

Contents

Summary	I
Zusammenfassung	III
Contents	V
1 Introduction	1
1.1 Ligand-binding of proteins	1
1.1.1 PDZ domains	4
1.1.2 Bromodomains	5
1.2 Computational methods and analysis tools	7
1.2.1 MD simulations	8
1.2.2 Cut-based one-dimensional free energy profiles and optimization of the reaction coordinate	9
1.3 Structure of the thesis	13
Bibliography	15
2 Peptide binding to the PDZ3 domain by conformational selection	
<u>Steiner, S. and Caffisch A. <i>Proteins: Structure, Function and Bioinformatics</i>, 80(11): 2562-2572, 2012</u>	21
3 Peptide unbinding from PDZ2	41
3.1 Introduction	41

3.2 Results and Discussion	42
3.3 Methods	48
Bibliography	51
4 Kinetic response of a photo-perturbed allosteric protein	
Buchli, B., Waldauer, S.A., Walser, R., Donten, M., Pfister, R., Blöchliger, N., <u>Steiner, S.</u> , Cafisch, A., Zerbe, O. and Hamm, P.; <i>Proceedings of the National Academy of Sciences</i> , 110(29): 11725-11730, 2013	53
5 Does bromodomain flexibility influence histone recognition?	
<u>Steiner, S.</u> , Magno, A., Huang, D. and Cafisch, A.; <i>FEBS letters</i> , 587(14): 2158-2163, 2013	69
6 Structured water molecules in bromodomains binding site can be dis- placed by cosolvent	
Huang, D., Rossini, E., <u>Steiner, S.</u> and Cafisch, A.; Article in press at <i>ChemMedChem</i>	91
7 Mechanism and kinetics of acetyl-lysine binding to bromodomains	
<u>Steiner, S.</u> , Magno, A. and Cafisch, A.; <i>Journal of Chemical Theory and Computation</i> , 9(9): 4225-4232, 2013	111
8 Conclusions	133
Acknowledgements	135
List of publications	137
Curriculum Vitae	139