5. Aim of the Work

It is widely accepted that the conformational transition from the native, mostly well defined and functional protein structure to the β-sheet rich amyloid form is the most crucial event in the entire process of amyloid formation. In this context, especially the impact of changed environmental conditions that can trigger these structural conversions has especially attracted the interest of many researchers in recent years. An elucidation of the molecular interactions that occur during the structural transformation and the consecutive formation of amyloids on a molecular level is still a challenge. The low solubility of amyloid forming peptides and the mostly poor synthetic accessibility restrict the spectrum of analytical techniques and, thus, hamper a detailed characterization. Therefore, the development of small peptide models with a native-like amyloid formation tendency, but improved properties is of paramount importance.

The aim of this work was to establish a coiled coil based model peptides that can be used to study the interplay between primary structure and environmental conditions on the amyloid formation process. The first step was to fuse the design principles of an idealized 26 residue coiled coil peptide with features known from β-sheets and amyloids to yield a peptide system that slowly associates into fibrils at stationary native-like conditions. Subsequently, functionalities that sensitively react on environmental conditions, namely, a varying pH or the presence of transition metal ions, should be developed and incorporated into the amyloid forming coiled coil based model peptide system. The gained sequences had to be investigated by a battery of biophysical techniques with regards to their pH or metal ion dependent amyloid formation properties.