Universität Bielefeld Fakultät für Physik

Physikalisches Kolloquium

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Insights into target recognition by CRISPR-Cas complexes from single-molecule mechanical measurements

The recently discovered CRISPR-Cas enzymes are promising tools in biotechnology and medicine. Central part of these enzyme systems are large protein complexes harboring a short RNA. The RNA promotes recognition of complementary nucleic acid targets by base pairing. The target recognition is, however, highly promiscuous, such that multiple mispairs between RNA and target strand are allowed. This causes technologically undesired off-target binding. Here we investigate the recognition of off-target sites by the CRISPR-Cas surveillance complex Cascade using mechanical experiments on single DNA molecules. This allows us to resolve the dynamics of the RNA base-pairing with the target. We find that mispairs act as barriers that stall the hybridization process but that can be overcome by thermal fluctuations. Based on these observations we developed a random walk model that can quantitatively describe the dynamics of the target recognition process by the investigated CRISPR-Cas system.

Montag, 08.01.2018, 16:15 Uhr
Ort: Hörsaal 6