Effects of amino acid substitution on chain packing in genetically engineered periodic polypeptides

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Abstract

Architecturally well-defined polymeric materials with precisely controlled chain length, sequence, stereochemistry and interchain interactions can be produced using the fidelity of biological protein synthesis. A set of periodic protein polymers of repeating unit sequence (AlaGly)$\sb3$-X-Gly, where X is Asn, Phe, Ser, Val, or Tyr, has been produced to examine the relation between amino acid residue volume and crystalline unit cell dimensions. The proteins were overexpressed in Escherichia coli and purified on the basis of acid/ethanol precipitation or insolubility in aqueous sodium dodecyl sulfate. The monodisperse populations of purified polypeptides were processed in the form of oriented crystalline mats by precipitation from formic acid under mechanical shear. Analysis by infrared spectroscopy and x-ray diffraction showed that the artificial proteins adopt a chain-folded lamellar structure comprised of anti-parallel β-sheets with polar orientation and three-residue folds at the lamellar surface; as seen for ((AlaGly)$\rm\sb3GluGly\rbrack\sb{36}$ (Krejchi, 1997). The x-ray diffraction signals for each of the (AlaGly)$\sb3$-X-Gly polymers were indexed on an orthorhombic unit cell with invariant a (hydrogen bond direction) and c (chain direction) axes. However, the b-axis (sheet stacking direction) spacing increased linearly with the volume of the substituted amino acid, indicating a linear relationship between the average intersheet stacking dimension and the volume of the residue at position X. Analysis of the Phe variant utilizing proton spin diffusion in solid state NMR spectroscopy, provided direct evidence for the confinement of Phe residues at the lamellar surface. The chain-folded lamellar architecture adopted by this family of periodic polypeptides accommodates a wide range of residues differing in charge, steric bulk, and hydrophobicity. These results provide a new approach to the controlled engineering of intermolecular interactions in polymeric solids. ^

Subject Area

Molecular biology|Biochemistry|Polymer chemistry

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