Genome Management and the Nucleosome

(Segal et al.)
Genomic material tightly packed in ordered arrangements.

These pictures of packaged DNA are a jumping off point for our models of the confined DNA.
HIV RNA Packing???

http://student.ccbcmd.edu/courses/bio141/lecguide/unit3/viruses/u2fig3a.html

(Turner and Summers)
Replication origins are confined!
The Chromosome as a Polymer Blob

$b = 2P$

1 μm
Electron Microscopy Images of the Nucleosome

Figure 4–23. Molecular Biology of the Cell, 4th Edition.
Dissecting the Nucleosome

- Linker DNA
- Core histones of nucleosome
- "beads-on-a-string" form of chromatin
- Nucleosome includes ~200 nucleotide pairs of DNA
- Released nucleosome core particle
- 146-nucleotide-pair DNA double helix
- Octameric histone core
- Dissociation with high concentration of salt
- Dissociation
  - H2A
  - H2B
  - H3
  - H4
Electron Microscopy of Higher Order Structures
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.
Atomic-Level Structure of the Nucleosome

(Richmond and Davey, 2003)
NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS EXTENDED LENGTH
Measurements of Equilibrium Accessibility

(Anderson and Widom)
The Role of DNA Sequence

(Cloutier and Widom)
Nucleosomes Care About Positioning

(Segal et al.)

(a) Collect nucleosome-bound sequences
   Centre align sequences
   Construct nucleosome-DNA interaction model
   Predict intrinsically encoded nucleosome organization
   Associate intrinsic encoding with biological function

(b) Validate model
   - In vitro experiments
   - Arbitrary alignment comparisons
   Compare intrinsic encoding with in vivo positions
   - Nucleosomes in literature
   - Global nucleosome maps
   - Cross-species comparisons
   - Occupancy experiments

---

(c) Relative affinity (fold to c1)
   c1, c2, c3

(d) Relative affinity (fold to d1)
   d1, d2, d3, d4, d5

(e) Relative affinity (fold to e1)
   e1, e2, e3

(f) Diagram of nucleosome organization
   - Dyad
   - TA dinucleotide
   - DNA sequence
Consequences of Nucleosome Positioning

(Segal et al.)