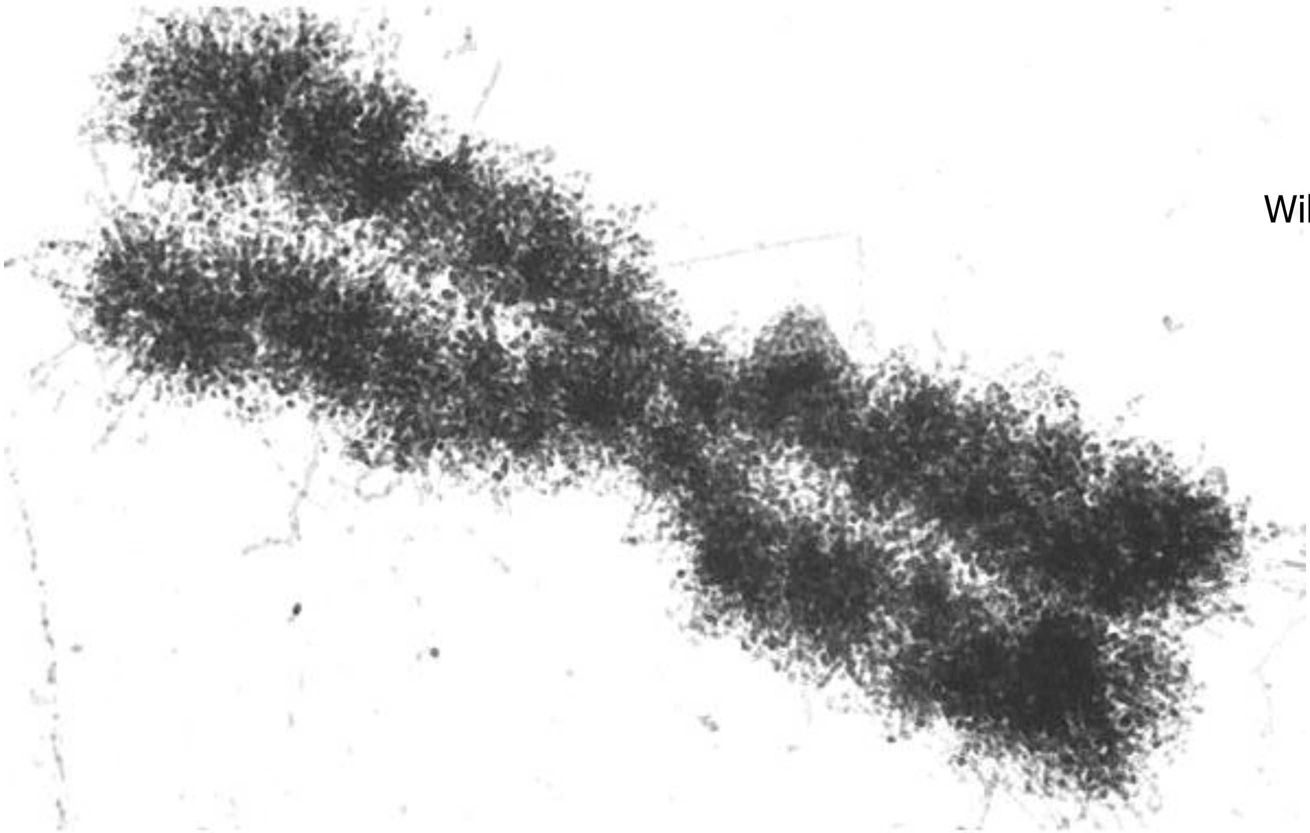
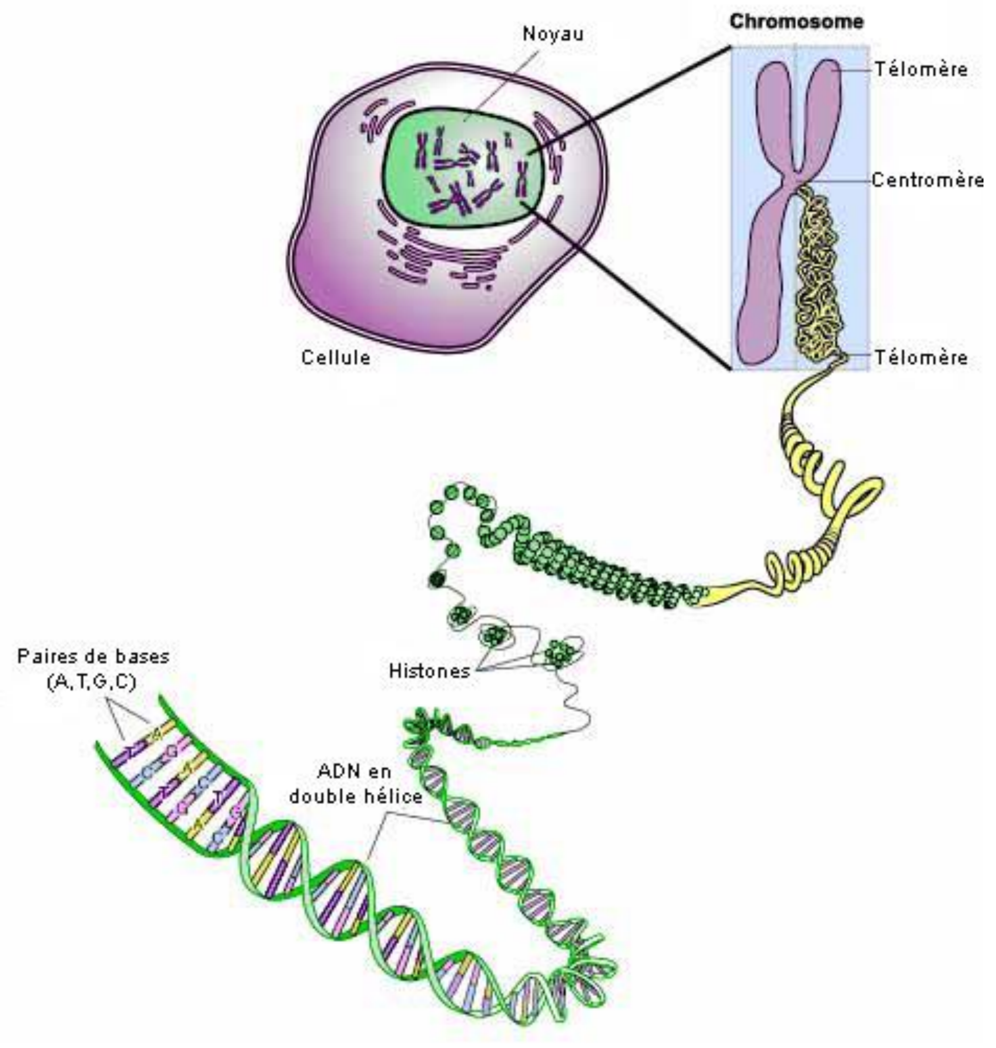
Chromosome

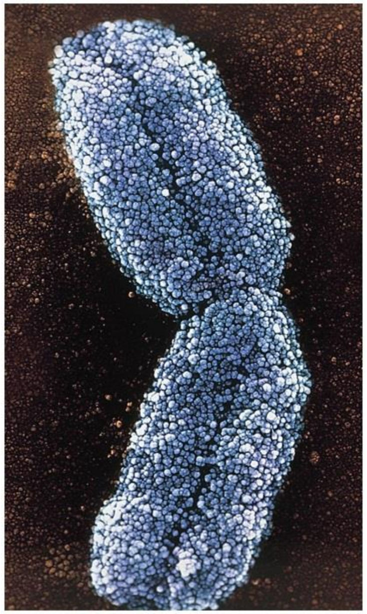


Wilhelm Gottfried Waldeyer
(1836 – 1921)

Basics of chromosome structure



Eukaryotic chromosomes

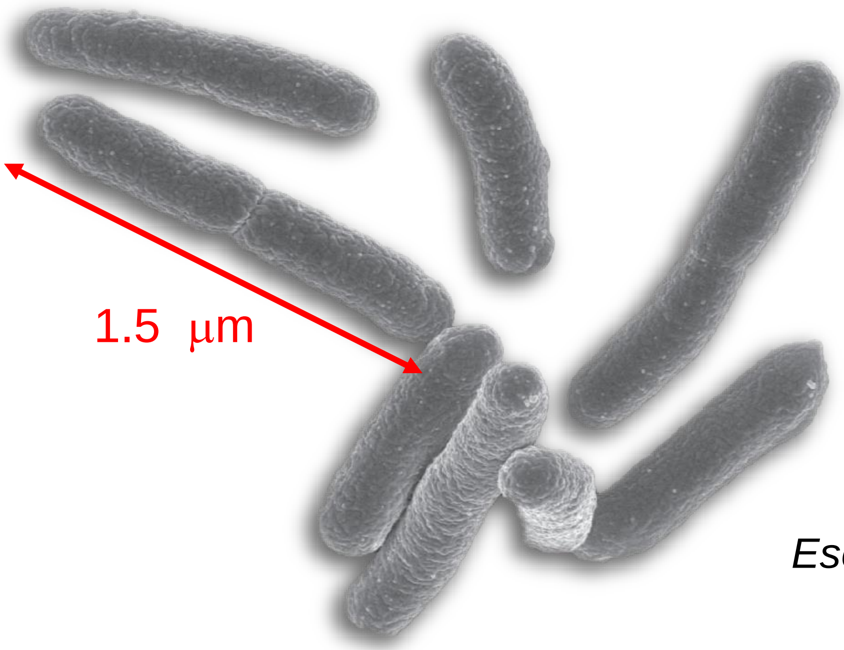


- Usually linear
- Variable in number
- DNA interacts with proteins to form chromatin
- Centromeres ensure segregation
- Telomeres cap ends
- Must be compacted to fit in nucleus

chromatin
(DNA & proteins)

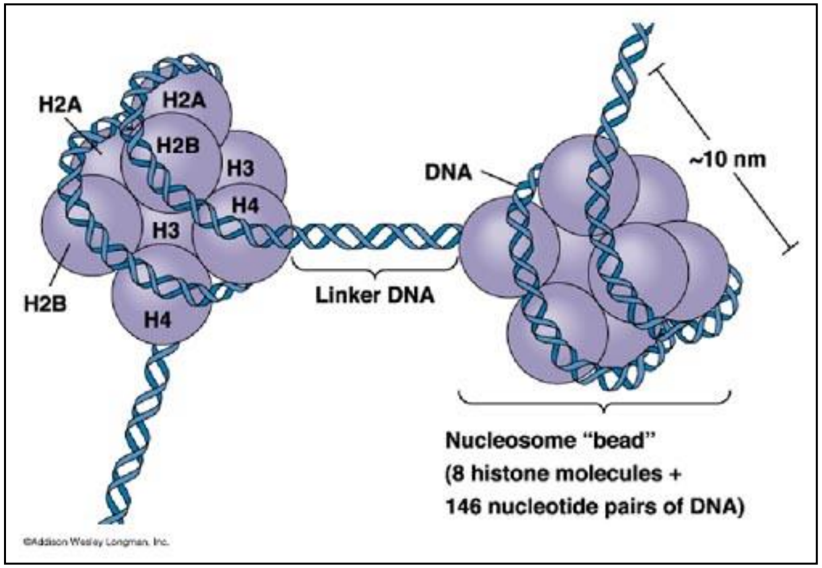
- highly coiled DNA
- histones
- non-histone chromosomal proteins (DNA & RNA polymerase, transcription factors, topoisomerases, histone modifying proteins)

Chromatin helps to fit the long DNA molecules into small cells or nuclei



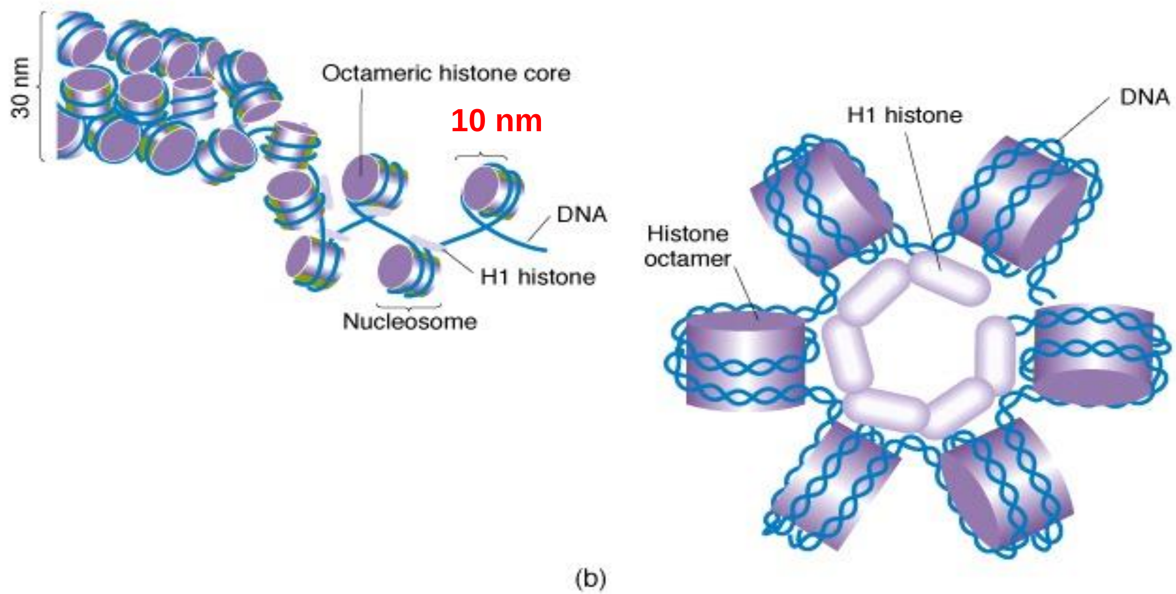
4.6×10^6 bp = 1.5 mm (a 1000-fold compression)

Histones and nucleosomes

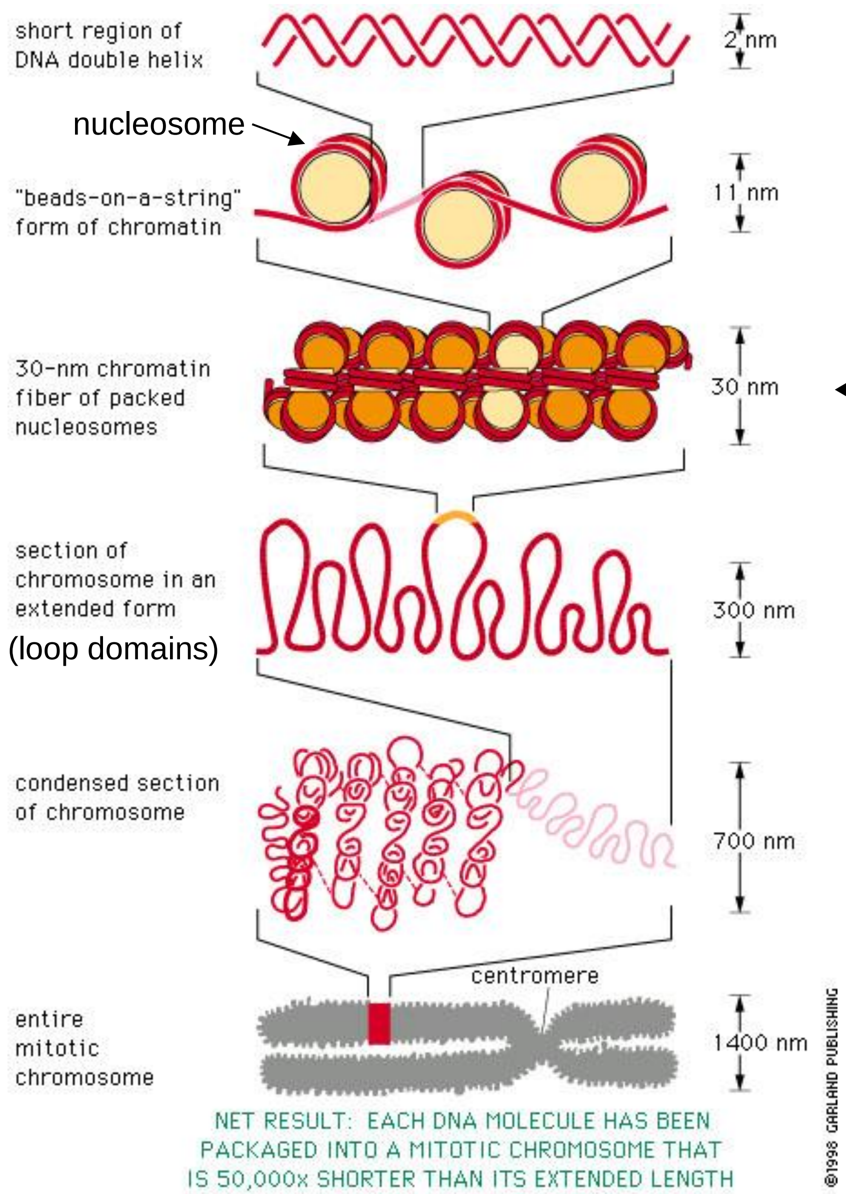


10-nm fibre

30-nm fibre

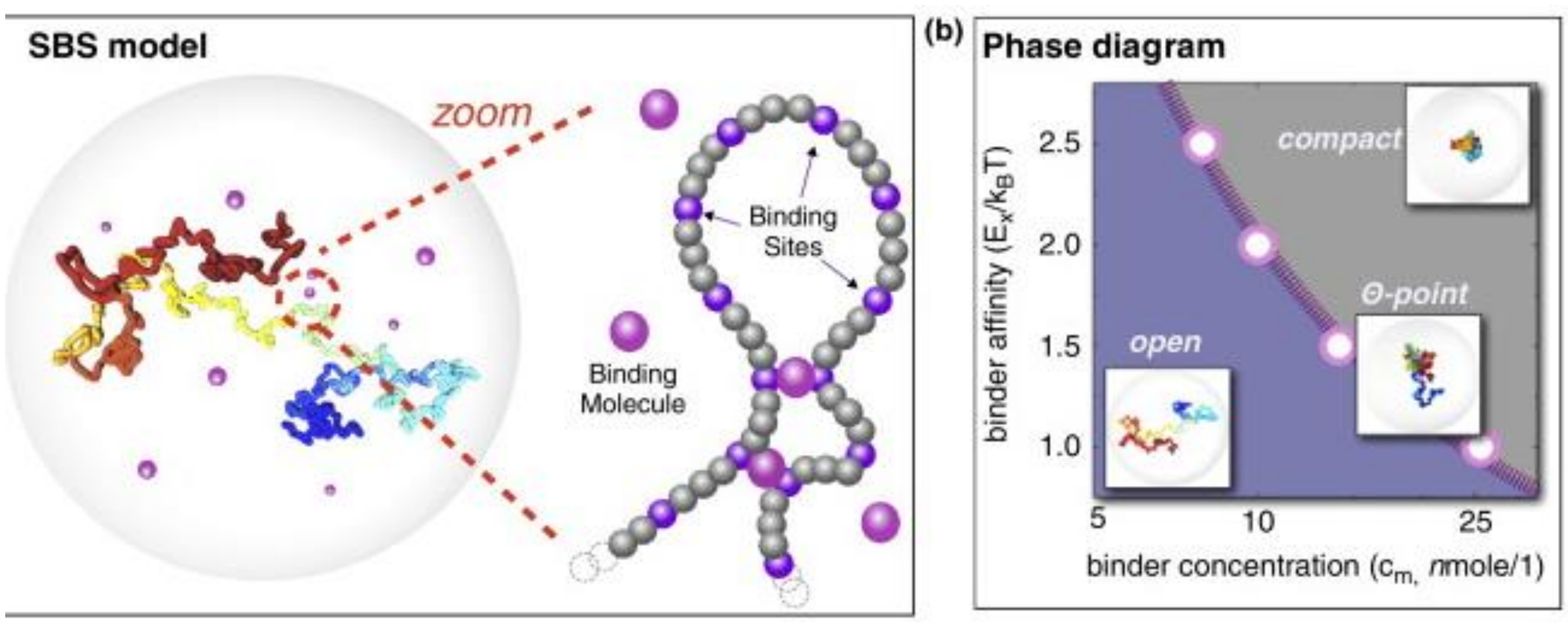


Chromosome packing



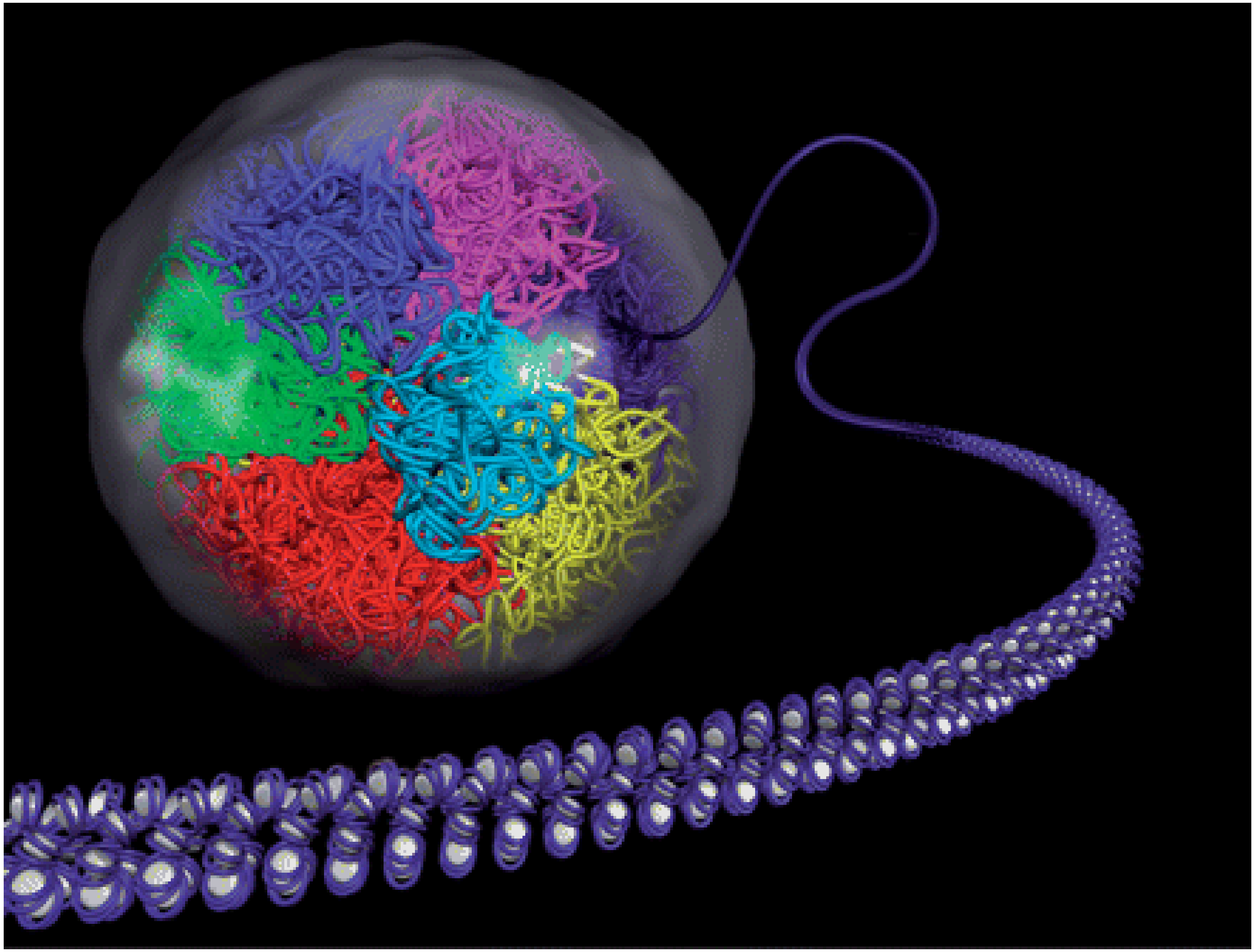
not a regular structure ?

Chromosome organisation:
Strings & Binders Switch (SBS) model



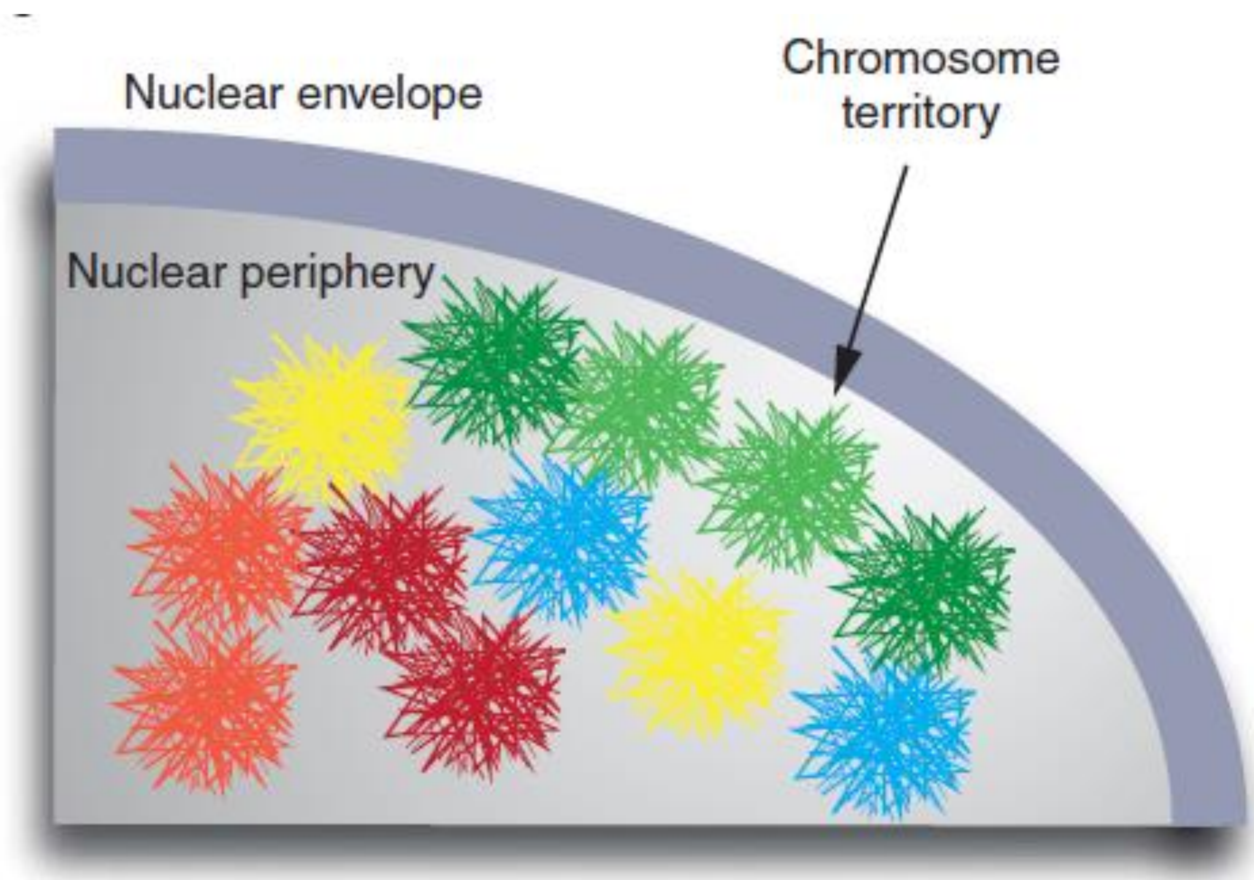
Barbieri M et al. (2012) Complexity of chromatin folding is captured by the strings and binders switch model. PNAS 109:16173-16178.

Interphase chromosomes - chromosome territories

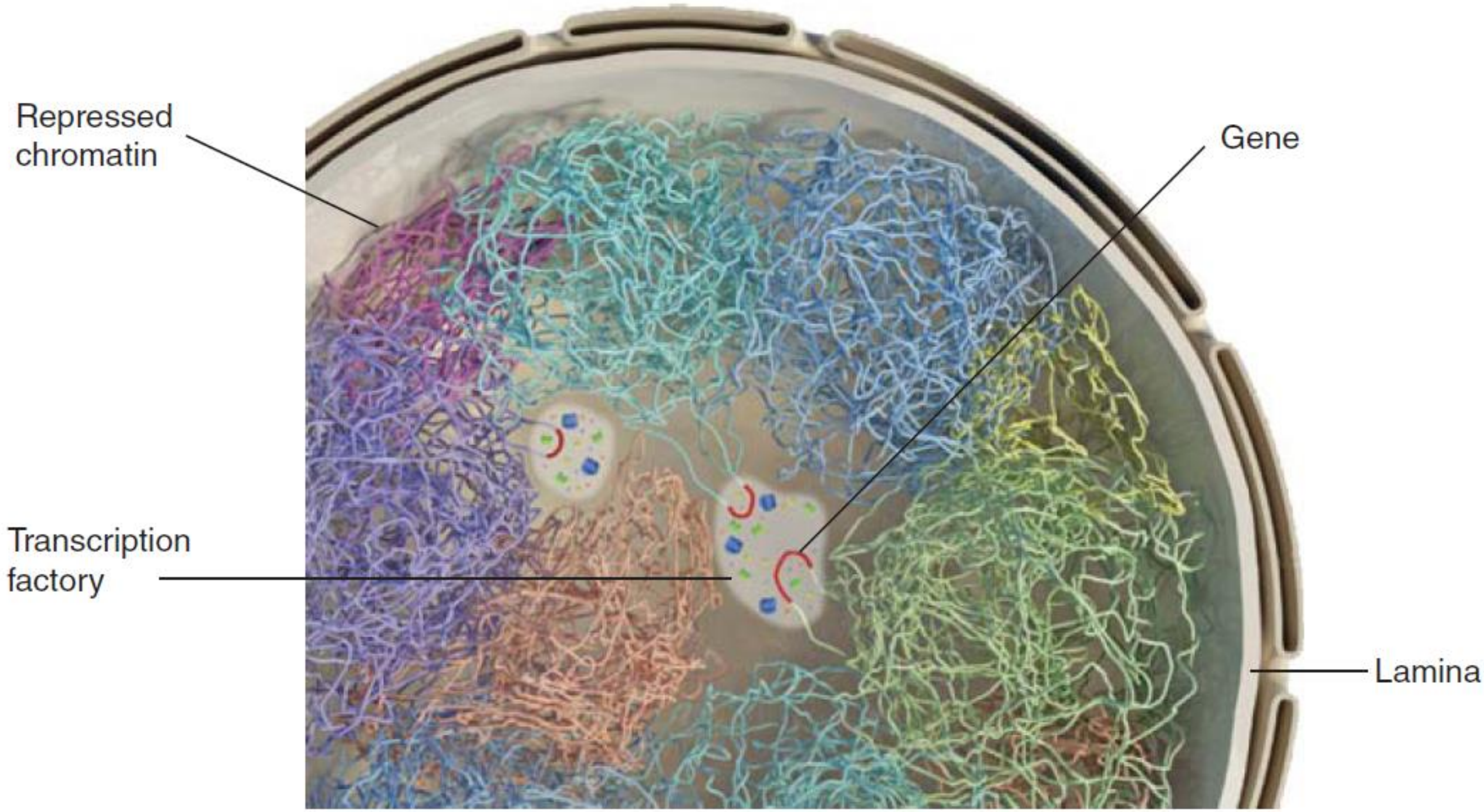


Chromosome territories

The distribution of chromosomes and genes is nonrandom with some chromosomes preferentially occupying internal positions and others occupying peripheral positions.

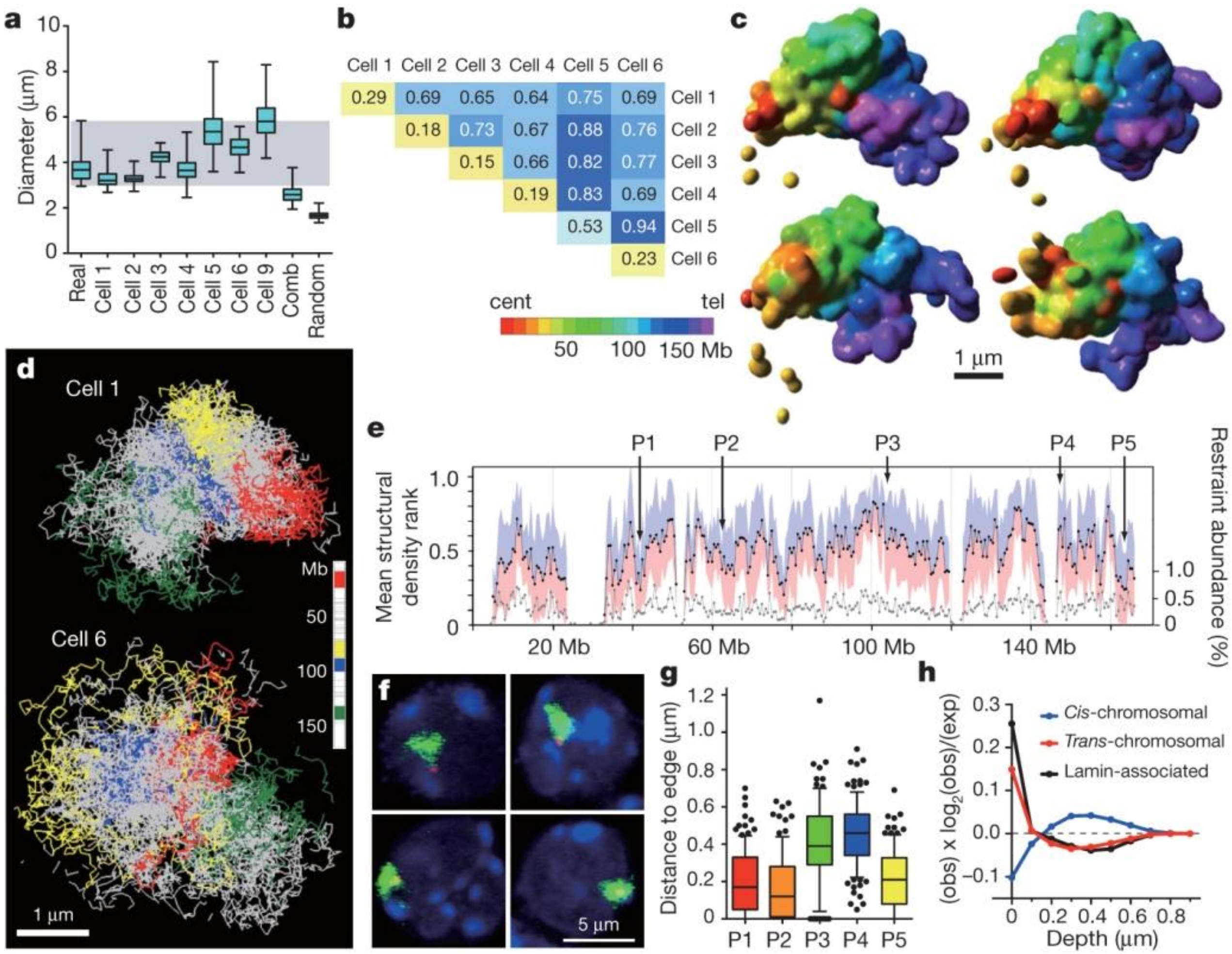


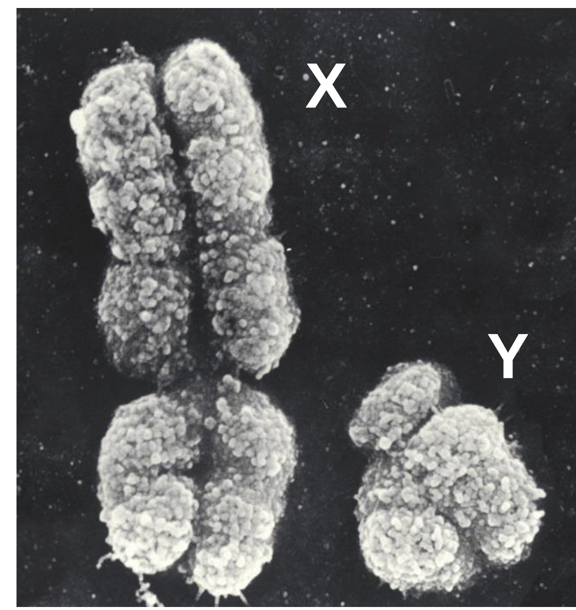
Chromosome territories



Chromosome territories

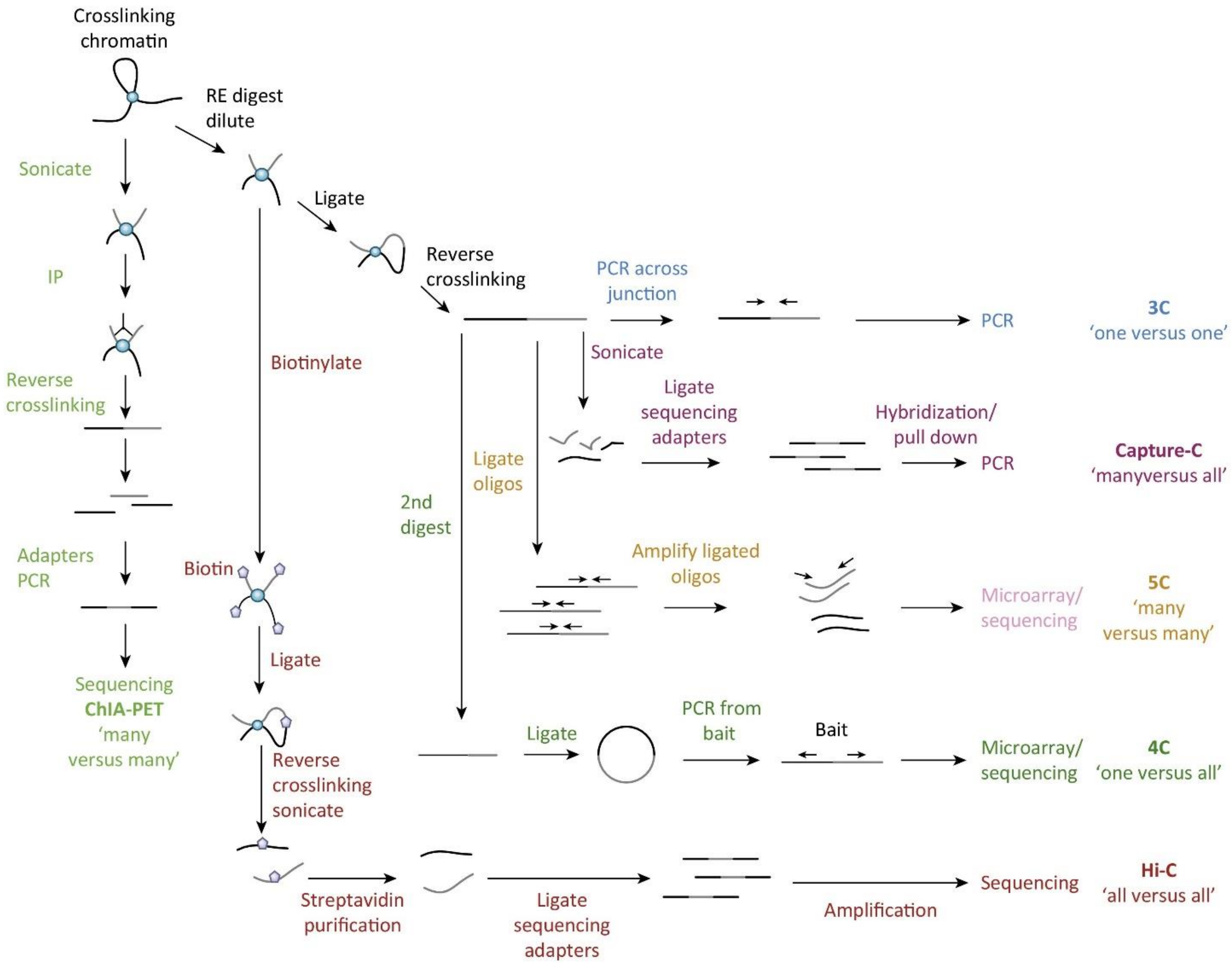
Structural modelling of X chromosomes





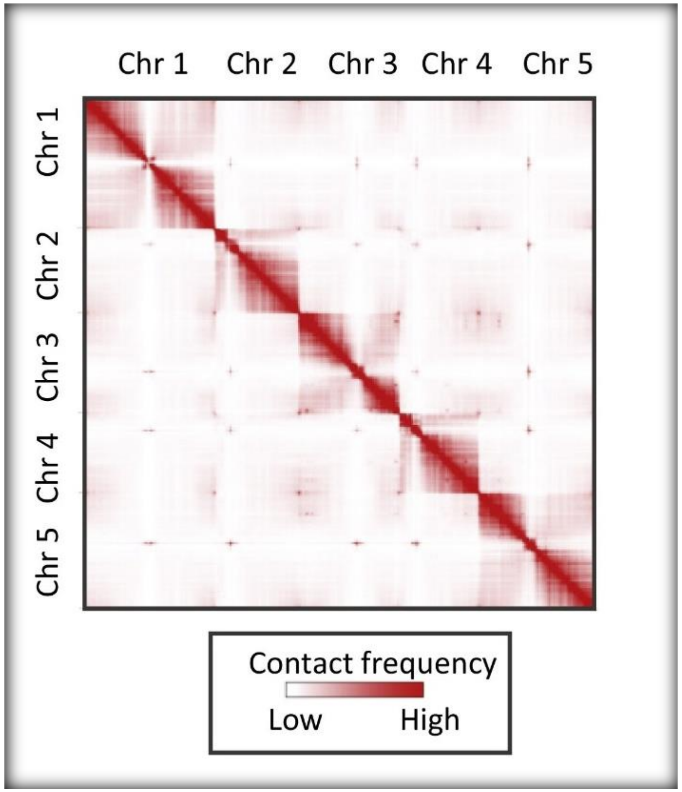
T Nagano *et al. Nature* (2013) doi:10.1038/nature12593

Chromosome Conformation Capture (3C) and 3C-Derived Methods



Trends in Plant Science

A Hi-C map of chromatin interaction frequencies



high levels of intra-chromosomal interactions

less frequent inter-chromosomal interactions

Chromosome territories

Chromosome territories - separate, yet interacting nuclear domains; important long-range chromatin interactions

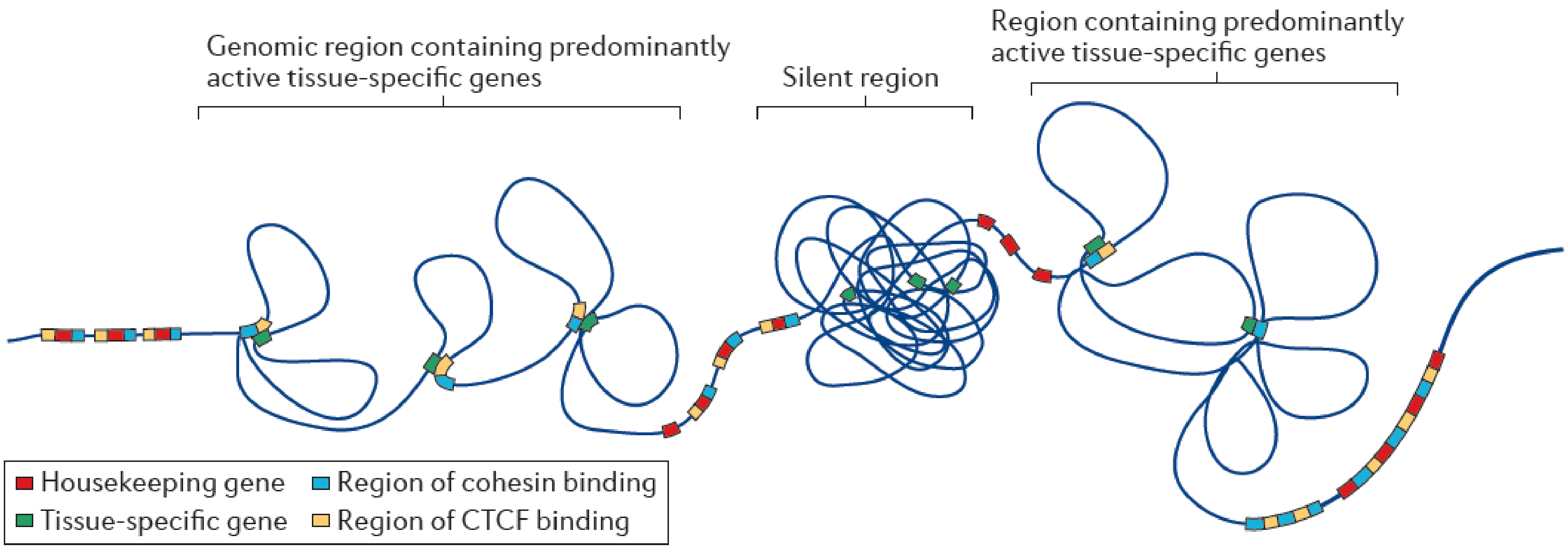
Territories partitioned in (i) megabasepair-long domains with frequent internal contacts = topological associated domains (TADs), and (ii) the lamina-associated domains (LADs) interacting with the nuclear lamina, and with other functional compartments

Specialized transcription factories = genes come together; proximity between different transcription units

Splicing factors (splicing nascent transcripts into messenger RNA) accumulated in splicing speckles - often associated with active genes

Repressed chromatin associates with heterochromatic regions

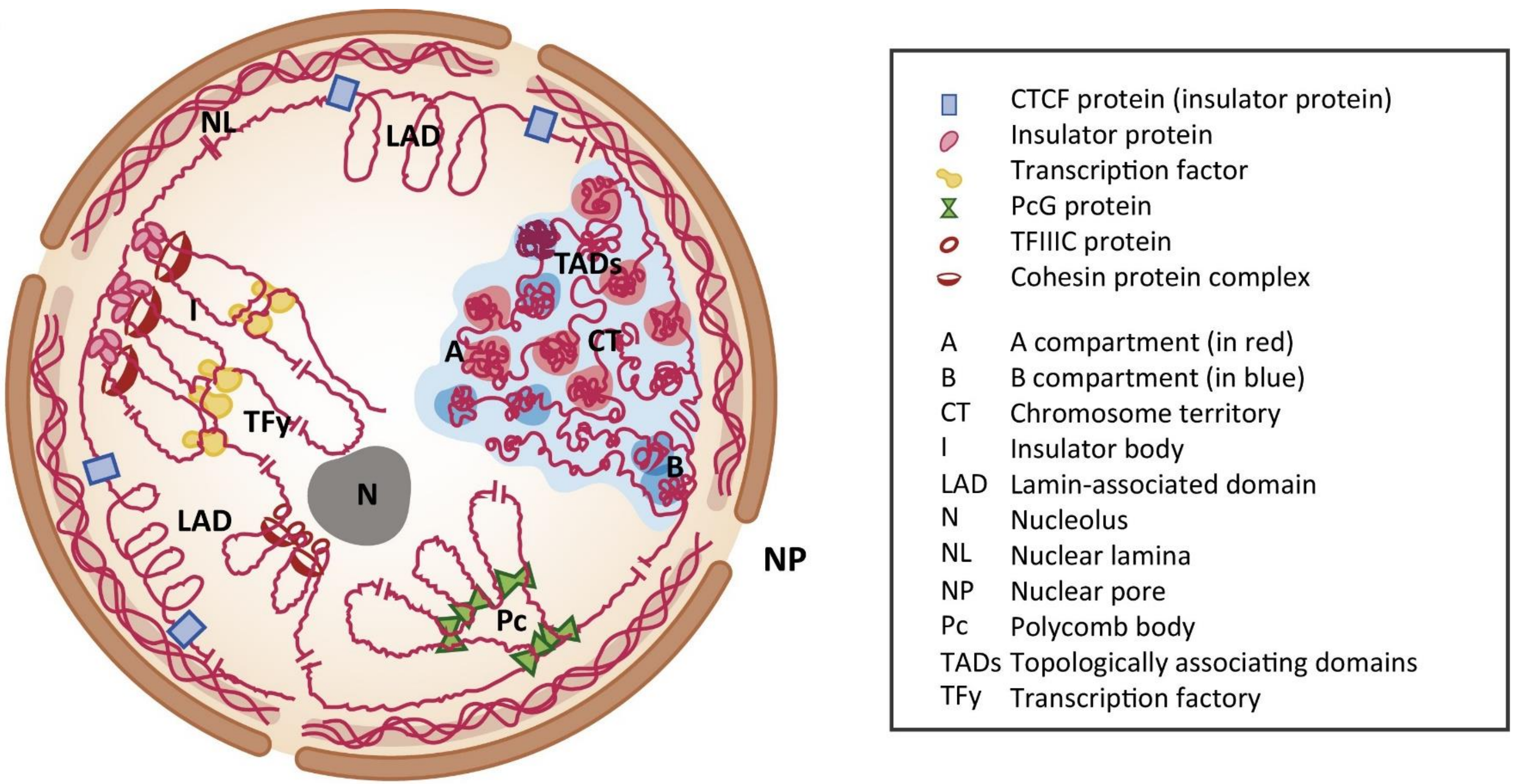
Topological associated domains (TADs)



- TADs show high levels of chromatin interaction and coincide with the presence of tissue-specific genes and their associated enhancers (the interactions of which with their cognate promoters are facilitated by the presence of cohesin and CCCTC-binding factor (CTCF))

- the border regions between TADs are enriched for housekeeping genes, which are often clustered together; show high levels of CTCF and cohesin binding, although only CTCF seems to prevent interactions between TADs.

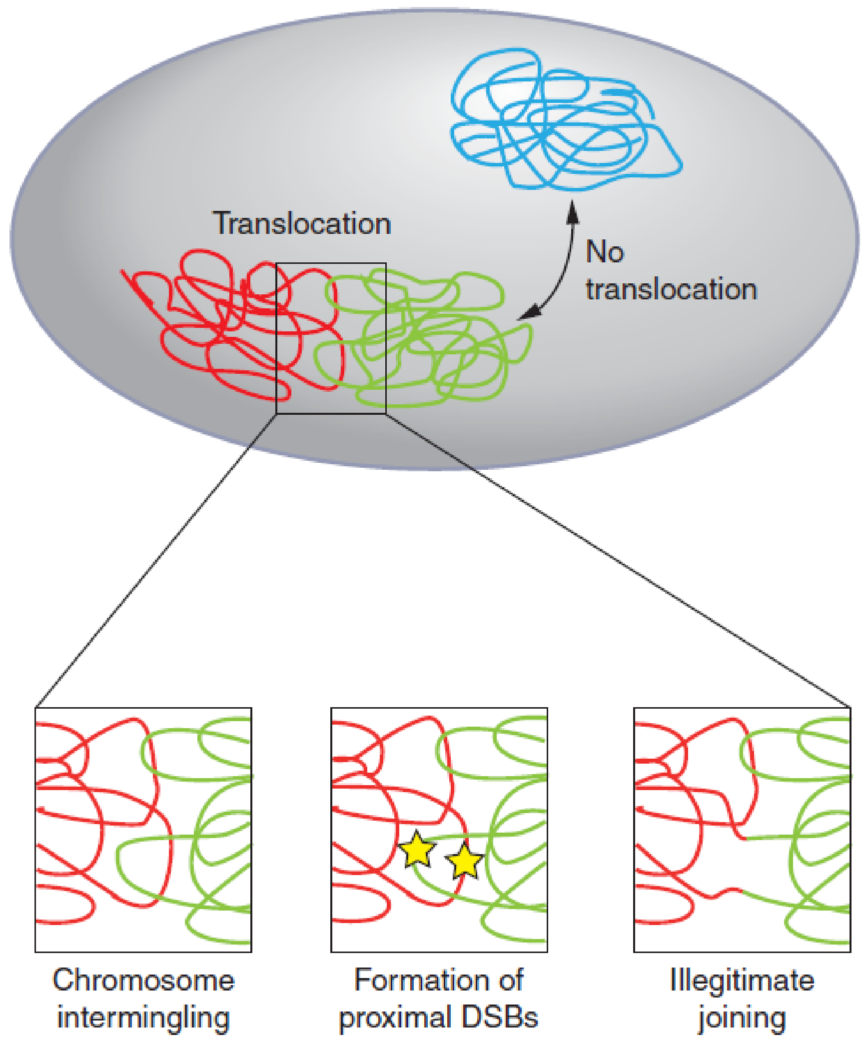
Model of nuclear organization (at different resolutions) described for animal models



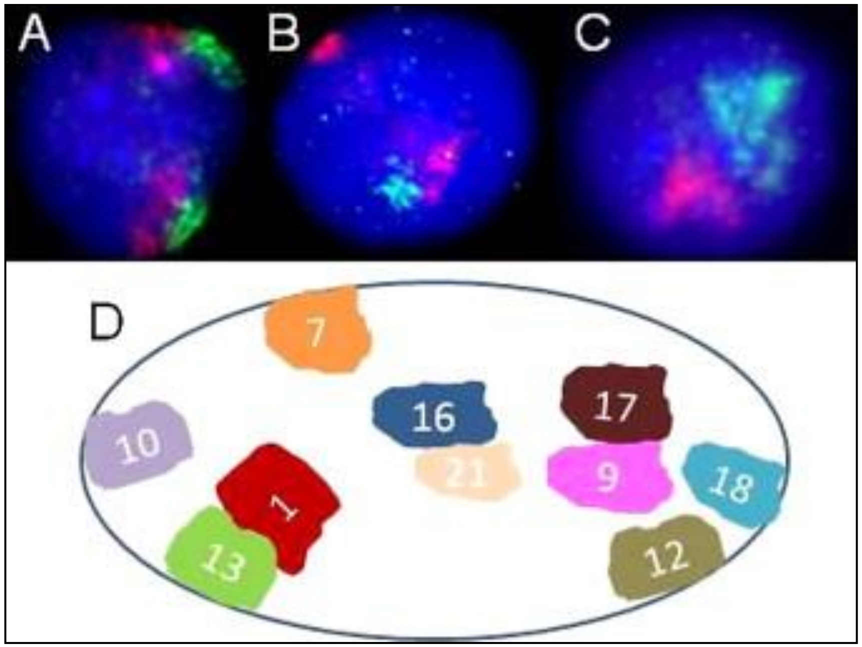
a particular locus can be surrounded by an active (A compartment) or repressive environment (B compartment)

Proximity of chromosome territories and chromosome translocations

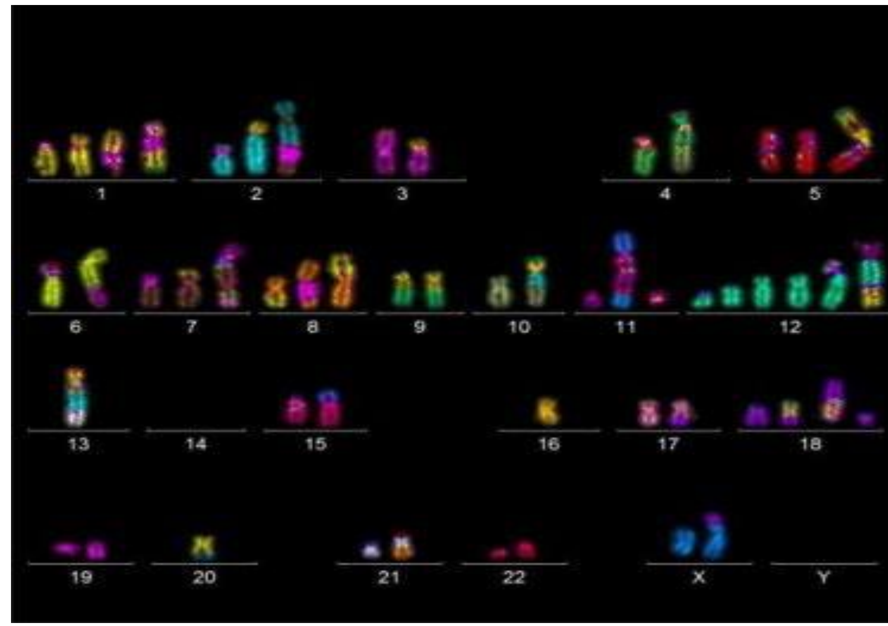
The nonrandom organization of genes and chromosomes contributes to the formation of translocations.



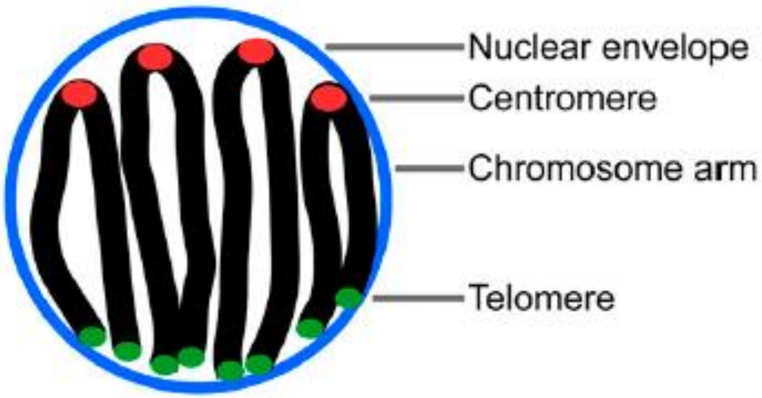
Foster et al. (2013): **Relative proximity of chromosome territories influences chromosome exchange partners in radiation-induced chromosome rearrangements in primary human bronchial epithelial cells**



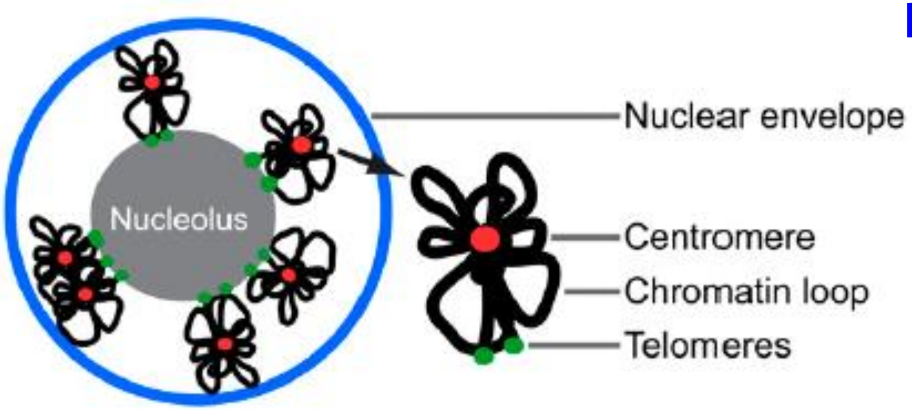
Relative interphase positions of chromosomes in NHBE cells. Panel A shows chromosomes 1 (red) and 13 (green), Panel B shows chromosomes 9 (green) and 17 (red) while Panel C shows chromosomes 16 (red) and 21 (green). Panel D outlines a 'map' of the relative positioning of chromosome territories in NHBE cells.



Chromosome organization at interphase (in plants)



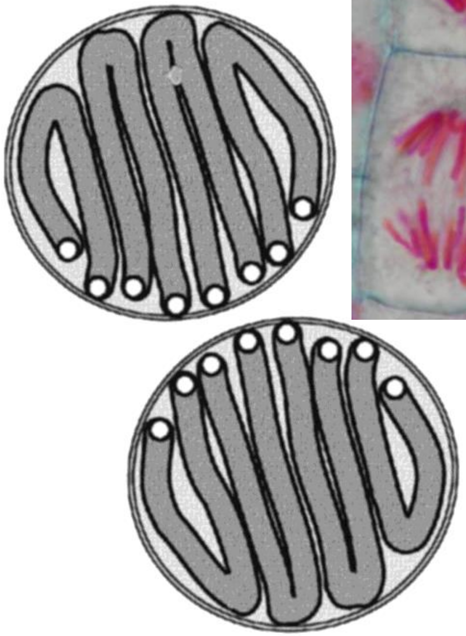
Rabl configuration

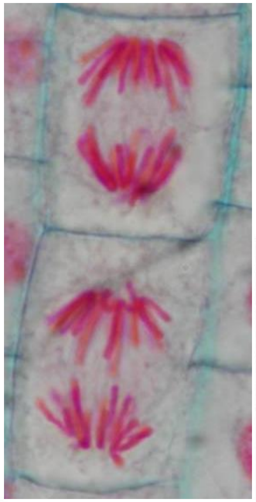


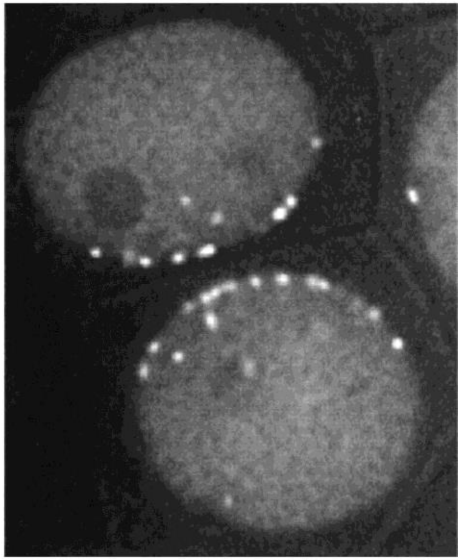
Radial loop model

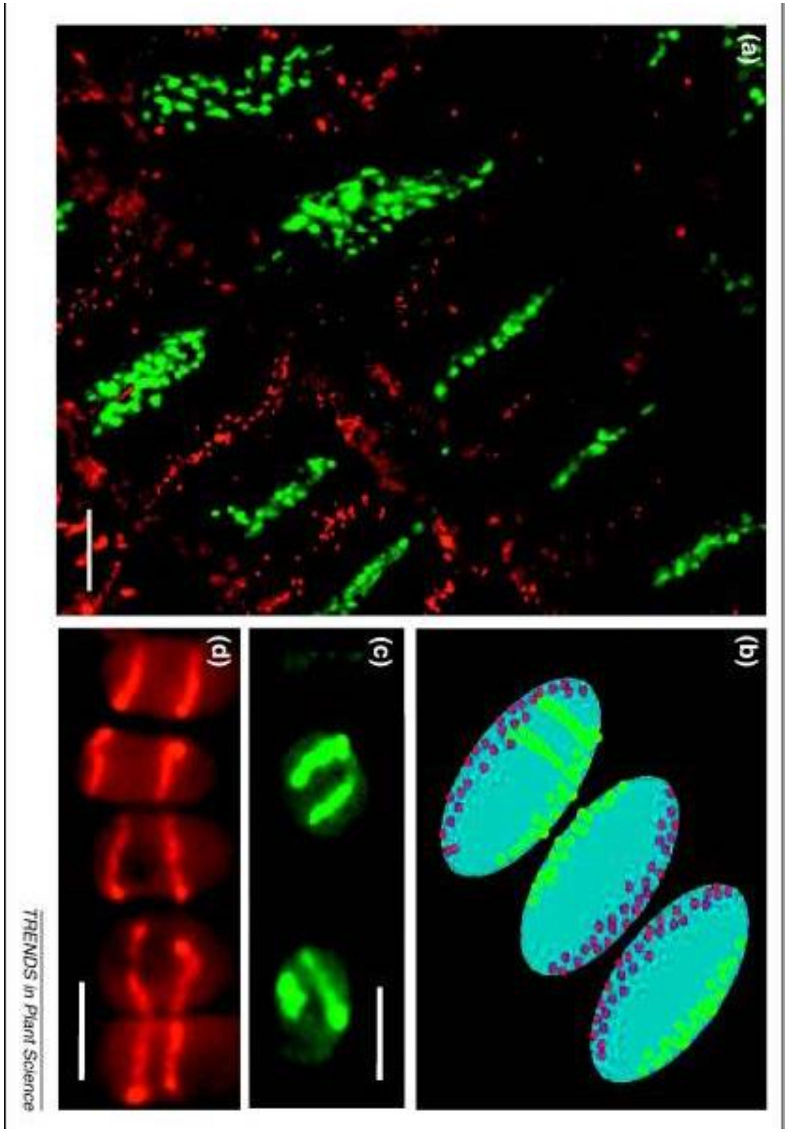
more organisation models ?

Rabl configuration



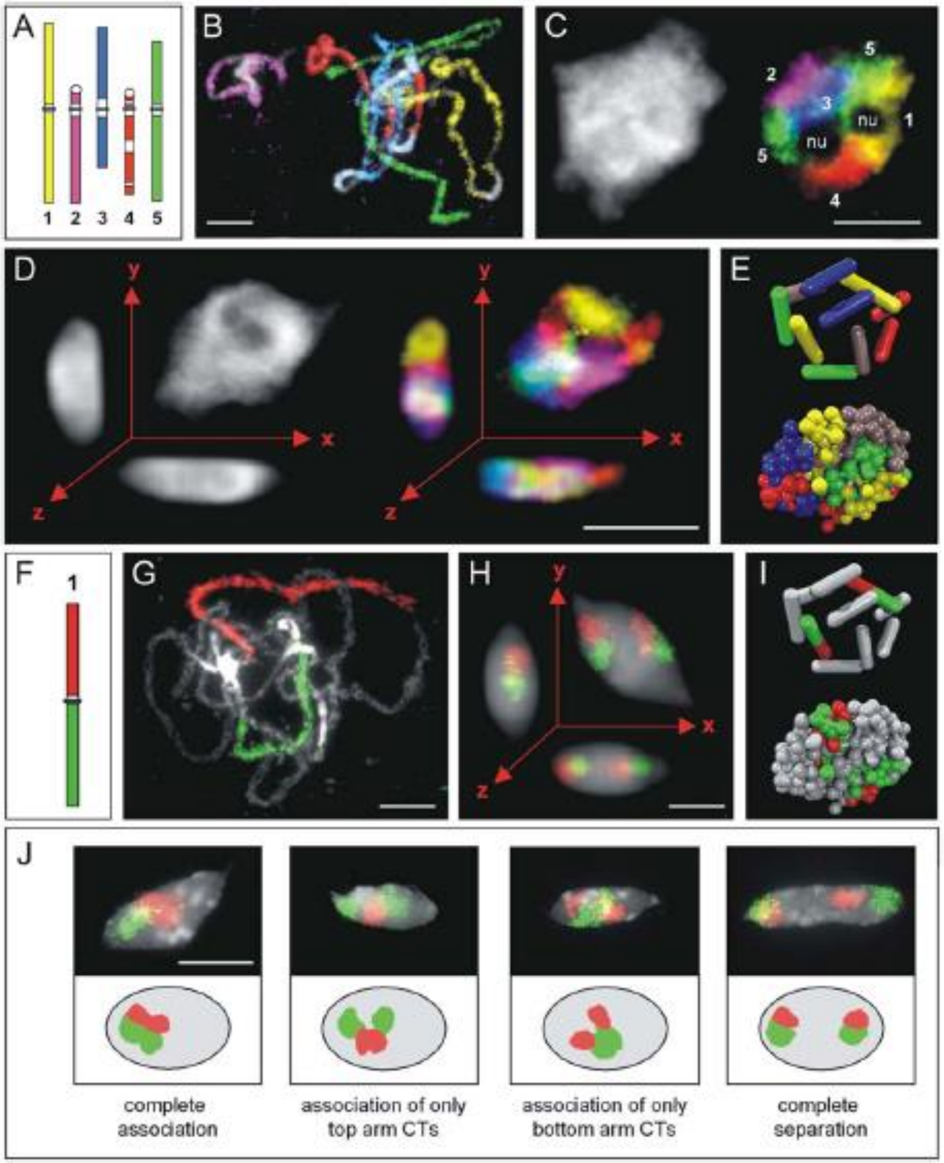






Cowan C R et al. Plant Physiol. 2001;125:532-538

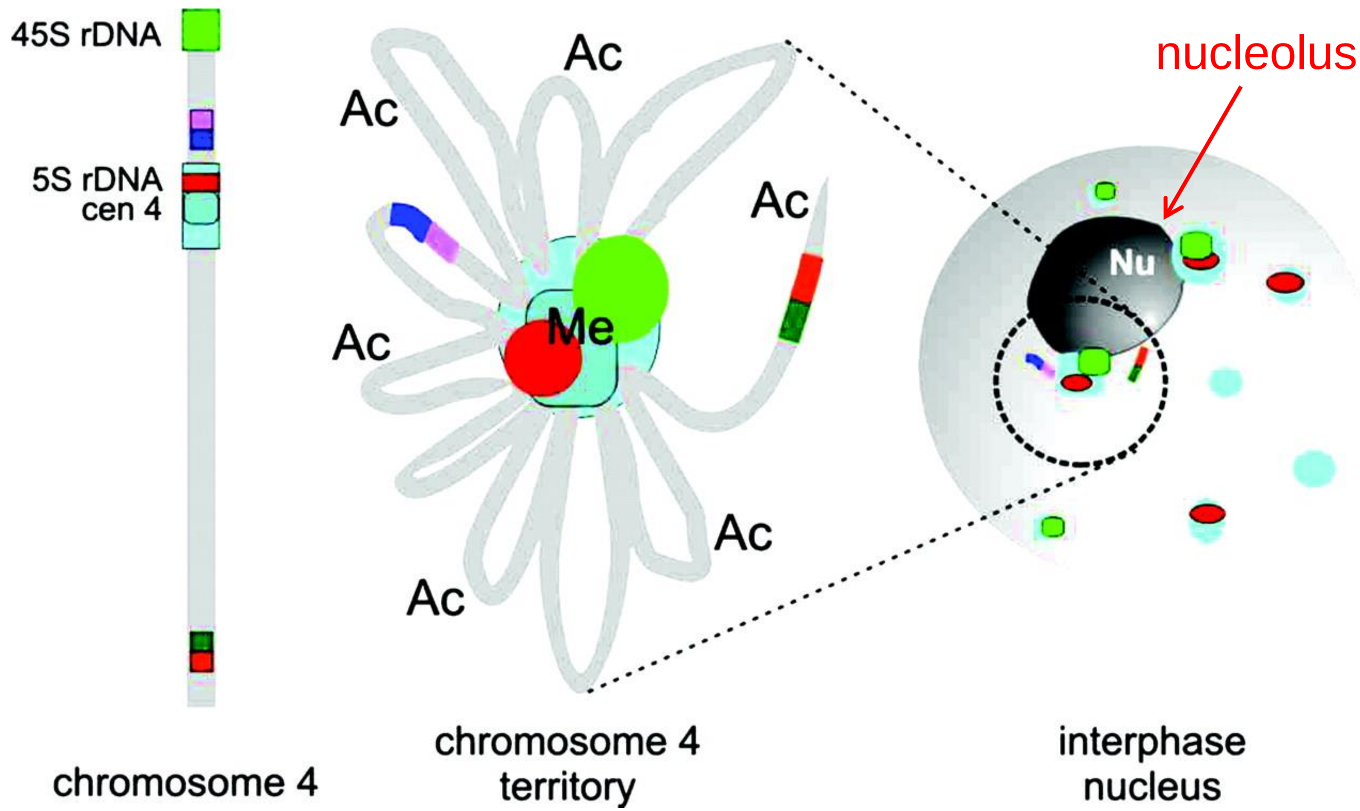
Chromosome territories - Arabidopsis



Pecinka et al. (2004) Chromosoma

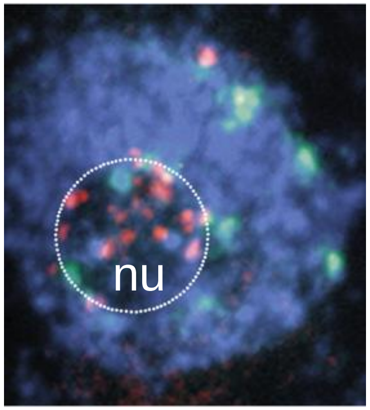
Interphase chromosomes in *Arabidopsis* are organized as well defined chromocenters from which euchromatin loops emanate

Paul Fransz*†, J. Hans de Jong‡, Martin Lysak*, Monica Ruffini Castiglione§, and Ingo Schubert*

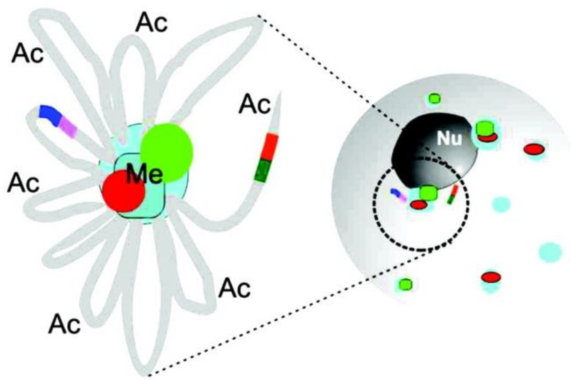


Identification of Nucleolus-Associated Chromatin Domains Reveals a Role for the Nucleolus in 3D Organization of the *A. thaliana* Genome

Pontvianne et al. (2016) Cell Reports

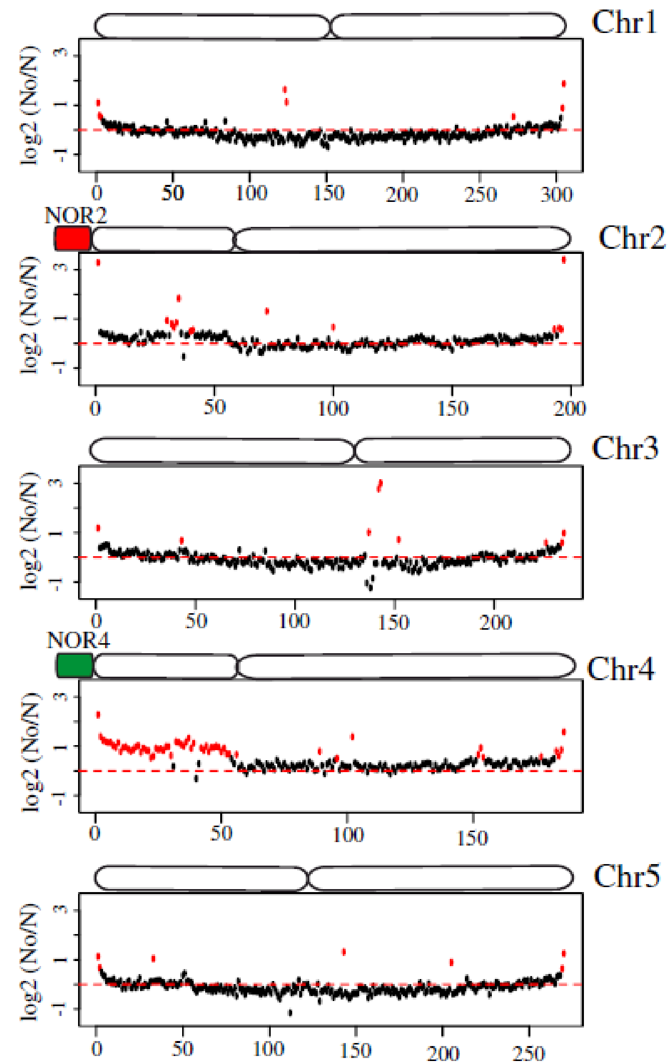


TELs clustered around nucleolus



radial loop model

NADs: nucleolus-associated domains



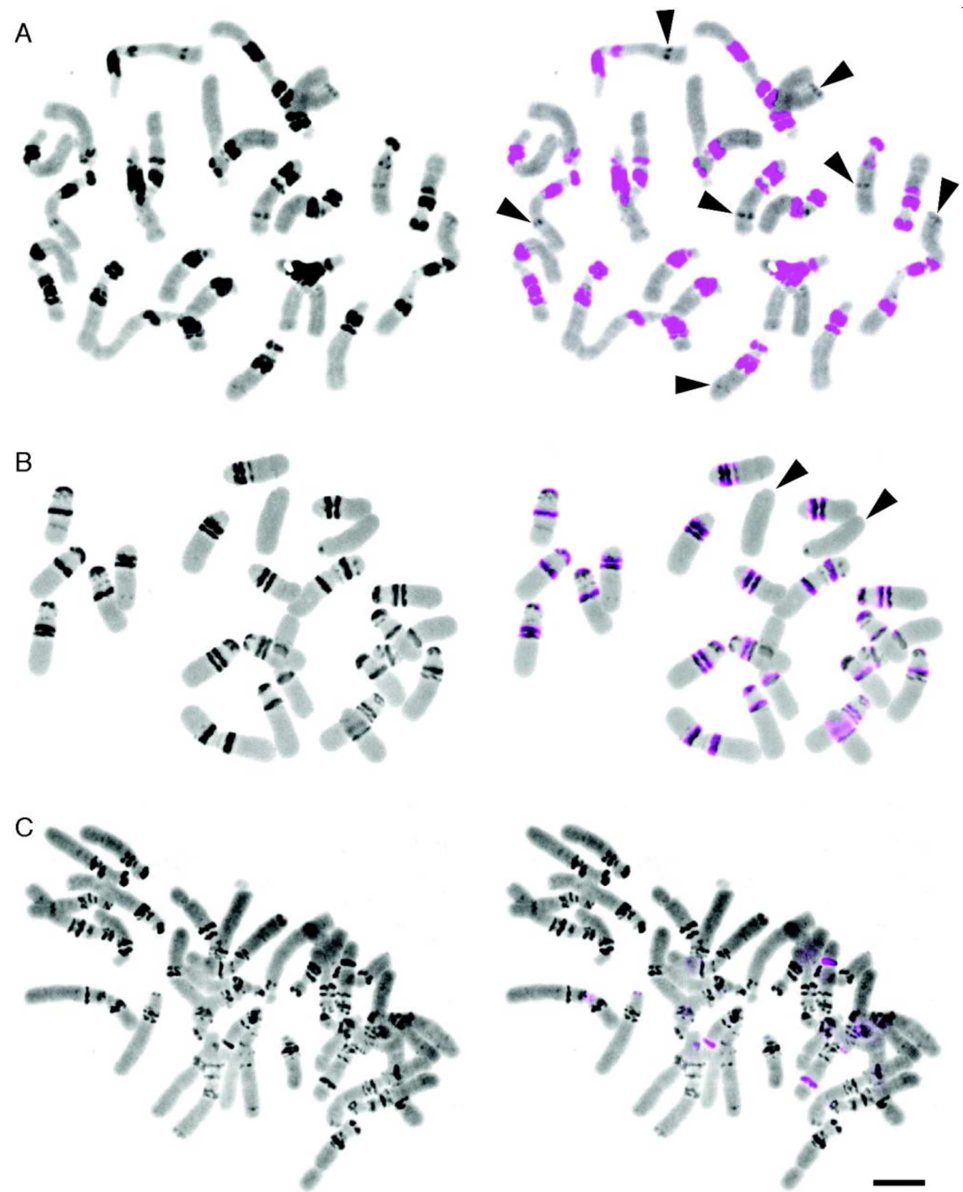
NADs : genomic regions with heterochromatic signatures and include transposable elements (TEs), sub-telomeric regions, and mostly inactive protein coding genes. However, NADs also include active rRNA genes and the entire short arm of chromosome 4.

Hypothesis: telomeres, NORs and NADs anchor chromatin loops to nucleolus

Chromatin and chromosomes

Heterochromatin and euchromatin

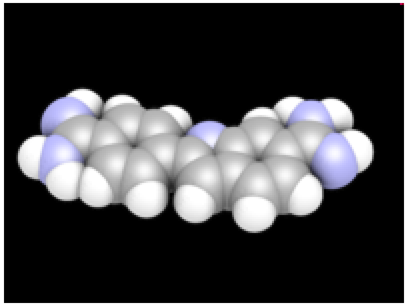
DAPI-stained chromosomes of *Fritillaria* spp. (B/W, inverted)

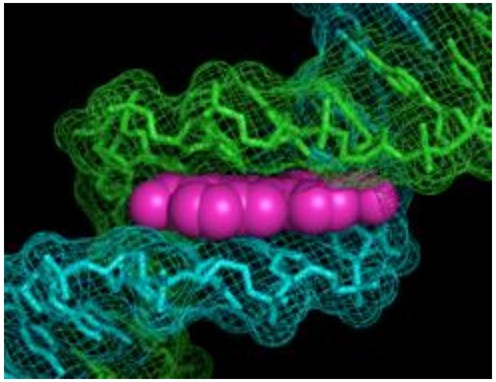


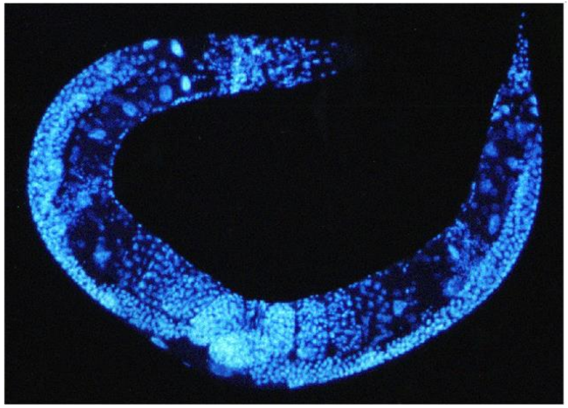
Chromosomes and nuclei stained by fluorescent dyes

4',6-Diamidino-2-phenylindole (DAPI)

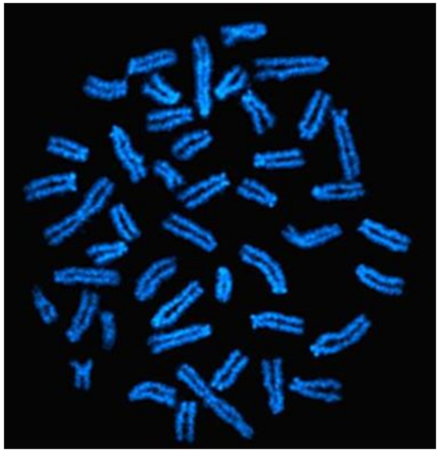
AT-specific fluorescent dye







Caenorhabditis elegans



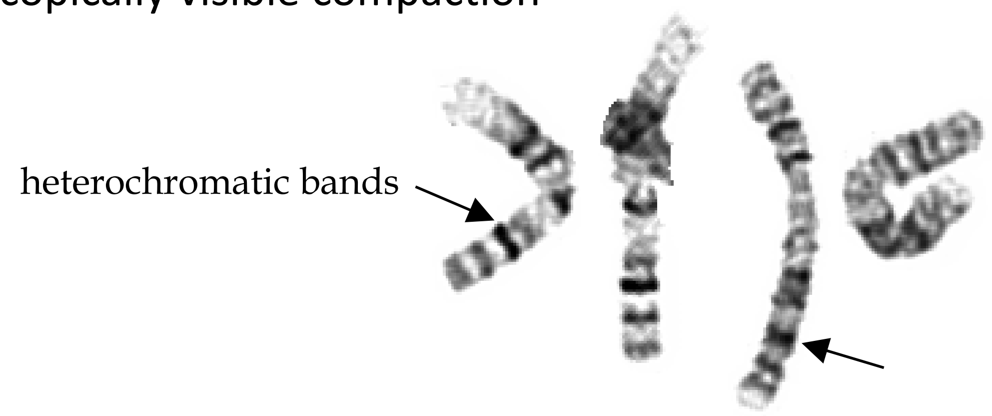
Chromatin structure: eu- and heterochromatin

• Traditional view: chromatin compaction limits or enhances access to transcription factors

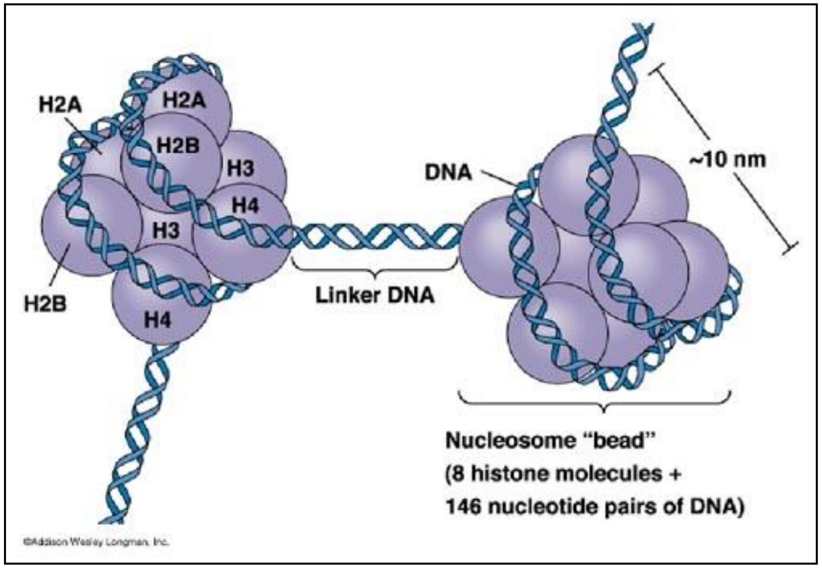
• Accessible chromatin is referred to as **euchromatin** and is active (Emil Heitz, 1928) (transcription facilitated)

• Inaccessible chromatin is called **heterochromatin** and is generally inactive (thought that regulatory proteins, e.g. transcription factors, cannot access DNA templates)

• Today - restriction of DNA accessibility is a local property of chromatin and not necessarily a consequence of microscopically visible compaction

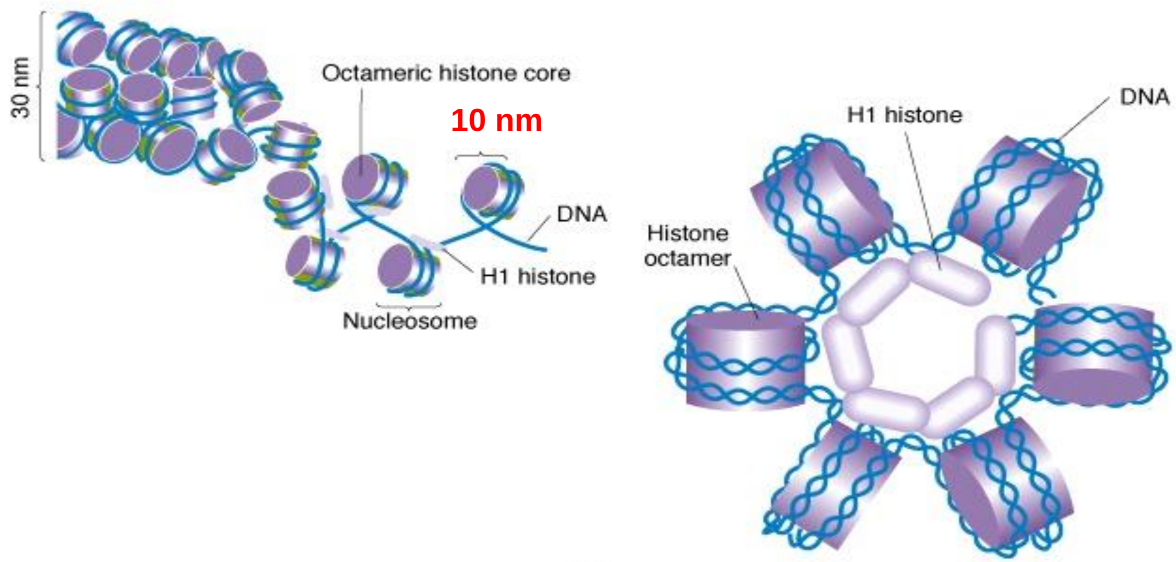


Histones



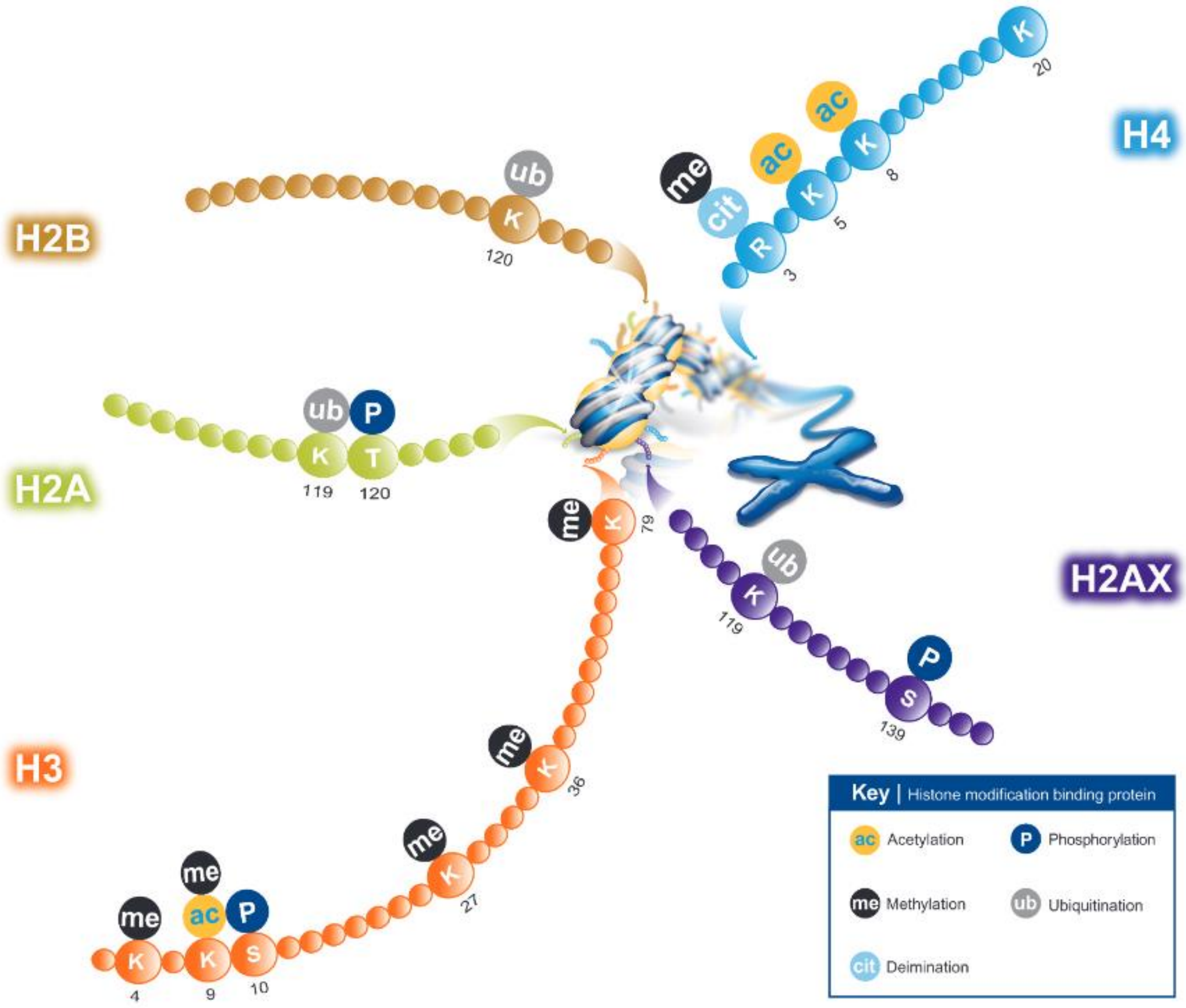
10-nm fibre

30-nm fibre

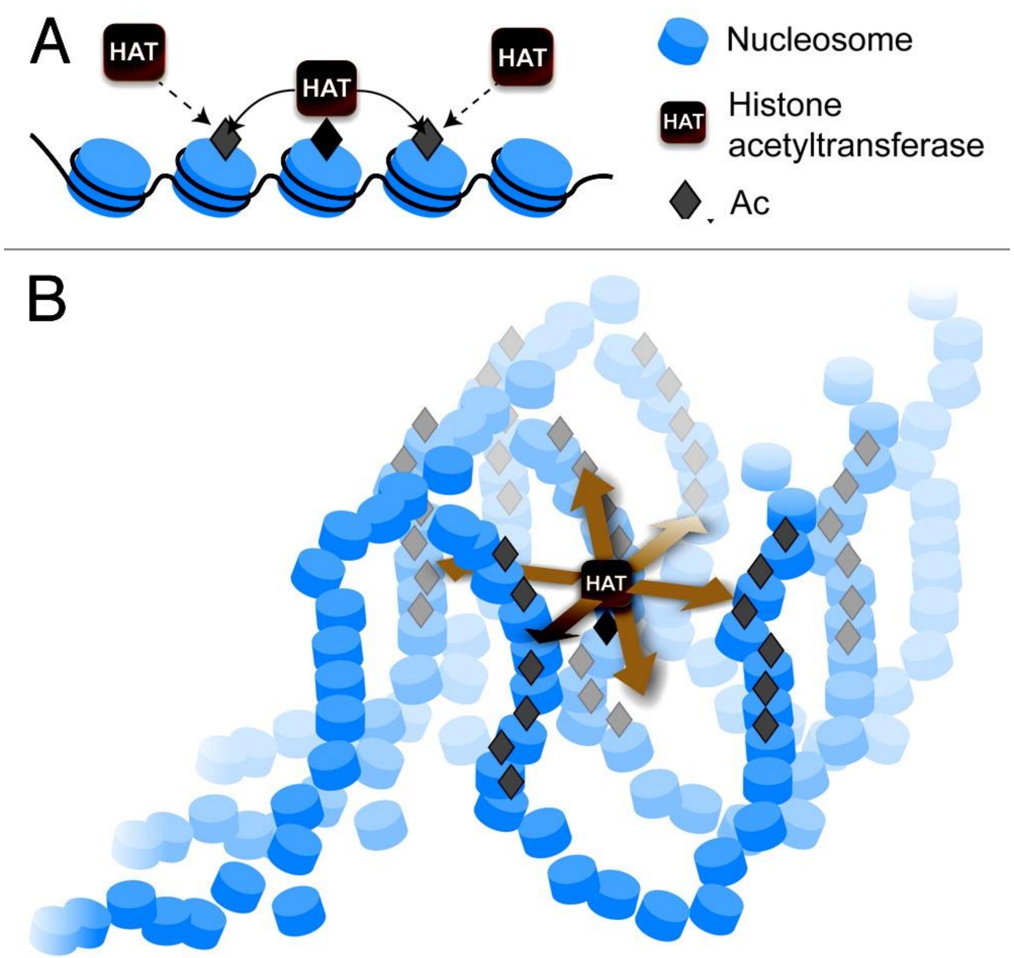


(b)

Histone modifications (marks)



10-nm fibers: mechanisms of signal spreading in chromatin



A classical view of the linear spreading of a signal in two directions along the chromatin fiber

3D spreading of a signal in all directions from a nucleation center resulting in modification of multiple chromatin regions both in cis and in trans

Histone modifications (marks)

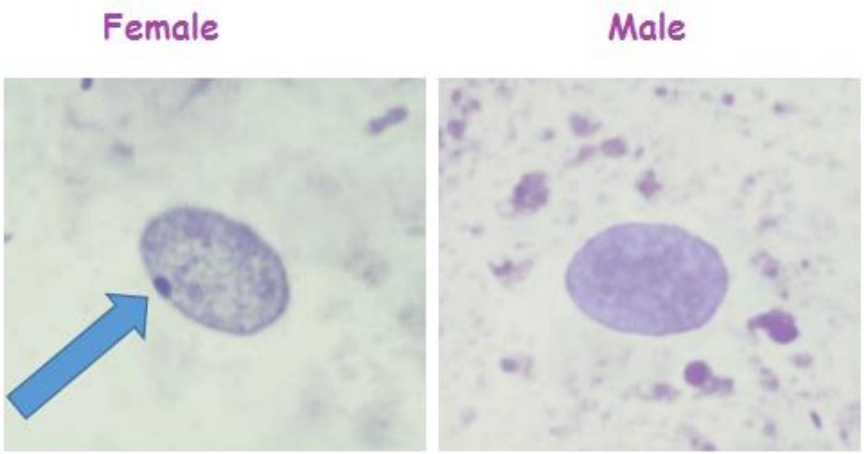
- acetylation — lysine (K) residues, arginine (R) residues
- methylation — lysine (K) residues [1, 2 or 3 methyl groups]
- phosphorylation — serine (S) and threonine (T) residues

Histone acetylation (ac) – usually higher gene expression

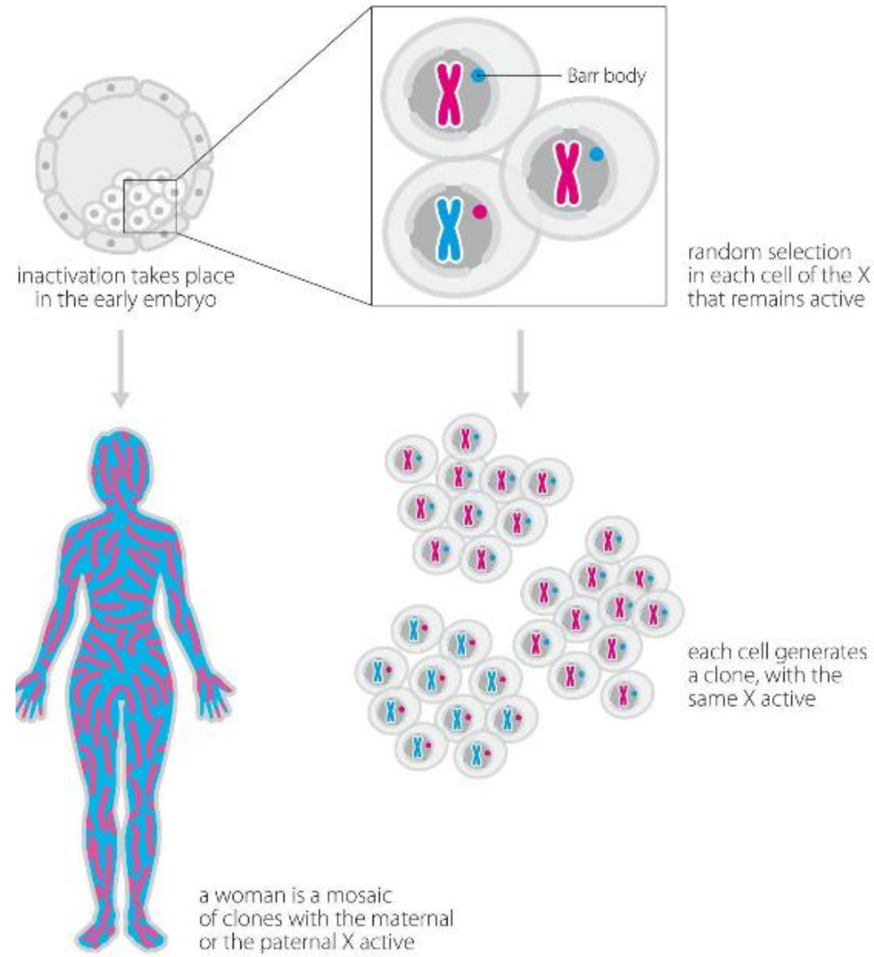
Histone methylation (m) – activation or repression of gene expression (often depending on the number of methyl groups – for example, H3K4m1, H3K4m2, H3K4m3)

Histone phosphorylation (ph) – most commonly during cellular responses to DNA damage (phosphorylated histone H2A separates large chromatin domains around the site of DNA breakage)

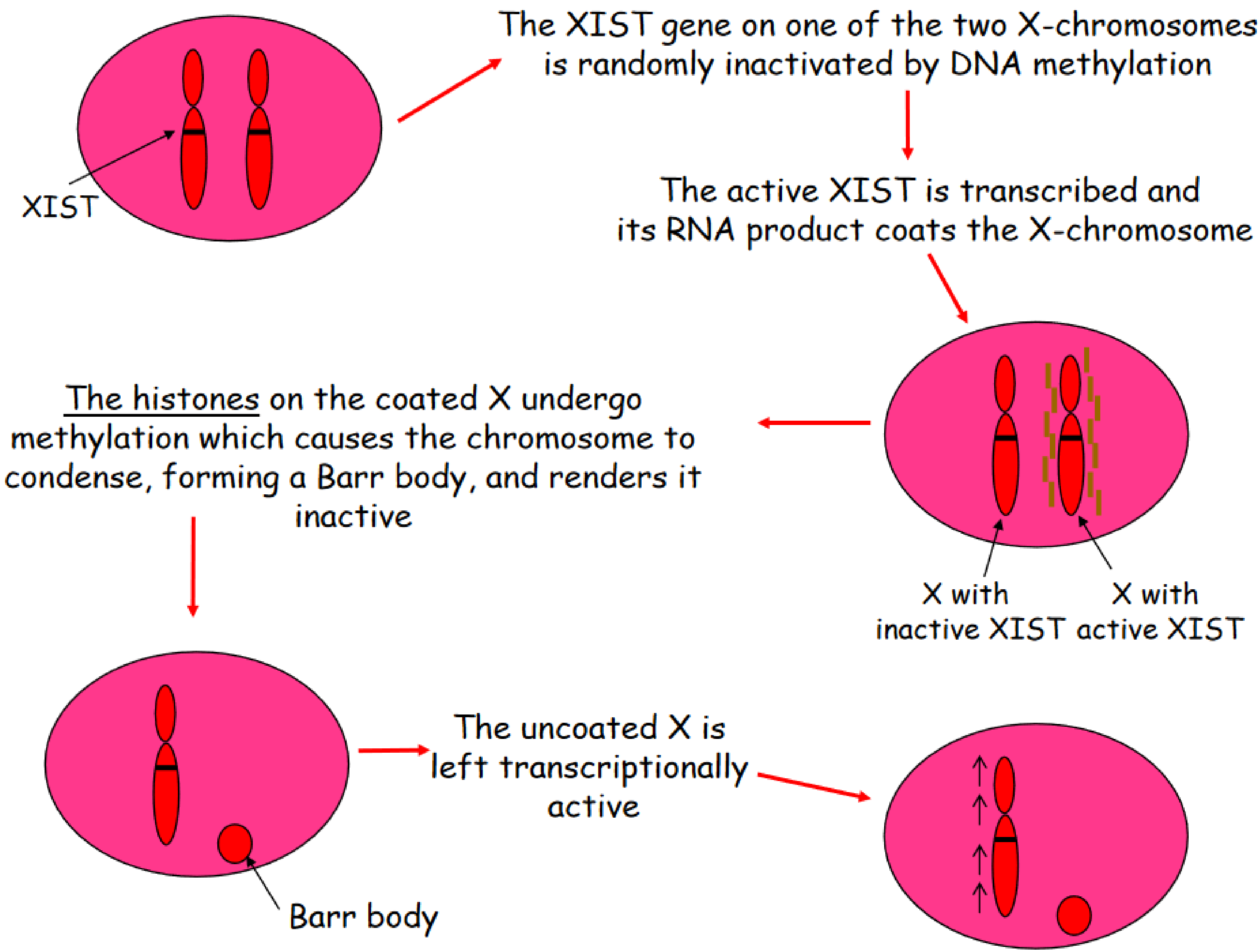
Methylation of X chromosome in mammals (Barr body)



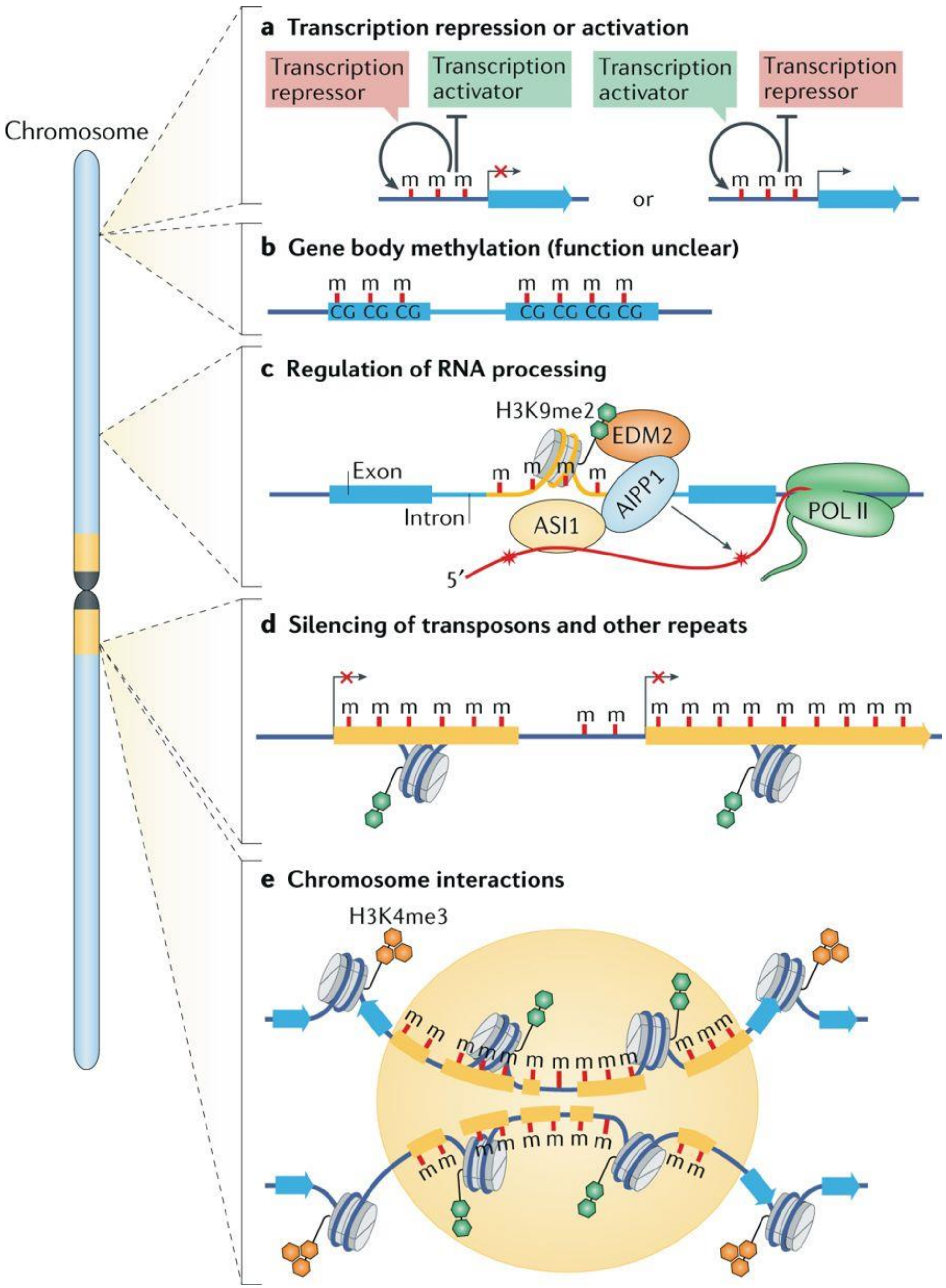
Barr body, an inactivated X chromosome



Methylation of X chromosome in mammals (Barr body)



DNA methylation in plants



Methylation at cytosines on the carbon no. 5 (within the pyrimidine ring) – m5C

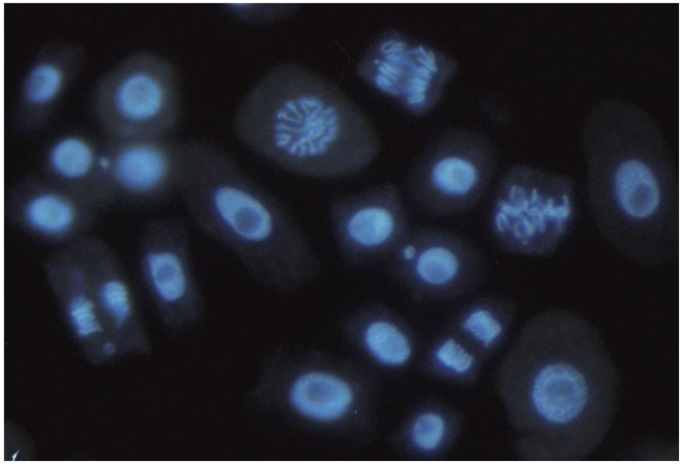
Arabidopsis (157 Mb) – c. 6% of the cytosine residues methylated

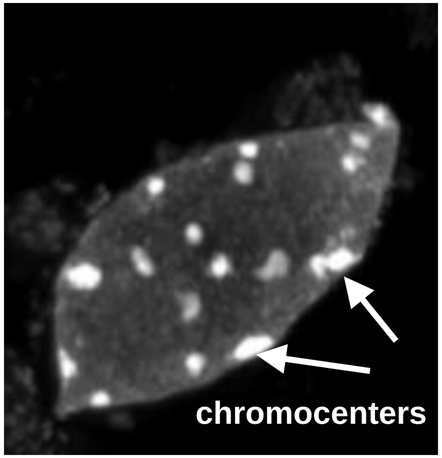
Maize (2 300 Mb) – c. 25%

Zhang et al. (2018) Dynamics and function of DNA methylation in plants. Nat Rev Mol Cell Biol 19: 489-506.

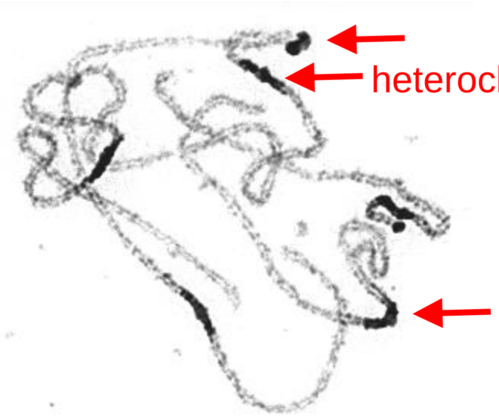
Heterochromatin in plant species

barley

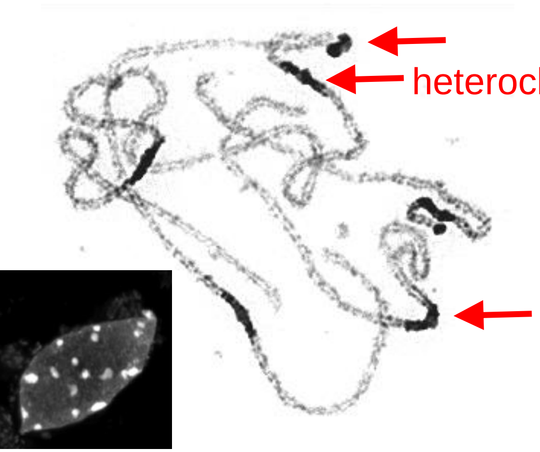


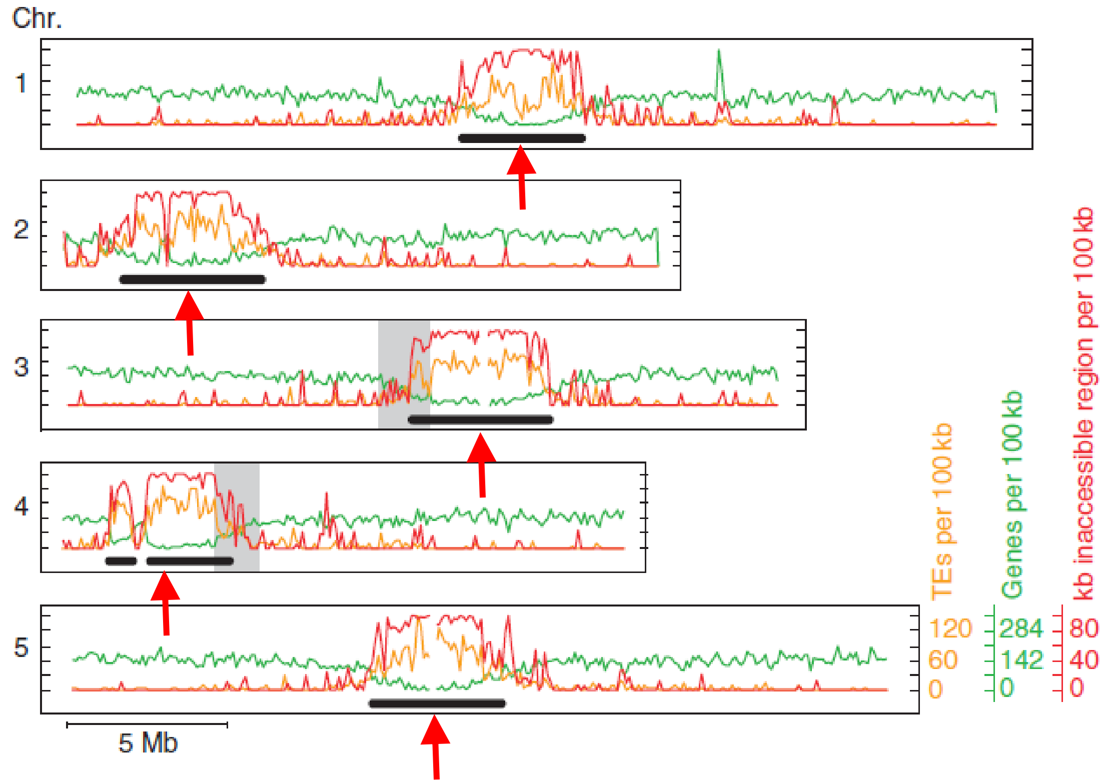


Arabidopsis

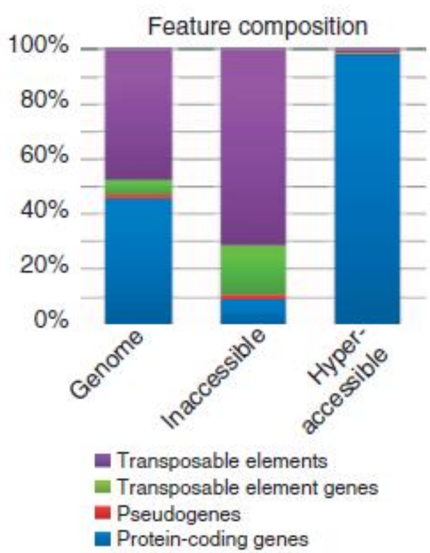


Heterochromatin in plant species: Arabidopsis





Genomic features in inaccessible and hyper-accessible regions



density of inaccessible region

protein-coding genes

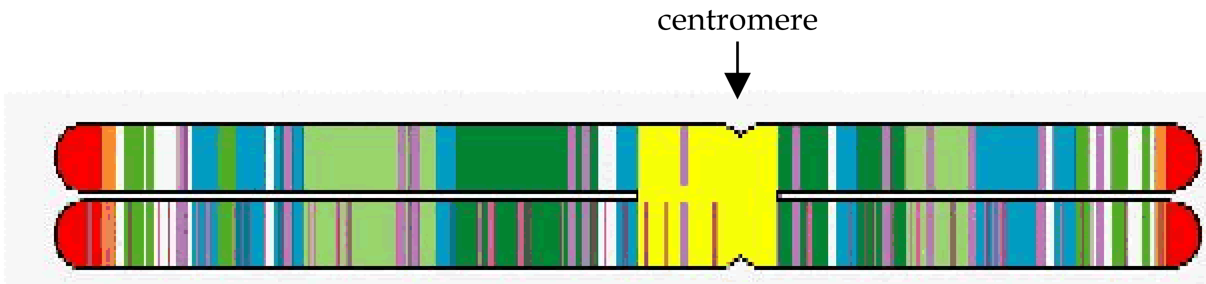
TEs along chromosomes

heterochromatin:
5-cytosine methylation,
dimethylation of H3 (H3K9me2)

euchromatin:
trimethylation of H3 (H3K9me3)

Shu et al. (2012), Nature Comm

Scheme of plant chromosome (after Haslop-Harrison)



Intercalary tandem repeats

Centromere associated tandem repeat

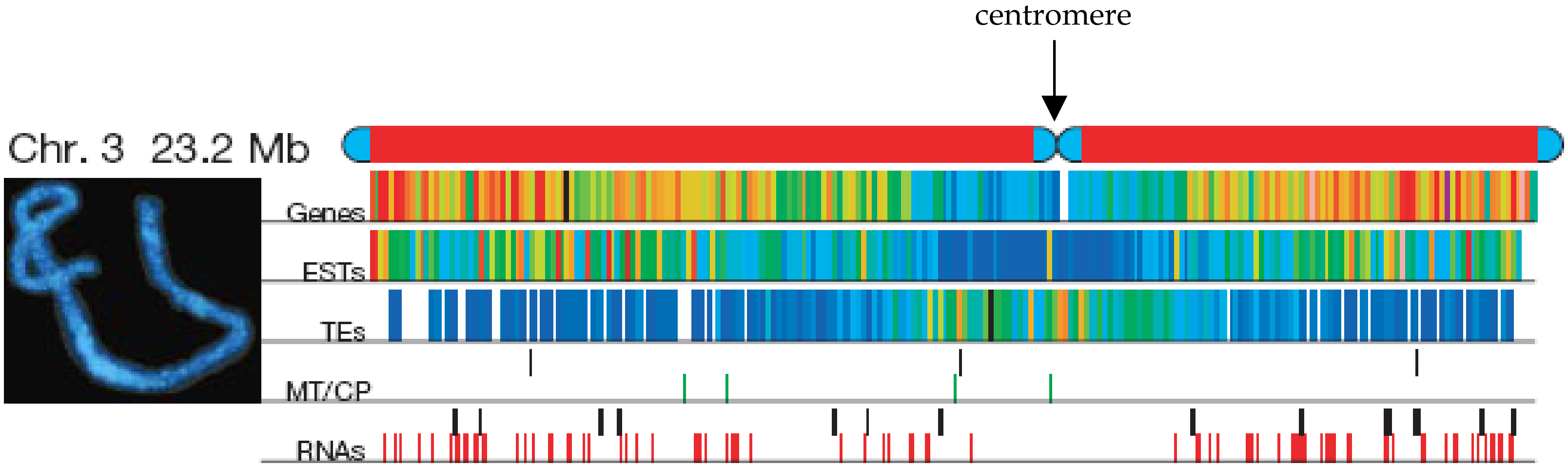
Telomeric and sub-Telomeric repeats

Dispersed tandem repeats

Dispersed Ty-1-copia-like retroelements LTR and microsatellites

Single and low-copy sequences Including genes

Arabidopsis chromosomes

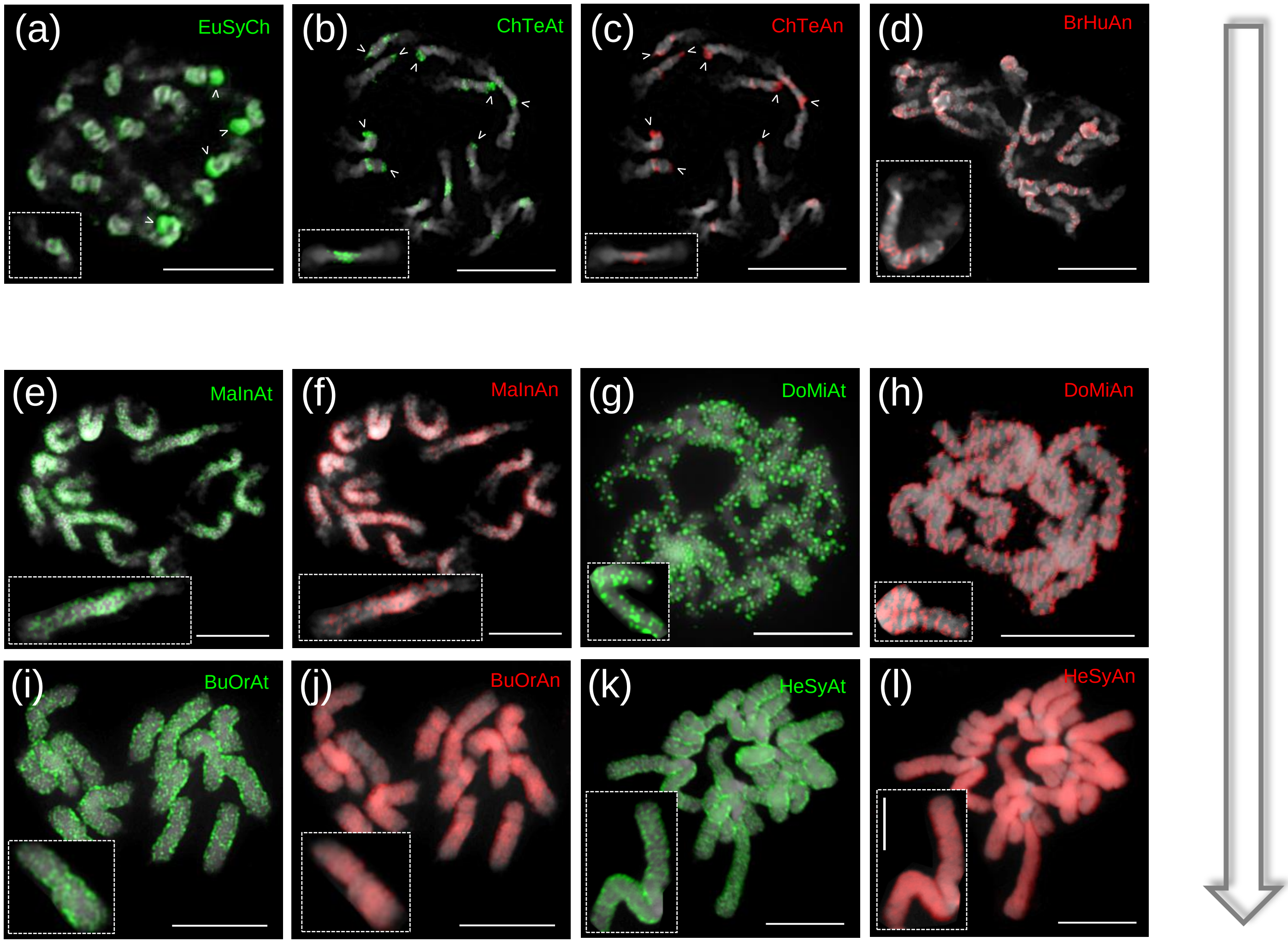


The frequency of features was given pseudo-colour assignments, from red (high density) to deep blue (low density).

Gene density (`Genes') ranged from 38 per 100 kb to 1 gene per 100 kb; Transposable element densities (`TEs') ranged from 33 per 100 kb to 1 per 100 kb.

Arabidopsis Genome Initiative, Nature 408, 2000

Chromosome structure



small genomes

(c. 150 – 600 Mb)

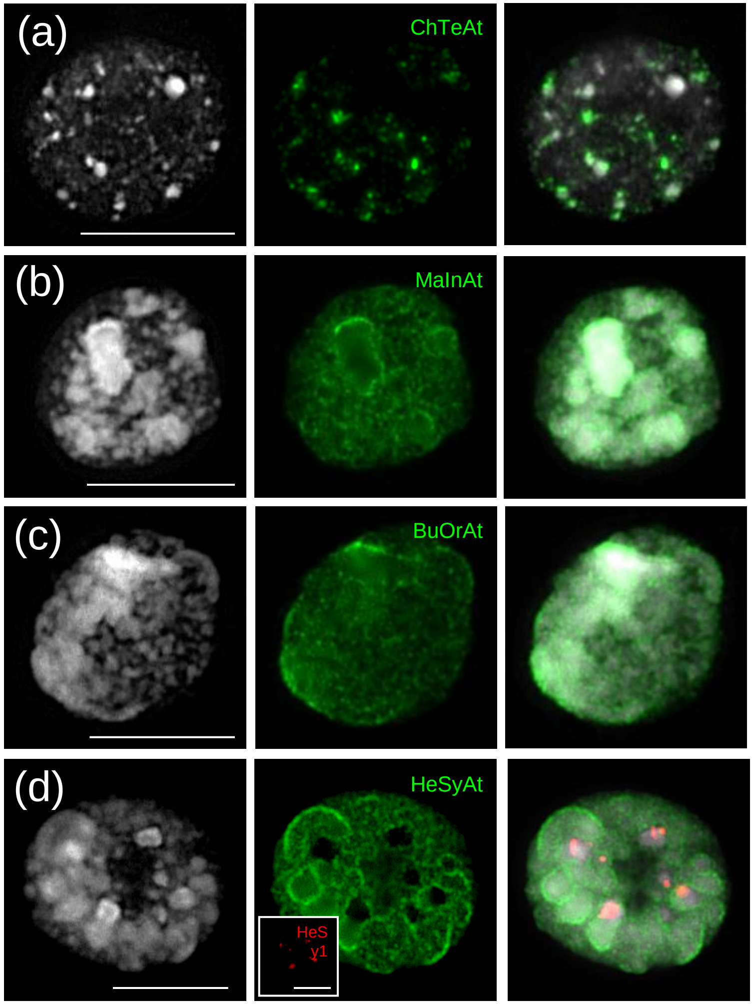
large(er) genomes

(> c. 1400 Mb)

Chromosome structure – different interphase organization

small genomes

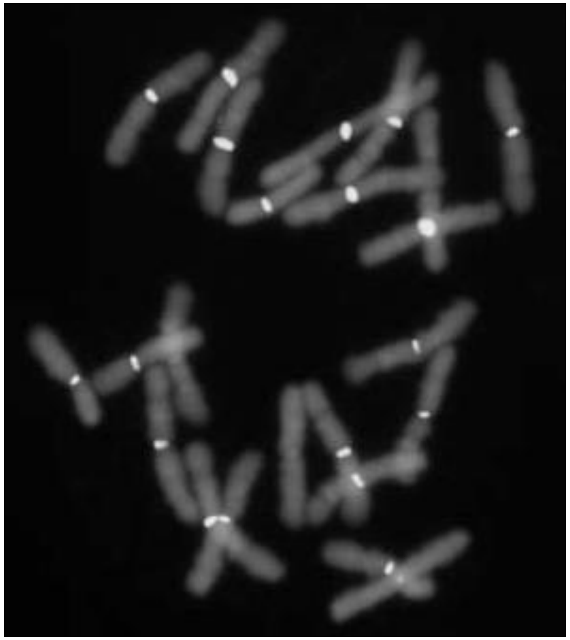
(c. 150 – 600 Mb)



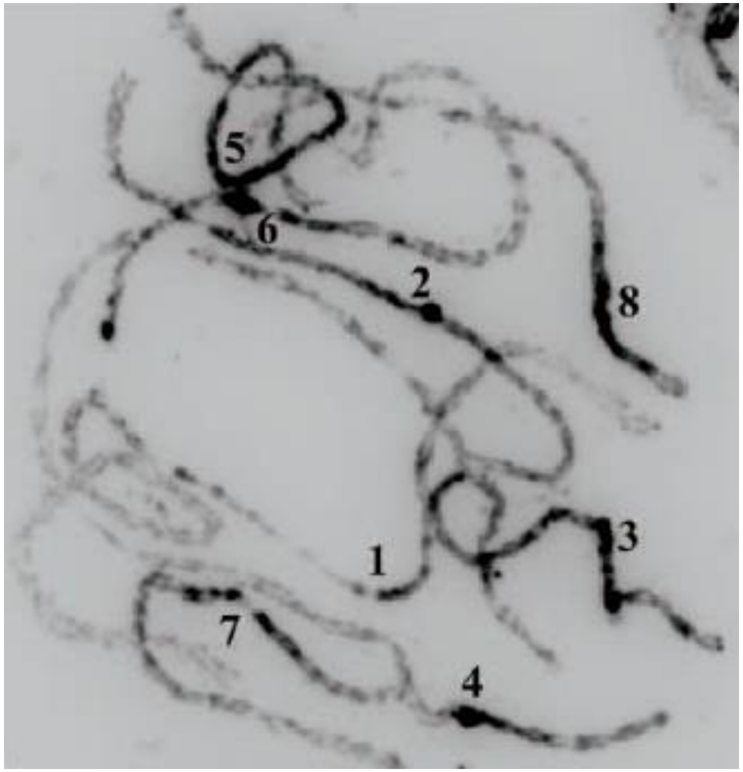
large(er) genomes

(> c. 1400 Mb)

Mitotic and meiotic chromosomes



mitotic chromosomes of *Pinus*

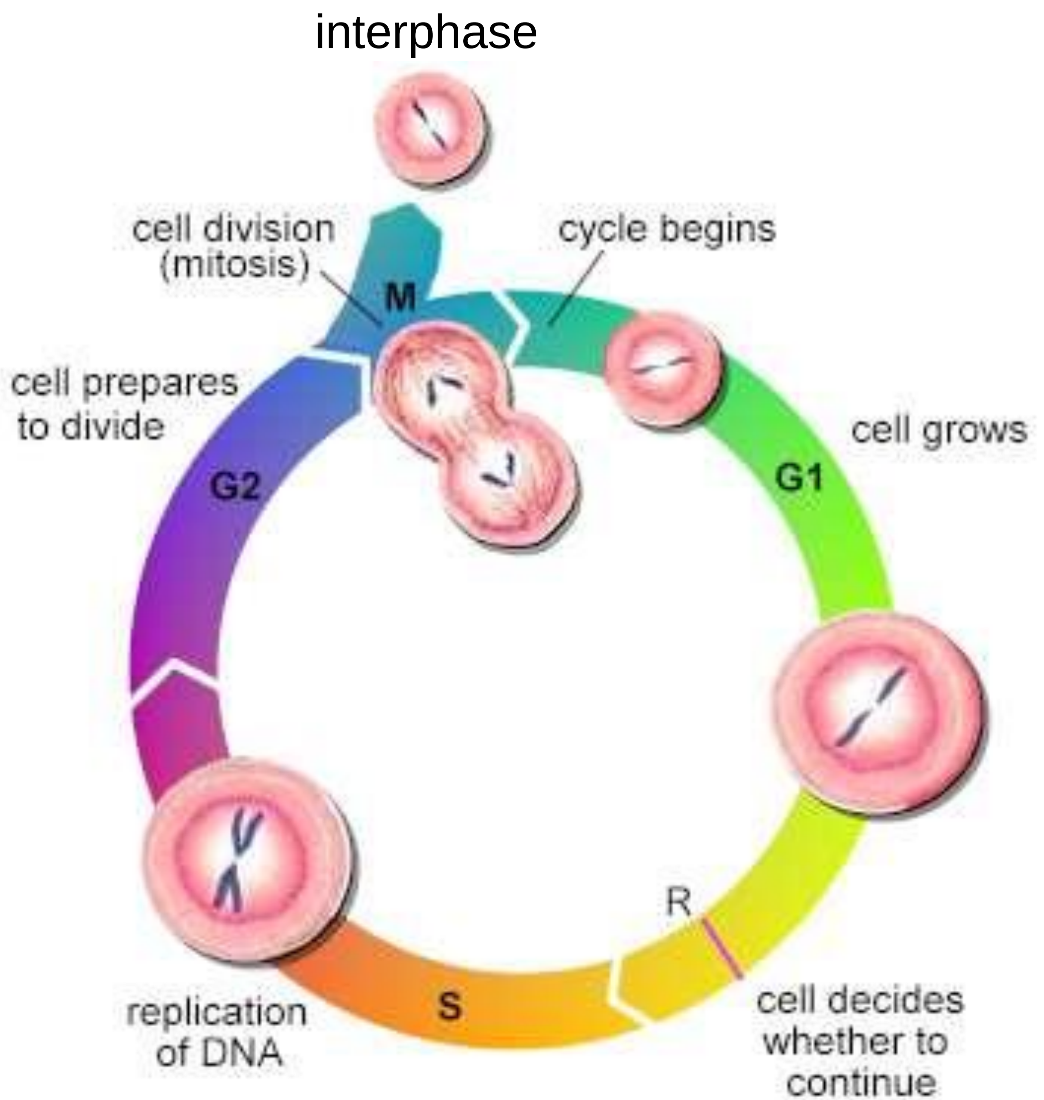


meiotic (pachytene) chromosomes of *Antirrhinum*

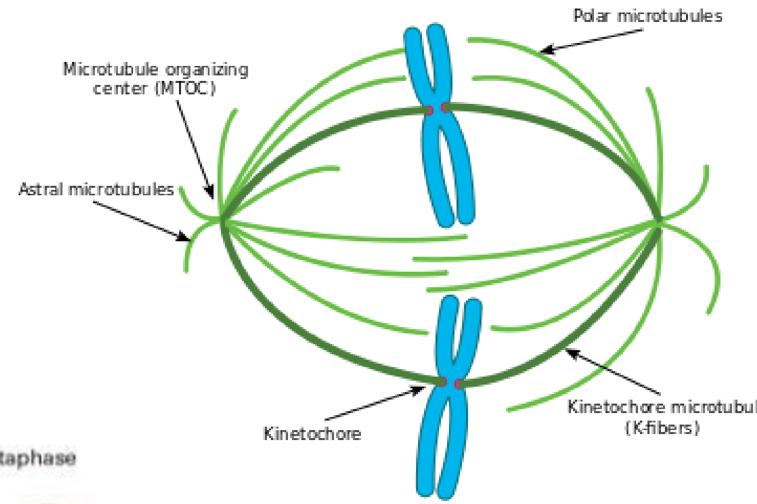
1 chromosome = 2 chromatids

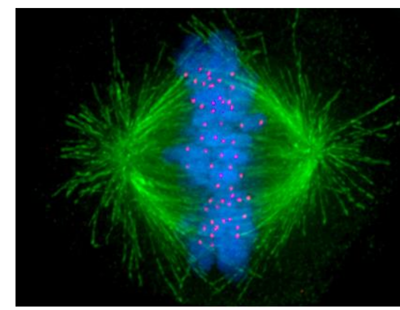
1 bivalent = 2 chromosomes = 4 chromatids

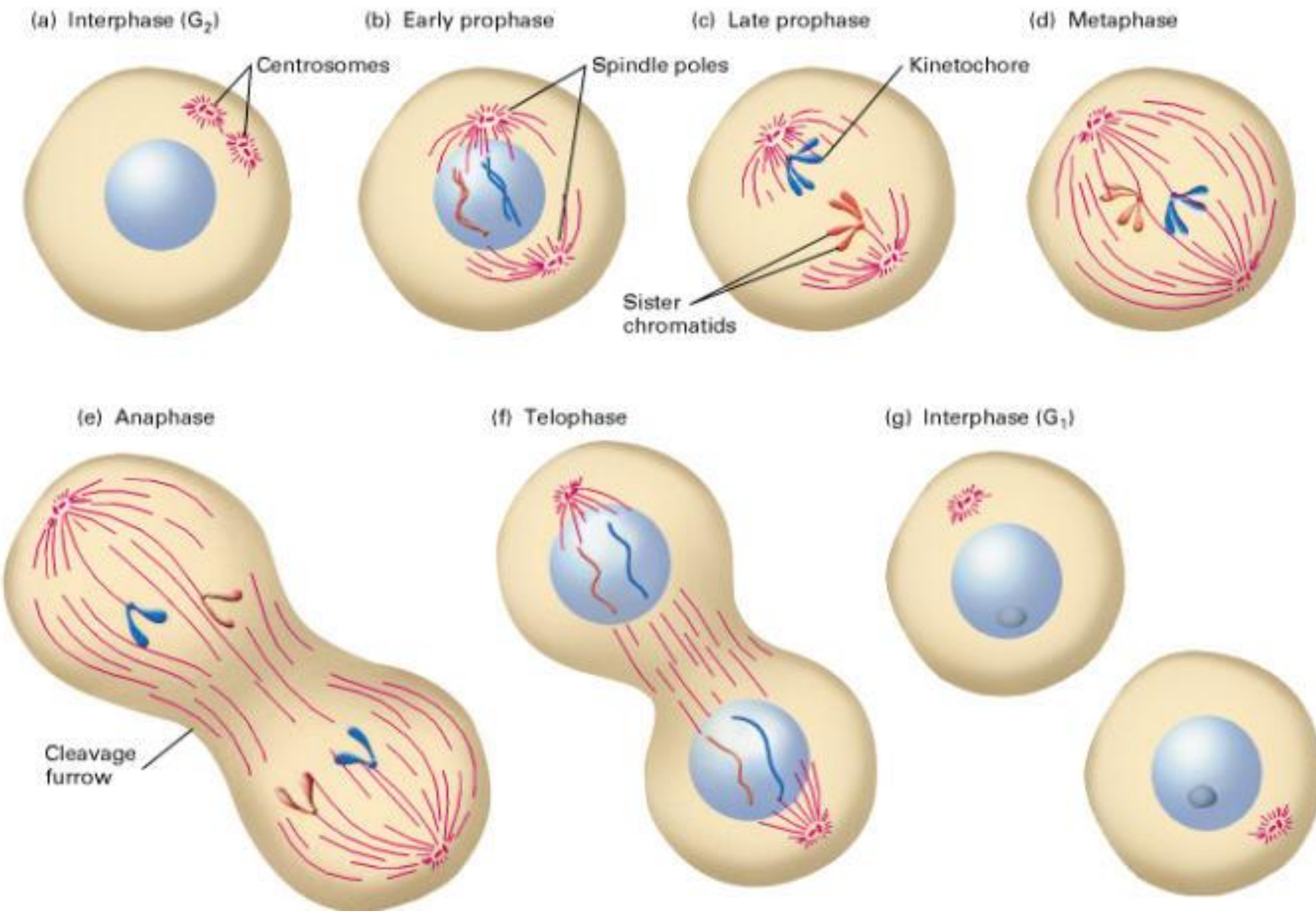
Cell cycle, chromosomes and chromatids



Mitosis


Polar microtubules
Microtubule organizing center (MTOC)
Astral microtubules
Kinetochore
Kinetochore microtubul
(K-fibers)




(a) Interphase (G_2)
Centrosomes
(b) Early prophase
Spindle poles
(c) Late prophase
Kinetochore
Sister chromatids
(d) Metaphase
(e) Anaphase
Cleavage furrow
(f) Telophase
(g) Interphase (G_1)

Meiosis

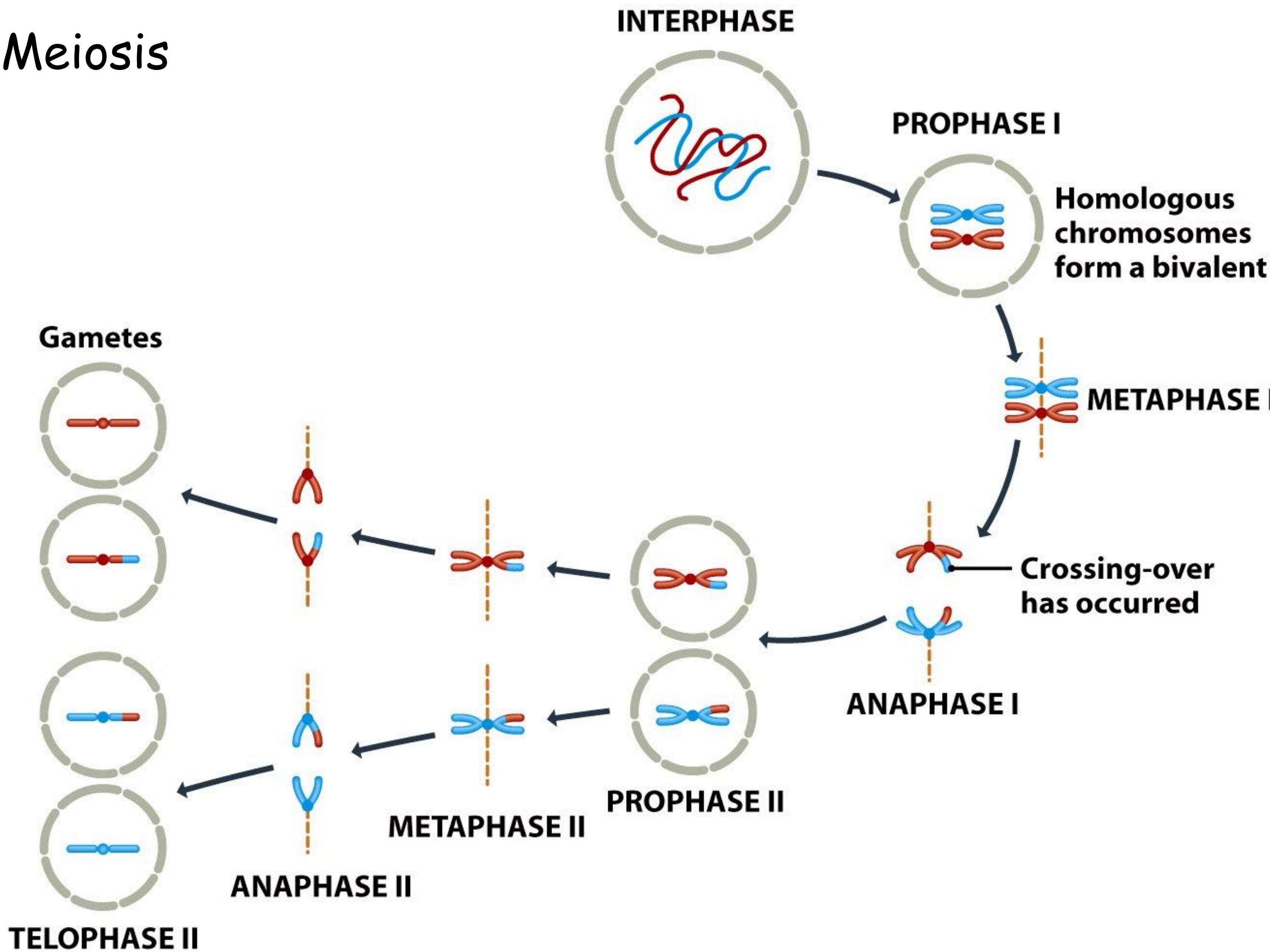
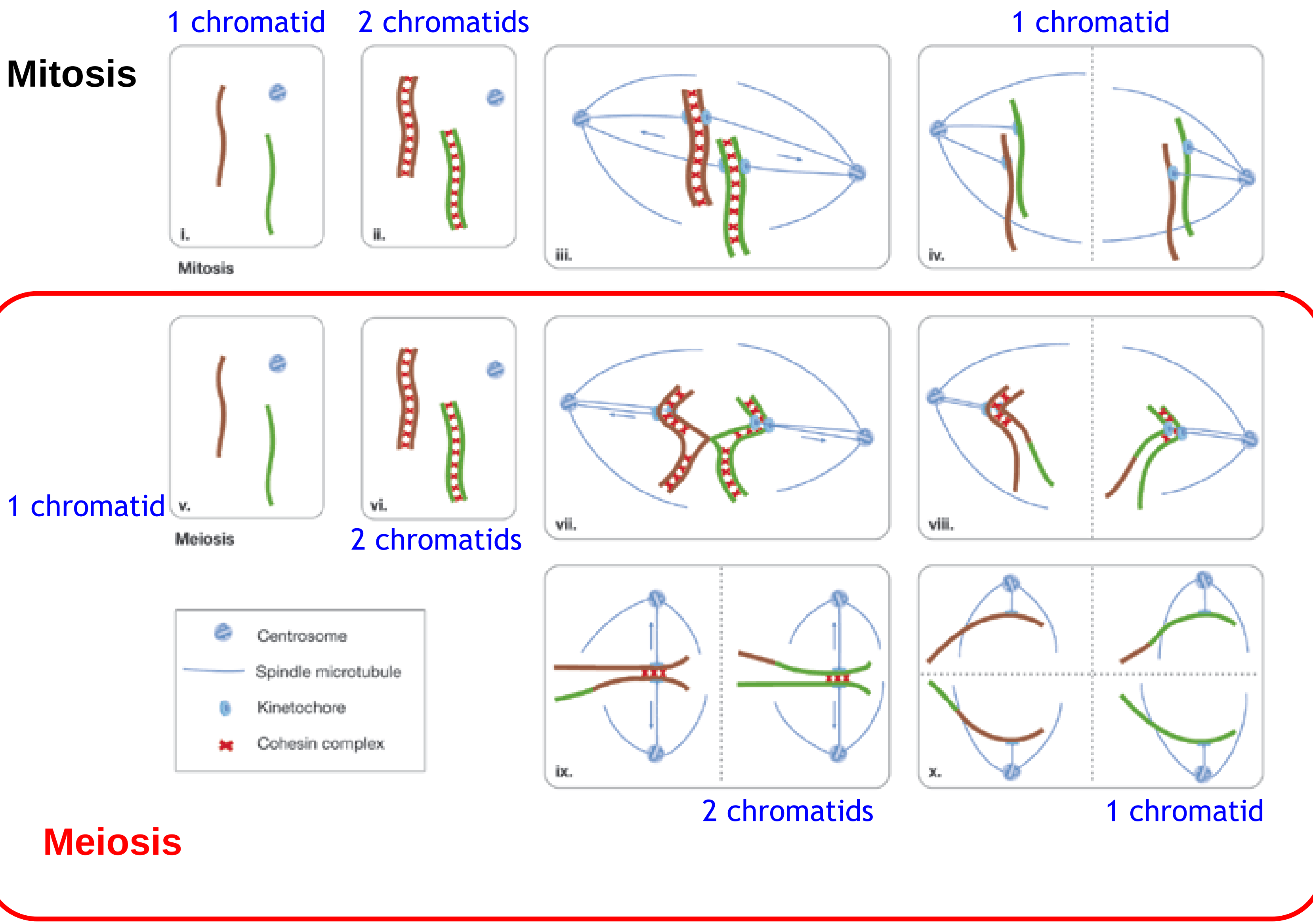
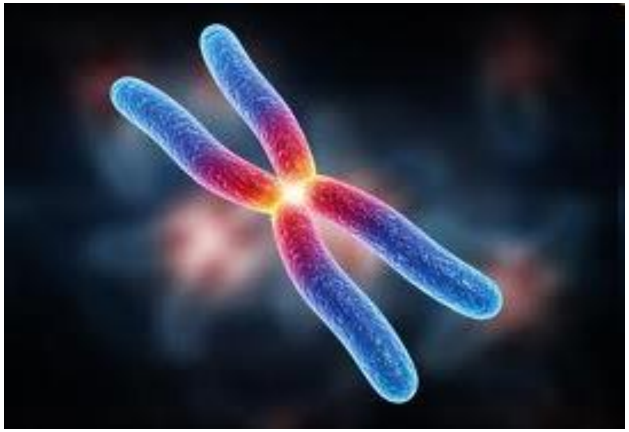


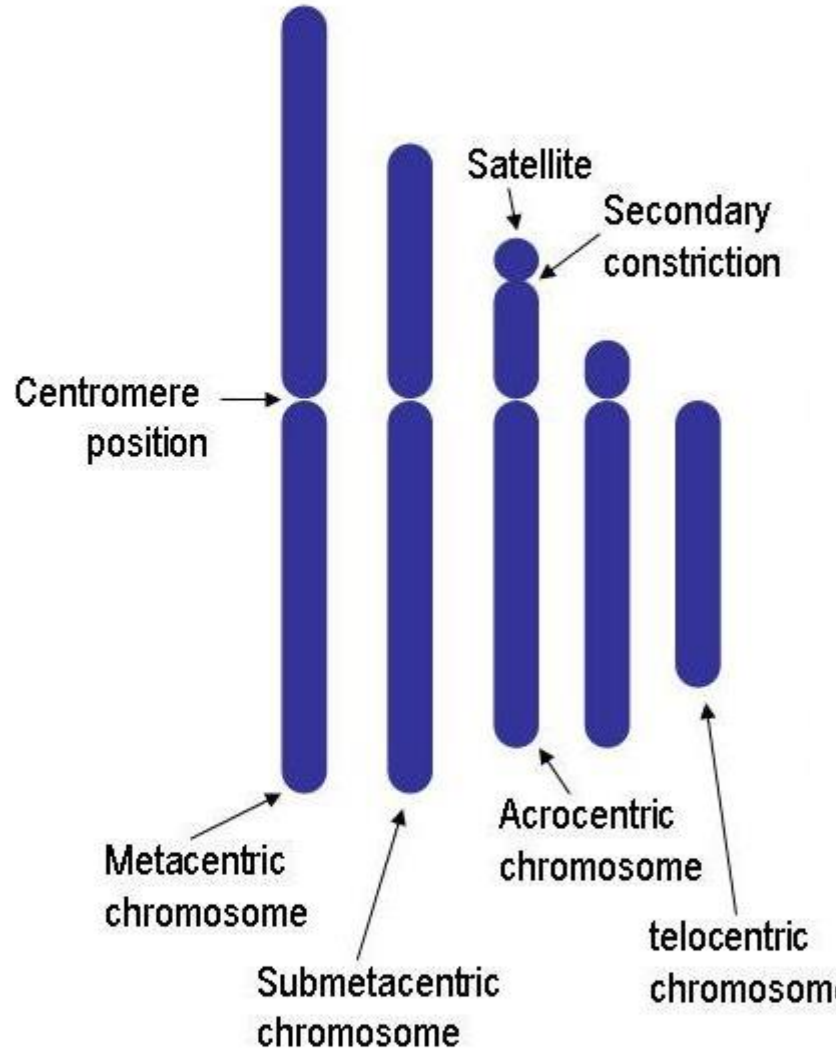
Figure 3.16 *Genomes 3* (© Garland Science 2007)

Chromosomes and chromatids during mitosis and meiosis

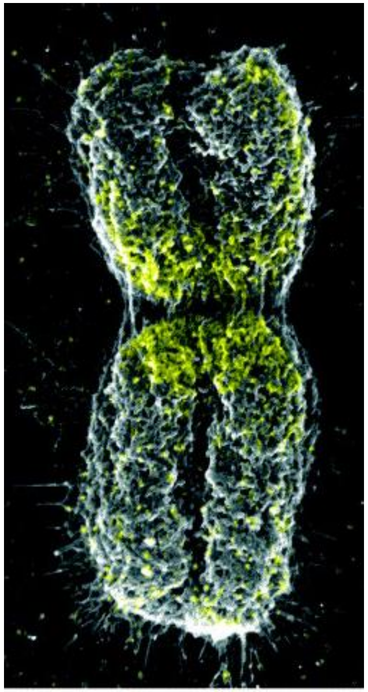


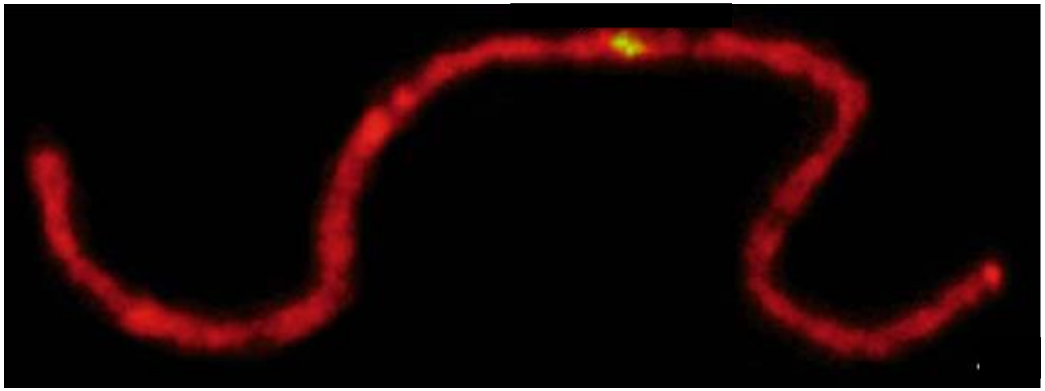
Chromosome morphology





Centromere structure, function & evolution





Centromere function

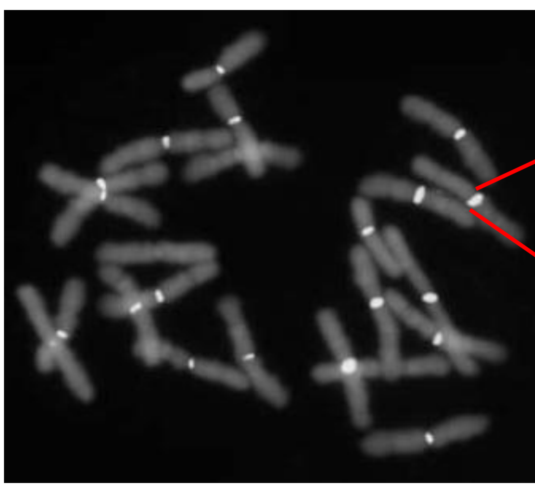
- chromosomes can be <u>monocentric</u> or <u>holocentric</u> (*Luzula*, *Eleocharis*, some insects)

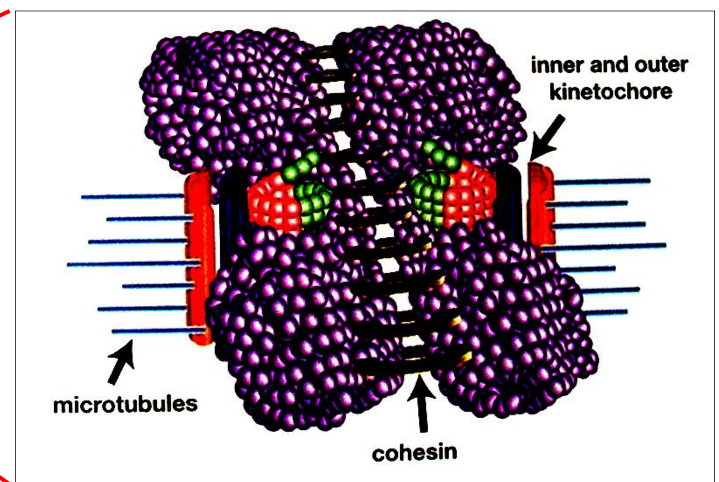
- <u>dicentric</u> chromosomes usuallly unstable (anaphase bridges >> breakage), one centromere has to be inactivated epigenetically (cf. dicentric Robertsonian fusions)

- <u>acentric</u> chromosome fragments are unstable at mitosis/meiosis and lost

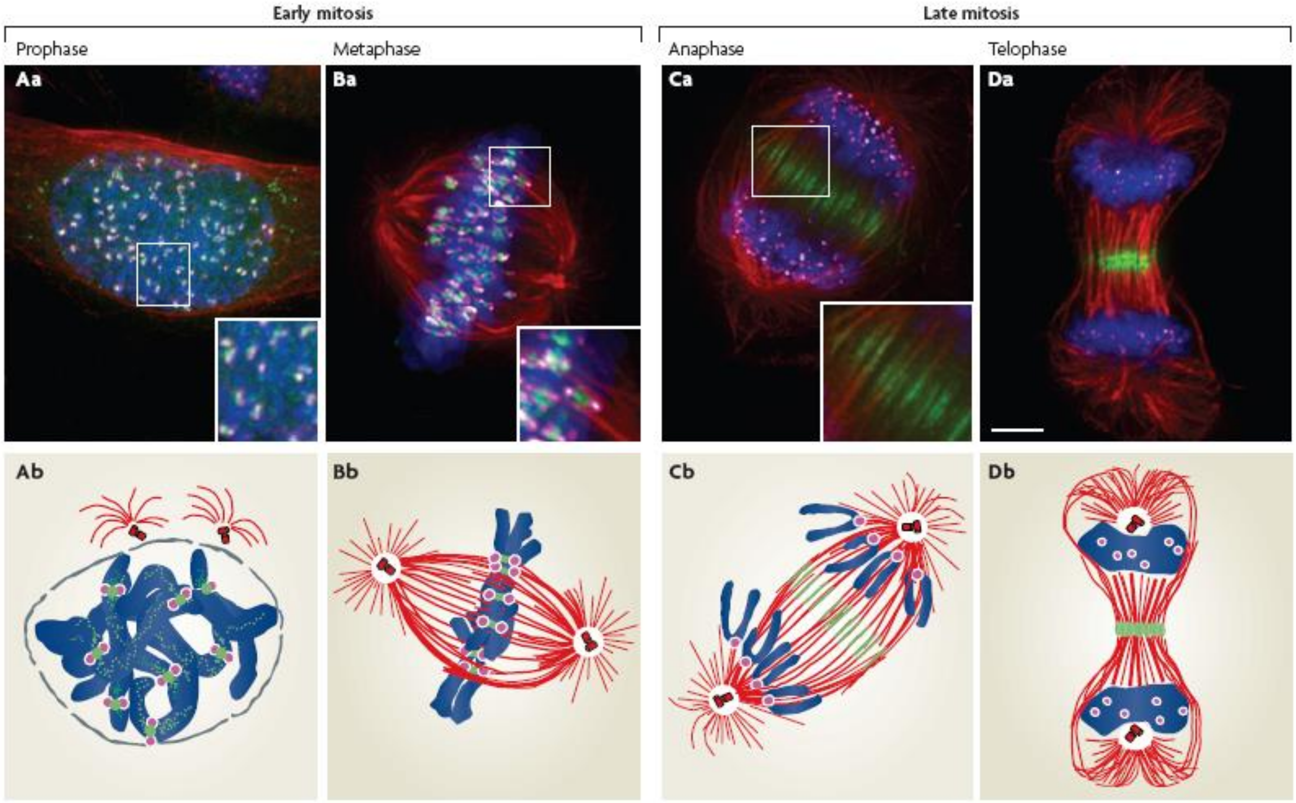
- <u>sister chromatid cohesion</u> throughout cell cycle until sister chromatid segregation at mitosis/meiosis II (centromeres enriched with cohesin)

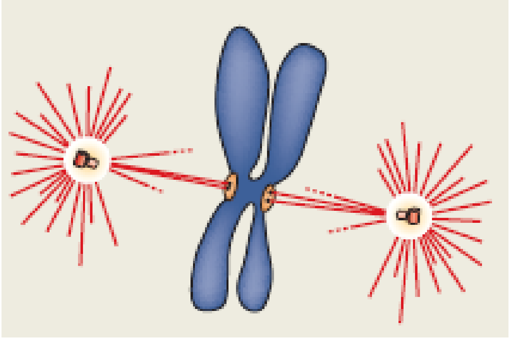
- sites of <u>kinetochore</u> formation ensuring correct chromosome position on mitotic/meiotic spindle: chromosome congression (kinetochore: spindle microtubules attached)





Centromere function: mitotic chromatid segregation

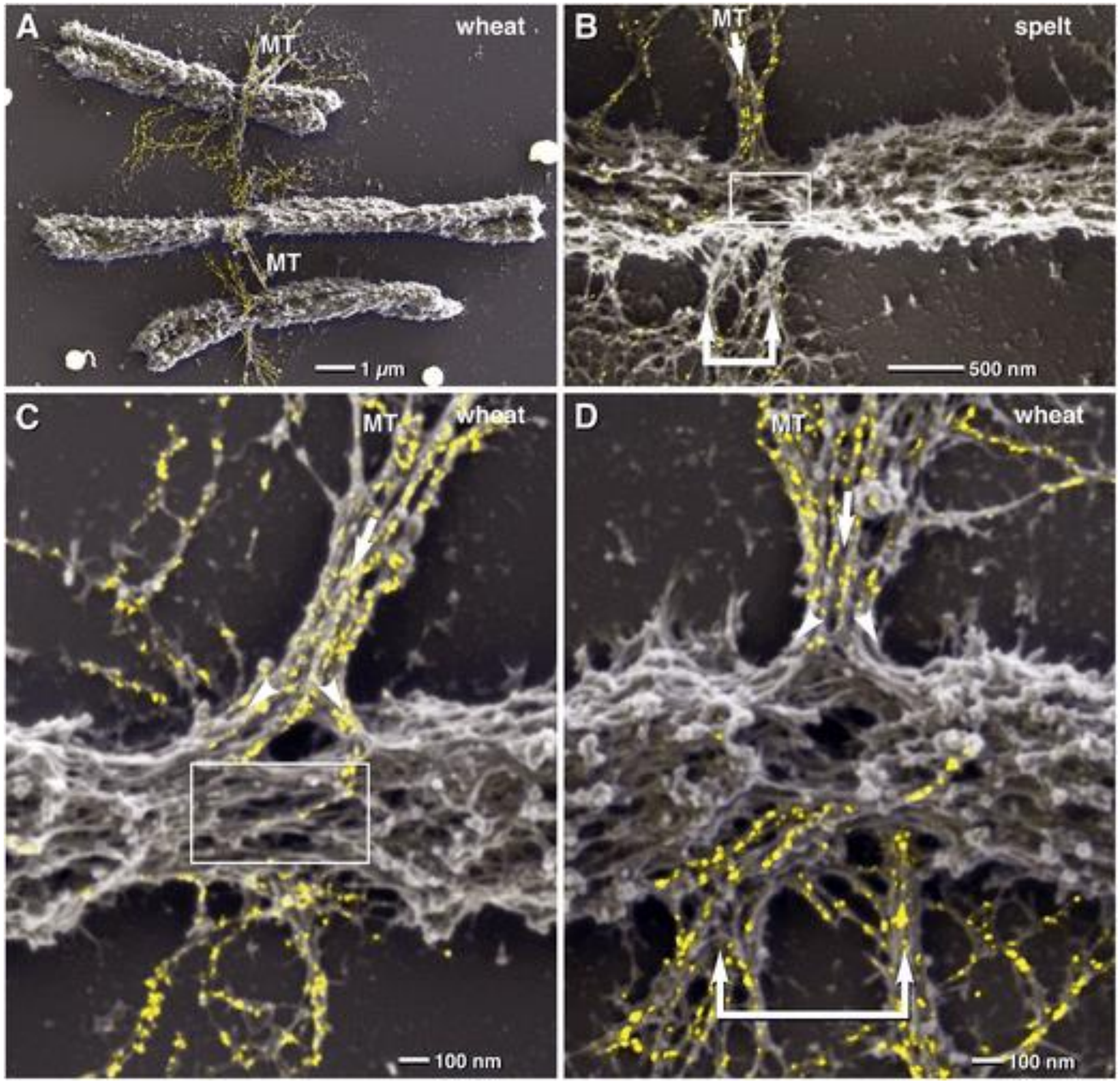




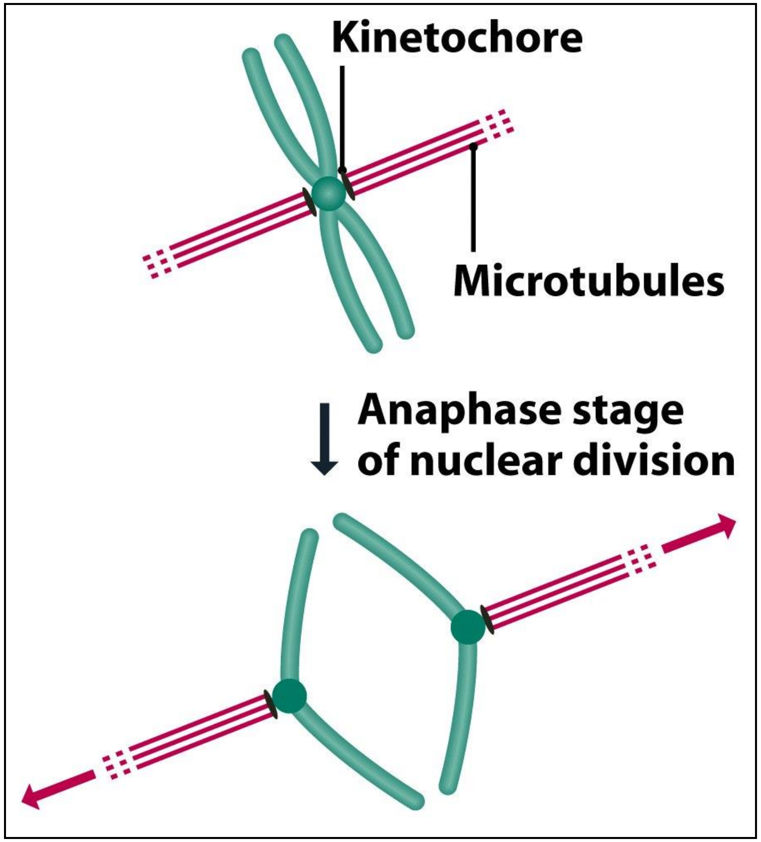
Chromosomal bi-orientation on a bipolar mitotic spindle

Accurate chromosome segregation requires that kinetochores from each sister chromatid bind microtubules that emanate from opposing spindle poles (amphitelic attachment). This is achieved by a process called chromosome bi-orientation. Incorrect attachments can lead to improper chromosome segregation and aneuploidy.

Centromeres and microtubules (monocentric chromosomes)



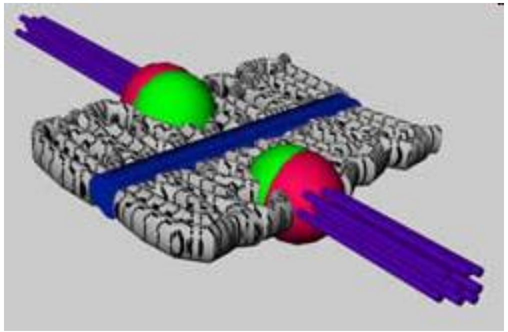
Wanner et al. (2015) Chromosoma



Kinetochore

inner kinetochore - associated with the centromere DNA; specialized form of chromatin persistent throughout the cell cycle

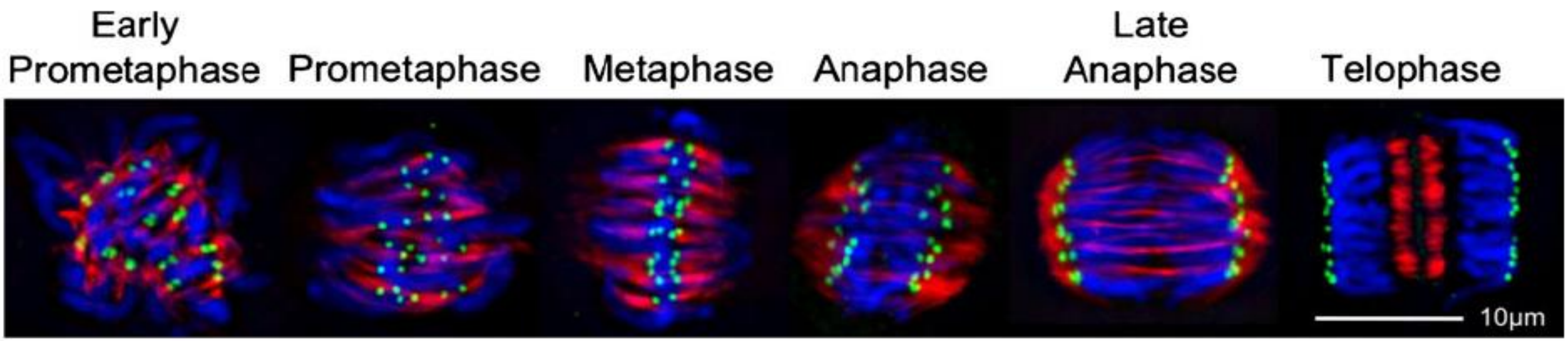
outer kinetochore - interacting with microtubules; functional only during cell division.



Even the simplest kinetochores consist of more than 45 different proteins!
Many conserved between eukaryotic species, including a specialized histone H3 variant (called CENP-A or CenH3) which helps the kinetochore associate with DNA.

Kinetochore

Mitosis in barley (immunofluorescence)

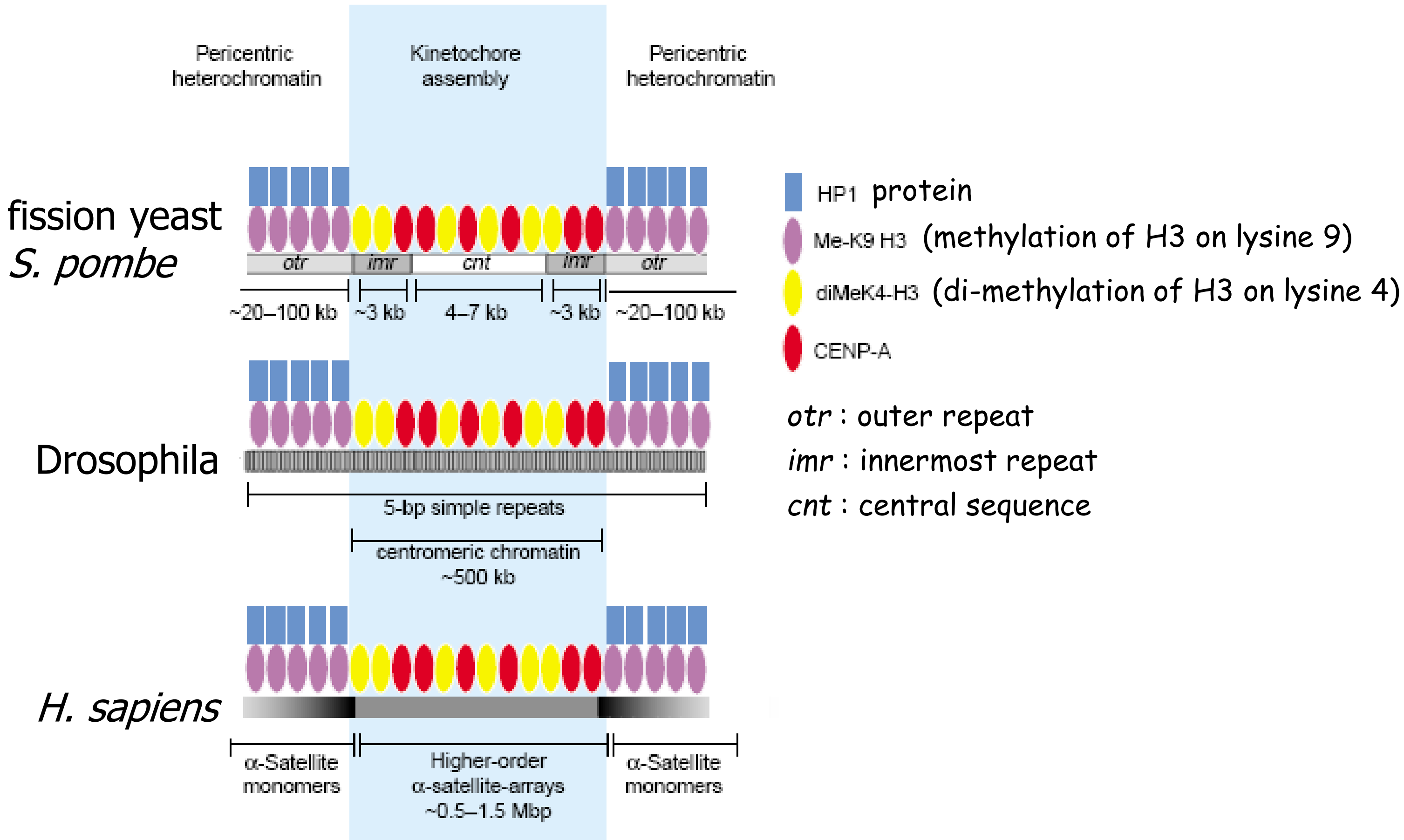


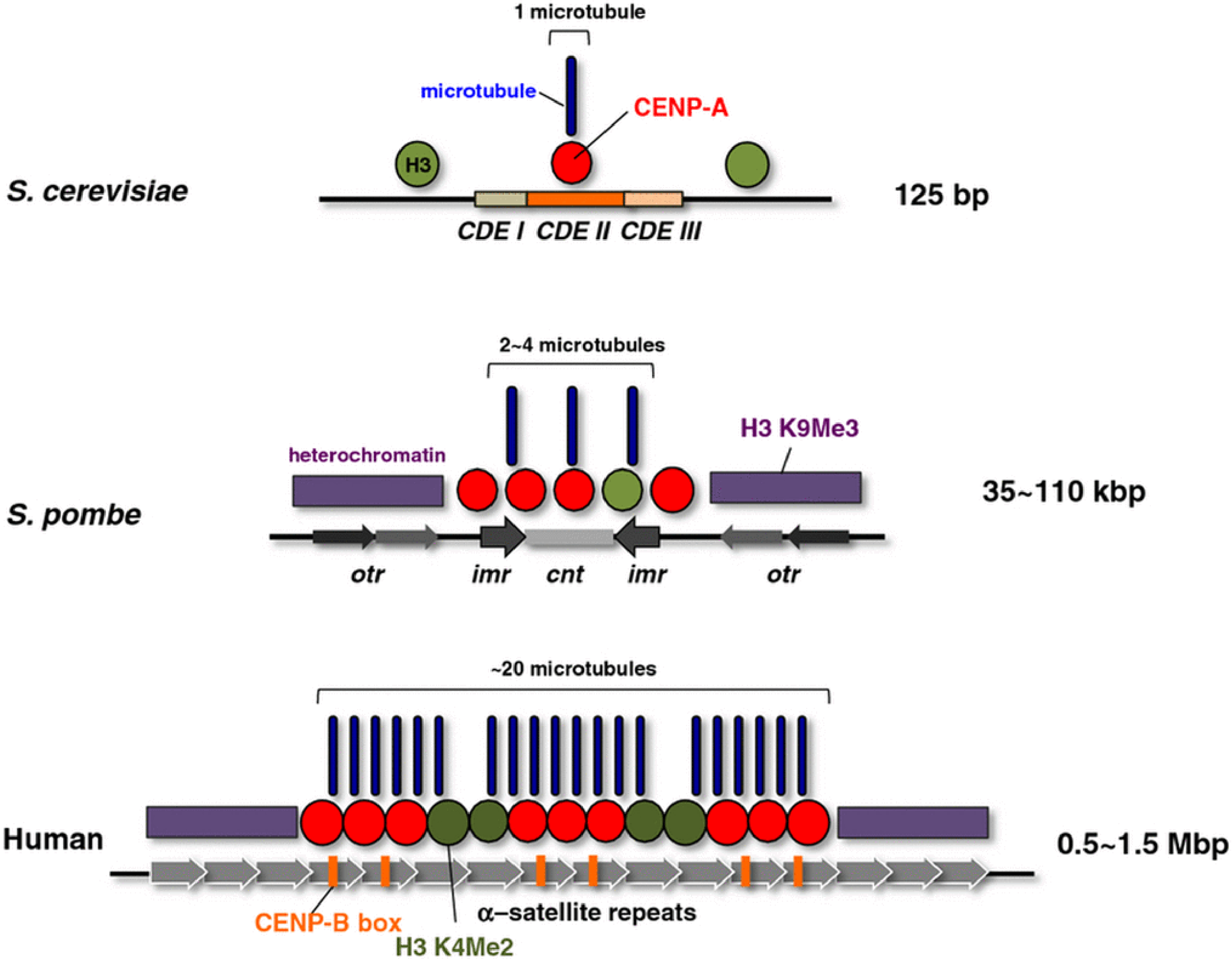
Microtubules (tubulin)
CENH3 (an inner kinetochore protein)
Chromosomes

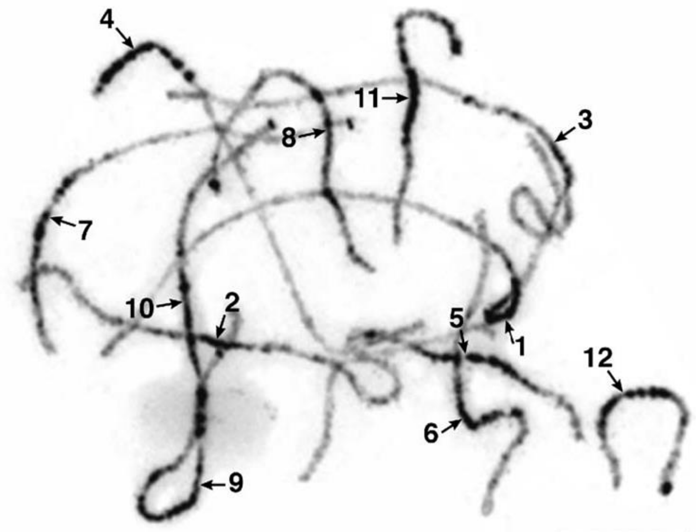
Microtubules interact with kinetochores even in the earliest stages of prometaphase (immediately following nuclear envelope breakdown).

Zhang and Dawe (2011) Mechanisms of plant spindle formation

The overall chromatin structure of the centromere is conserved among different species



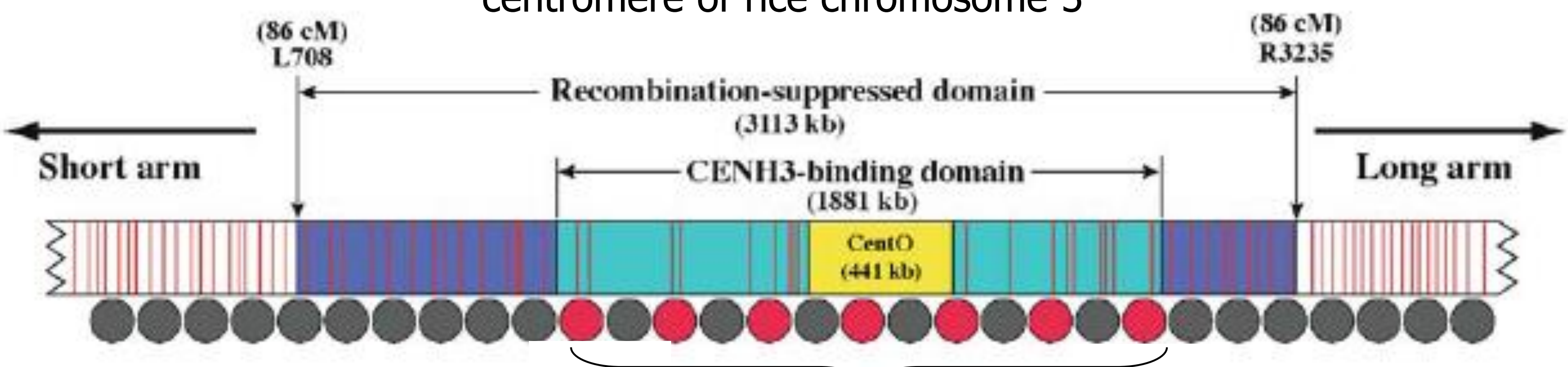

1 microtubule
microtubule
CENP-A
H3
S. cerevisiae
125 bp
CDE I
CDE II
CDE III
2~4 microtubules
heterochromatin
H3 K9Me3
S. pombe
35~110 kbp
otr
imr
cnt
imr
otr
~20 microtubules
Human
0.5~1.5 Mbp
CENP-B box
α–satellite repeats
H3 K4Me2



Structure of plant centromeres

In monocentric chromosomes, the centromere is characterized by a single CenH3-containing region within a morphologically distinct primary constriction. This region usually spans up to a few Mbp composed mainly of centromere-specific satellite DNA.

centromere of rice chromosome 3

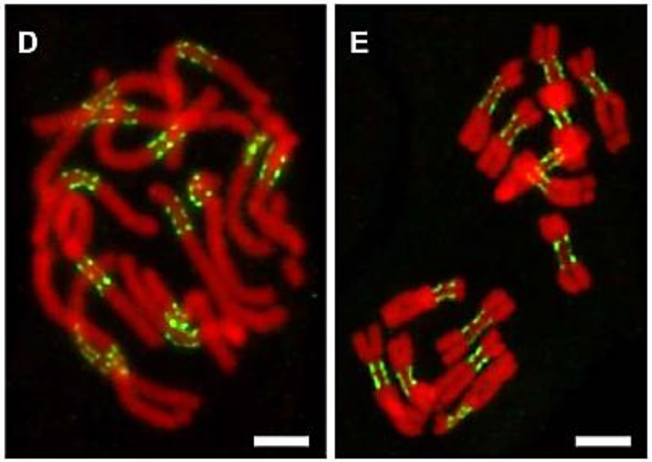


The CENH3-binding domain contains active genes (red bars), but with a lower density than the flanking domains.

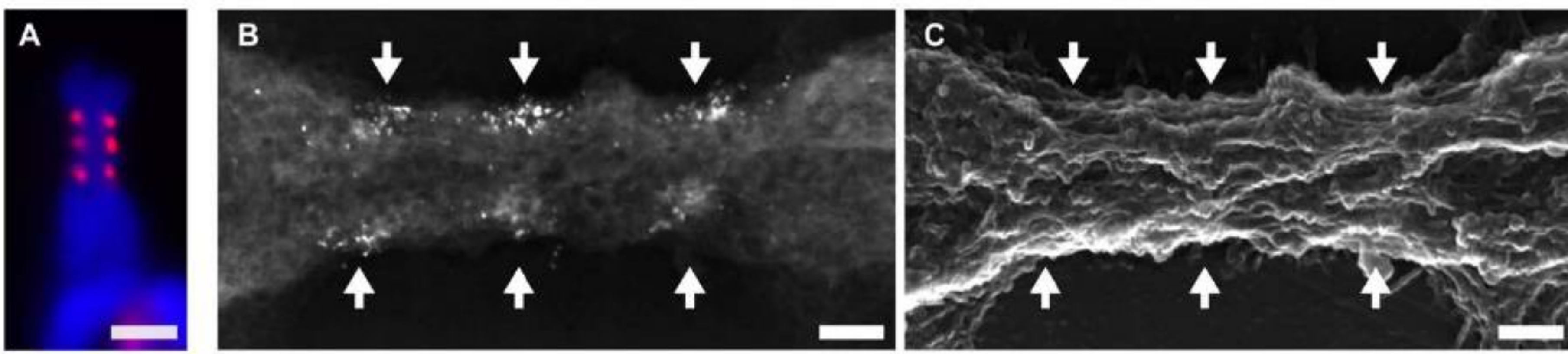
CENH3 (CENP-A)-associated and H3-associated nucleosomes

Rice centromeres contain a satellite repeat CentO and centromere-specific retrotransposon CRR.

Pea: monocentric chromosomes with multiple centromere domains

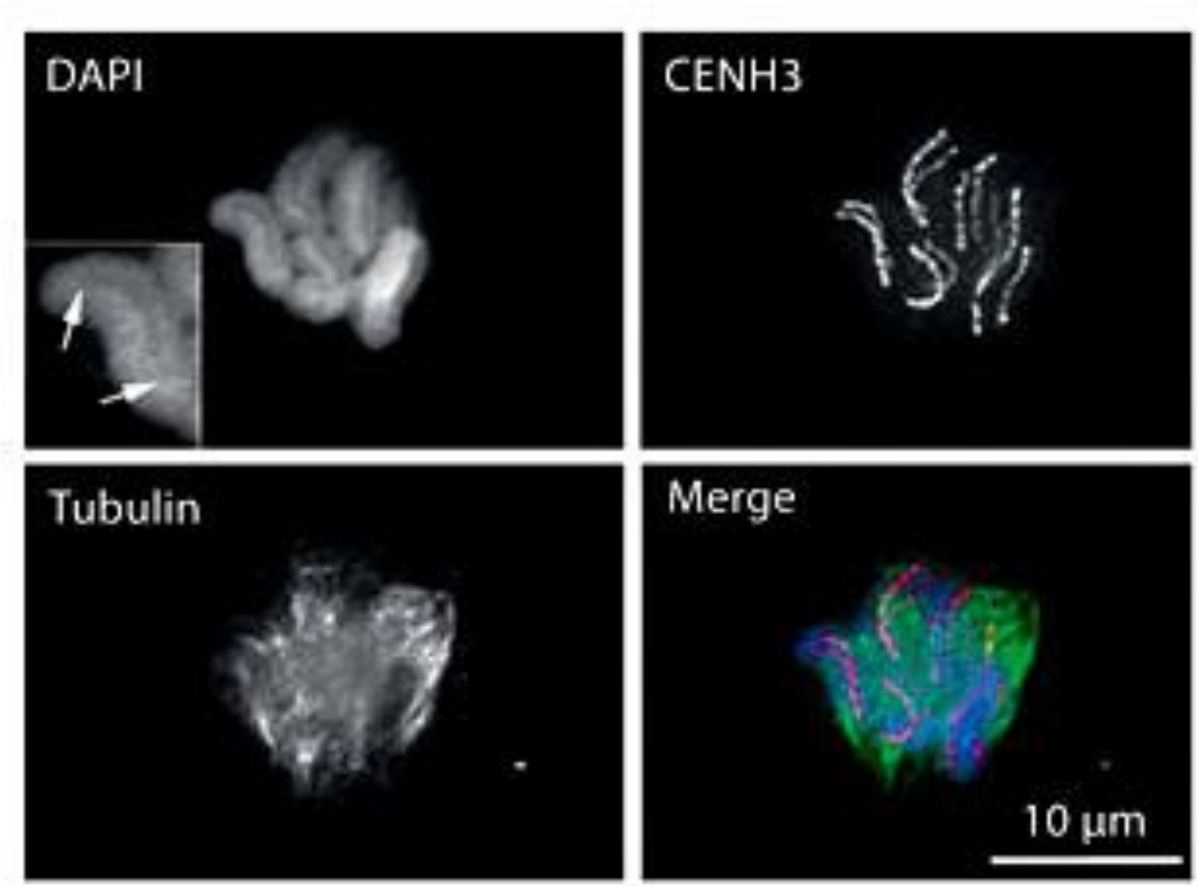


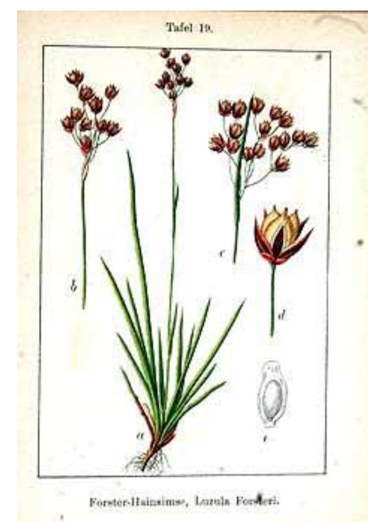
- long primary constrictions that contain 3–5 explicit CenH3-containing regions
- the size of the chromosome segment delimited by two outermost domains varies between 69 Mbp and 107 Mbp (several factors larger than any known centromere length)
- 13 distinct families of satellite DNA and one family of centromeric retrotransposons (unevenly distributed among pea chromosomes)



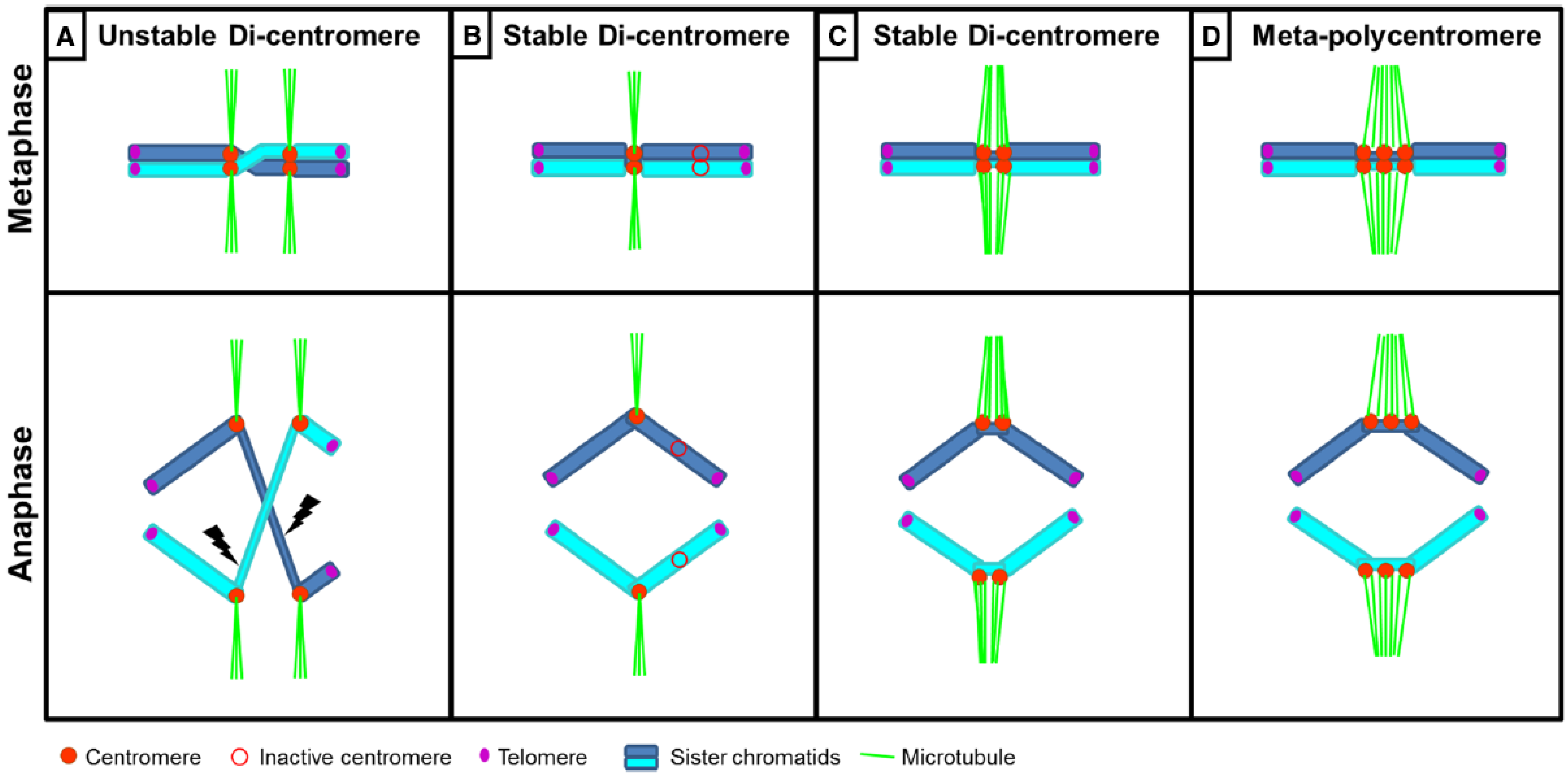
Neumann et al. (2012) PLoS Genet

Holokinetic Chromosomes Do Not Possess a Localized Centromere





Chromosomes with more than one centromere: consequences and solution

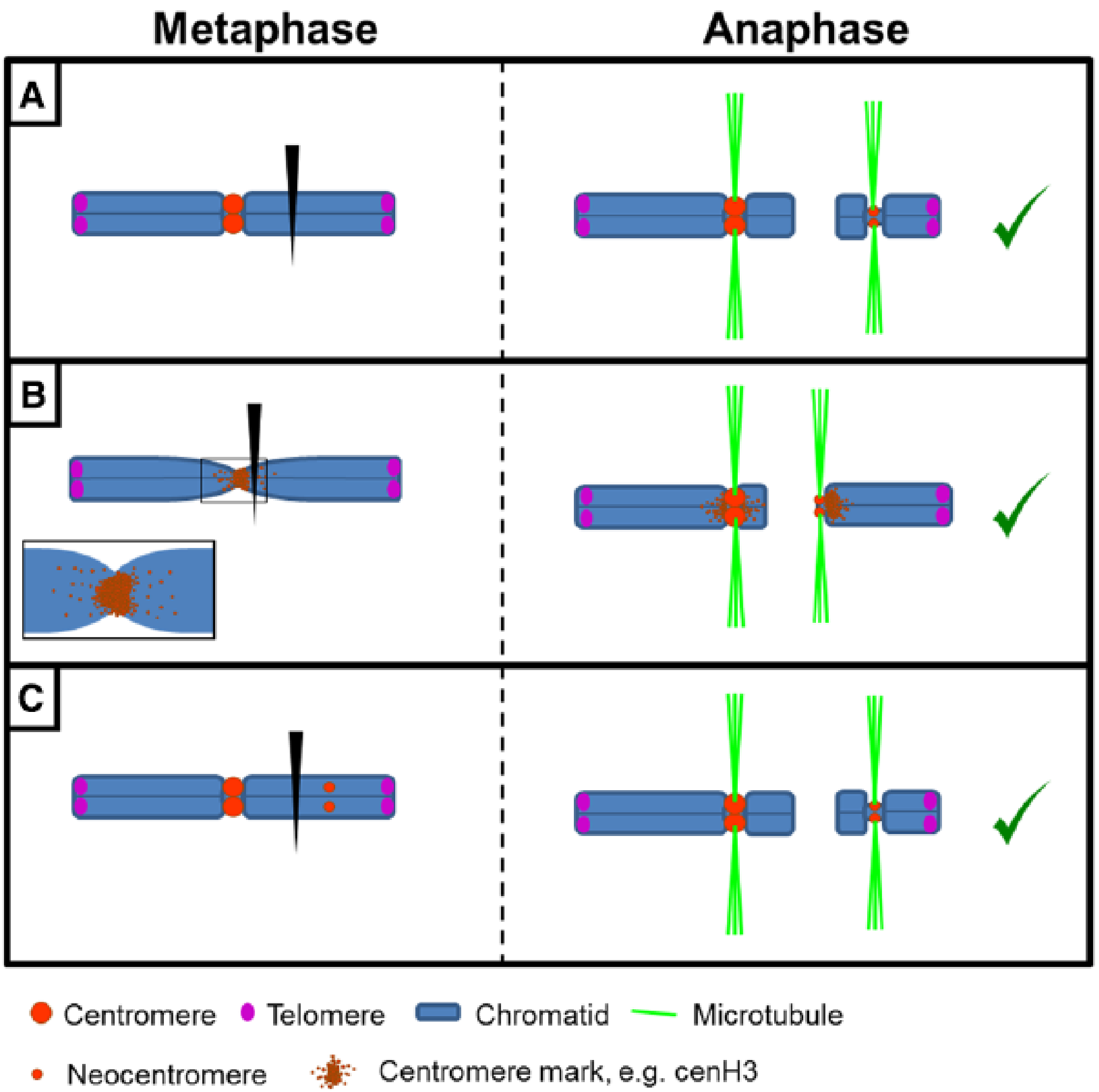


Neocentromeres

Two meanings in literature:

- a de novo centromere formation occurring after chromosome breakage or endogenous centromere inactivation
- kinetic motility of terminal or subterminal heterochromatin, which is pulled to the cell poles during meiosis in plants (heterochromatic knobs)

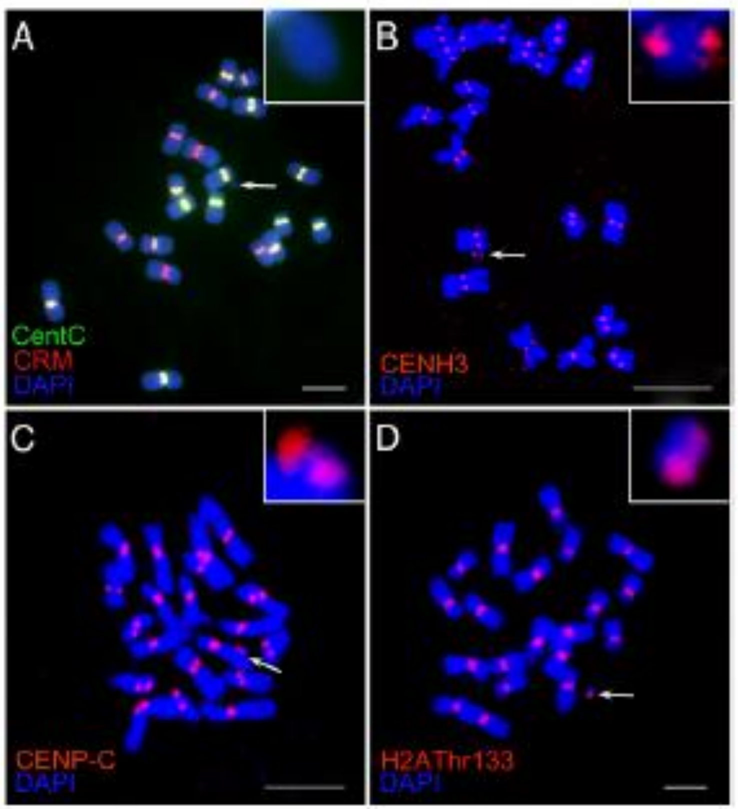
Formation and behavior of de novo centromeres



PNAS 2013

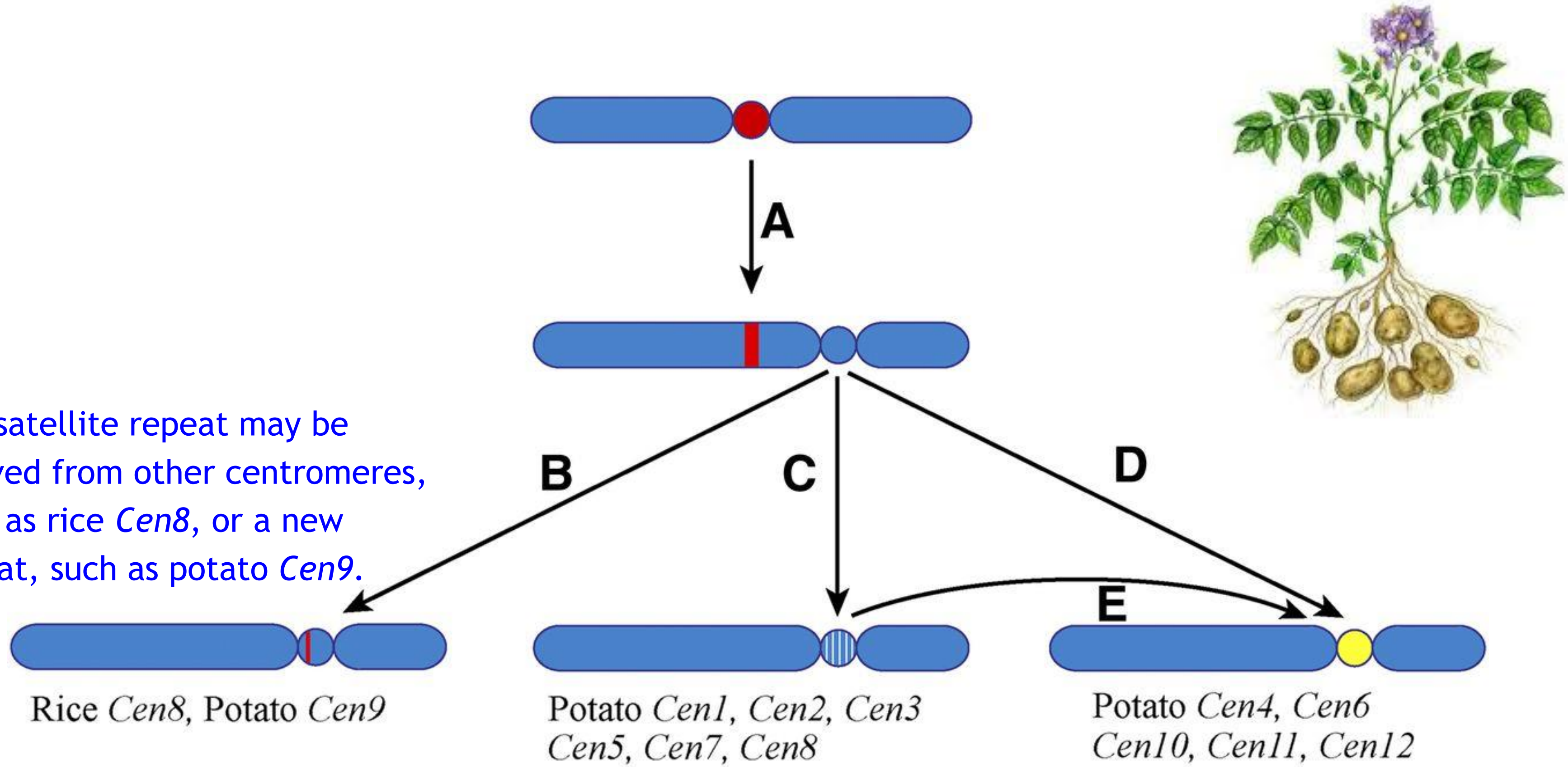
De novo centromere formation on a chromosome fragment in maize

Shulan Fu[a,1], Zhenling Lv[a,1], Zhi Gao[b,1], Huajun Wu[c], Junling Pang[c], Bing Zhang[a], Qianhua Dong[a], Xiang Guo[a], Xiu-Jie Wang[c], James A. Birchler[b,2], and Fangpu Han[a,2]



The small chromosome has no detectable canonical centromeric sequences, but contains a site with protein features of functional centromeres such as CENH3, the centromere specific H3 histone variant, and CENP-C, a foundational kinetochore protein, suggesting the de novo formation of a centromere on the chromatin fragment.

A Model of Centromere Evolution



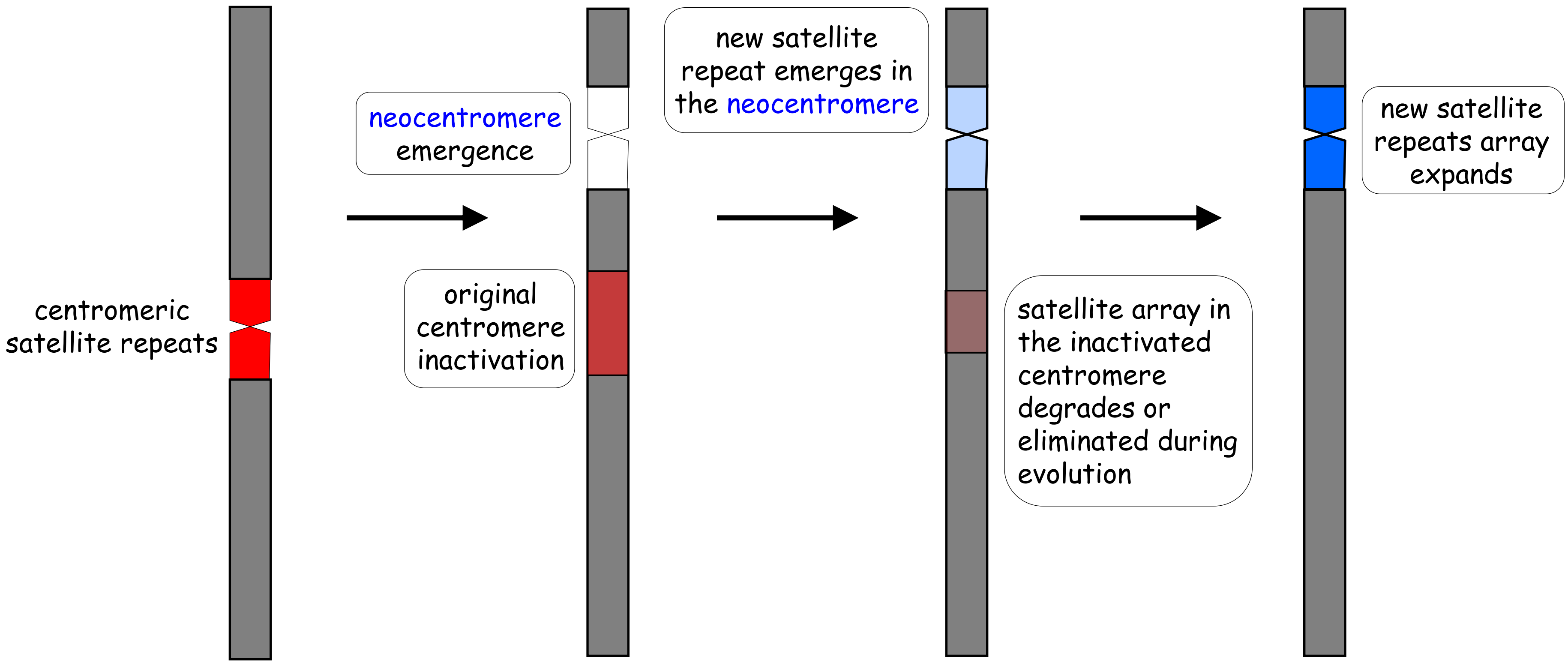
The satellite repeat may be derived from other centromeres, such as rice *Cen8*, or a new repeat, such as potato *Cen9*.

Centromeres may survive for several million years without satellite repeat invasion (slow evolution through DNA mutations and accumulation of transposable elements).

A de novo DNA amplification of a satellite repeat, possibly based on an eccDNA-mediated mechanism, and insertion of the repeat (yellow) in the CENH3 domain can turn an evolutionarily new centromere into a repeat-based centromere.

Gong Z et al. Plant Cell (2012)

A model of neocentromere-mediated centromere evolution in plants (rice)



Centromere repositioning in curbit species

- centromere repositioning (CR) extensively documented in mammalian species (e.g. 5 CRs in the donkey after its divergence from zebra)

- scarce reports on CR in other eukaryots including plants

- centromeres of cucumber and melon chromosomes are associated with distinct pericentromeric heterochromatin

Cucumis melo
2n = 24

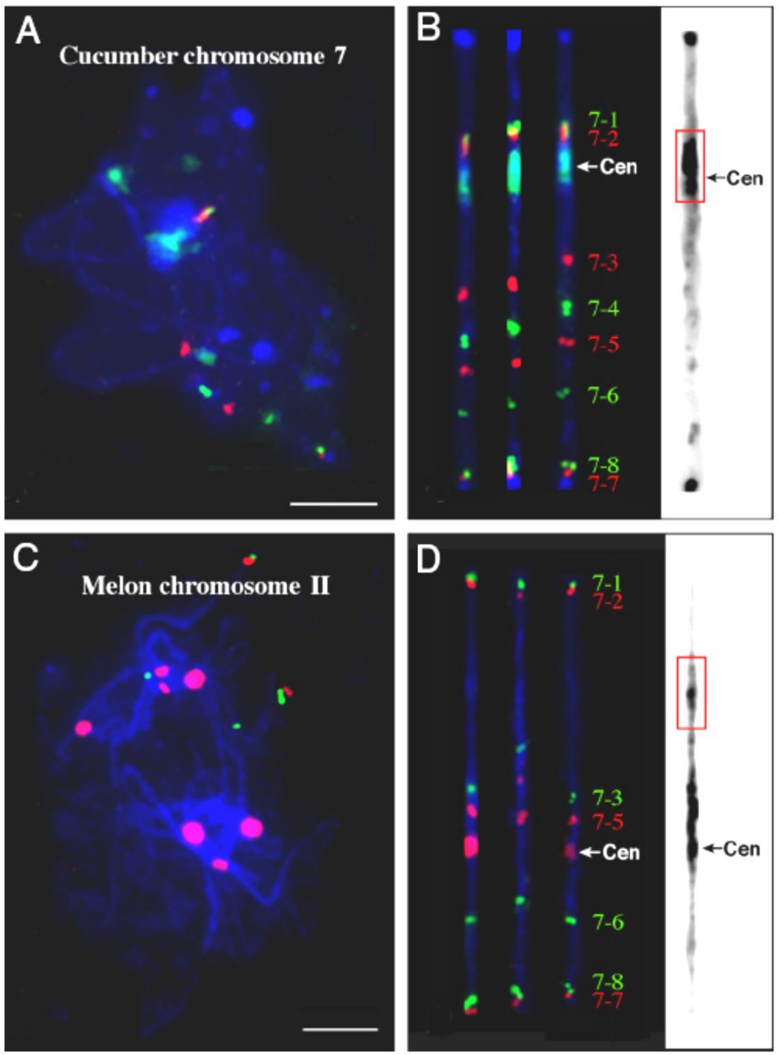
- centromere activation or inactivation were associated with a gain or loss of a large amount of pericentromeric heterochromatin

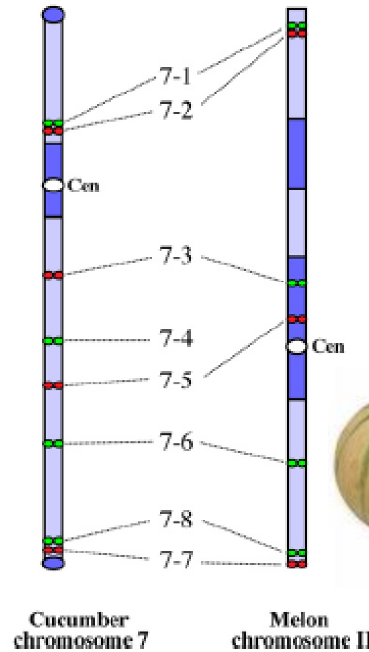
Cucumis sativus
2n = 14

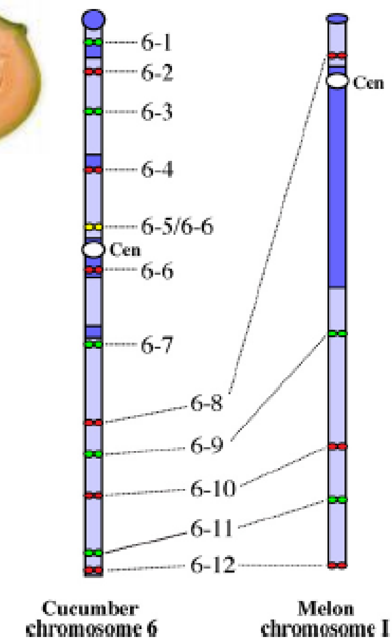
Centromere repositioning in curbit species

Cross-species fosmid FISH in cucumber and melon (*Cucurbitaceae*)

Fosmids (40 kb) are based on the bacterial F-plasmid. The cloning vector is limited, as a host (usually *E. coli*) can only contain one fosmid molecule. Low copy number offers higher stability than comparable high copy number cosmids.

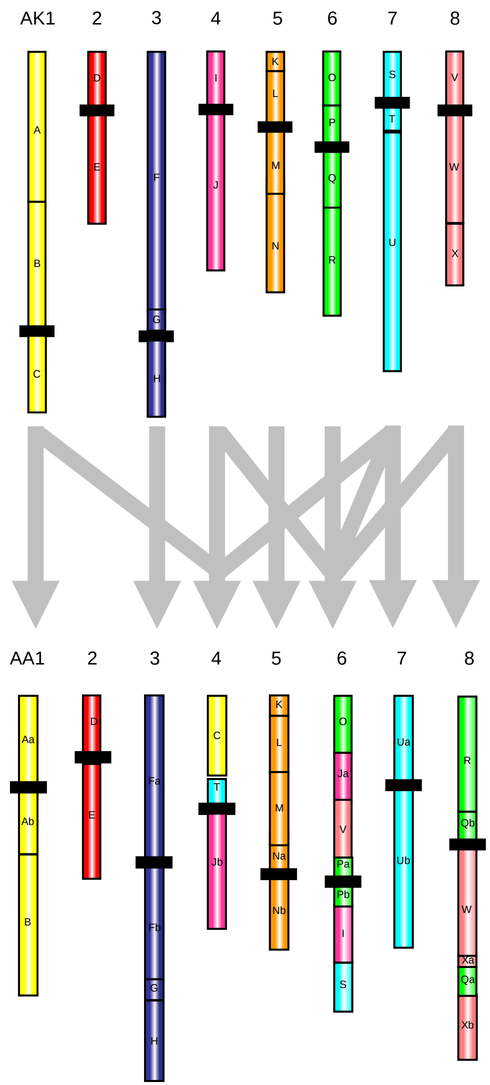






Han et al. 2009, *PNAS* 106

Arabis alpina - centromere repositioning



5 reciprocal translocations

4 pericentric inversions

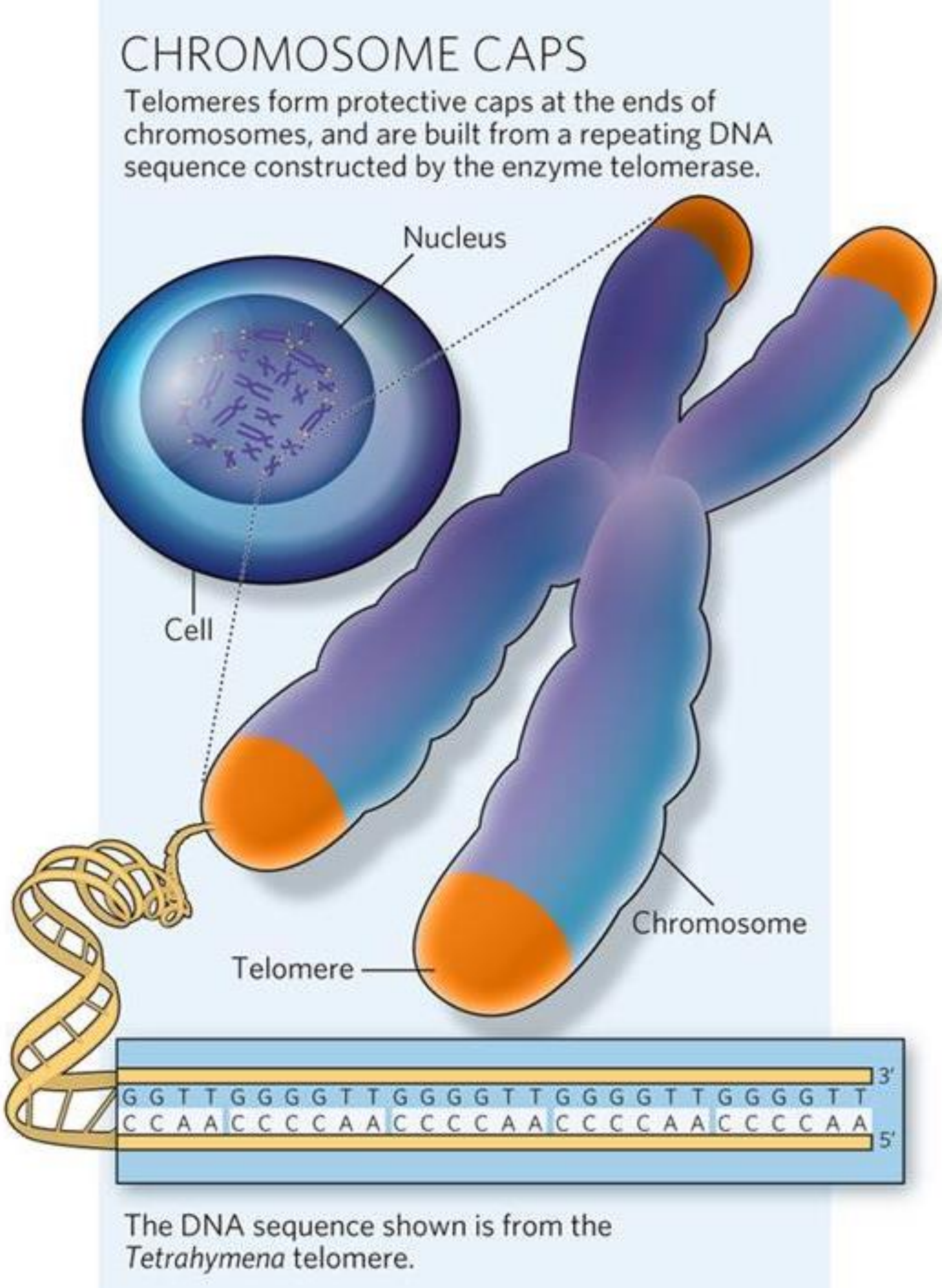
3 centromere repositions

1 centromere loss

1 new centromere emergence (?)

Willing et al., Nature Plants 2015

Telomeres



CHROMOSOME CAPS
Telomeres form protective caps at the ends of chromosomes, and are built from a repeating DNA sequence constructed by the enzyme telomerase.
Nucleus
Cell
Chromosome
Telomere
3'
G G T T G G G G T T G G G G T T G G G G T T G G G G T T
C C A A C C C C A A C C C C A A C C C C A A C C C C A A
5'
The DNA sequence shown is from the *Tetrahymena* telomere.

Telomeres

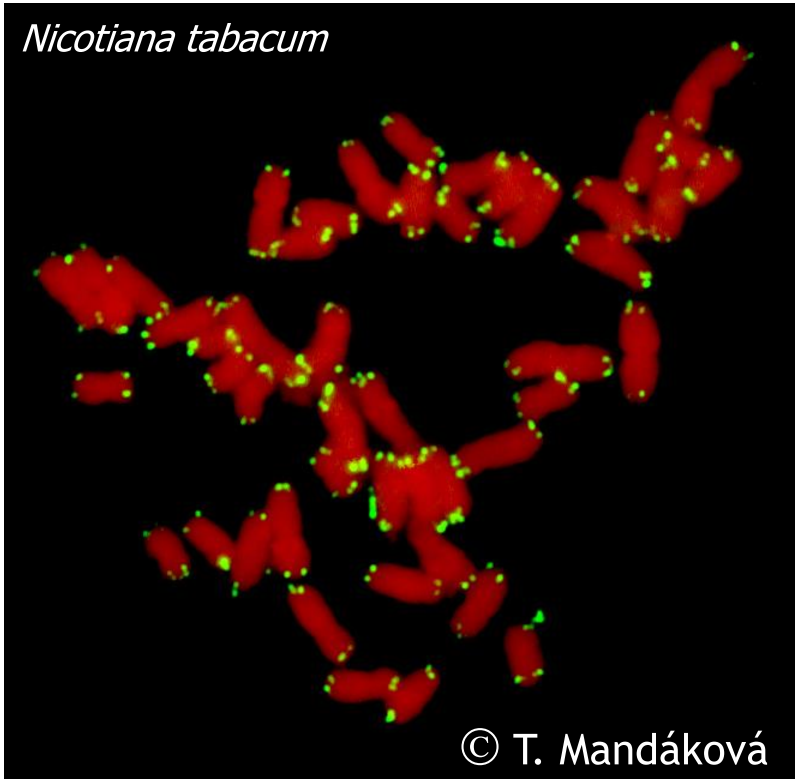
Elizabeth H. Blackburn

Carol W. Greider

Jack W. Szostak

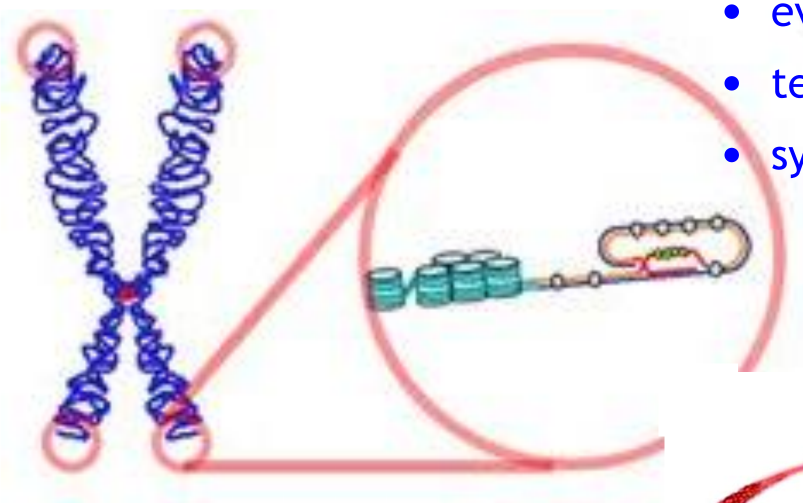
The Nobel Prize in Physiology or Medicine 2009 was awarded jointly to Elizabeth H. Blackburn, Carol W. Greider and Jack W. Szostak ***"for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase".***

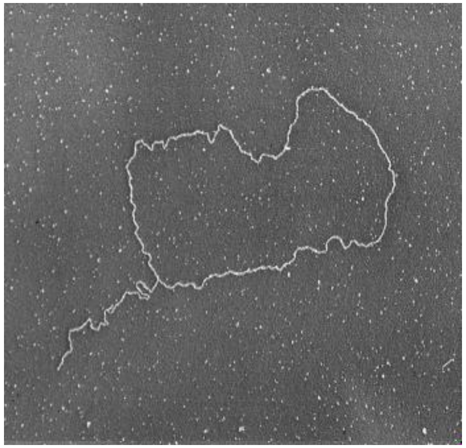
Telomeres

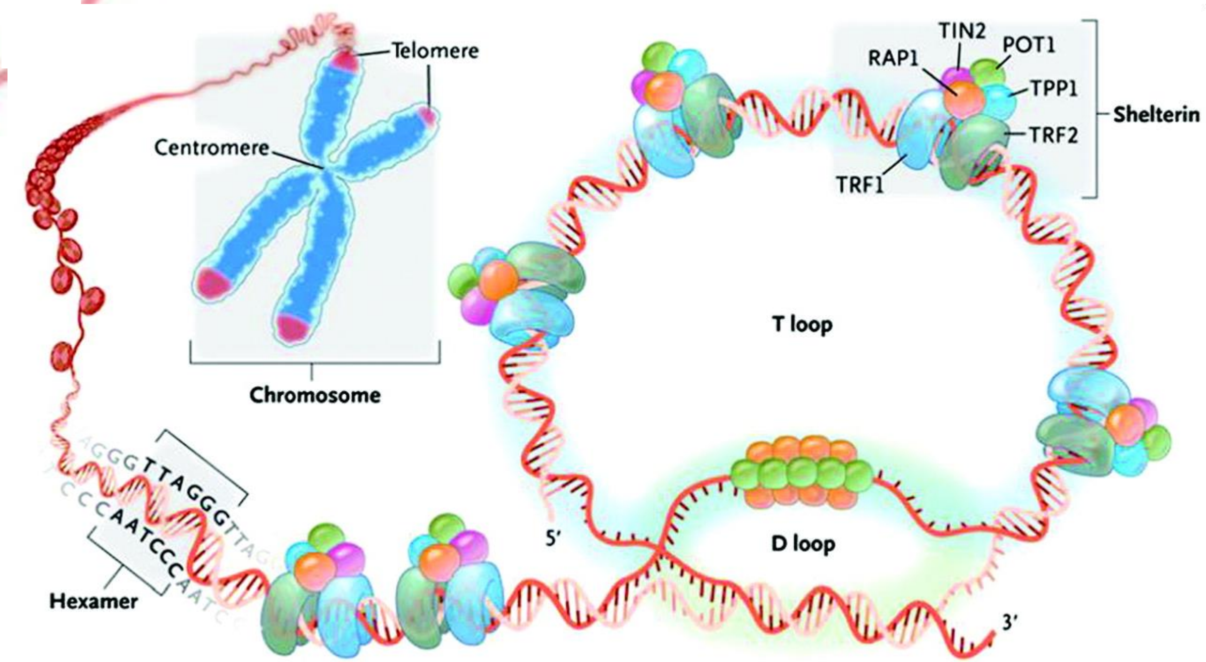


Keywords on telomeres

- solving chromosome shortening (loss of DNA sequences)
- protects against DNA repair (repair of double-strands)
- evolutionary conserved telomeric repeats
- telomere-binding proteins (shelterin complex)
- synthesis by the telomerase enzyme

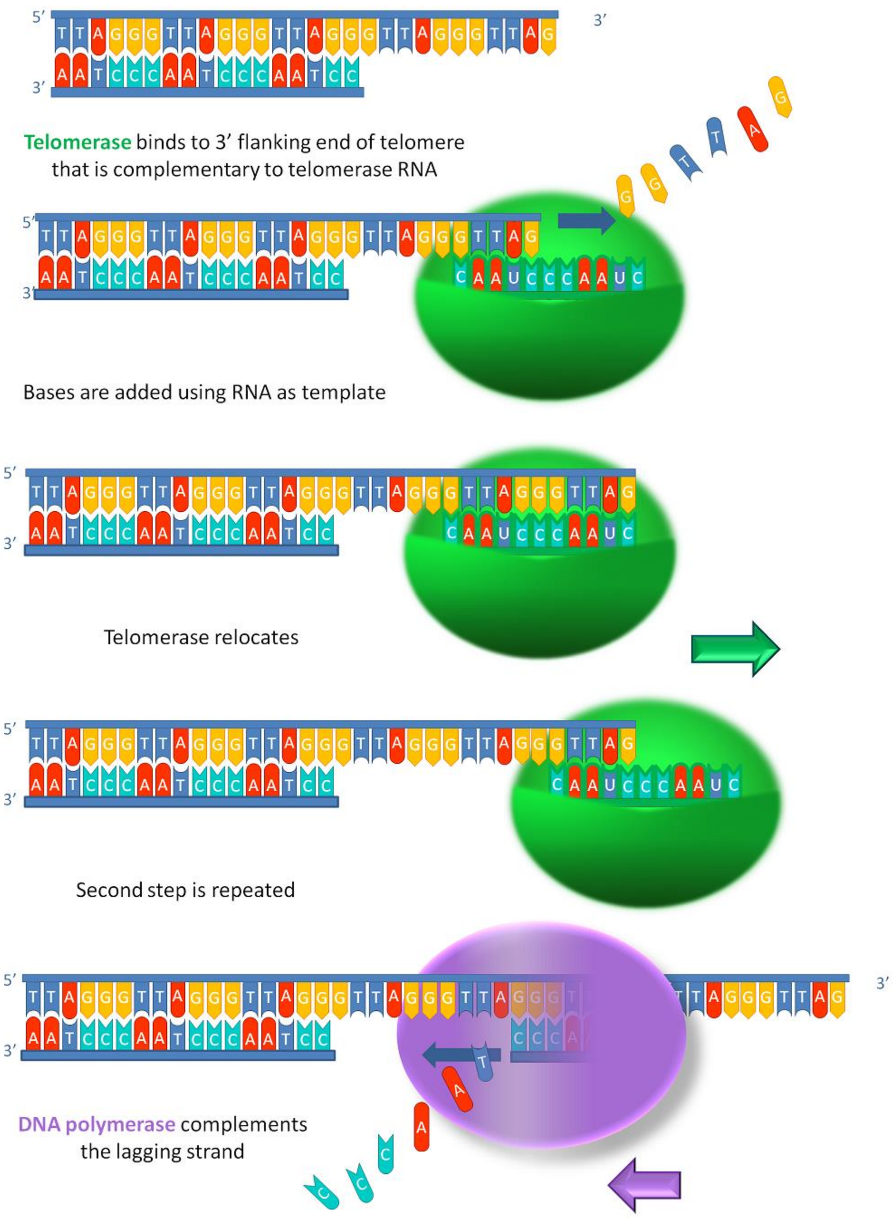






Telomeres are made by telomerase

- ribonucleoprotein, enzyme
- adds telomeric repeats (e.g. TTAGGG in all vertebrates) to the 3‘ end of DNA strands at the ends of eukaryotic chromosomes
- preventing constant loss of DNA sequences from chromosome ends
- composed of own RNA and reverse transcriptase (TERT)

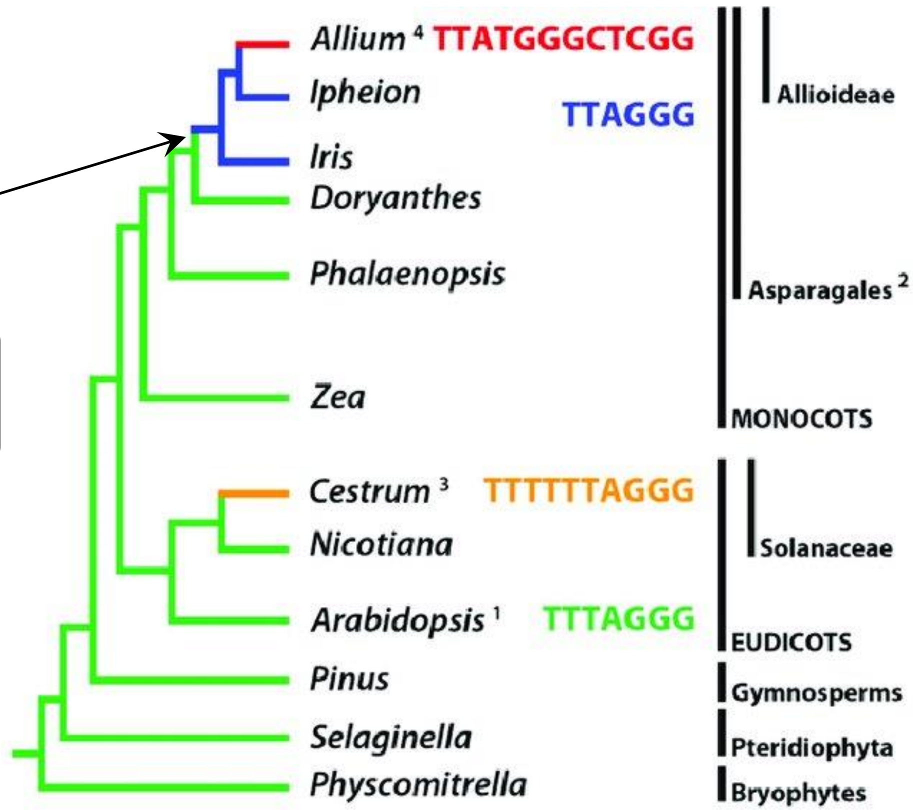


Telomeres of plants

Sequences of telomere repeats

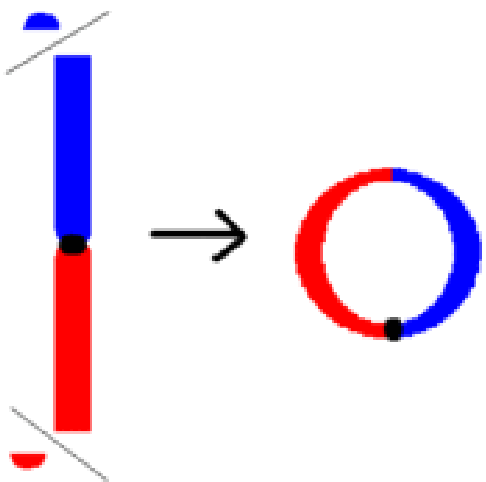
human	TTAGGG
Tetrahymena	TTGGGG
Arabidopsis	TTTAGGG

mutation altering the RNA template subunit of telomerase, c. 80 million years ago



Telomeres – when something goes wrong

telomere dysfunction → ring chromosomes



Wikipedia:

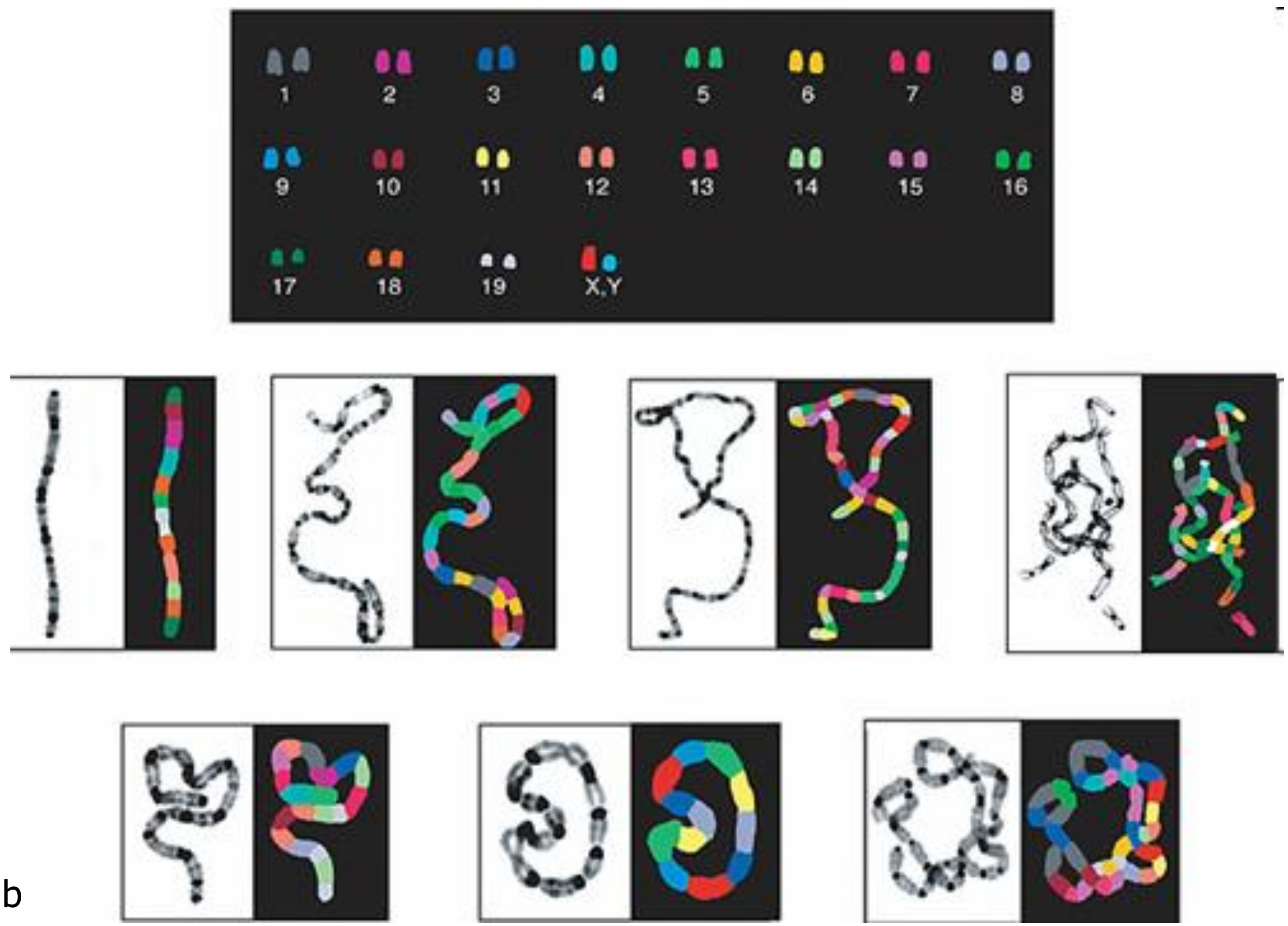
Human genetic disorders can be caused by spontaneous ring chromosome formation; although ring chromosomes are very rare, they have been found in nearly all human chromosomes.

Disorders arising from the formation of a ring chromosome include **ring chromosome 20 syndrome** where a ring formed by one copy of chromosome 20 is associated with **epilepsy**; ring chromosome 14 and ring chromosome 13 syndrome are associated with **mental retardation** and **dysmorphic facial features**; ring chromosome 15 is associated with mental retardation, **dwarfism** and **microcephaly**. Ring formation of an X-chromosome causes **Turner syndrome**.

Symptoms seen in patients carrying ring chromosomes are more likely to be caused by the deletion of genes in the telomeric regions of affected chromosomes, rather than by the formation of a ring structure itself.

Telomeres – when something goes wrong

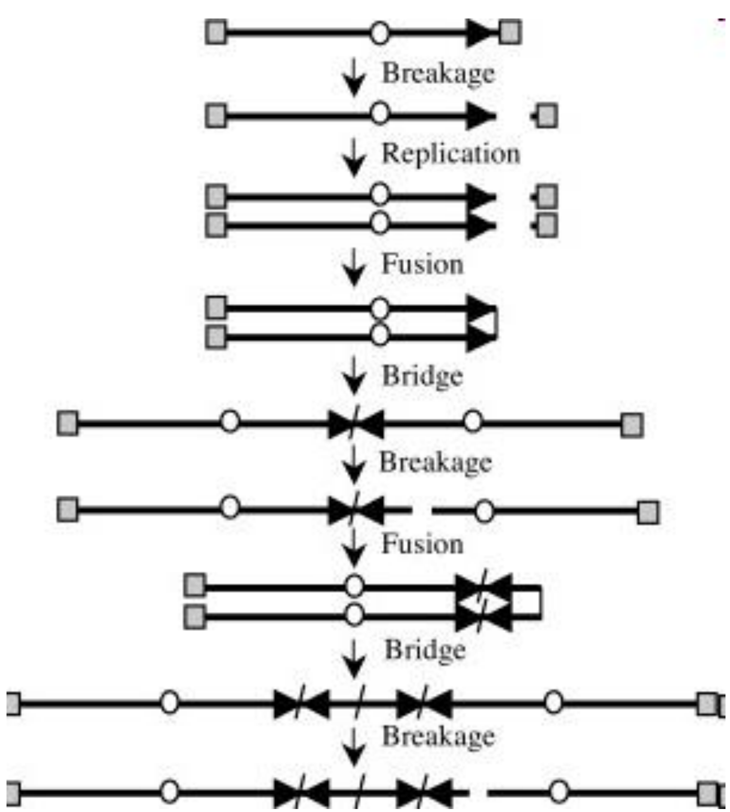
In the absence of a protein protecting telomeres, chromosomes fuse abnormally



data from the T. De Lange lab

Telomeres – when something goes wrong

Breakage-fusion-bridge cycle



The telomeres (gray squares), centromeres (circles), subtelomeric sequences (horizontal arrows)

1. telomere dysfunction
2. sister chromatid fusion (2 centromeres)
3. bridge during anaphase
4. breakage
   (breakage occurs at locations other than the site of fusion, resulting in large inverted repeats on the end of the chromosome in one daughter cell and a terminal deletion on the end of the chromosome in the other daughter cell)
5. fusion, bridge, breakage,…

… the B/F/B cycles will continue until the chromosome acquires a new telomere, most often by translocation

Murnane JP (2012) Telomere dysfunction and chromosome instability

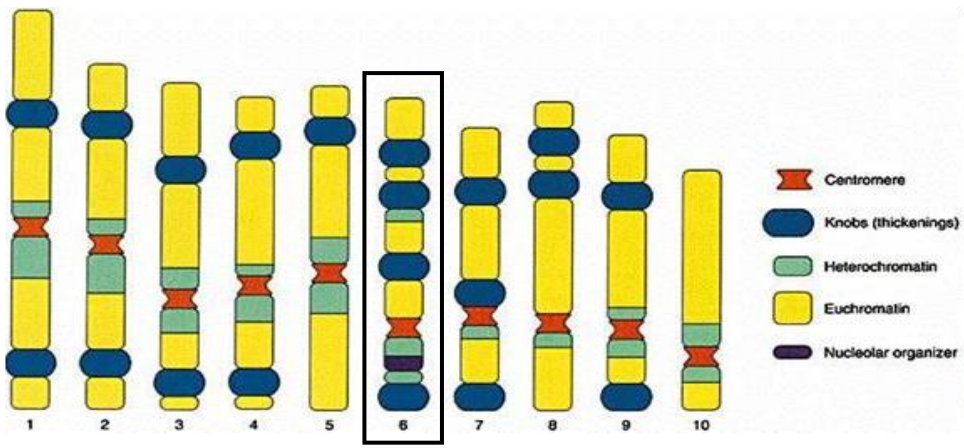
rDNA loci on chromosomes

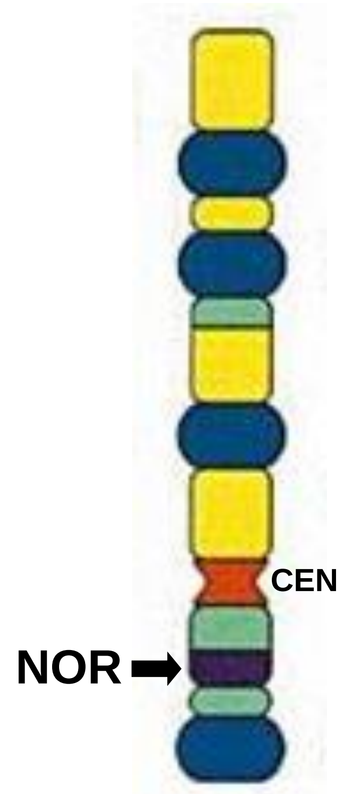
rDNA = ribosomal DNA = *genes coding* ribosomal RNAs

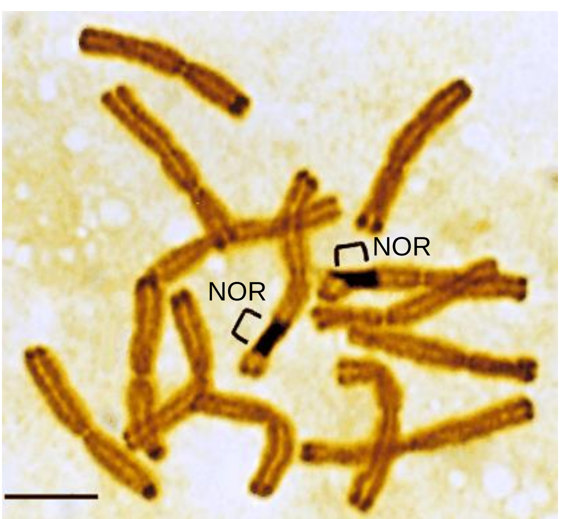
- routinely detected by FISH
- diagnostic value, position and the number usually species-specific
- 45S rDNA usually in different position on chromosome(s) than 5S rDNA
- 45S formed at nucleolar organizing regions (NORs) associated with nucleolus

Physical mapping of 45S rDNA (red) and 5S rDNA (green) to metaphase chromosomes of *Larix leptolepis*. Chromosomes counterstained with DAPI (blue) (Zhang *et al.* 2010)

Satellite (SAT) chromosomes, secondary constrictions



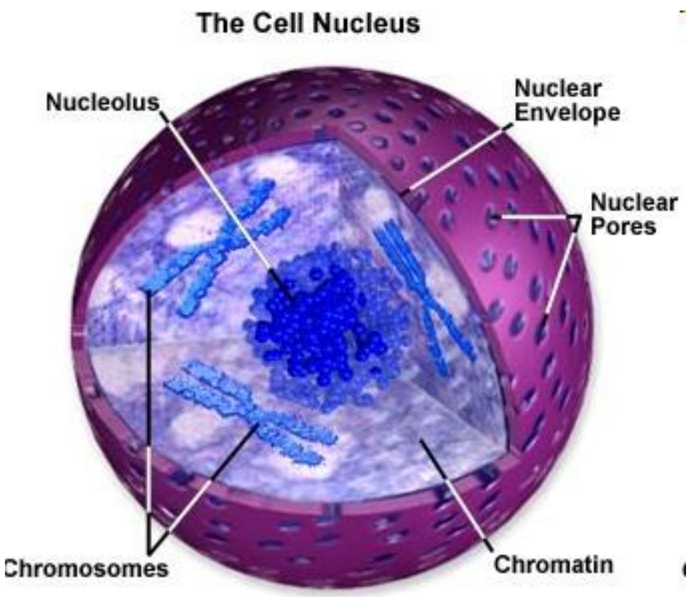




Satellites (different from satellite repeats), **satellite chromosomes**: chromosomes with nucleolar organizing region (NOR) = secondary constriction. Short chromosome part beyond the NOR is called a satellite (trabant).

SAT chromosome: *Sine Acid thymonucleinico* (without thymonucliec acid or DNA). Because of relative deficiency of DNA in the nucleolar organizing region, NORs show less intense staining.

Nucleolus



- ribosomal DNA (rDNA = rRNA genes) is transcribed and ribosomes are assembled within the nucleolus

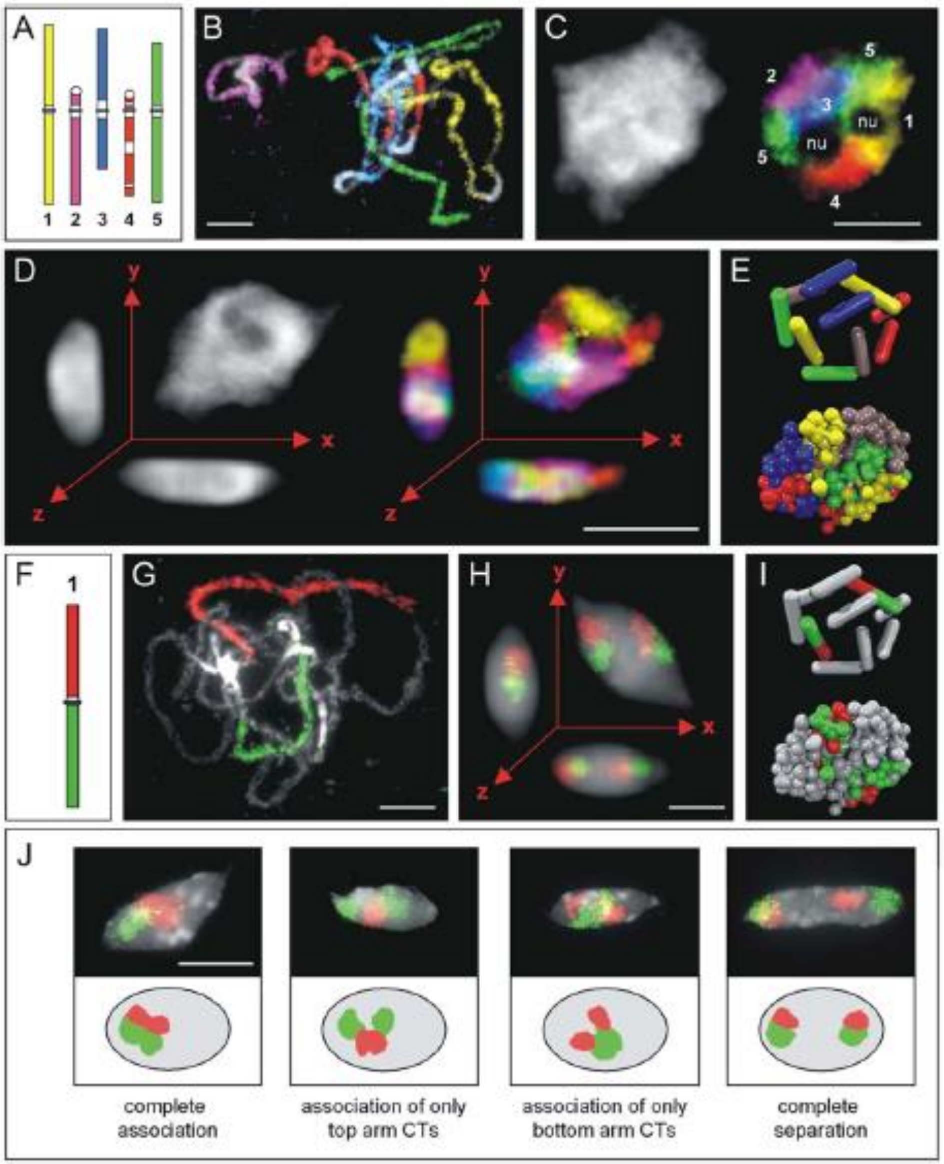
- ribosomes are exported to the cytoplasm. They remain free or associate with the endoplasmic reticulum (rough endoplasmic retictulum).

- one or several nucleoli in a nucleus

- after a cell division, a nucleolus is formed around nucleolar organizing region (NOR) on some chromosomes (chromosomes are brought together by nucleolar organizing regions)

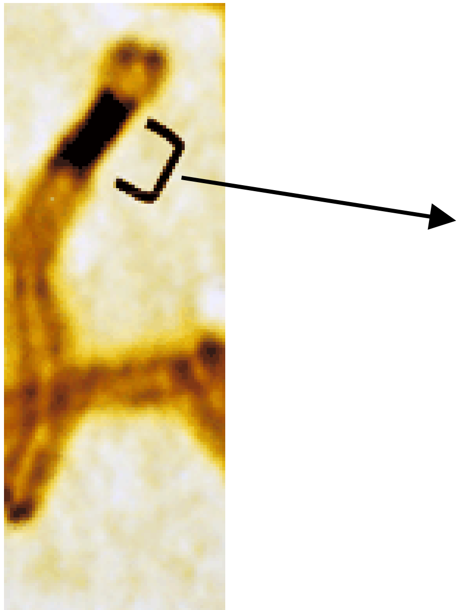
- cell division: nucleolus disappears

Chromosome territories in Arabidopsis: NOR-bearing chromosomes associated more frequently than all other chromosomes

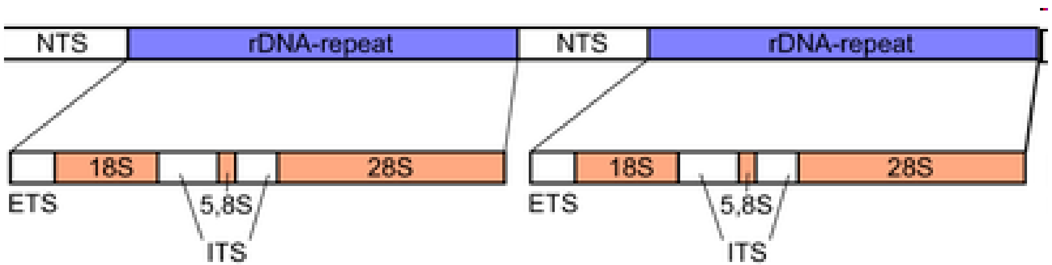


Pecinka et al. (2004) Chromosoma

45S and 5S ribosomal DNA (rDNA)



Structure of the 45S rDNA tandem repeat



18S, **5.8S**, and **28S** - genes coding **18S**, **5.8S**, and **28S** RNA molecules

NTS - nontranscribed spacer

ETS - external transcribed spacer

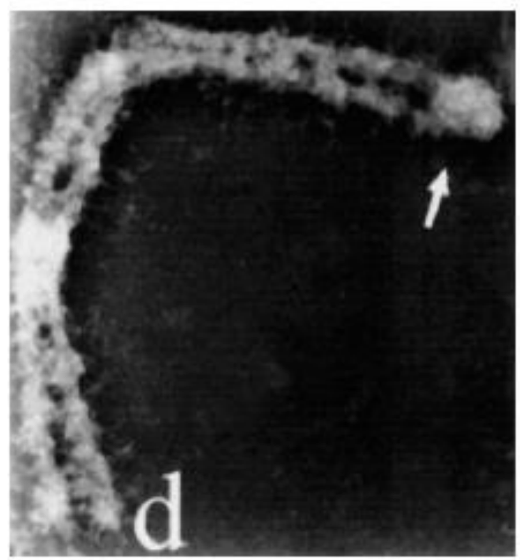
ITS - internal transcribed spacers 1 and 2

transcription of rDNA→ 45S pre-rRNA→ processing→ 18S RNA, 5.8S and 28S RNA molecules

Ribosomes – proteins and RNA molecules. In eukaryotes, small (40S) and large (60S) subunit. The 18S rRNA in the small subunit, large subunit contains 3 rRNA types (**5S**, 5.8S, and 28S rRNA).

In eukaryotes, the 5S rRNA gene is separated from the 45S rRNA genes. But together in *Artemisia*, gymnosperms, and some other plants.

Heterochromatin and heterochromatic knobs

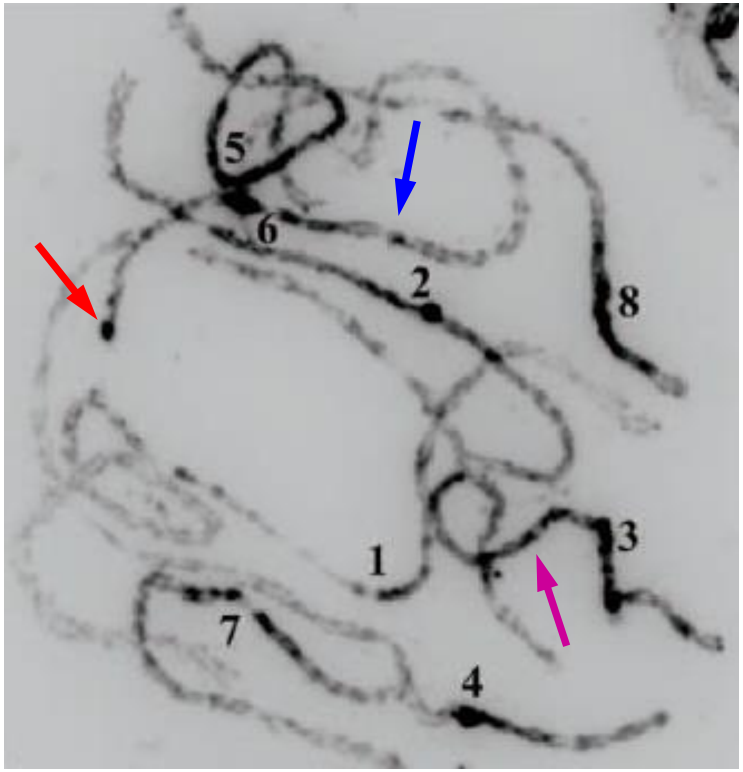


Het knobs are located on chromosomes:

a) terminally

b) insterstitially

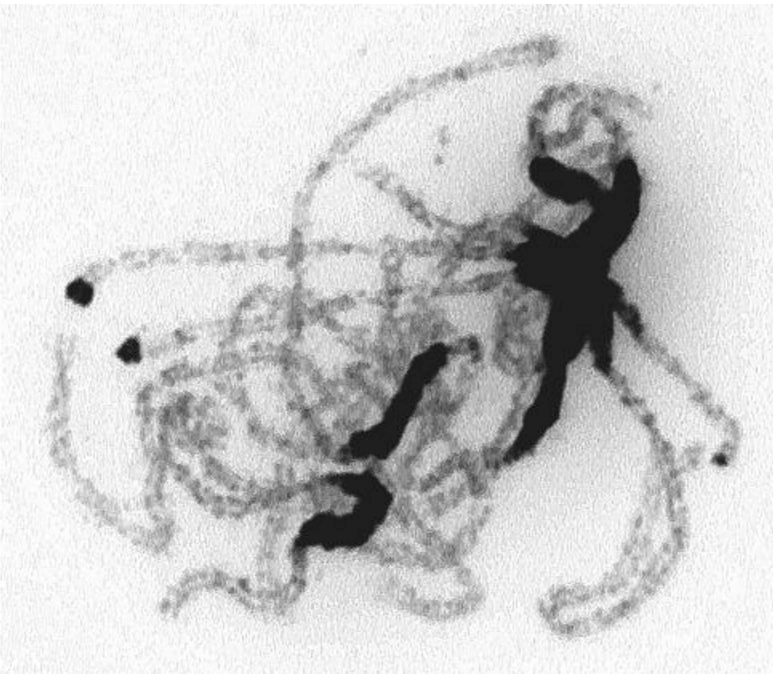
c) at pericentromeres



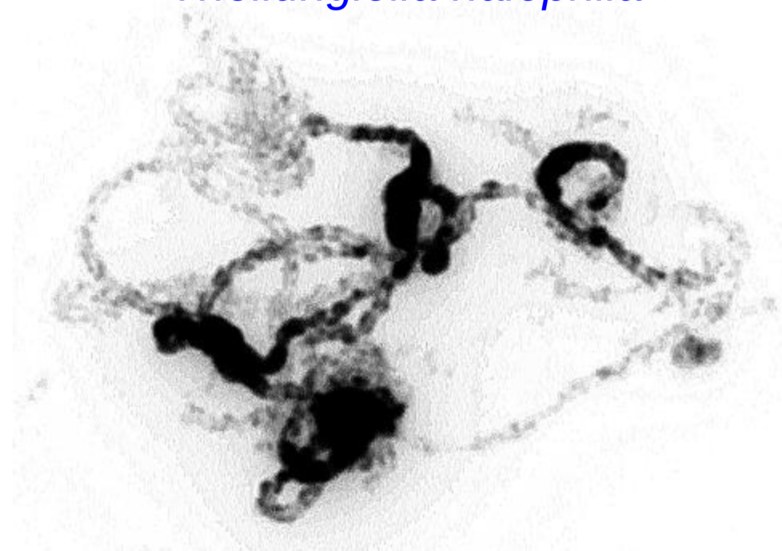
meiotic (pachytene) chromosomes of *Antirrhinum*

Het knobs in *Brassicaceae* species

Myagrum perfoliatum

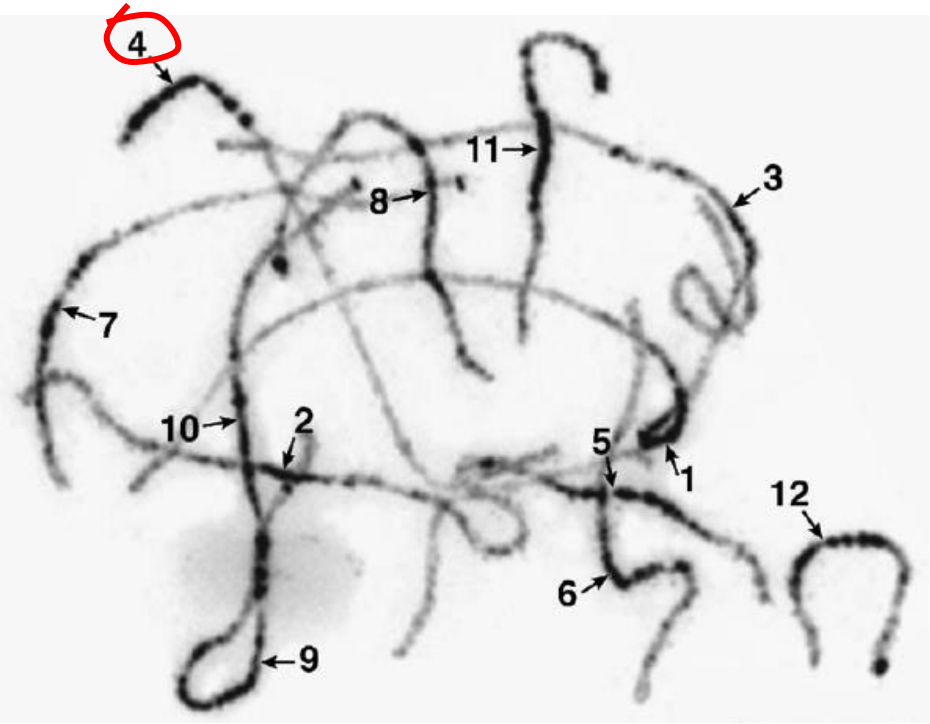


Thellungiella halophila

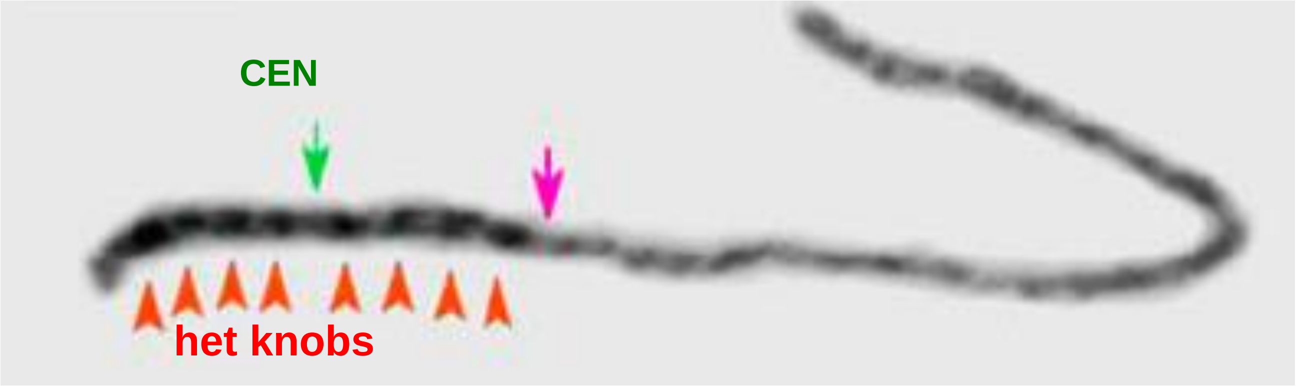


Mandáková & Lysak (2008), Plant Cell

Het knobs in rice

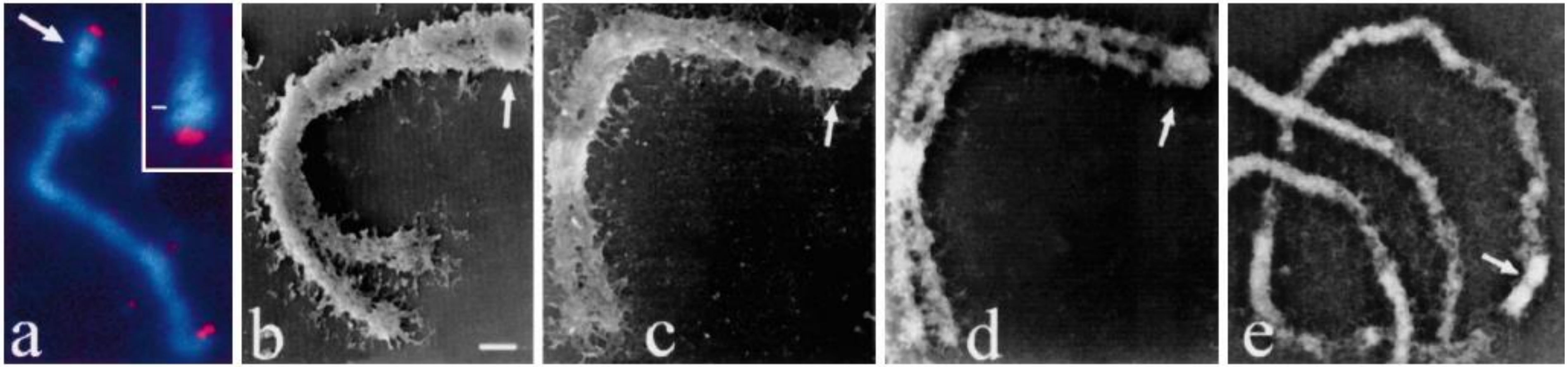


rice chromosome 4



Jiao et al. 2005, *Plant Cell* 17

Heterochromatic segment 1 found in *Brachycome dichromosomatica* (*Asteraceae*)

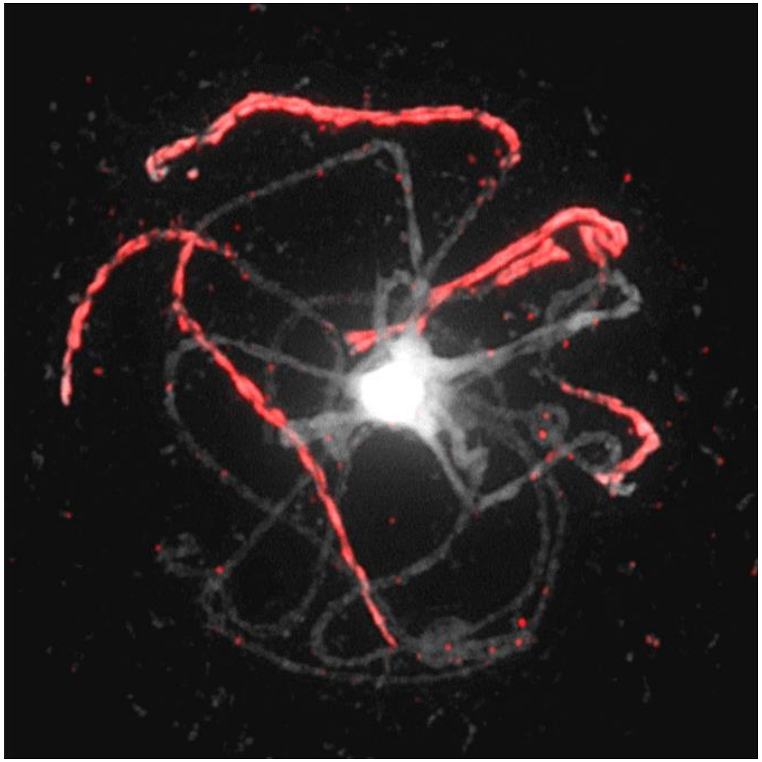


The terminal knob contains the Bds1 tandem repeat.

Houben et al. 2000, *Chromosoma* 109

Large Heterochromatin Knobs (Segments) in *Ballantinia antipoda*

174-bp satellite repeat



Het knobs

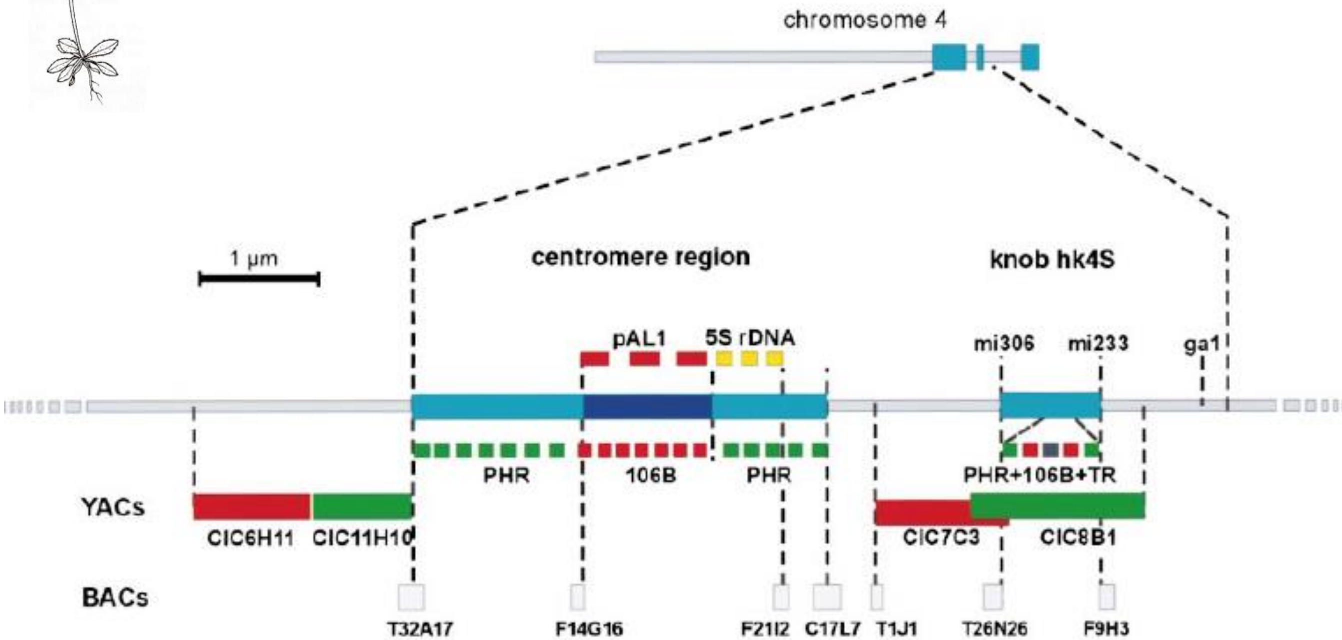
? origin

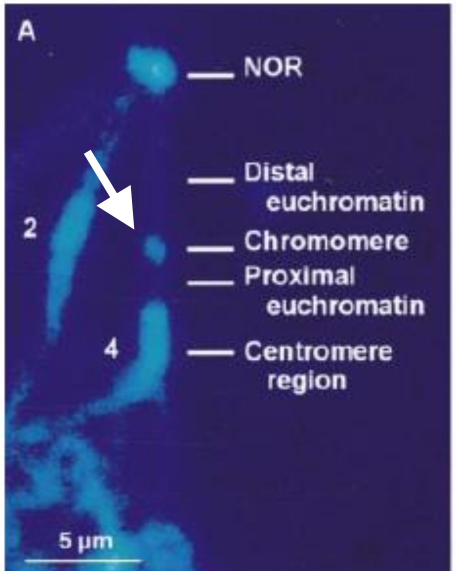
? composition

? function (if any)

Het knob hk4S in Arabidopsis

The hk4S originated by an inversion event that relocated pericentromeric sequence to an interstitial position.





Fransz et al. 2000, *Cell* 100

Het knobs were discovered by McClintock in maize

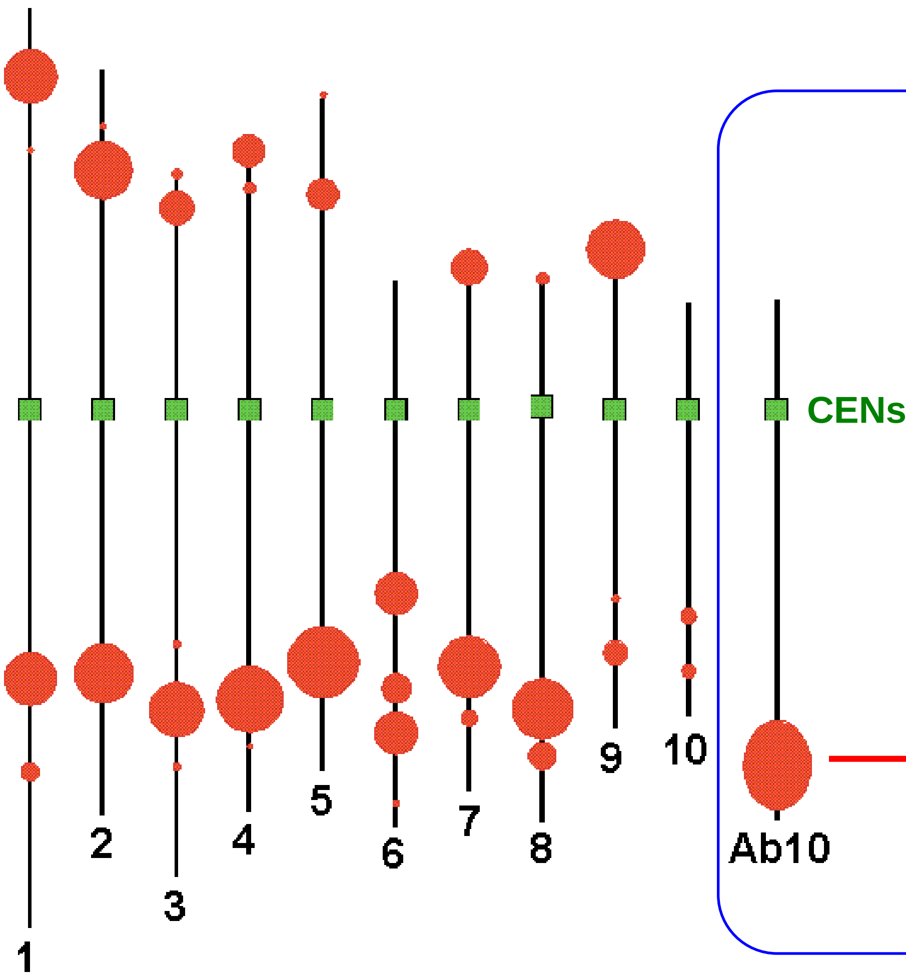
Barbara McClintock
(1902-1992)

America's most distinguished cytogeneticist, was initially denied acceptance to Cornell University's Dept. of Plant Breeding because she was a woman. Eventually allowed to study plant genetics, McClintock received her Ph.D. from Cornell in 1927, and later formulated one of the most important genetic theories of the 20th century.

McClintock B (1929) Chromosome morphology in *Zea mays*. *Science* 69

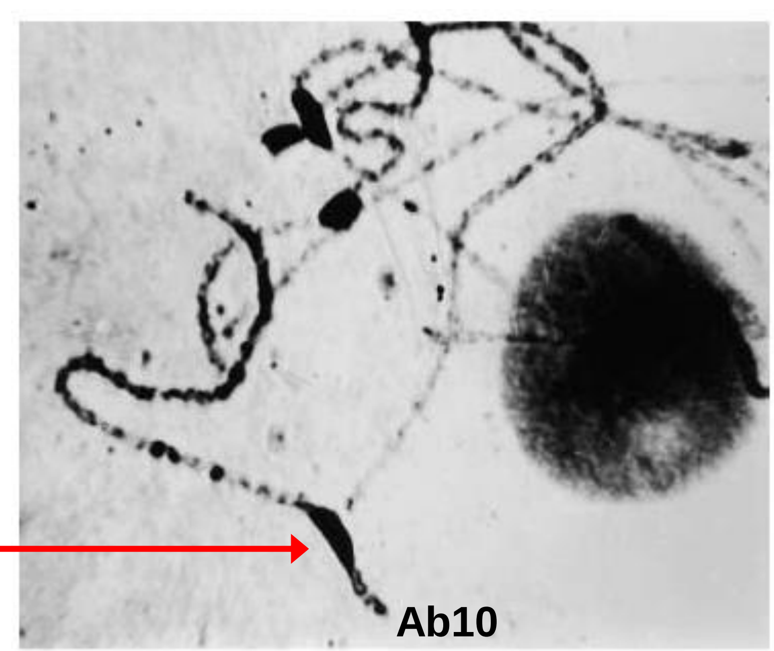
Het knobs in maize

- knobless and knobb-bearing accessions
- the number, size and position of knobs are variable and they are found in 23 locations on the ten maize chromosomes



abnormal chromosome 10

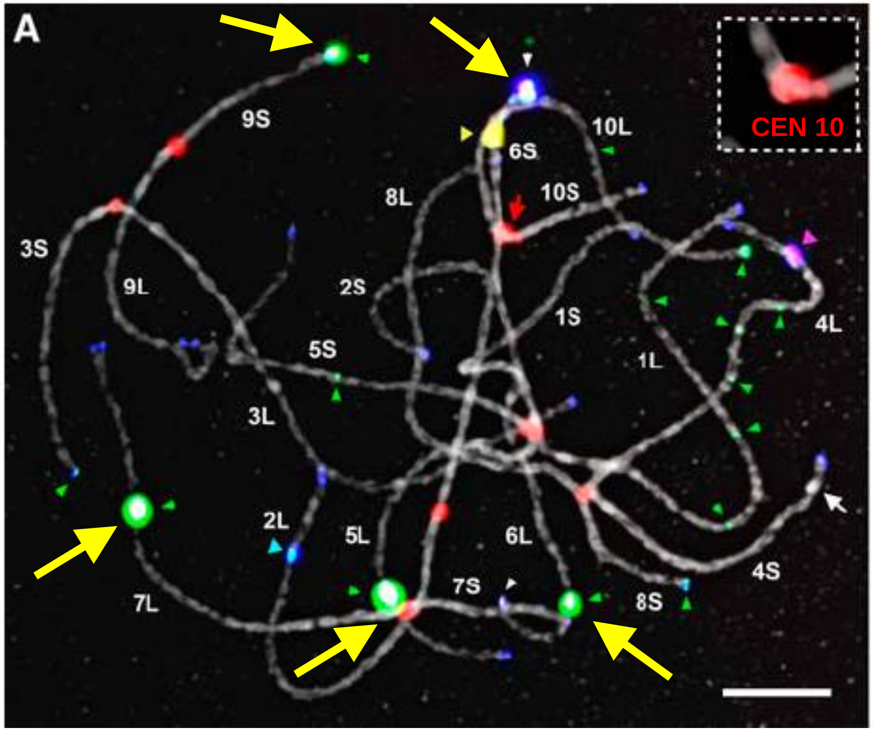
(discovered by Albert Longley; 1937, 1938)



Rhoades 1952

Het knobs in maize

the 180-bp and TR-1 (350-bp) tandem repeats are the major components of knob heterochromatin (Peacock et al. 1981, Ananiev et al. 1998) + different retrotransposons



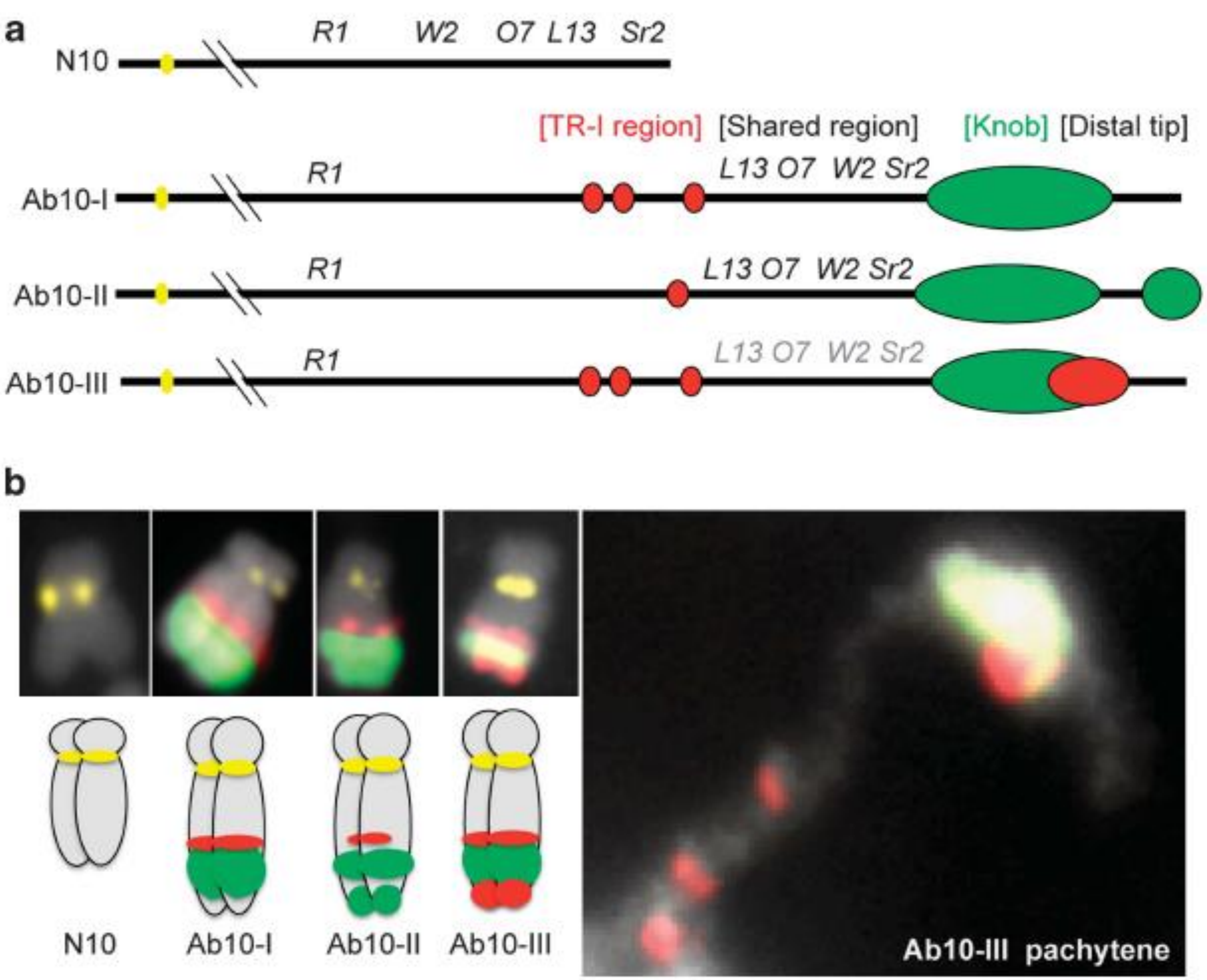
mFISHed pachytene chromosomes of the Kansas Yellow Saline (KYS) inbred line

180-bp repeat (green)

TR-1 element (pink)

Wang et al. 2006, *Plant Cell* 18

Structural variants of maize chromosome 10 (Ab10)



TR-1 repeat

knob 180 repeat

Kanizay et al. (2013) Heredity

Meiotic drive (transmission distortion)

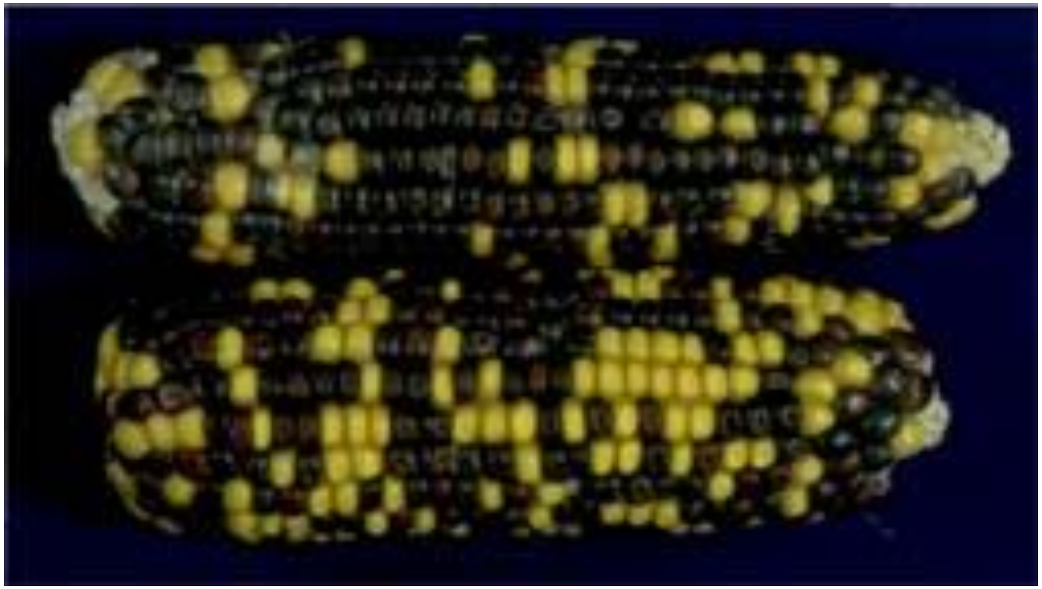
described by **Marcus Morton Rhoades**

Rhoades MM (1942) Preferential segregation in maize. *Genetics* 27: 395–407.

Birchler et al. 2003, *Genetics* 164

Meiotic drive

The ability of one homolog to enhance its probability of transmission at the expense of its partner (e.g. in Aa heterozygote, A-bearing gametes are produced more frequently than a-bearing gametes).



preferential transmission of the Ab 10 chromosome

the 1:1 segregation (normal chromosome 10)

Meiotic drive in maize

Preferential transmission of the knob-bearing chromosomes during female meiosis. But only if the Ab 10 chromosome is present.

heterozygote for Ab 10

↓

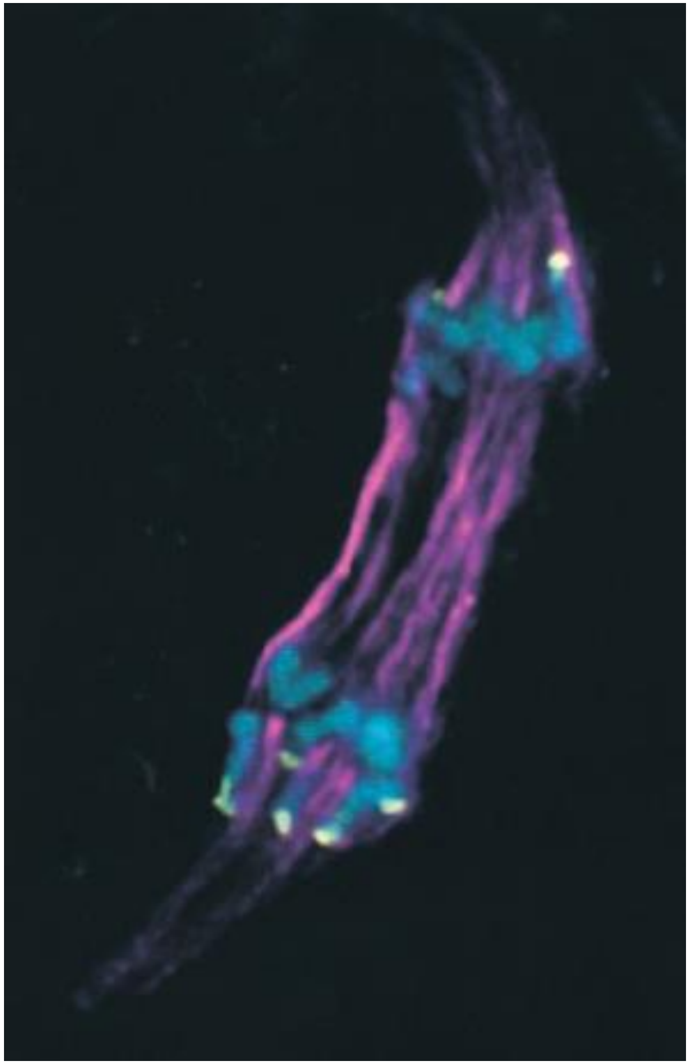
crossing-over located between
the knob and centromere

↓

cross-over products that carry the knob
on only one of its two chromatids
(heteromorphic dyad)

↓

pseudokinetochore activity of the knob direct the
knob-bearing chromatides to two of the four products
of meiosis II



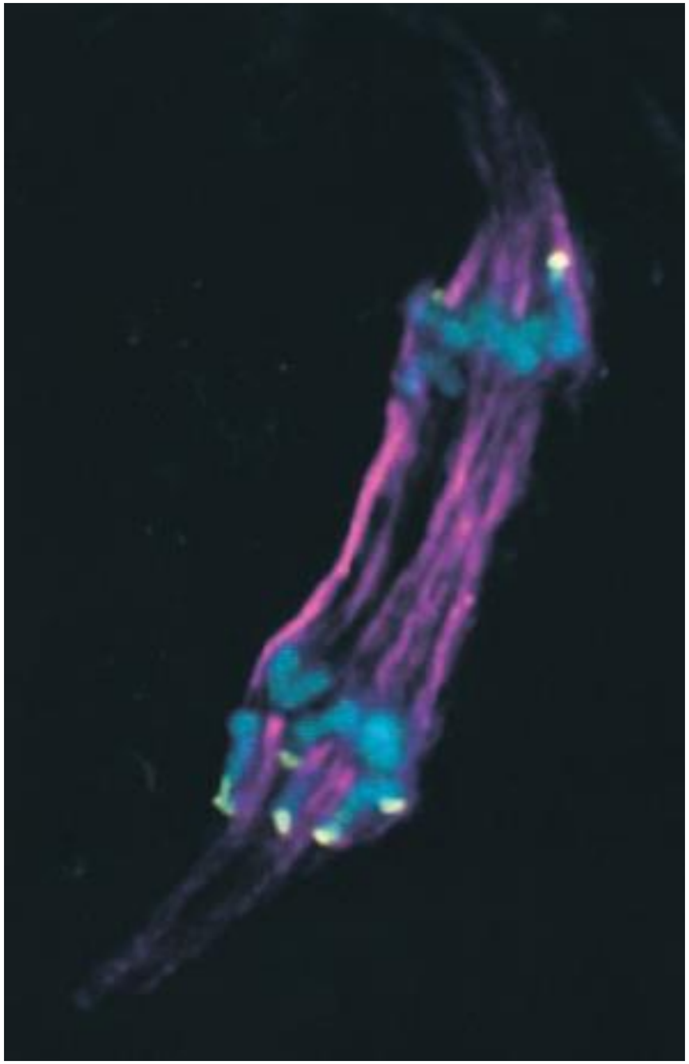
Birchler et al. 2003, *Genetics* 164

Megasporogenesis and meiotic drive in maize

Female meiosis (megasporogenesis) is asymmetric:

-out of 4 haploid products only one will become the egg; other three degenerate

- **the outermost (basal) megaspore** differentiates into the megagametophyte via a few mitoses to produce the egg, polar nuclei, and associated cells

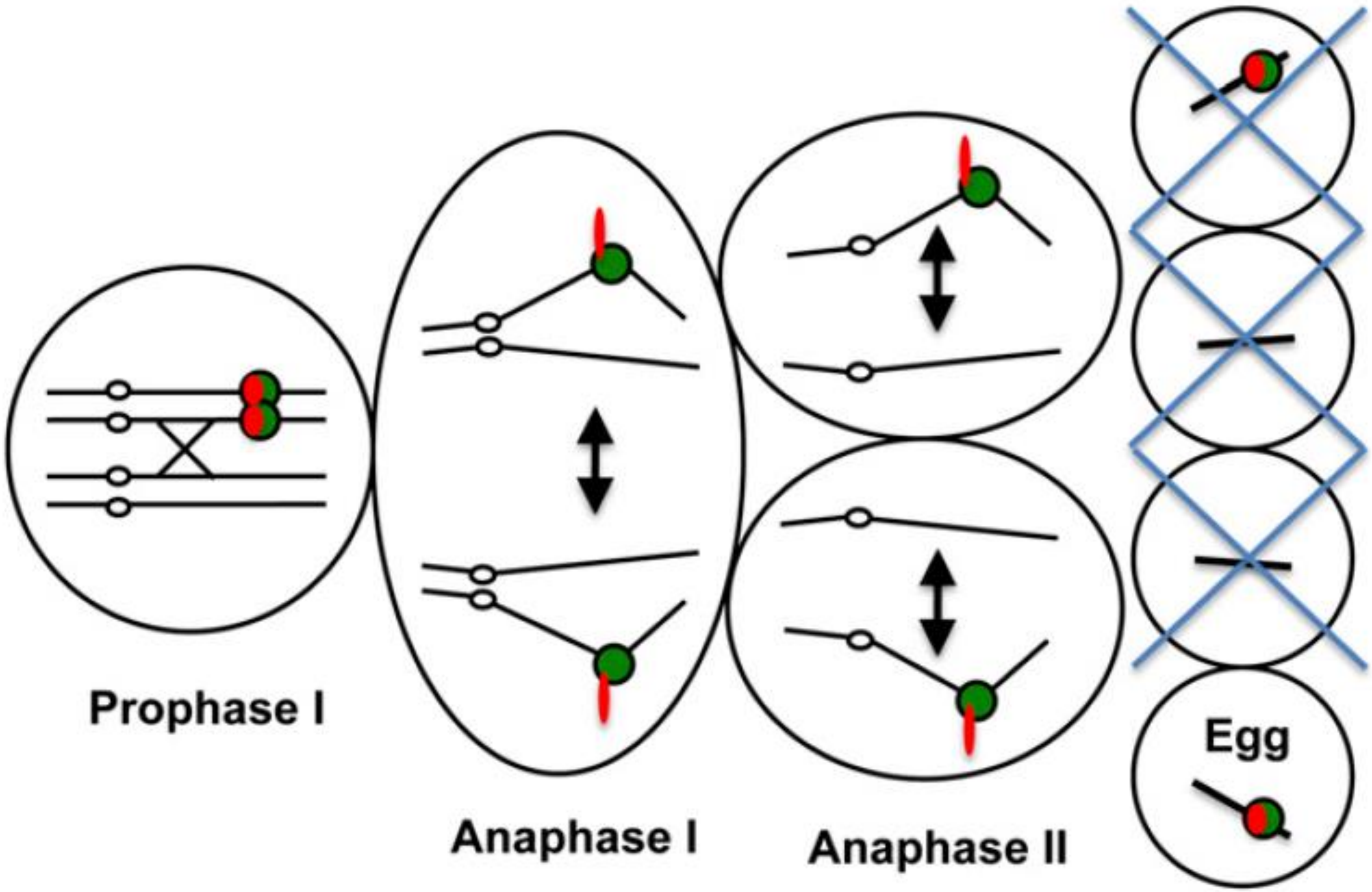


Birchler et al. 2003, *Genetics* 164

Knob-bearing chromatids are pulled towards the **outermost megaspores** during meiosis II ahead of the centromeres.

Consequently, instead of a 50% expected ratio of transmission in a heterozygote, knob transmission in female meiosis varies from 59 to 82%.

Meiotic drive in maize



Female gametogenesis