

Comparison between force signal and DNA sequence: A proposed novel mechanism for DNA sequence determination

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Mol Switch Deliverable D4.3

Summary

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Due to recent theoretical (Lubensky and Nelson, Phys.Rev.E65,031917(2002)) and experimental (Danilowicz et al., PNAS,100, 1694 (2003)) results, it appears that the unzipping of DNA at constant force exhibits multiple metastable intermediates that makes its sequencing by that technique a very challenging task with little chance of success.

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Aims of Deliverable

With the help of magnetic tweezers we will unwind a large palindromic DNA, generating a cruciform structure. We will then pull on that molecule with optical tweezers and measure the force required to break successive bonds (between 20 and 30 pN). Because the extent of the resulting denaturation bubble, i.e. the length of the single strands, is controlled by amount of coiling, we will be able to control the amount of elastic energy they store and should in principle be able to achieve the sensitivity required for the detection of the breaking of a single base-pair. Preparation of proteins and DNA substrates. The attachment of these substrates to suitably derivatised AFM tips, or surfaces, will be confirmed using local facilities. Force measurement of the same phenomena using the same palindromic DNA, but with a calibrated AFM system (see Workpackage 2), will allow confirmation of the accuracy of the force measurements.

Tasks scheduled:

1. Show the influence of DNA sequence upon stability of dsDNA formation and separation forces using the Magnetic Tweezer Setup for force measurement.

Results achieved:

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Conclusion:

Due to recent theoretical (Lubensky and Nelson, Phys.Rev.E65,031917(2002)) and experimental (Danilowicz et al., PNAS,100, 1694 (2003)) results, it appears that the unzipping of DNA at constant force exhibits multiple metastable intermediates that makes its sequencing by that technique a very challenging task with little chance of success.