

Dynamics of the Autoinhibited Transcription Factor RfaH

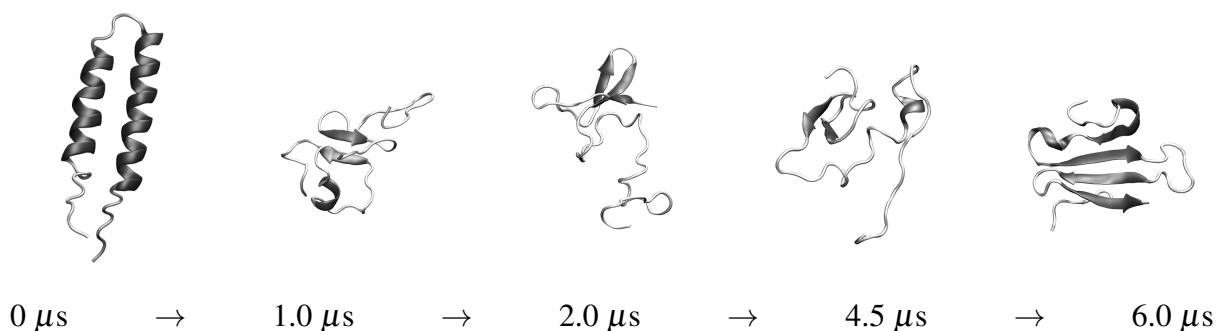
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Transcription factors control the flow of genetic information from DNA to messenger RNA rendering understanding of their function highly important for the modulation and optimization of protein expression. Molecular and structural biology have provided a wealth of information for transcription factors, however, the dynamic processes underlying their activation are yet not fully understood.

We applied molecular dynamics (MD) simulations to supplement the structural information available for the transcription factors RfaH from *Escherichia coli* and NusG from *Thermotoga maritima*. Both proteins are autoinhibited proteins; in NusG, the β -barrel C-terminal domain (CTD) is tightly bound to the larger N-terminal domain (NTD), whereas RfaH consists of a structurally similar NTD and a bound CTD in α -helical conformation[1]. Upon activation of RfaH, the CTD is released and undergoes a large-scale $\alpha \rightarrow \beta$ structural transition[2].

Investigation of RfaH under different environmental conditions revealed that not only high temperatures, but also a decrease in ionic strength significantly enhances CTD dynamics. Despite this enhanced dynamics, none of the conditions investigated caused CTD dissociation suggesting that this process needs to be triggered by the interaction with DNA or other proteins of the transcription machinery. Further, we were able to see a transition from the α - to a β -conformation in a microsecond long MD simulation of the isolated CTD.



[1] Belogurov, G.A., Mooney, R.A., Svetlov, V., Landick, R. and Artsimovitch, I., *EMBO J*, **2009**, 28, 112–122.

[2] Burmann, B.M., Knauer, S.H., Sevostyanova, A., Schweimer, K., Mooney, R.A., Landick, R., Artsimovitch, I. and Rösch, P., *Cell*, **2012**, 150, 291–303.