Histone core of nucleosome

Linker DNA of nucleosome
**Table 24–3**

<table>
<thead>
<tr>
<th>Histone</th>
<th>Molecular weight</th>
<th>Number of amino acid residues</th>
<th>Content of basic amino acids (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1*</td>
<td>21,130</td>
<td>223</td>
<td>29.5</td>
</tr>
<tr>
<td>H2A*</td>
<td>13,960</td>
<td>129</td>
<td>10.9</td>
</tr>
<tr>
<td>H2B*</td>
<td>13,774</td>
<td>125</td>
<td>16.0</td>
</tr>
<tr>
<td>H3</td>
<td>15,273</td>
<td>135</td>
<td>9.6</td>
</tr>
<tr>
<td>H4</td>
<td>11,236</td>
<td>102</td>
<td>10.8</td>
</tr>
</tbody>
</table>

*The sizes of these histones vary somewhat from species to species. The numbers given here are for bovine histones.*
**Figure 19.2** Individual nucleosomes are released by digestion of chromatin with micrococcal nuclease. The bar is 100 nm. Photograph kindly provided by Pierre Chambon.
Figure 19.3 The nucleosome consists of approximately equal masses of DNA and histones (including H1). The predicted mass of the nucleosome is 262 kD.

<table>
<thead>
<tr>
<th>Protein</th>
<th>Mass (kD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2A</td>
<td>28 kD</td>
</tr>
<tr>
<td>H2B</td>
<td>28 kD</td>
</tr>
<tr>
<td>H3</td>
<td>30 kD</td>
</tr>
<tr>
<td>H4</td>
<td>22 kD</td>
</tr>
</tbody>
</table>

200 bp DNA = 130 kD  
Length = 67 nm

Total protein = 108 kD

H1 = 24 kD

6 nm

11 nm

Figure 19.4 The nucleosome may be a cylinder with DNA organized into two turns around the surface.

DNA ‘leaves’

DNA ‘enters’
Figure 19.5 The two turns of DNA on the nucleosome lie close together.

2 turns of DNA, each 2 nm diameter, occupy most of height (6 nm)

Axis of symmetry

Protein = 3.2 nm
Radius of gyration
DNA = 5.2 nm

Sites 80 bp apart on linear DNA are close together on nucleosome
**Figure 19.7** Micrococcal nuclease digests chromatin in nuclei into a multimeric series of DNA bands that can be separated by gel electrophoresis. Photograph kindly provided by Markus Noll.

**Figure 19.8** Each multimer of nucleosomes contains the appropriate number of unit lengths of DNA. Photograph kindly provided by John Finch.
Figure 19.9 Micrococcal nuclease reduces the length of nucleosome monomers in discrete steps. Photograph kindly provided by Roger Kornberg.
**Figure 19.12** Sites for nicking lie at regular intervals along core DNA, as seen in a DNase I digest of nuclei. Photograph kindly provided by Leonard Lutter.

**Figure 19.13** Two numbering schemes divide core particle DNA into 10 bp segments. Sites may be numbered S1 to S13 from one end; or taking S7 to identify coordinate 0 of the dyad symmetry, they may be numbered −7 to +7.

**Figure 19.14** The most exposed positions on DNA recur with a periodicity that reflects the structure of the double helix. (For clarity, sites are shown for only one strand.)
[Diagram showing the process of DNA supercoiling and interaction with histone core.]

(a) DNA with a Histone core.

(b) Bound negative supercoil (solenoidal) and Unbound positive supercoil (plectonemic).

(c) One (net) negative supercoil after treatment with topoisomerase.

\[ \Delta Lk = 0 \]
Higher order structure

A. Winding of DNA into bead like particles
   1. 10 nm fiber - does not require H1 histone under low ionic conditions
   2. Packing ratio (length of DNA/length of unit) is ~6
   3. Part of euchromatin, heterochromatin, and chromosomes - invariant
B. Coiling of series of beads into a helical array
   1. 30 nm fiber requires H1 and greater ionic conditions
   2. packing ratio of ~40
   3. basic component of both mitotic chromosome and interphase chromatin
   4. easily interconverted into 10 nm structure by changing salt concentration
C. Packing of 30 nm fiber
   packing ratio of > or = 1000 in euchromatin and < or = 10,000 for heterochromatin
Chromatin Assembly

Factors required for assembly
1. Nucleoplasmin - acidic protein
   there are several chaperones like this one
2. Topoisomerase I
3. ATP dependent remodeling
Phasing of Nucleosome

A. Definition of nucleosome phasing - the binding of nucleosomes to a specific region of DNA rather than the more normal random binding of nucleosomes to DNA
   1. Translational positioning
   2. Rotational positioning

B. Nucleosome phasing occurs because of
   1. binding is influenced by sequence specific topology
   2. the first nucleosome in a region is preferentially assembled at a particular site
      a. because region excluded by prior protein-DNA complex or other higher order structure
      b. followed by sequential assembly of nucleosomes
      c. phasing would be expected to be well maintained close to boundary, but not farther away (variability in linker)
      d. example is the central region of Tetrahymena rDNA
Figure 27.24  Acetylation of lysine or phosphorylation of serine reduces the overall positive charge of a protein.
Sites of histone acetylation

**H2A**
- **Vertebrates**: SGRGKQGGKARAKAK
- **Yeast**: SGGKGGKAGSAAKAS

**H2B**
- **Vertebrates**: PEPAKSAPAPKGGSKKAVTKT
- **Yeast**: SSAAEKKPASKAPAEEKKPAAKK

**H3**
- **Vertebrates**: ARTKQTARKSTGGKAPRKQLATKAA
- **Yeast**: ARTKQTARKSTGGKAPRKQLASKAA

**H4**
- **Vertebrates**: SGRGKGGKGLGKGGAKRHRK
- **Yeast**: SGRGKGGKGLGKGGAKRHRK
Histone acetyltransferases (HATs)

A. cytoplasmic HATs (Type B)
   i. acetylate newly synthesized H3 and H4 histones before depositing on to DNA
   ii. after binding to DNA the acetyl groups are removed

B. nuclear HATs (Type A)
   i. have been found to be required for gene activation
   ii. part of TFIID has HAT activity (TAFII250)
   iii. these HAT proteins are usually large multi-subunit complexes
      two classes: the GNAT and MYST families
Figure 1. The known post-translational covalent modifications of histones (H2A, H2B, H3 and H4). Lysine (K) methylation (Me) is represented in red. Acetylation (Ac), phosphorylation (P) and ubiquitination (Ub) are indicated in green, blue and orange, respectively. Arginine (R) methylation is represented in black. Modifications shown above each amino acid correlate with activation, whereas the lysine methylation shown below correlates with repression. The highest degree of methylation possible for each residue is displayed. Note that in H4, K20 methylation might also participate in activation.