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STEPWISE CHEMICAL CONTROL IN THE FORMATION OF BETA-PEPTIDE ASSEMBLIES

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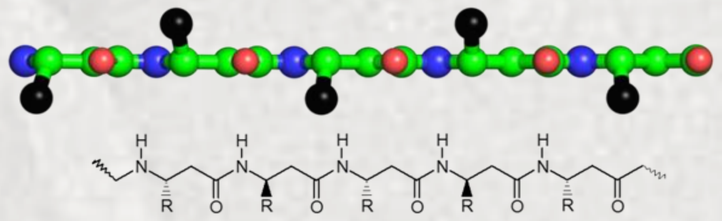
ABSTRACT

Peptidic foldamers are an important class of synthetic macromolecules and have gained high attention in different areas of nanotechnology, drug delivery and molecular biology. Small **manipulations in peptide sequences**: length, charge or amino acid chirality can lead to the formation of different morphological assemblies. We have recently demonstrated[1,2] that acyclic, lysine-rich, short beta-peptides can achieve nanostructures that closely mimic both the oligomerization and the filament formation of natural peptides. **Here, we show** how systematic small variations could affect assemblies formation. **Molecular dynamics simulations** combined with **electron microscopy** confirmed distinct levels of macromolecular structures: from oligomers to fibrillar bundles, by applying **single point mutations** or **N-terminal chemical modifications** in the sequences. These results suggest that the self-assembly process could be fine-tuned by sequence modification, allowing widespread applications where specific levels of assembly stages need to be maintained.

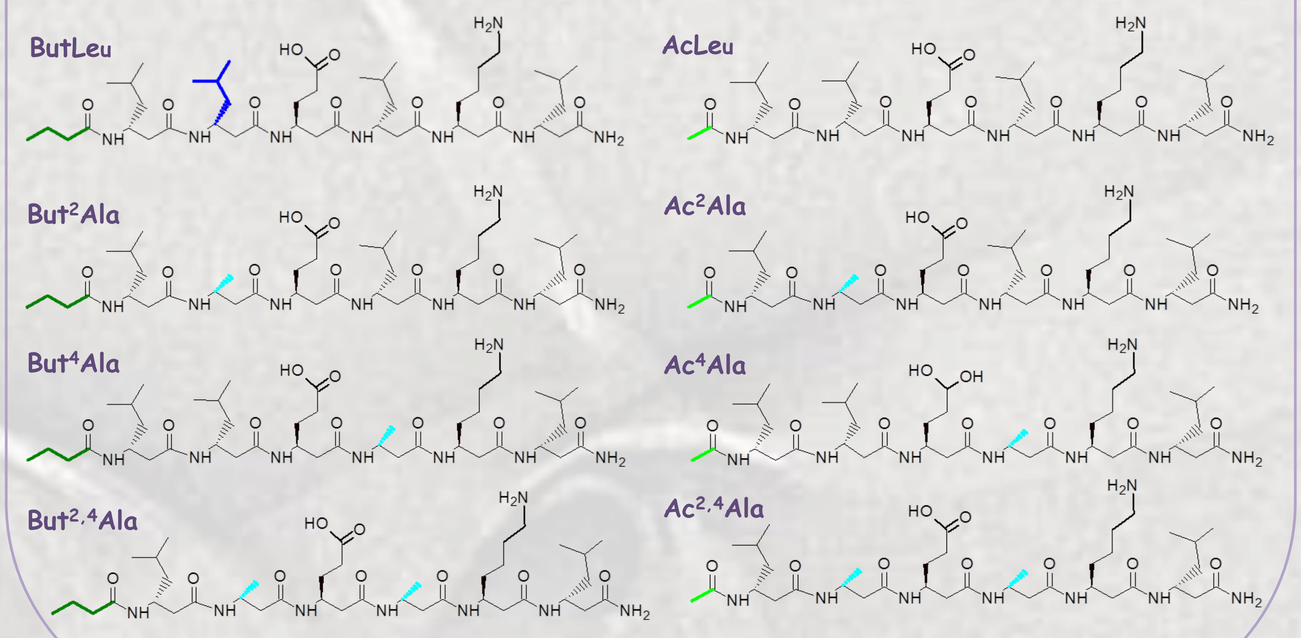
EXPERIMENTAL DESIGN

- lysine-rich, acyclic, **beta-hexapeptide** sequences, with alternating side chain chirality



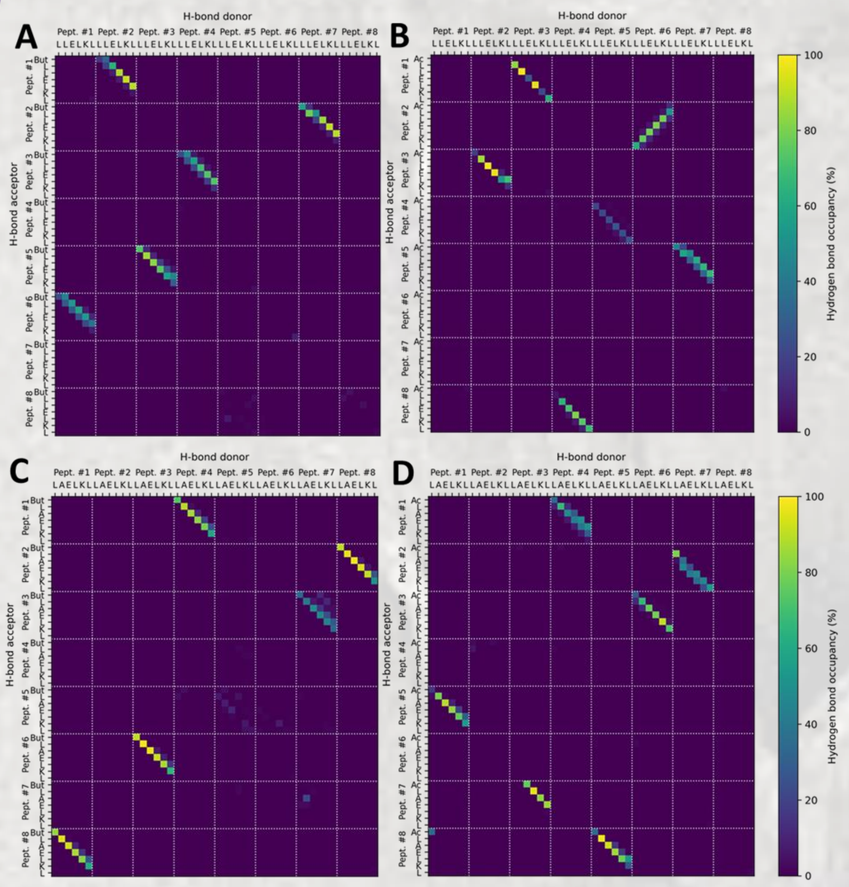
β³-heterochiral

- synthesized **β³-sequences**



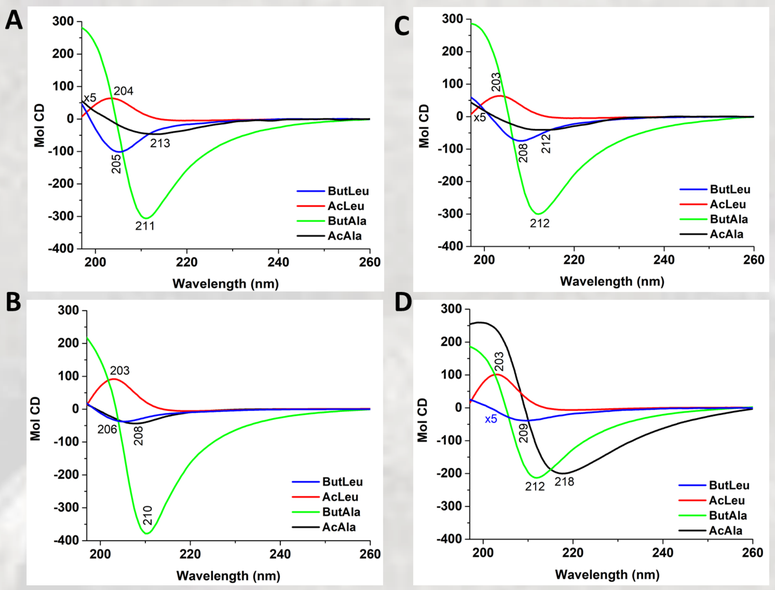
RESULTS - STRUCTURE & MORPHOLOGY

* MD simulations



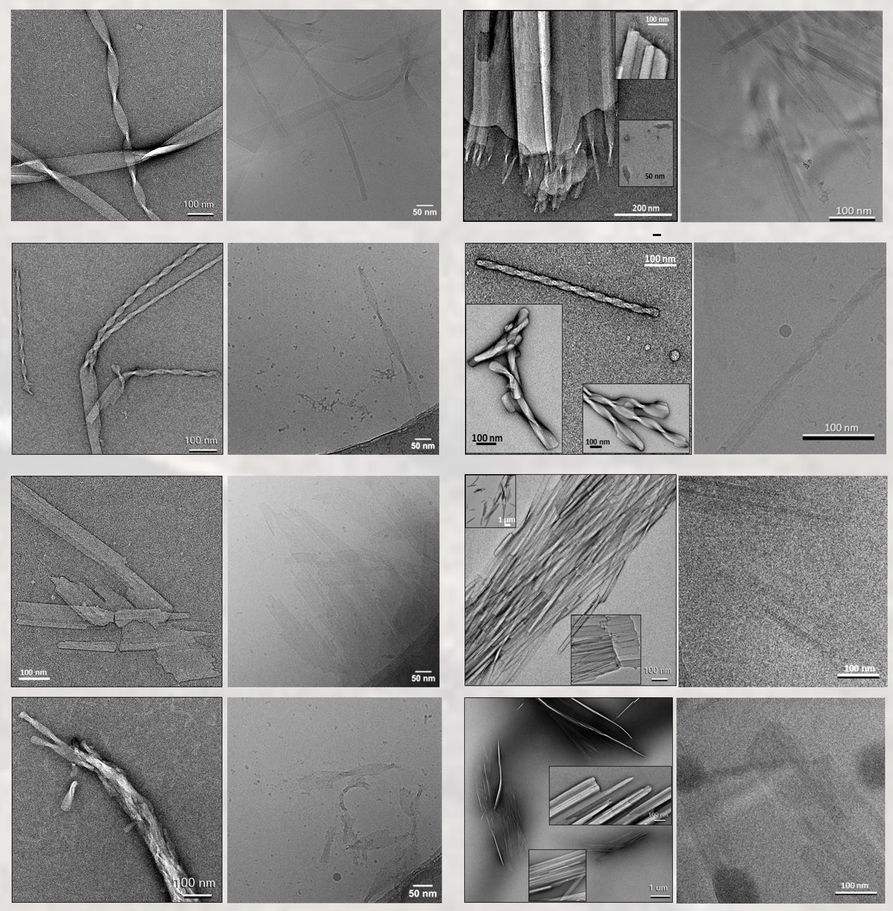
Interchain hydrogen bonds occupancy in octameric oligomers: ButLeu (A), AcLeu (B), ButAla (C) and AcAla (D).

* Molecular Spectroscopy secondary structure



CD spectra at a nominal peptide concentration of 100 μM (A and C) and 500 μM (B and D), respectively.

* Electron microscopy



TEM & cryo-EM images of ButLeu (A), AcLeu (B), ButAla (C) and AcAla (D).

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