding free energies when self-consistently parametrizing both the protein and ligand.

Journals

- *J. Chem. Phys.* **152**, 225101 (2020)
  Edge Expansion Parallel Cascade Selection Molecular Dynamics Simulation for Investigating Large-amplitude Motion of Proteins

  Kenichiro Takaba, Akio Kitao

  A new adaptive sampling method is proposed to explore the large-amplitude motions of proteins with a focus on domain motions. The proposed method repeats multiple MD simulations from structures that are located at the boundary of a principal component space with the concept of nodes and edges which are designed to expand as the adaptive sampling cycles increase.

INVITED TALKS

- **Application of Molecular Dynamics and Fragment Molecular Orbital Method in Drug Discovery**
  392th CBI seminar and workshop: Application of molecular dynamics in drug discovery
  March 2018, Tokyo, Japan

  Practical application of MD simulations in drug discovery projects such as docking pose validation, predictions of protonation states, and protein-ligand interaction profiling are discussed. Furthermore, application of fragment molecular orbital method (FMO) is introduced as a tool to analyze the protein-ligand interactions based on quantum mechanics providing better understanding of the protein-ligand system. Additionally, an example is shown where systematic averaging of FMO-based interaction energies over multiple conformers generated by MD simulations can be used as a convenient scoring method to predict the protein-ligand binding affinity.

- **Validation of Supervised Molecular Dynamics and its Usefulness in Drug Discovery**
  MOE Forum 2017
  July 2017, Tokyo, Japan

  Supervised molecular dynamics (SuMD) [Sabbadin et al. 2014] is an adaptive sampling method to explore the protein-ligand recognition pathway which utilizes a tabu-like supervision algorithm on the protein–ligand distance. In this study, accelerated MD was combined with the original SuMD to speed up the binding event by lowering the dehydration barrier of the binding site. Furthermore, the

original SuMD was extended for protein-ligand dissociation (rSuMD) where the wrong docking poses tend to dissociate faster than the correct binding poses, suggesting that rSuMD may be useful for post processing of structure-based virtual screening to decrease the false positive hits.