DNA Folding.

DNA is a very long polymer!

Human DNA is about 2m long. It is made of 46 (2×23) chromosomes, so on average each chromosome is

$$\frac{2}{46} = \frac{1}{23} \simeq 0.04 \text{ m} \Rightarrow 4 \text{ cm} = 10^{-2} \text{ m}$$

Recall that the Kuhn's length of DNA is 100 nm $= 10^{-7}$ m and we have that DNA is, in total

$$\frac{2}{10^{-7}} = 2 \cdot 10^{7} \text{ Kuhn lengths}$$

and each chromosome is

$$\frac{4 \cdot 10^{-2}}{10^{-7}} = 4 \cdot 10^{5} \text{ Kuhn lengths}$$

here we use Gaussian SAW might be more appropriate but also give larger values. Gaussian is conservative.

The end-to-end distance is thus

Full DNA

$$\bar{R}_{ee} = \sqrt{\langle \vec{R}_{ee}^{\,2} \rangle} = l_k N^{1/2} =$$

$$= 100 \cdot 10^{1/2} (10^6)^{1/2} \text{ nm} =$$

$$= 100 \cdot 3 \cdot 10^{3} \text{ nm} = 3 \cdot 10^{5} \text{ nm} = 300 \ \mu\text{m}$$

$$\bar{R}_{ee} = \sqrt{\langle \vec{R}_{ee}^{\,2} \rangle} = l_k N^{1/2}$$

$$= 100 \cdot 2 \cdot 10^{1/2} (10^4)^{1/2} \text{ nm} =$$

$$= 2 \cdot 100 \cdot 3 \cdot 100 \text{ nm} = 6 \cdot 10^{4} \text{ nm} = 6 \ \mu\text{m}$$

But the nucleus is a few microns across!

Clearly DNA by itself cannot fit the nucleus. Not even a chromosome

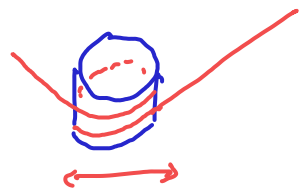
⇒ Need to make it compact.

(1) DNA-binding proteins can interact with each other, resulting in effective attractive interactions that allow DNA to collapse.

$$\bar{R}_{ee} \sim \ell_k N^{1/3} \simeq 100\,\text{nm} \cdot (10^7)^{1/3} = 100\,\text{nm} \cdot 10^{1/3} \cdot 10^2 \simeq 100 \cdot 2 \cdot 10^2\,\text{nm} = 20\,\mu\text{m}$$

it is getting closer to the correct size.

Actually DNA is wrapped around histones



⇒ it is strongly bent over very short lengthscales!

~10 nm

It is possible thanks to the strong electrostatic interaction: positive histones and negative DNA

In this way, for each histone step (10 nm), we advance about $2 \cdot \pi \cdot d \simeq 60$ nm ⇒ 6x shorter.

($d \downarrow 10$ nm)

This is great, but there is then a second problem:

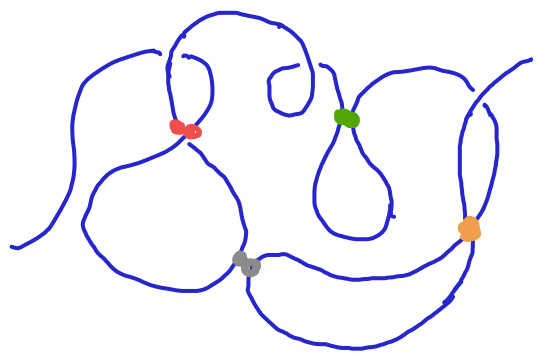
DNA collapse cannot be random!

DNA must be read, copied etc. To do so it must be packed in an ordered way, so that it is easy.

⇒ problem similar to protein folding.

Starting the end of the 2000's, there has been a series of works (initiated by Job Dekker at MIT) to experimentally map the structure of DNA in the nucleus.

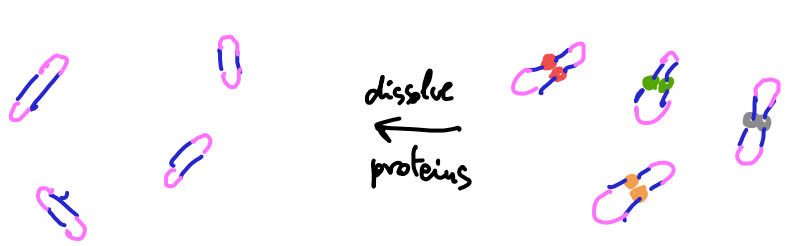
The basic idea :



→ chemically "freeze"

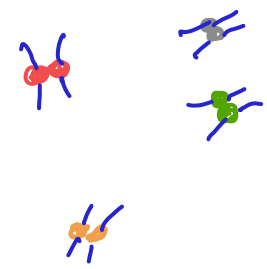
The crossing interactions cannot be disrupted anymore

↓ enzyme to cut DNA



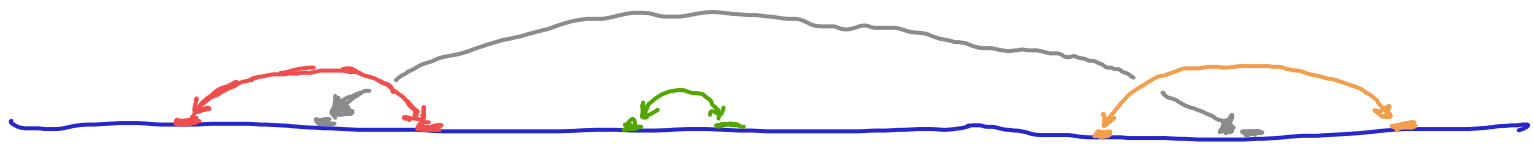
dissolve proteins ←

enzyme + nucleotides to form circles ←



are the only parts that are preserved

↓ sequencing and identification of the original parts on DNA



Doing the same on very many cells (10^5), and averaging, it has been discovered that the way DNA is "folded" in the nucleus is highly reproducible, depends on the tissue, on the line of the day, etc but it is not random.

Part of the job is accomplished by carefully placing the regions for protein binding : it's a little bit as designing the sequence of a protein.

Yet this is not sufficient, and indeed, and there are a number of proteins that constantly remodel DNA using the energy from ATP.

Just like chaperones for proteins, these molecules can maintain the overall chromatin in a steady conformational ensemble different from the one at equilibrium.

↑
DNA in the nucleus

As Schroedinger wrote in "What is Life?" : "Living matter evades the decay to equilibrium".