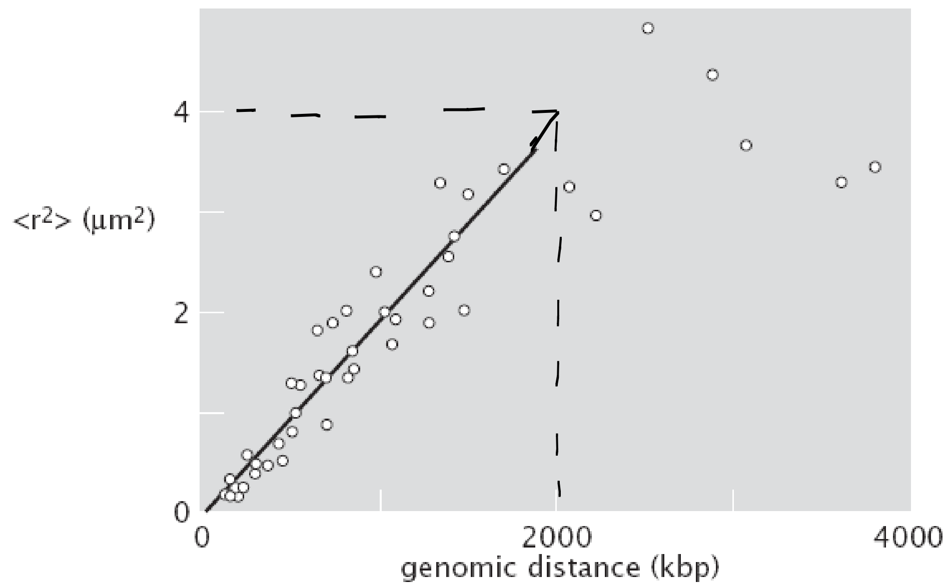
Note Title 7/4/2007

Lecture 3: Rods, ropes and chromosomes

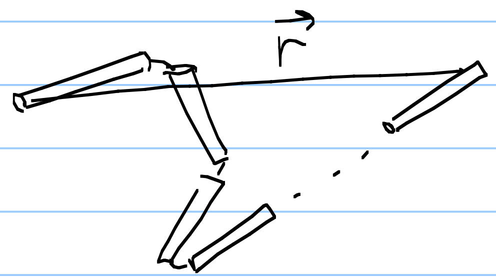
a. Chromosomes as random-walk polymers

Distance measurements on human chromosome 4



van den Engh et al.
Science '92

What do we learn about the structure/organization of the chromosome?



$$\langle \vec{r}^{\,2} \rangle = N b^2$$

$$= N_{genome}/\nu \; b$$

$$= N_{genome} \boxed{b/\nu}$$

$\gamma = b/\nu$ (gyration coefficient) Need better name!

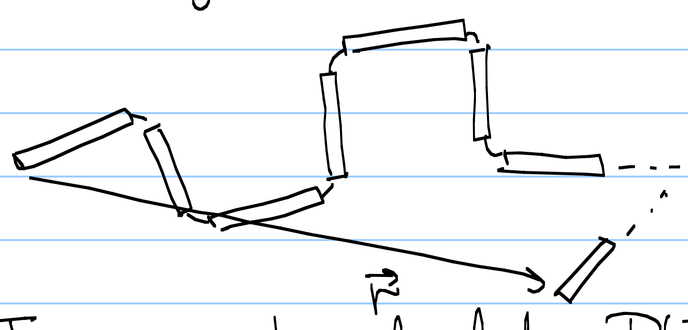
$$\gamma \approx \frac{4\ \mu m^2}{2000\ kbp} = 2 \times 10^{-3}\ \mu m^2/kb$$

Compilation of chromosome parameters:

Fiber Structure	Source	Compaction $1/\nu$ (kb/ μm)	Persistence Length ξ (10^{-3} μm)	Gyration Coefficient γ (10^{-3} μm^2/kb)
dsDNA[a]	*in vitro* [11]	2.96	40–47	27.2–32
dsDNA[a]	*in vitro* [12]	2.86	53	37
dsDNA[a]	*in vitro* [14]	2.90 – 2.96	15–86	10–60
dsDNA	this paper	2.94	50	**34**
10 nm [h]	this paper	8.0	30	**7.4**
chromatin[a]	*in vitro* [15]	2.9[f]	30	20.4
chromatin	*in vivo* [69]	NA	NA	~ 4[e]
chromatin	*theory* [65]	120	220	3.6
30 nm[b]	*in vivo* [44]	145	197	2.72
30 nm[c]	*in vivo* [21]	90[d]	28	0.62
30 nm	*theory*[66]	108–137	196–272	1.4–2.5
30 nm	compilation[63]	90–116[g]	137–440	2.4–9.8
30 nm	this paper	91	126	**2.8**

Need precision experiments in vivo!

b. Distributions contain more information than averages!



$$P(\vec{r}) = \left(\frac{3}{2\pi N g \gamma}\right)^{3/2} e^{-\frac{3r^2}{2Ng\gamma}}$$

Two ways to calculate $P(\vec{r})$:

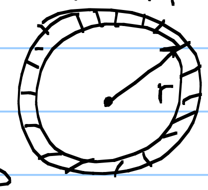
i. $\langle\vec{r}\rangle = 0$, $\langle\vec{r}^{\,2}\rangle = Nb^2$, and $P(\vec{r})$ = gaussian

ii. $\frac{\partial P}{\partial N} = \frac{b^2}{6}\frac{\partial^2 P}{\partial \vec{r}^{\,2}}$ and $P(\vec{r}, N=0) = \delta(\vec{r})$

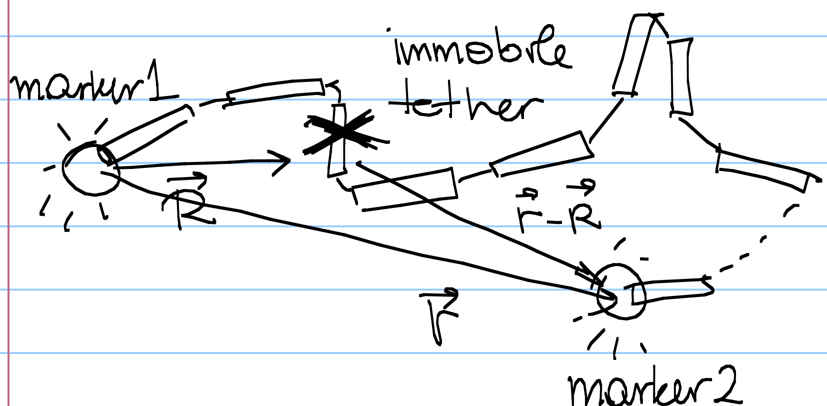
One rarely, if ever has access to 3D positional information and instead one measures $|\vec{r}|$ and its distribution.

$$P(|\vec{r}|) = \left(\frac{3}{2\pi N_g \gamma}\right)^{3/2} \underbrace{4\pi r^2}_{\text{volume element in spherical coordinates}} e^{-\frac{3r^2}{2N_g\gamma}}$$

$dV = 4\pi r^2 dr$



c. Chromosome tethering

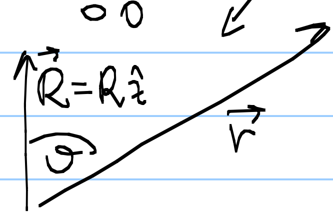


$$P(\vec{r}) = \mathcal{N}\, e^{-\frac{3(\vec{r}-\vec{R})^2}{2N_g'\gamma}}$$

$\mathcal{N}$: normalization

N_g': # of base pairs from tether to 2nd marker

$$P(|\vec{r}|)\, dr = \mathcal{N} r^2 dr \int_0^{\pi}\int_0^{2\pi} \sin\theta\, d\theta\, d\varphi\; e^{-\frac{3(\vec{r}-\vec{R})^2}{2N_g'\gamma}}$$

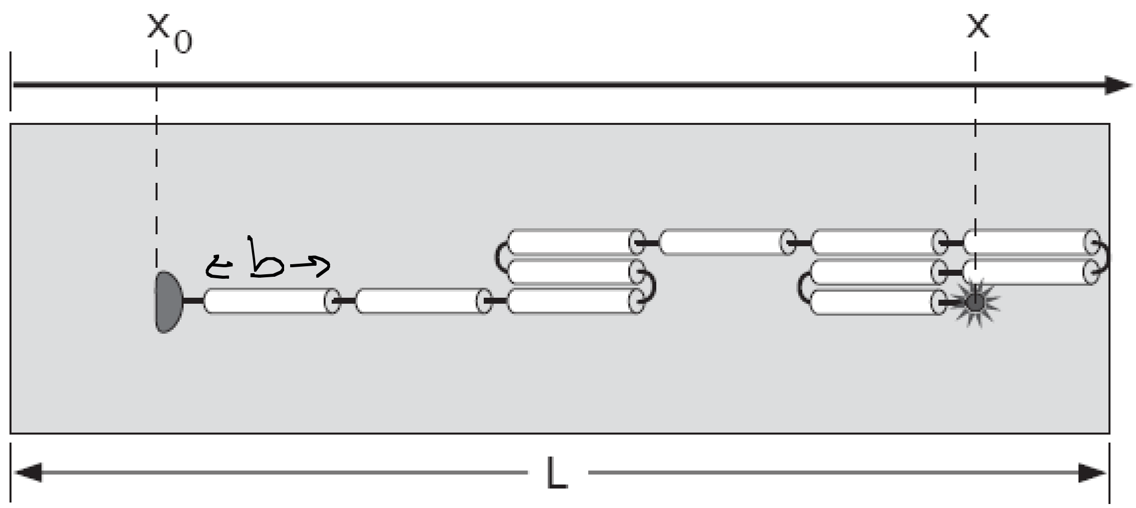


$$(\vec{r}-\vec{R})^2 = r^2 + R^2 - 2rR\cos\theta$$

$$P(|\vec{r}|) = 2\pi\left(\frac{3}{2\pi N_g\gamma}\right)^{1/2} \frac{r}{R}\left[e^{-\frac{3(r-R)^2}{2N_g\gamma}} - e^{-\frac{3(r+R)^2}{2N_g\gamma}}\right]$$

d. Chromosome tethering and confinement

1d random-walk polymer model in a box



(*) $$\frac{\partial G(x,N)}{\partial N} = \frac{b^2}{2}\frac{\partial^2 G}{\partial x^2} \quad \text{where } P(x,N) = \frac{G(x,N)}{\int_0^L G(x,N)\,dx}$$

Initial condition: $G(x, N=0) = \delta(x-x_0)$

Boundary conditions: $G(0,N) = G(L,N) = 0$!

(Why absorbing and not reflecting? Subtle...)

Solve using Fourier series

$$G(x,N) = \sum_{n=1}^{\infty} A_n(N) \sin\frac{n\pi x}{L} \quad \Rightarrow \text{sub into } (*)$$

$$\frac{\partial A_n(N)}{\partial N} = -\frac{b^2}{2}\left(\frac{n\pi}{L}\right)^2 A_n(N)$$

$$\Rightarrow \quad A_n(N) = A_n(0)\, e^{-\frac{b^2}{2}\left(\frac{n\pi}{L}\right)^2 N}$$

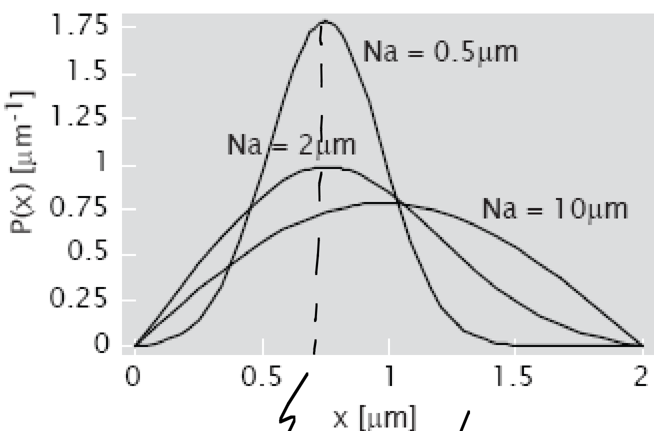
↳ from initial condition

$$A_n(0) = \frac{2}{L} \sin \frac{n\pi}{L} x_0$$

($b \to a$: change of notation !)

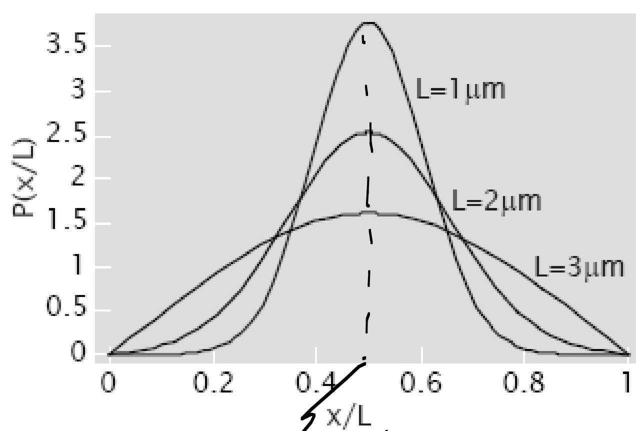
$$\Rightarrow \quad P(x;N) = \frac{1}{L} \, \frac{\sum_{n=1}^{\infty} \sin\left(\frac{n\pi}{L} x_0\right) \sin\left(\frac{n\pi}{L} x\right) \exp\left(-\left(\frac{n\pi}{L}\right)^2 \frac{a^2}{2} N\right)}{\sum_{n=1}^{\infty} \sin\left(\frac{n\pi}{L} x_0\right) \frac{1}{n\pi}(1-\cos(n\pi)) \exp\left(-\left(\frac{n\pi}{L}\right)^2 \frac{a^2}{2} N\right)}$$

Plots of $P(x,N)$ assuming Kuhn length of $a = 100$ nm :



$X_0 = 0.75 \mu m$

$L = 2 \mu m$



$X_0/L = 1/2$

$Na = 1 \mu m$