Attacking Alzheimer's: Developing New Drugs Using Computational Modeling of Beta-Amyloid Protein Binding

Tripathi, Sanidhya (School: Arkansas School for Mathematics, Sciences and the Arts)

Alzheimer’s Disease (AD) is an irreversible, progressive neurodegenerative disorder that occurs gradually and results in symptoms such as memory loss and decreased thinking abilities. The common pathological hallmark leading to AD is the accumulation of Amyloid-Beta (Aß) plaques. Due the accumulation of the plaques on the brain, their insolubility leads to abnormalities in the patient. If a molecule binds to the Aß protein, it could lead to potential treatment. To propose new treatments for AD, the IC50 value is an essential parameter to know, because it determines the effectiveness and strength of binding to a protein. In this study, novel molecules were identified that bind to the active site of Aß. First, a correlation between reported IC50 values of fourteen chemicals and their energy gap, dipole moment, and total energy were analyzed. The best correlation was discovered between 1/IC50 values and total energy (R2 = 0.9279). Then, each identified molecule was virtually modified and its new IC50 value was determined utilizing Gaussian 09, a molecular modeling program, which was used to predict total energies. Some of the most useful modifications included the addition of oxygen (-O), chlorine (-Cl), and fluorine (-F) atoms. The results of this study can be used as a tool to finding novel, medically relevant new molecules for other neurodegenerative diseases and assist researchers in developing new drugs to treat AD.

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