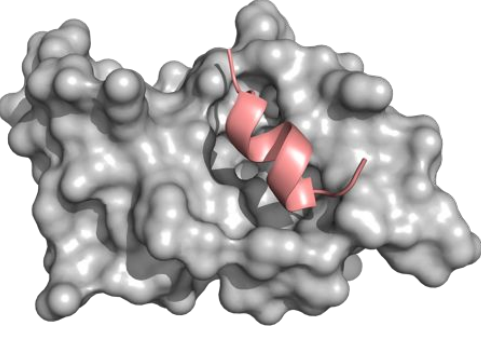
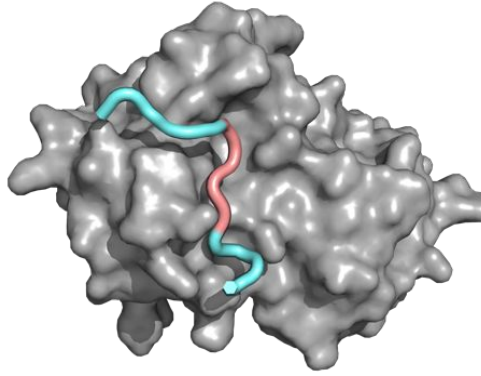
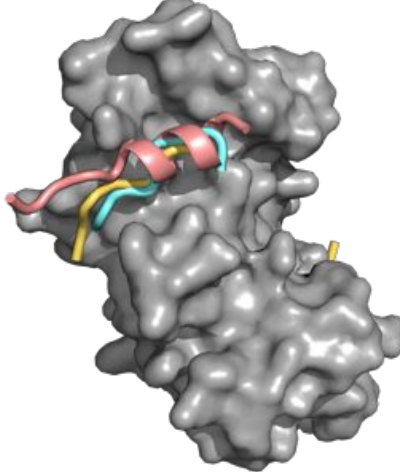
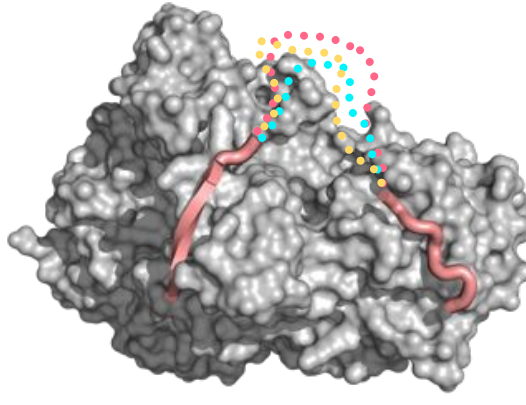
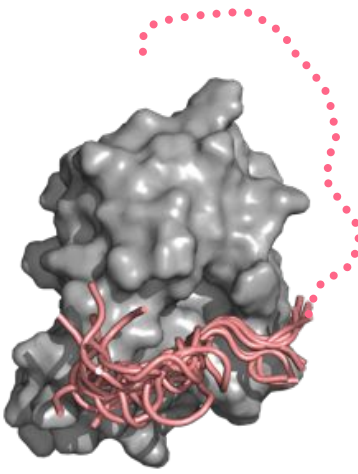
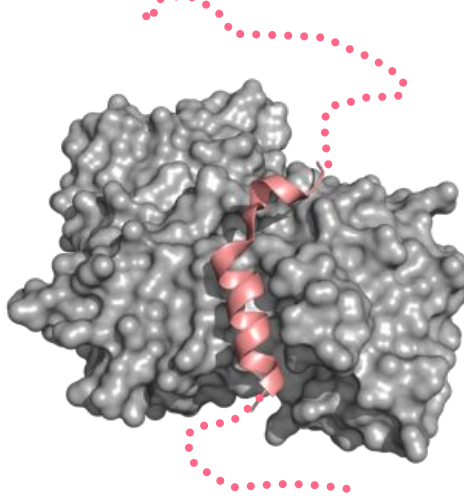
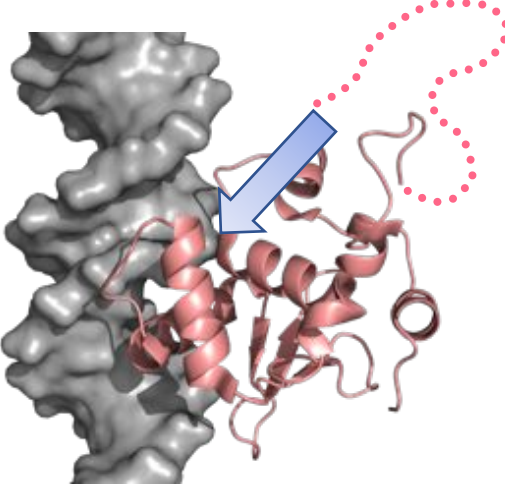
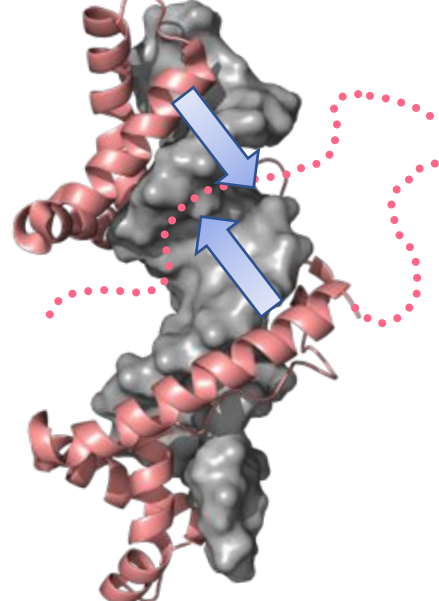
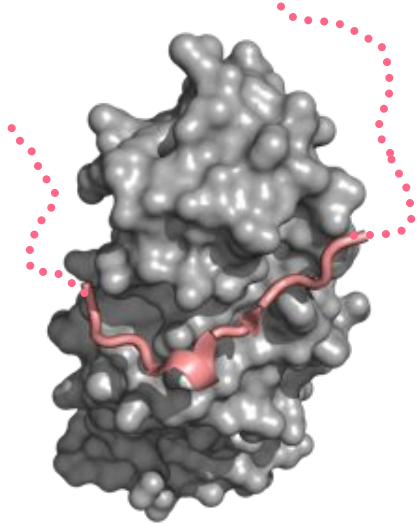
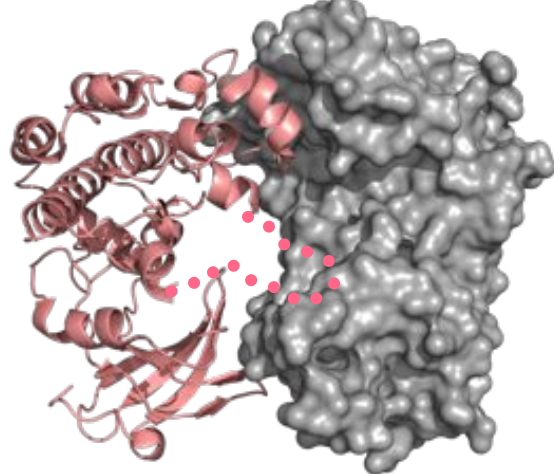
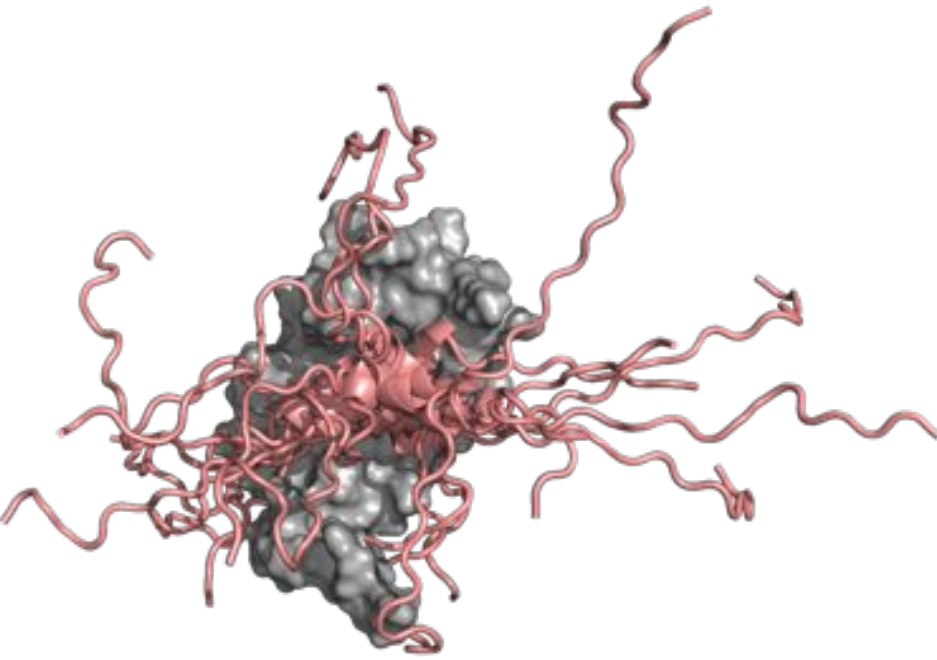
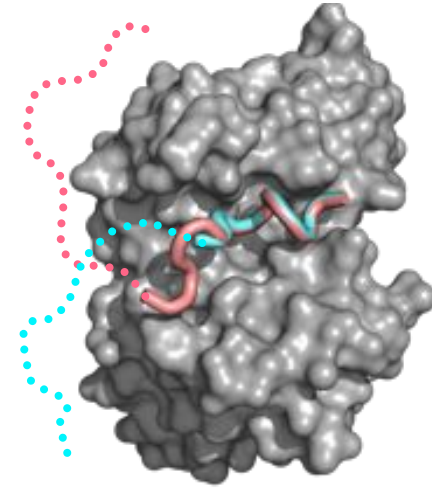
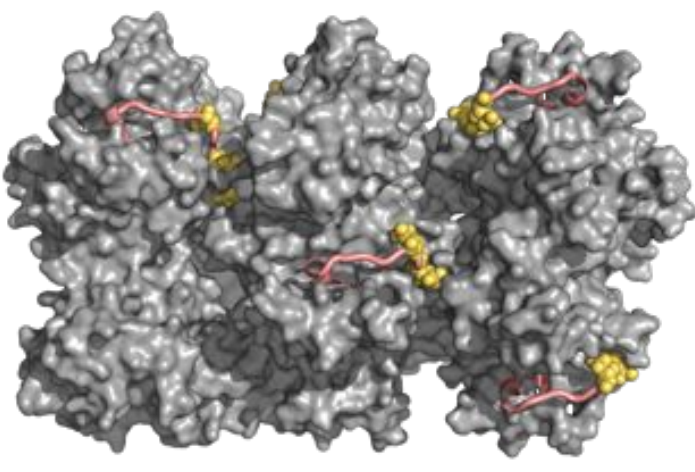
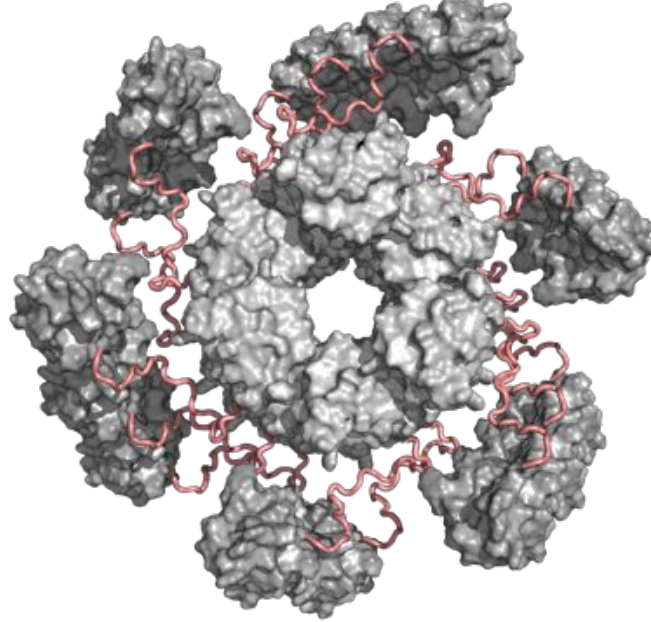


Period	Proposal	Representative structures		References
Phase 0 (2004 – 2007)	Short recognition elements for ID interactions	 p53 – Mdm2 (1ycq) <i>preformed structural element</i>	 p27^{Kip1} – Cyclin (1su) <i>linear motif</i>	Fuxreiter et. al. (2004) J. Mol. Biol. 338, 1015-26. Fuxreiter et. al. (2007) Bioinformatics 23, 950-6.
Phase 1 (2008)	Fuzzy complexes: conformational heterogeneity in protein interactions	 MKK7 – JNK1 (5csf,5csi,5csj) <i>polymorphism</i>	 Ste5 – Fus3 (2f49) <i>dynamic disorder</i>	Tompa and Fuxreiter (2008) Trends Biochem. Sci. 33, 2-8.
Phase 2 (2008 – 2012)	Functional implications of fuzziness	 SF1 – U2AF⁶⁵ (1o0p) <i>affinity improvement</i>	 WH2 – actin (3u9d) <i>polymerization, sequestration</i>	Fuxreiter and Tompa and (2012) Adv Exp Med Biol. 725, 1-14. Fuxreiter and Tompa and (2011) <i>book</i> New York: Landes BioScience/Springer
Phase 3 (2011 – 2012)	Molecular mechanisms of fuzzy interactions	 Ets-1 – DNA (1mdm) <i>entropy modulation</i>	 HMGB1 – DNA (2gzk) <i>competitive binding</i>	Fuxreiter et. al. (2011) Trends Biochem. Sci. 36, 415-23 . Fuxreiter (2012) Mol Biosyst. 8, 168-77 .
Phase 4 (2012 – 2017)	Context-dependence of fuzzy interactions	 PiP5K1c – AP-2 (3h1z) <i>tissue-specificity (AS)</i>	 RIP3 – MLKL (4m69) <i>programmed necrosis (PTM)</i>	Buljan et. al. (2012) Mol Cell. 46, 871-83. Miskei et. al. (2017) FEBS Lett. 591, 2682-95.
Phase 5 (2015 – 2017)	Stochastic structure-function relationships	 GCN4 – Med15 (2lpb) <i>fuzzy interface increases transcription by synthetic activator domains</i>	 MSP2 – mAB6D8 (4qy8, 4qxt) <i>transient interactions enable strain-specificity of malaria antigens</i>	Sharma et. al. (2017) FEBS Lett. 589, 2533-42. Miskei et. al. (2017) Nucleic Acids Res. 45:D228-D35.
Phase 6 (2016 – 2018)	Fuzziness in higher-order protein assemblies	 Ire1 oligomer (3fbv) <i>autophosphorylation driven oligomerization</i>	 ASC inflammasome (3j63) <i>shift from autoinhibition to polymerization</i>	Wu and Fuxreiter (2016) Cell 165:1055-66. TuuSzabo, Fuxreiter (2018) BioRxiv. doi: 10.1101/248062.