



Review

# Biophysical characterization of DNA binding from single molecule force measurements

Kathy R. Chaurasiya<sup>a</sup>, Thayaparan Paramanathan<sup>a</sup>, Micah J. McCauley<sup>a</sup>,  
Mark C. Williams<sup>a,b,\*</sup>

<sup>a</sup> Department of Physics, Northeastern University, 111 Dana Research Center, Boston, MA 02115, United States

<sup>b</sup> Center for Interdisciplinary Research on Complex Systems, Northeastern University, 111 Dana Research Center, Boston, MA 02115, United States

Received 16 February 2010; received in revised form 19 May 2010; accepted 20 May 2010

Available online 4 June 2010

Communicated by M. Frank-Kamenetskii

## Abstract

Single molecule force spectroscopy is a powerful method that uses the mechanical properties of DNA to explore DNA interactions. Here we describe how DNA stretching experiments quantitatively characterize the DNA binding of small molecules and proteins. Small molecules exhibit diverse DNA binding modes, including binding into the major and minor grooves and intercalation between base pairs of double-stranded DNA (dsDNA). Histones bind and package dsDNA, while other nuclear proteins such as high mobility group proteins bind to the backbone and bend dsDNA. Single-stranded DNA (ssDNA) binding proteins slide along dsDNA to locate and stabilize ssDNA during replication. Other proteins exhibit binding to both dsDNA and ssDNA. Nucleic acid chaperone proteins can switch rapidly between dsDNA and ssDNA binding modes, while DNA polymerases bind both forms of DNA with high affinity at distinct binding sites at the replication fork. Single molecule force measurements quantitatively characterize these DNA binding mechanisms, elucidating small molecule interactions and protein function.

© 2010 Elsevier B.V. All rights reserved.

**Keywords:** Force spectroscopy; DNA binding; DNA melting; DNA replication; Nucleic acid chaperones

## Contents

1. Introduction	300
1.1. Single molecule force spectroscopy techniques	301
1.2. Stretching single DNA molecules	301
1.2.1. Models of polymer elasticity	302
1.3. Force-induced structural transitions	302
1.3.1. Glyoxal binds ssDNA bases exposed in the force-induced melting transition	303
1.3.2. Visualizing force-induced melting with intercalators and SSBs	304

\* Corresponding author at: Department of Physics, Northeastern University, 111 Dana Research Center, Boston, MA 02115, United States. Tel.: +1 (617) 373 3677; fax: +1 (617) 373 2943.

E-mail address: [mark@neu.edu](mailto:mark@neu.edu) (M.C. Williams).

2.	DNA binding ligands: Small molecules . . . . .	304
2.1.	Cross-linkers . . . . .	305
2.2.	Intercalators . . . . .	305
2.3.	Groove binders . . . . .	309
2.4.	Multiple and complex binding modes . . . . .	309
2.5.	Classification of different binding modes . . . . .	311
3.	Double-stranded DNA binding proteins . . . . .	312
3.1.	Packaging DNA: Histones and chromatin . . . . .	312
3.1.1.	Fundamental interactions: Histones and nucleosomes . . . . .	312
3.1.2.	Higher order interactions: Unraveling chromatin . . . . .	313
3.2.	Bending DNA and distorting chromatin: High mobility group proteins . . . . .	313
3.2.1.	HMGB alters the elasticity of dsDNA . . . . .	314
3.2.2.	Distributions of bending angles and enhanced DNA flexibility . . . . .	315
3.2.3.	Stabilizing dsDNA . . . . .	316
3.3.	The bacterial nucleoid: Comparisons to eukaryotes . . . . .	318
3.3.1.	IHF binds with sequence specificity . . . . .	318
3.3.2.	HU and non-specific binding . . . . .	318
3.3.3.	Non-specific H-NS binding dynamically bridges DNA . . . . .	319
4.	Single-stranded DNA binding proteins . . . . .	319
4.1.	Bacteriophage SSB proteins . . . . .	319
4.1.1.	T7 gp2.5 and T4 gp32 preferentially bind ssDNA . . . . .	320
4.1.2.	T7 gp2.5 and T4 gp32 slide on dsDNA in search of exposed ssDNA . . . . .	321
4.1.3.	DNA binding mechanisms of bacteriophage SSB proteins . . . . .	323
4.2.	Bacterial SSB proteins . . . . .	324
4.2.1.	<i>E. coli</i> SSB binding modes to ssDNA are salt-dependent . . . . .	324
4.2.2.	<i>B. subtilis</i> DnaD preferentially binds ssDNA . . . . .	324
5.	Proteins that bind both double and single-stranded DNA . . . . .	325
5.1.	Nucleic acid chaperones in retroviruses and retrotransposons . . . . .	325
5.1.1.	Retroviral nucleocapsid proteins . . . . .	325
5.1.2.	HIV-1 NC destabilizes dsDNA and dissociates rapidly from ssDNA . . . . .	325
5.1.3.	Rapid kinetics of retroviral NCs correspond to efficient nucleic acid chaperone activity . . . . .	327
5.1.4.	HTLV-1 NC binds cooperatively to ssDNA . . . . .	328
5.1.5.	Target-site primed reverse transcription in the retrotransposon LINE-1 requires the ORF1 protein . . . . .	328
5.1.6.	ORF1p increases DNA melting transition width and aggregates ssDNA . . . . .	329
5.1.7.	ORF1p mutants which induce strong DNA aggregation inhibit nucleic acid chaperone activity . . . . .	329
5.2.	DNA recombinases . . . . .	329
5.2.1.	Human recombinase Rad51 binds ssDNA and dsDNA dynamically . . . . .	330
5.3.	DNA polymerases . . . . .	330
5.3.1.	<i>E. coli</i> DNA polymerase alpha binds both ssDNA and dsDNA . . . . .	330
5.3.2.	(HhH) <sub>2</sub> domain binds dsDNA and the predicted OB fold binds ssDNA . . . . .	332
5.3.3.	Quantitative binding affinities for double- and single-stranded DNA . . . . .	332
6.	Conclusions . . . . .	332
	Acknowledgements . . . . .	333
	References . . . . .	333

## 1. Introduction

Single molecule methods have provided a clearer understanding of a wide range of fundamental biological processes, including DNA replication, transcription, and repair. Single molecule force spectroscopy began with the capture and manipulation of single DNA molecules. Techniques such as optical tweezers, magnetic tweezers, and atomic force microscopy (AFM) apply forces to single molecules, probing conformational changes and structural dynamics in a variety of conditions. Such measurements explore the interactions of DNA with molecules ranging from small ligands to complex proteins. Quantifying the thermodynamics and kinetics of these interactions leads to substantial insights into DNA binding mechanisms in important biological systems.

Download English Version:

<https://daneshyari.com/en/article/1871059>

Download Persian Version:

<https://daneshyari.com/article/1871059>

[Daneshyari.com](https://daneshyari.com)