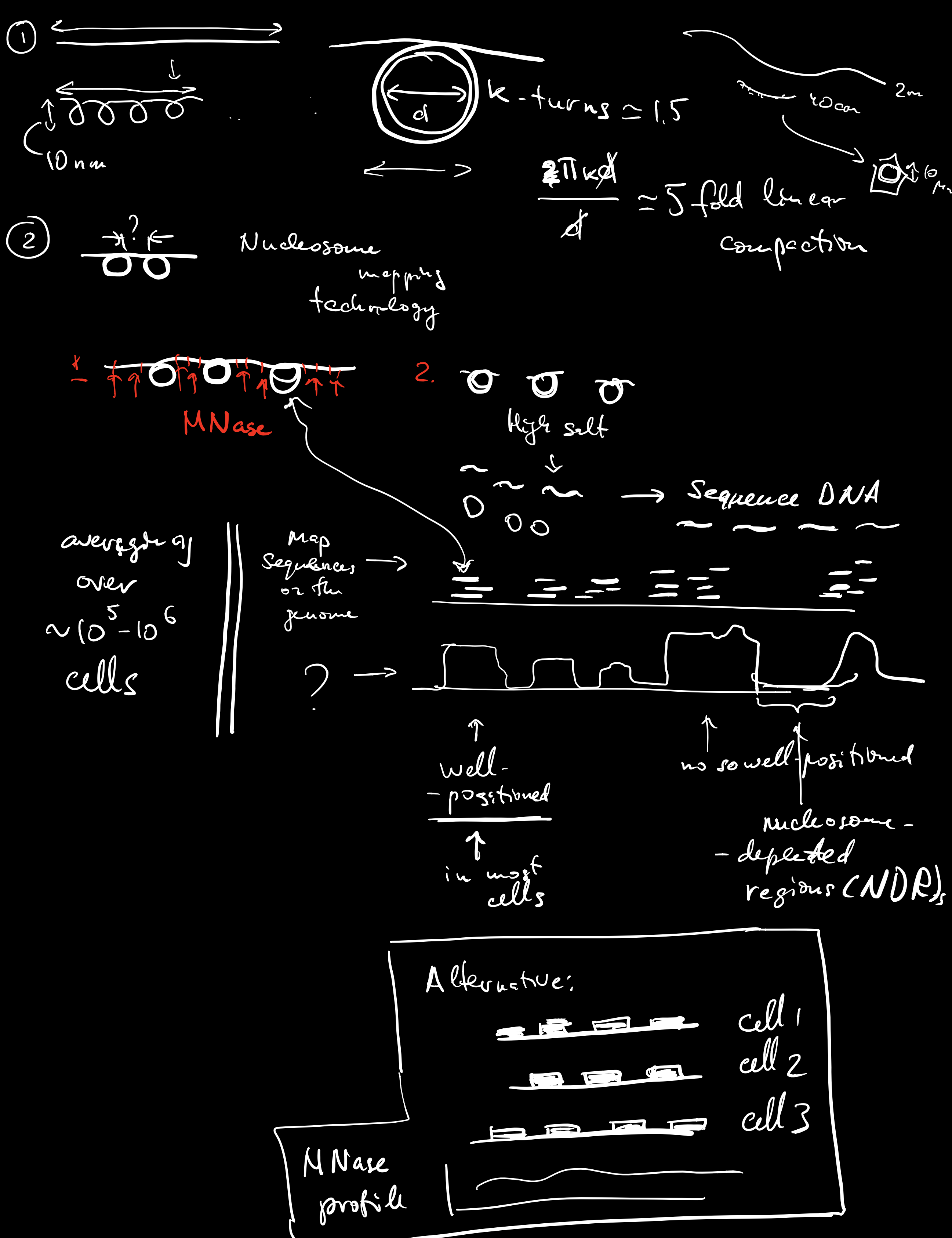


1
10 nm
k-turns ≃ 1.5
2m
10cm
10 μm
2πkd / d ≃ 5 fold linear compaction
2
Nucleosome mapping technology
1. MNase
2. High salt
Sequence DNA
averaging over ~10^5-10^6 cells
Map sequences on the genome
?
well-positioned
in most cells
no so well-positioned
nucleosome-depleted regions (NDR)s
Alternative:
cell 1
cell 2
cell 3
MNase profile

* Some nucleosomes are well-positioned

Why -? ① Sequence! [tightly packed DNA]

② Depletion by other proteins (processes)

① Sequence

1980s Nucleosome-positioning sequences

— AT — AA — AT —

5bp turn of the helix

10 bp

→ Mechanical properties to make them more for nucleosome binding

①

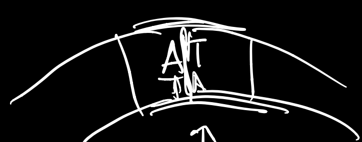
more flexible

needs to be bent

Strong AA/AT periodicity in nucleosome-bound sequences

②

"pre-bent" DNA



↑ more flexible

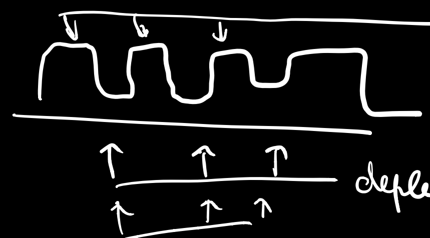
→ NDR (depleted regions)

- stiff: AAAAAA...

TTTTTT...

Experimental tests: (Jon Widom)

- design and test in vitro
- in vivo: MNase profile

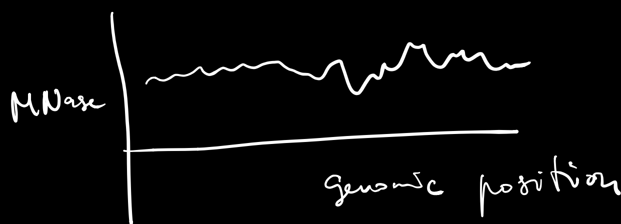


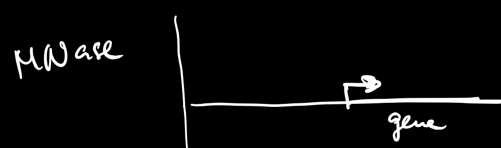
enriched —AT—AA— (10 or 5bp)

depleted —AAAAAAA— —CCCCCCC— circularization assay

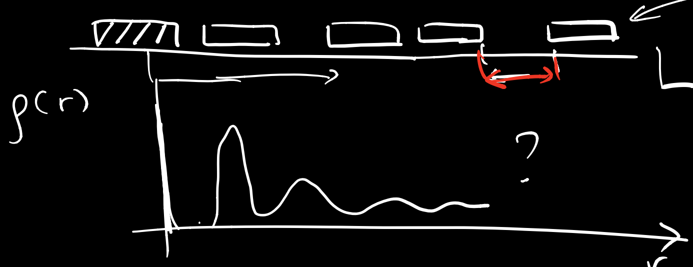
any not periodic seq...

Observed





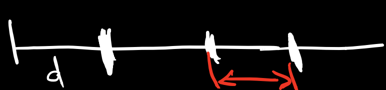
* Statistical positioning of nucleosomes (Tonks gas)



N nucleosomes each of length b

$$d = \frac{L - Nb}{N} \leftarrow \text{aver. spacing}$$

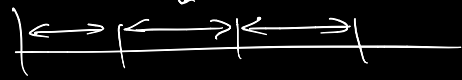
*



$L \rightarrow L - Nb$

$$p(r) = e^{-r/d} \frac{1}{d}$$

P_k ← exp distribution with average d

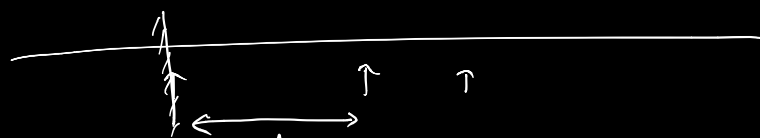


sum of k exp random variables ← Gamma distribution

$k>0$ Erlang distribution

$$\Rightarrow P_k = \frac{r^{k-1}}{d^k (k-1)!} e^{-r/d}$$

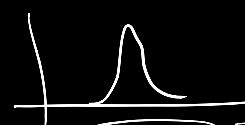
$r \to r - bk$



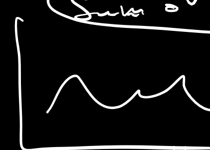
$\rho = \frac{N}{L}$

$$\rho_k(r) = P_k(r-bk)\,\Theta(r-bk)\,\rho \;\leftarrow$$

(k)



Sum over k

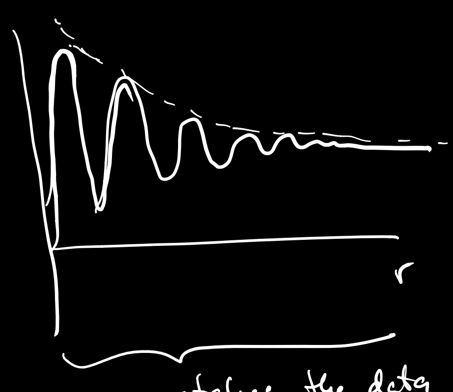


$$\rho(r) = \delta(r) + \sum_{k=1}^{N} \rho_k(r) \;\leftarrow$$

$$= \delta(r) + \sum_{k=1}^{N} \frac{(r-bk)^{k-1}}{\left(\frac{1-b\rho}{\rho}\right)^k (k-1)!} e^{-\frac{r-bk}{\frac{1-b\rho}{\rho}}}$$

$$d = \frac{L-Nb}{N} = \frac{1}{\rho} - b$$

$$\frac{r}{b} = x$$



– mechanisms enzymes act ⇒ unknown

$\frac{N}{L} = \rho$, b } d

$b = 150\text{bp} \quad d \simeq 50\text{bp}$

ρ – has not been directly measured

$\rho_b = \frac{N_b}{L} \sim$ 95% in higher eukaryotes