

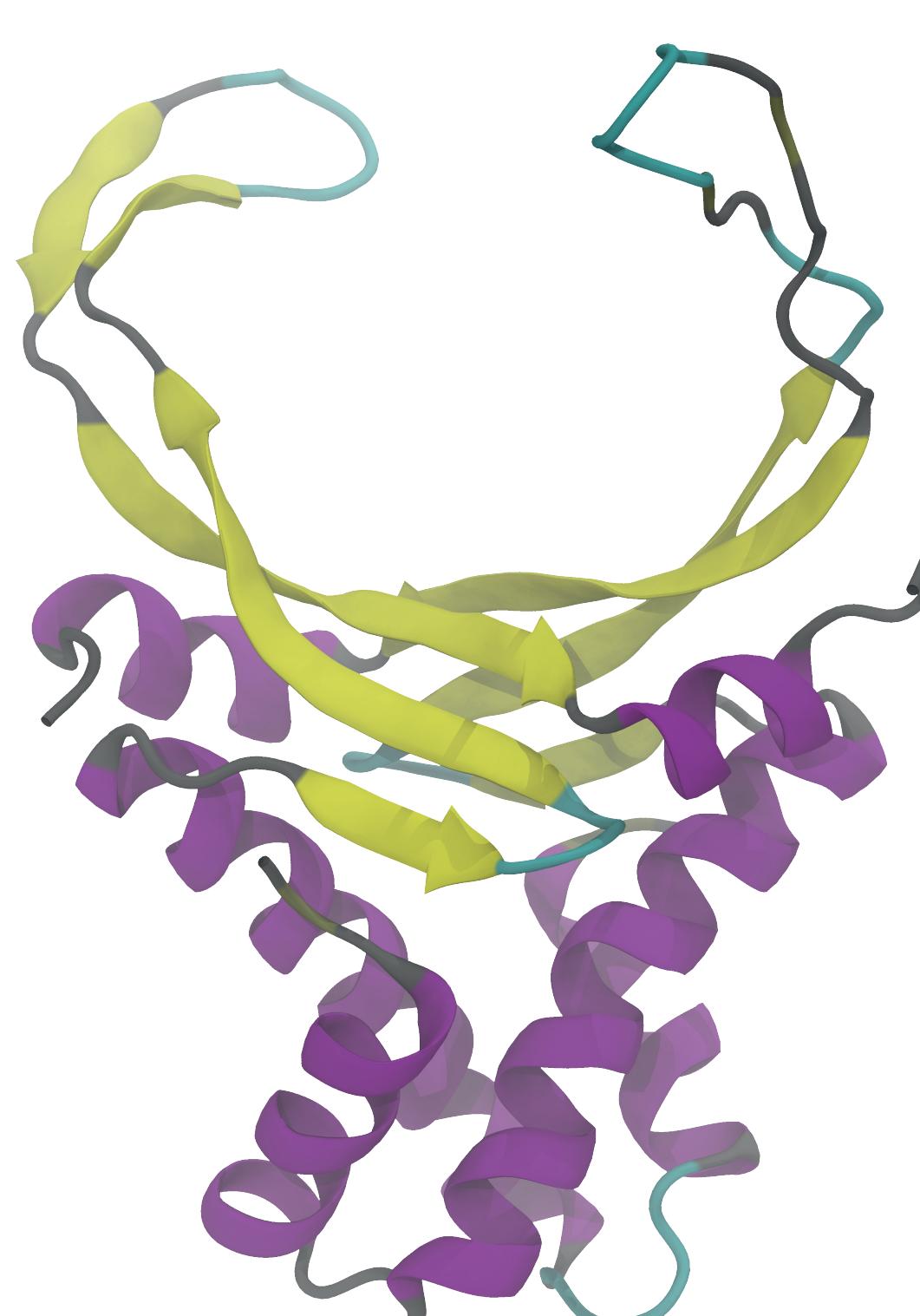
Atomistic simulations reveal modality of IHF–DNA binding

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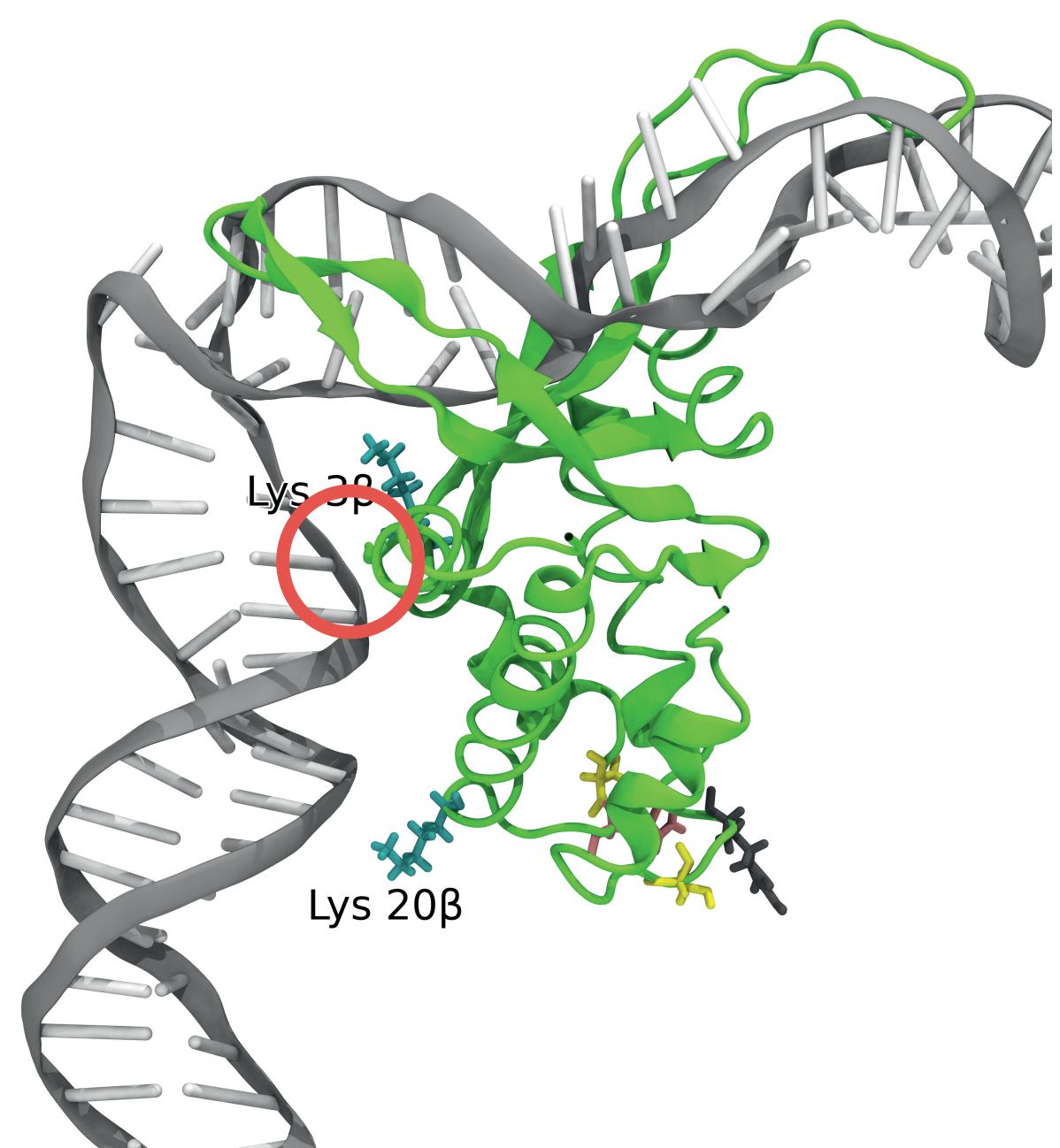
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Integration host factor (IHF)

- > Prokaryotic nucleoid-associated protein
- > Functional analogue of histones
- > Bends DNA by $\sim 160^\circ$
- > Binds specifically by indirect readout
- > IHF & HU regulate around 120 *E. coli* genes [1]
- > Stabilises biofilms [2]



IHF binds DNA in 3 substates



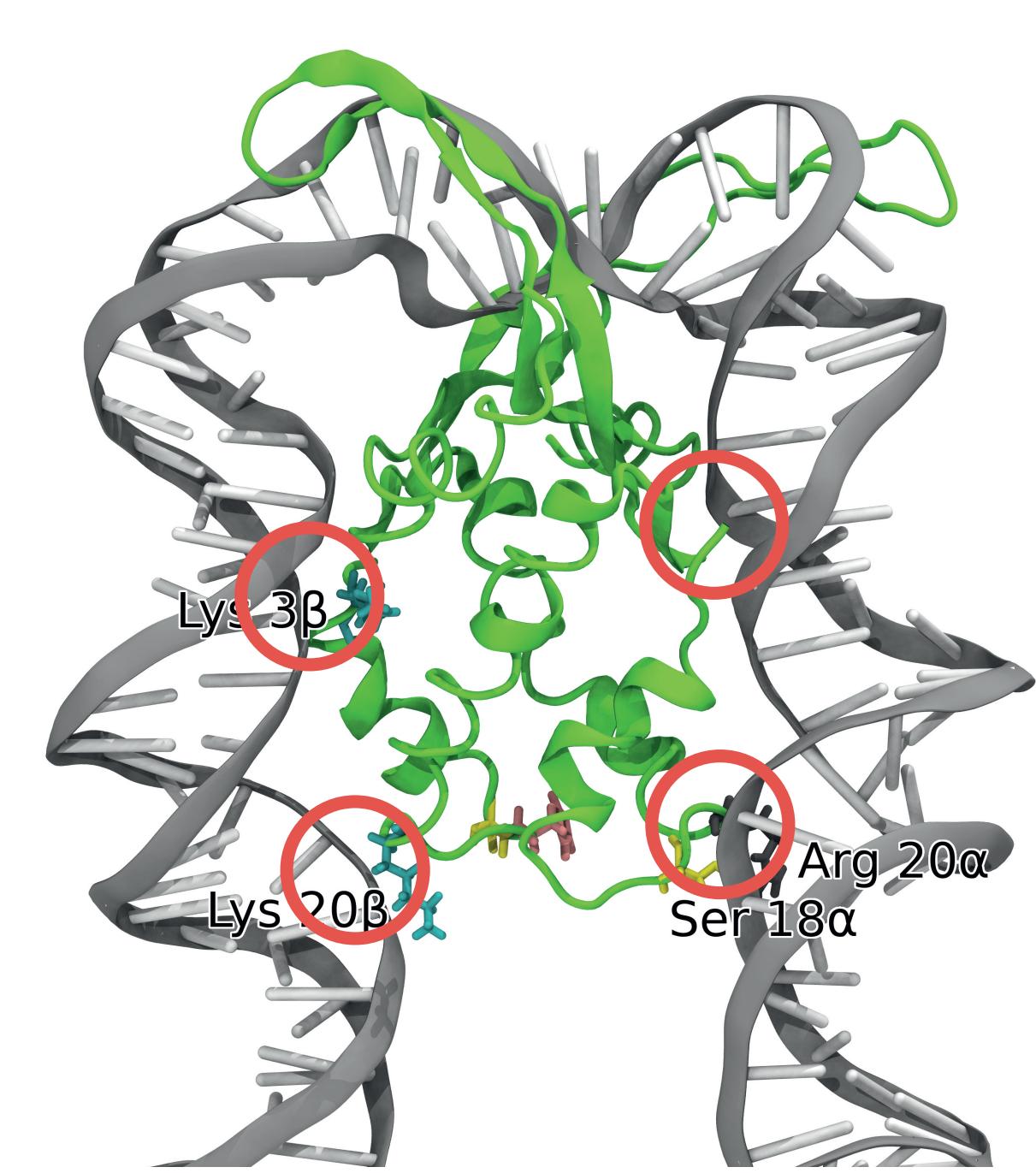
- > “Unwrapped” state
- > $\sim 60^\circ$ bend
- > Bending within range for naked DNA
- > The A-tract makes a single contact with IHF
- > Highest free energy

“Half wrapped” state
 $\sim 120^\circ$ bend



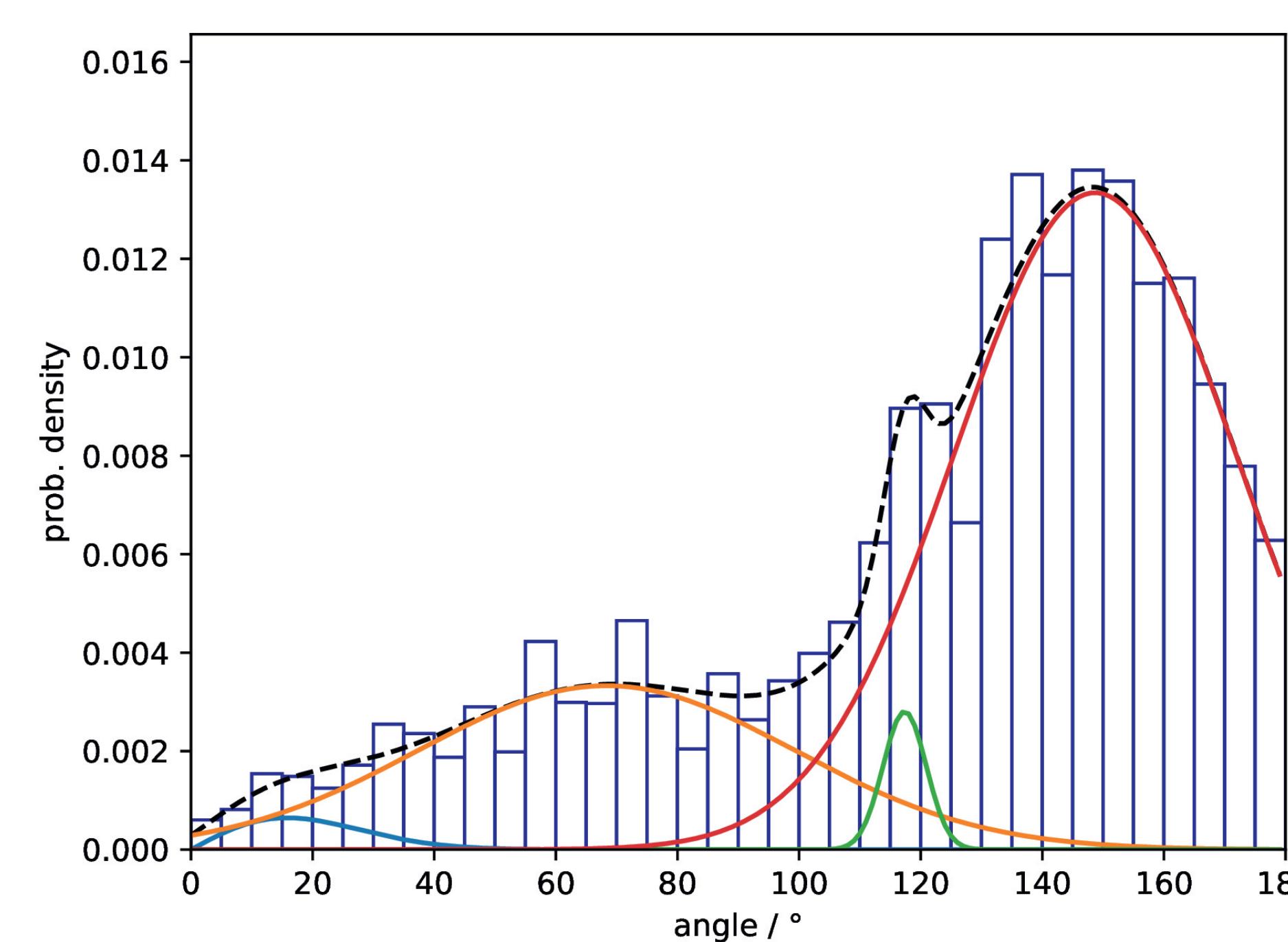
Novel observation confirms existing FRET data [3]

IHF binds only the A-tract to one side of the binding site



- > “Fully wrapped” state
- > $\sim 160^\circ$ bend
- > Known from crystal structure
- > DNA binds to both sides of the protein
- > Lowest free energy

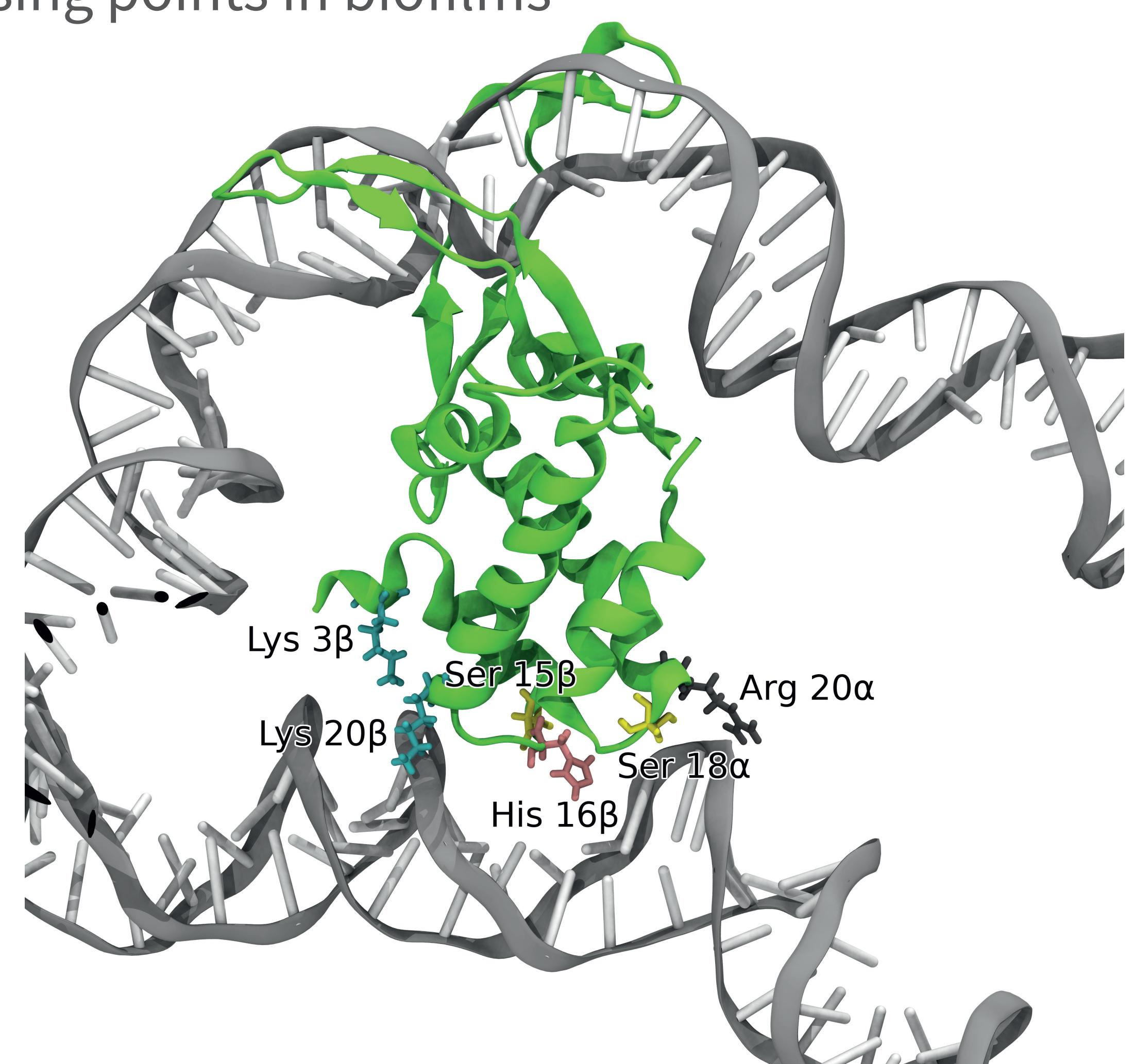
- > Following binding, the DNA–IHF complex progresses downwards through these metastable states



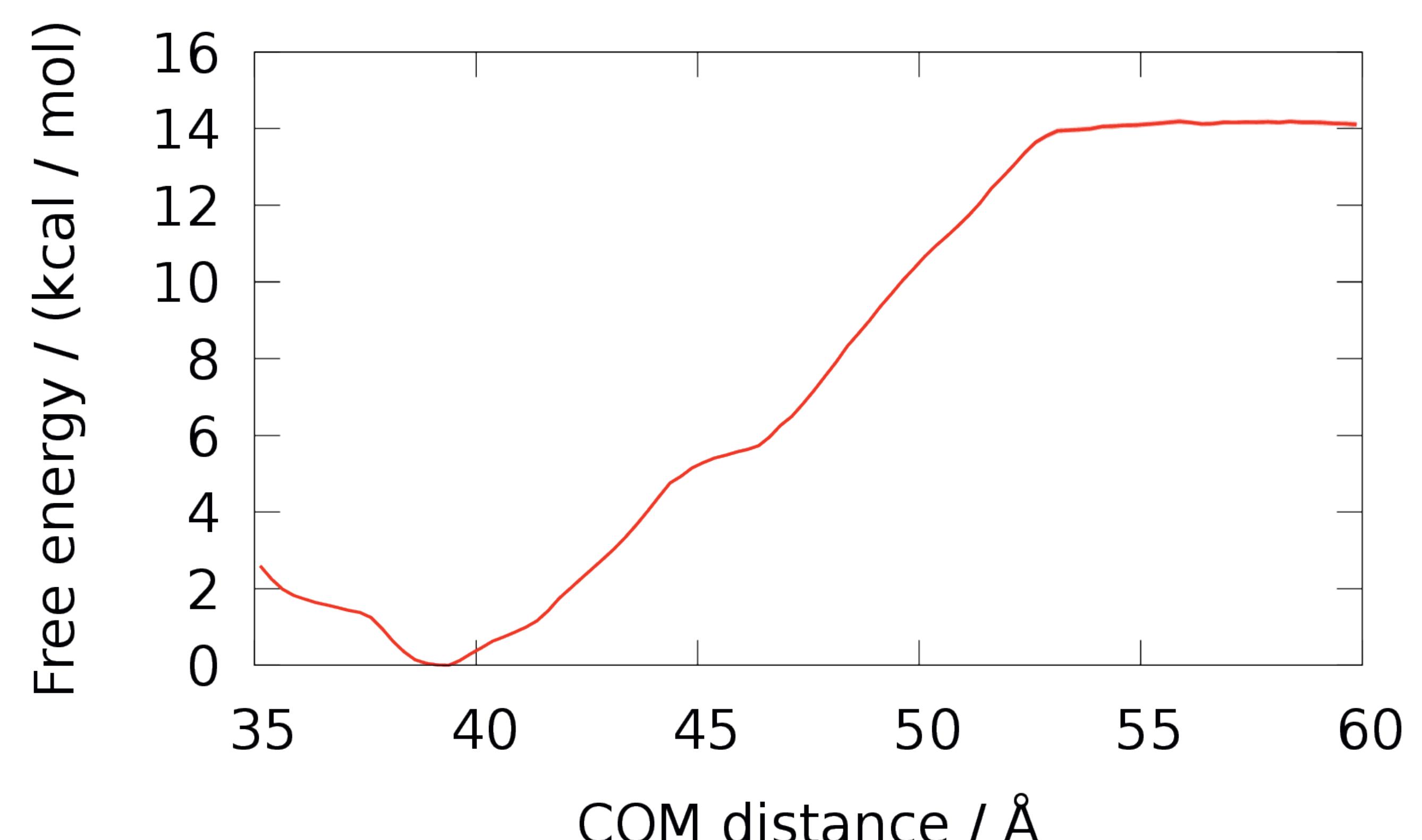
Corresponding peaks appear in the histogram of bend angles across several simulations. Here, a 2D projection of the trajectories was used for comparison with AFM data.

IHF can bridge DNA

- > A single IHF molecule can bind at least two pieces of DNA, forming a bridge between them
- > Bridges constrain DNA structure & topology
- > Could explain why IHF exists at extracellular DNA crossing points in biofilms



- > IHF bridges involve nonspecific hydrogen bonding with the DNA backbone
- > Umbrella sampling simulations demonstrate that bridging is energetically favourable



Methods

- > Atomistic molecular dynamics simulations using AMBER
 - \$ Explicit & implicit solvent
- > Free-energy calculations using umbrella sampling & weighted histogram analysis method (WHAM)
- > Results agree with measurements from atomic force microscopy (AFM) by S. Yoshua

References

1. Swinger K K, Rice P A 2004 *Curr. Opin. Struct. Biol.* **14** 28
2. Novotny L A et al. 2013 *PLoS ONE* **8** e67629
3. Connolly M et al. 2018 *J. Phys. Chem. B* **122** 11519