Journal Name

COMMUNICATION

Supporting Information

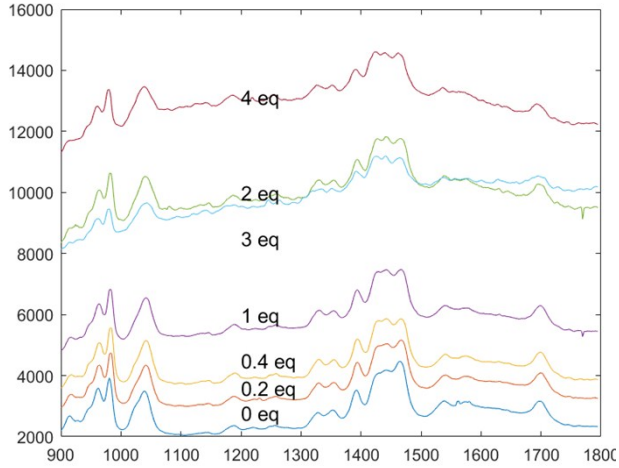

Fig. S1. Raw UVRR spectra. The processed UVRR spectra in Fig. 3 were obtained by smoothing and subtraction of autofluorescence.

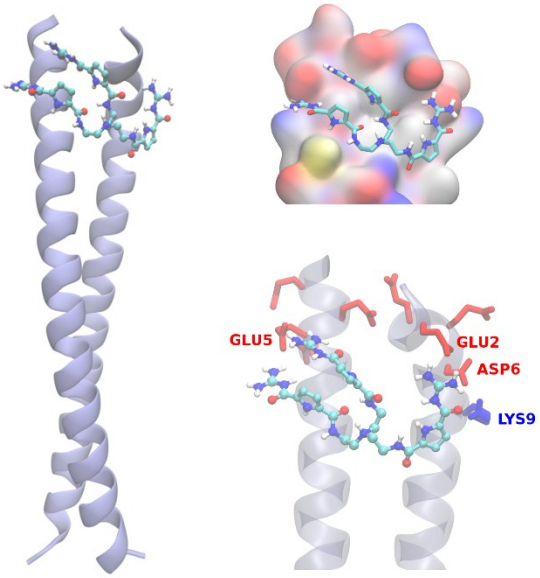

Fig. S2. Predicted binding mode of the tri-armed GCP-based supramolecular ligand with the Leucine Zipper dimer near N-terminus. Overview of the entire protein-ligand complex(Left). Corresponding molecular surface representation, same colour code as in Figure 4 (Top right). Individual acidic and basic sidechains involved in protein-ligand interactions are shown (Bottom right).

Docking studies

The best binding pose (Figure 6) showed a binding affinity of -8.1 kcal/mol, which indicates strong binding of the ligand, according to benchmarking studies of AutoDock Vina results against free energy calculations (see reference 15, main text). The next best pose (Figure S2) showed a binding affinity of -7.4 kcal/mol.

Re-clustering the docked conformations

The AutoDock Vina program performs a clustering of docked conformations internally. As a result, the output consists of best ranking conformations and their binding affinity values. We have analyzed these conformations from 5 flexible docking trials (total of 100 conformations) and calculated the histogram of root mean squared deviation (rmsd) of the ligand. We used a 3.0 Å cutoff for clustering of data. The clustering analysis showed that the population of the highest occupied cluster for the docking performed in the middle region of Leucine Zipper dimer is 6% and for the docking performed at the N-terminal region is 5%. This indicates that the docked conformations are highly scattered. This is due to the fact that there is no well defined binding pocket in the Leucine Zipper dimer and the supramolecular ligand exhibits high degrees of freedom. Because of these reasons, we used the binding affinity as the main selection criterion for the identification of best binding poses.

Rigid docking

A rigid docking with a search space covering the entire Leucine Zipper dimer was performed. The best binding pose in terms of docking score is shown in Figure S3. It is interesting to note that, the binding site predicted by the rigid docking approach that performs a conformational search over the entire protein surface is the same as the binding site predicted by flexible docking. This further supports that the binding mode we identified earlier is favorable. The binding affinity calculated for this mode using the rigid docking approach is -6.7 kcal/mol.

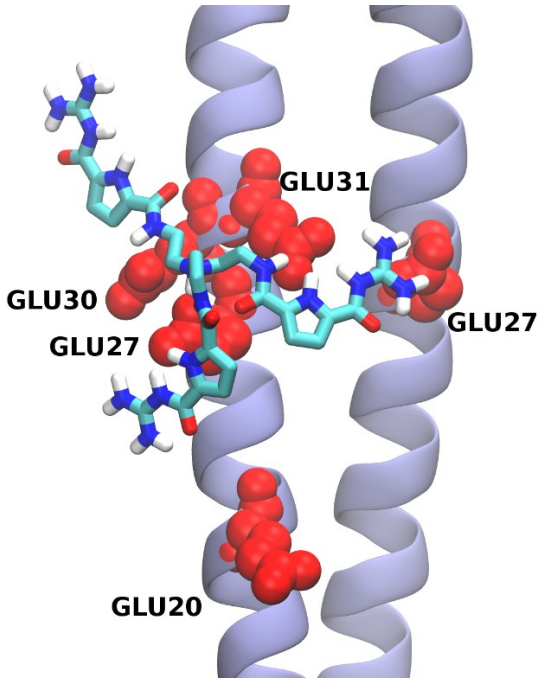

Figure S3. The predicted binding mode of the supramolecular ligand with the Leucine Zipper dimer obtained from rigid docking (covering the entire protein surface) corroborates the result from the flexible docking calculations. The key GLU residues involved in binding (Figure 4) are shown as red spheres.