3 Aim of the Work

As discussed in Chapter 2, fluorocarbon-substituted amino acids are very interesting building blocks in peptide and protein chemistry e.g. as NMR label, to significantly improve the metabolic stability and the biological activity of peptides and peptidomimetics or to stabilize protein structure and dictate ther folding of these biomolecules. However, the applicability of fluorinated amino acid side chains for the rational design of protein domains and peptide-protein interaction surfaces is severely limited due to a lack of knowledge about fundamental properties of C-F containing moieties. Issues such as the capability of organic fluorine to act as hydrogen bond acceptor, the steric demand of fluoroalkyl groups, the influence of fluorine substitution on hydrophobicity of alkyl moieties, as well as the polarization of alkyl hydrogen atoms in proximity to the fluorination site are extensively discussed in literature. A further controversy deals with the nature of structural protein stabilization by perfluorination of hydrophobic interaction cores.

The aim of this work was to develop a peptide-based screening system that can be applied for the systematic investigation of the properties fluoroalkyl-substituted amino acid side chains exert in a native protein environment. The model system was evaluated in respect to its sensitivity towards differently modified amino acid side chains and to the reproducibility of the results from the applied screening methods. With this peptide-based screening system a systematic scan of side chain-modified as well as $C^{\alpha,\alpha}$-dialkylated amino acids that vary in side chain length and degree of fluorination, regarding their interaction properties with native polypeptides, should be performed.
Based on this model system, libraries had to be screened to find the preferred interaction partners for the investigated fluorinated building blocks out of the pool of the twenty canonical amino acids. Therefore, a phage display screening system was to be developed and applied.