Figure S1:

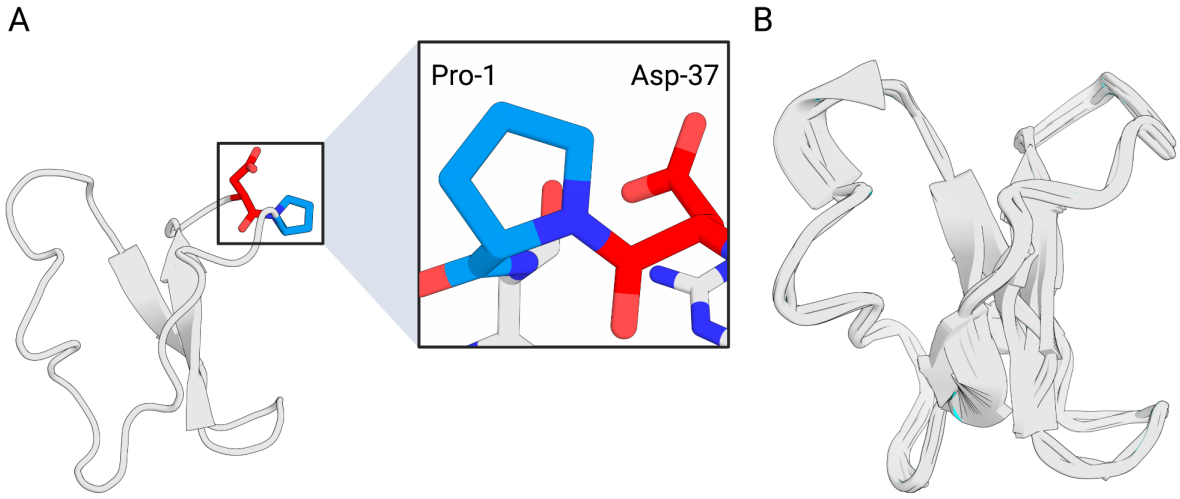

Figure S1: Cyclic offset to relative positional encoding in AfCycDesign enforces N-to-C terminal cyclization and is invariant to circular permutations of the sequence

(A) Peptide structures predicted with AfCycDesign show correct bond connectivity and geometry at the termini. (B) Cartoon overlay of 37 predicted models for each circularly permuted sequence of a native peptide with cyclic offset applied in AfCycDesign.

Figure S2:

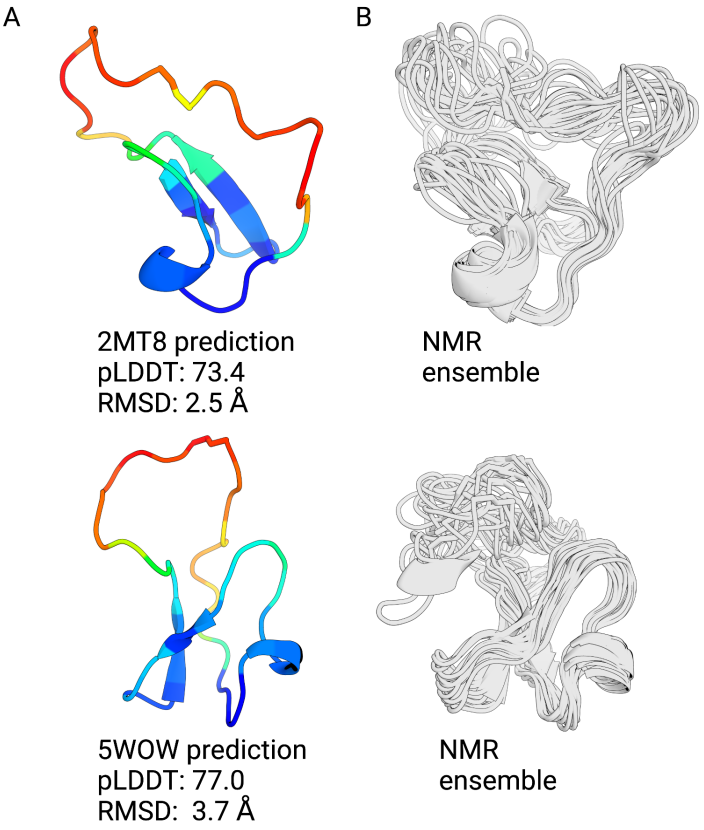

Figure S2: Regions predicted with low confidence match the flexible regions in the NMR structures

(A) Representative peptides with pLDDT lower than 0.85. Cartoon representations are colored from regions of high confidence (blue) to low confidence (red) based on per residue pLDDT. RMSD is calculated against all ensemble members, and the lowest backbone heavy atom RMSD is reported. (B) NMR ensemble of the peptide aligned to the predicted model.

Figure S3:

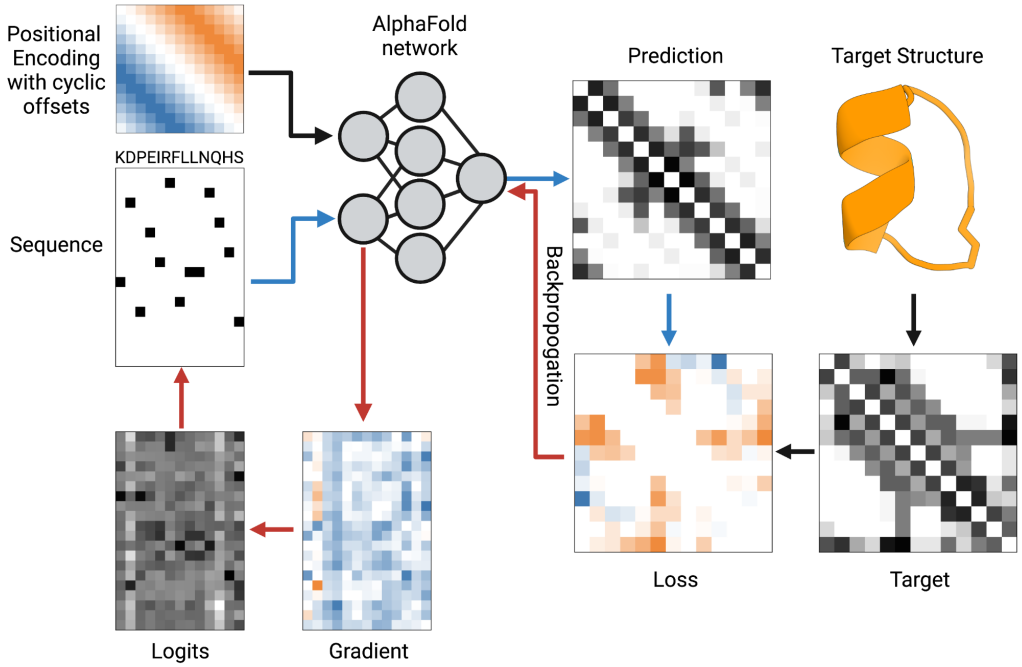

Figure S3: Overview of the sequence design approach in AfCycDesign
Given the input sequence and relative positional encoding with cyclic offset, AlphaFold is used to predict the distogram (distribution of distances between every pair of positions). The loss is defined as the categorical-cross entropy (CCE) between the output distogram and the desired distogram extracted from the desired structure. At each iteration, the gradient is computed to minimize the CCE. The gradient is then applied to a proxy variable we term "logits". The one-hot encoding of the argmax of the logits is then used as the input sequence for the next iteration.