Multiple-binding-site mechanism explains concentration-dependent unbinding rates of DNA-binding proteins

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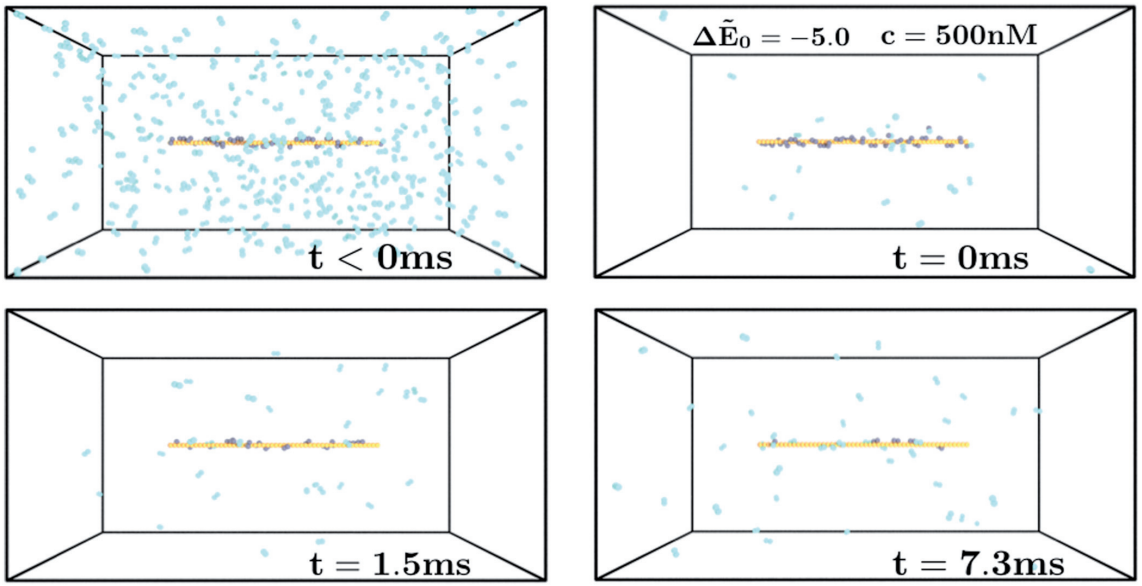
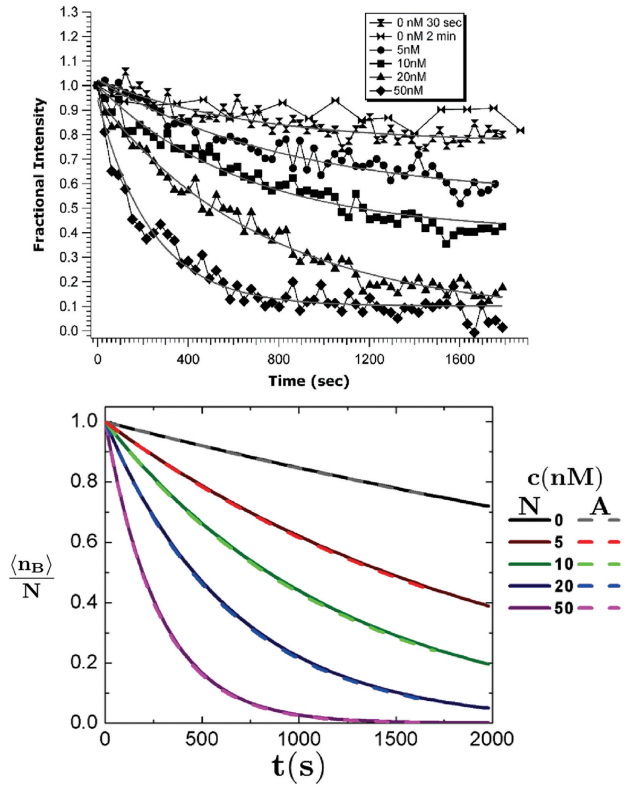
Recent experimental work has demonstrated concentration-dependent unbinding rates of proteins from DNA using direct fluorescence visualization of the bacterial nucleoid protein Fis (Graham, et al. 2011). Using a combination of coarse-grained simulation and theory we demonstrate that such behavior can be explained by taking into account the dimeric nature of the protein, which permits partial dissociation and exchange with other proteins in solution. Concentration-dependent unbinding is generated by this simple model, quantitatively explaining experimental data. This effect is likely to play a major role in determining binding lifetimes of proteins *in vivo* where there are very high concentrations of solvated molecules.





Simulations of dimeric binding (left) are performed where initially bound proteins (dark blue) are tagged and slowly leave the simulation box. The leaving of these tagged molecules demonstrates quantitative matching between experimental data (Graham, et al. 2011, upper right) and both numerical and analytical calculations (bottom right).

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