## 4 Joint AIC - SILS Conference



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## Exploring weak interactions realm with cyclic peptoids

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A variety of non-covalent interactions, such as hydrophobic effect, hydrogen bonding, Coulombic contacts, and van der Waals interactions, influence the proper protein folding [1]. Many investigations have shown that these conventional forces cannot be the only ones influencing protein folding, implying the involvement of weaker interactions. Thus, a plethora of "non-conventional" forces such as  $n\boxtimes\pi^*$  interactions [2], C5 hydrogen bonds [3], and C-HIXXXO hydrogen bonds [4] have emerged as co-protagonists to overall protein stabilization. Cyclic peptoids have recently been reported to be a simple and useful tool for the understanding of the aforementioned non-conventional interactions [5]. These N-substituted oligomeric glycines are peptidomimetic compounds that stand out due to their unique properties [6]. Aside from the possible applications, their solid state assembly has been extensively studied in recent years, revealing their ability to organize in a range of supramolecular structures [7].

The crystal structures of four cyclic dodecapeptoids, decorated with a different combination of propargyl and methoxyethyl side-chains, revealed an unprecedented cccctcccct (c = cis, t = trans) amide bond configuration (Figure 1), defining two enantiomorphic right- and left-handed polyproline type I helices bridged by trans residues. It was demonstrated that this conformation is supported by the same type of non-conventional contacts that are essential for protein folding, establishing peptoids as an exceptional framework to explore the impact of weak interactions governing molecular self-organization.

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