THREAT AGENT DEFEAT MODELING AND TESTING

Non-canonical Amino Acid Parameterization Engine For Charmm Potentials

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Non-canonical or non-proteinogenic amino acids (ncAAs) provide numerous opportunities for rational introduction of additional functionality into peptides and proteins, either through solid phase peptide synthesis or genetic-code expansion and heterologous expression of encoded the protein modification. These novel biomolecules present both opportunities and challenges for chemical and biological defense. Modeling of these highly engineered biomolecules is essential, whether for designing beneficial new macromolecules or being able to understand and respond to future threats. In either case, structural characteristics of ncAA-containing peptides and proteins are often difficult to evaluate due to the limited availability of empirically resolved structures. In the absence of empirical data, modeling through scoring functions or molecular dynamics potentials, such as CHARMM, is commonly employed. Central to these models are sets of parameters that describe the internal degrees of freedom in a molecule, which are not readily available for ncAAs. In this work, we introduce a software package to generate CHARMM compatible parameters for ncAAs from quantum DFT calculations. Our motivation for this software is to reduce user intervention and analysis as much as feasible to efficiently generate potential parameters. Eighteen canonical and 94 non-proteinogenic residues were parameterized and evaluated in this work.

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