HU Binding Coupled Bending of DNA

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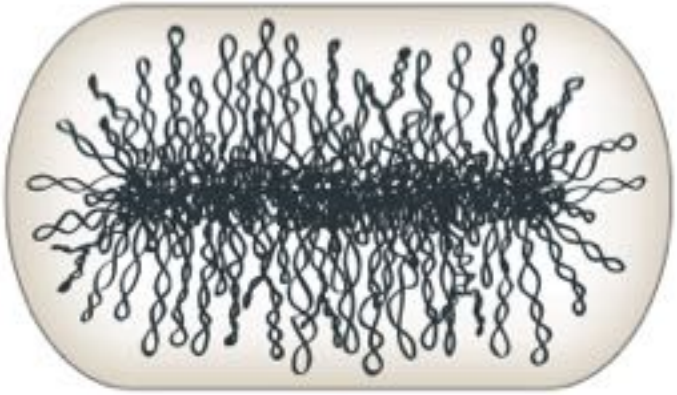
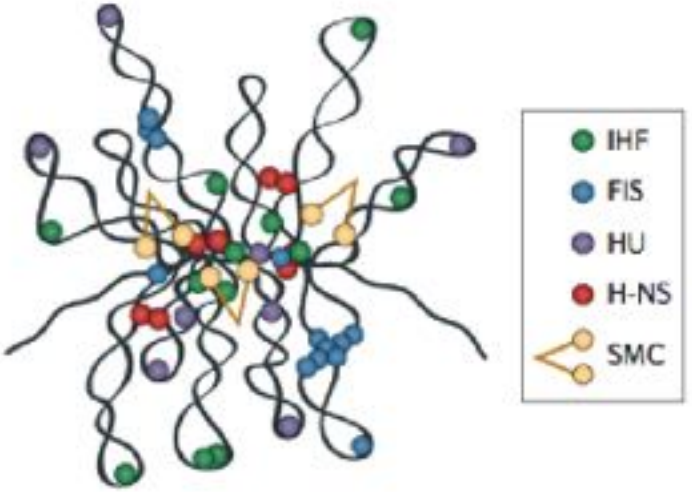
Introduction

- Double stranded DNA: one of the stiffest biomolecules (Persistence length ~ 50nm ~ 150bp)



Packaging of DNA into cells (prokaryotic)

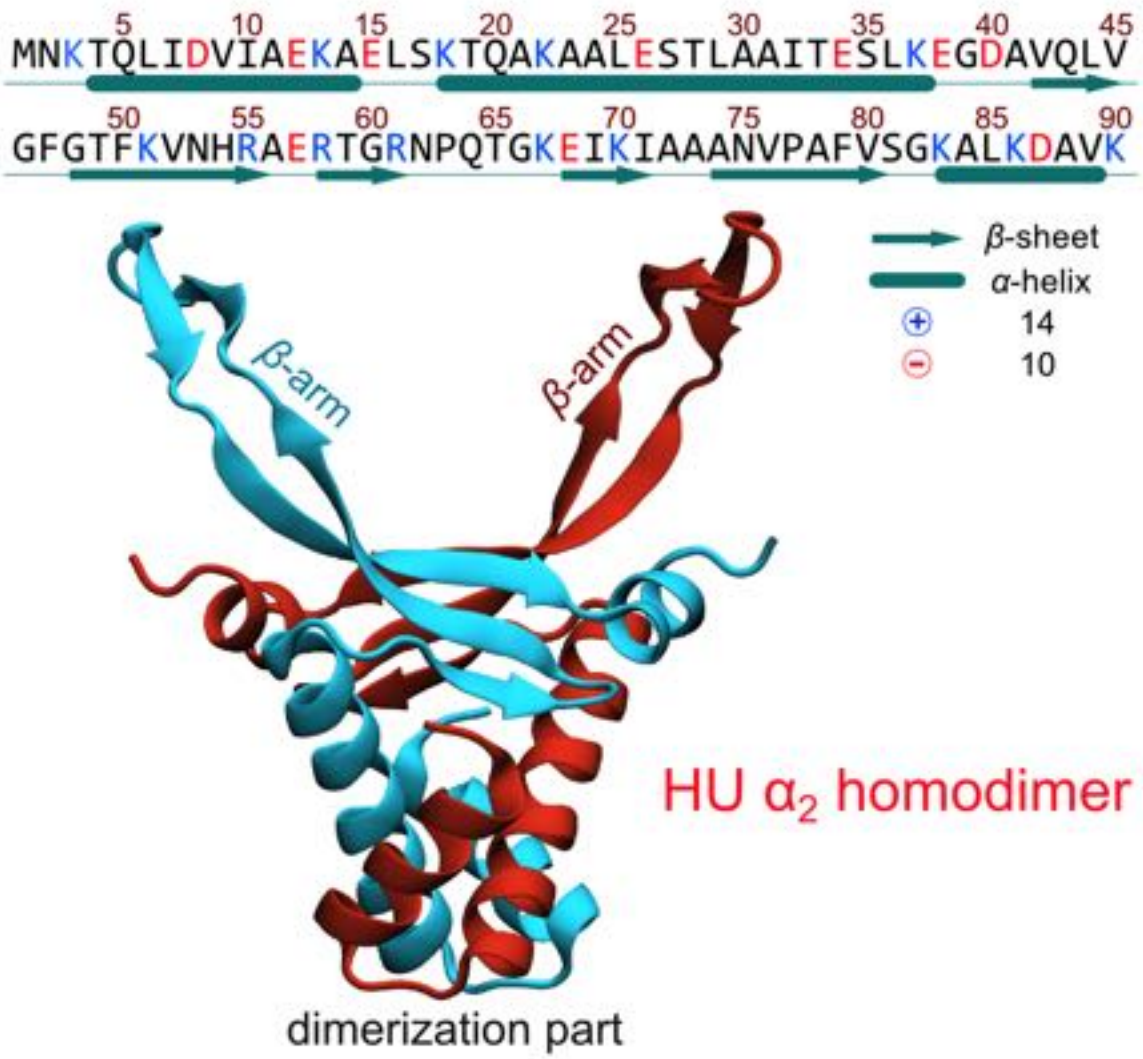


"Architectural" DNA-binding proteins

Wang, X. *et al.* (2013) *Nat. Rev. Genet.* **14**, 191.

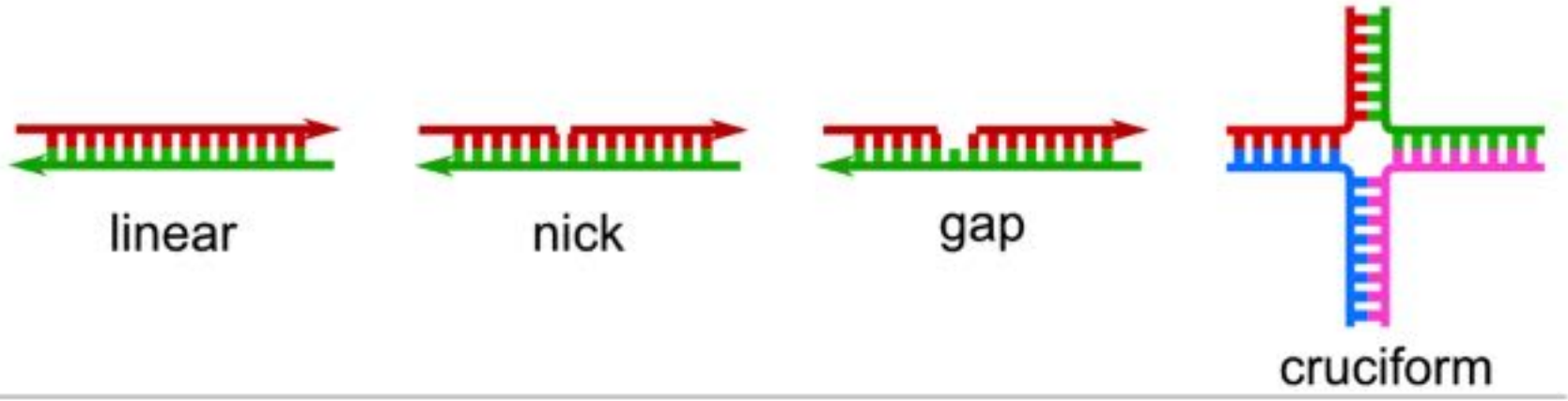
Introduction

- HU: one of the most abundant "architectural" proteins



Introduction

- HU-DNA binding specificity:
  Sequence: Slight preference for A/T-rich DNA.
  Structure: Strong preference for cruciform or gap/nick.

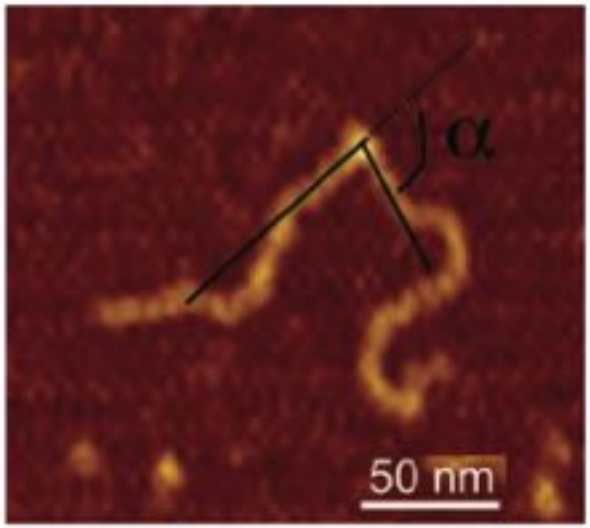


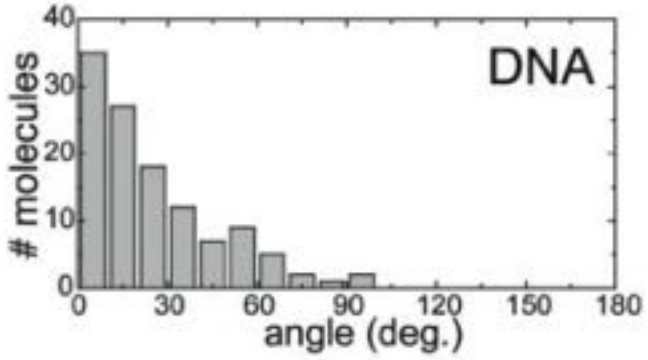
	linear	nick	gap	cruciform
K_d (nM)	9000	40.0	11.0	25.0

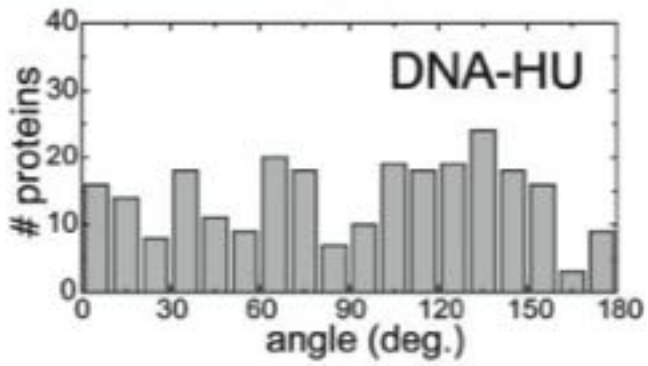
Prieto, A. I. *et al.* (2012) *Nucleic Acids Res.* **40**, 3524.
Pinson, V. *et al.* (1999) *J. Mol. Biol.* **287**, 485.

Introduction

- HU enhances DNA bending (AFM experiment)



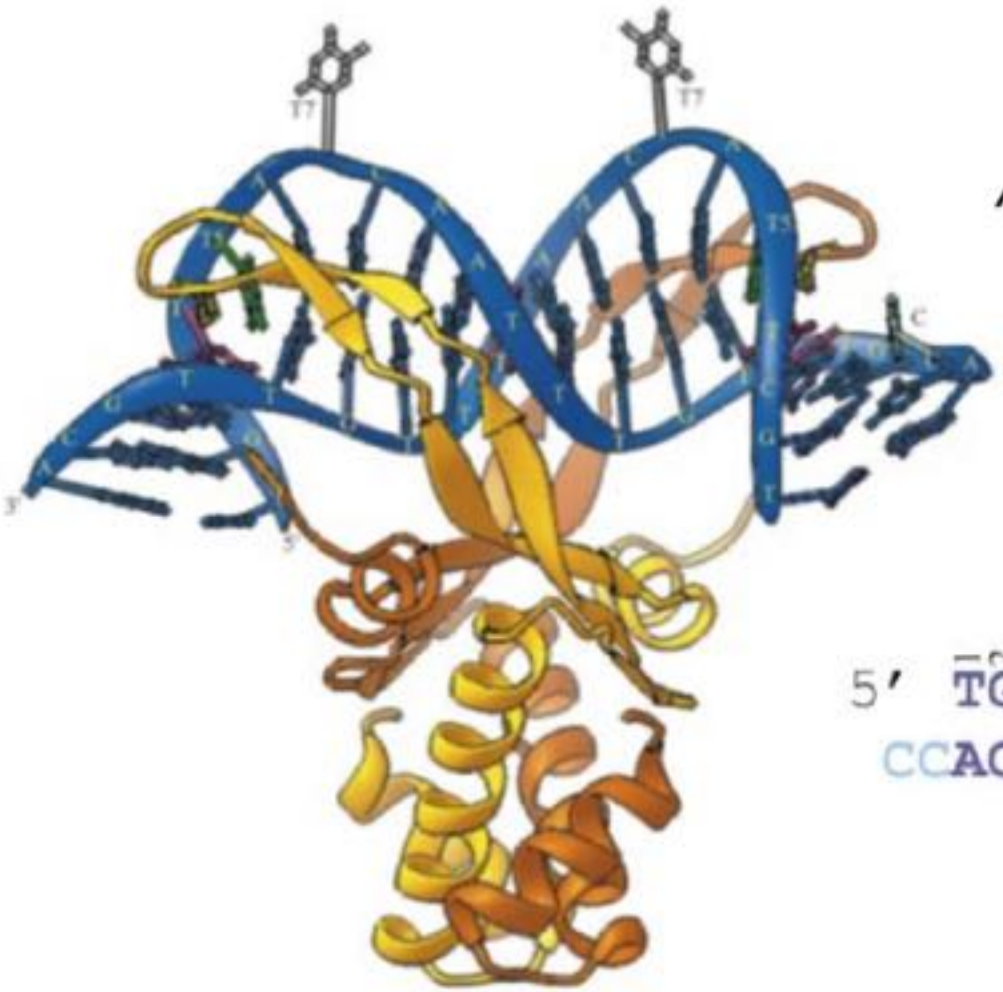




van Noort, J. *et al.* (2004) *Proc. Natl. Acad. Sci.* **101**, 6969.

Introduction

- HU-DNA complex structure:



crystal structure of
Anabaena HU bound to DNA

PDB: 1P71

Motivation

- How does HU bind to and slide on DNA?
- How does DNA conformation change in response to HU binding?
- What's the relationship between HU binding and DNA conformational change?

Coarse-Grained Models and Methods

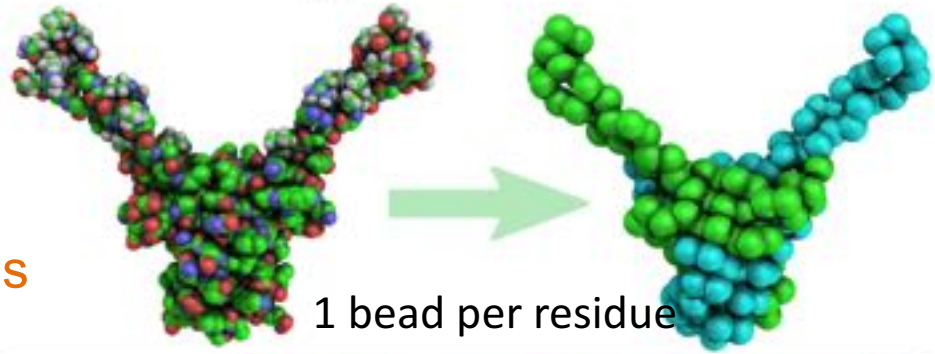
- CG Protein: AICG2+

  W. Li *et al.* (2014) *PNAS*.

- DNA: 3SPN.2C

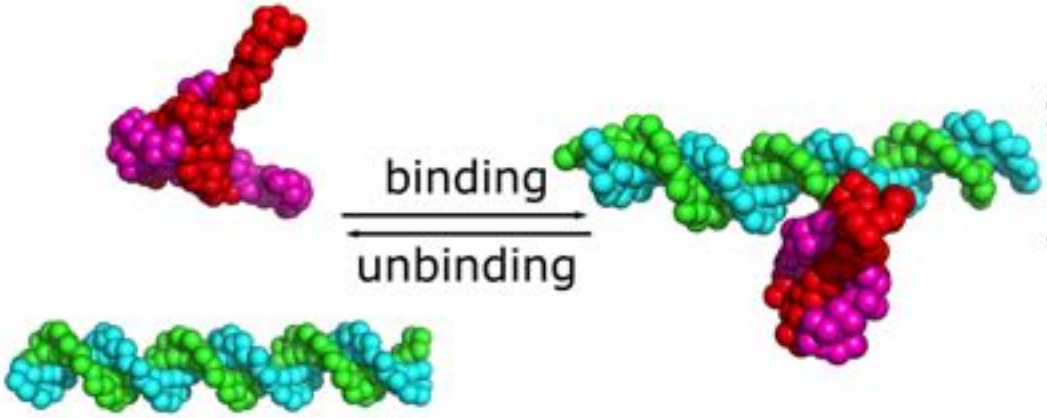
  Sequence dependent properties

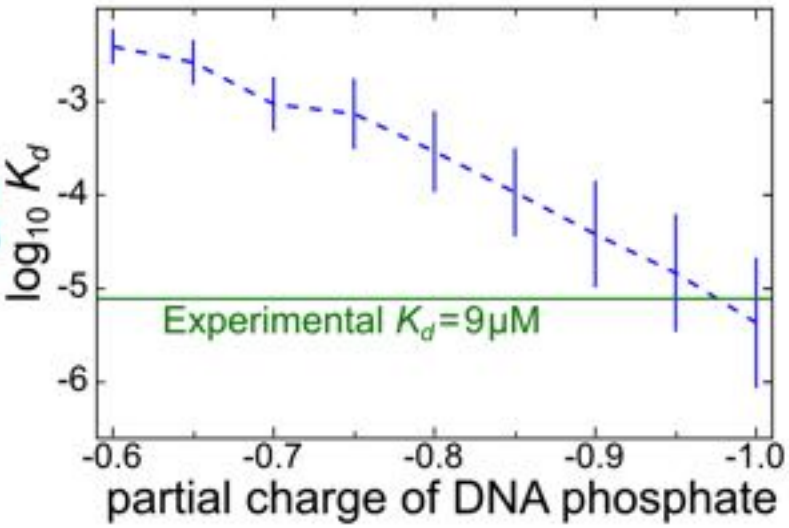
  G. Freeman *et al.* (2014) *JCP*.



- Intermolecular interactions:

  electrostatic + excluded volume





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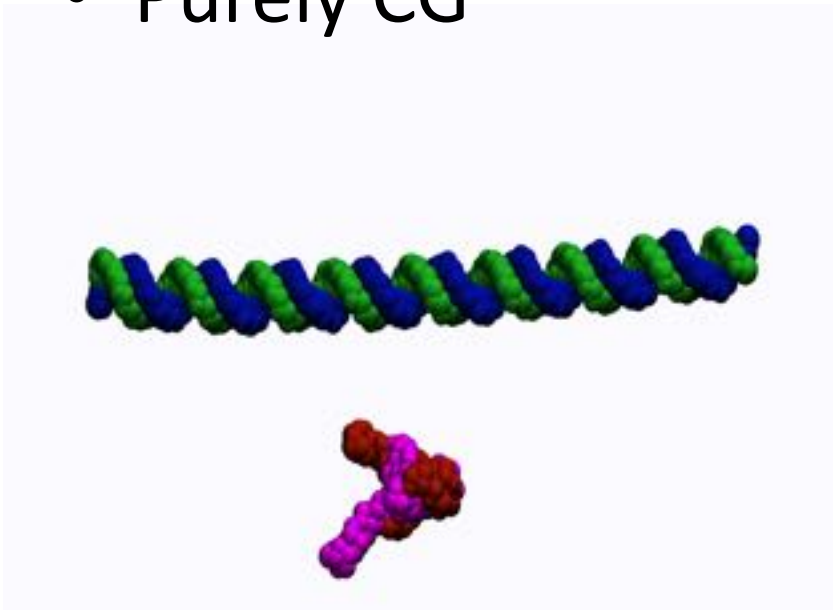
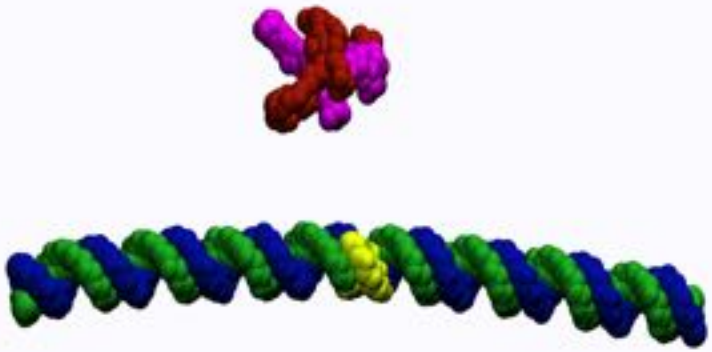
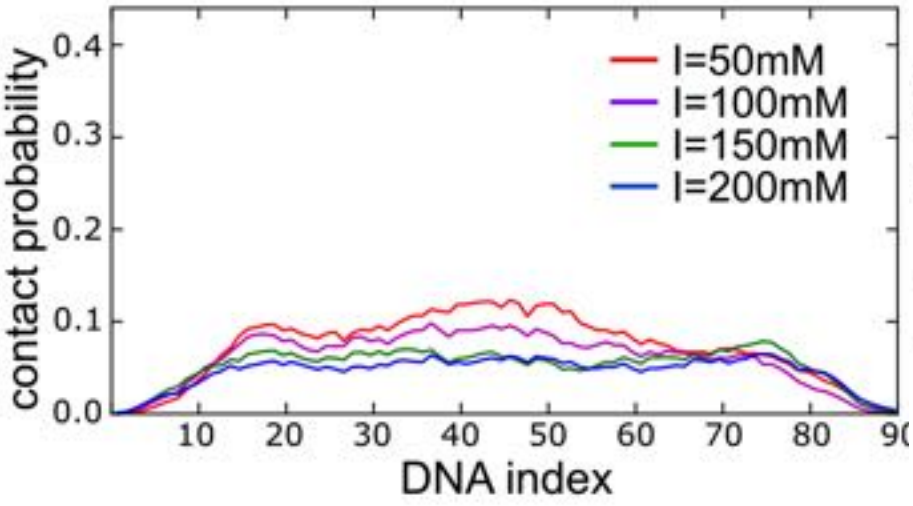
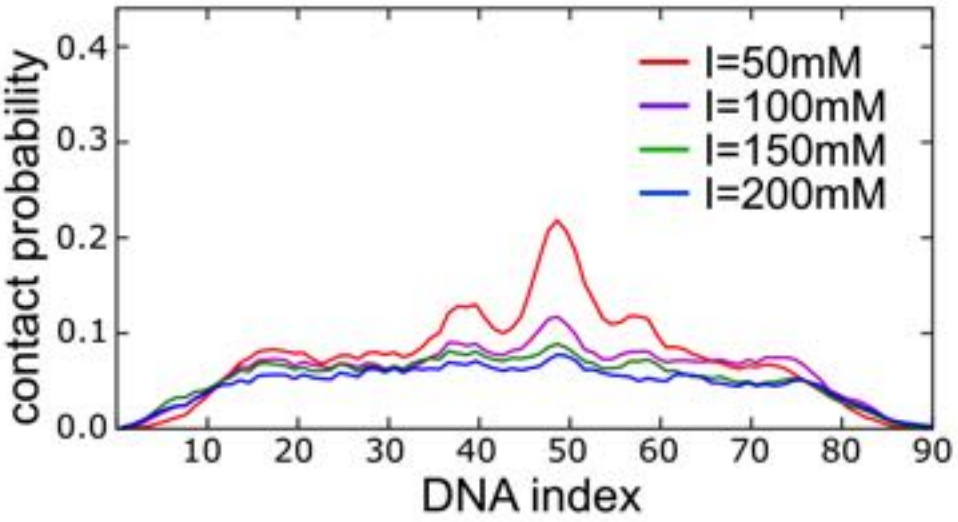
HU Prefers A/T Rich Region

- Purely CG
- A/T region at center









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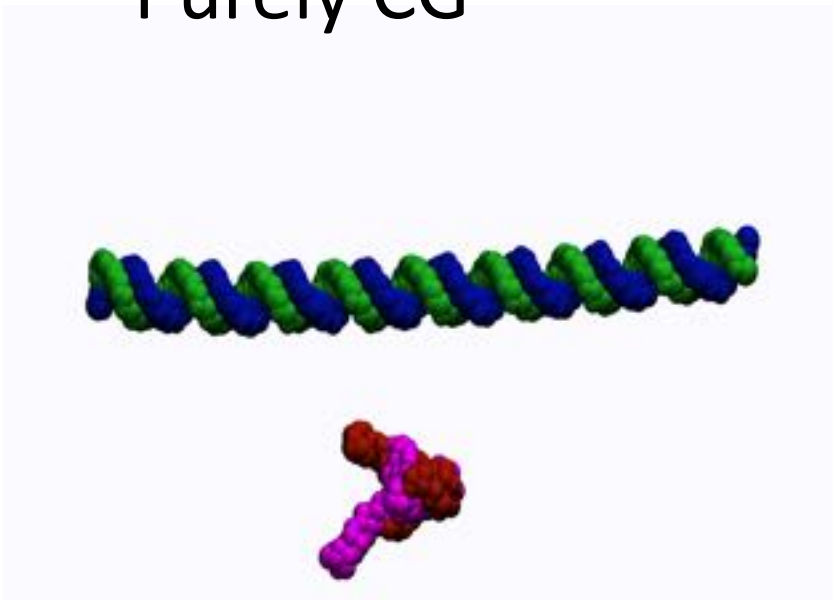
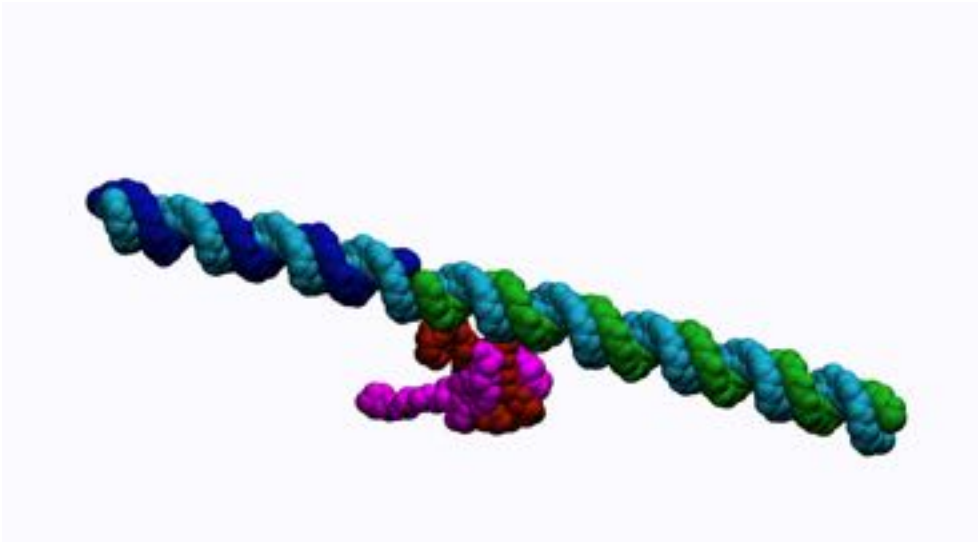
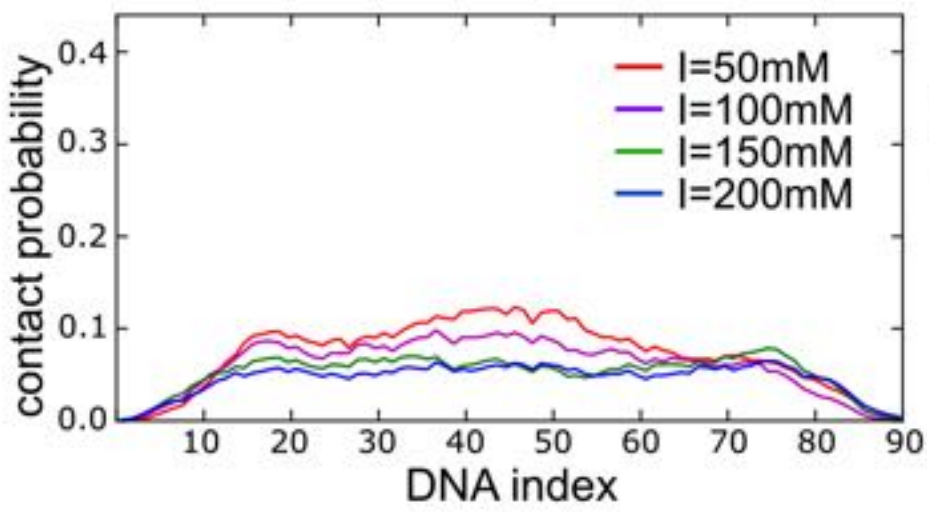
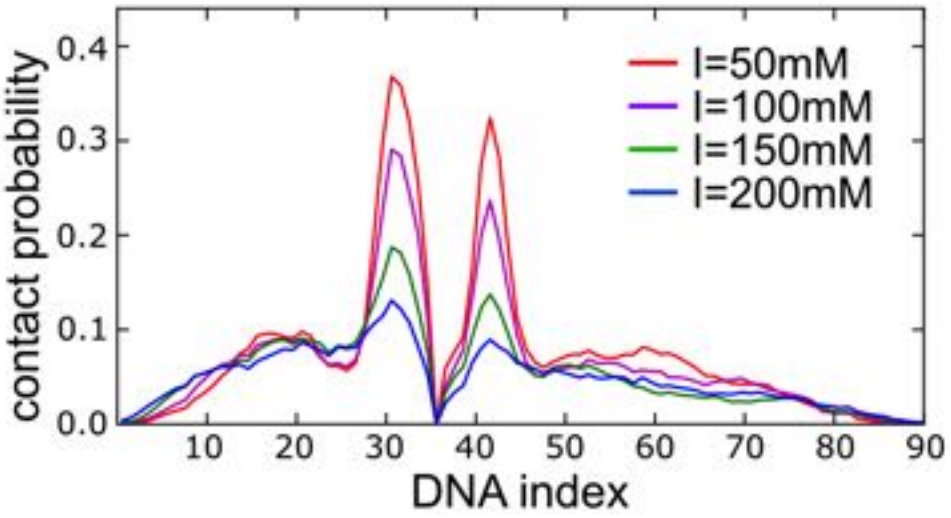
HU Favors Gap in DNA

- Purely CG
- Gap at index 36









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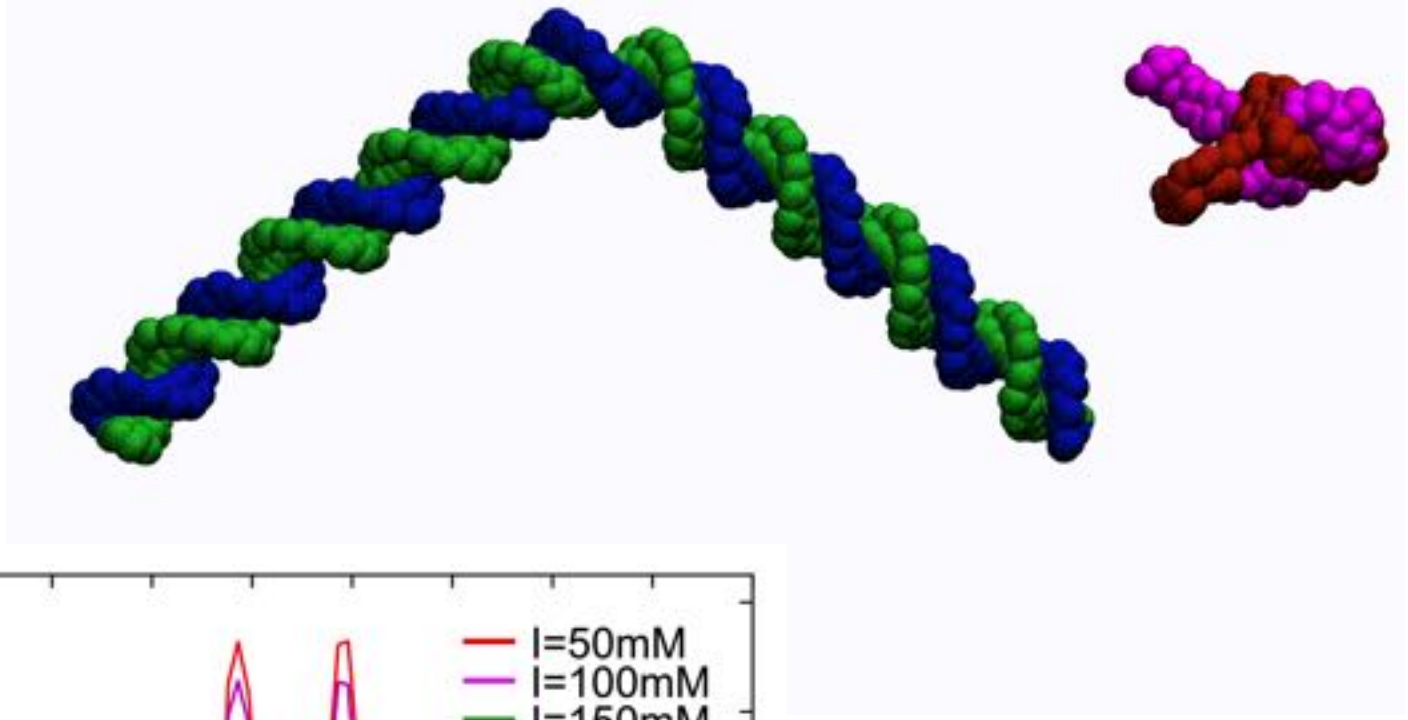
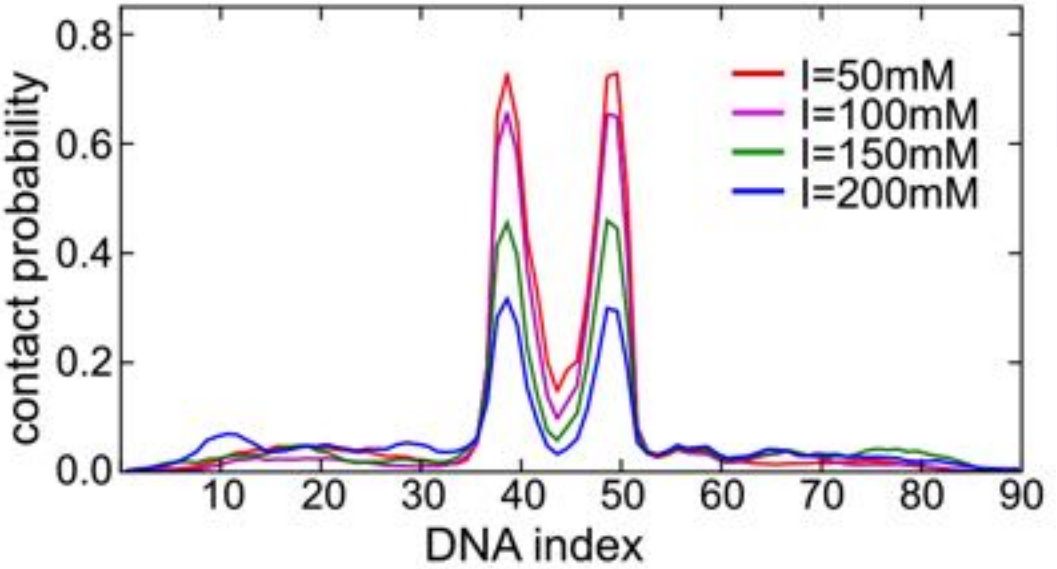
Summary of HU Binding Specificity

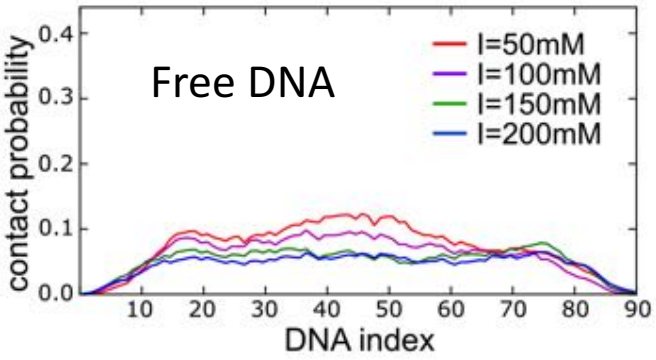
- Slight preference for A/T rich sequence
- Strong preference for gap/nick

- New questions:
  Origin of A/T specificity: sequence or structure?
  Origin of gap preference: topology or flexibility?

HU Binding to Fixed Bent DNA







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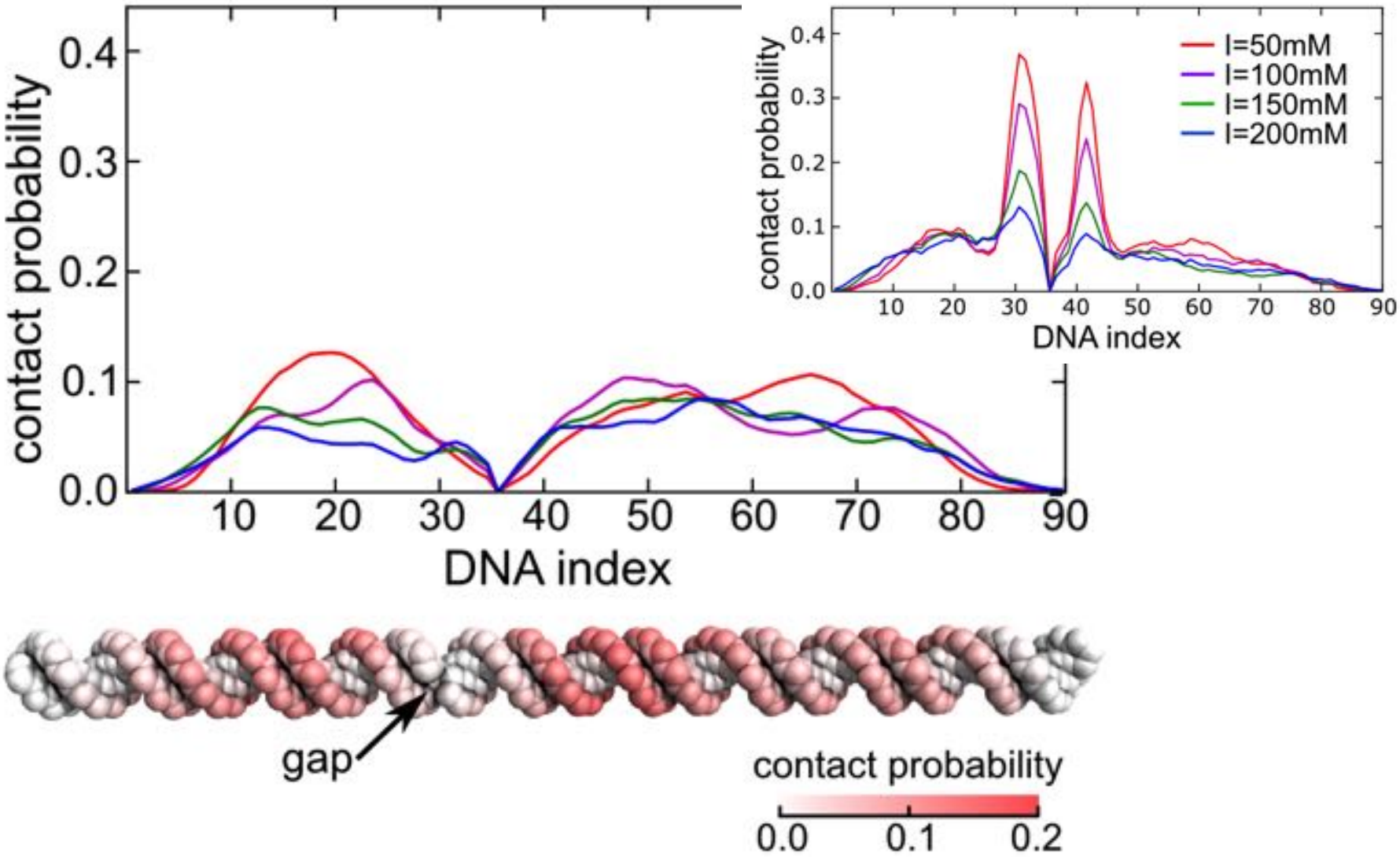
HU Binding to Fixed Straight Gapped DNA



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Summary of HU Binding Specificity

Answers to the questions:

- Origin of sequence specificity: structure properties.
- Origin of gap preference: flexibility.

"Bendability"

New question:

How does HU affect conformation of DNA?

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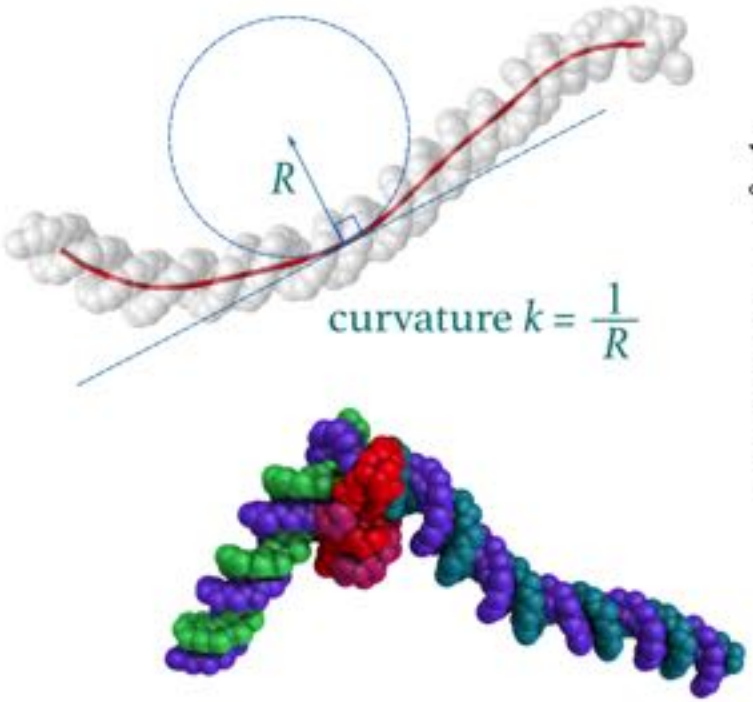
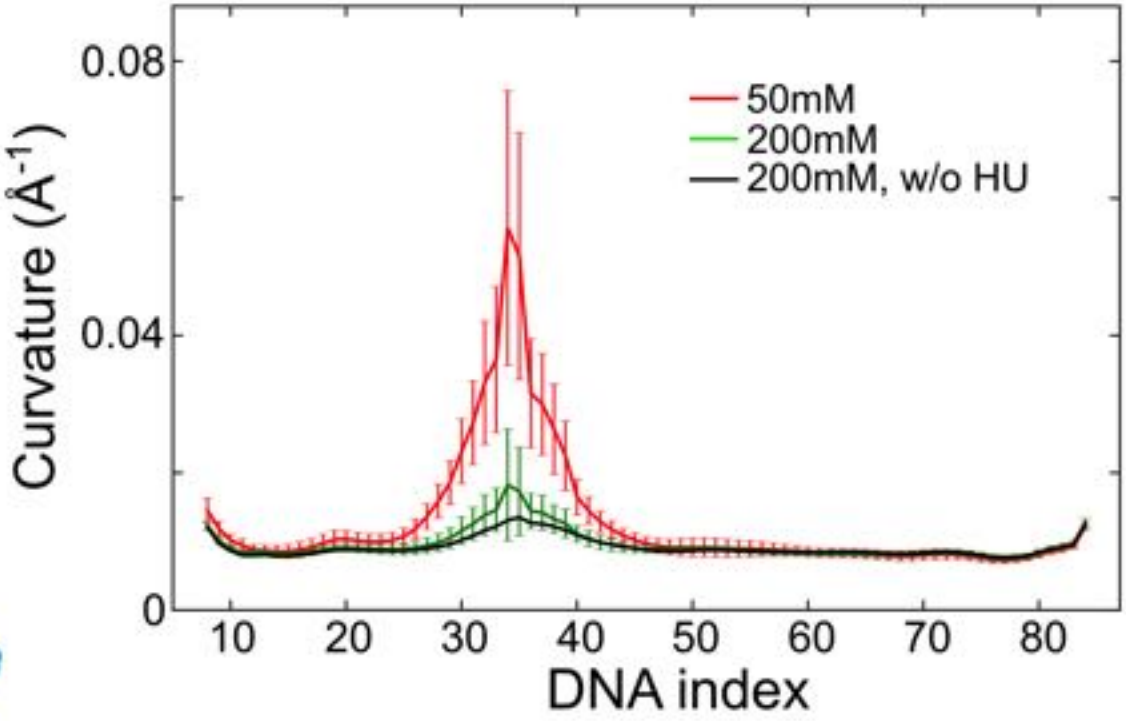
HU Enhances Bending of Gapped DNA





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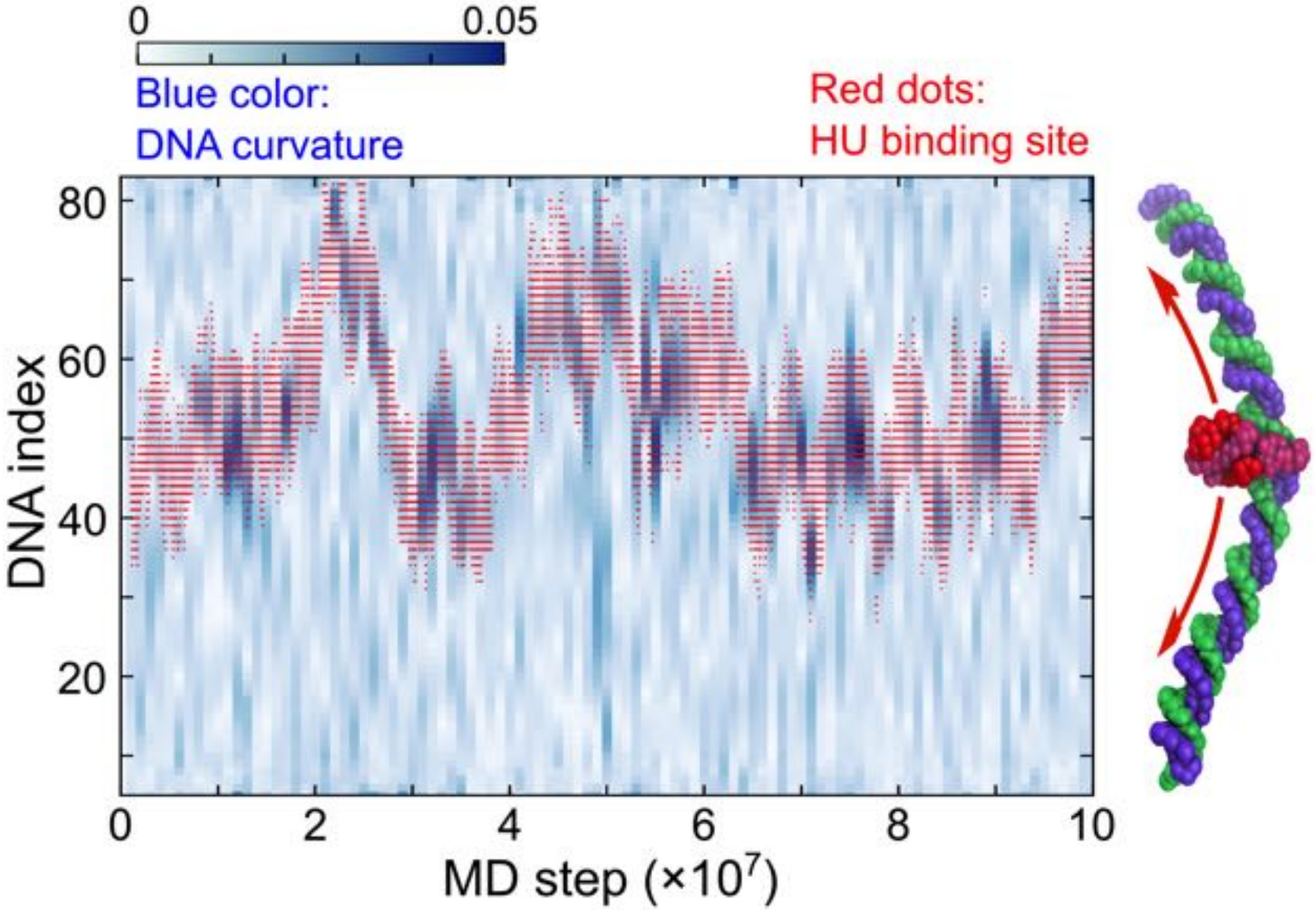
Coupling of Binding and Bending



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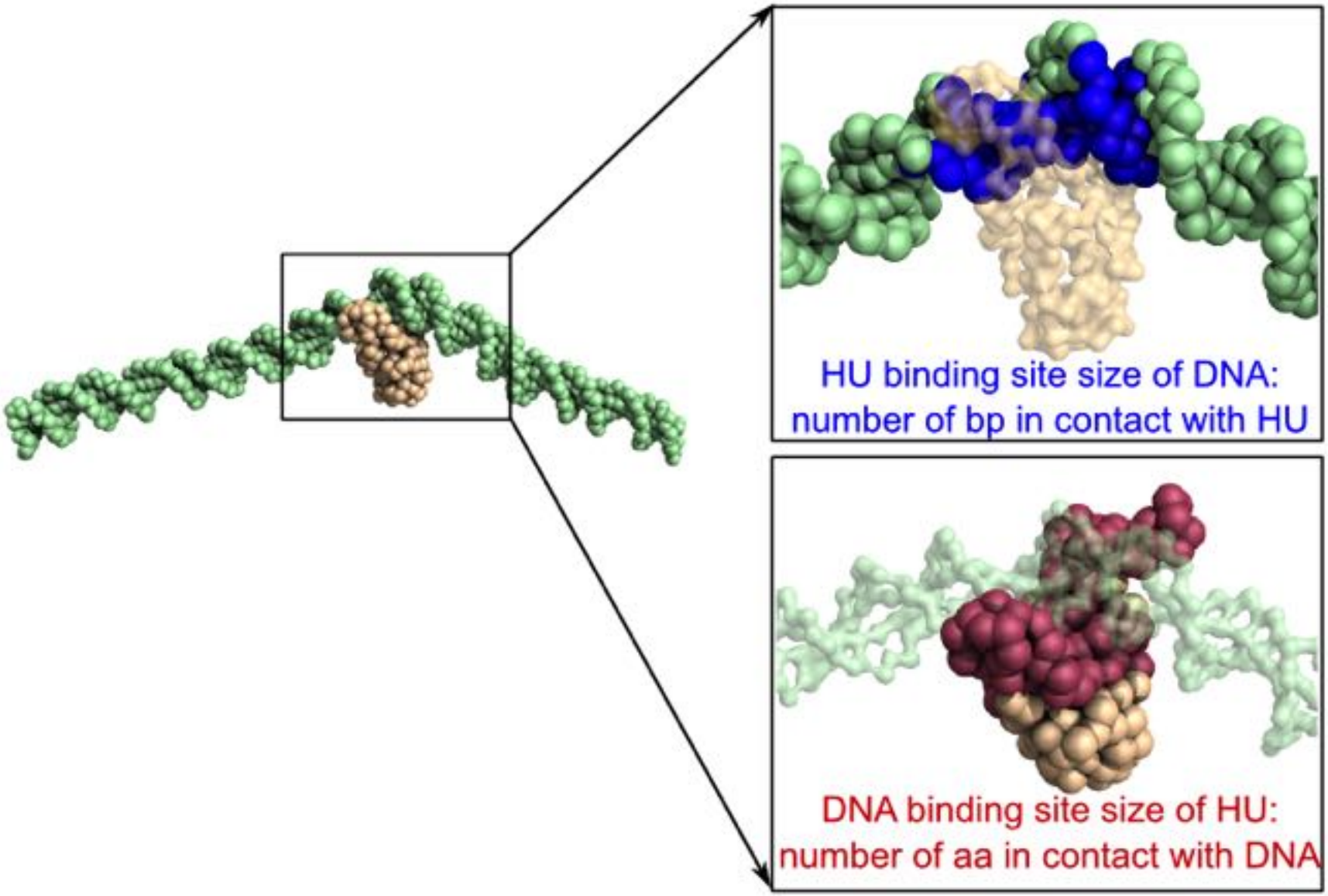
HU Binding & DNA Bending

- HU binding statistically facilitates DNA bending
- HU binding is dynamically coupled to DNA bending

HU-DNA Binding Site Size



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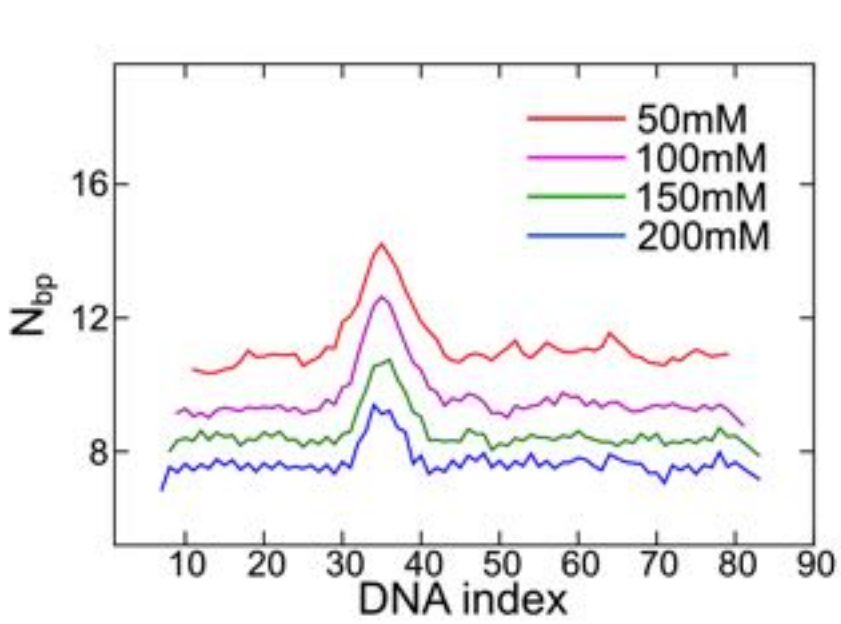
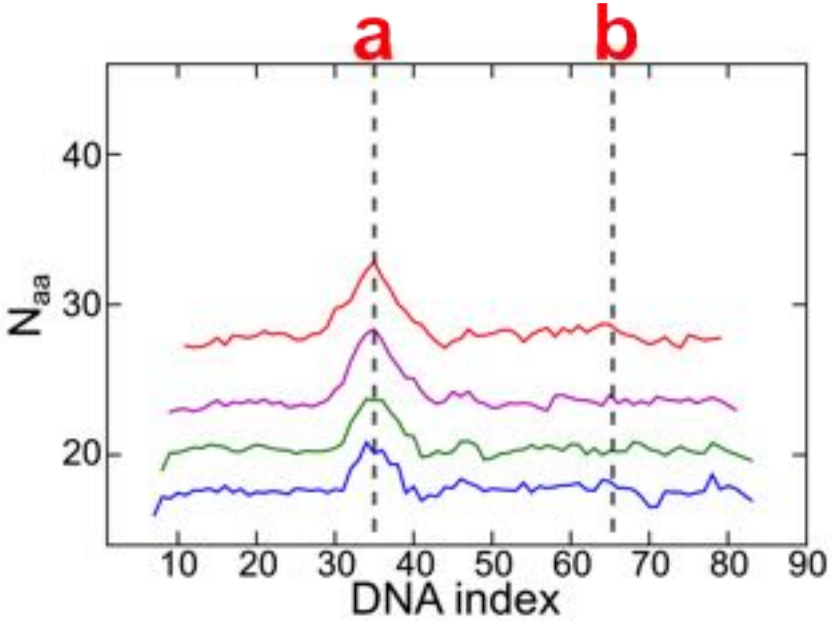
Binding site of HU-Gaped DNA





HU binds to position a

HU binds to position b

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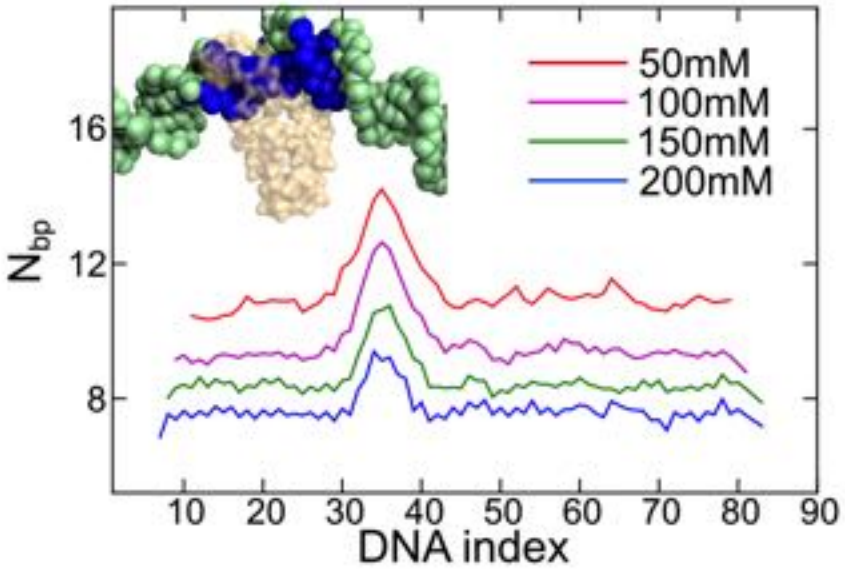
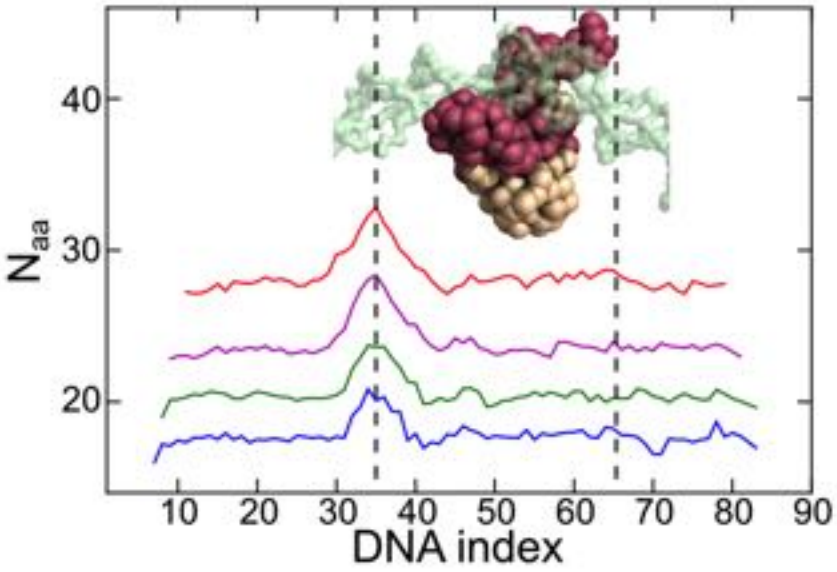
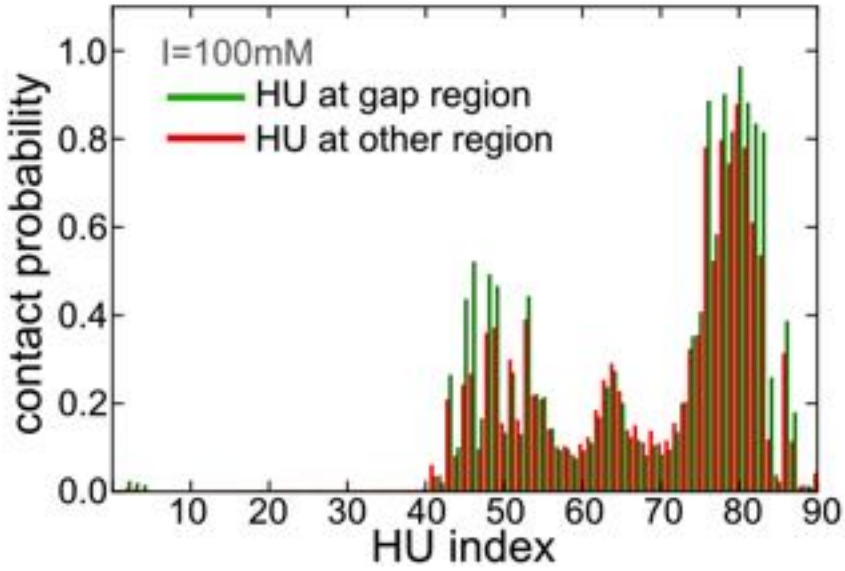
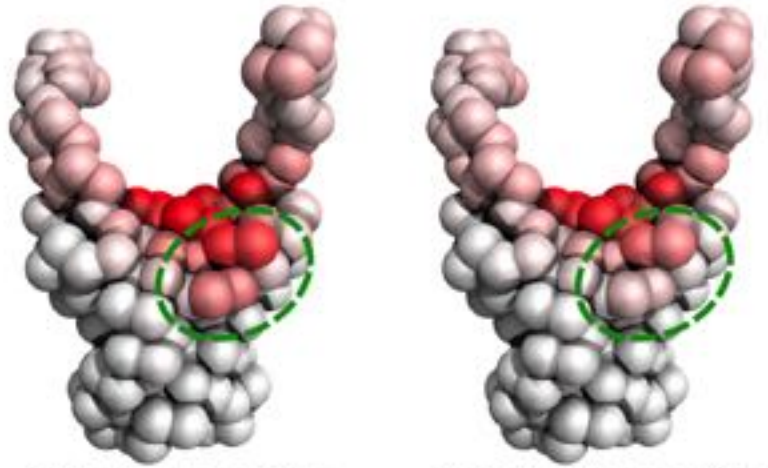
Binding Site of HU-Gaped DNA









Conclusions

- **HU selects “bendable” DNA structures;**
- **HU binding is highly coupled to DNA bending;**
- **HU facilitated DNA bending by contributing larger contact interface.**