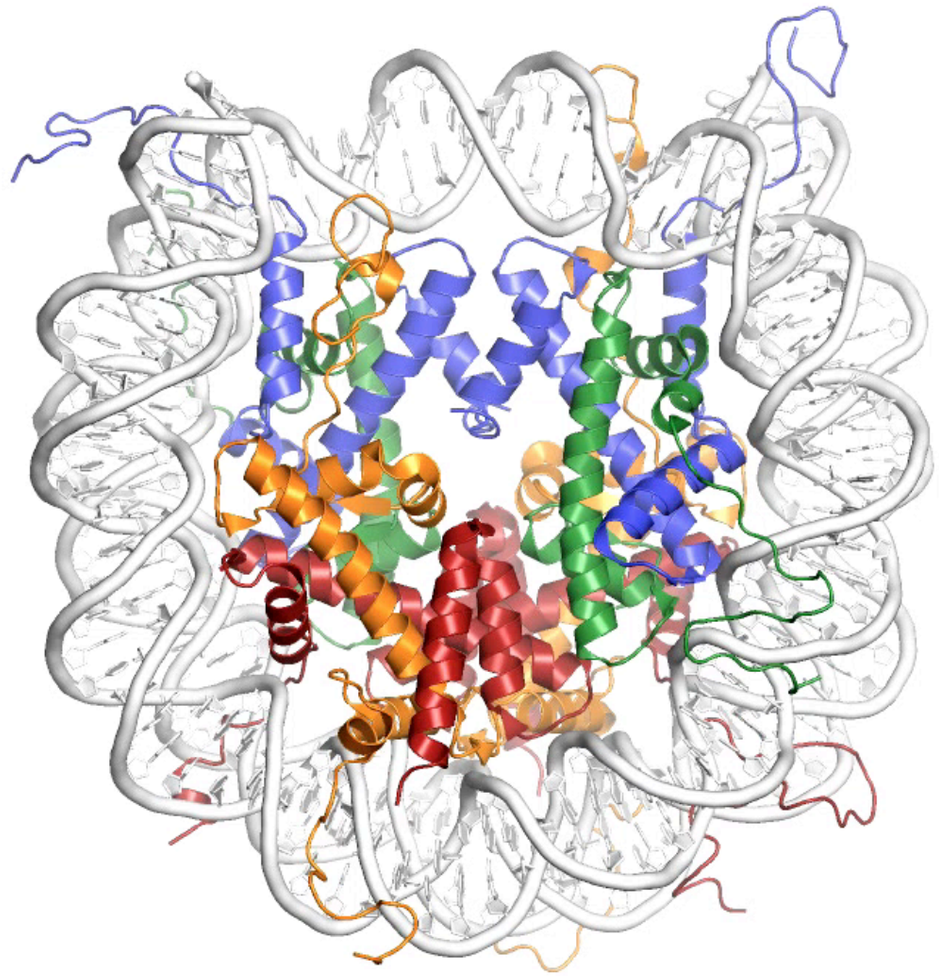
Regulation of a nucleosome-sliding machine

Greg Bowman
Biophysics Department
Johns Hopkins University

Eukaryotic DNA is packaged into nucleosomes



Luger et al., Nature (1997)

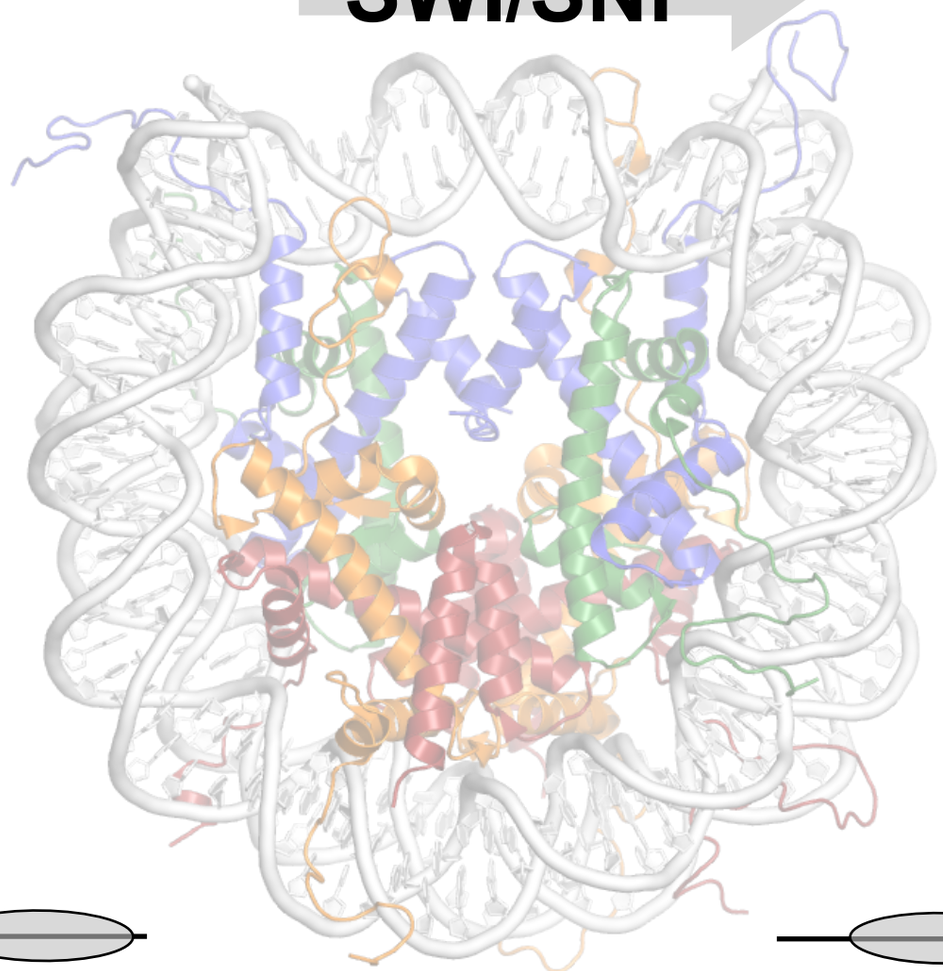
Chromatin remodelers reorganize the nucleosomal barrier

assembly

disassembly

Chd1, Iswi

SWI/SNF



Chd1
Iswi
SWI/SNF
INO80

INO80

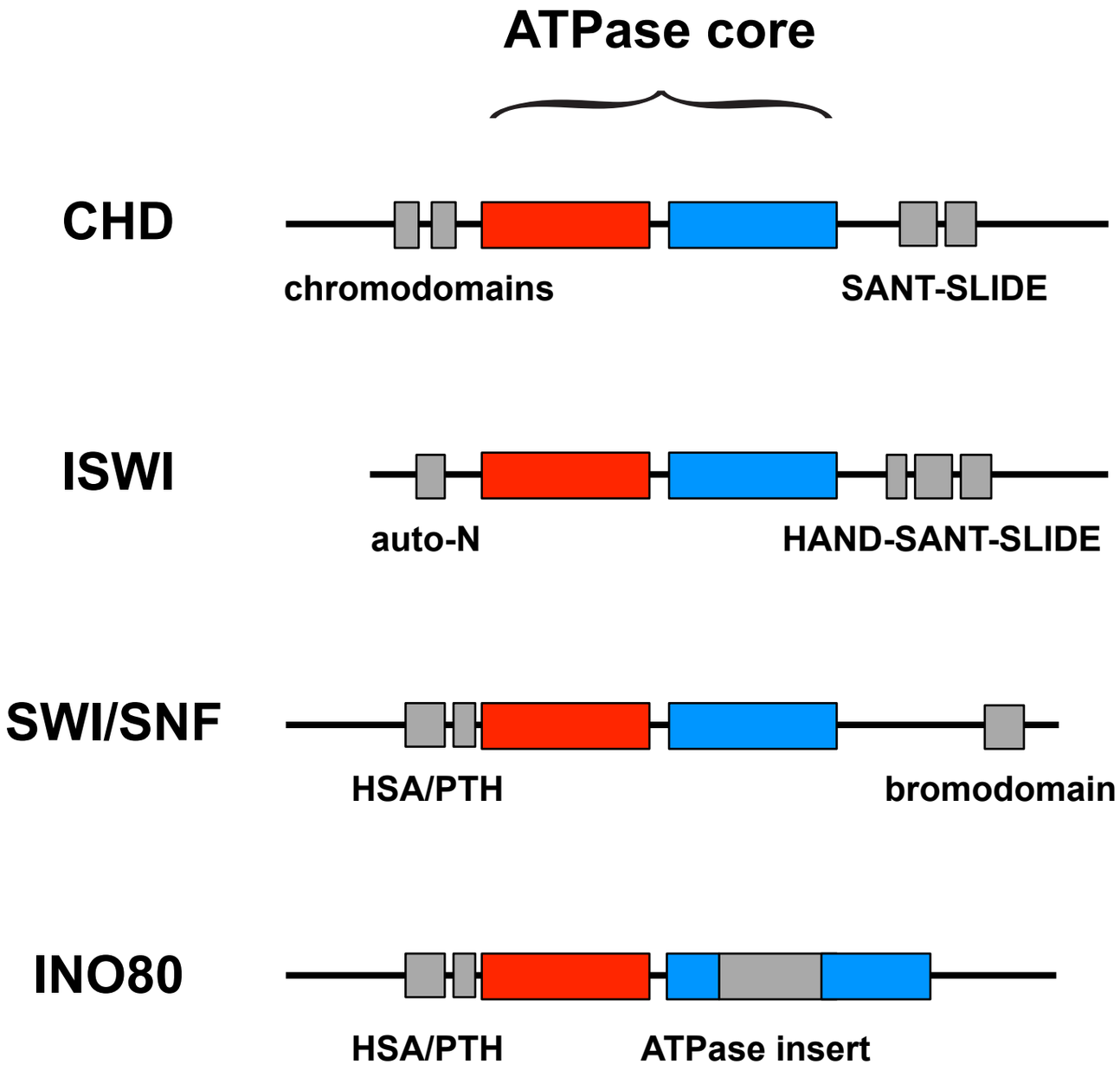
SWR1

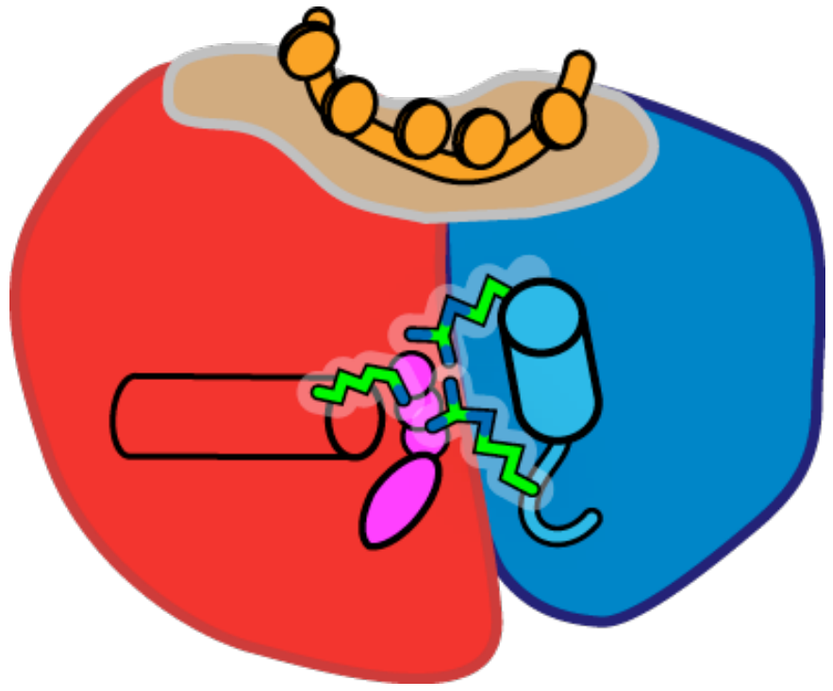
sliding

histone replacement

Luger et al., Nature (1997)

The remodeler ATPase motor is a member of Helicase Superfamily 2 (SF2)





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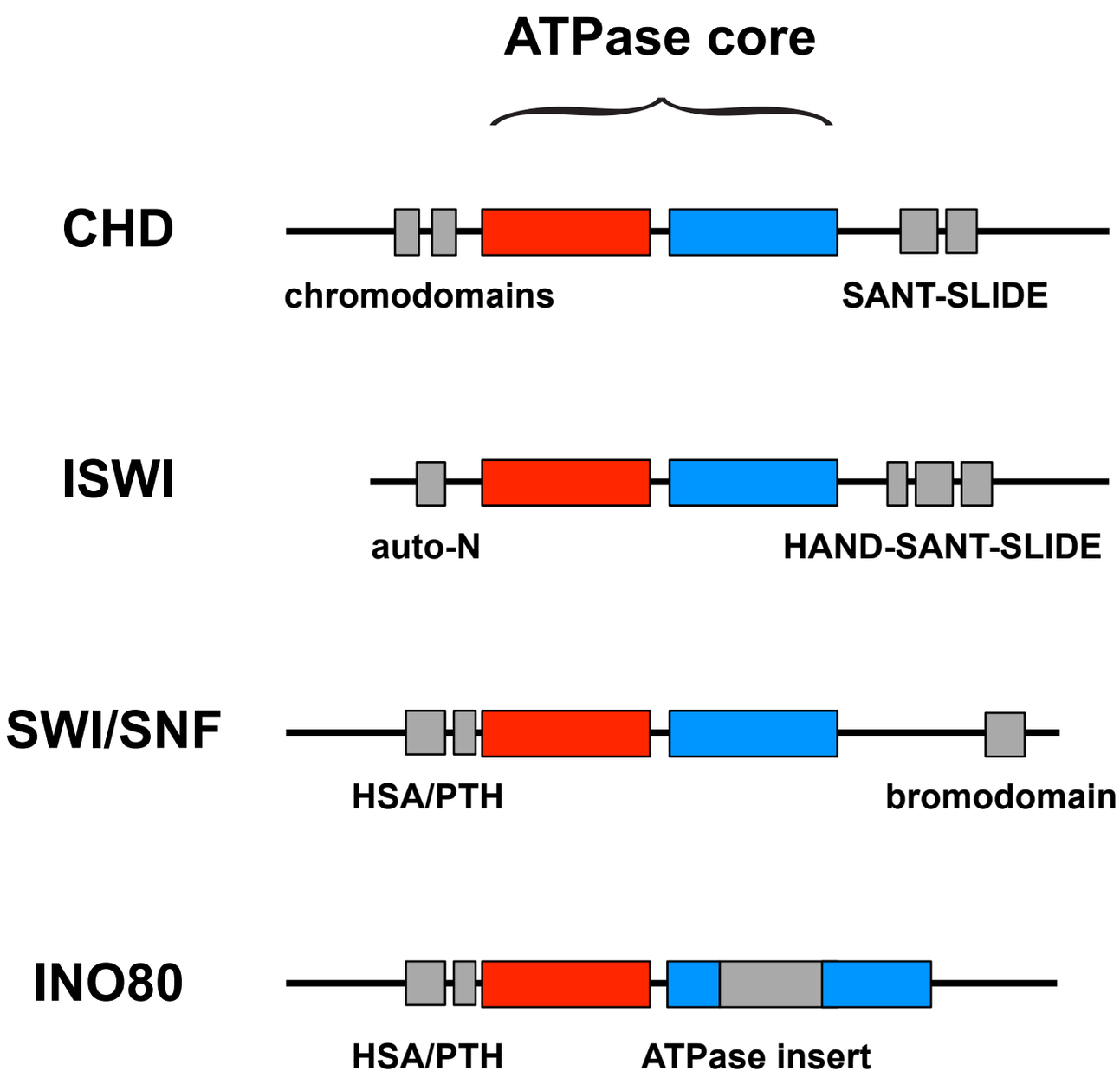
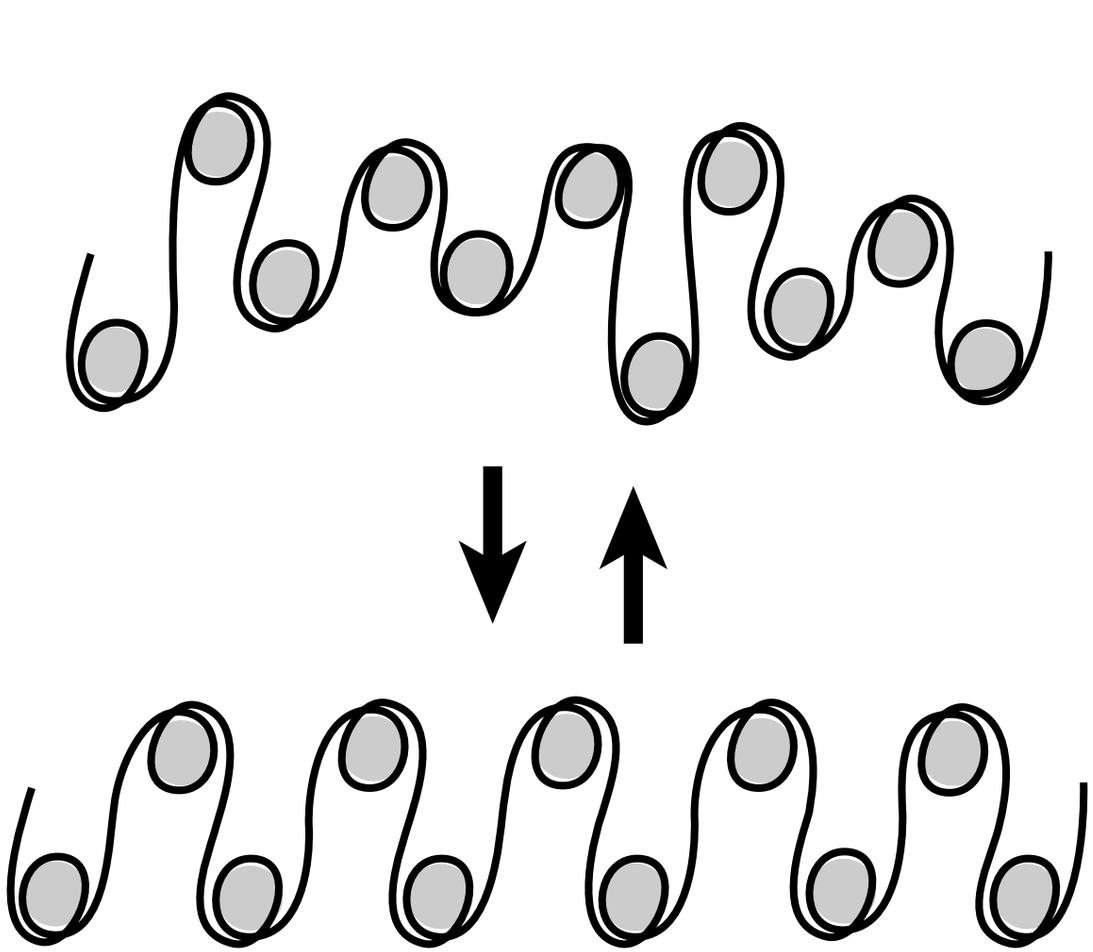
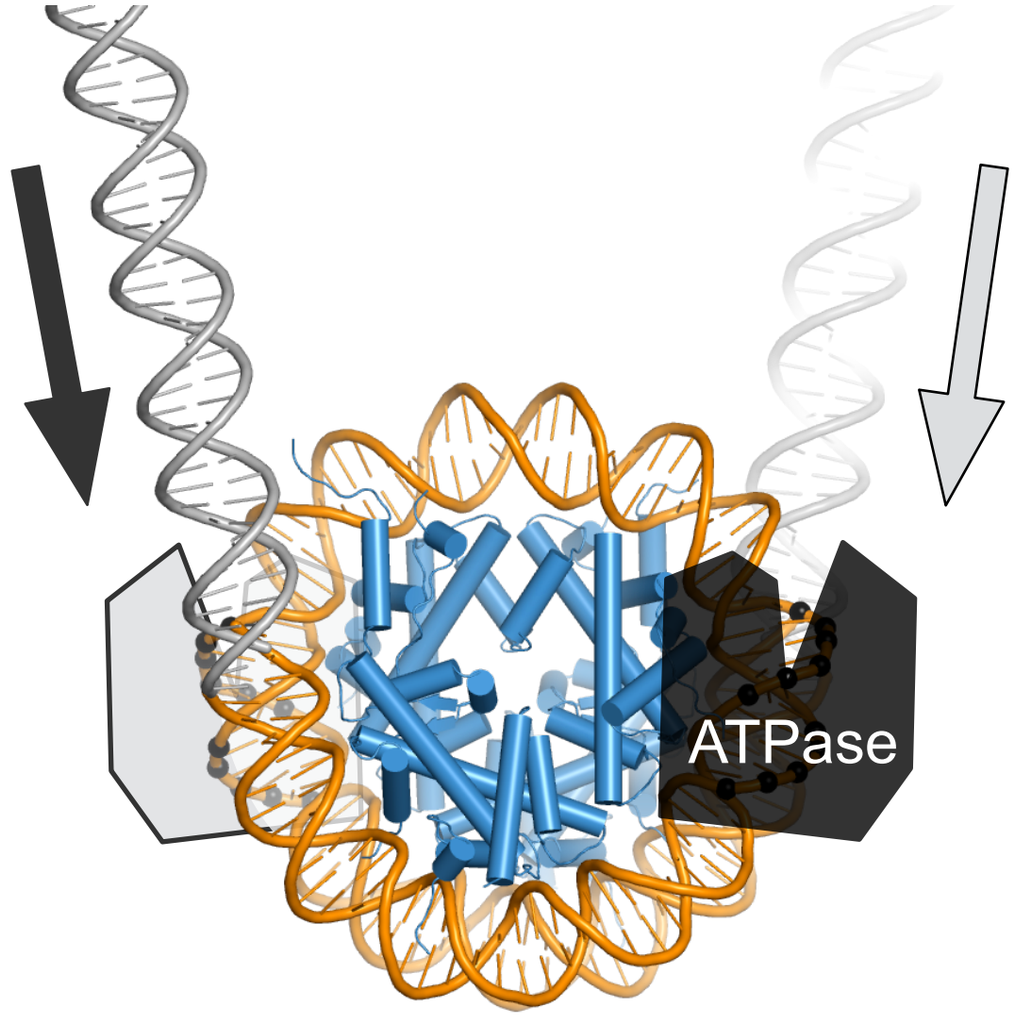


Lee & Yang, Cell (2006)

ATPase motors pull DNA onto the nucleosome





Schwanbeck et al., JBC (2004)

Saha et al., NSMB (2005)

Zofall et al., NSMB (2006)

Dang & Bartholomew, MCB (2007)

McKnight et al., MCB (2011)

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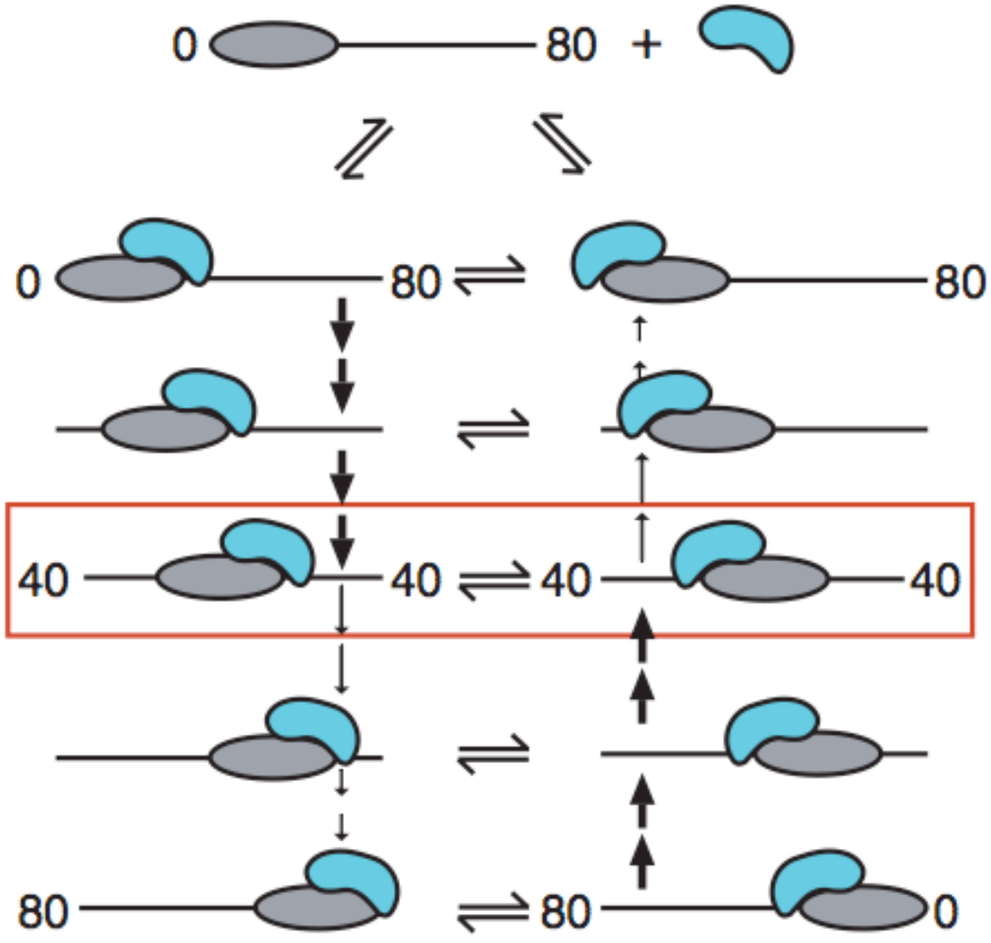
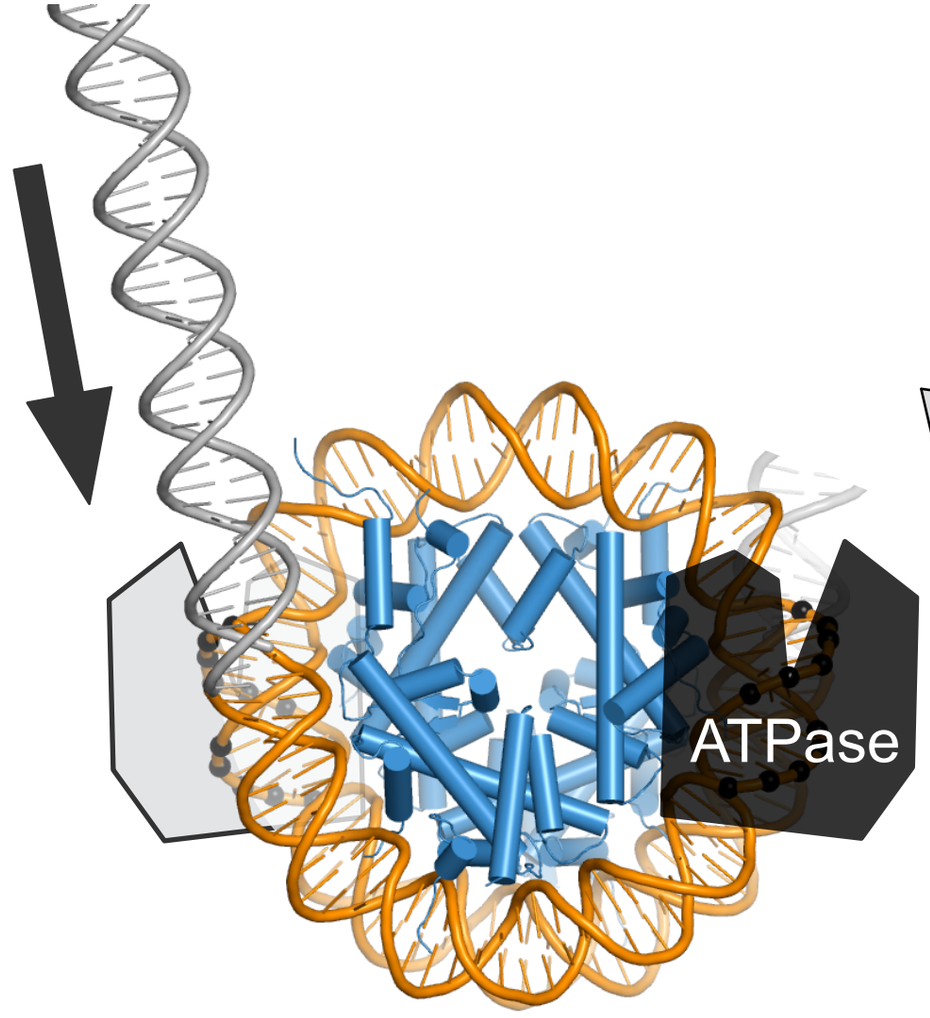


Yang et al., NSMB (2006)



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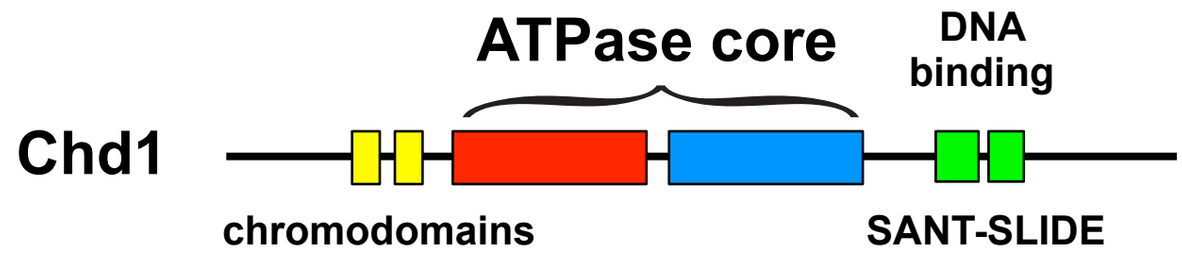
Saha et al., NSMB (2005)

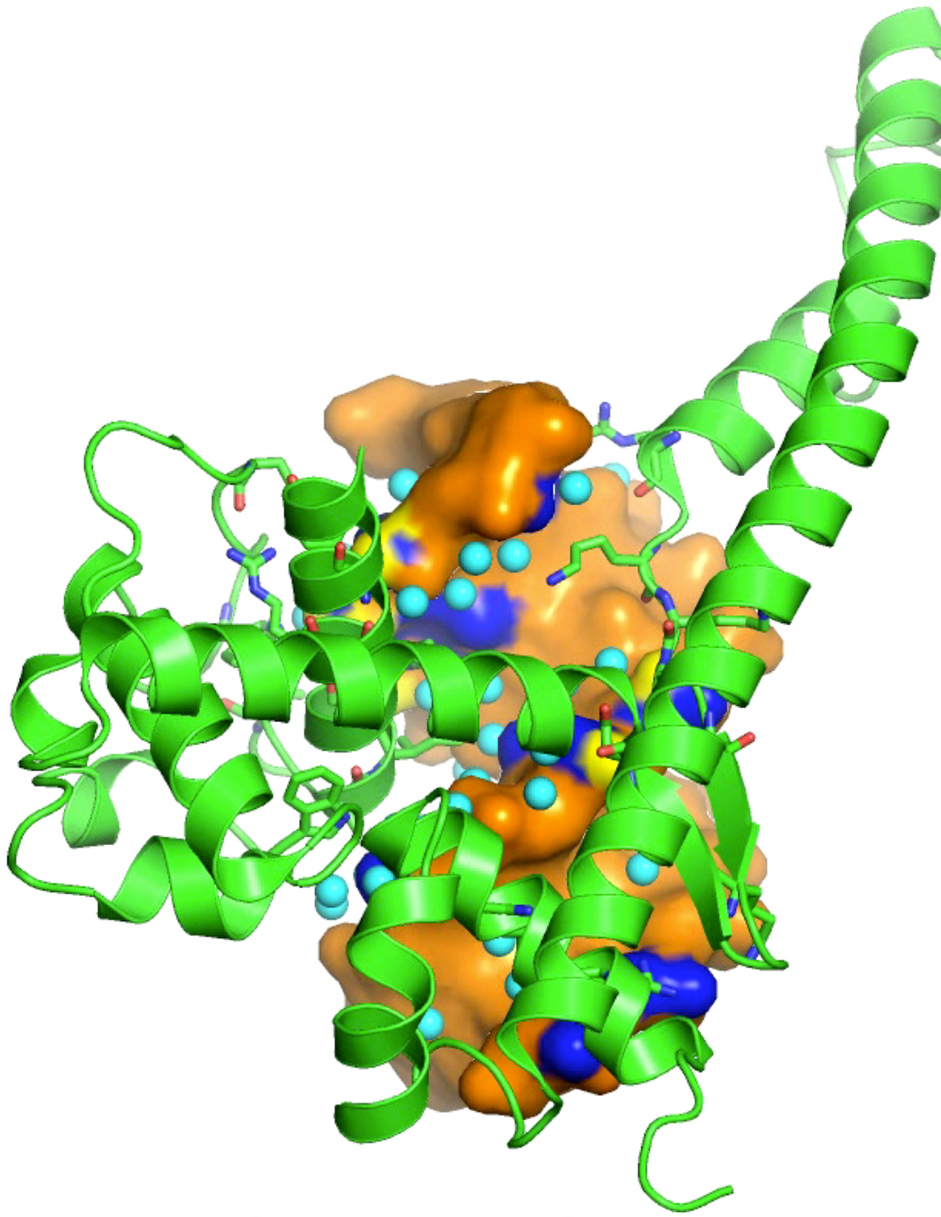
Zofall et al., NSMB (2006)

Dang & Bartholomew, MCB (2007)

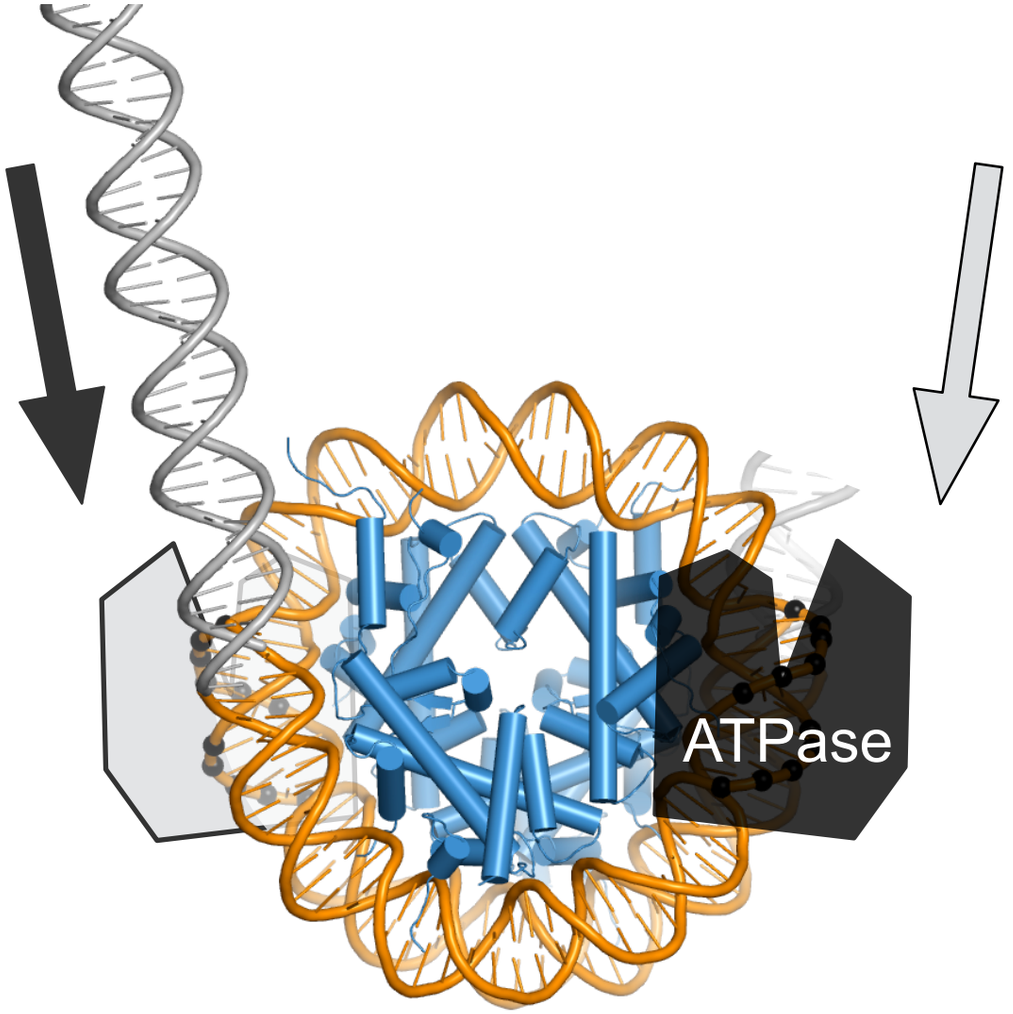
McKnight et al., MCB (2011)

How does Chd1 sense DNA outside the nucleosome?

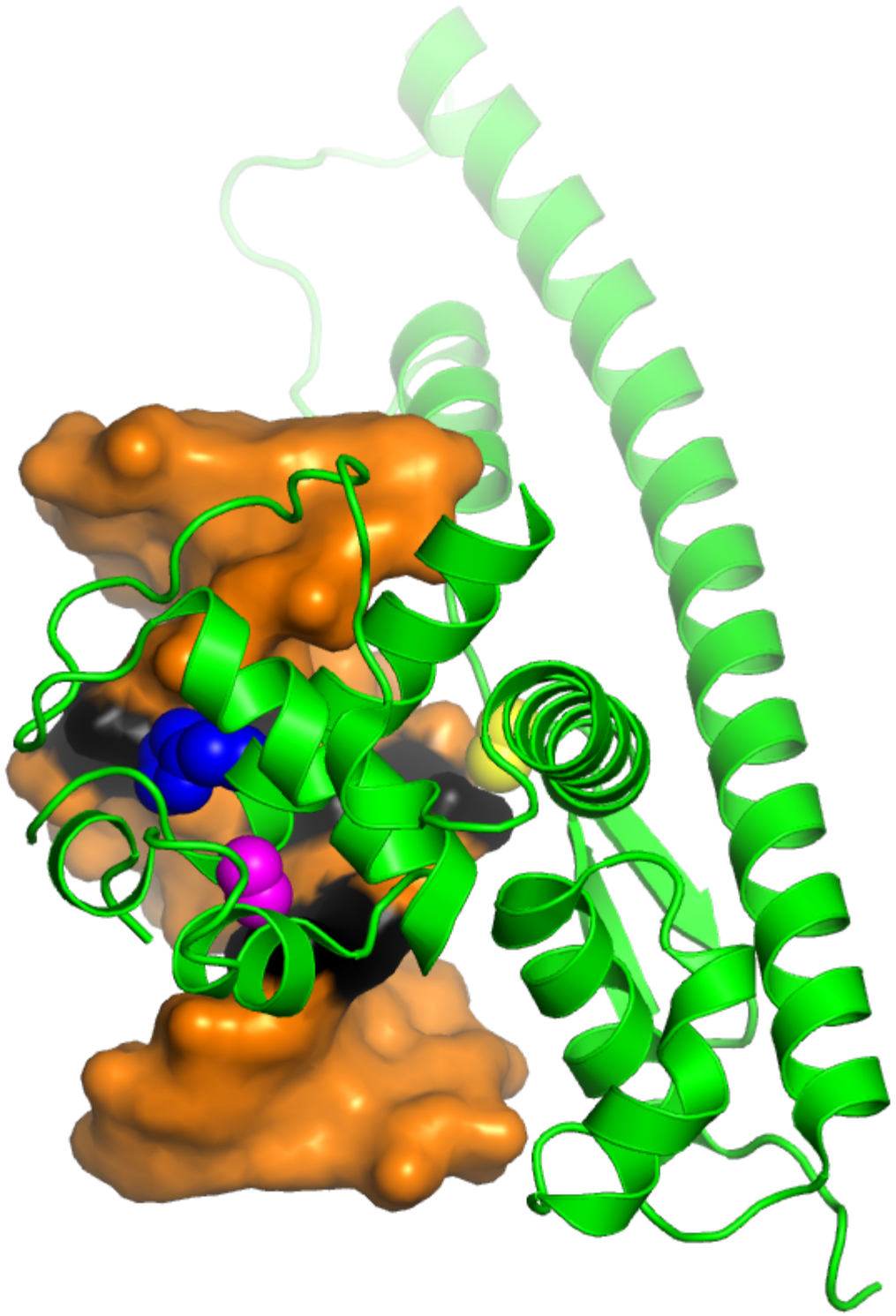


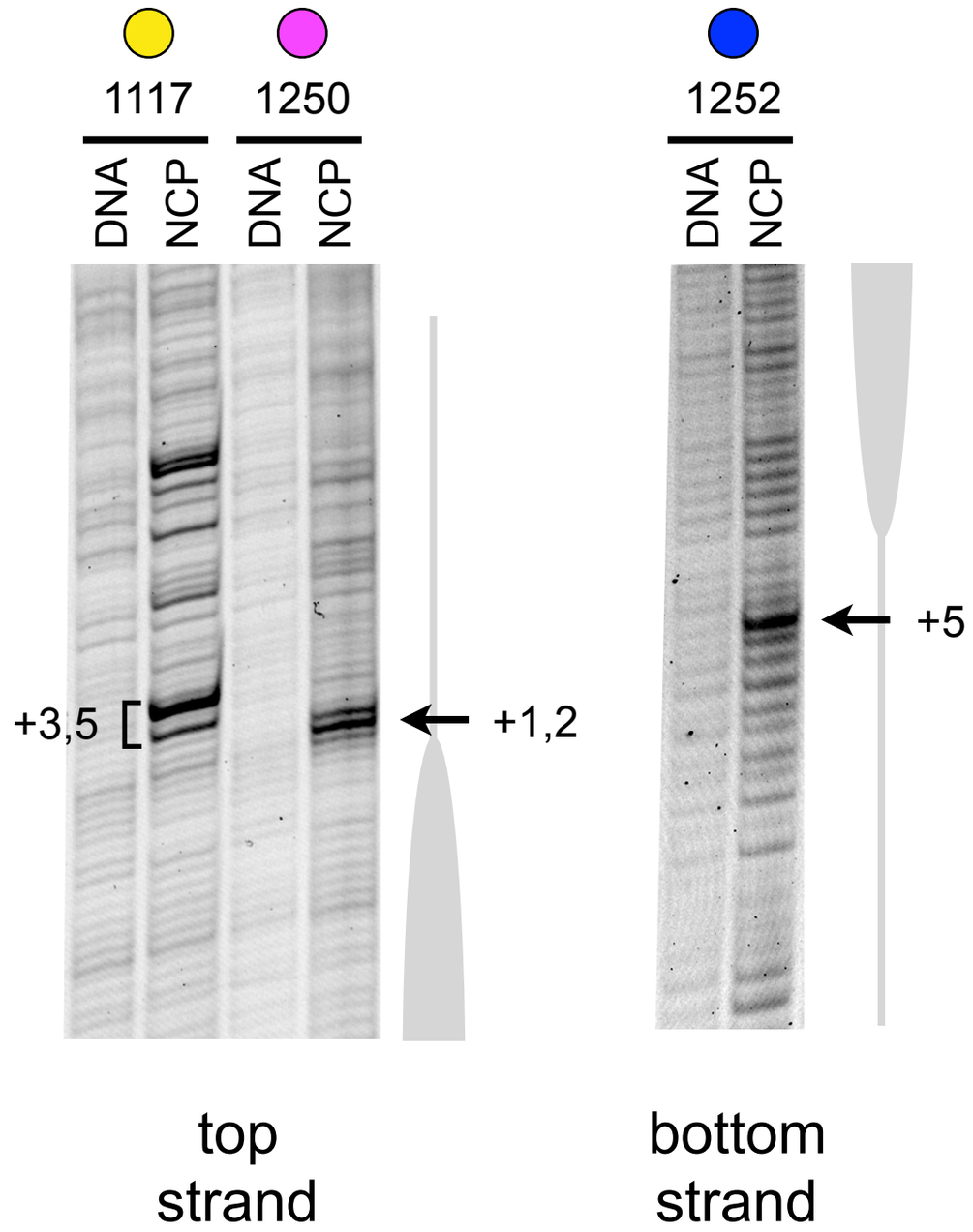


Sharma et al., JBC (2011)



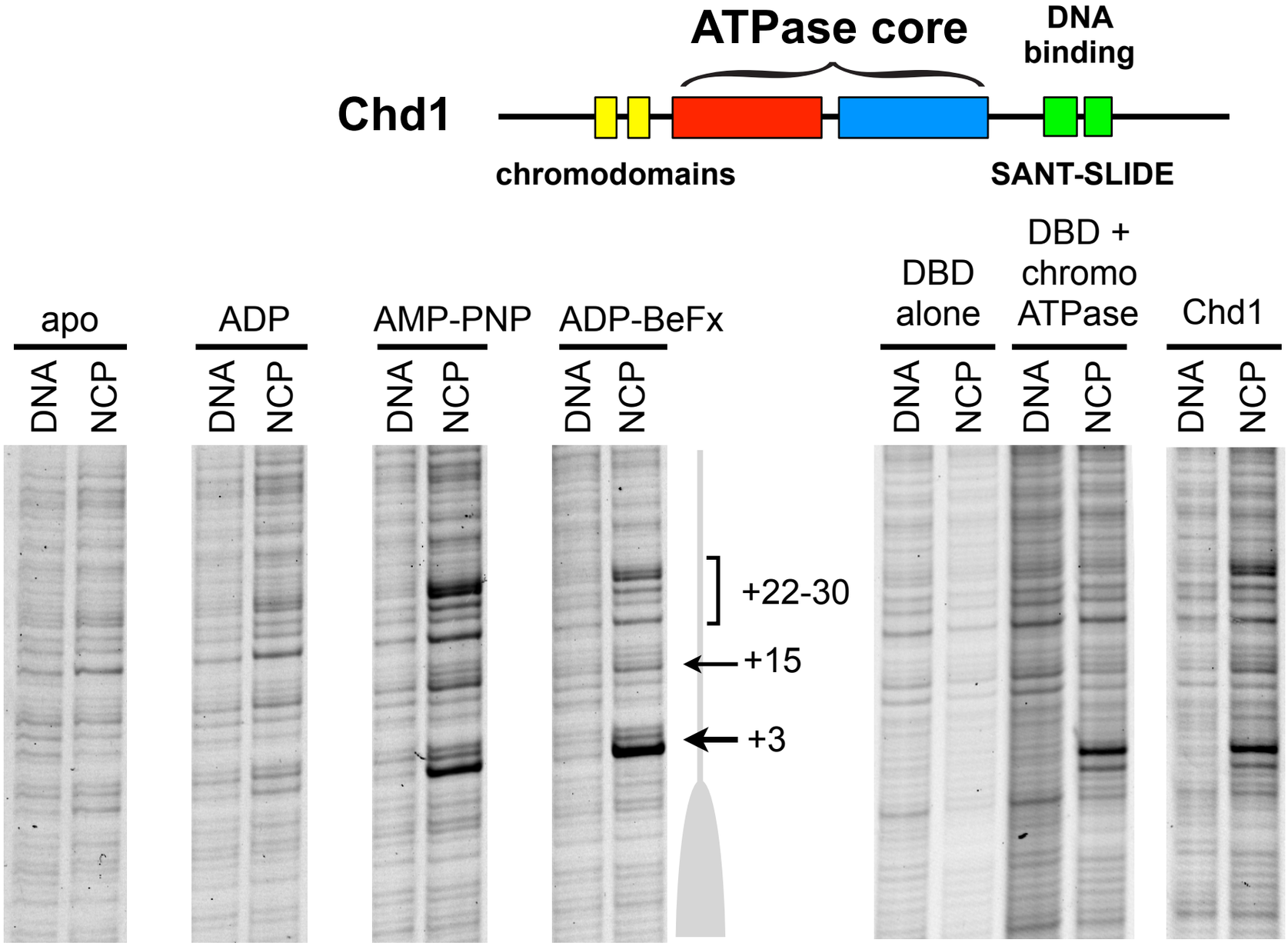
The Chd1 DNA-binding domain makes specific contacts at the nucleosome edge



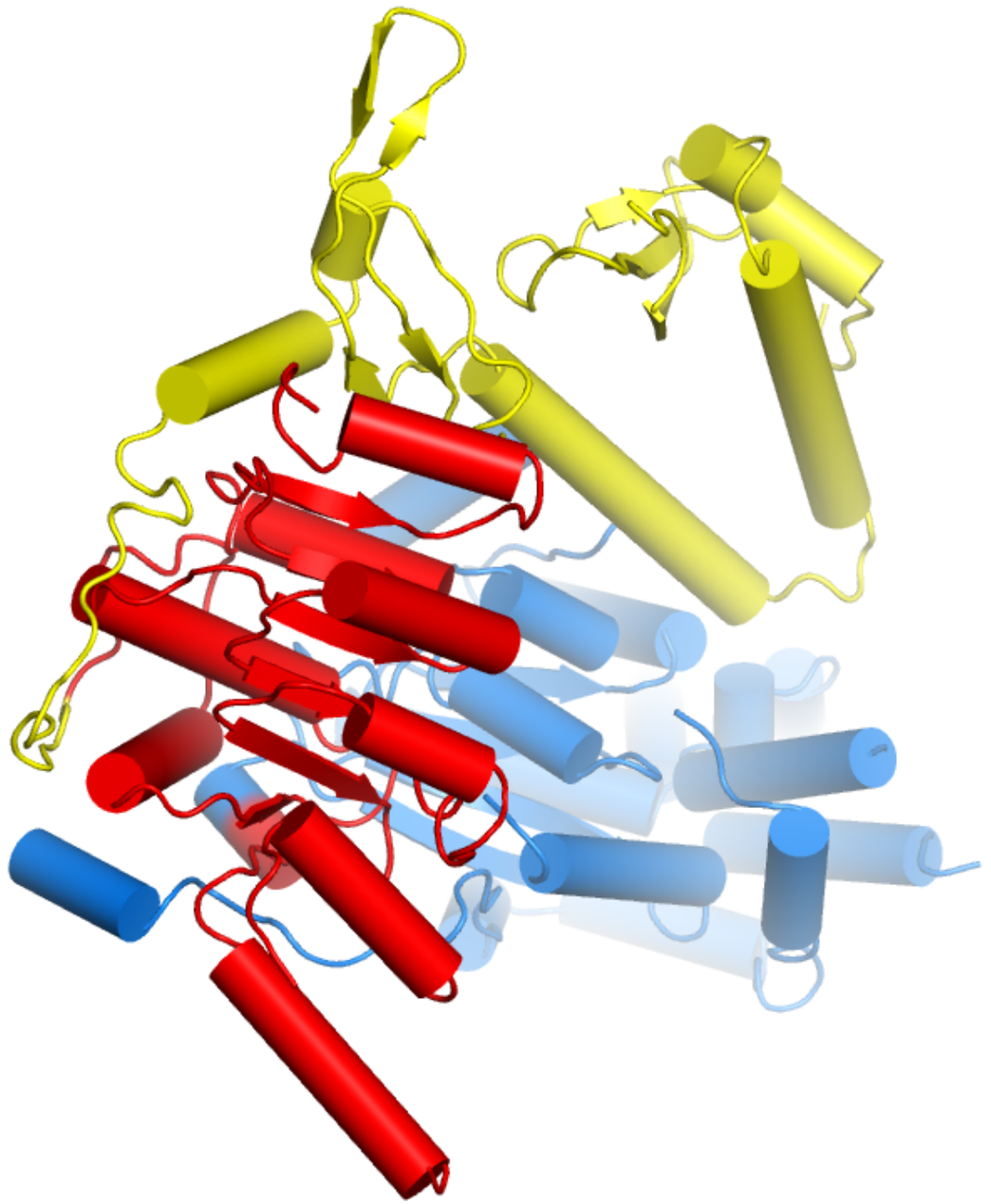


Nodelman et al., Mol Cell (2017)

The Chd1 DNA-binding domain can be stabilized by the chromo-ATPase in trans



Cross-linking defines the positions of the Chd1 ATPase on the nucleosome



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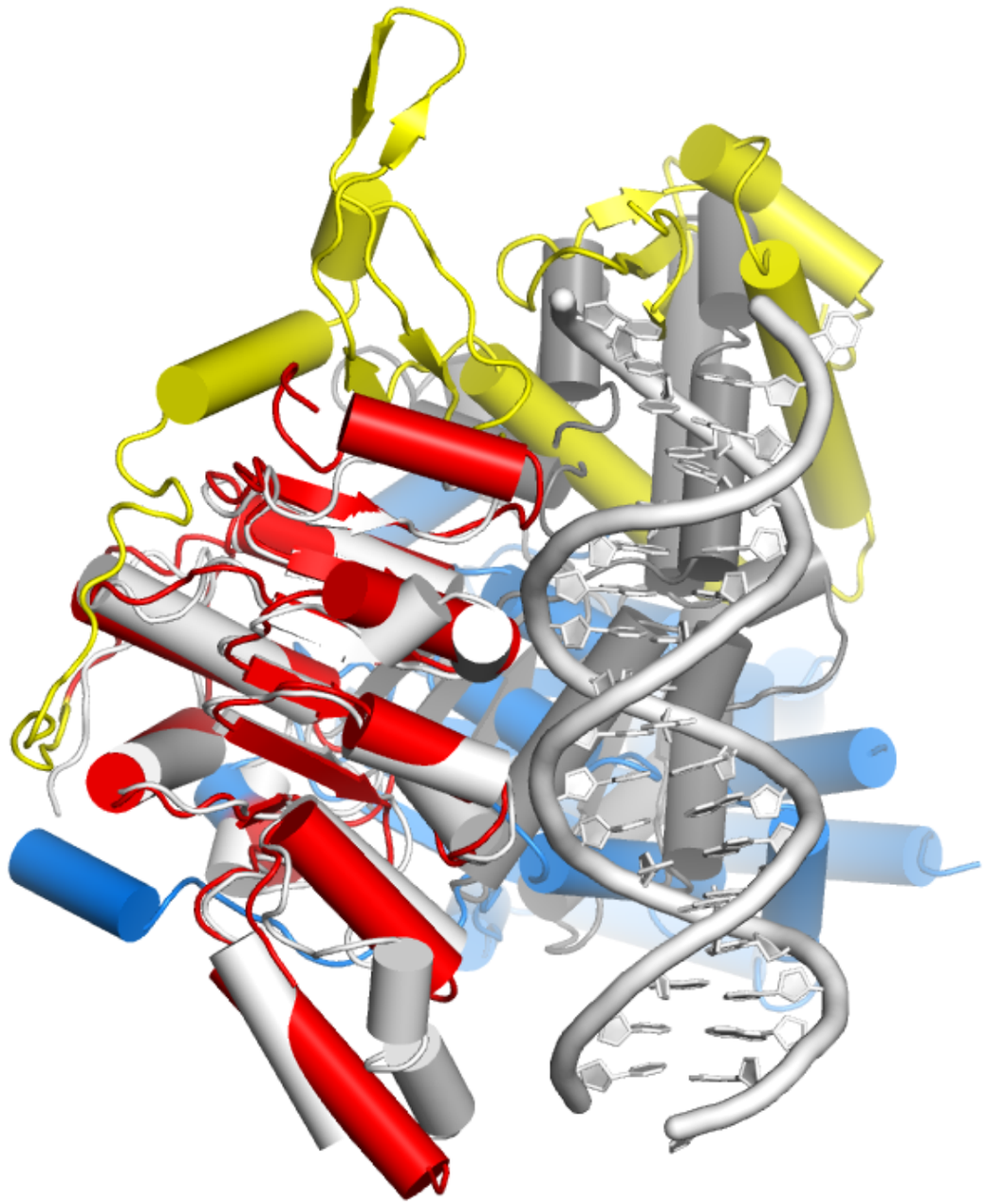

○ modeled DNA from Rad54 structure

Dürr et al., Cell (2005)

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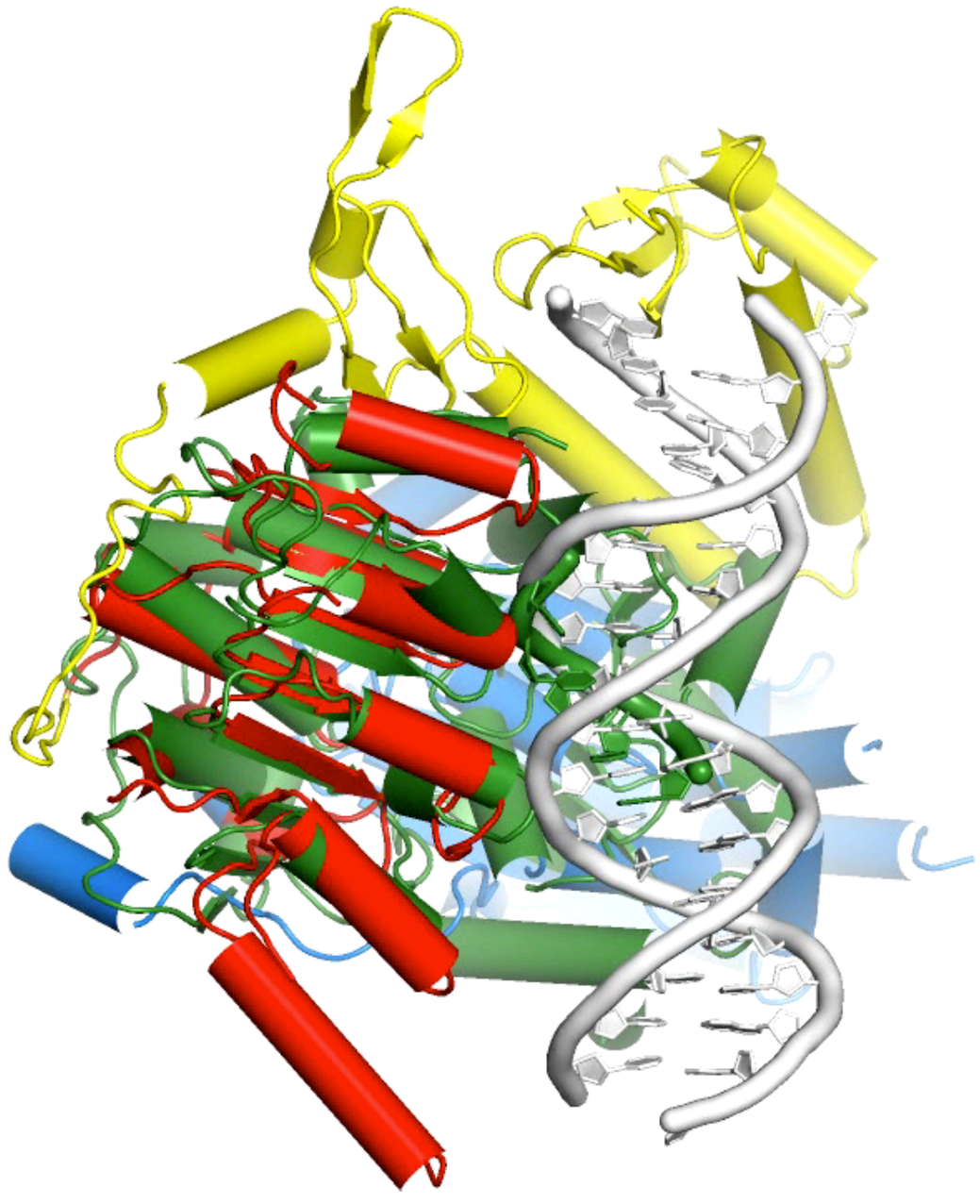

- ATP-bound closed from of Vasa DEAD-box helicase

Sengoku et al., Cell (2006)

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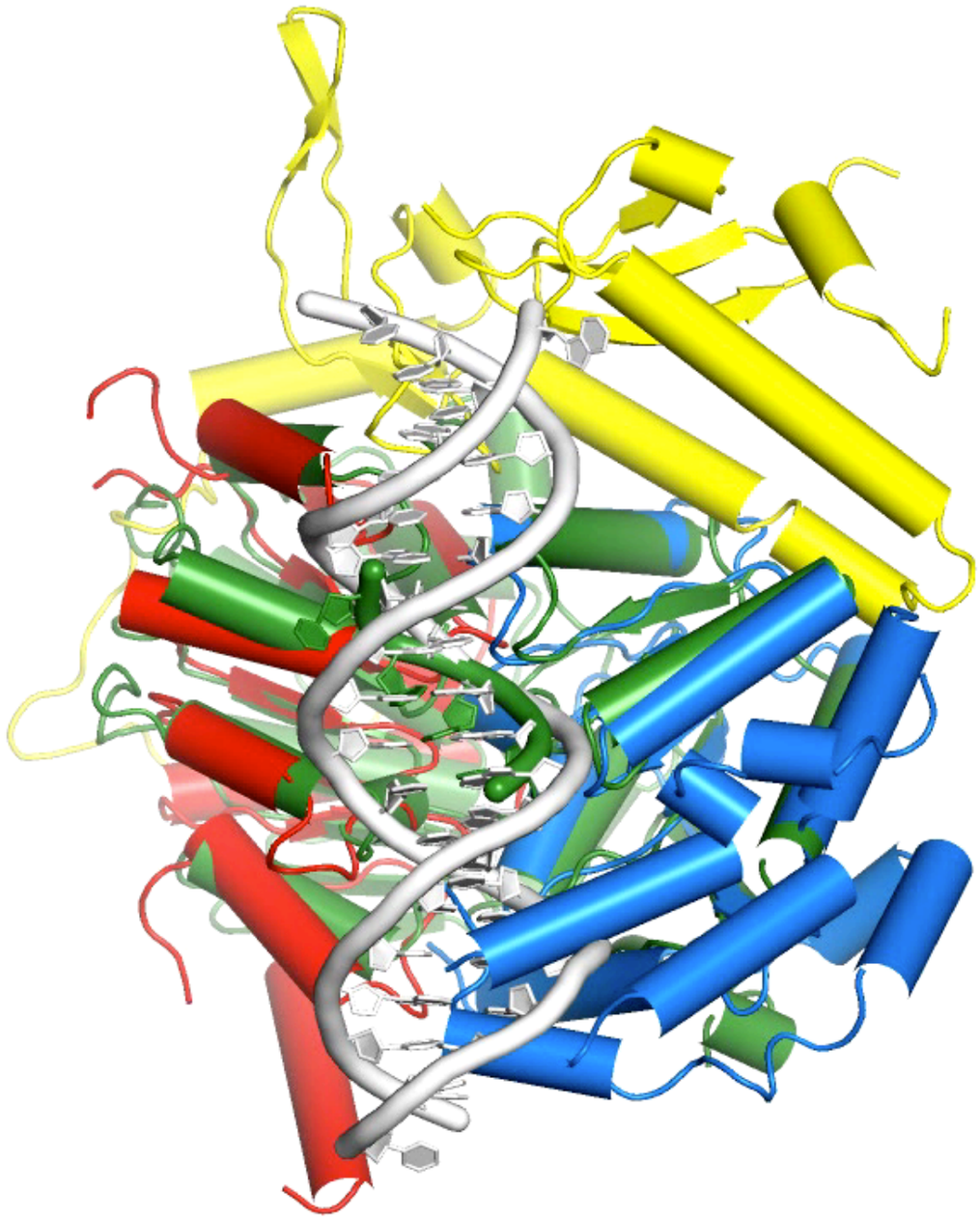

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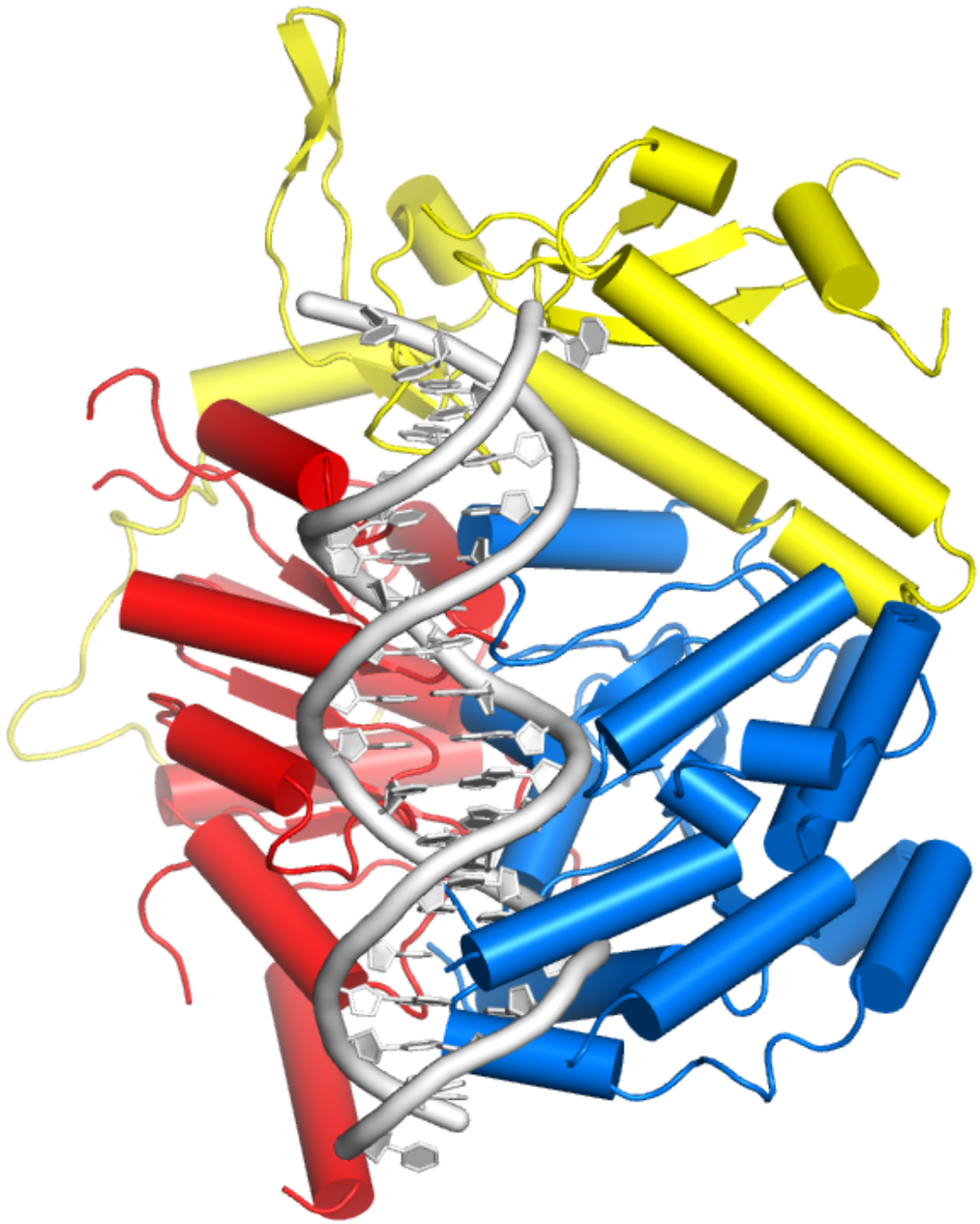

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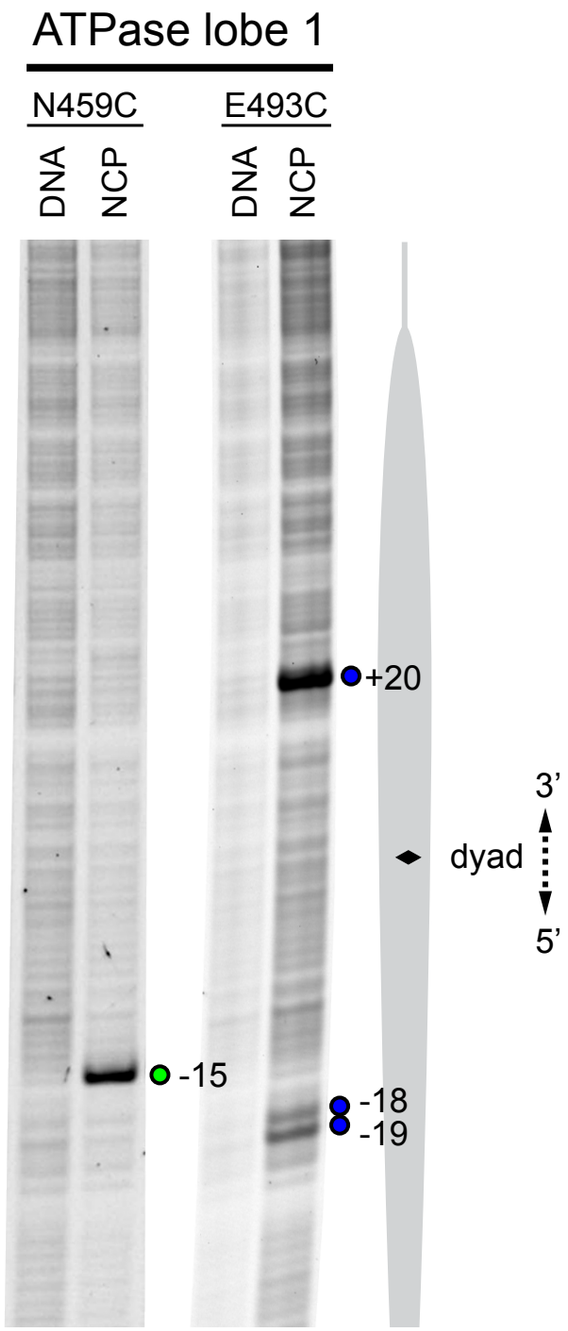

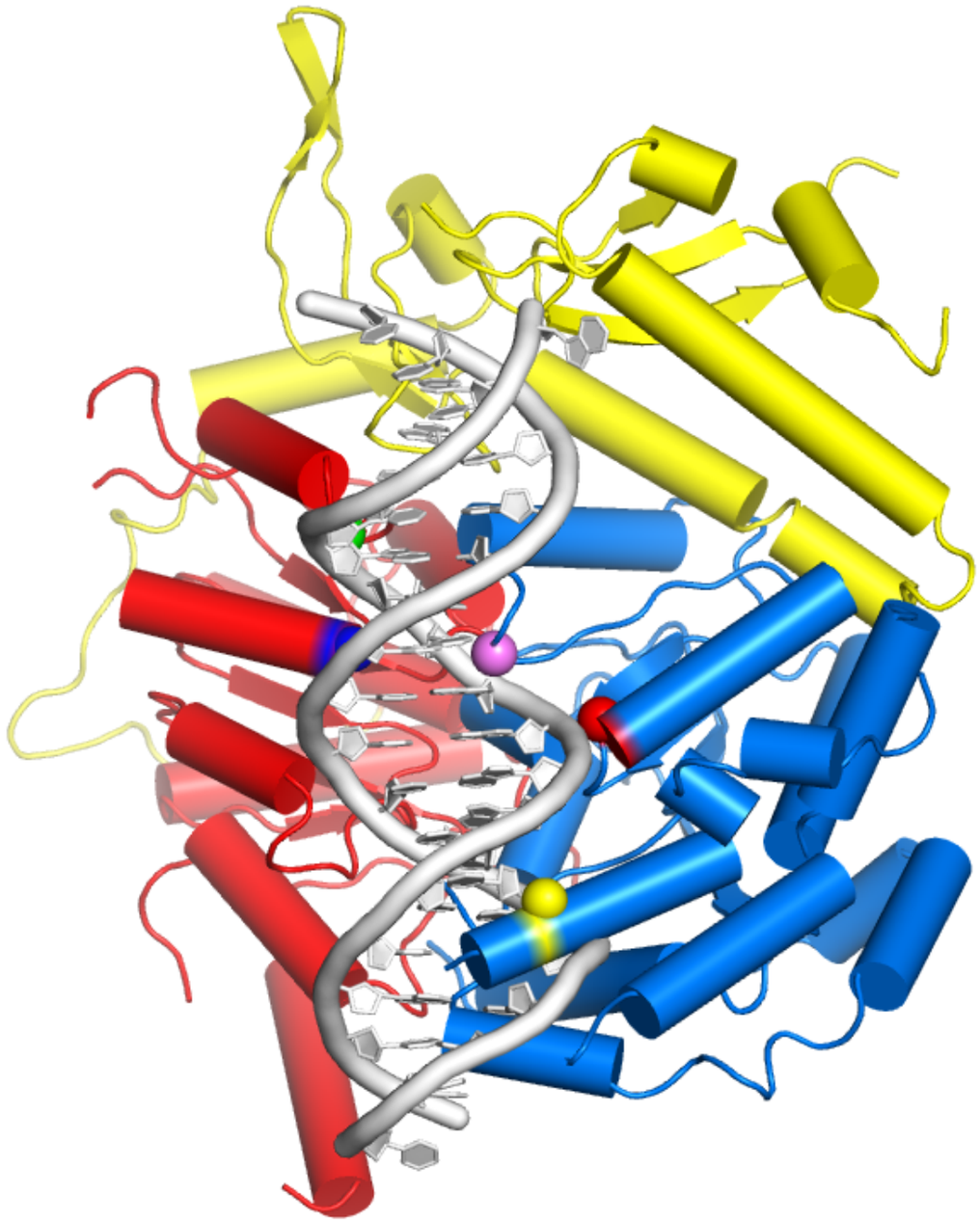

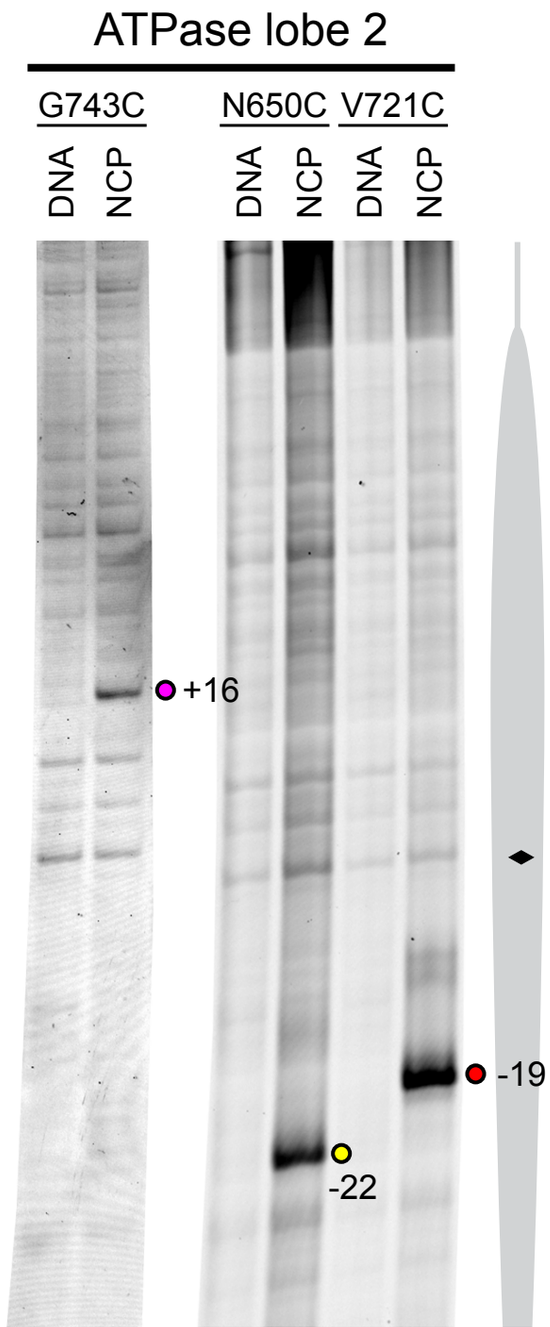

Nodelman et al., Mol Cell (2017)

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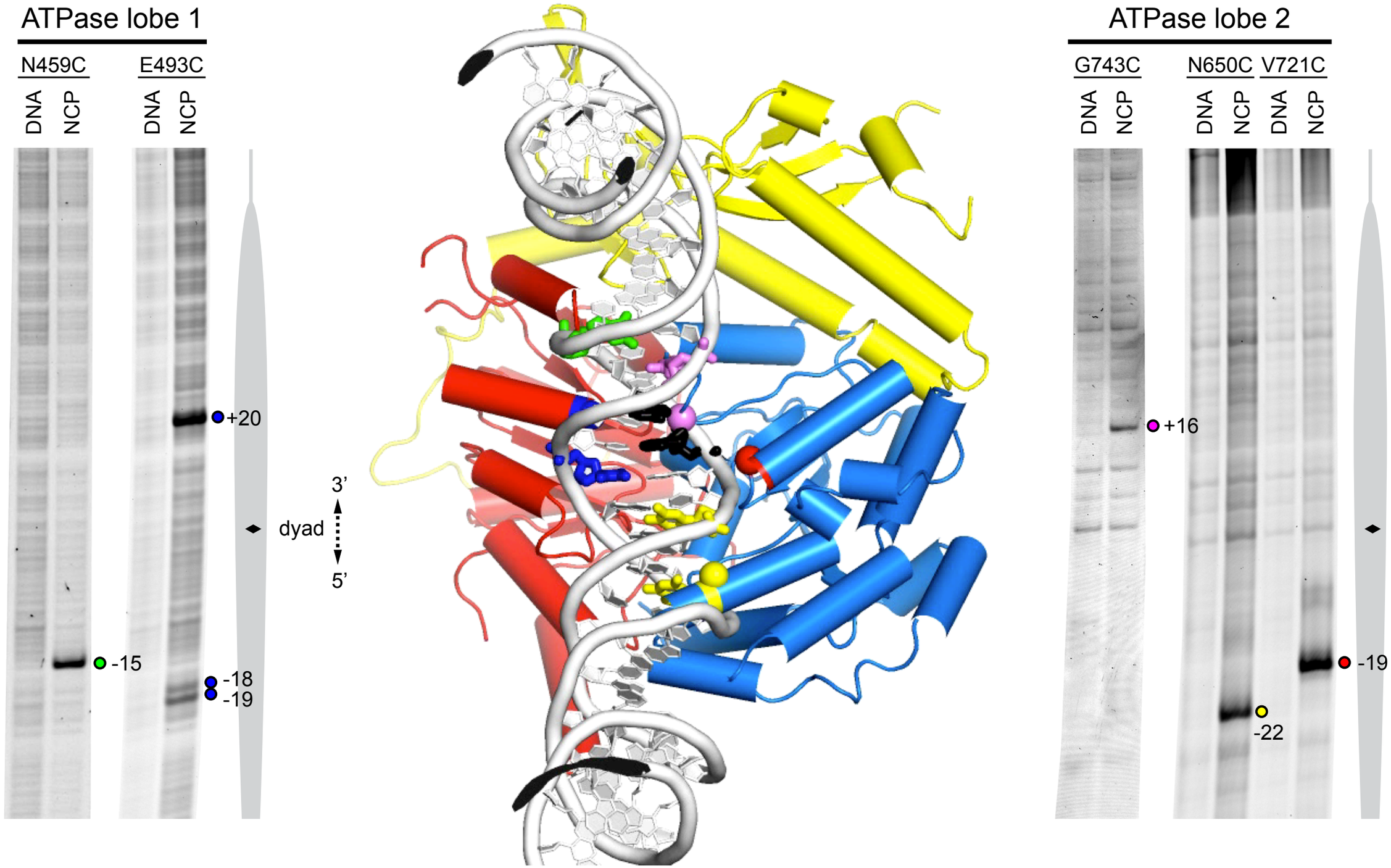

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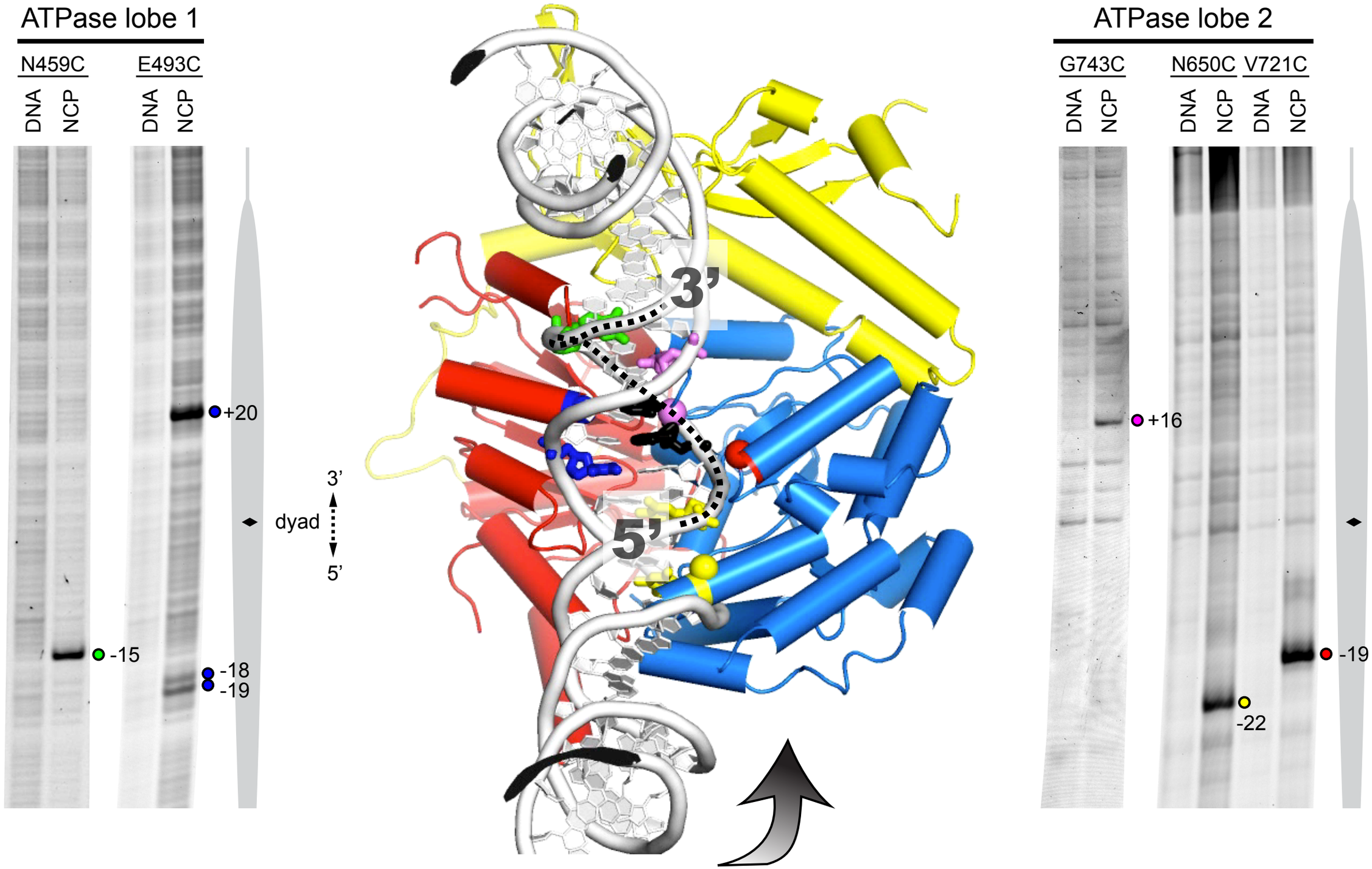
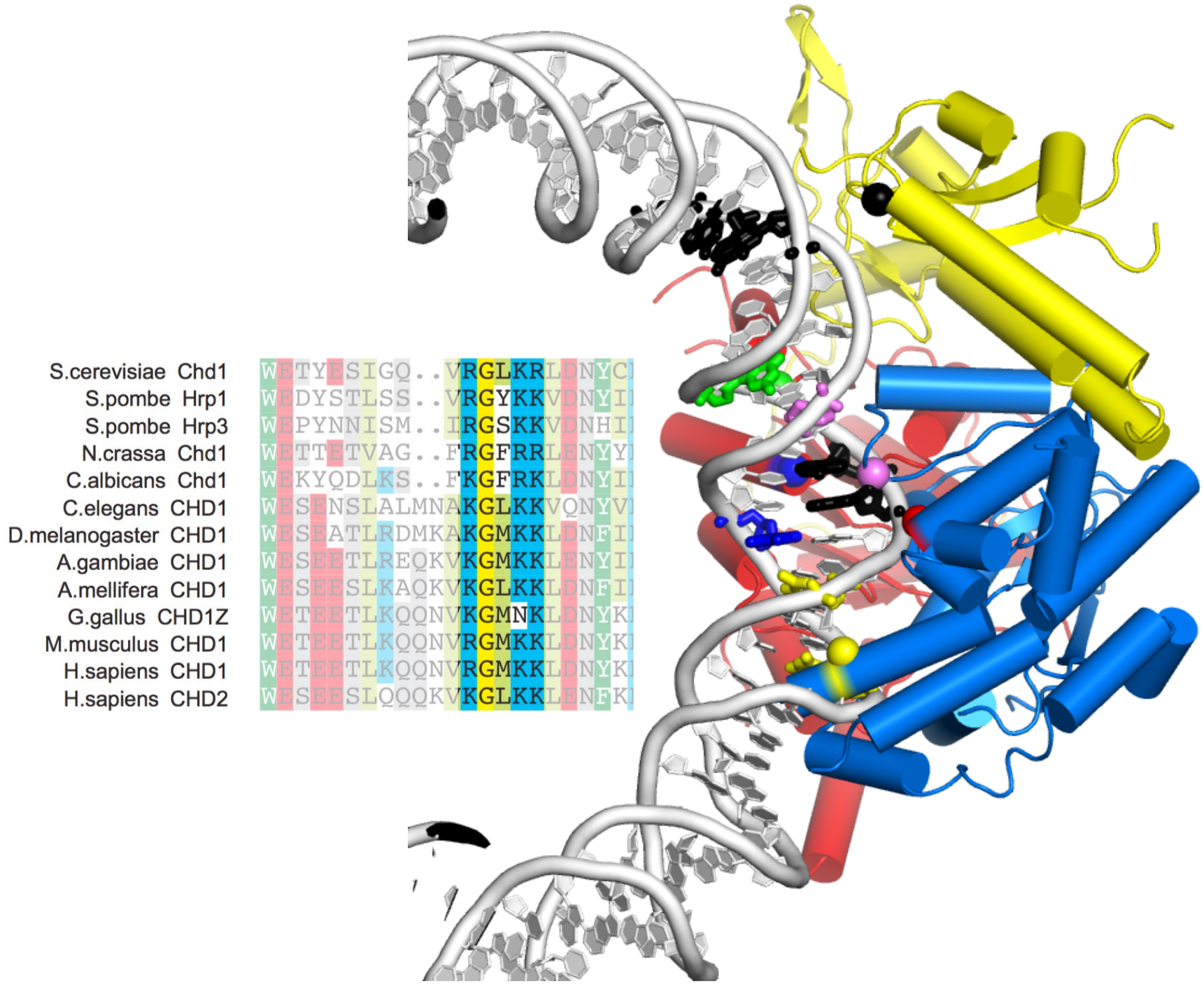
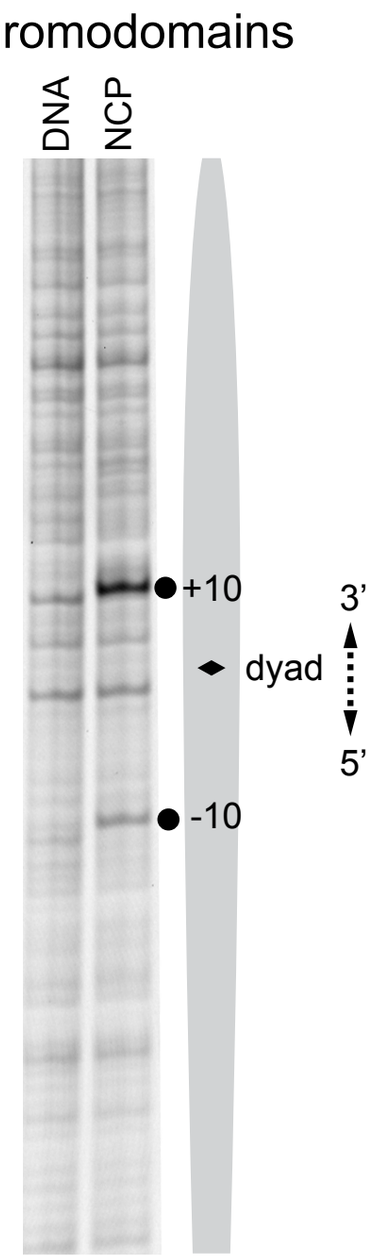


Nodelman et al., Mol Cell (2017)

The Chd1 chromodomains also cross-link to nucleosomal DNA





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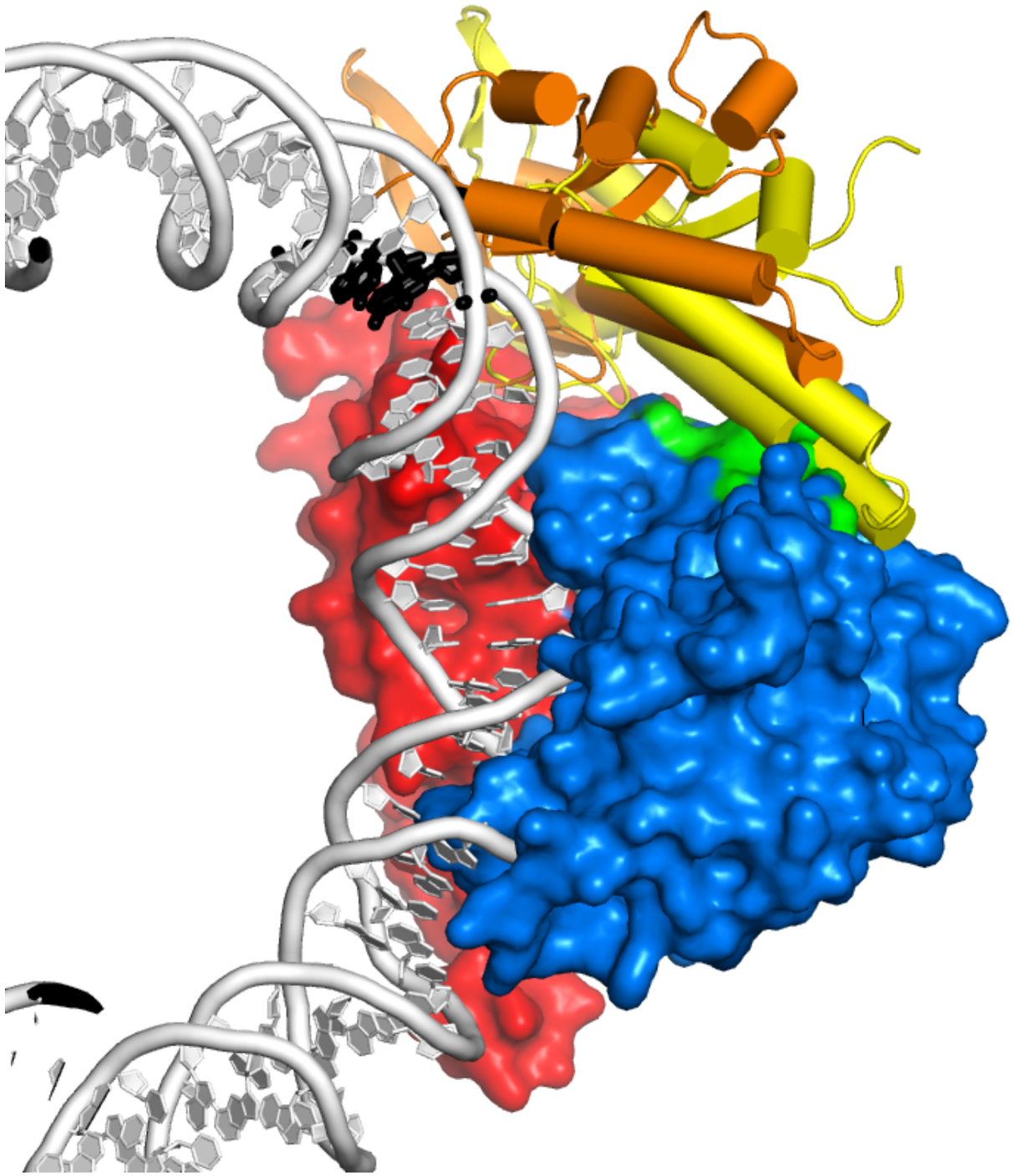
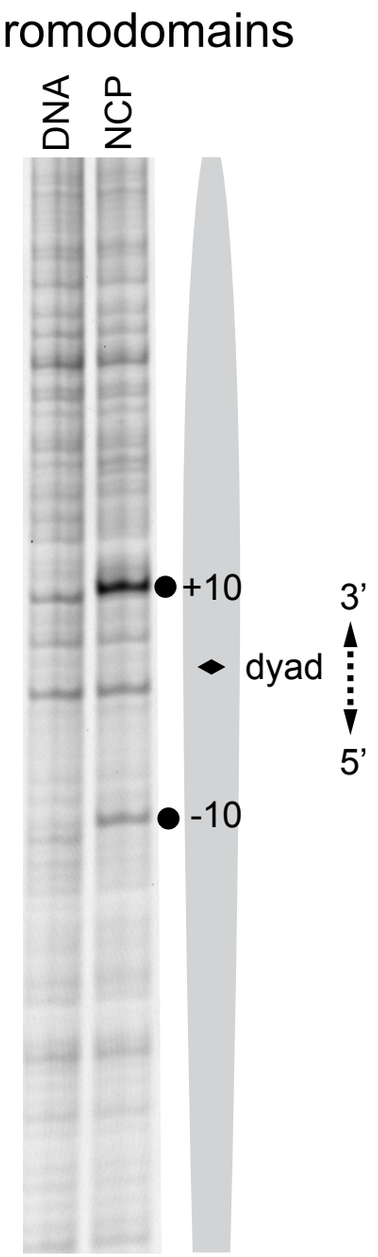
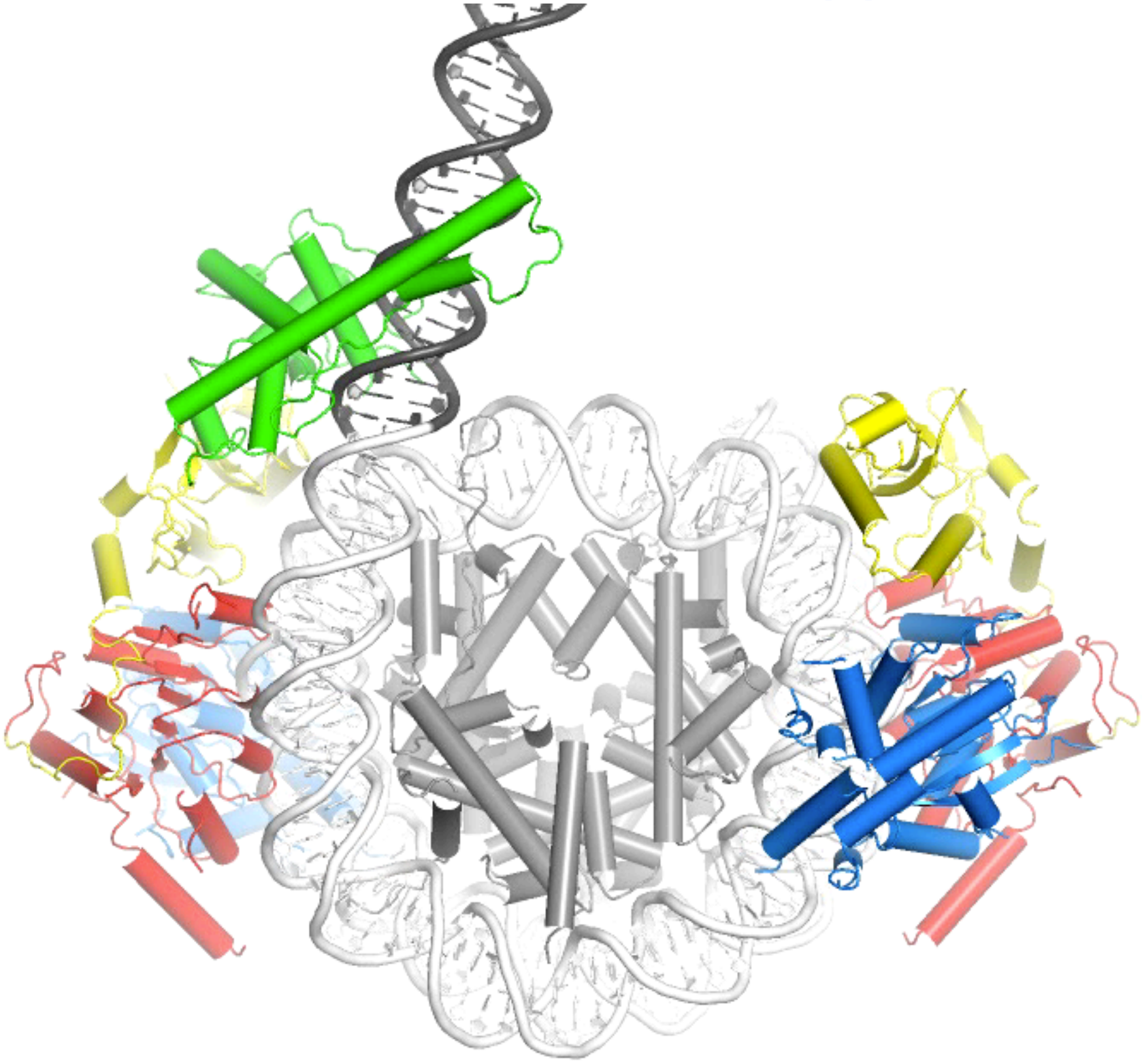


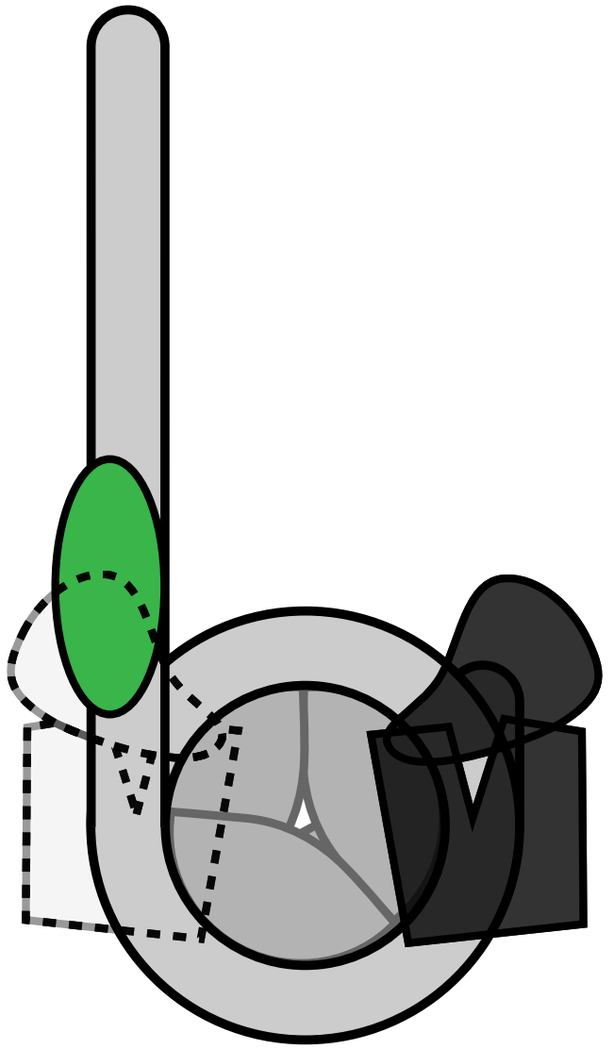


Nodelman et al., Mol Cell (2017)

Cross-linking places the DNA-binding domain closest to the ATPase on the opposite DNA gyre



Contacts across the DNA gyres suggests an inhibitory mechanism



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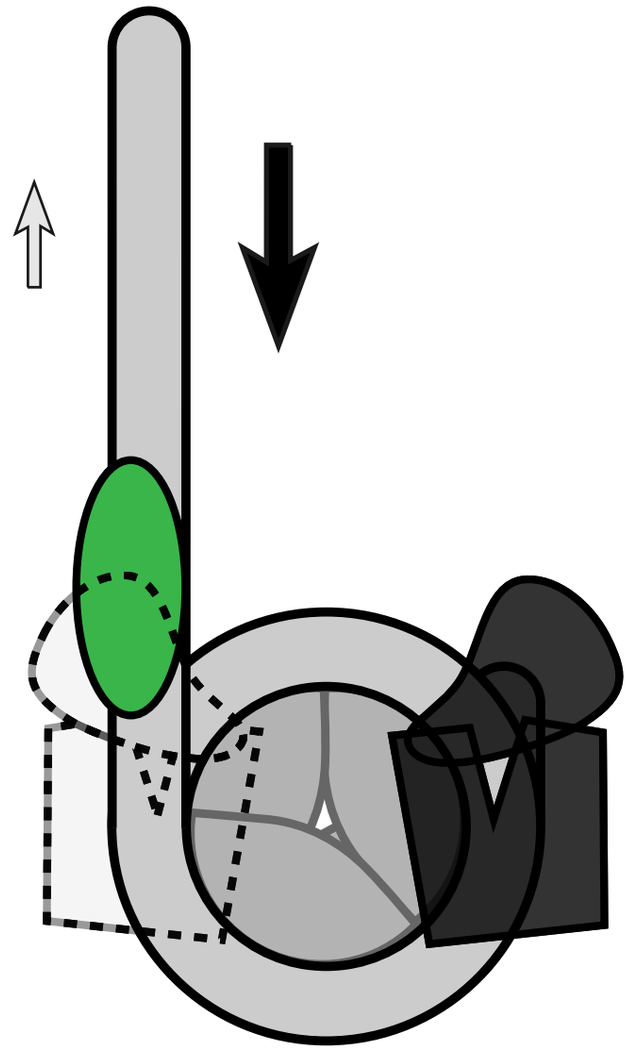

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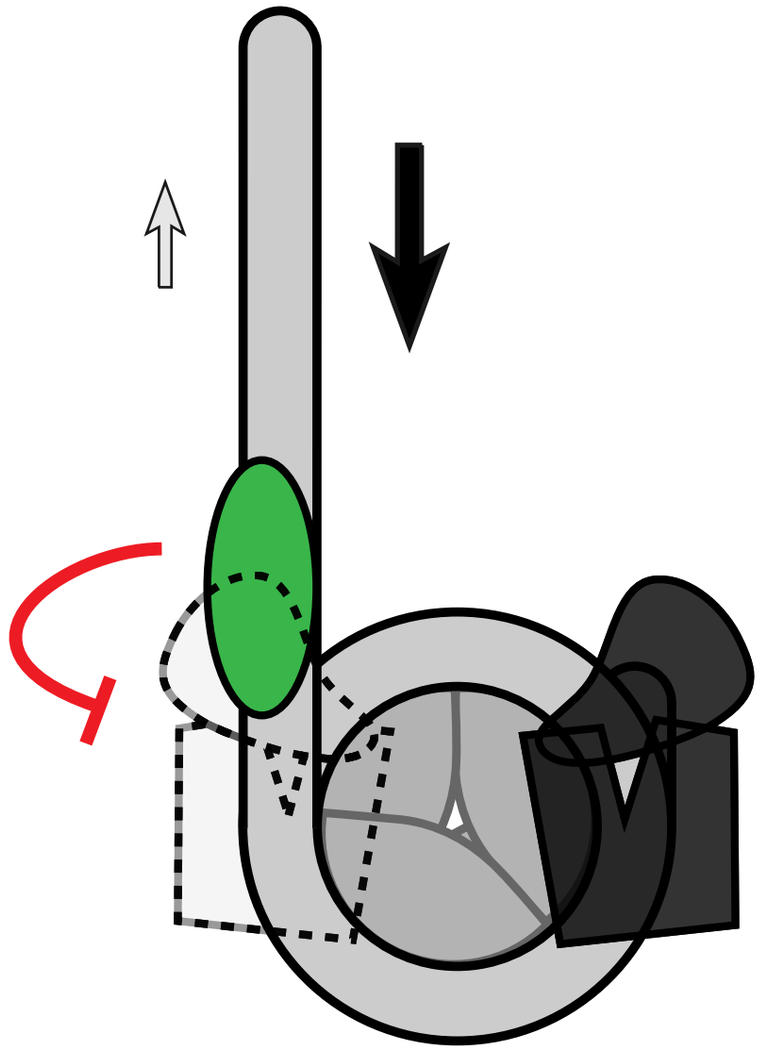

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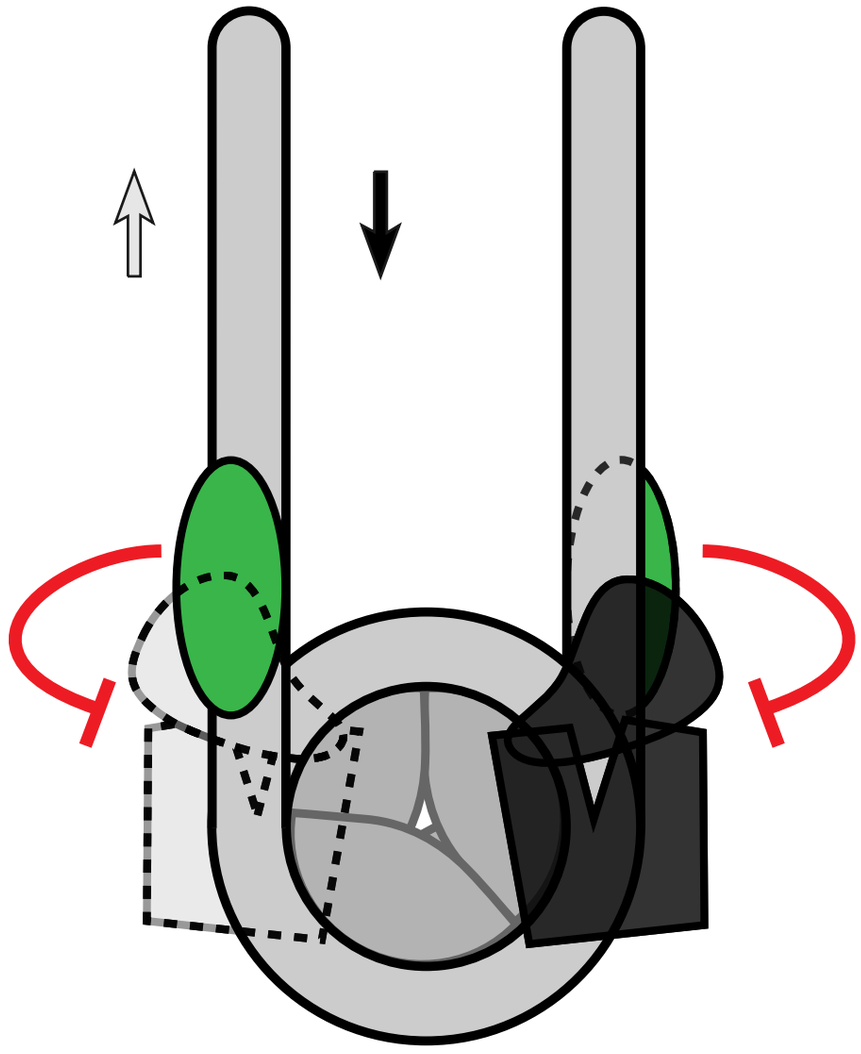
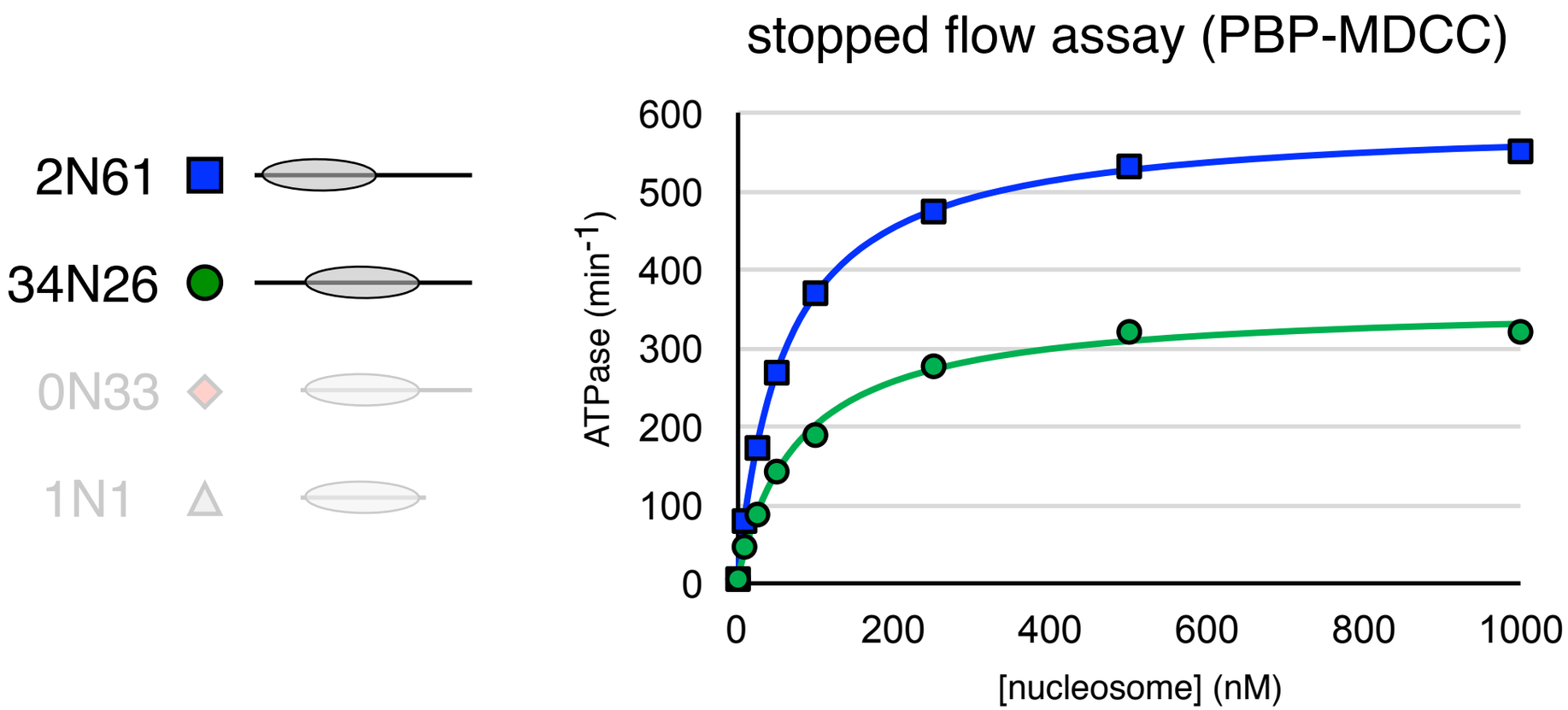


The absence of exit DNA stimulates ATPase activity of Chd1



Nodelman et al., Mol Cell (2017)

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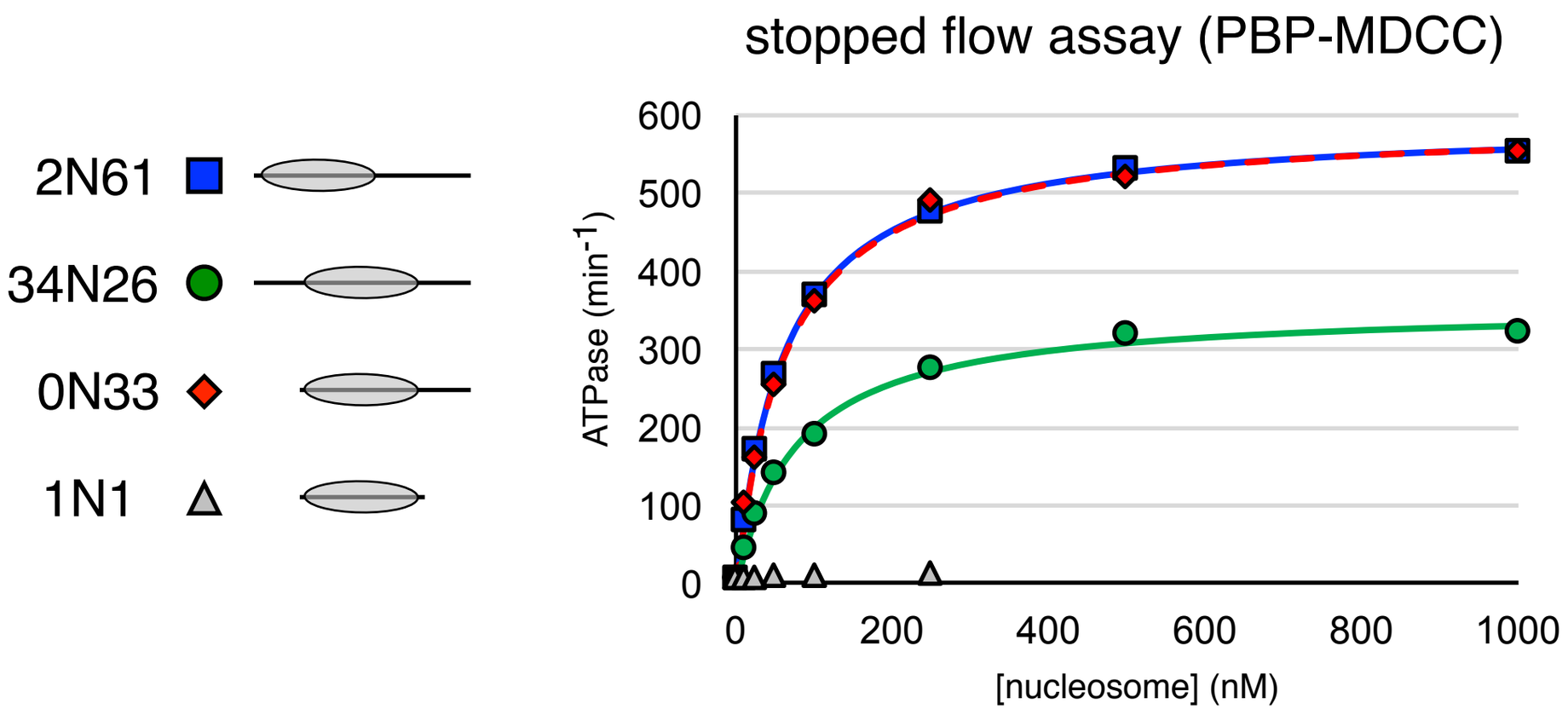

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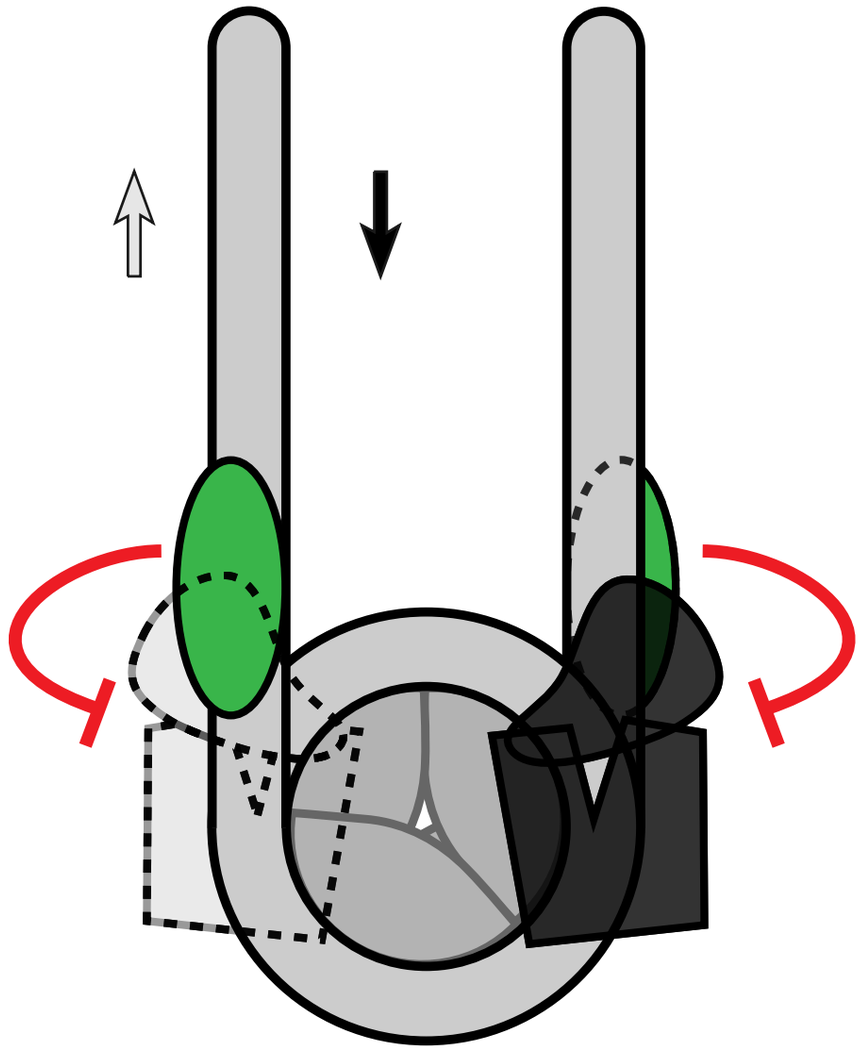

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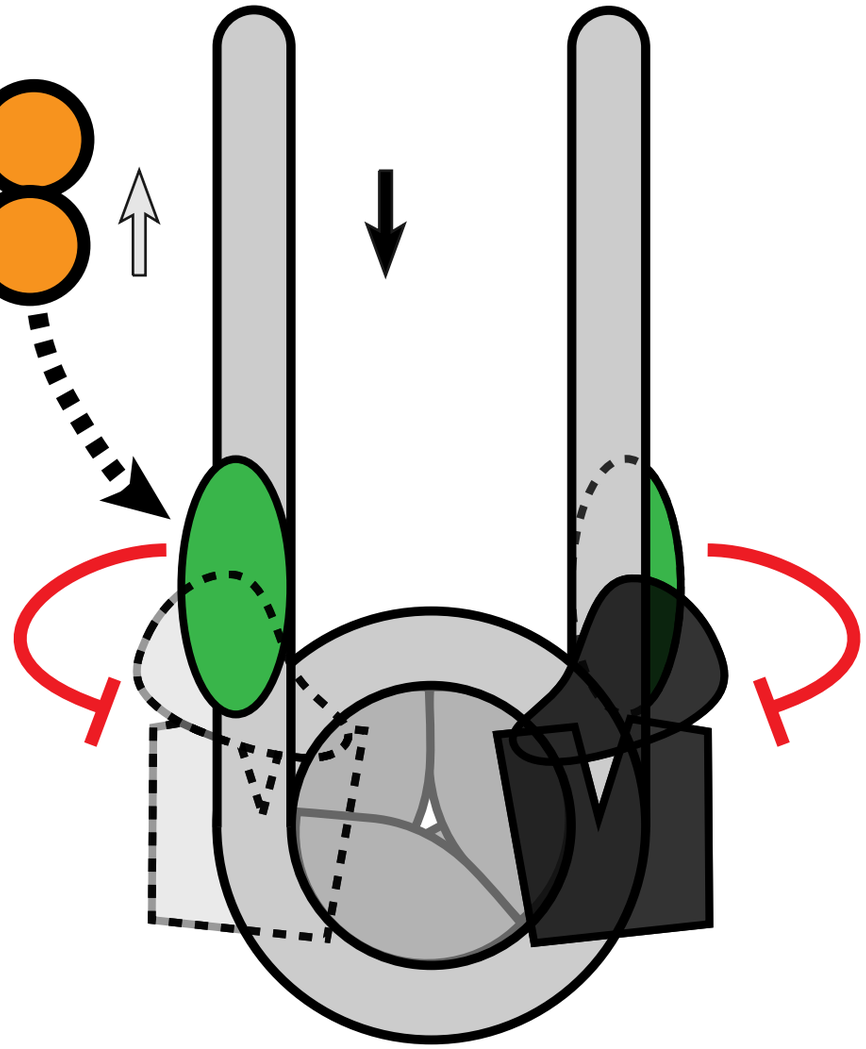

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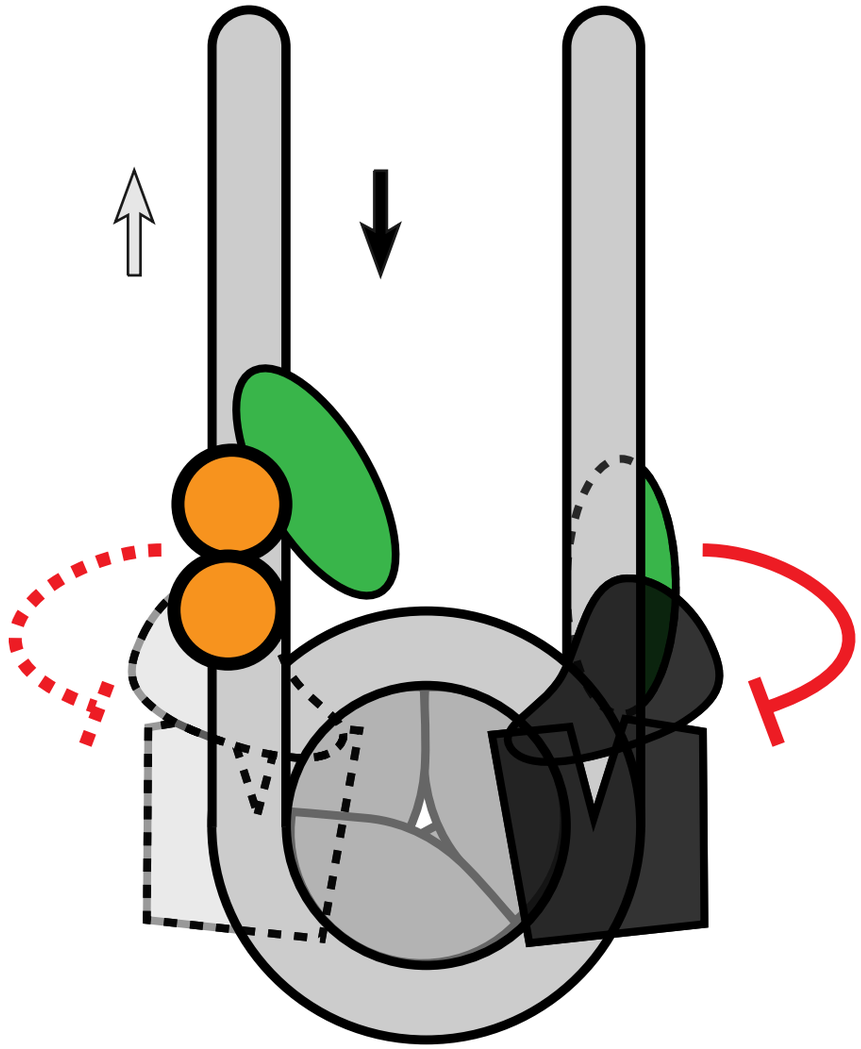

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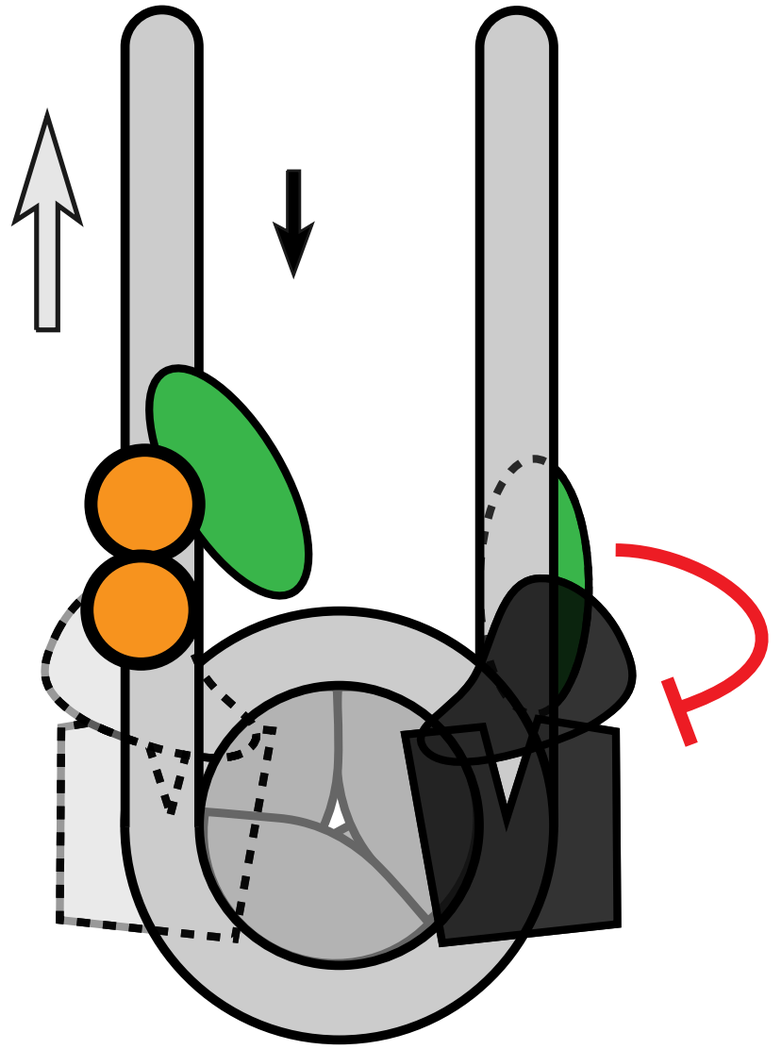
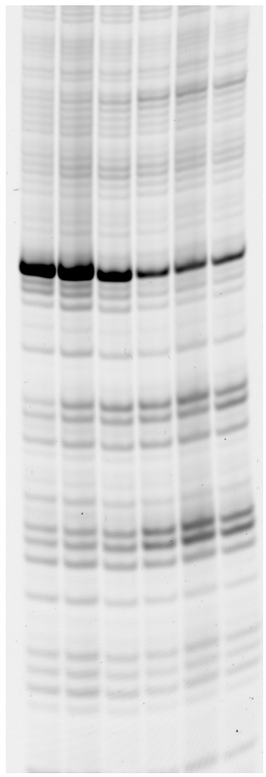


Lac repressor increases the rate of sliding away from LacO

time

no LacI



Nodelman et al., NAR (2016)

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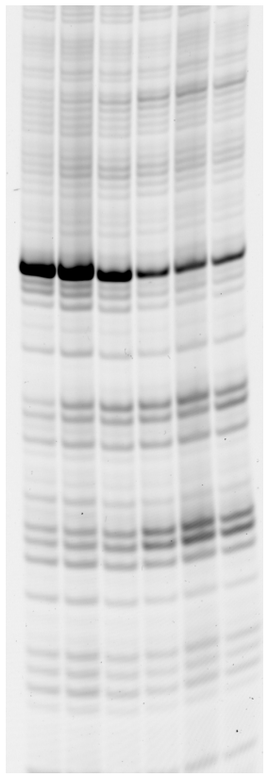
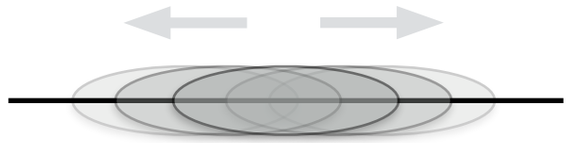
time

no LacI





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time

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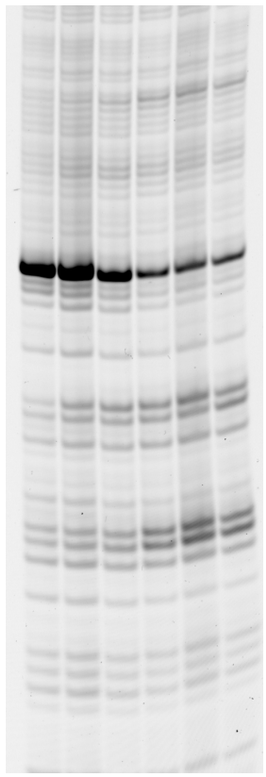

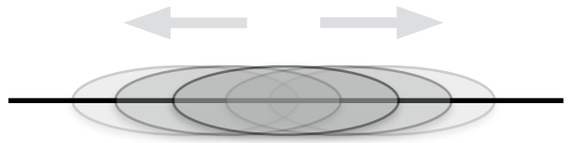

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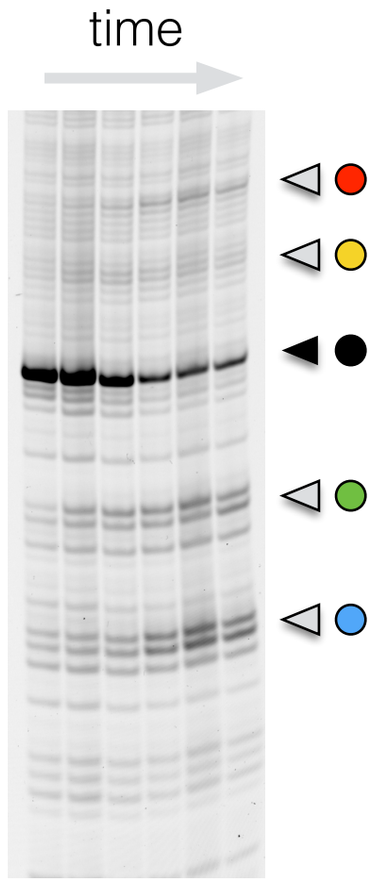
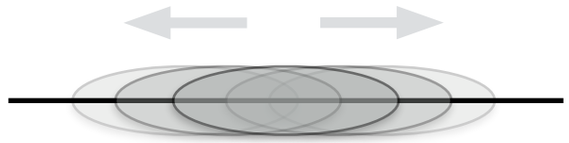
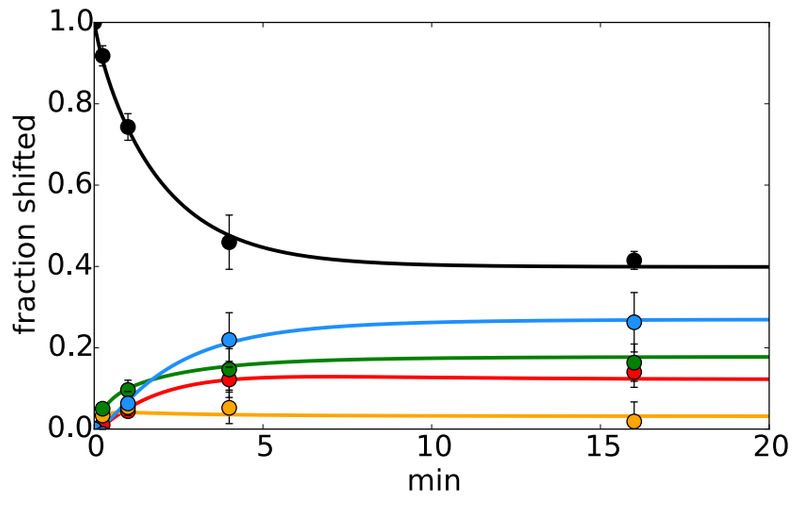
no LacI





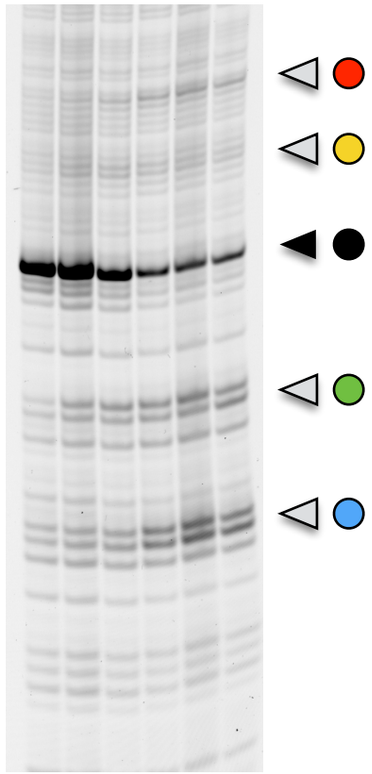


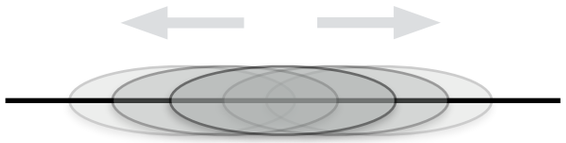
Nodelman et al., NAR (2016)

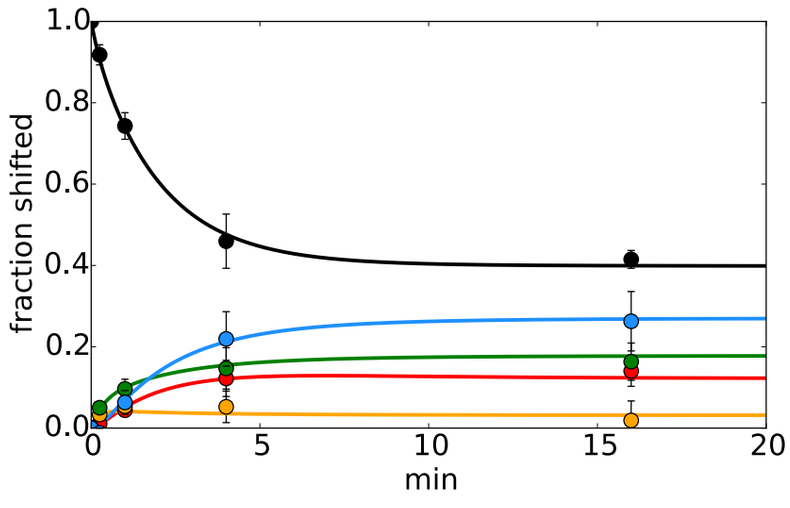
Lac repressor increases the rate of sliding away from LacO

time

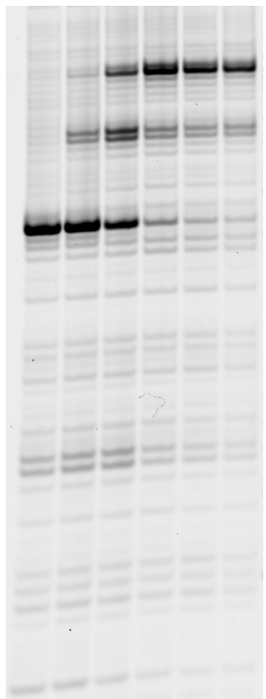
no LacI







plus LacI



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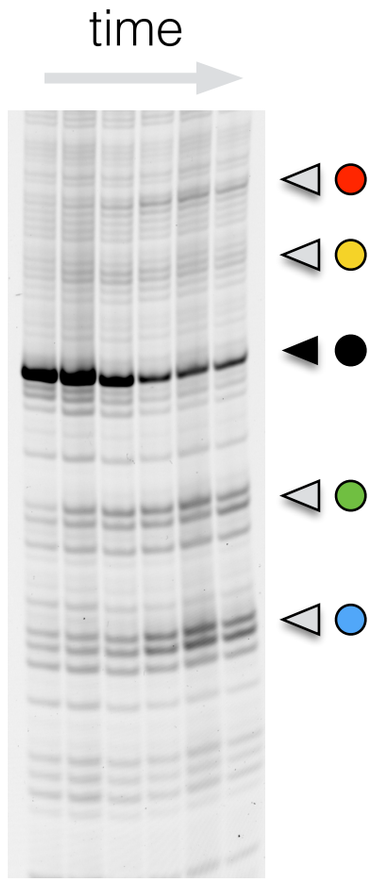
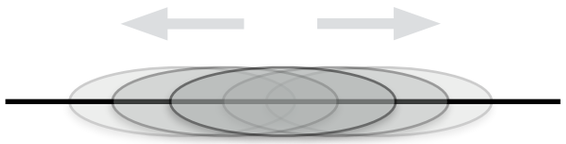
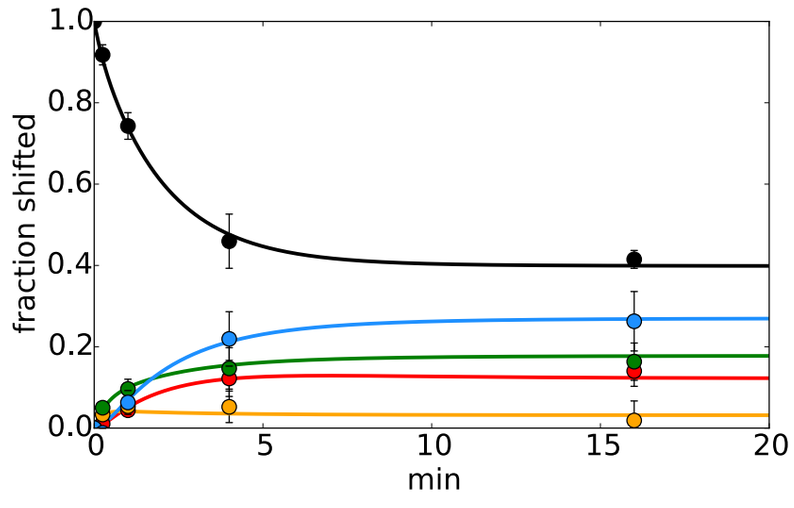
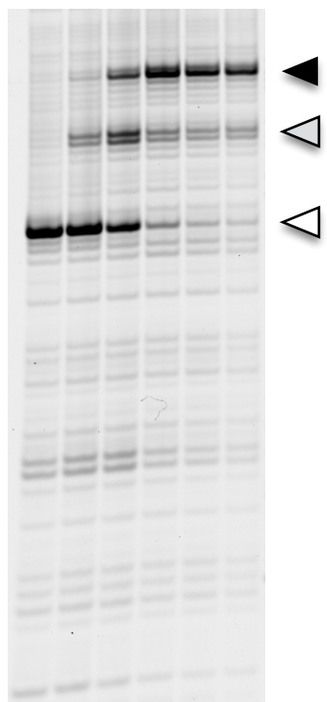
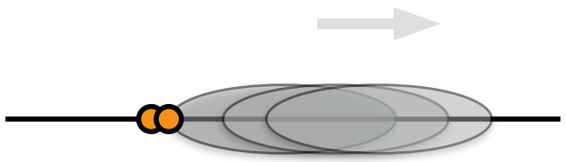






plus LacI



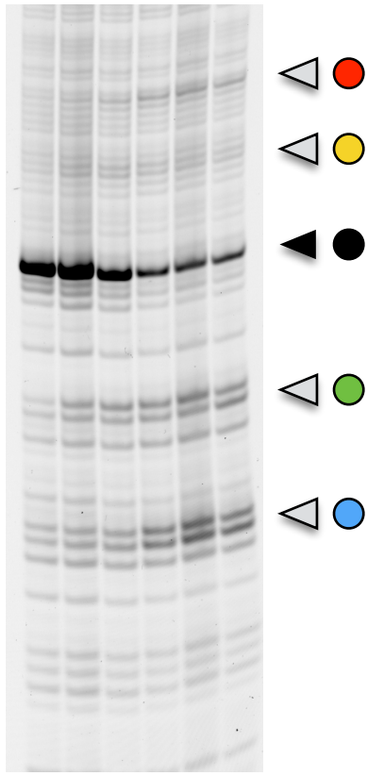


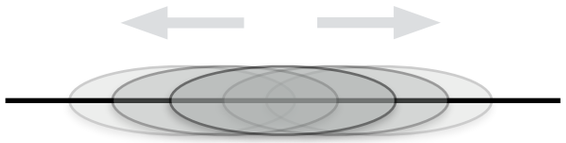
Nodelman et al., NAR (2016)

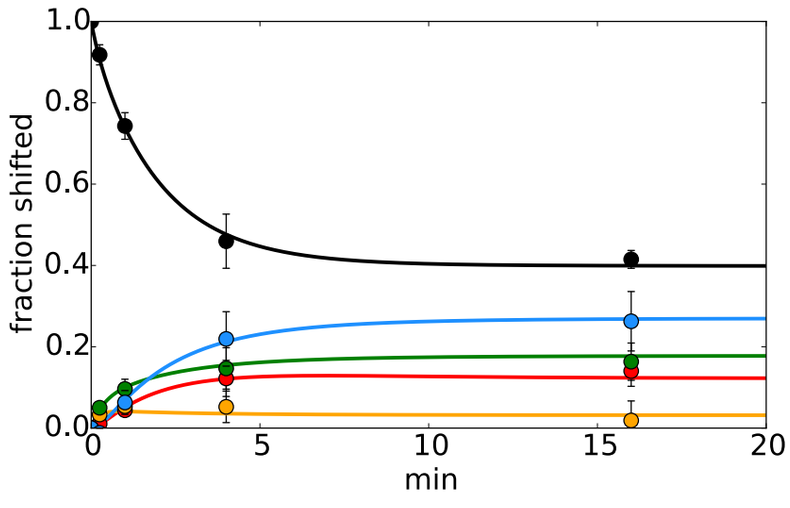
Lac repressor increases the rate of sliding away from LacO

time

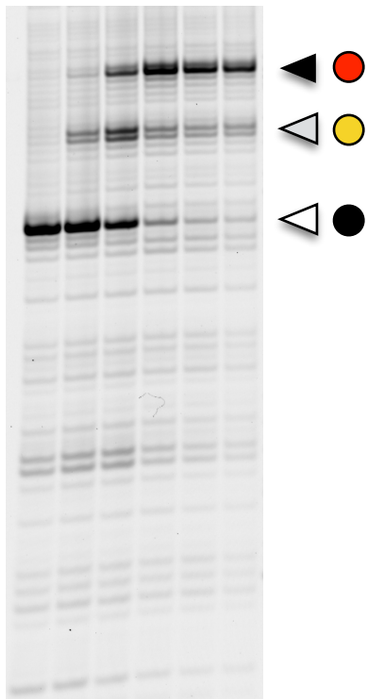
no LacI

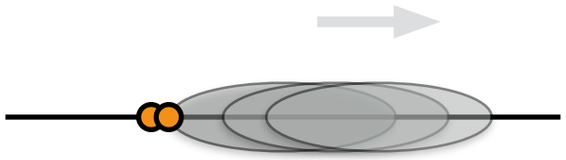






plus LacI

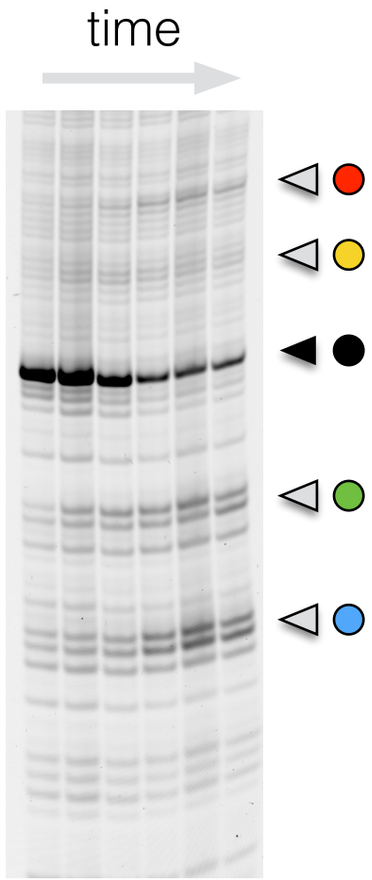


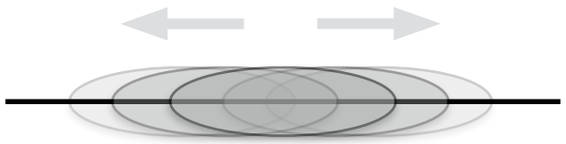


Nodelman et al., NAR (2016)

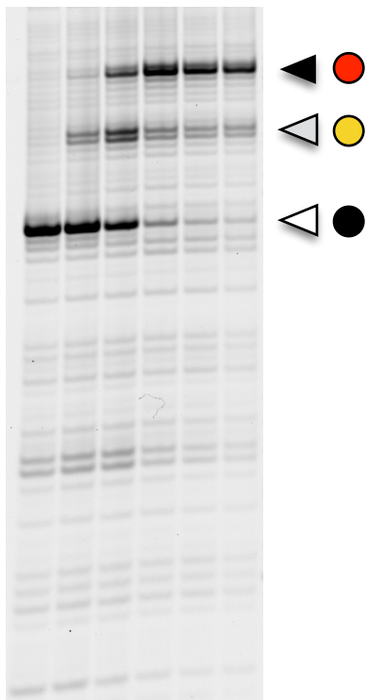
Lac repressor increases the rate of sliding away from LacO

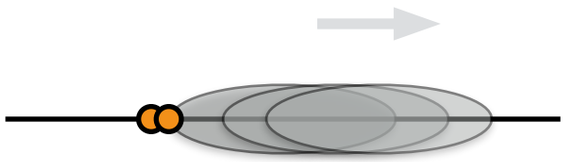
no LacI

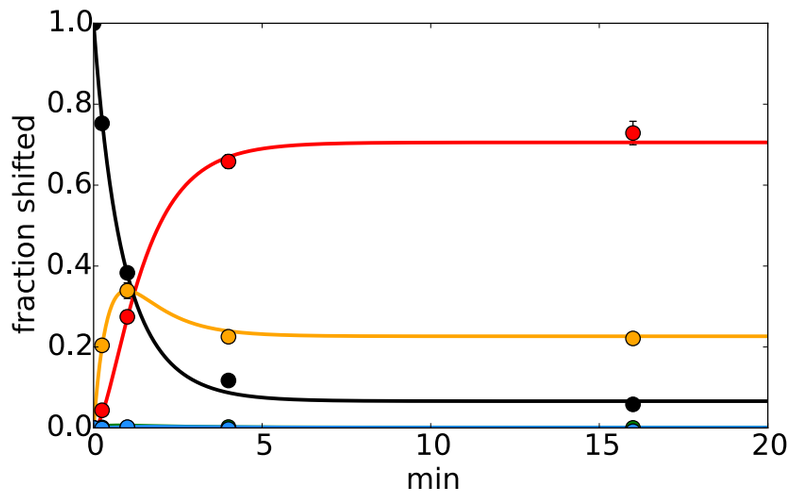




plus LacI



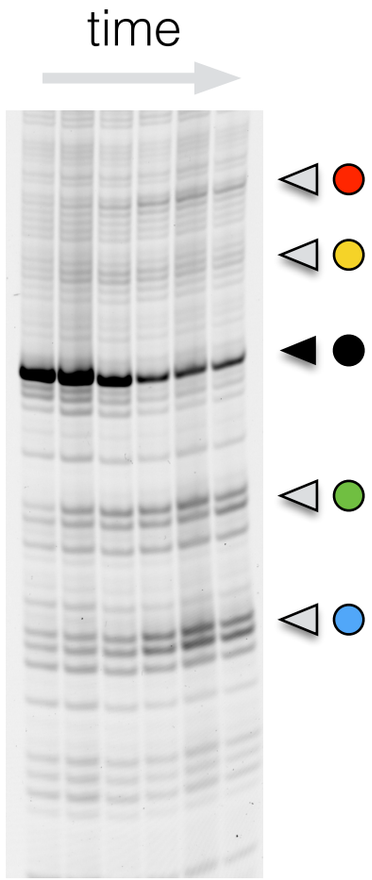


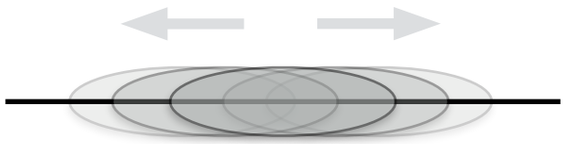


Nodelman et al., NAR (2016)

Lac repressor increases the rate of sliding away from LacO

no LacI





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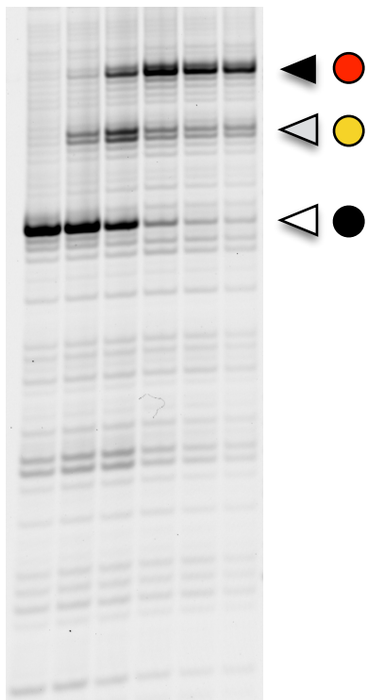
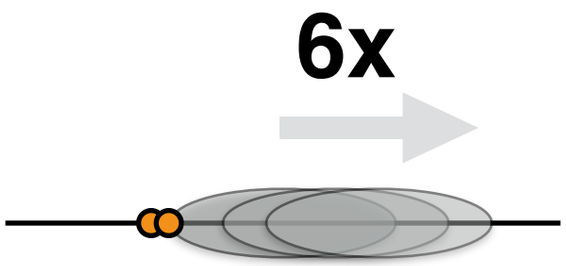
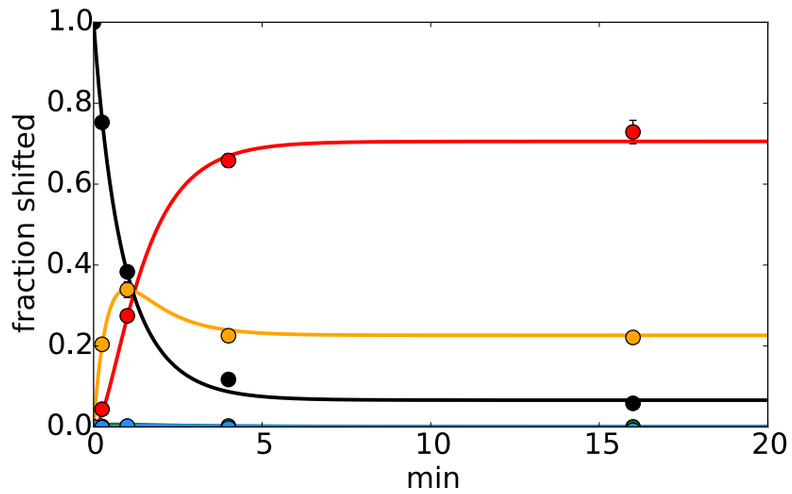
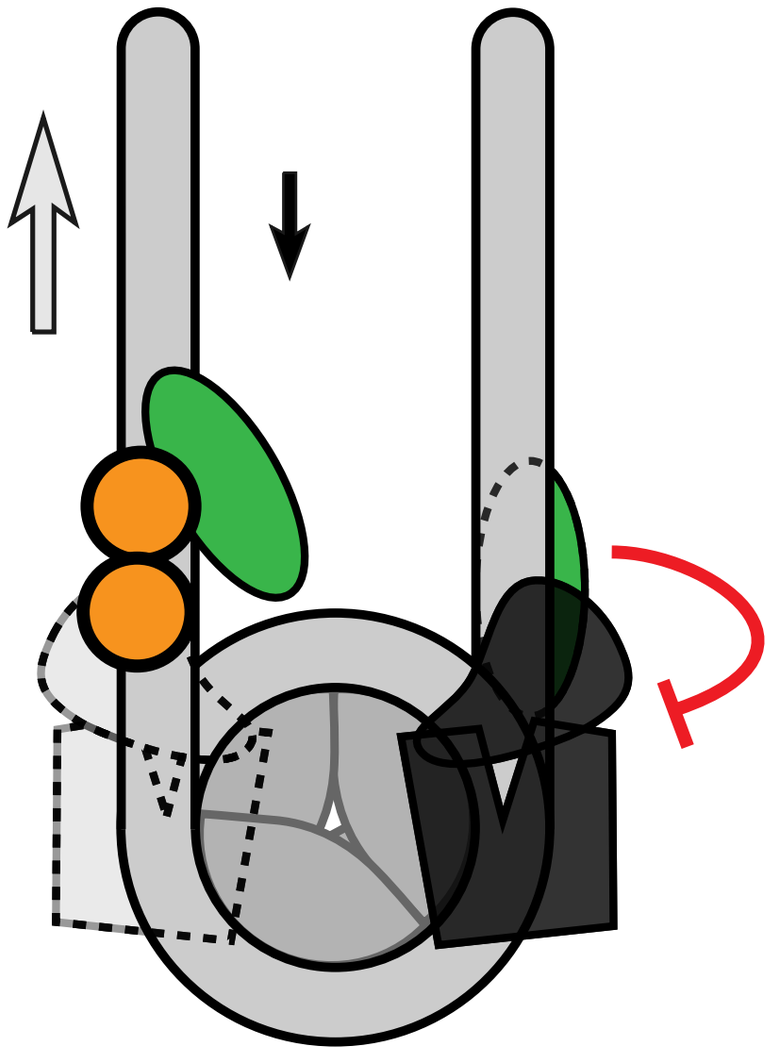


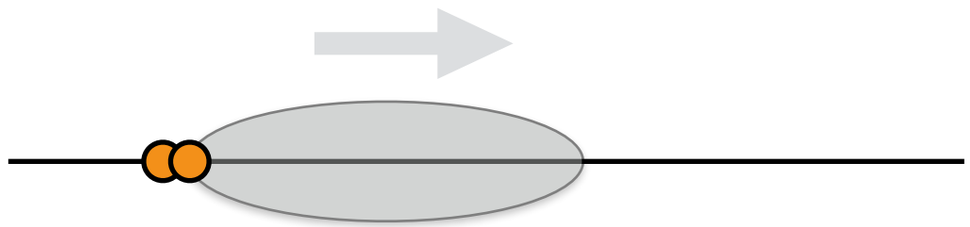




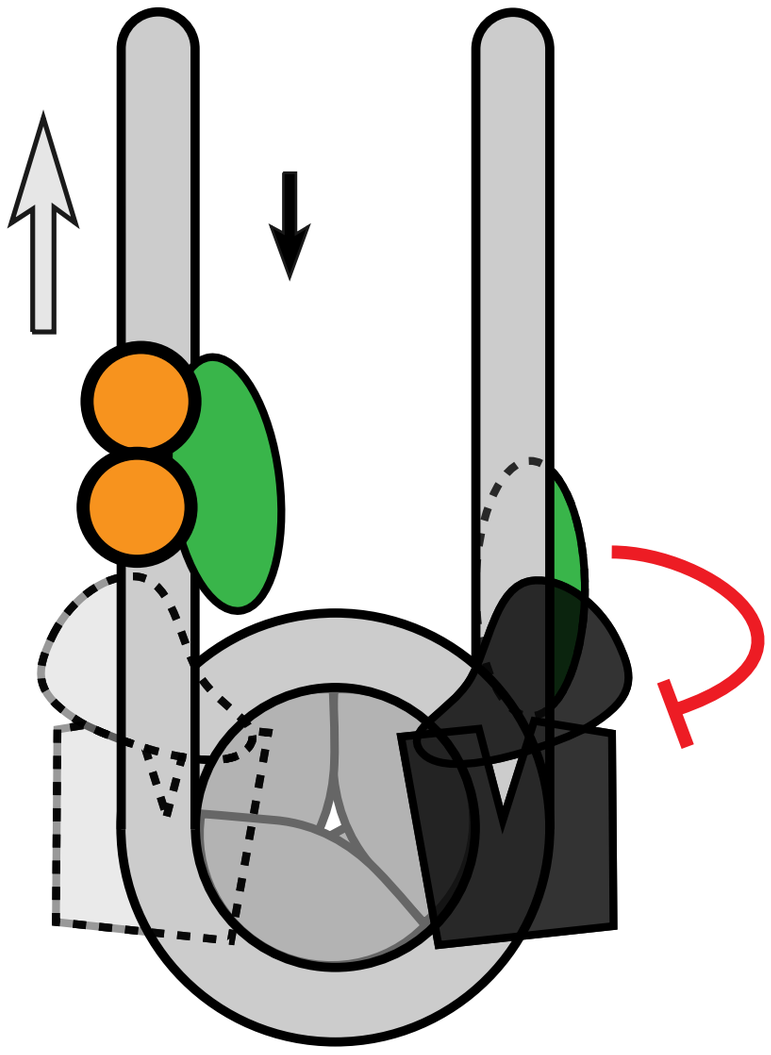
Nodelman et al., NAR (2016)

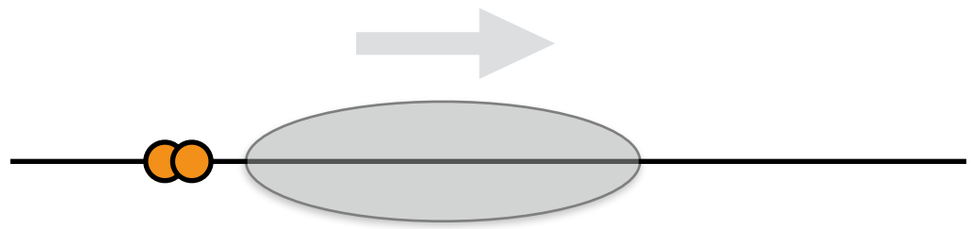
Exit-side inhibition stimulates nucleosome sliding away from bound transcription factors





Exit-side inhibition stimulates nucleosome sliding away from bound transcription factors





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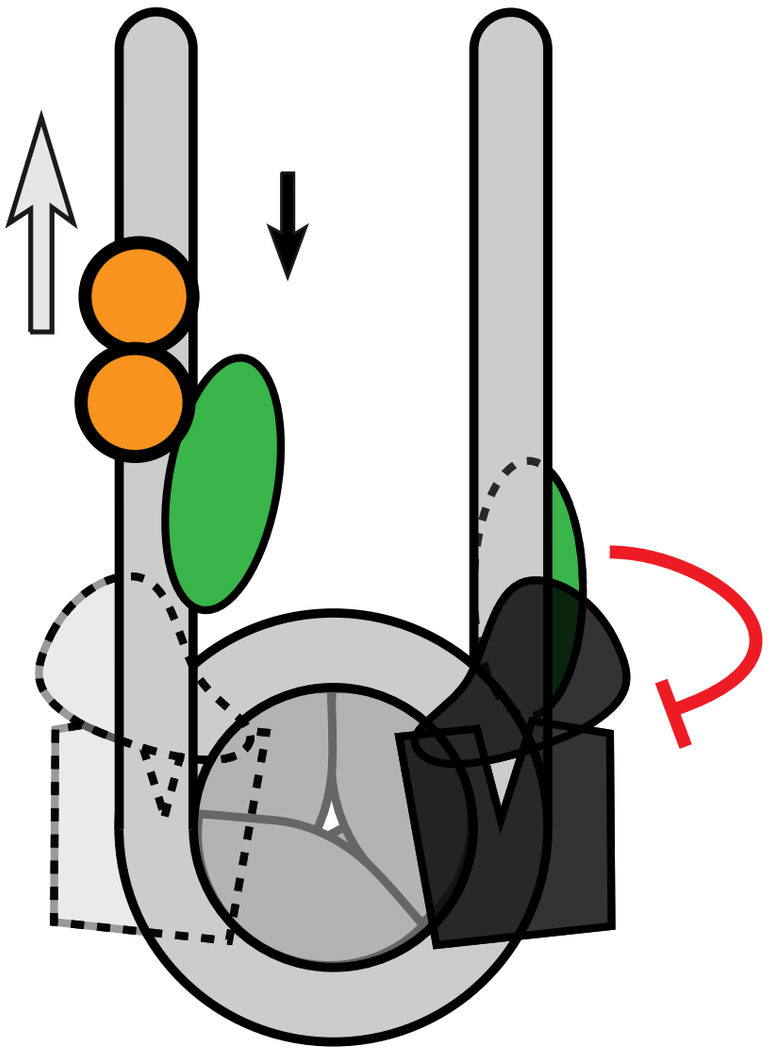
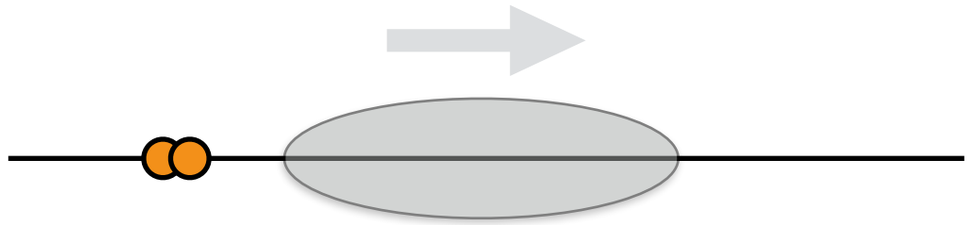
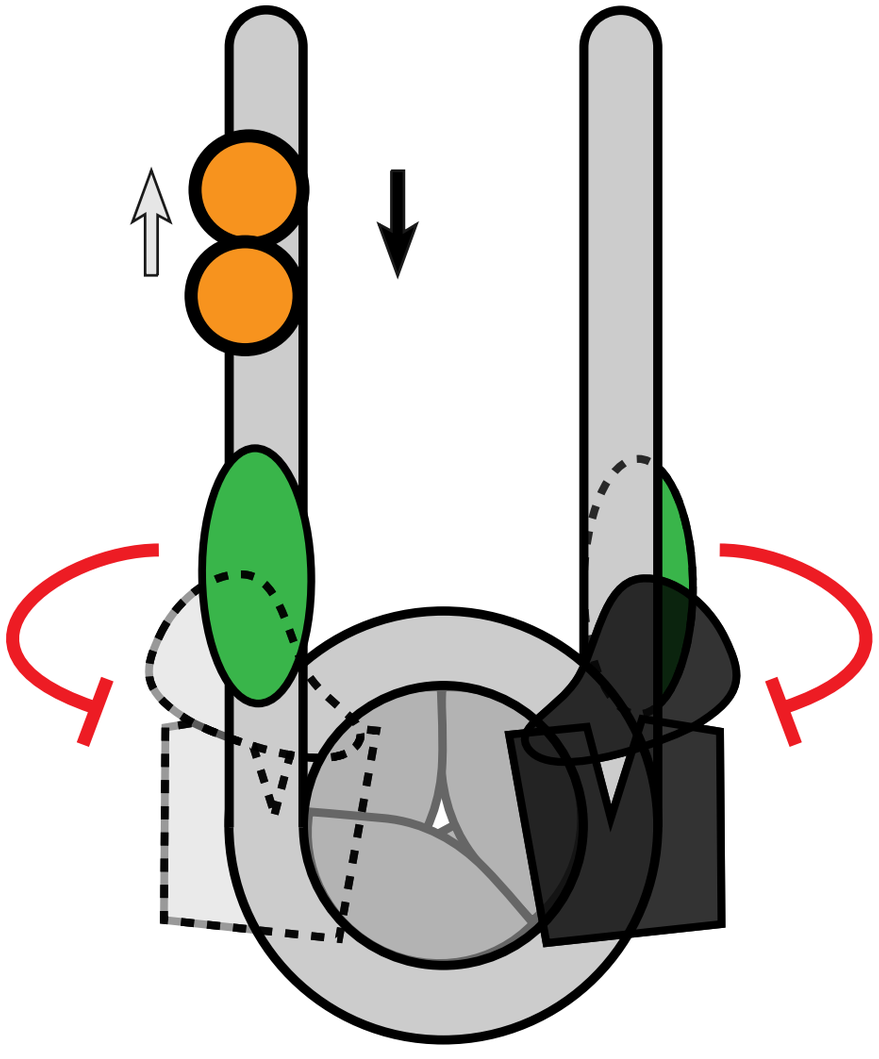
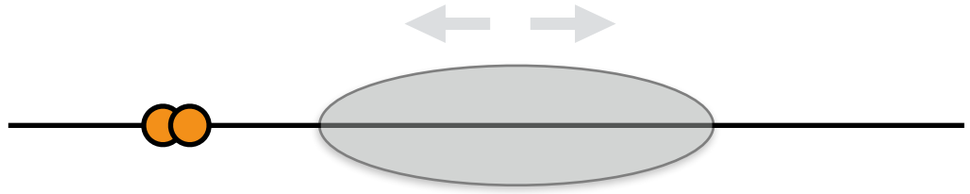


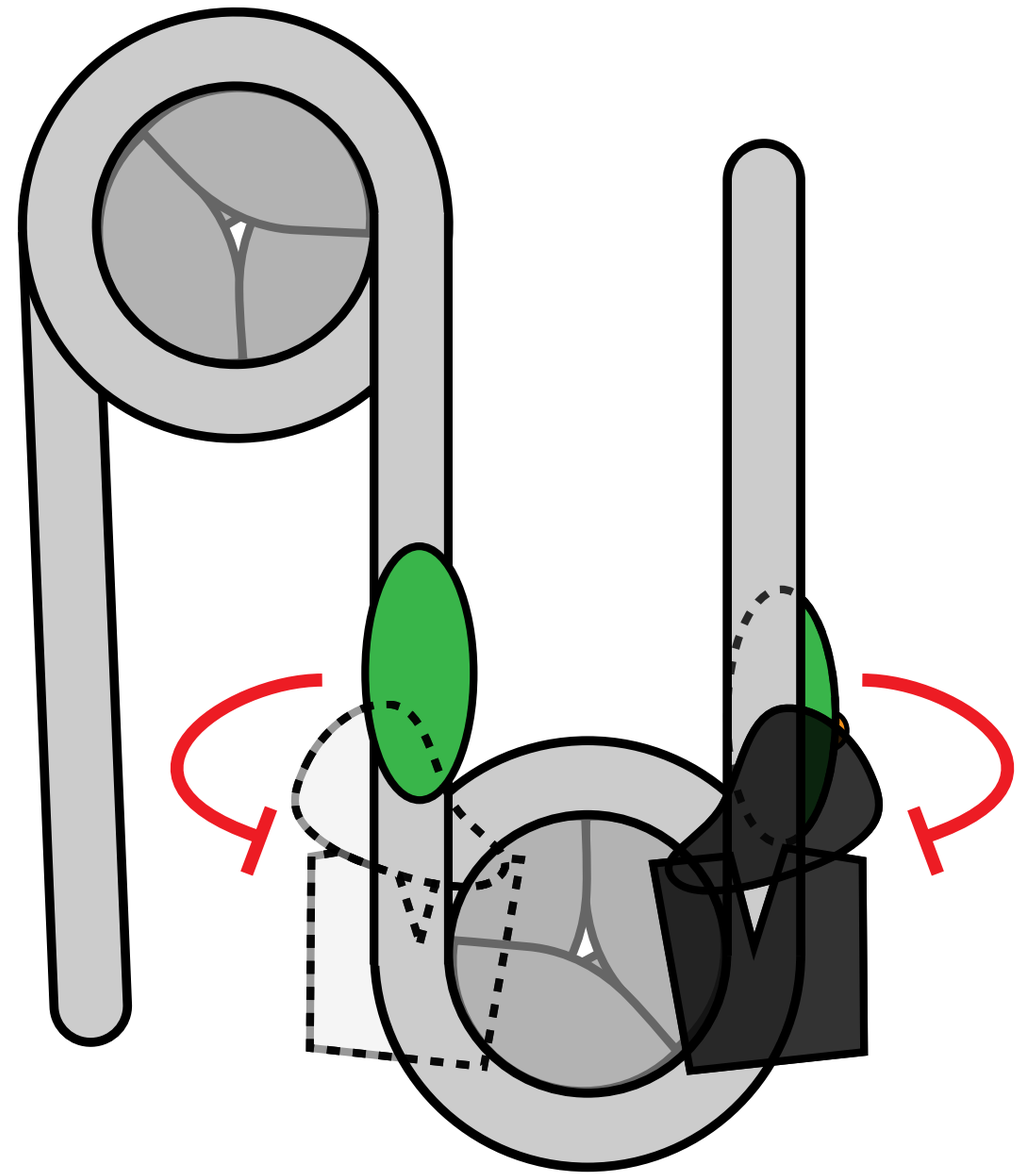


Exit-side inhibition stimulates nucleosome sliding away from bound transcription factors





Does exit-side inhibition also regulate nucleosome spacing by Chd1?



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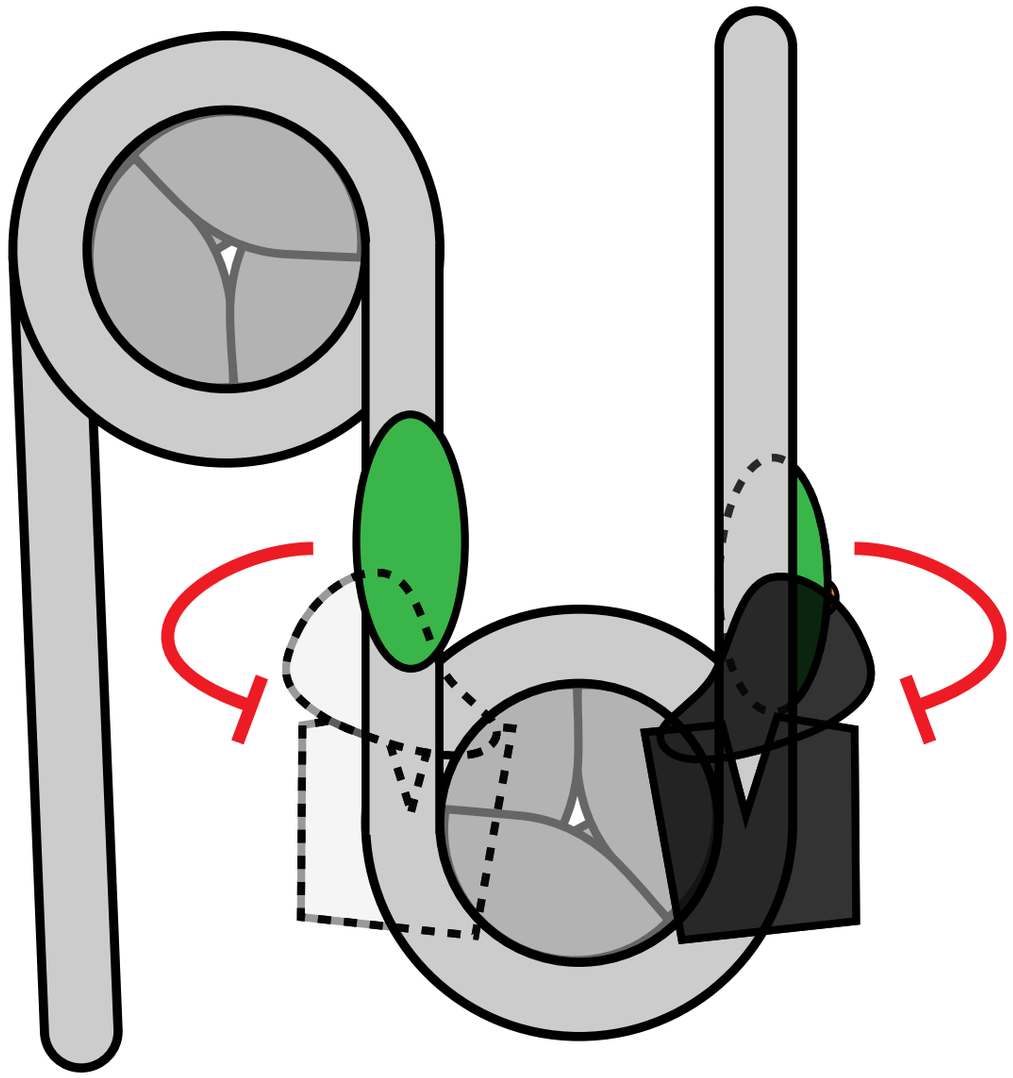

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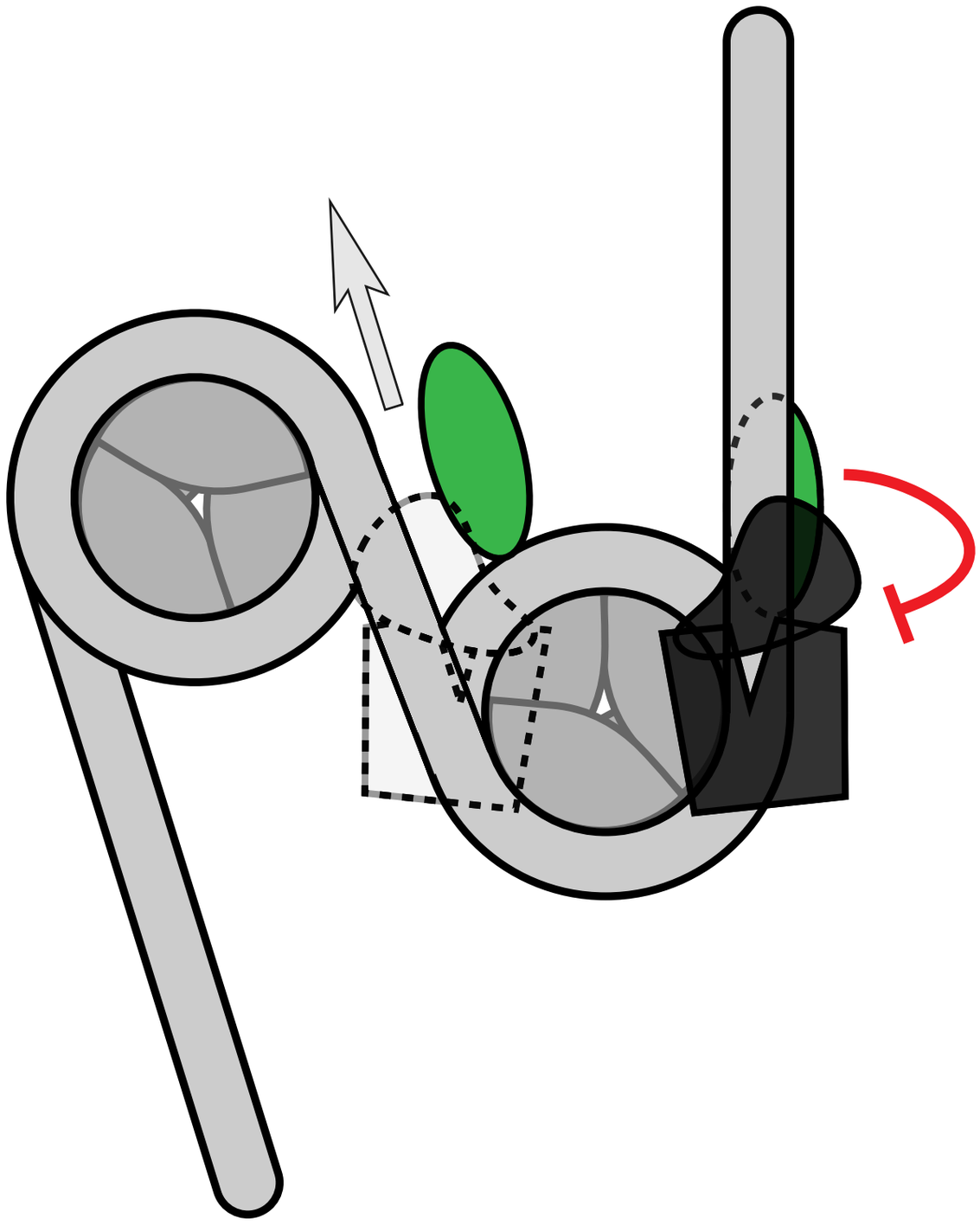

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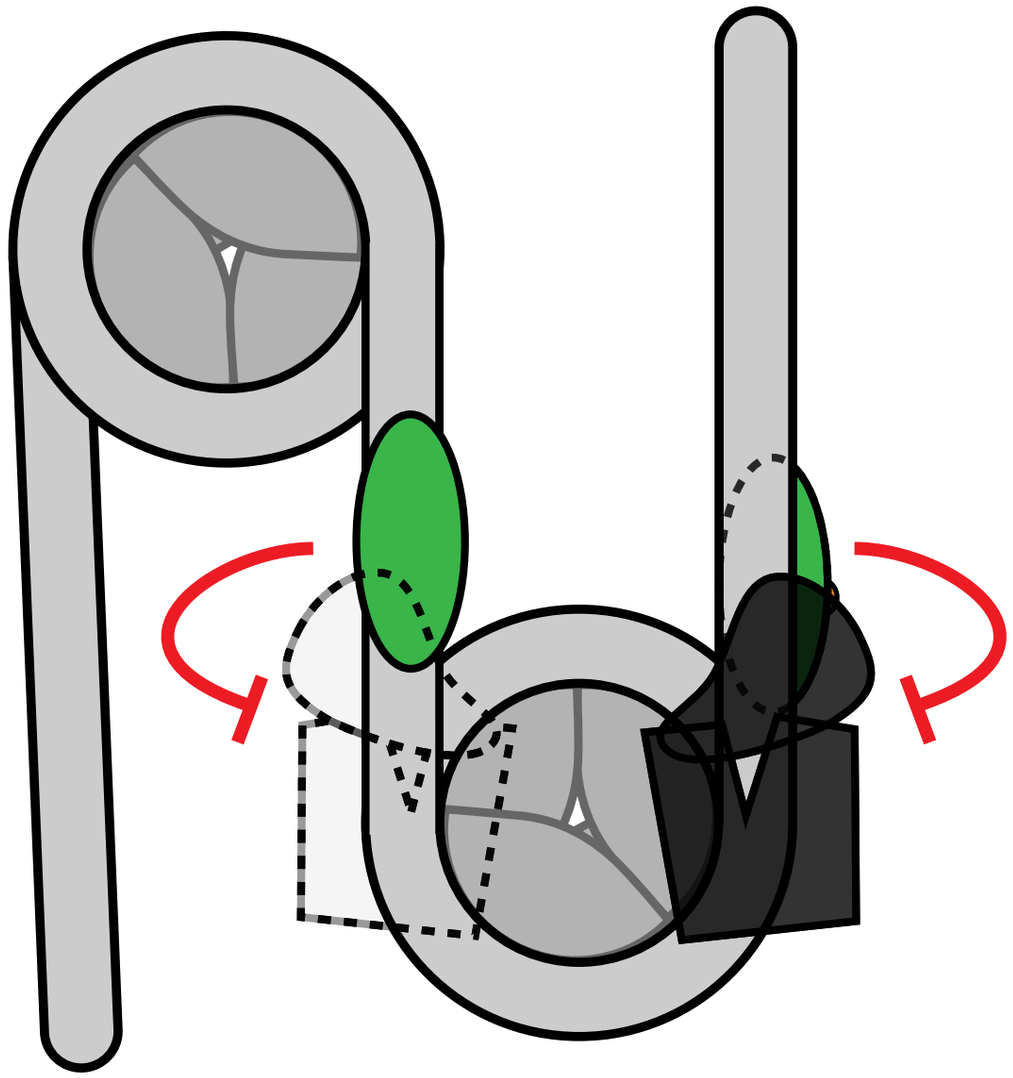

Acknowledgements

current group

Rob Levendosky
Jessica Winger
Ilana Nodelman
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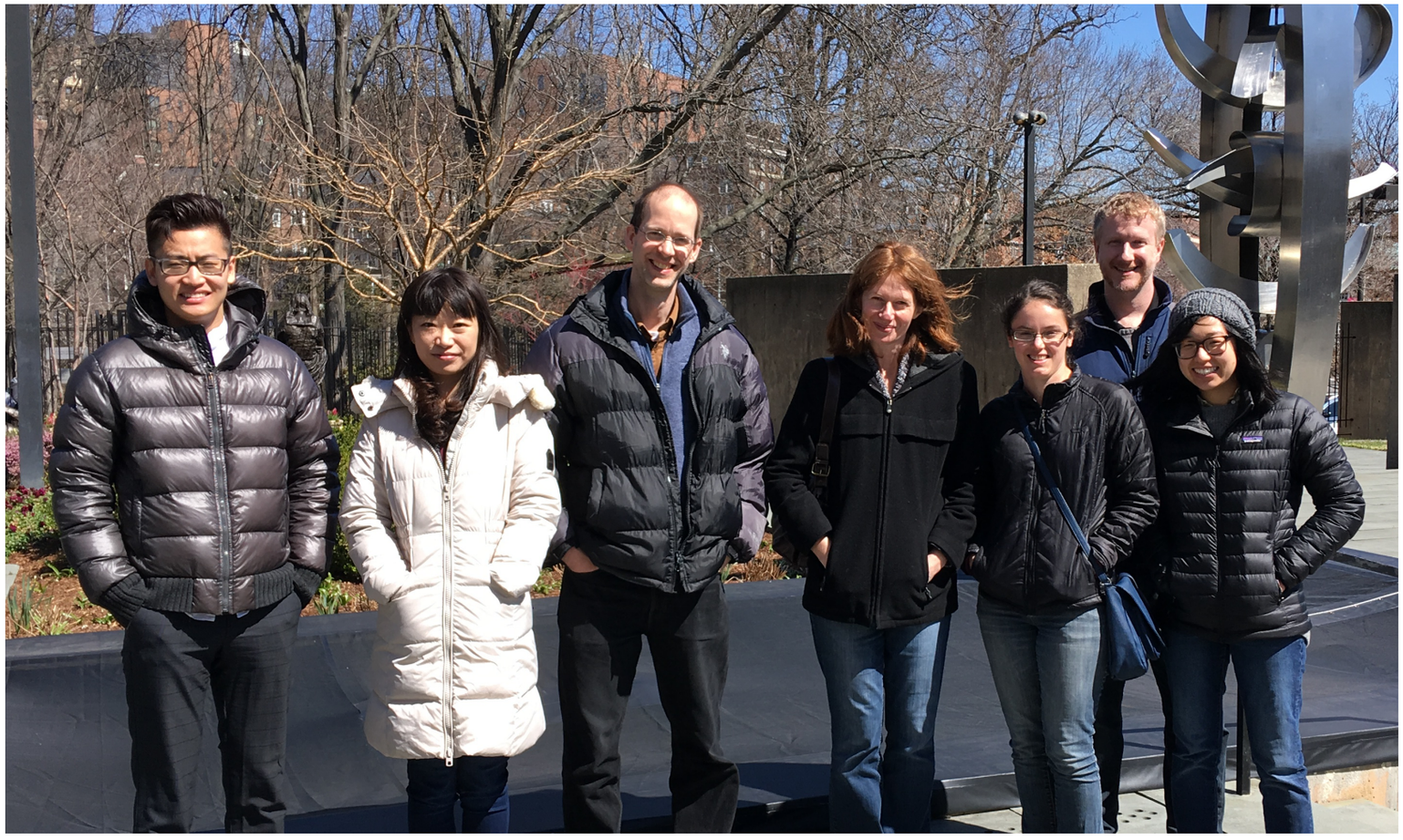

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