BB 101: MODULE II

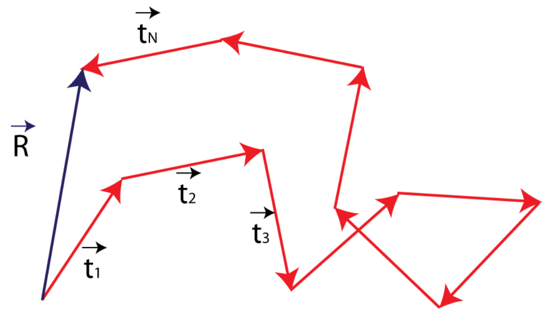
PHYSICAL BIOLOGY

Review of Lecture 4

- Diffusion Equation using Fick's law and Continuity Equation
- Free diffusion from a point source
- Need for active transport
- Einstein Relation and its significance
- Conformation of polymers as random walk

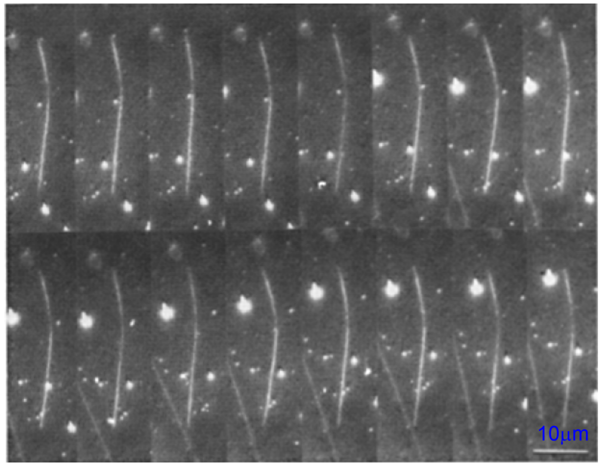
Conformation of polymers as random walk

- In last lecture, we treated polymers as freely jointed chain

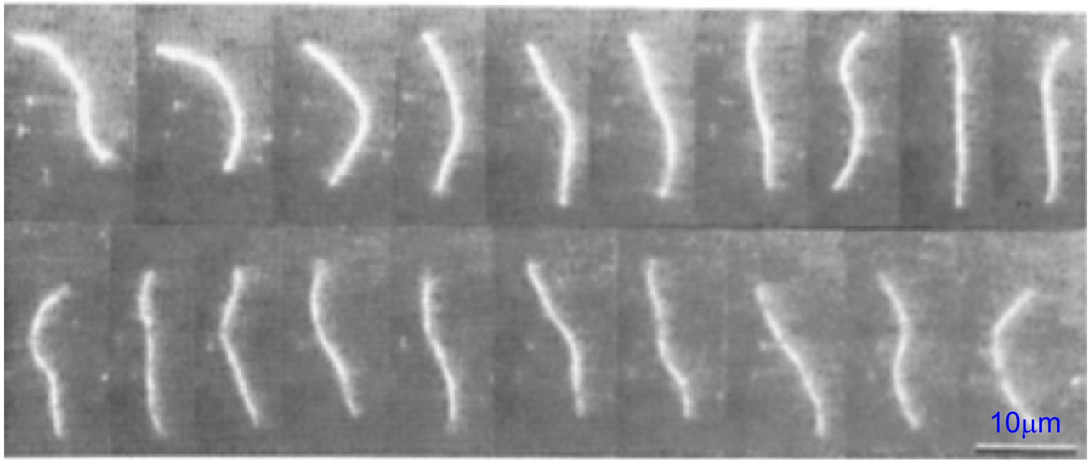


- Each conformations look like a random walk
- Thermal forces can bend the polymer
- Under what conditions thermal forces can bend filaments?
- Under what conditions we can treat polymers as freely jointed chain?

Thermal bending of bio-polymers



Microtubule



Actin Filaments

Figure Source: Gittes F, Mickey B, Nettleton J, Howard J, *J Cell Biol* ***120**, 923–934 (1993).*

Thermal bending of bio-polymers

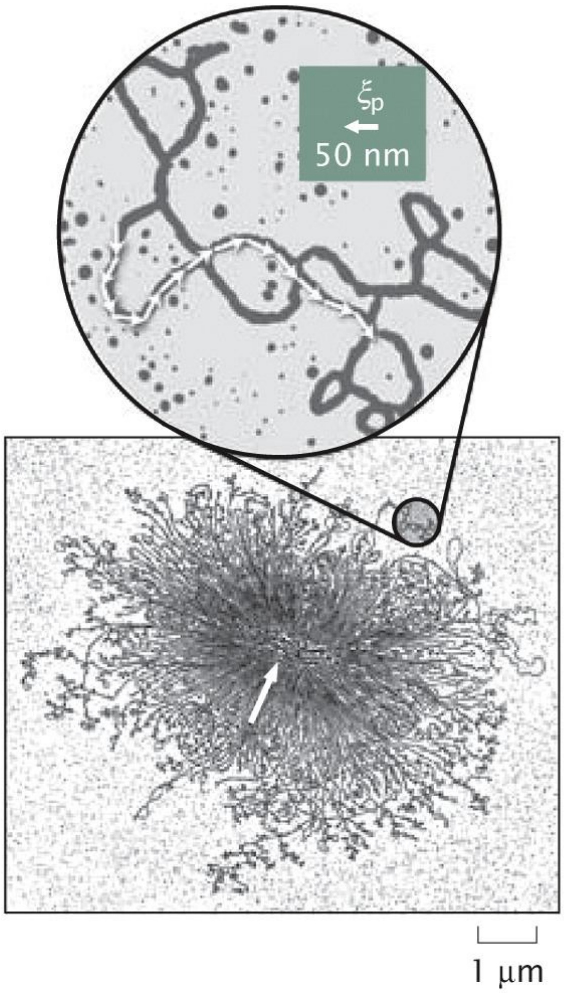


Figure 8.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Bacterial DNA

Random Walk!

Thermal bending of bio-polymers: DNA looping

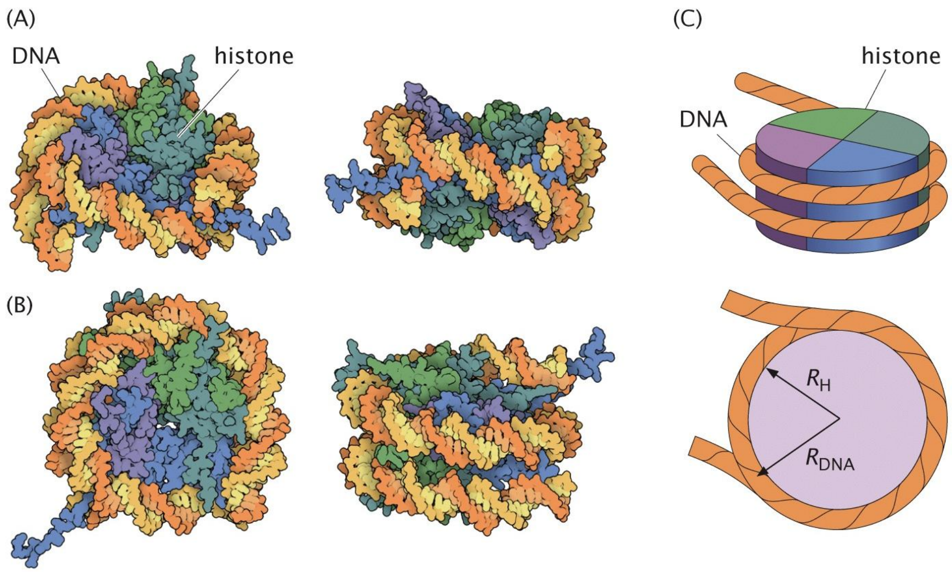


Figure 10.21 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

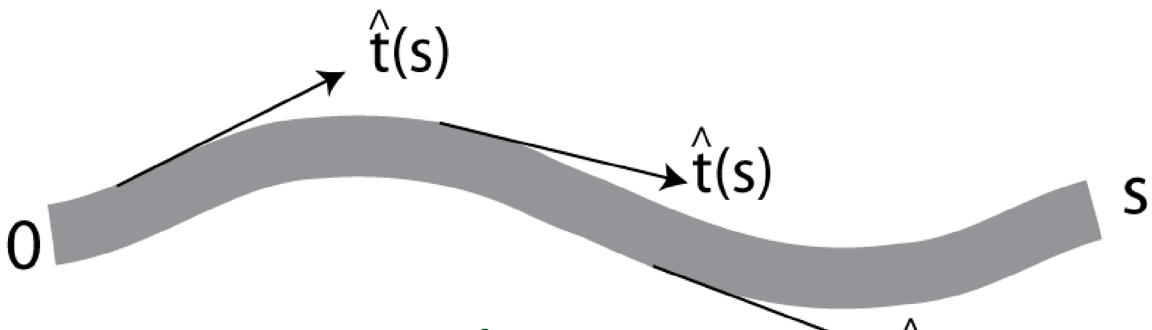
DNA is like a elastic rod. It is not easy to bend a elastic rod

Requires energy !!!

1. What is the energy required to bend DNA in loops?

2. Is the required energy comparable to thermal energy?

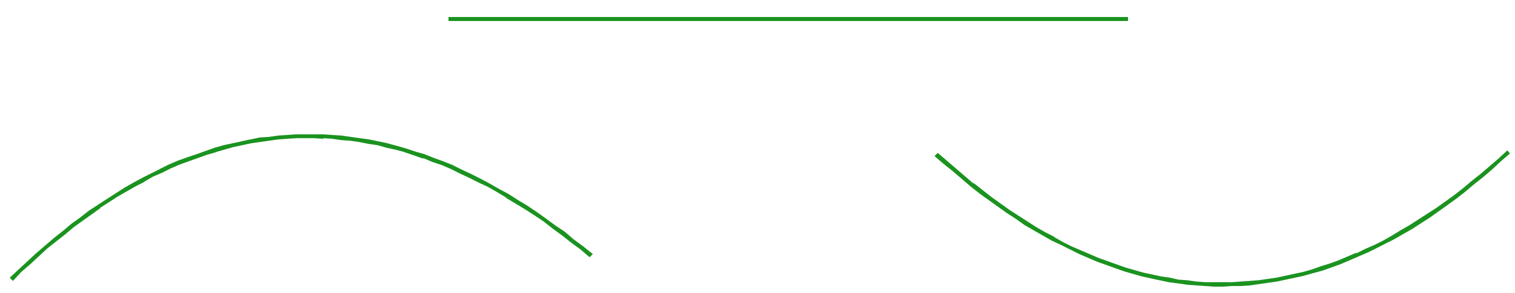
Worm Like Chain model for polymers



Unit tangent vector $\hat{t}(s)$ will be different at different points along the chain

$\frac{\partial \hat{t}}{\partial s}$ **quantifies change in $\hat{t}(s)$**

Slope and Curvature

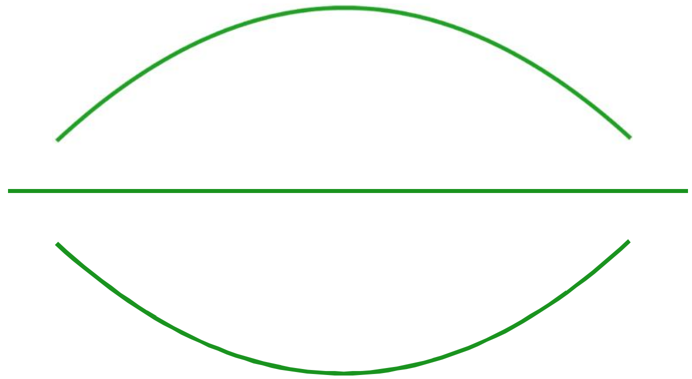


- Slope: First derivative-measures amount of bend at every point

- Curvature: Second derivative- measures the change in the slope

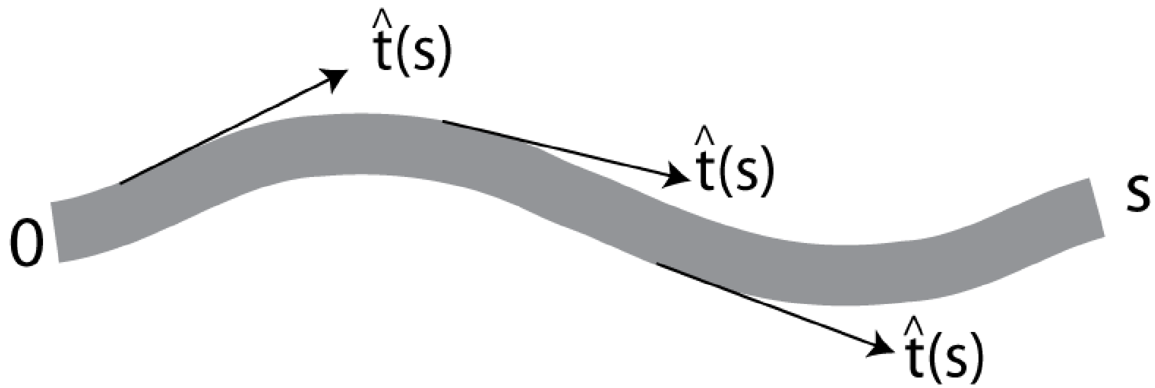
- Curvature is different for a convex or concave curve

Slope and Curvature



- Energy to bend a filament to a concave shape is equal to the energy to bend it to a convex shape
- Energy required is proportional to magnitude of curvature

Worm Like Chain model for polymers



$$\boldsymbol{E_b \propto \left|\frac{\partial \hat{t}}{\partial s}\right|^2}$$

$$\boxed{\boldsymbol{E_b = \frac{k_b}{2}\int_0^L \left|\frac{\partial \hat{t}}{\partial s}\right|^2 ds}}$$

Similar to $\mathrm{E} = \frac{1}{2}kx^2$

***k_b* = Bending stiffness**

What is unit of k_b?

Bending stiffness

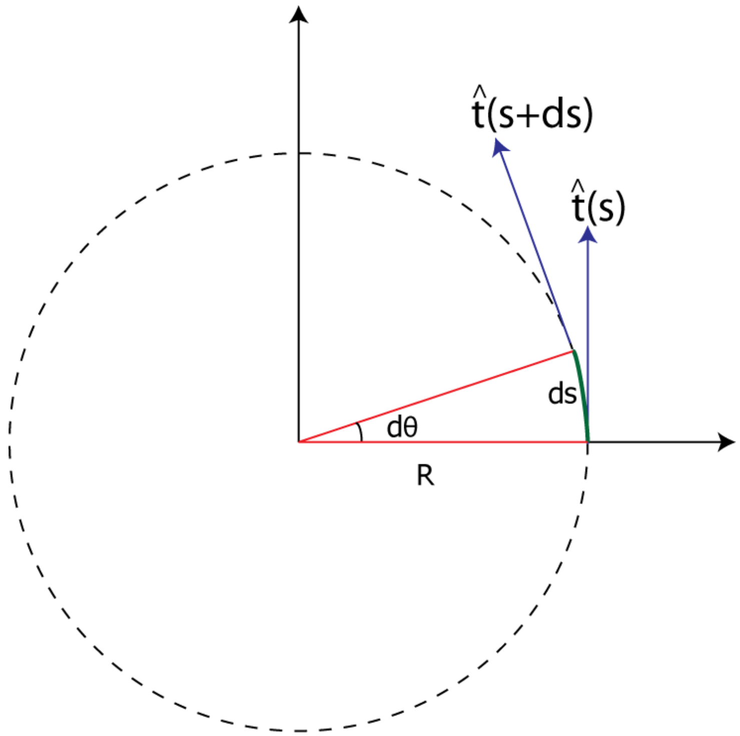
- "Bending stiffness" or "bending modulus" is a parameter that depends on the material property of the filament

- Similar to Young's modulus or spring constant

- The chemical interactions between the atoms in DNA decide the value of k_b

.

Energy required to bend DNA into an arc of a circle ?



$$\left|\frac{\partial \hat{\boldsymbol{t}}}{\partial \boldsymbol{s}}\right| = ?$$

$\boldsymbol{d\hat{t}}$ changes by **dθ** has a magnitude equal to $\frac{ds}{R}$

Energy required to bend DNA in a circle

$$\boxed{E_b = \frac{k_b}{2}\int_0^L \left|\frac{\partial \hat{t}}{\partial s}\right|^2 ds}$$

$$\left|\frac{\partial \hat{t}}{\partial s}\right| = \frac{1}{R}$$

$$E_b = \frac{\pi k_b}{R}$$

Can thermal energy bend DNA into a circle

$$E_b = \frac{\pi k_b}{R}$$

$k_b = 300$Å kcal mol^{-1} ≈ 210 x 10^{-30} Jm

$k_B T$≈ 4.1 pN nm

R ~160 nm

Thermal energy can bend DNA into circles of radius 160 nm !!!

Puzzle of DNA Packaging

- Each of us has enough DNA to reach from here to the sun and back, more than 300 times.

- How is all of that DNA packaged so tightly into chromosomes and squeezed into a tiny nucleus?

How did we arrive at this number?

- Thermal energy can't alone pack the entire DNA

Human Genome

- most cells in the body with 23 pairs of chromosomes. That makes a total of 6 billion base pairs of DNA per cell

- Because each base pair is around 0.34 nanometers long (a nanometer is one-billionth of a meter), each diploid cell therefore contains about 2 meters of DNA [$(0.34 \times 10^{-9}) \times (6 \times 10^{9})$]

- Moreover, it is estimated that the human body contains about 50 trillion cells—which works out to 100 trillion meters of DNA per human

Sun is 150 billion meters from Earth.
Circumference at Earth's equator 40000 Km

How is this possible?

DNA Packaging Puzzles

- Tight Packaging: Protection from damage and uncontrolled reading
- Processes such as transcription require frequent access to DNA
- It has to be rapid and localized
- Need pack and re-pack very often

How is this done?

How is the DNA Packaged in a chromosome?

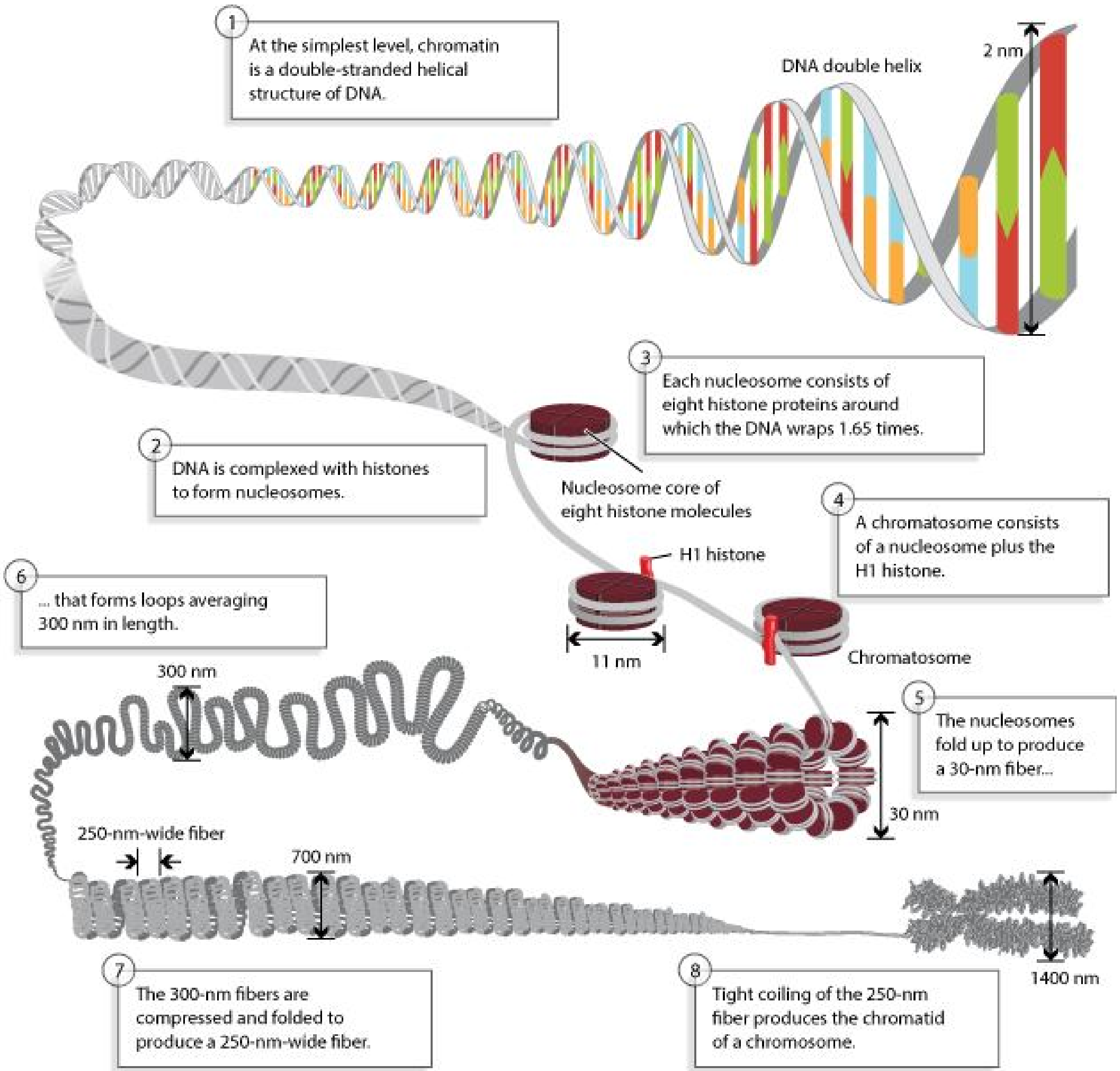


Figure Source: http://www.nature.com/scitable/topicpage/dna-packaging-nucleosomes-and-chromatin-310

How is the DNA Packaged in a chromosome?

Watch the video of DNA packaging on following link
http://www.hhmi.org/biointeractive/dna-packaging

Result: Each DNA is packaged into chromosome which is 10000 fold smaller than its extended length

- We know a few things. However, we know very little!
- How this packaging is being achieved within a short time with remarkable accuracy?
- What are the physical laws and rules governing this packaging?

Summary

- Worm Like Chain (WLC) for a polymer
- Energy required to bend a filament
- Thermal energy can bend DNA into circles
- However, thermal energy can not alone pack DNA into nucleus
- DNA is tightly packed into chromosome, around 10000 fold reduction