Design and optimization of mimetic peptide probes

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The design and generation of peptides capable of mimicking the binding sites of proteins represents a promising strategy for the exploration and modulation of protein interactions. Synthetic peptides have proven an excellent type of molecule for the mimicry of protein sites because such peptides can be generated as exact copies of protein fragments and can be subjected to further optimization.

We applied this approach to an oligomeric protein complex that is composed of hexameric protein rings and plays an important role for viral replication.
We investigated the different binding regions of the oligomer interface and designed mimetic peptides that contain the key interacting residues. The peptides were optimized for stronger binding to the interaction partner. For validation, the optimized and non-optimized peptides were compared with respect to their binding behavior using molecular dynamics simulations.

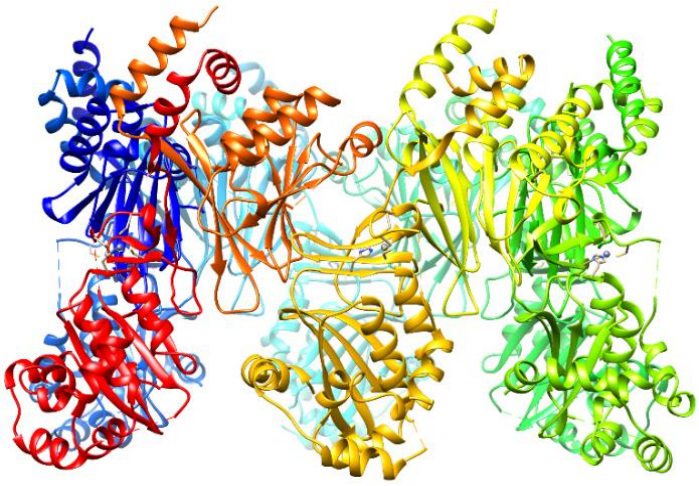

Figure: Hexameric protein ring

The computer-assisted analyses showed increases in binding stability for both suggested peptides with respect to the number of total contacts. The evaluation of the respective RMSDs supports this finding. While the total number of contacts in the optimized peptides were higher, the initial structural properties of the interactions were not preserved during the course of the simulation. This suggests that additional modifications may be required to increase the conformational stability of the suggested peptides.