PHARMACOPHORE MODEL DEVELOPMENT FOR THE IDENTIFICATION OF NOVEL ACETYLCHOLINESTERASE INHIBITORS

Kamau, Edwin¹²; Mustata, Gabriela¹.

¹ Bioengineering & Bioinformatics Summer Institute, Dept. of Computational Biology, University of Pittsburgh, Pittsburgh, PA 15260

² Dept. of Chemistry and Biochemistry, Kennesaw State University, Kennesaw, GA 30144

Clearly established as one of the successful computational tools in rational drug design, pharmacophore modeling has become an integrated part of drug discovery. The work described herein focuses on the use of ligand-based pharmacophore modeling to identify novel acetylcholinesterase inhibitors against Alzheimer’s disease. Starting with a small training set of known dual inhibitors of the Torpedo californica acetylcholinesterase (TcAChE), we generated a series of ligand-based pharmacophore models using the Molecular Operating Environment (MOE) software. The models were further used to screen the lead-like subset of the ZINC database. The top 100 molecules will be virtually screened against the TcAChE three-dimensional structure using Molegro Virtual Docker in order to prioritize hits for experimental testing.