Lecture 2.
Cell cycle. Interphase chromosome

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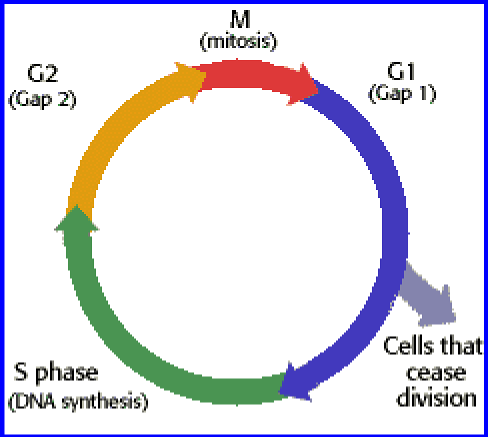


The Cell cycle

The average mammalian cell cycle lasts about 17–18 hours.

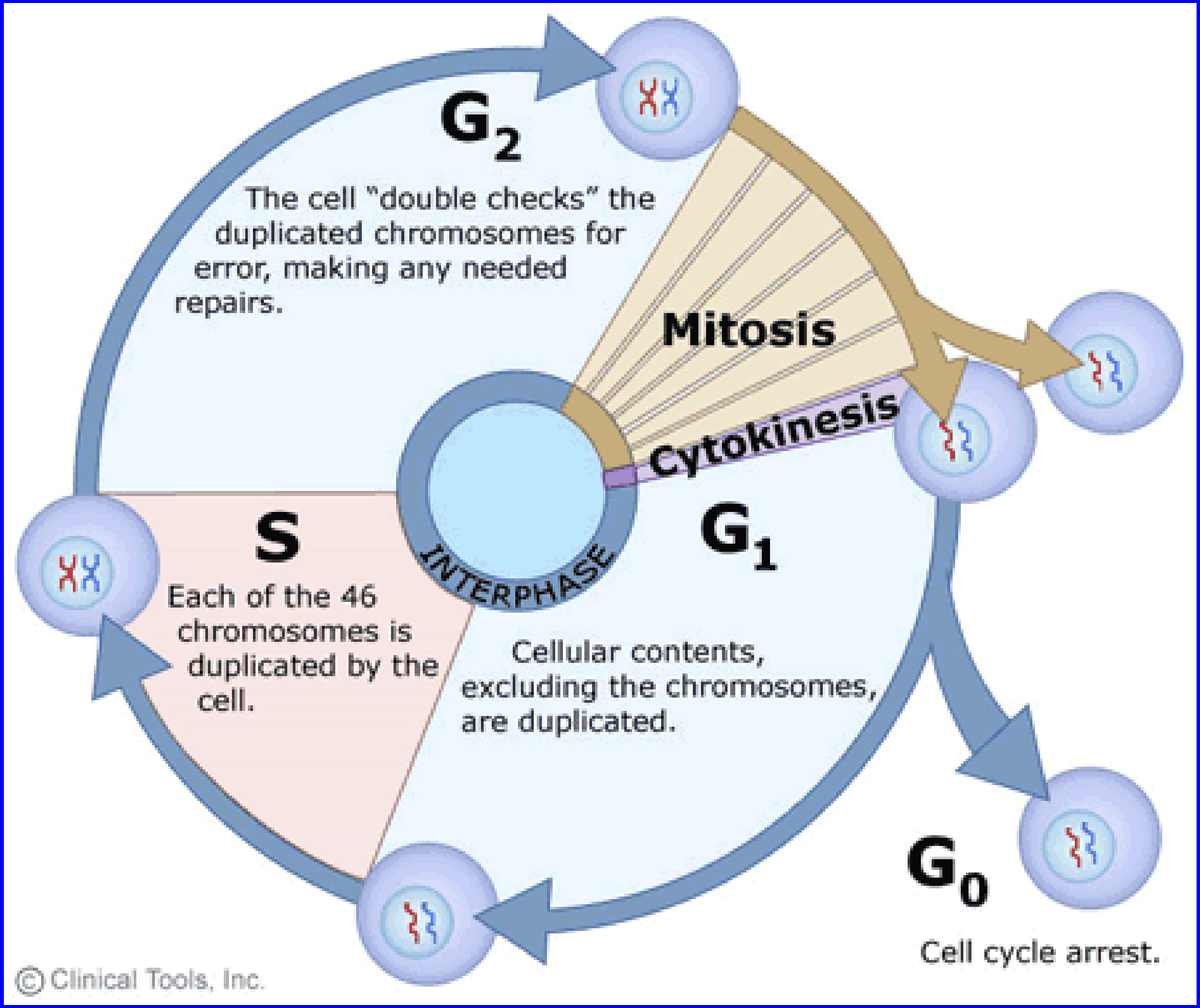
The first stage, G1, lasts about 9 hours. Chromosomes exist as single chromatids during this stage. Cells are metabolically active during G1, and this is when protein synthesis takes place. A cell might be permanently arrested at this stage if its does not undergo further division. This arrested phase is referred to as gap zero (G0).

The synthesis phase (S) lasts about 5 hours in mammalian cells. This is when DNA synthesis occurs. The DNA replicates itself and the chromosomes then consist of two identical sister chromatids.

Gap 2 lasts about 3 hours. During this phase, the cell prepares to undergo cell division. The completion of G2 represents the end of the interphase.

The final step in the cell cycle is mitosis. This stage lasts only 1–2 hours in most mammalian cells.

The Cell cycle



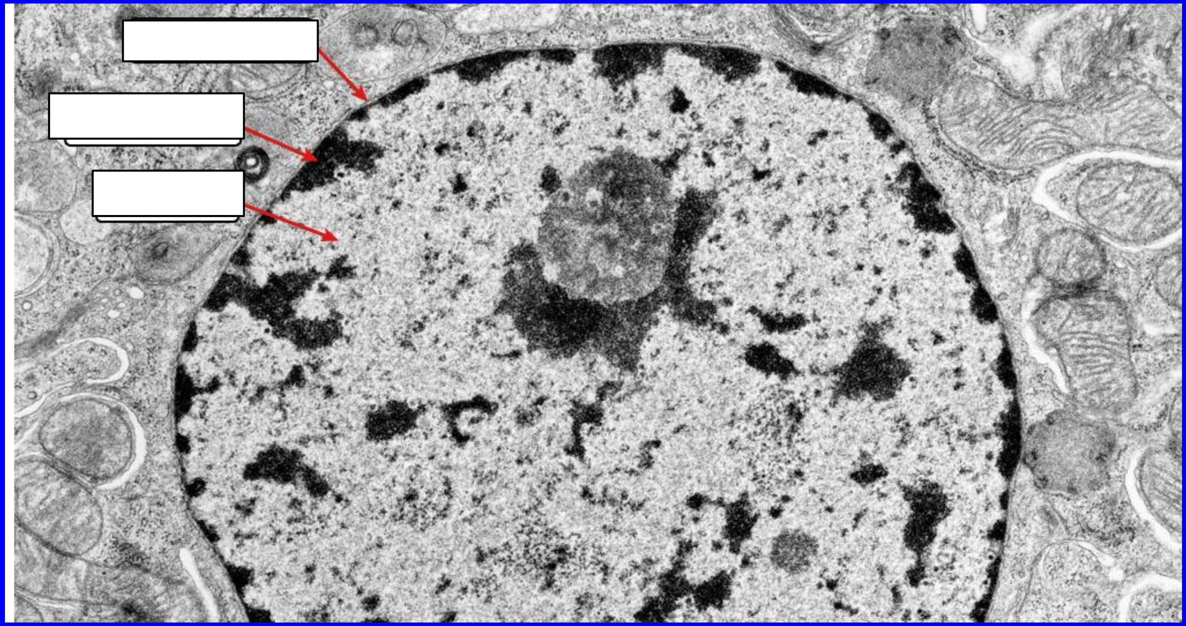
Chromatin

Euchromatin

Heterochromatin

Constitutive

Facultative



Emil Heitz,
1892-1965

Euchromatin

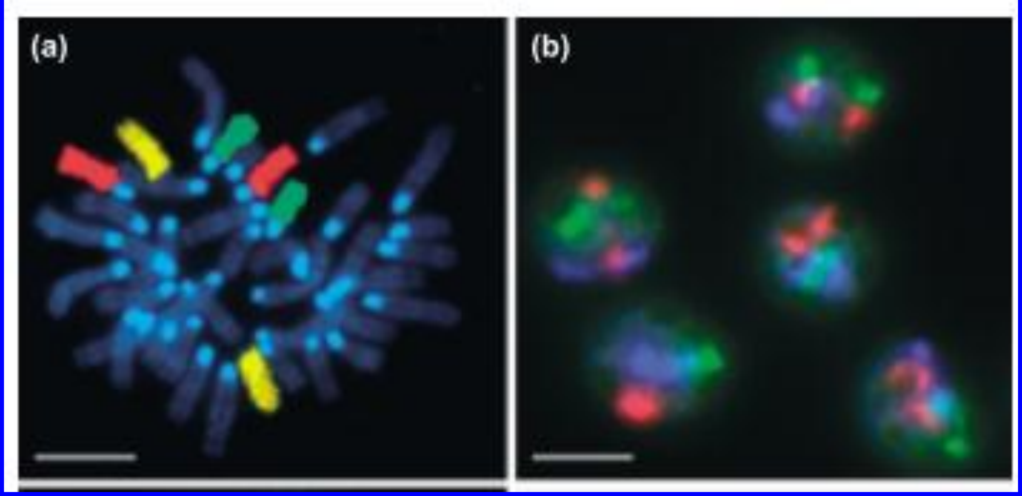
- ✓ Eucromatin is the lightly packed form of chromatin that rich in gene concentration
- ✓ It is often active transcription
- ✓ Euchromatin comprises the most active portion of the genome within nucleus, 92% of the human genome is euchromatin.
- ✓ The structure of Euchromatin is reminiscent of an unfolded set of beads represent Nucleosomes. Nucleosomes consist of eight proteins kown as Histones, with approximately 147 base pairs of DNA wound around them.
- ✓ In Euchromatin the wrapping is loose so that the raw DNA may be accessed.
- ✓ The basic scructure of Euchromatin is an elongated, open 10 nm micro fibril
- ✓ Euchromatin participates in the active transcription of DNA to mRNA products

Heterochromatin

- ✓ Heterochromatin appear relatively condensed and stained deeply with DNA specific strains.
- ✓ It is tightly packed form of DNA.
- ✓ Heterochromatin play a role in the expression of genes.
- ✓ Transcriptionally inactive.
- ✓ Facultative heterochromatin is the result of genes that are silenced through a mechanism such as histone methylation or siRNA through RNAi.
- ✓ Constitutive heterochromatin is usually repetitive and forms structural functions such as centromeres or telomeres

Chromosome territories

✓ The genetic material that makes up a single chromosome is not distributed in a disorderly fashion throughout the interphase nucleus. Instead, each chromosome occupies a finite, mutually exclusive fraction of the nuclear volume and represents a structural unit referred to as a ***chromosome territory*** (Fig. b). The size of a chromosome territory is roughly determined by its DNA content but is also affected by other factors such as its overall transcriptional status.

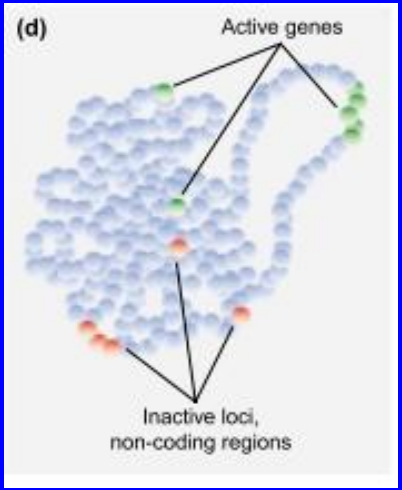


The physical nature of chromosomes.
(a) The distinct physical nature of chromosomes is evident in mitotic cells, when chromosomes condense. Fluorescent detection of specific chromosomes (12, red; 14, yellow; 15, green; DNA, blue) in a metaphase spread of normal mouse lymphocytes.
(b) During interphase, chromosomes are organized in physically distinct chromosome territories. Chromosomes 12 (green), 14 (red) and 15 (blue) were detected in mouse fibroblasts.

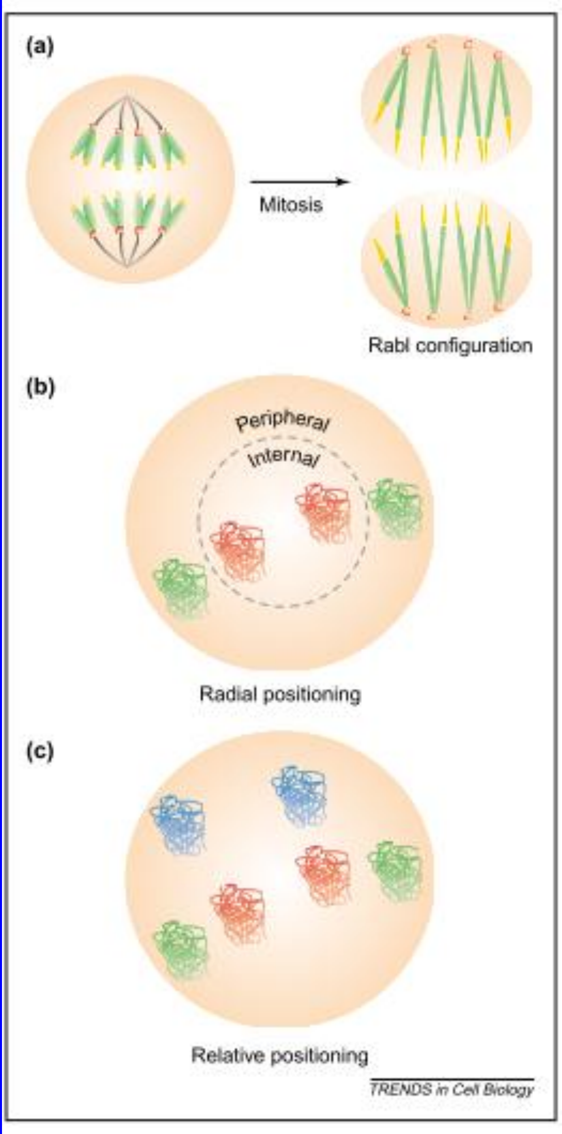
Chromosome territories

✓ The replication domains are ~1 Mb in size and constitute a distinct level of chromosome territory organization, because they are maintained during consecutive cell cycles. The chromatin fibre within chromosome territories has been suggested either to exist in the form of loops of 30–150kb, which in turn form rosettes to give the 1 Mb replication domains, or to form ~3 Mb giant loops that observed during anaphase is maintained throughout are generated by a random walk of the fibre and are held together at their bases.

✓ Chromosome territories are permeable to proteins. Active transcription sites are scattered throughout chromosome territories and are not concentrated on the surface of chromosome territories. The genes can be found anywhere within a chromosome territory, regardless of their transcriptional activity (Fig. d).



Non-random chromosome positioning



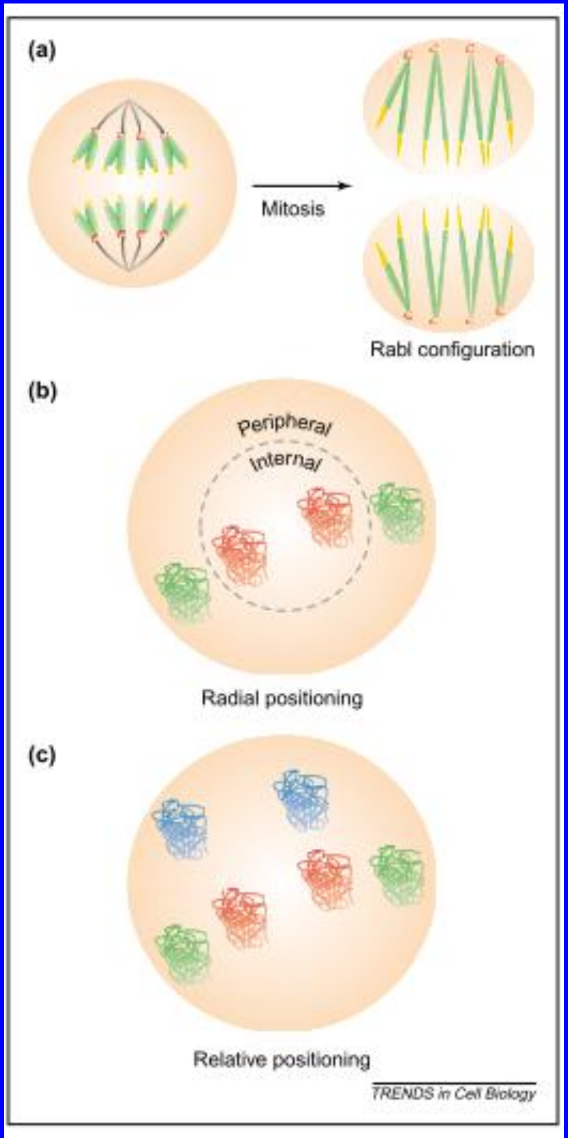
a) In the Rabl configuration, centromers (red) and telomeres (yellow) are aligned at opposite sides of the nucleus. The Rabl configuration is established during anaphase and is maintained during interphase;

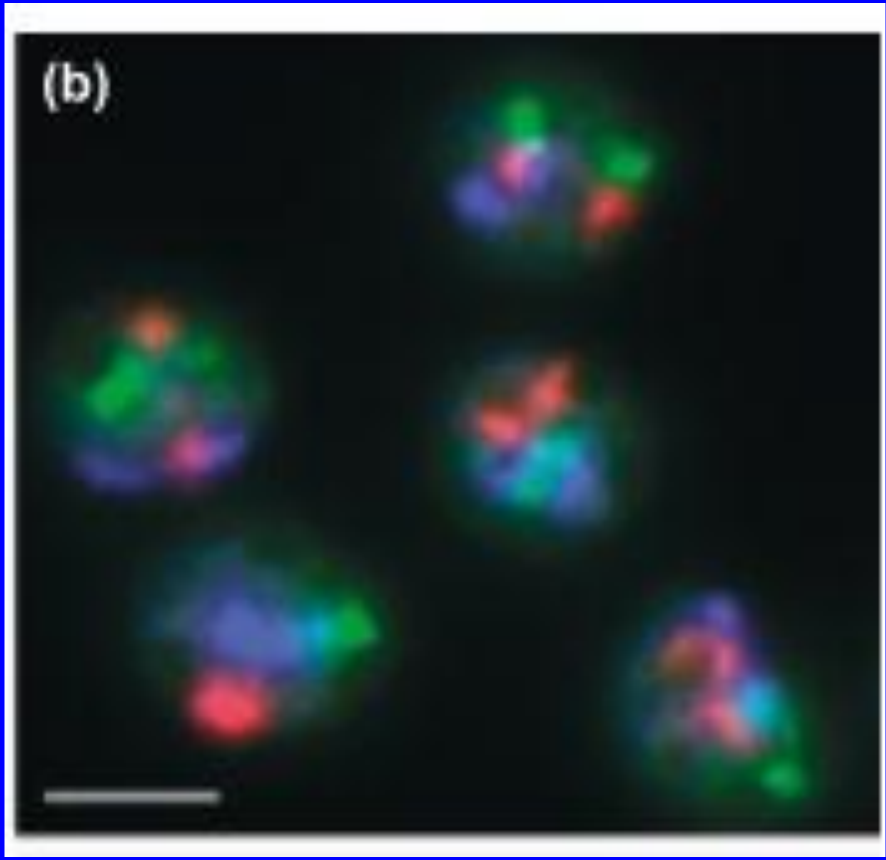
b) Radial positioning of chromosomes results in the preferential localization of chromosome territories towards either the periphery or the interior of the nucleus depending on their size or gene density;

c) Relative positioning places chromosome territories in preferential positions relative to each other.

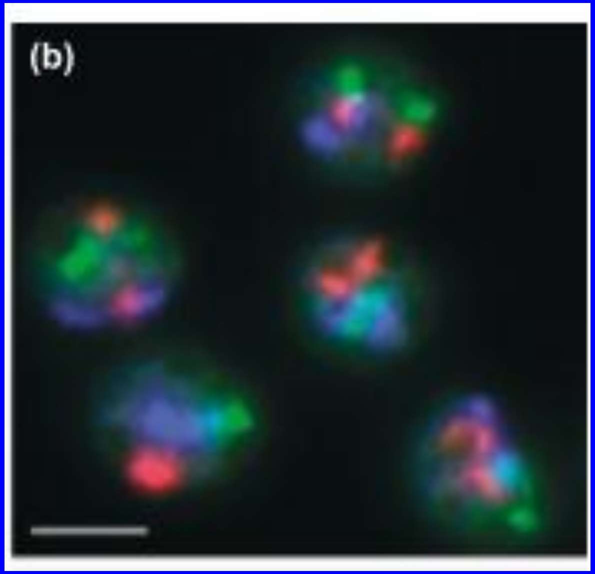
None of these models is mutually exclusive.

Non-random chromosome positioning





Non-random chromosome positioning



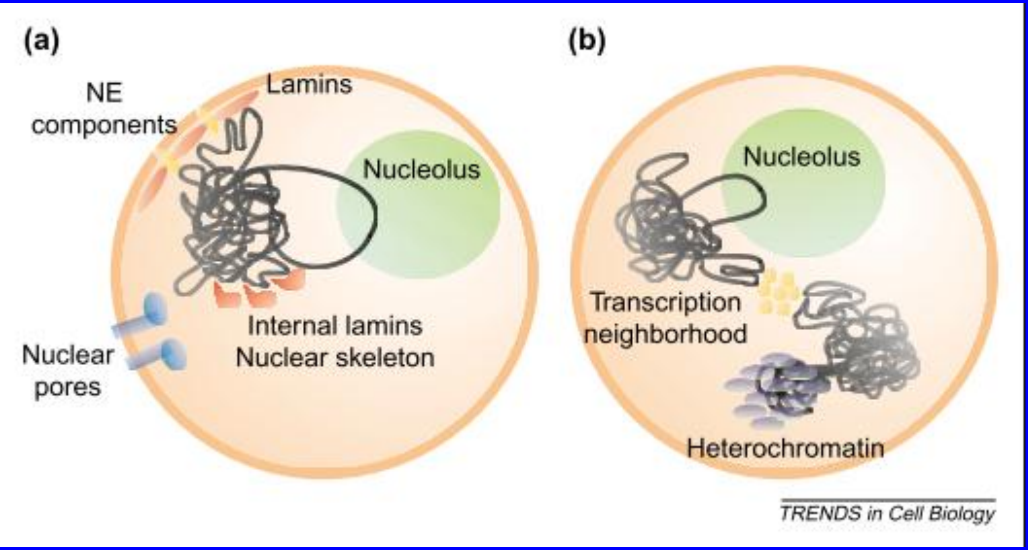
Why is it so difficult to answer the apparently simple question of whether and how chromosomes are arranged in the nucleus?

1) The different organisms, tissues and even cell types might arrange their chromosomes according to different rules.

2) In most experimental systems, the observed patterns are heterogeneous and are often only observed in a subpopulation of cells.

3) The three-dimensional nature of interphase nuclei, the relatively large number if chromosomes and the absence of fixed reference points within the nucleus make spatial pattern recognition and analysis difficult.

Attachment and functional roles for chromosome positioning



a) Tethering of chromosome territories to nuclear structures restricts their movement and contributes to maintenance of chromosome positioning.

b) Chromosome territories might be positioned within the nucleus in order to place specific genes in particular nuclear neighborhoods that favour the expression or silencing of genes.

Thank you for attention!