

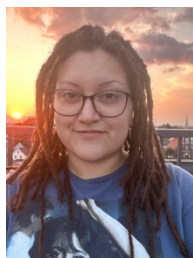
Palindromic Peptides: Anion Recognition and Stimuli-Responsive Hydrogel

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Abstract: Peptides offer remarkable functional versatility depending on their molecular environment. Here, we demonstrate how a single library of linear palindromic hexapeptides exhibits environment-dependent functionality, switching between selective anion recognition in a low-dielectric solvent and stimuli-responsive hydrogelation in aqueous solution. Inspired by natural proteins that bind anions within low-polarity microenvironments using hydrogen bonds, we designed minimalist scaffolds composed of canonical amino acids (glycine, phenylalanine, and serine) to encourage folding-driven binding without relying on complex cyclic or cage-like architectures. Peptides were synthesized via solid-phase peptide synthesis and characterized by NMR, LC-MS, and circular dichroism. NMR and CD titrations along with molecular dynamics simulations revealed sequence-dependent, selective binding of chloride in acetonitrile. Conversely, in aqueous media, anion selectivity was lost, but one sequence uniquely underwent self-assembly into a pH-stimuli-responsive hydrogel. Rheology and electron/atomic force microscopies (TEM, SEM, AFM) confirmed the formation of a mechanical network with distinct nanoscale morphology and elasticity in the kPa to MPa range. These findings highlight how minimalist linear peptides can bridge host–guest chemistry and materials science through solvent-driven functional switching. Future work will focus on extending the sequence-dependent selective recognition to other biologically relevant anions in solution state, and further study mechanical properties such as the stiffness of the hydrogel, along with examining enzymatic degradation for potential drug delivery system.