(ii) *Non - histones* : These make up about 20% of the total chromosome mass. The number of non - histones vary from 12 to 120. These proteins show variation from one species to the other and even in different tissues of the same organism. Clearly, they have not been conserved during evolution as the histone proteins. This class of proteins include many important enzymes such as DNA and RNA polymerases etc.

7-10 EUKARYOTIC CHROMOSOME STRUCTURE

The length of DNA in the nucleus is far greater than the size of the compartment in which it is contained. To fit into this compartment, the DNA has to be condensed in some manner. The degree to which DNA is condensed is expressed as its packing ratio.

Packing ratio is the length of DNA divided by the length into which it is packaged. For example, the shortest human chromosome contains $4 \cdot 6 \times 10^7$ bp of DNA (about 10 times the genome size of *E. coli*). This is equivalent to 14,000 μm of extended DNA. In its most condensed state during mitosis, the metaphase chromosome is about 2 μm long. This gives a packing ratio of 7000 (14000/2). Thus any model for chromosome structure must be able to account for among other things, the packaging of a long DNA molecule into such a small metaphase chromosome.

Typical Early Model : One of the earliest models of chromosome structure is presented based on light microscope studies. According to this model, the basic component of chromosome structure is *chromonema* (pl. chromonemeta). The chromonema is composed of chromatin and contains genes. The variation in chromosome length and thickness was proposed to be due to coiling and uncoiling of chromonemata. Each chromatid of a chromosome may contain two or more chromonemata, which run across through the centromere. In case of metaphase chromosomes, chromonemata are surrounded by an *amorphous matrix* , the outerside of which is enclosed in a membrane called *pellicle.* However, electron micrography of metaphase chromosome do not show any evidence for the existence of matrix or pellicle. Clearly, this model of chromosome structure is inadequate and of historical interest only.

7-11 ULTRA STRUCTURE OF CHROMOSOME

E.M. studies of both intact and sectioned metaphase and nterphase chromosomes have revealed that 300A° diameter

chromatin fibres are the basic units of chromosome structure. The organization of such chromatin fibres is best explained by the folded - fibre model of chromosome structure.

(A) Folded - fibre model :

This model was proposed by Du Praw in 1965 and is widely accepted. According to this model, chromosomes are made up of chromatin fibres of about 230A° diameter. This chromatin fibre is produced by coiling of single DNA double helix, and the coils of DNA molecule are stabilized by proteins. Each chromosome contains a single enormously long chromatin fibre, which folds in various ways to yield the metaphase chromosome structure.

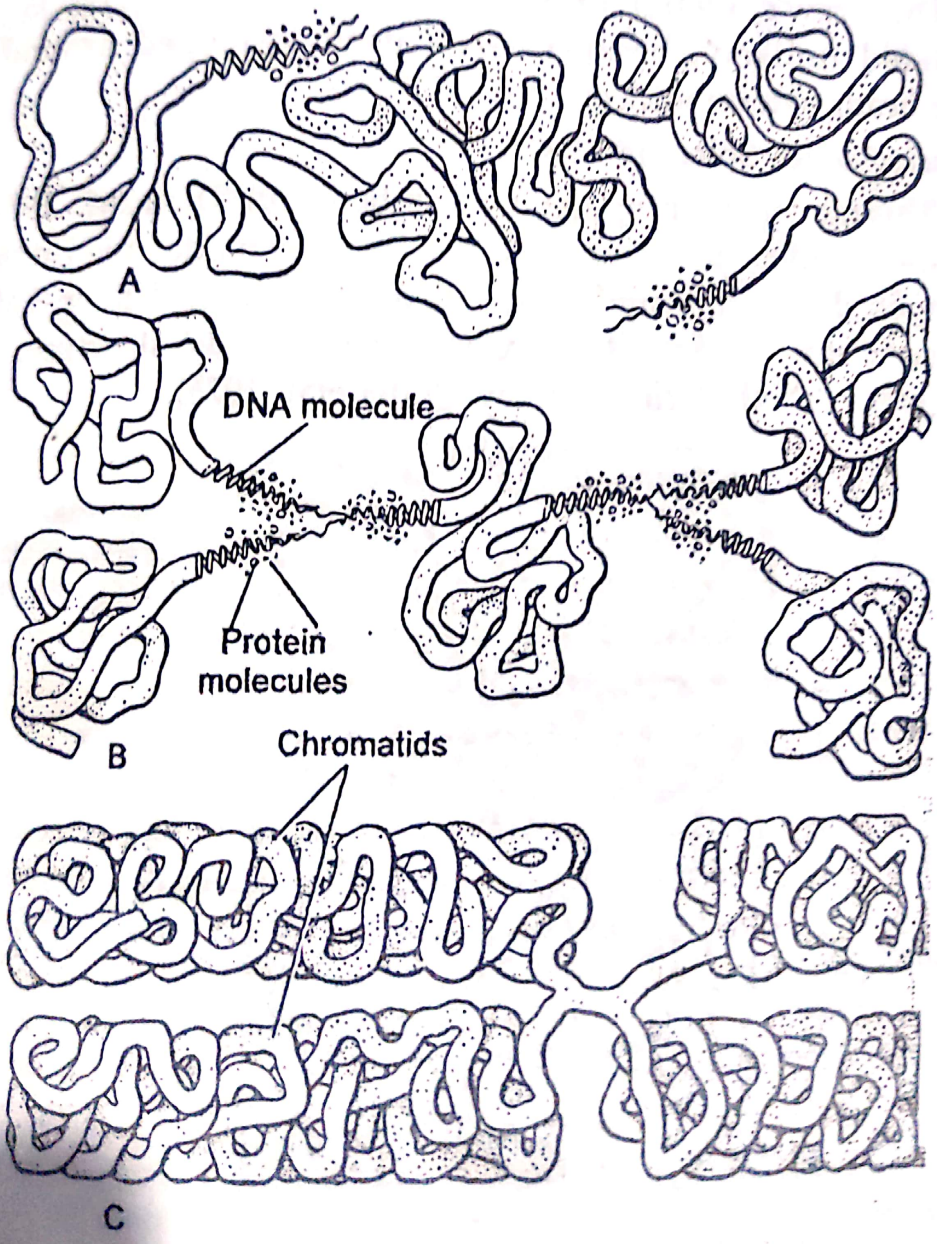


Fig. 7·6 : Dupra's folded fibre model of chromation in interphase
(A & B) Interphase, (c) Metaphase

The details of this model are as follows :

(i) The 20A° DNA double helix is specially packed in protein o form a *fibril*. This fibril further coils to form a fibre of 100 A°. his fibre is called Type A fibre. The DNA is packed inside the ype A fibre in a packing ratio of 6 : 1.

(ii) Type A fibre then coils in a packing ratio of 10 : 1 to form a ype B fibre of 200 – 250 A° diameter. The total packing ratio of NA in type B fibre averages 56 : 1.

(iii) Now the Type B fibre is extensively folded to form the hromated.

Du Praw's model of DNA - histone association is now onsidered unlikely, because DNA itself is looped around the istone beads to form nucleosomes.

B) Nucleosome - Solenoid Model :

This model was proposed by Kornberg and Thomas in 1974 and s the most widely accepted. According to this model, the chromatin s composed of a repeating unit called *nucleosome*. Under E.M, the hromatin fibres appears to have a "string of beads" structure. These eads were called *Nucleosomes* by Qudet etal (1975).

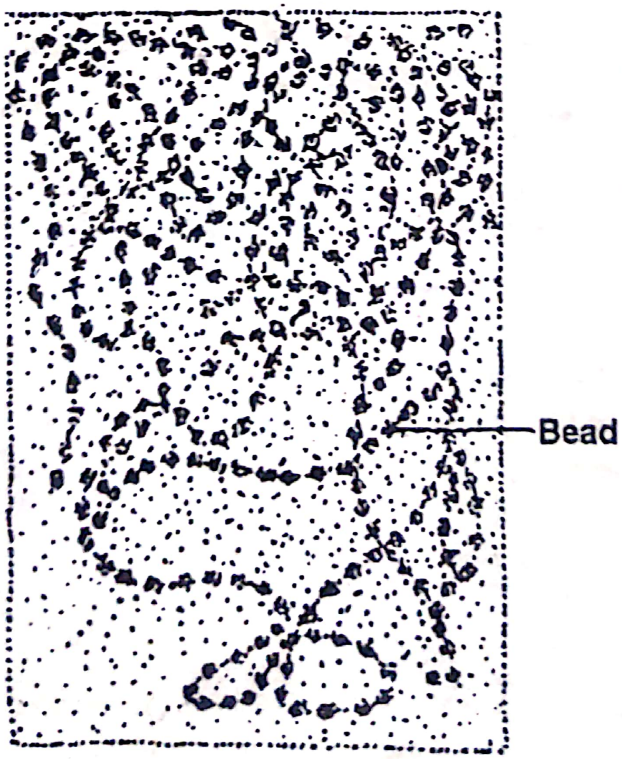


Fig. 7·7 : Beaded appearance of DNA

The nucleosome is an oblate particle of about 57A° high and 110 A° diameter. It consists of a *core* particle of histone proteins and

a small *spacer* or *linker DNA*. The core particle consists of an octamer of histone proteins composed of two molecules each of histones H_2 A, H_2 B, H_3 and H_4. The surface of the core particle is tightly wrapped like a ribbon by 1·75 turns of DNA (146 bp). The nucleosomes are linked together by small fragments of DNA molecule called *linker DNA*. Its length is 15 -114 bp, depending on

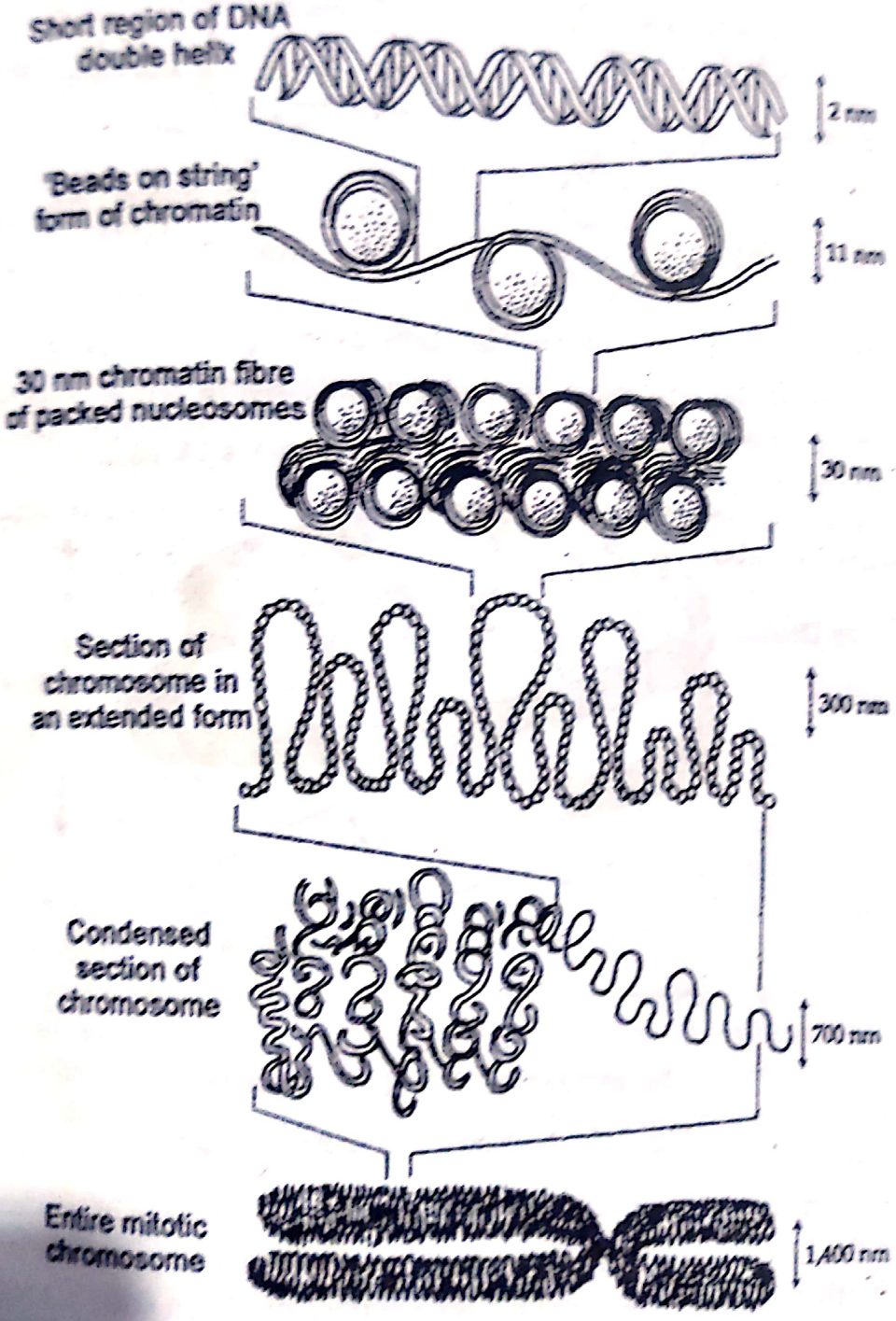
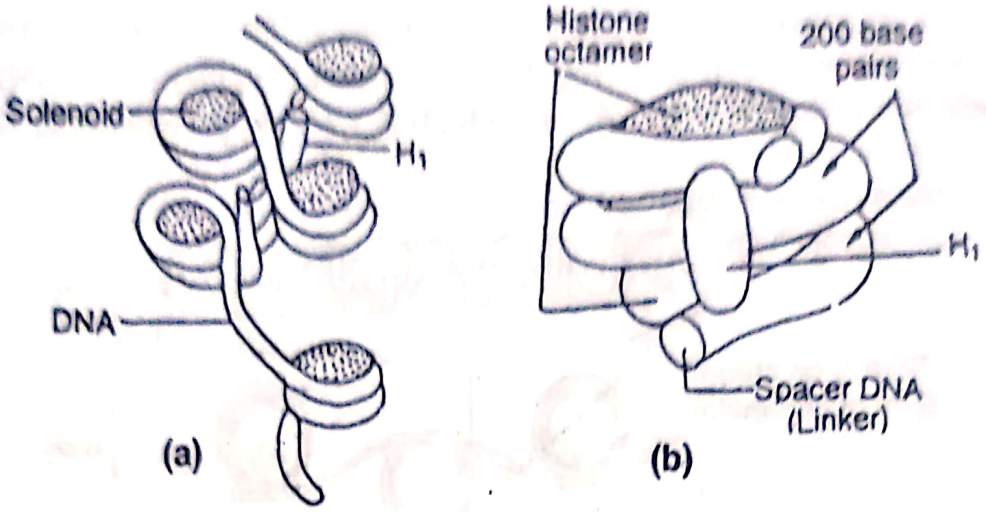
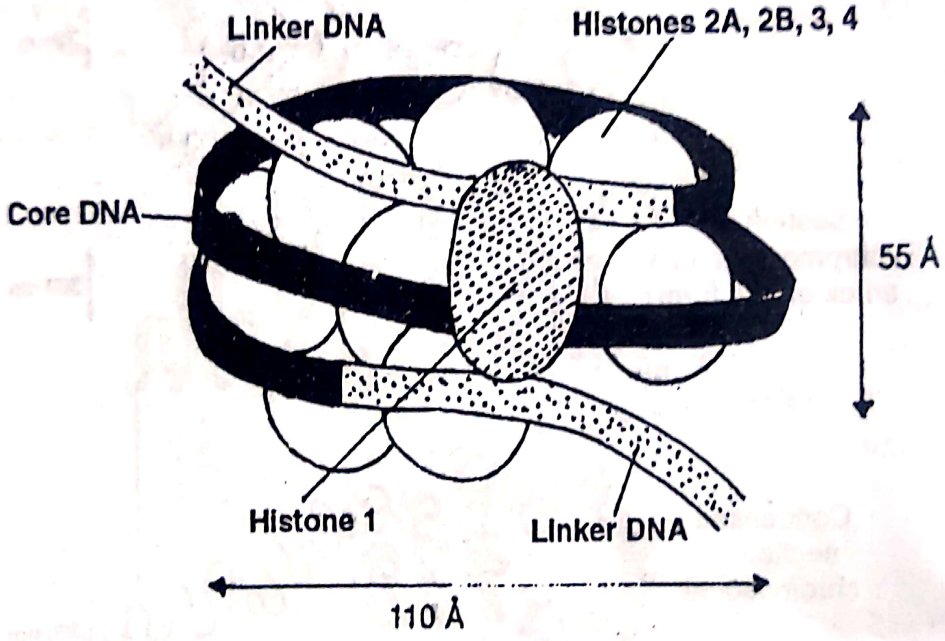


Fig. 7·9 : Levels of packaging of DNA

the cell type. Another protein histone protein H_1 is bound to the linker DNA.



(a) nucleosome chain
(b) structure of single nucleosome.



Schematic diagram of Nucleosome

Fig. 7·8 : Nucleosome solenoid model

Assembly of DNA and histones is the first stage of shortening of the DNA strand in a chromosome ; a sevenfold reduction in the length of DNA. The beaded flexible fibre of 11 nm wide is roughly five times the width of free DNA. The second level of folding is the shortening of the 11 nm fibre to form a solenoidal supercoil with six

nucloeosome per turn, called the 30 nm fibre (The supercoiled nucleosome is called *solenoid*). The further folding of the 30 nm fibre is less well understood.

7.12 FUNCTIONS OF CHROMOSOMES

The main function of chromosomes is to carry the genetic information from one cell generation to another. Another important function is to *protect* the genetic material (DNA) from being damaged during cell division. *Gene action* in eukaryotes is belived to be regulated through histone and non histone proteins associated with chromosomes. The specialized structure of telomeres prevents end to end interactions between chromosomes. This ensures stability of the different chromosomes.

Semi conservative replication of a linear DNA molecule inevitably leaves a short sequence at the two ends of this molecule in unreplicated state. This will lead to progressive shortening of the molecule after every round of replication. Chromosome organization avoids this shortening as follows. The telomeres are made up of several copies of short repeating sequence. The enzyme telomerase adds copies of this sequence at the chromosome ends. Therefore the shortening that occurs due to replication is adequatelyy compensated for by telomerase action, and the chromosome length is maintained.