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Unifying Concepts in Catalysis

UniCat Colloquium

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Macromolecular binding in competition: how the energetic cost of a 'menage a trois' stabilizes molecular pairs

The specificity of molecular recognition is important to molecular self-organization. In the highly crowded molecular environment of the cell, a myriad of different molecular receptor pairs recognize their binding partner with astonishing accuracy. It is usually admitted that the affinity of recognizer pairs only depends on the nature of the binding molecules, and that the corresponding binding constants are sufficient to describe their interaction. Here, we consider the molecular recognition of short DNA oligonucleotide single strands in thermal equilibrium. We experimentally show that a better matching oligonucleotide can prevail against a disproportionally more concentrated competitor that exhibits reduced affinity due to a mismatch. The magnitude of deviation from the simple picture above may reach several orders of magnitude. The effective molecular affinity of a given strand remains elevated only as long as the better matching competitor is not present. We investigate the situation using different fluorescence based techniques. We interpret our observations based on an energy-barrier of entropic origin that occurs if two competing oligonucleotide strands occupy the same probe simultaneously.

In a second part of my talk, I will present recent experiments on in vitro expression. We have constructed a methylation dependent transcription regulator, using the methylation binding-domain, MBD, from the human transcriptional element MeCP2. Although regarding their structure, prokaryotic and eukaryotic transcriptional elements seem to have nothing much in common, MBD performs as a highly efficient regulator in an E. coli, in vitro transcription-translation system. In spite of its small footprint of about two base-pairs, the performance is highly specific to the human BDNF promoter sequence. We attribute this striking observation to cooperative transitions within DNA. However, to understand the problem entirely, we believe that the competition of binding microstates needs to be addressed along the same lines as in the first part of this talk.

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TU Berlin, Institute of Chemistry
Straße des 17. Juni 115, 10623 Berlin

Building C, Lecture Hall **C 264**

Prof. Budisa (TUB)
Organizer

Coffee and cake will be served 30 minutes before the lecture. Guests are cordially invited to attend!
Prof. Dr. Matthias Driess - Chair of the Cluster of Excellence UniCat - www.unicat.tu-berlin.de