Conformational Adaptation of Linear Peptides for Anion Recognition in Water

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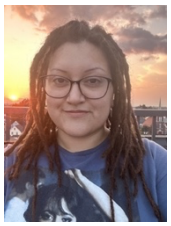

Abstract: Proteins bind anions in water through hydrogen bonds within low-polarity microenvironments which envelope the anion of interest, a feature often mimicked by synthetic cyclic or cage-like receptors. However, these designs diverge from naturally occurring peptide structures, limiting biological relevance and versatility. To address this, we designed linear hexapeptides using canonical amino acid residues to enable conformational dynamics that incline selective anion recognition. Glycine provided flexibility and backbone NH donors, phenylalanine promoted π–π stacking, and serine contributed additional hydrogen bonds (see figure) Peptides were synthesized via solid-phase peptide synthesis, purified by prepHPLC, and characterized using NMR, LCMS, and circular dichroism. Further binding studies were conducted with the aforementioned spectroscopy which are all dispatched in titration assays. Computational methods such as molecular dynamics and density functional theory are used to supplement our understanding of binding interface contacts. Our studies demonstrate selective binding of hydrogen sulfate in water, highlighting sequence-dependent selective recognition through minimalist peptide scaffolds. Future work will extend this approach to other biologically relevant anions and compare binding modes with nature's anion binding proteins through structural database analysis.