

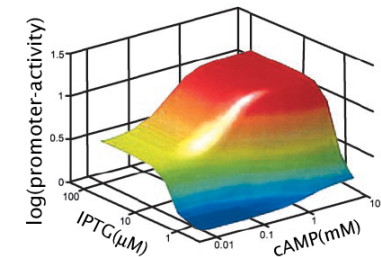
The Other Codes on DNA: It's not all about codons!

Species	Genome size	% coding sequences
<i>C. elegans</i>	100 MB	14
<i>D. melanogaster</i>	175 MB	<10
<i>Homo sapiens</i>	2.9 GB	1.2
<i>A. Thaliana</i>	~145 MB	21

Shapiro and von Sternberg (2005)

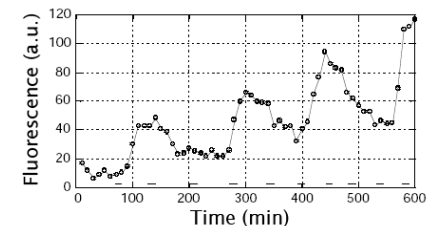
- Small changes in the architecture of these regulatory regions can lead to dramatic phenotypic changes.
 - Very inspiring work by Sean Carroll and David Kingsley.
- Quantitative data demands quantitative models!

How much?



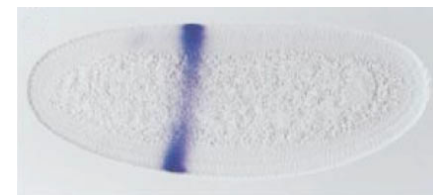
Setty *et al.* (2005)

When?



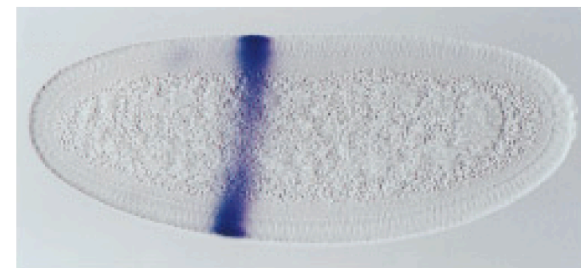
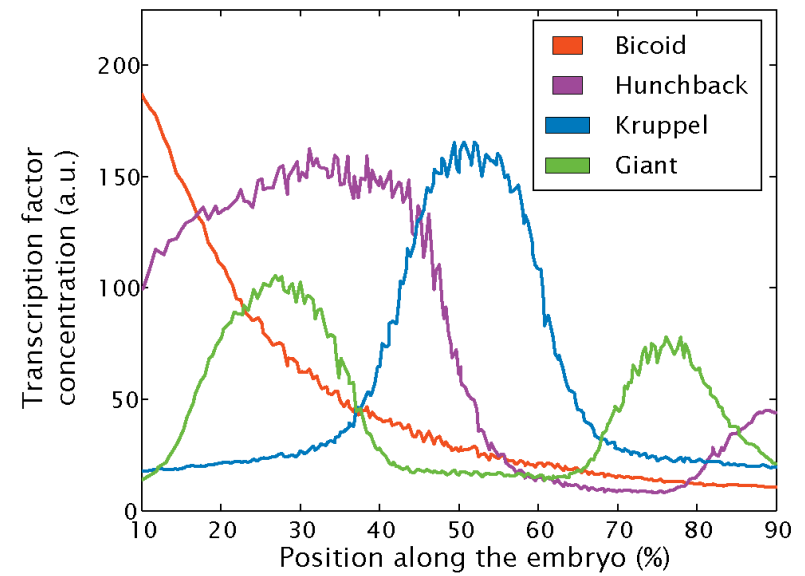
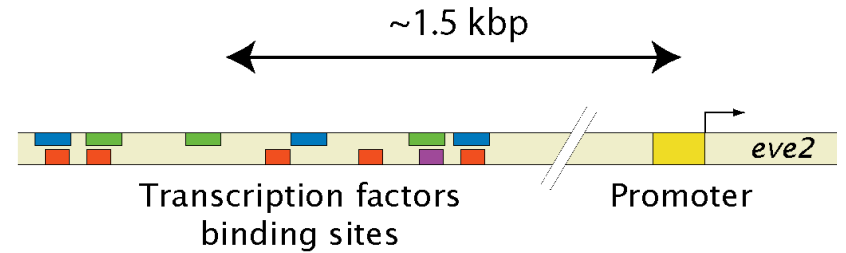
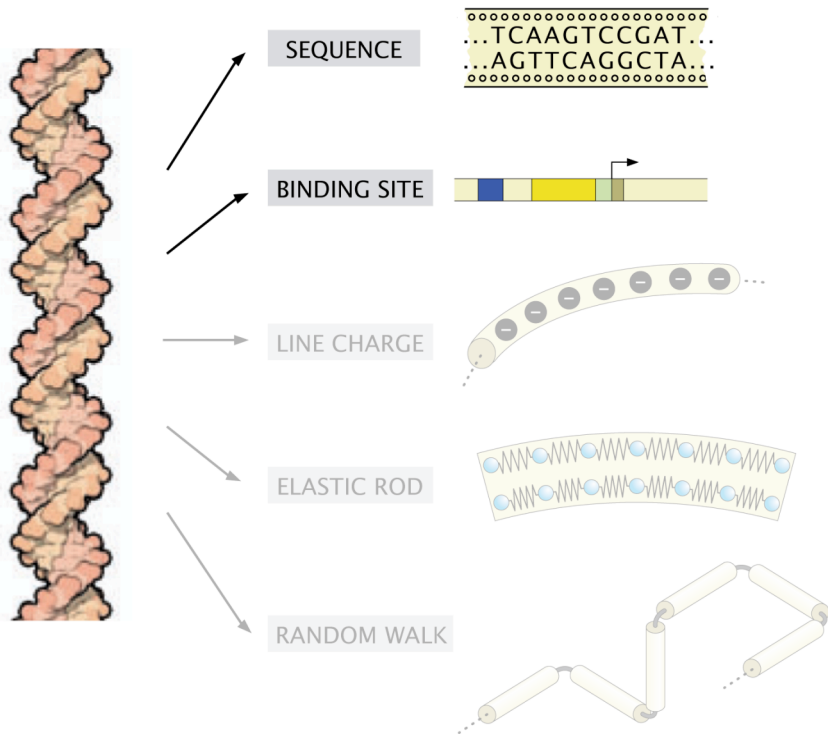
Elowitz *et al.* (2002)

Where?

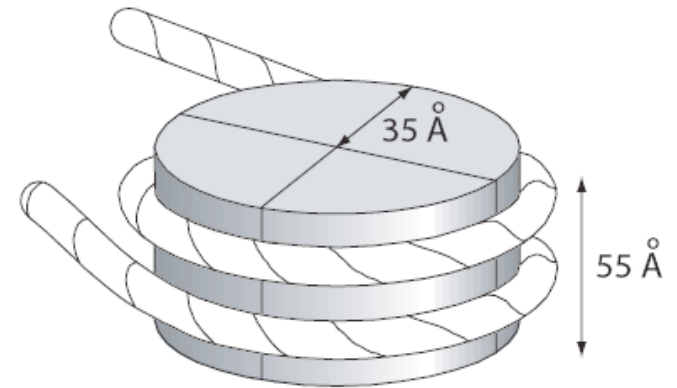
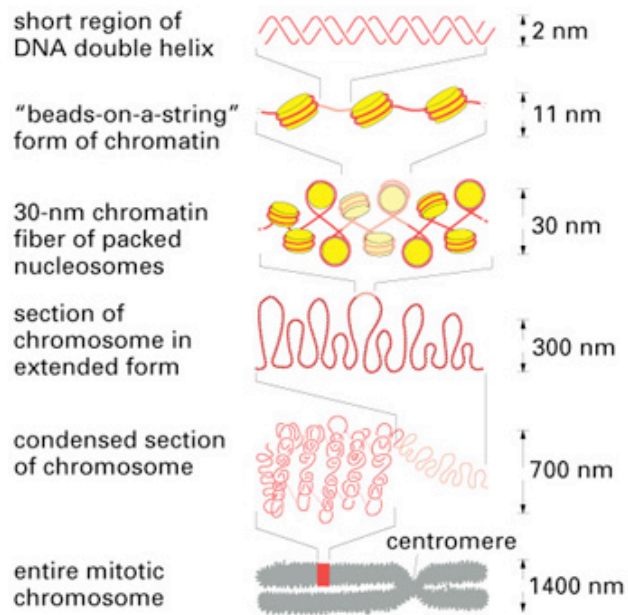


DNA Sequence Architecture

Regulation of *eve2* in *D. melanog*

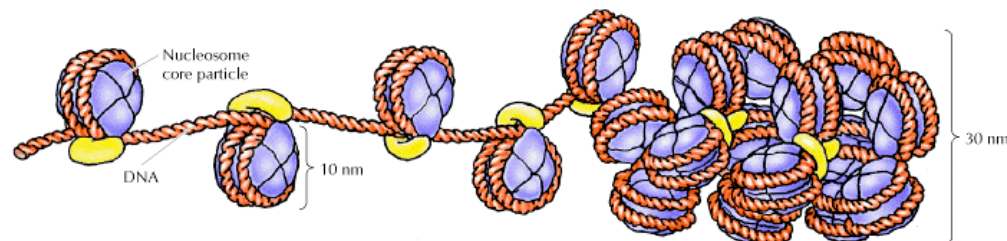


DNA packaging in eukaryotes



NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS EXTENDED LENGTH

Figure 5-24 Essential Cell Biology, 2/e. (© 2004 Garland Science)



Electron Microscopy of Higher Order Structures

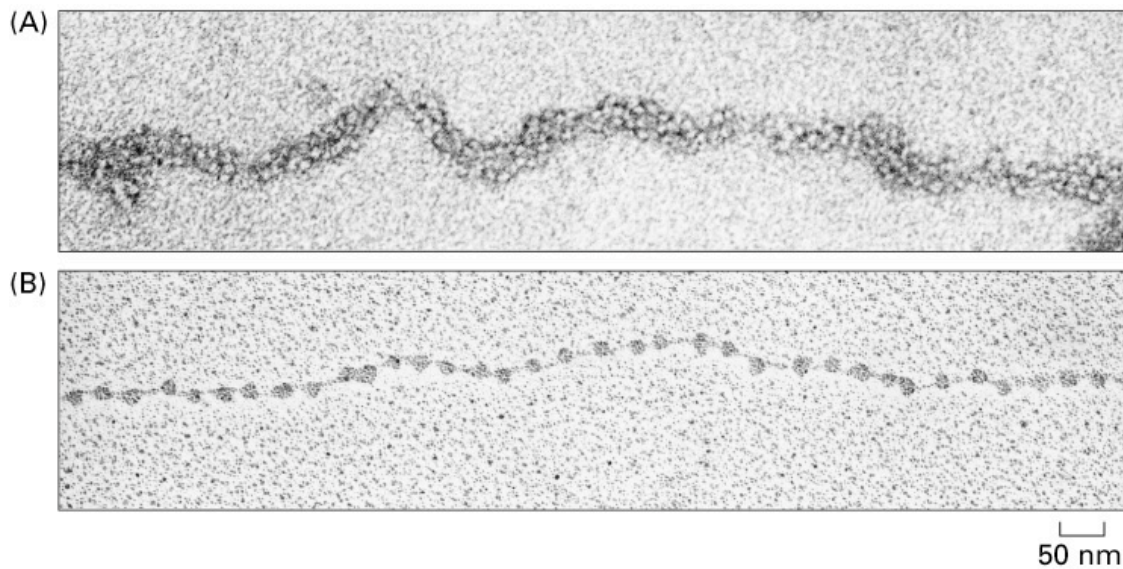
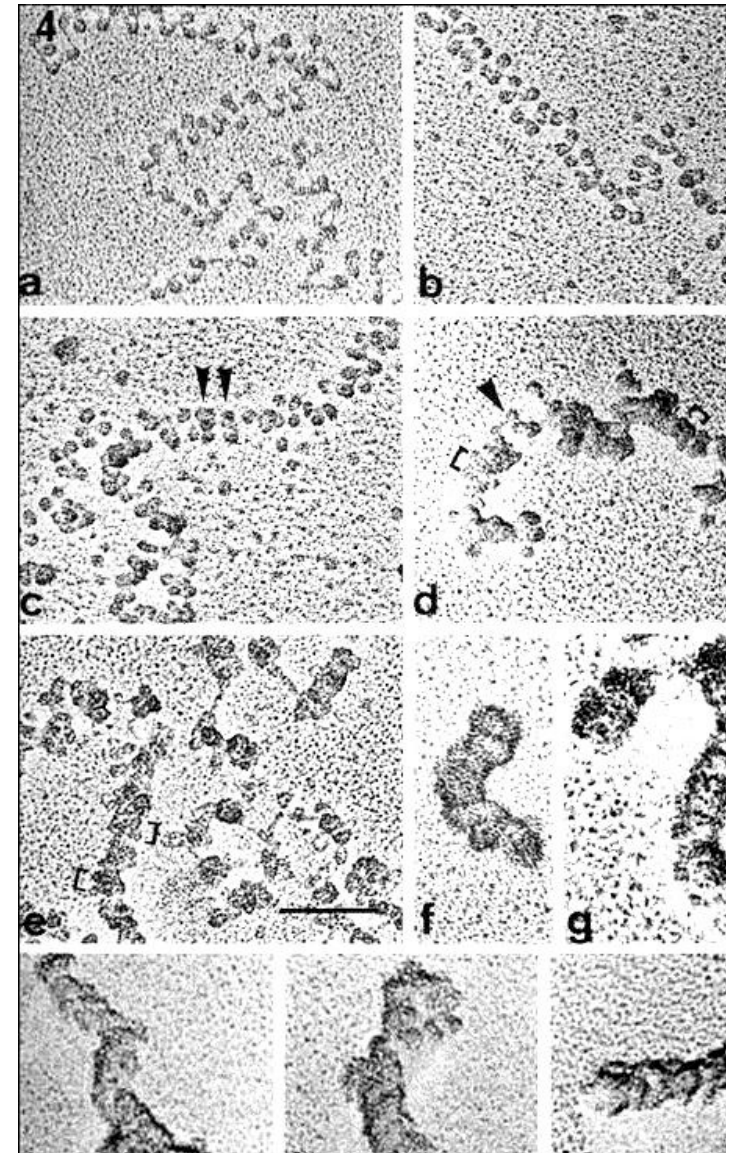
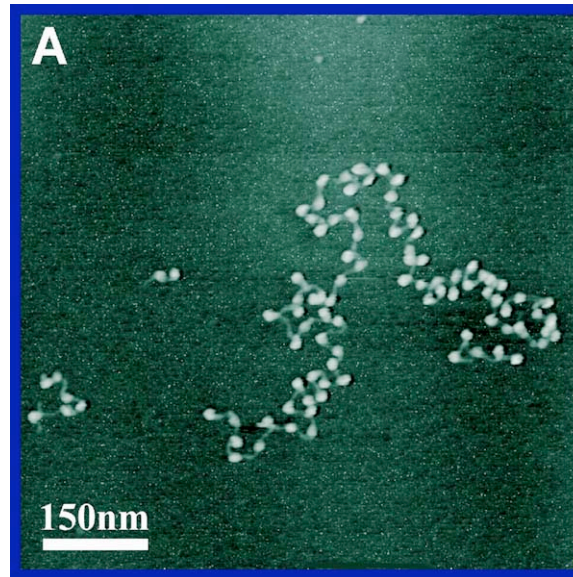


Figure 4-23. Molecular Biology of the Cell, 4th Edition.



AFM Images of the Nucleosome



This image was obtained with purified chromatin fragments from chicken erythroid, using the cryo-AFM. It is seen that all the linker DNA is resolved directly, and the lateral dimensions of the nucleosome are similar to those determined by electron microscopy, and are only slightly greater than that from crystallography. The resolution here is generally higher than that at room temperature. This was at low salt. The orientation of the nucleosomes appears to be random. With this purification (low salt), linker histones are supposed to be retained.

Atomic-Level Structure of the Nucleosome

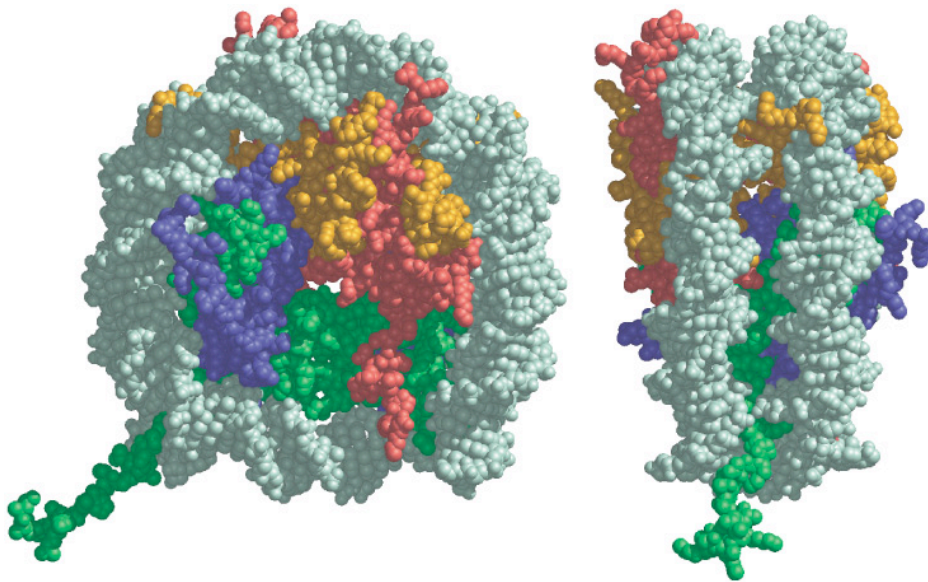
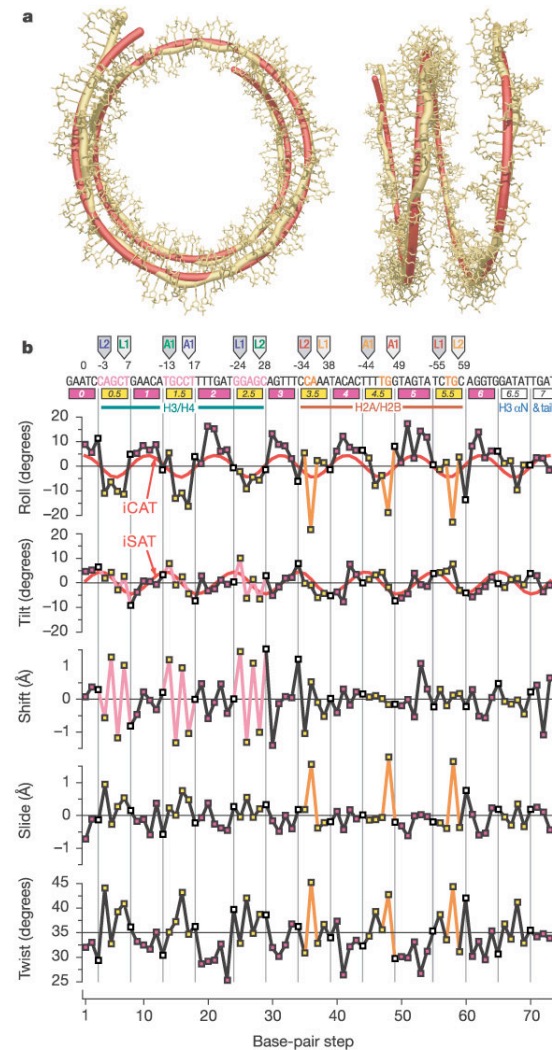
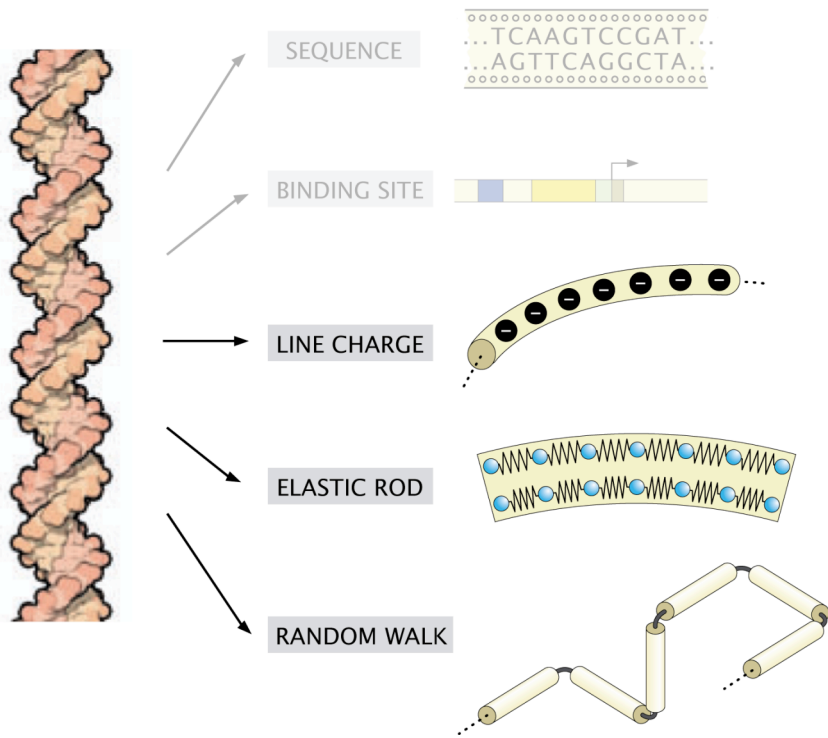


Figure 4-25. Molecular Biology of the Cell, 4th Edition.

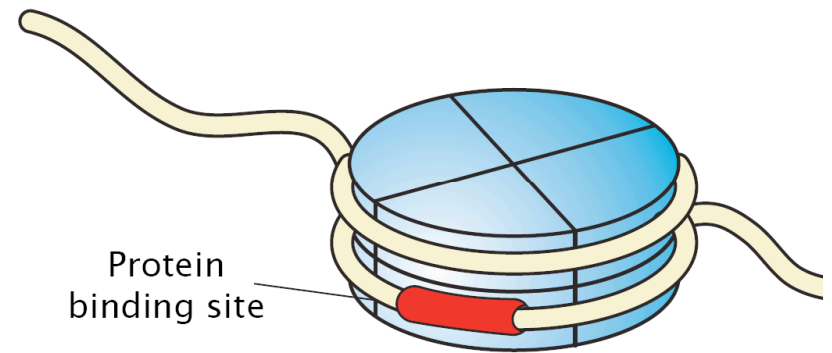


DNA Physical Architecture

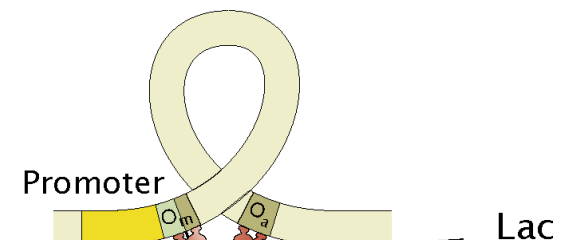
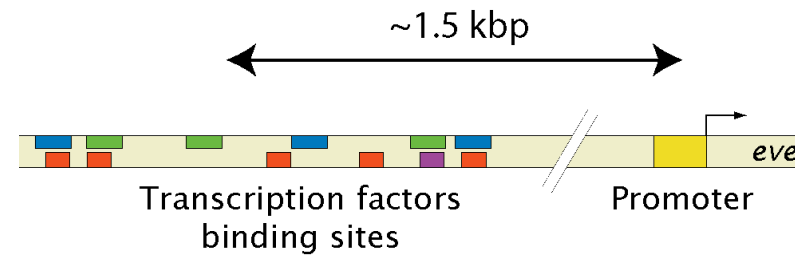


PBOC

Nucleosomal DNA accessibility and packaging

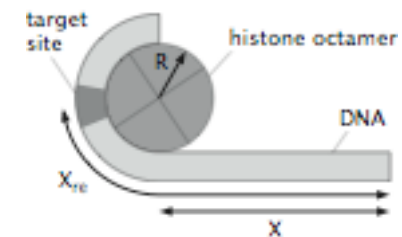
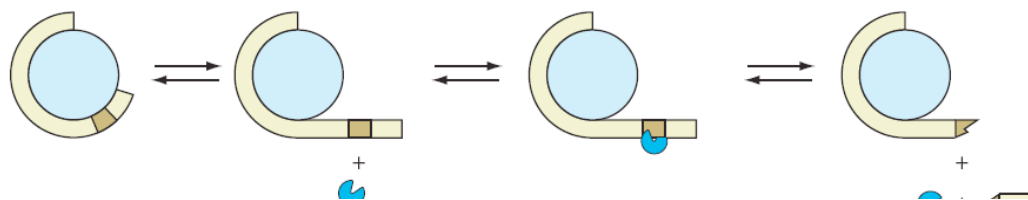
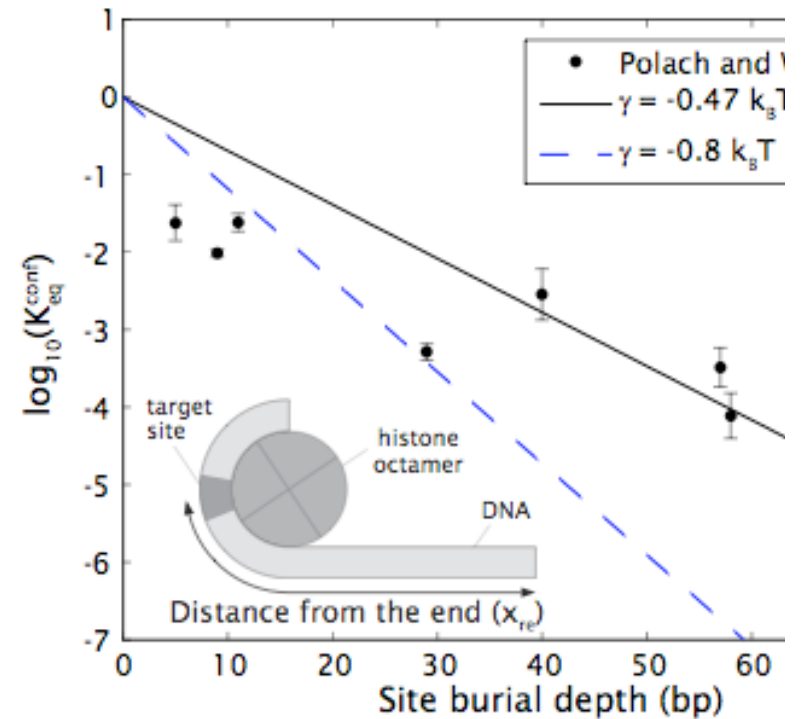
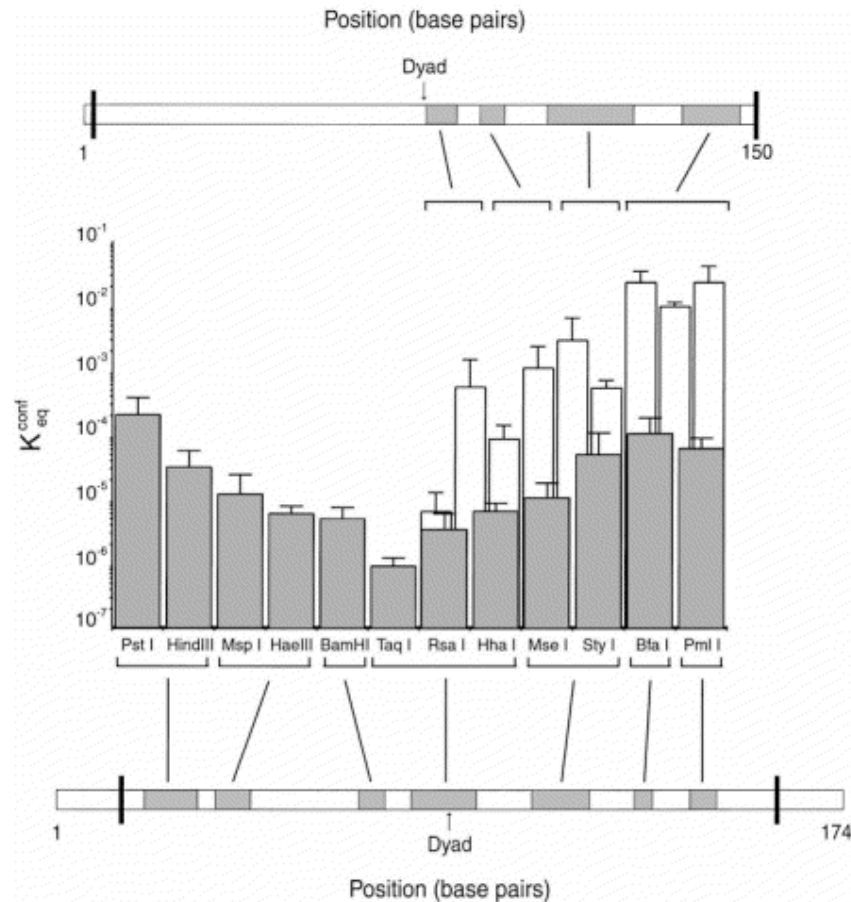


Action at a distance in transcriptional regulation

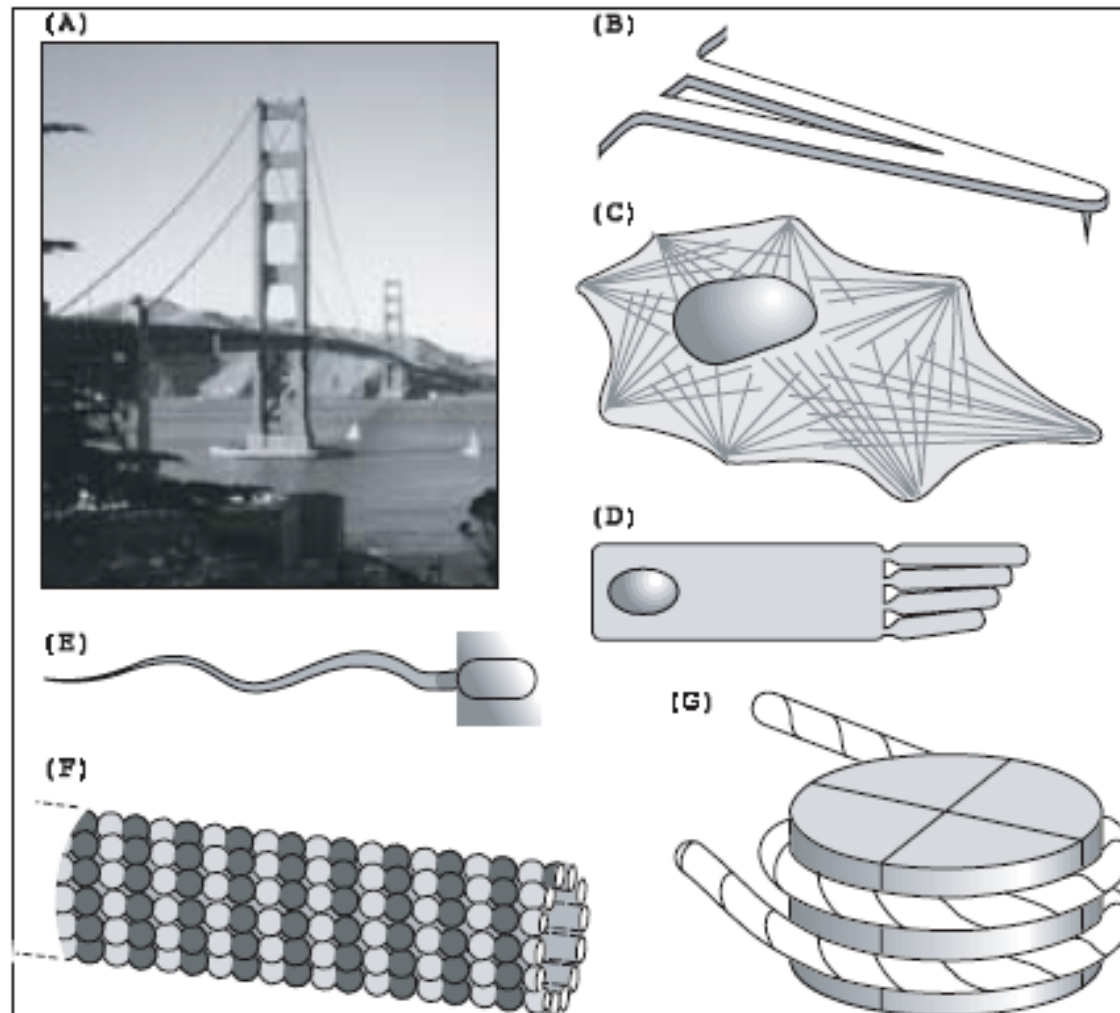


Measurements of Equilibrium Accessibility

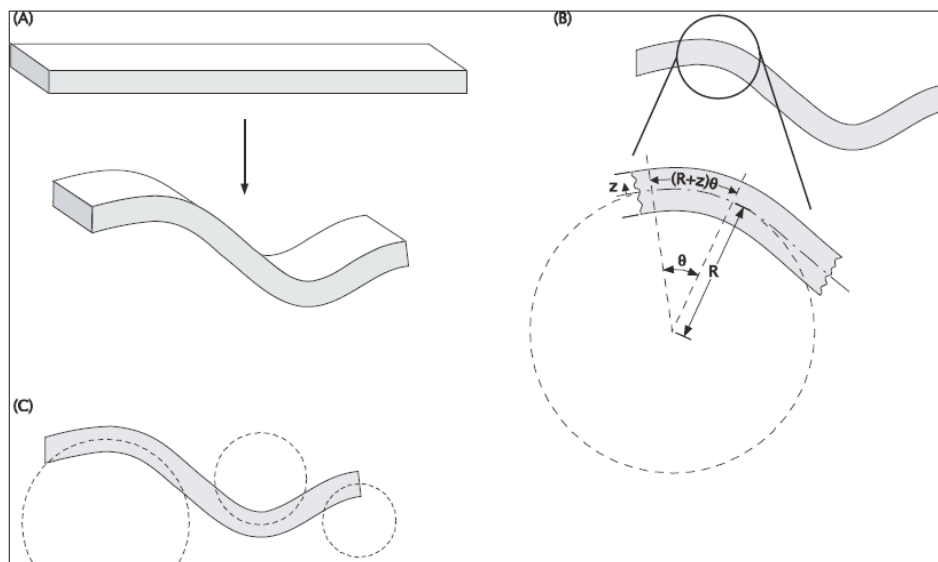
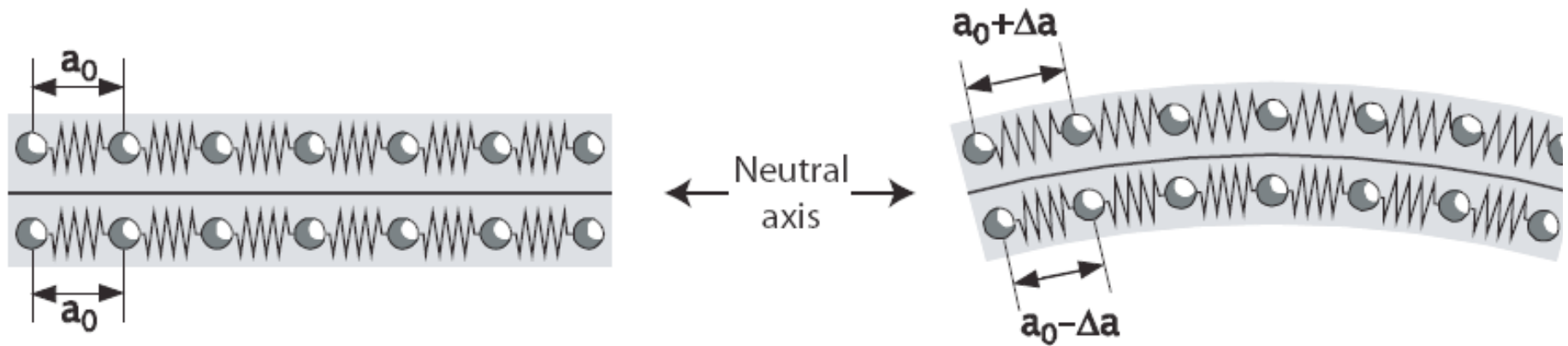
(Anderson and Widom)



Linear beam theory

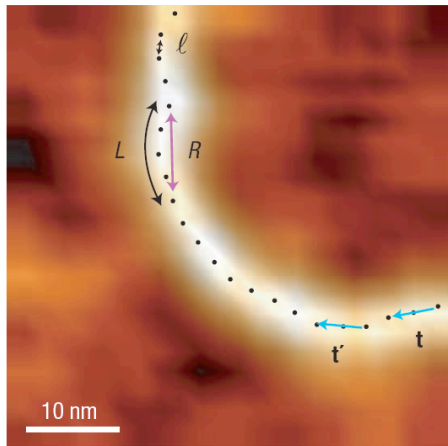
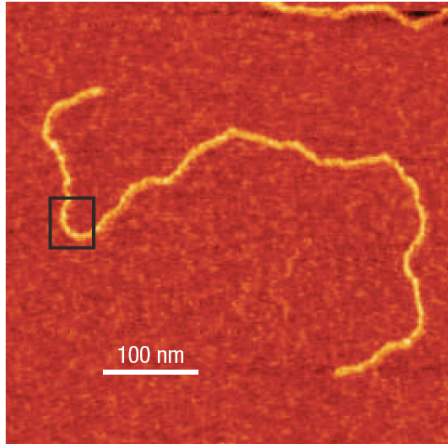


Linear beam theory



Measuring the flexural rigidity

Tracking the equilibrium polymer



Wiggins *et al*

Show buckling
movie by Dogterom

Evolution of Nucleosomal Positioning Sequences

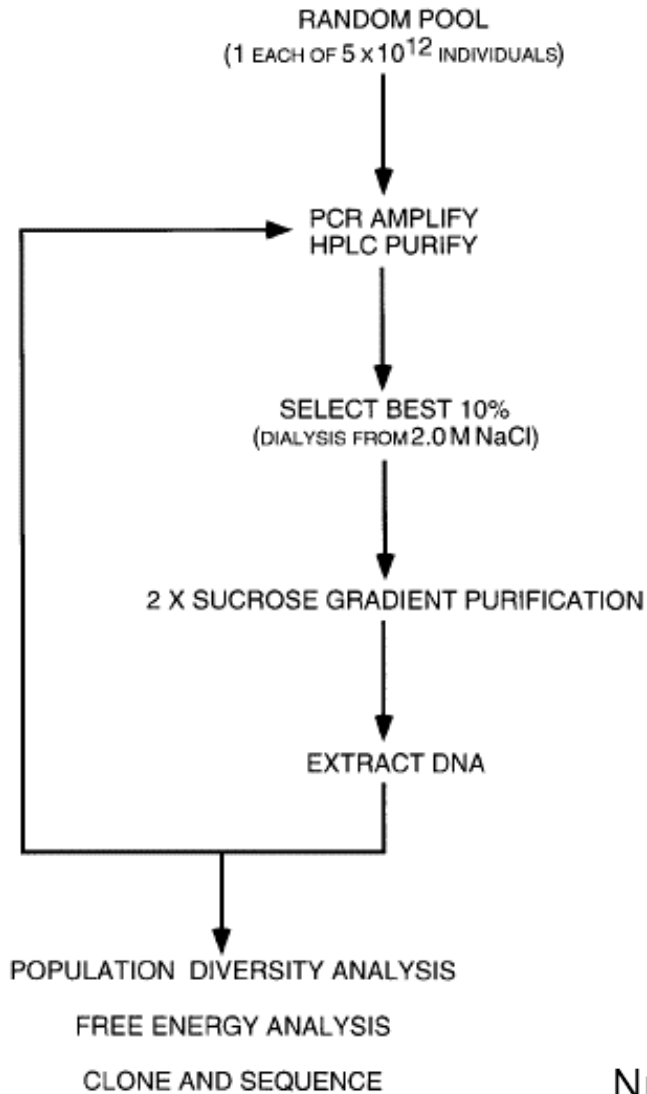
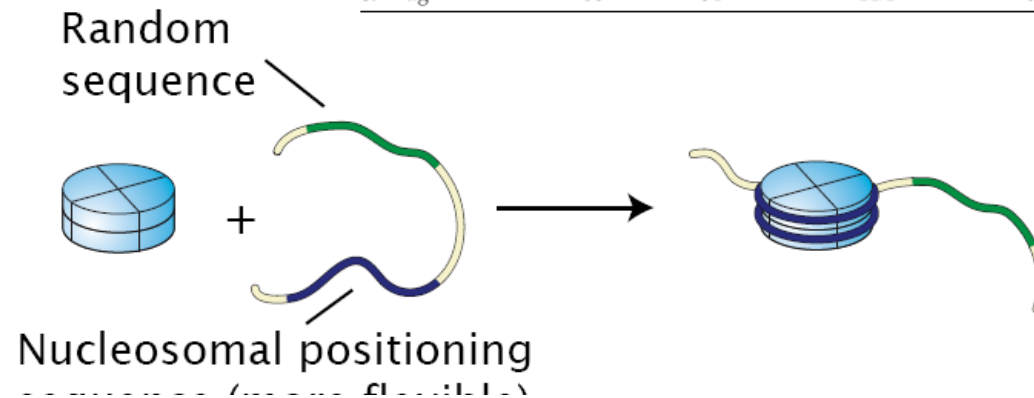


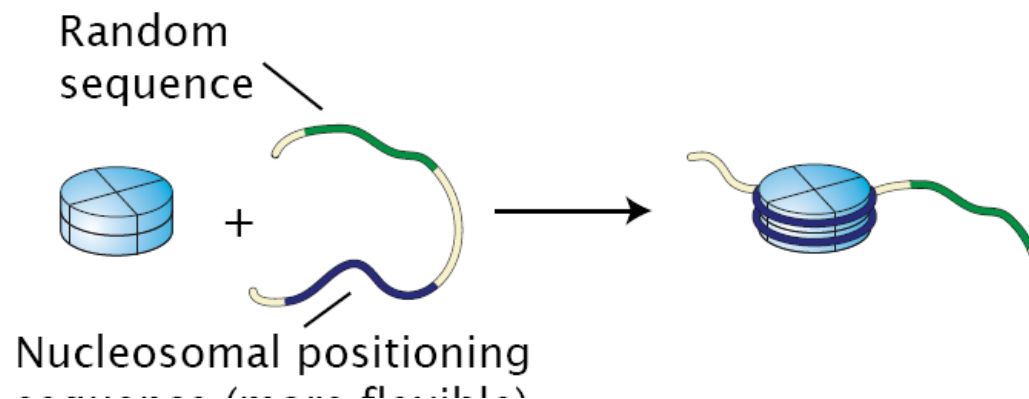
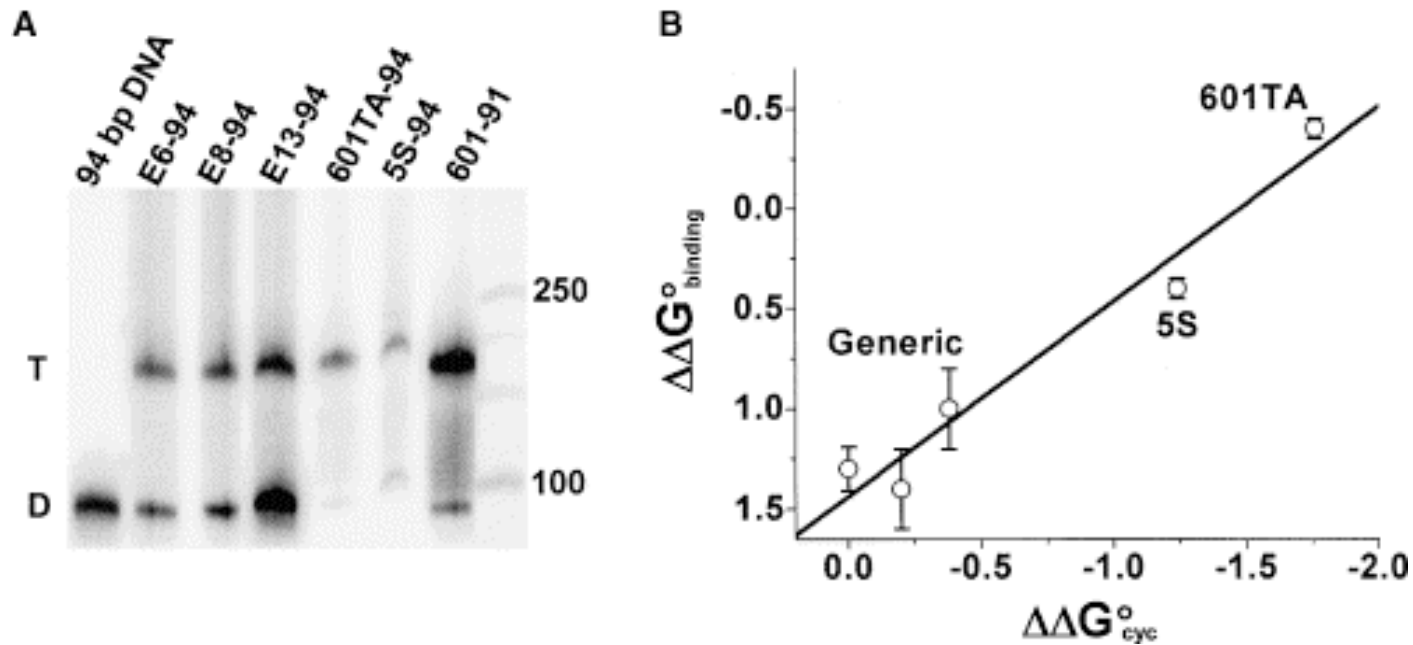
Table 3. Top 30 correlated dinucleotides in selected sequences

Dinucleotide pair	λ	Occurrences	Mean random	σ	δ
ta ta	10	180	46.5	6.5	20.6
ta ta	20	122	43.2	6.8	11.5
ct ta	11	131	52.9	6.9	11.4
ct ag	2	152	66.6	8.1	10.5
ta ag	11	131	52.6	7.8	10.0
aa ta	9	109	46.4	6.8	9.2
tc ta	2	124	57.1	7.4	9.0
ta ga	2	124	58.1	7.4	8.9
ta tt	9	109	47.3	7.0	8.9
ag ta	9	114	55.1	6.8	8.6
ta ct	9	114	53.4	7.3	8.3
ta ct	19	109	50.0	7.3	8.1
aa ta	19	93	43.9	6.2	7.9
ta gc	3	124	64.6	7.5	7.9
ag ct	6	124	62.3	8.5	7.3
ag ta	19	109	49.5	8.1	7.3
gc ta	3	124	65.2	8.1	7.3
ct ta	1	357	251.3	15.1	7.0
ta tt	19	93	44.5	7.0	7.0
ta ag	1	357	252.4	15.2	6.9
ta ga	12	103	52.8	7.3	6.9
tc ta	12	103	52.1	7.3	6.9
tt ta	11	88	45.4	6.1	6.9
ct ag	12	106	60.4	6.8	6.7
ct ag	14	114	59.2	8.2	6.7
ct ct	10	116	62.1	8.2	6.6
ct ta	21	96	49.8	7.0	6.6
cg ta	14	108	59.3	7.6	6.5
ct ag	4	120	64.1	8.5	6.5
ct ag	60	84	44.4	6.2	6.4



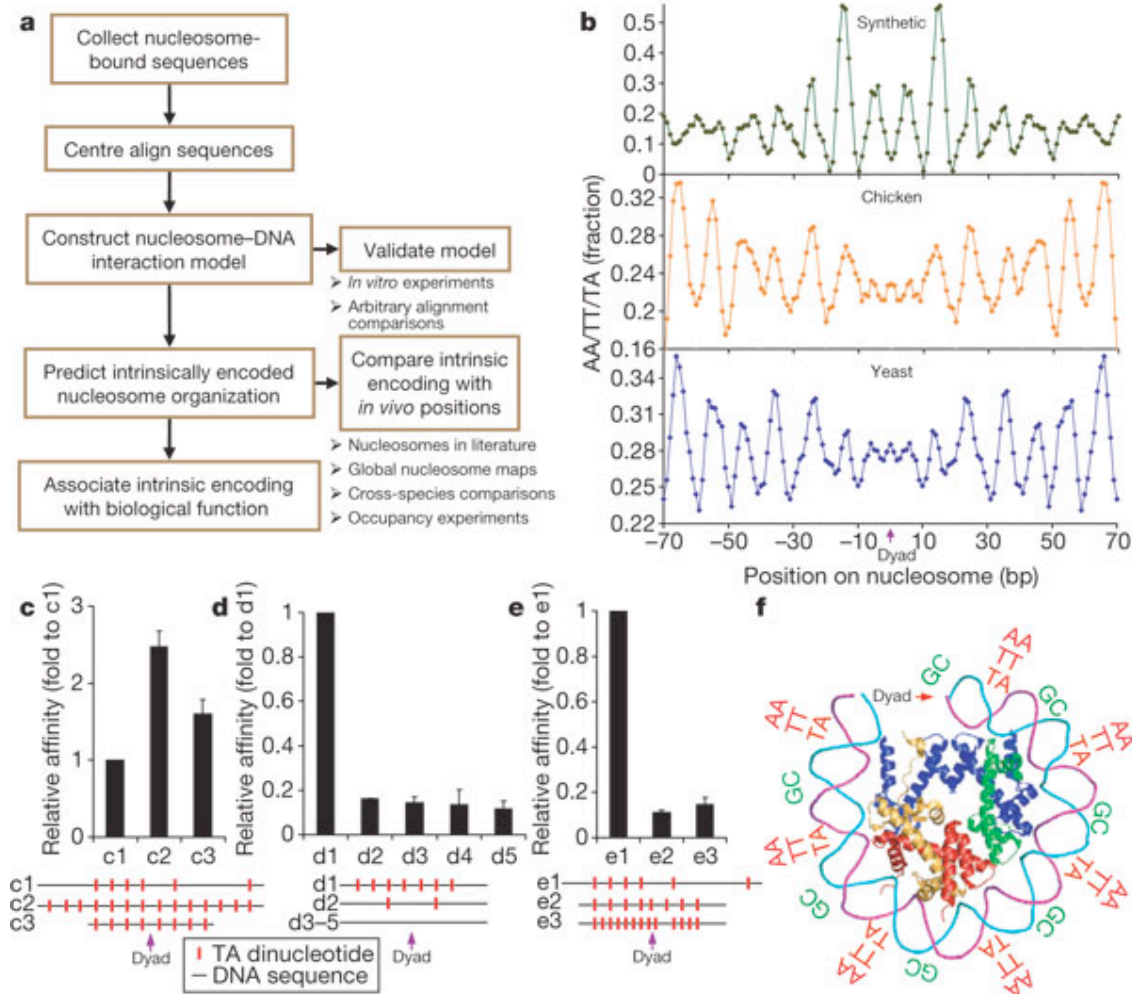
The Role of DNA Sequence

(Cloutier and Widom)



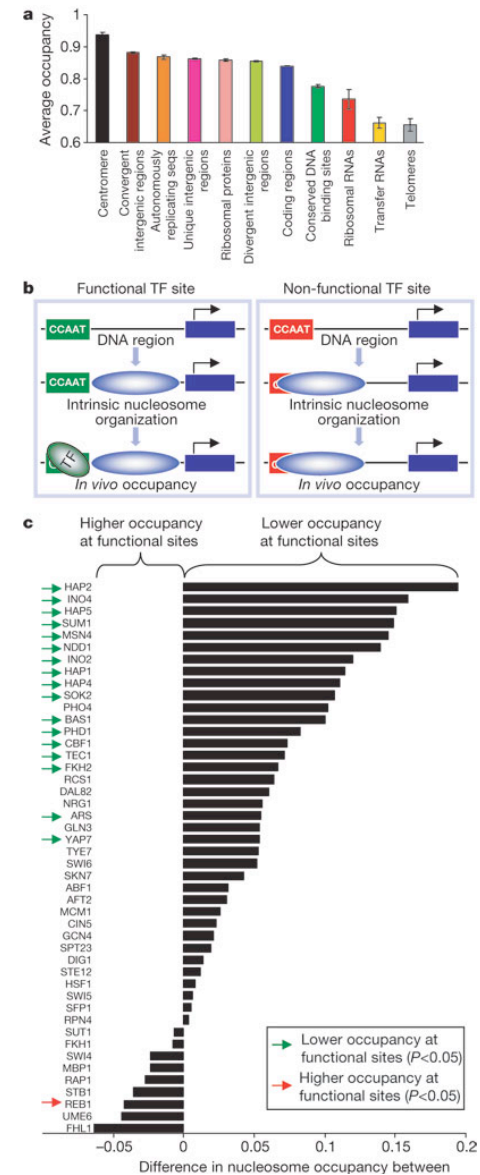
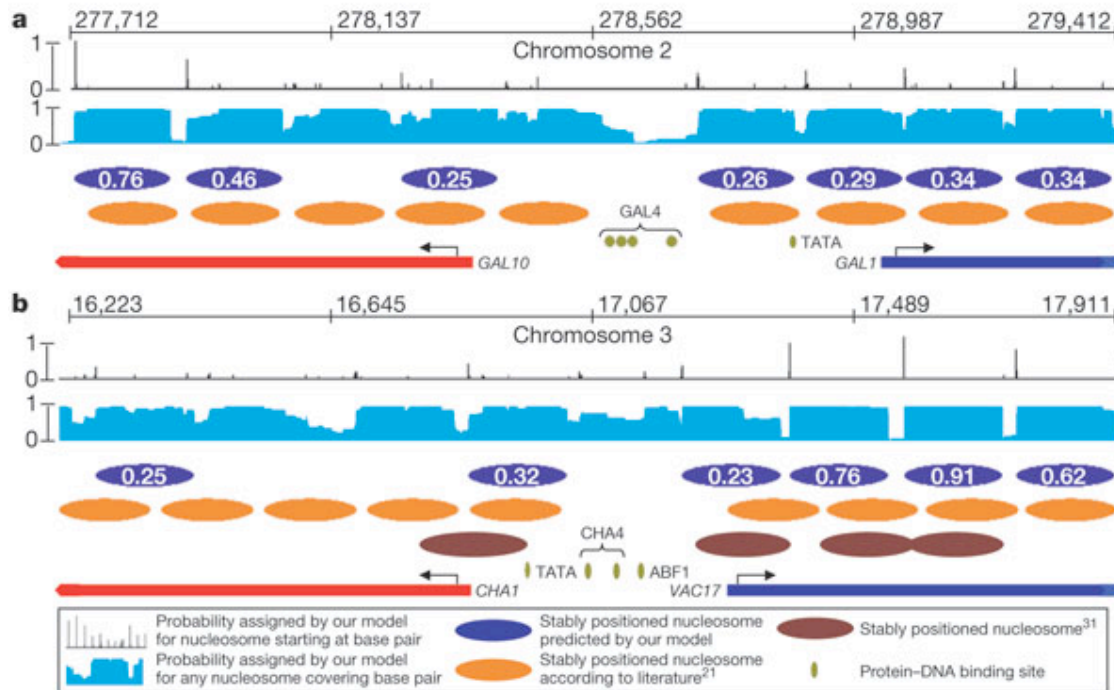
Nucleosomes Care About Positioning

(Segal *et al.*)



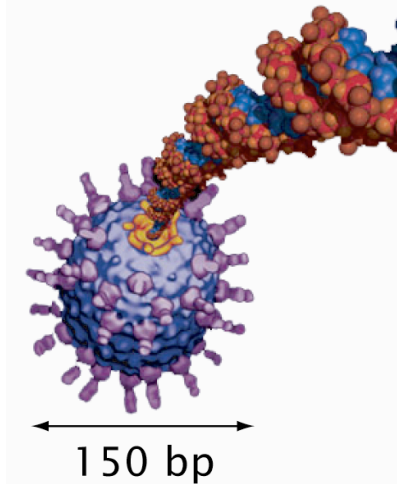
Consequences of Nucleosome Positioning

(Segal *et al.*)



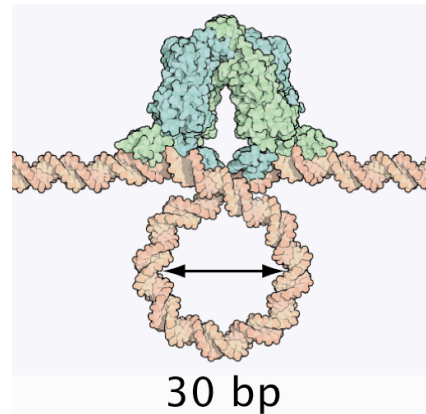
DNA in a Tight Squeeze: DNA Bending is Ubiquitous

Viral DNA packaging

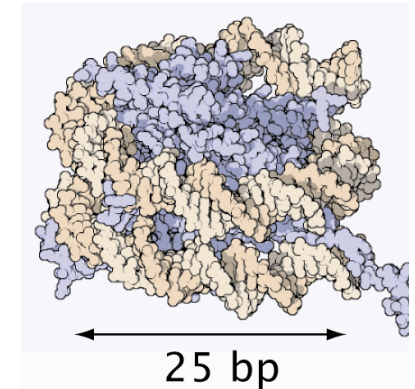


Bustamante *et al.*

Gene Regulation



Eukaryotic DNA Packaging



David Good

- Understanding tightly bent DNA goes beyond just transcriptional regulation!

The Chromosome as a Polymer Blob

