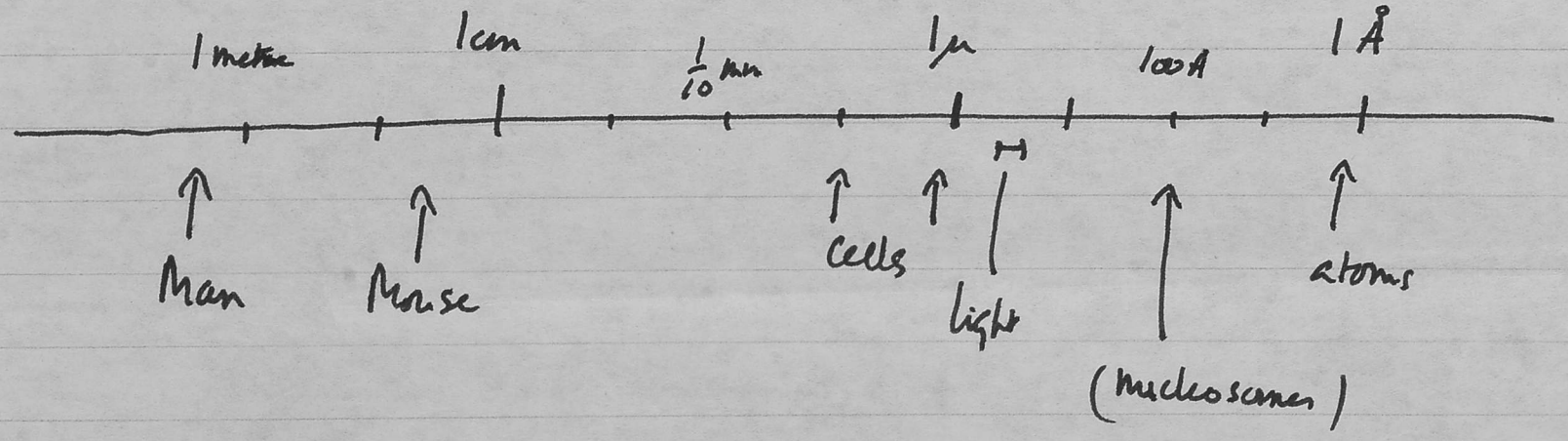
1

Salk Trustees. Thursday 20 Jan 1977

Genes in lower and higher organism

Preamble

Sizes



What are genes made of nucleic acid.?

Nucleic acid. Two great families. DNA RNA
(long thin high chain molecules)

each a backbone + side groups = Bases, 4 types.
(slightly different)
Double Helix Base-pairing

Life's instructions written in a language with only 4 letters

How big are the instructions?
ie. how many bases (= b.p) in the nucleic acid.

a very small virus SV40 ~ 5000 bp (1 page)
others E. Coli 3×10^6, for book
Drosophila 10^8 large encyclop.
haploid { Man 3×10^9 Small Library
Amphibians - large eel. 10^{11} bp.

In lower organisms eg bacteria
(yeast is a 'higher' organism : so is man)

most DNA codes for proteins
a quite different ~~chain~~
family of chemicals.
– machine tools of cell.

(20 amino acids
triplet
genetic dictionary
(≡ code))

S.V. 40 has ~~jus~~ 5–6 (??) genes
E. Coli ~~has~~ prob. has ≃ 3000 genes.

on this basis ~~man~~ Man would have 3 million genes. (10^6)

But genetic estimates only approximate give ≃ 50,000

Why this difference? (Same sort of
problem in Drosophila, ETC.)

Thus major problem is
What is all ~~that~~ this DNA for ?

(1) Some must be "junk" ie have a less specific
function (newspaper for wrapping up fish & chips)

Some Crabs have lots of ATATAT up to 40%.

We ourselves have junk DNA ie simple sequence
but only 10?% (varies in diff organisms)

(2) Some DNA of intermediate complexity

Function also unknown.
Is it for regulation?
complexity of higher organisms!
does this mean more DNA needed for control.
ie more administration ~~attention~~ ?

don't yet know.

(3) Much of this DNA is 'unique'

but not all codes for protein
ie "Spacer" DNA

Also repetitive sequences.
but not in all cases. esp. haemoglobin

Thus there is a major area of our ignorance.
Many approaches
in entire only two A G. need to sequence ~~DNA~~ a "gene"

~~B~~ Gene and test its function in the test-tube.

But minute amounts ∴ need to multiply up esp.
~~Stan~~ 'cloning' technique (genetic engineering).
put in a "virus" (plasmid) make many copies (dangers)

B packaging.

total length of DNA per cell 2×100 cm.

has to fit in a cell with a nucleus $\angle 10\,\mu$

need to package for cell division ——— S

DNA multiplication first
then chromosomes assorted
then cells divides

} picture of mitosis.

Better picture of chromosomes (mouse) ——— S

(Notice bands)

Contraction ratio (packaging ratio) $\hat{\sim} 10^4 : 1$

How is this done.

Area of Rapid Progress

Special proteins used to help this folding up.

main type called "histones".

4 main types Mw ~ 13,000 (~ 1000 atoms each + H)

go together (x2) & make a ball about 80 Å diameter

DNA wound on outside of ball

Balls now called nucleosome.
(Griffith) SV 40 ——— S

Fifth type of histone. When added, makes
balls pack together SV 40 ——— S
to form a filament.
≅ 100 Å diameter.

Balls + their DNA (~~other~~ - 140 bp)
\ Same throughout Nature
have been crystallized

with spacer repeat is ≅ 200 bp
? varies.

Approx 2 DNA turns / ball

Contraction ratio : ~ 1:7 SV 40. ——— S

Must be more levels of coiling

next level less certain: called a "Solenoid" ——— S
a filament wound round to form a tube thick walled
tube (pack 5 to 6 balls / turn)
diameter ≅ 300 Å Total contraction ratio
≅ 40

6

<u>Next level</u>

very new, somewhat speculative

(Bak + Zeuthen in Denmark)

~~the~~ again a coil, but this time a

<u>thin walled</u> tube. <u>4000</u> Å (wall 300 Å)

this can be seen in the light microscope

<u>fairly regular</u> (not double look) ——— S

e/m pictures, <u>consecutive</u>, appear to support this

<u>Water</u> →

sort of shape.

This last makes a big contraction ratio ~ ×40

∴ 40 × 40 ~ <u>1600</u>.

<u>final level</u> : prob. the tube folds (in a collapsed sort of way)

prob. to give <u>another</u> type coil

<u>hence banding</u> in early photo.

perhaps ×5. 7×6×40×5 ≃ ~~8~~ <u>8,000</u>

~~rough~~ which is figure required.

Thus may now understand packaging for

mitotic chromosomes. But these are "silent".

Really interesting ones are functioning ones. These

are at least partly uncoiled.

How is packaging done?

due to special proteins eg Histones

but prob other proteins help.

Cross-ties ??

do some of these persist in functioning state

or is packaging used to help control function

ie to keep some sets of genes silent in

tissues where they're not needed!

Don't know: but progress now likely to be

rapid. Might have general answer within 5 years.