# EUKARYOTIC CHROMOSOME STRUCTURE

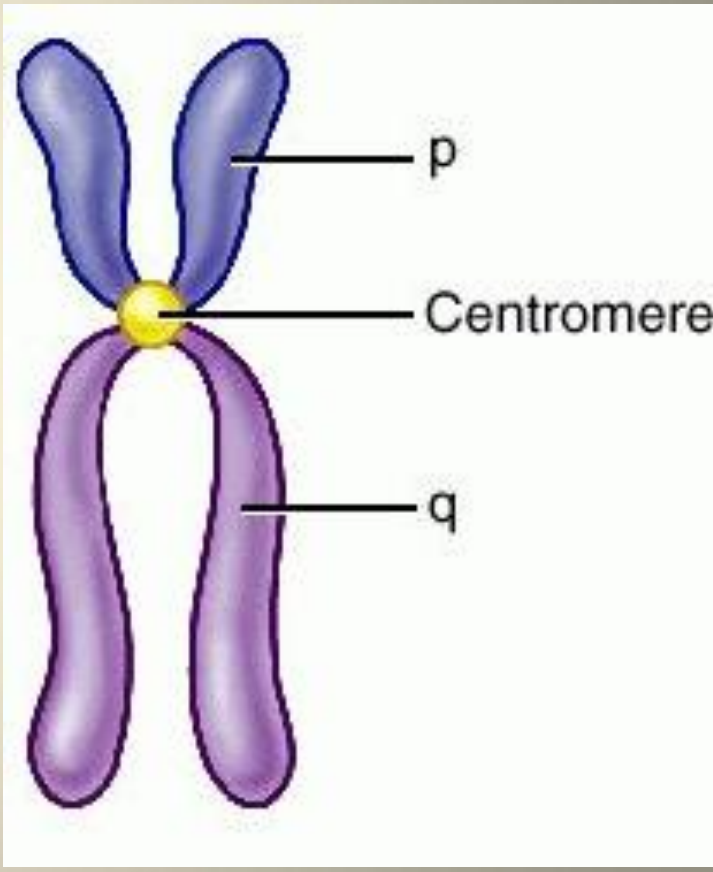
Levels of packing
Chemical Modifications
Epigenetics

# Comparing Prokaryotic and Eukaryotic DNA

| | Prokaryote | Eukaryote |
|---|---|---|
| DNA | Circular  | Linear |
| Location of DNA | Not in nucleus<br>Nucleoid region (similar to nucleus in eukaryote but not surrounded by a membrane) | Contained in nucleus |
| DNA bound with proteins? | No. Naked. | Yes |

# Chromosome Structure

- 2 arms, divided at centromere:
  - p arm – petit arm
  - q arm – long arm
- Centromeres:
  - region where sister chromatids are connected
  - made up of repetitive sequences

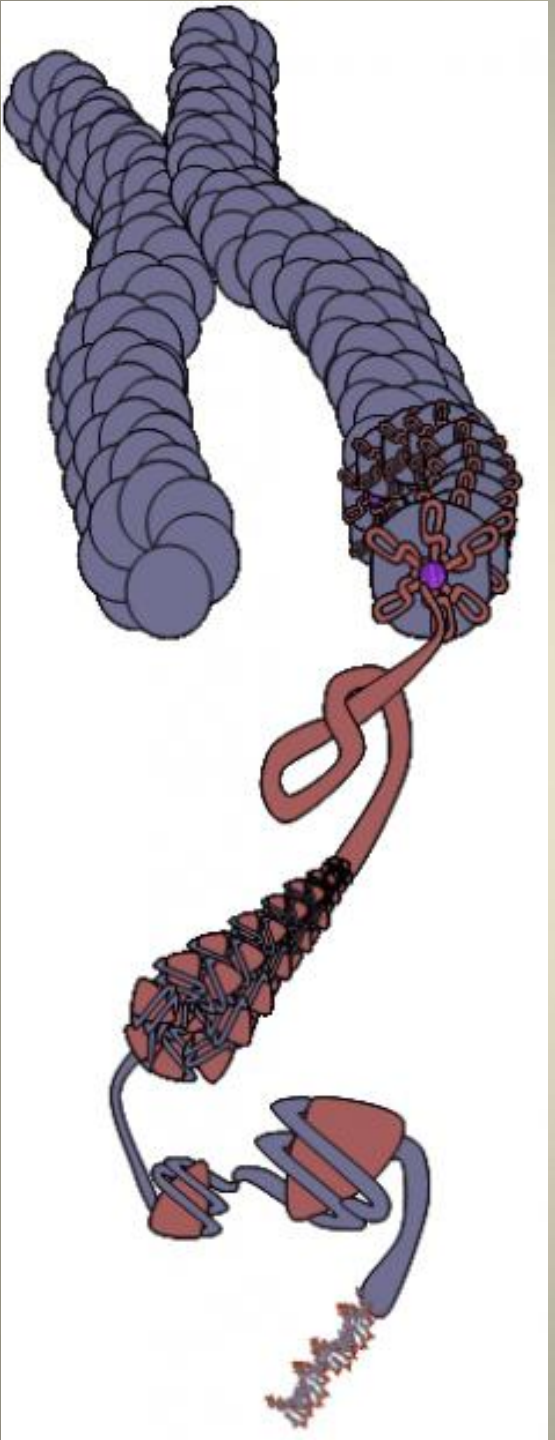


# Activity: DNA Packing

- Materials:
  - Thread
  - Scissors
  - pill covers
- Instructions:
  - Cut out 20 m of thread
  - Put the thread in the pill cover

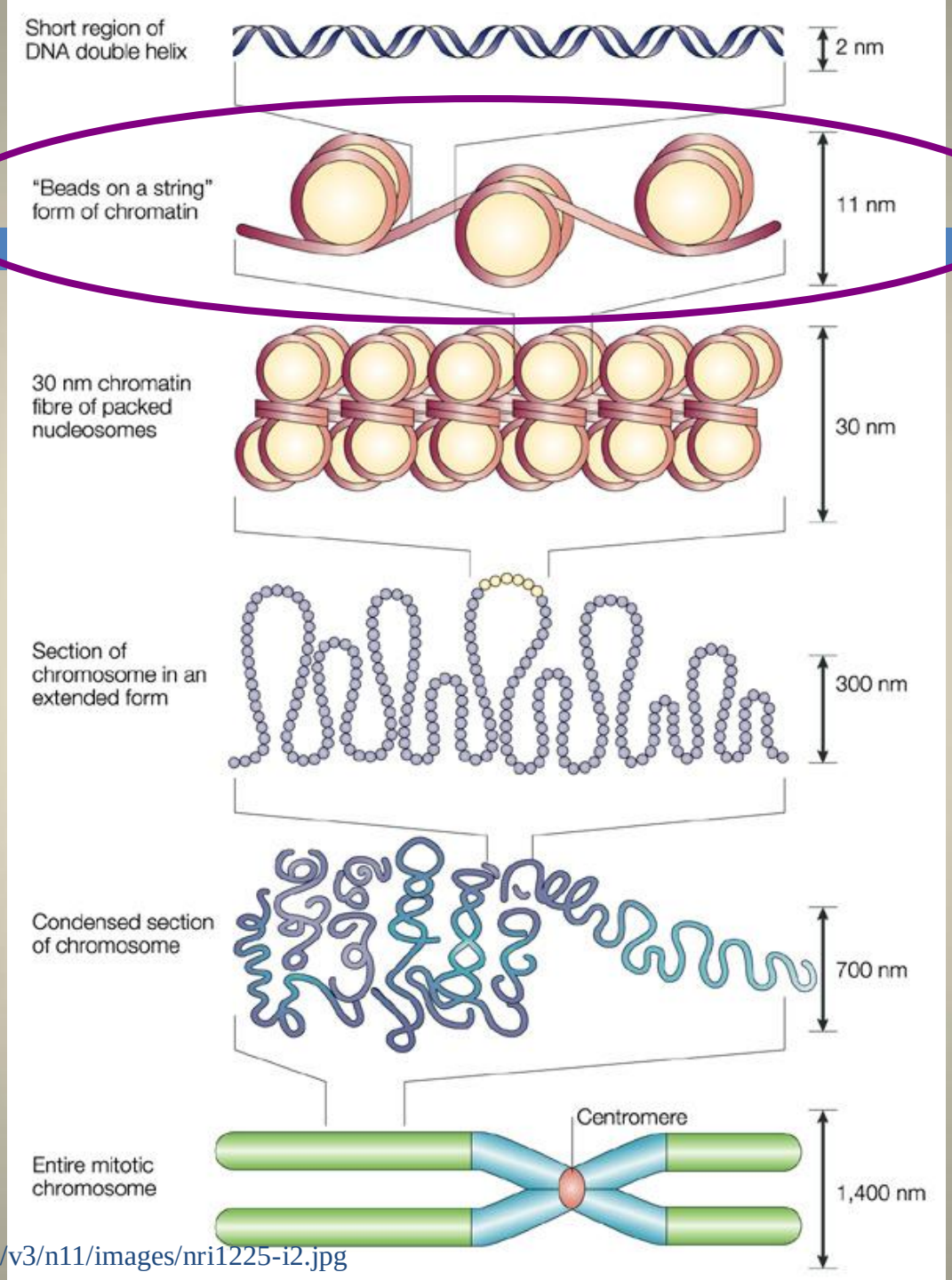
# DNA Packing Animation

- Try to ignore the strange music
  http://www.youtube.com/watch?v=N5zFOScowqo



# Levels of DNA packing

- 1st level: nucleosome
- 2nd level: solenoid / chromatin
- 3rd level: looped domain
- 4th level: metaphase chromosome



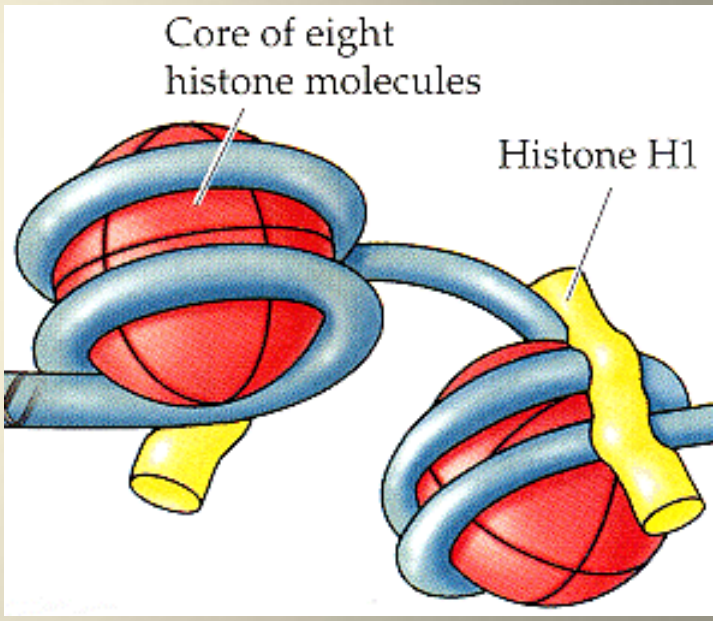

http://www.nature.com/nri/journal/v3/n11/images/nri1225-i2.jpg

# Histones

- Proteins around which DNA coils to form chromatin
- Contain positively charged R-groups which bind to the negatively charged DNA (phosphate groups)
  - DNA backbone has a negative charge
  - histones have a positive charge
- 5 types
  - Core: H2A, H2B, H3, H4
  - Linker: H1

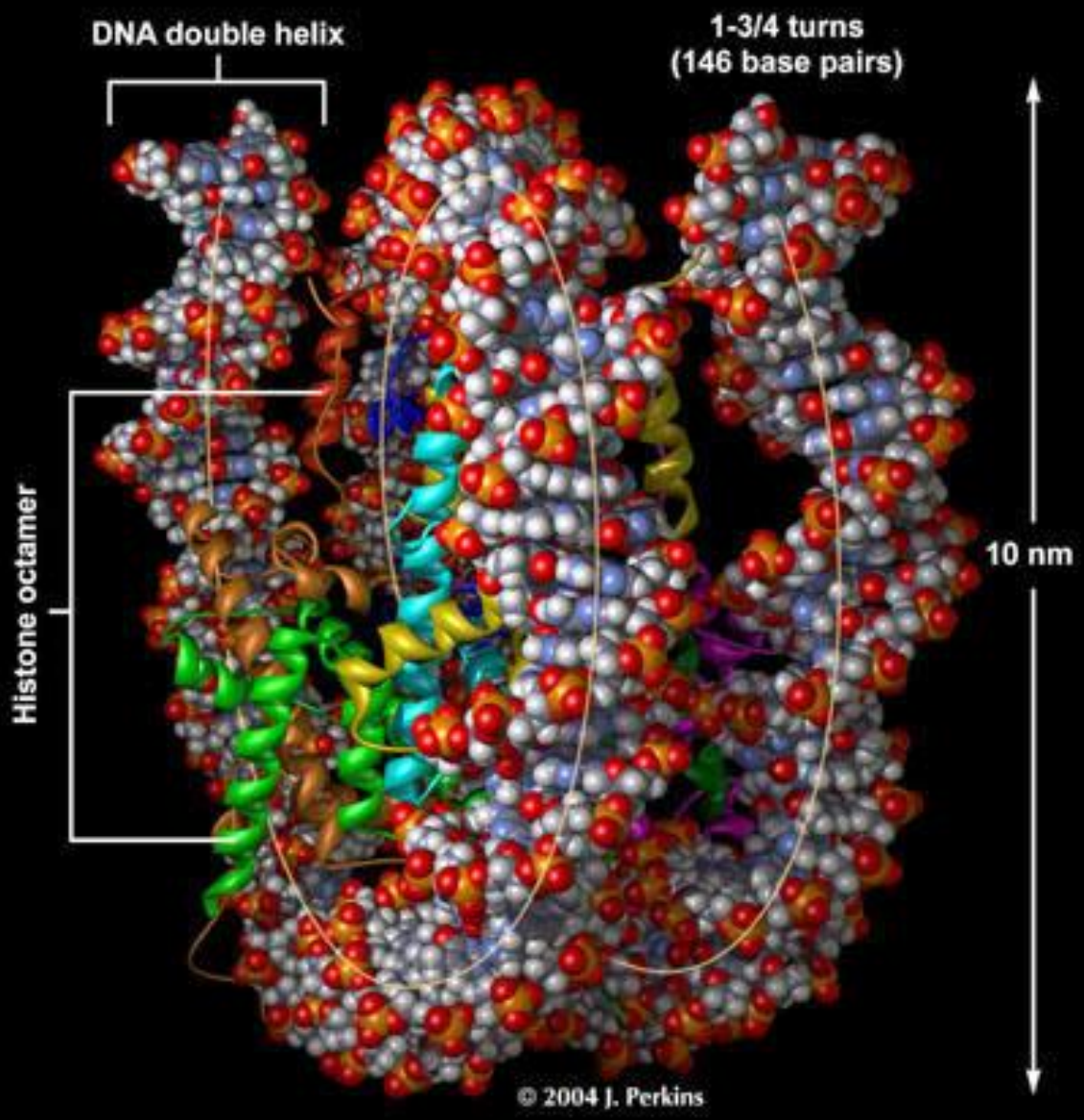
# First level of packing: Nucleosome

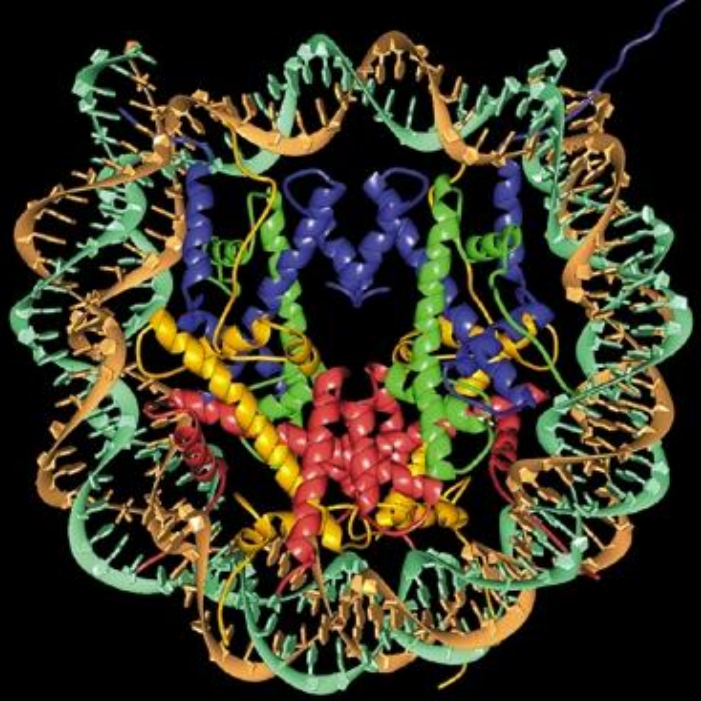
- Nucleosome = DNA + core histones
- DNA wrapped twice around an octamer of core histones consisting of:
  - 2 of each core histone: H2A, H2B, H3, H4
  - Note: H1 is not part of the nucleosome, but is attached to the DNA near the nucleosome
- 10 nm in diameter




http://biology.kenyon.edu/courses/biol114/Chap01/chrom1.gif

# A NUCLEOSOME



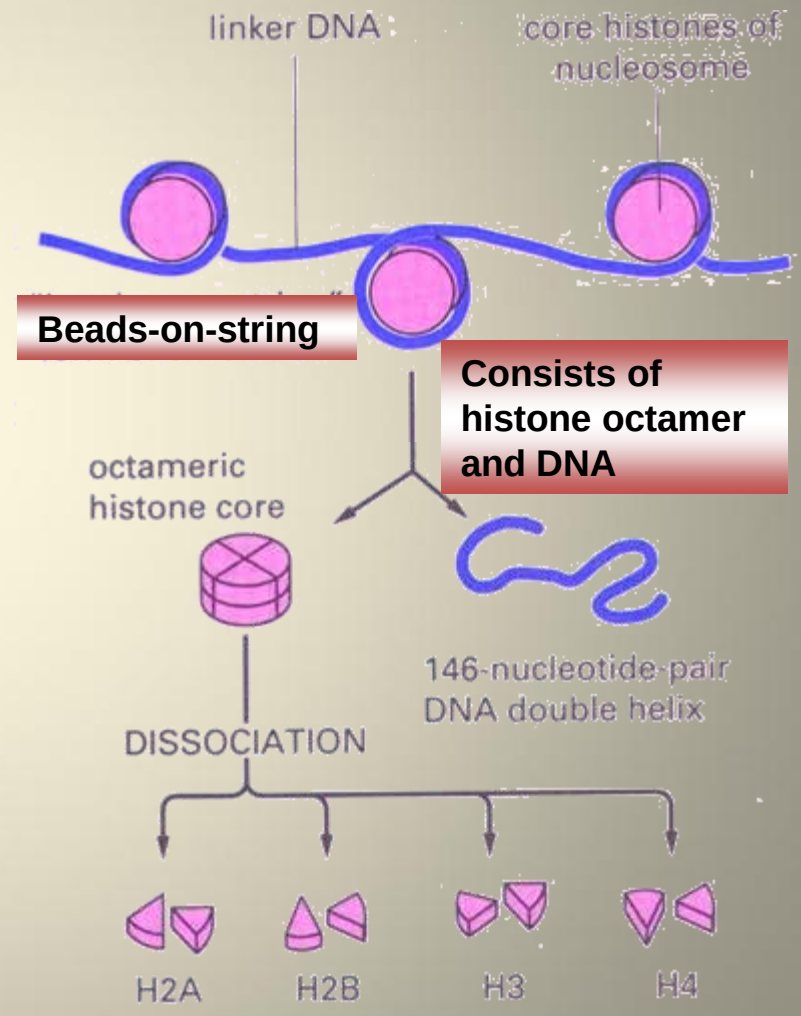



http://bio.research.ucsc.edu/people/boeger/images/research%20interest%20images/nucleosome%20bigger.jpg

http://bioweb.wku.edu/courses/Biol566/Images/NucleosomeF09-30A.JPG

# Beads-on-a-string

- A nucleosome looks like a bead (histone) with string wrapped around it (DNA)

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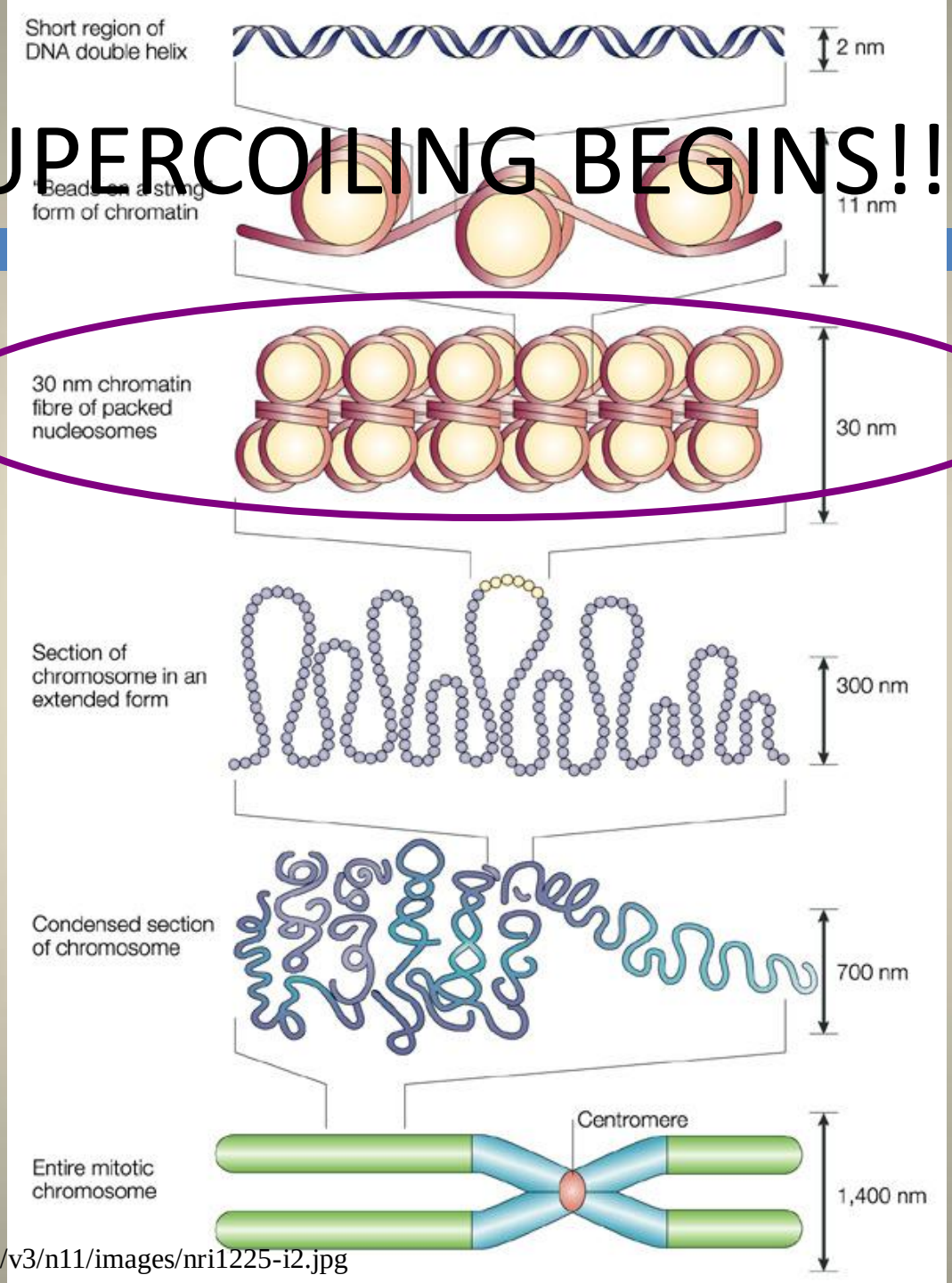
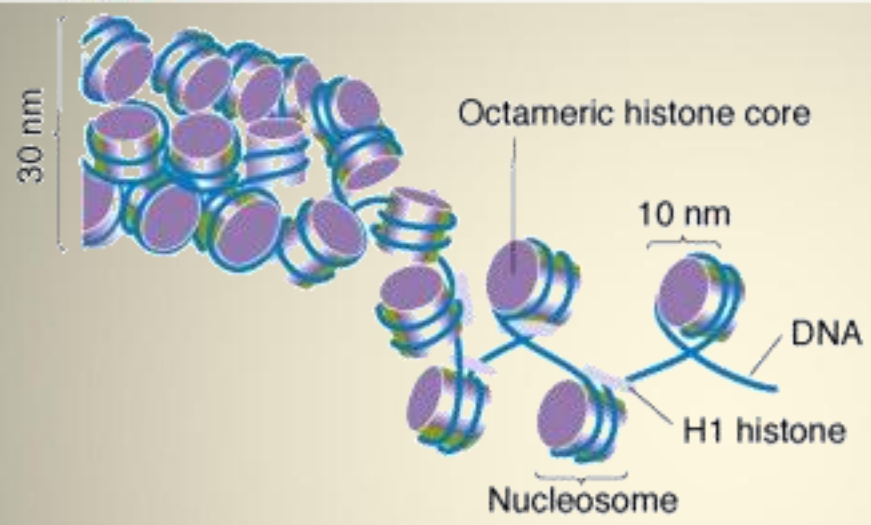
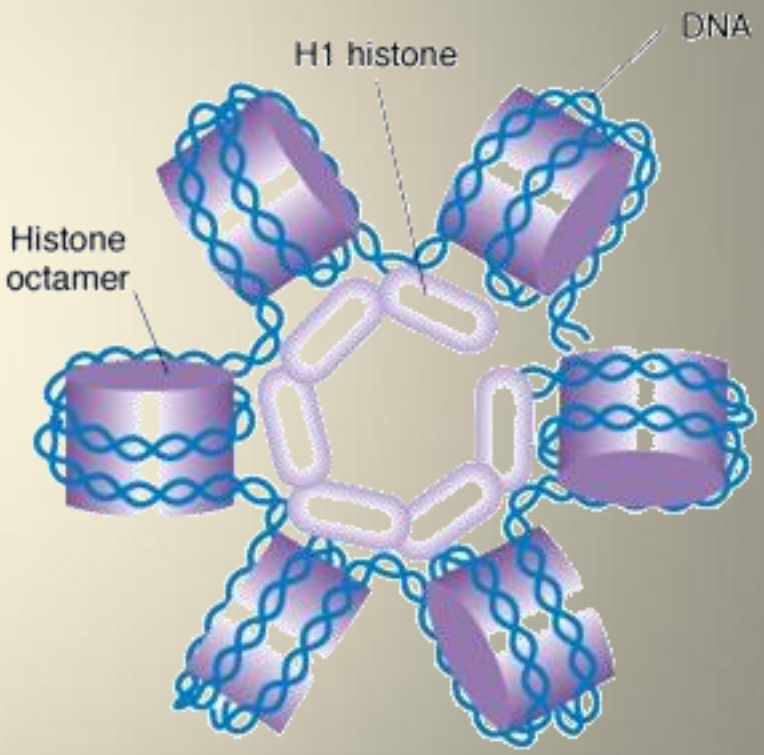
# SUPERCOILING BEGINS!!!




http://www.nature.com/nri/journal/v3/n11/images/nri1225-i2.jpg

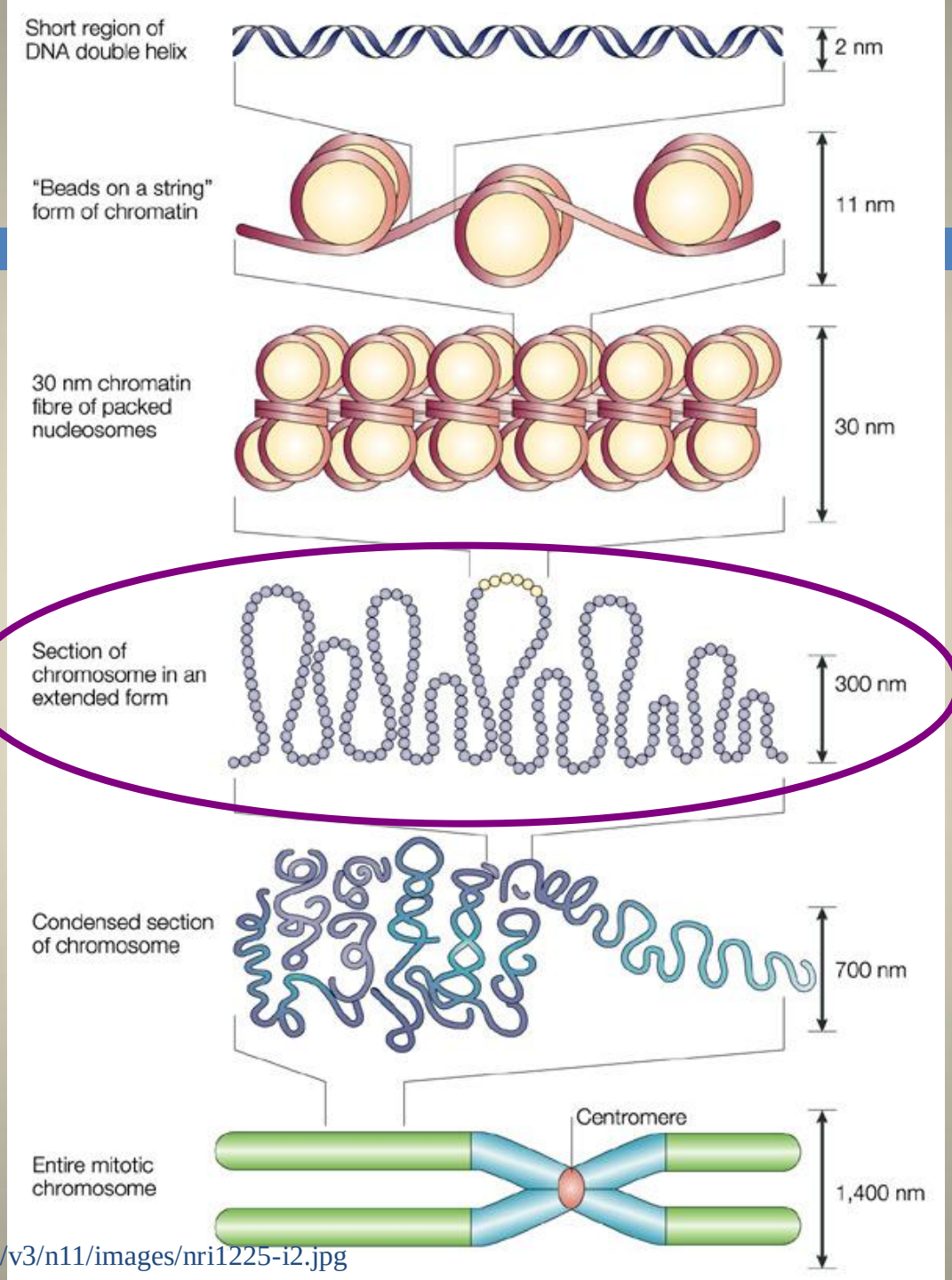
# Second level of packing: Solenoids / chromatin




- Solenoid: H1 histones aggregate causing 6 nucleosomes to coil together
- 30 nm in diameter
- stack on top of each other forming the chromatin fiber

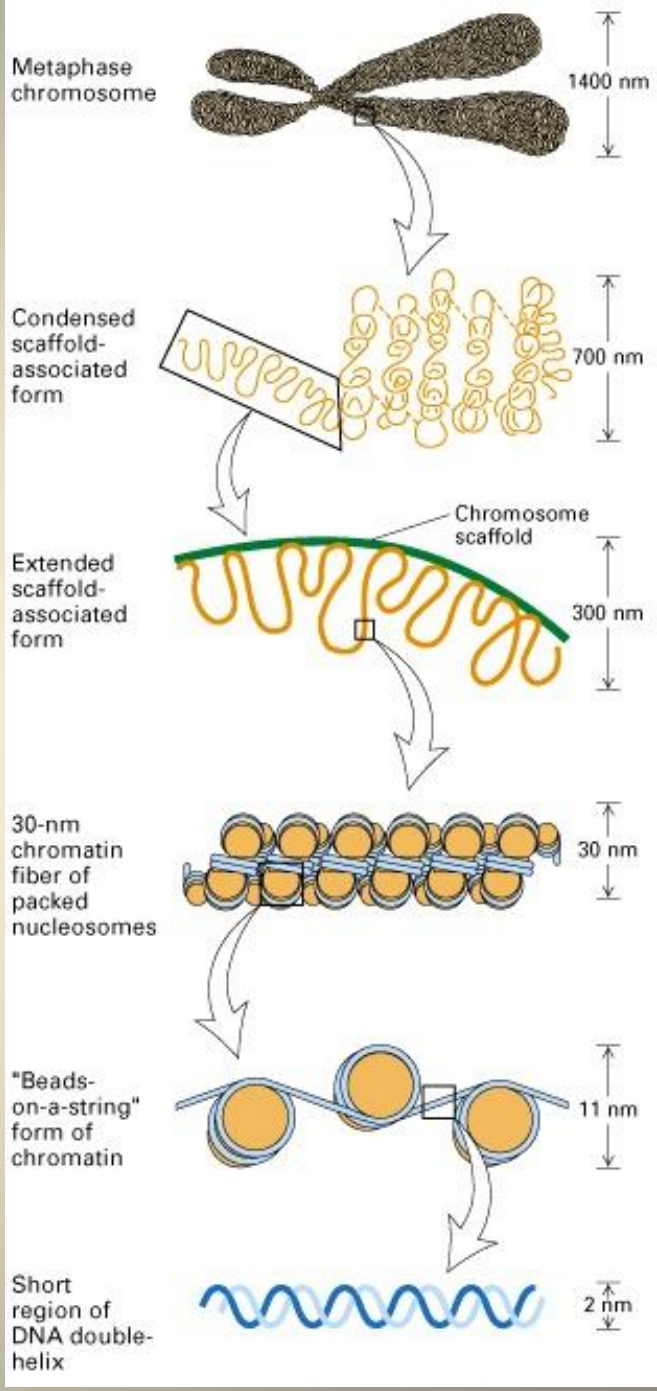
http://www.bio.miami.edu/dana/104/nucleosome.jpg



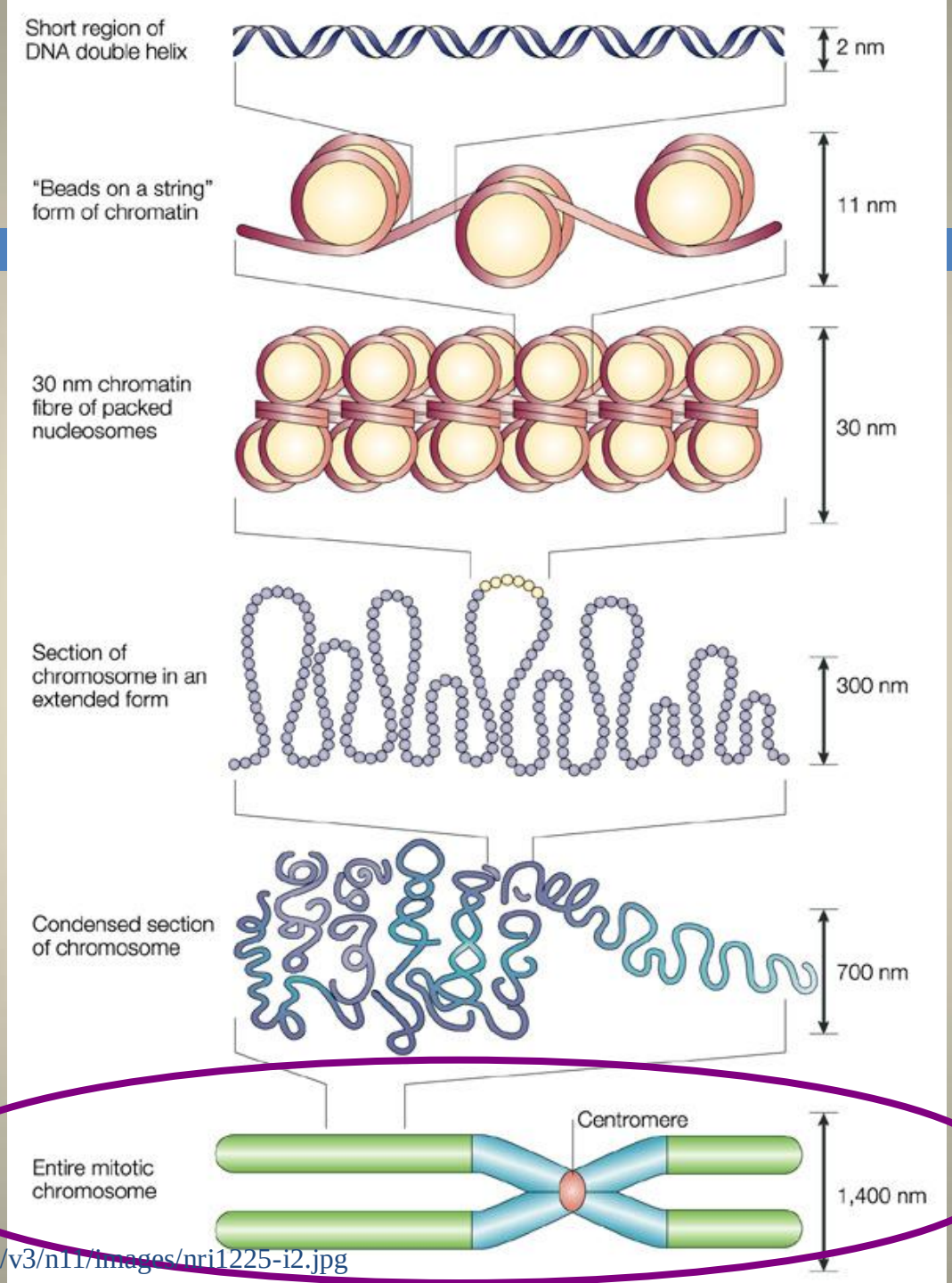

http://www.nature.com/nri/journal/v3/n11/images/nri1225-i2.jpg

# Third level of packing: looped domains

- Chromatin fibers forms loops which attach to nonhistone proteins
- Nonhistone proteins form a scaffold
- 300 nm in diameter




http://bioweb.wku.edu/courses/Biol566/Images/ChromatinF09-35.JPG




http://www.nature.com/nri/journal/v3/n11/images/nri1225-i2.jpg

# Fourth level of packing: Metaphase Chromosome

- Looped domains coil and fold, further compacting chromatin
- Result in the characteristic metaphase chromosome seen in karyotypes
- Such packing occurs during mitosis

# DNA Packing Video


http://www.hhmi.org/biointeractive/dna/DNAi_packaging_vo2.html

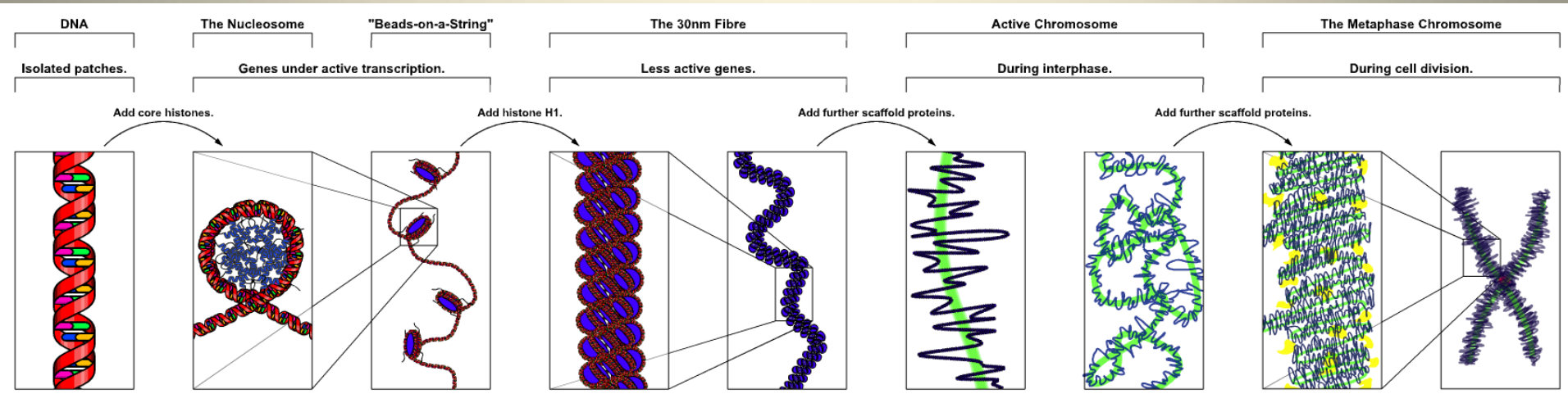
# Tutorial

- Discovery of chromosome packaging

  http://www.dnaftb.org/dnaftb/29/concept/index.html

# Gene Regulation Topics

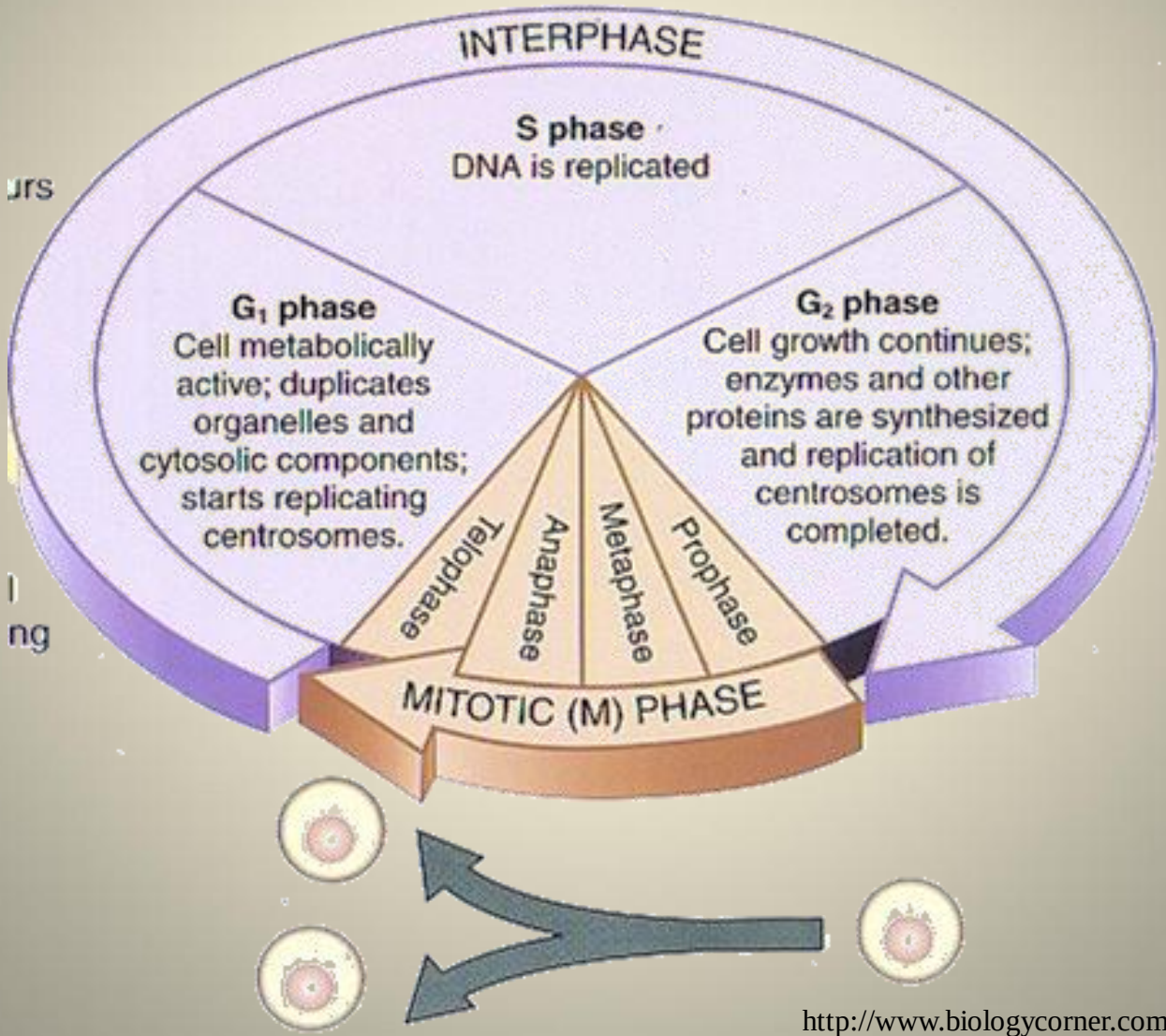
- Review cell cycle
- Metaphase chromosome in mitosis
- Interphase chromatin in G1, S, G2
  - DNA replication
  - transcription



# Gene Regulation Defined

- The ability to control whether a gene is actively being transcribed or not
- This regulation can occur at the:
  - Structural level (e.g. supercoiling of DNA)
  - Molecular level (e.g. negative feedback to suppress enzymatic activity)

# Cell Cycle



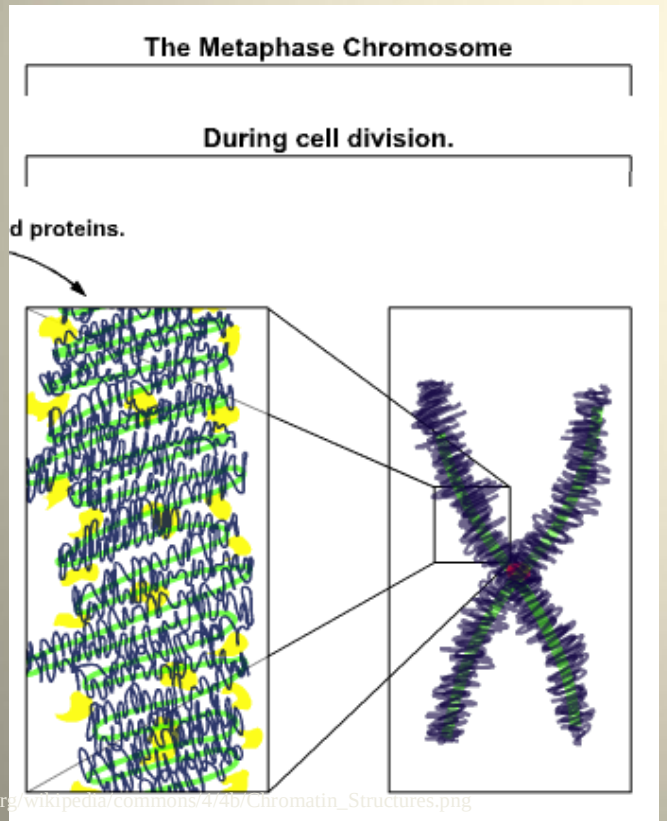

http://www.biologycorner.com/resources/cellcycle2.jpg

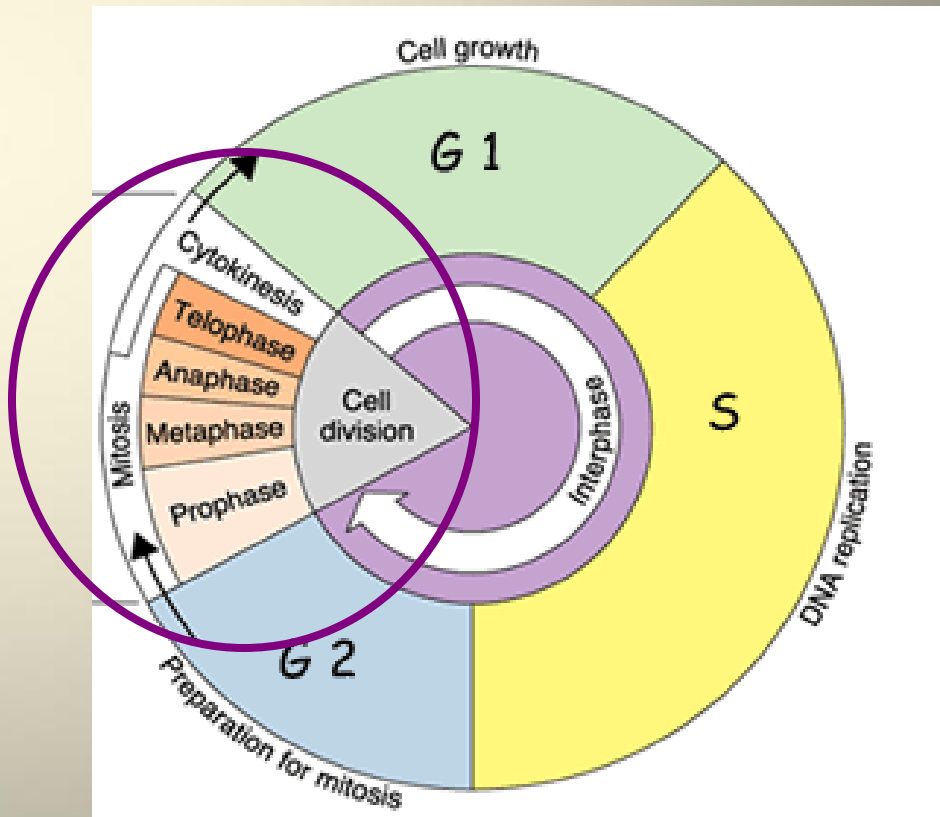
# Supercoiling

- For a gene to be expressed (transcribed), the chromosome at that region must be uncoiled
- Different levels of supercoiling affects transcription
- Allows control over which genes are expressed

# Mitosis: PMAT

- DNA is “inactive” because it is in the most condensed form (metaphase chromosome)
- thus information is inaccessible



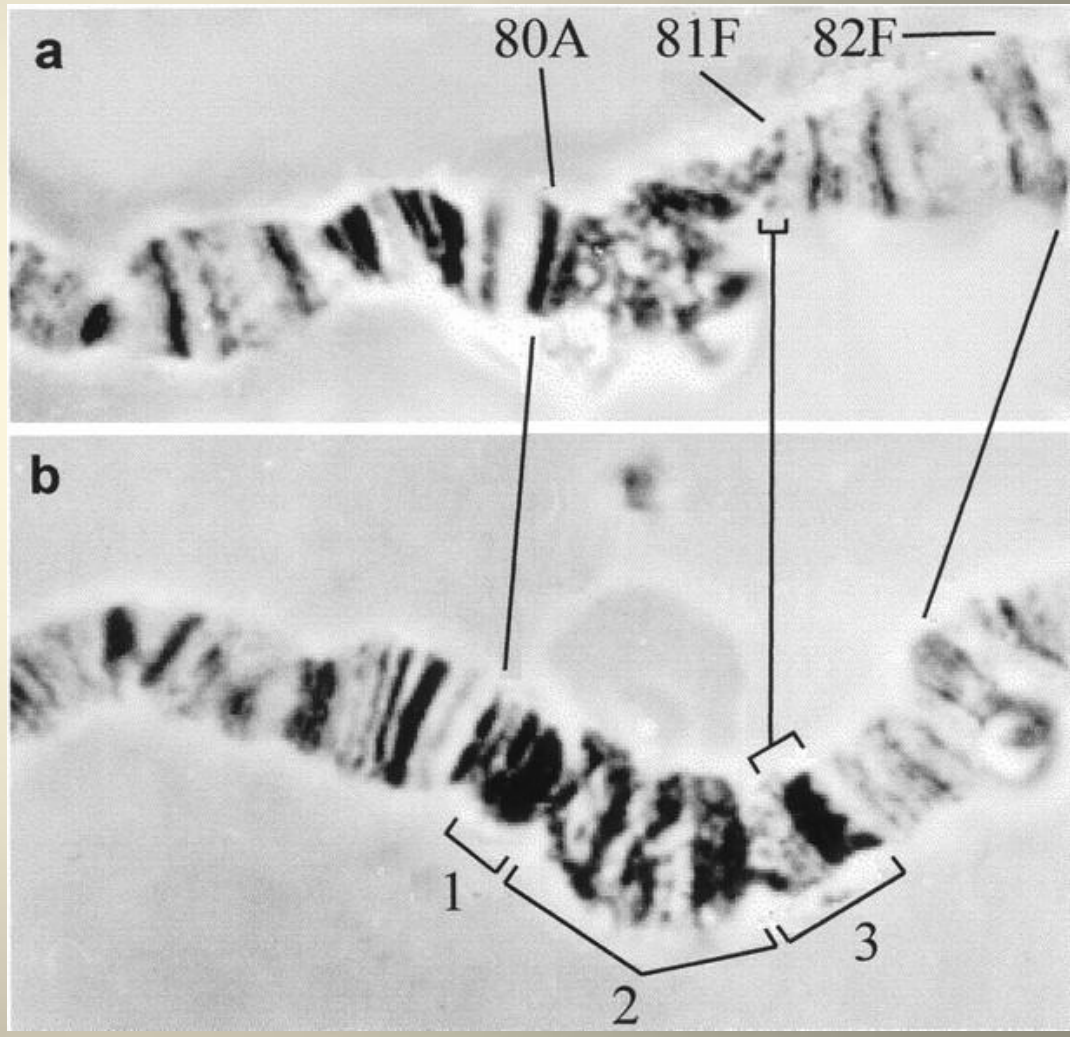

http://upload.wikimedia.org/wikipedia/commons/4/4b/Chromatin_Structures.png

# Interphase Chromatin

- Much less condensed than during mitosis
- Scaffold may be less defined (e.g. attach to inside of nuclear envelope)
- But order still exists:
  - Each chromosome occupies a restricted area with the nucleus
  - Nucleosome structure stays intact throughout cell cycle
  - Most still maintain the solenoid and looped domain structures

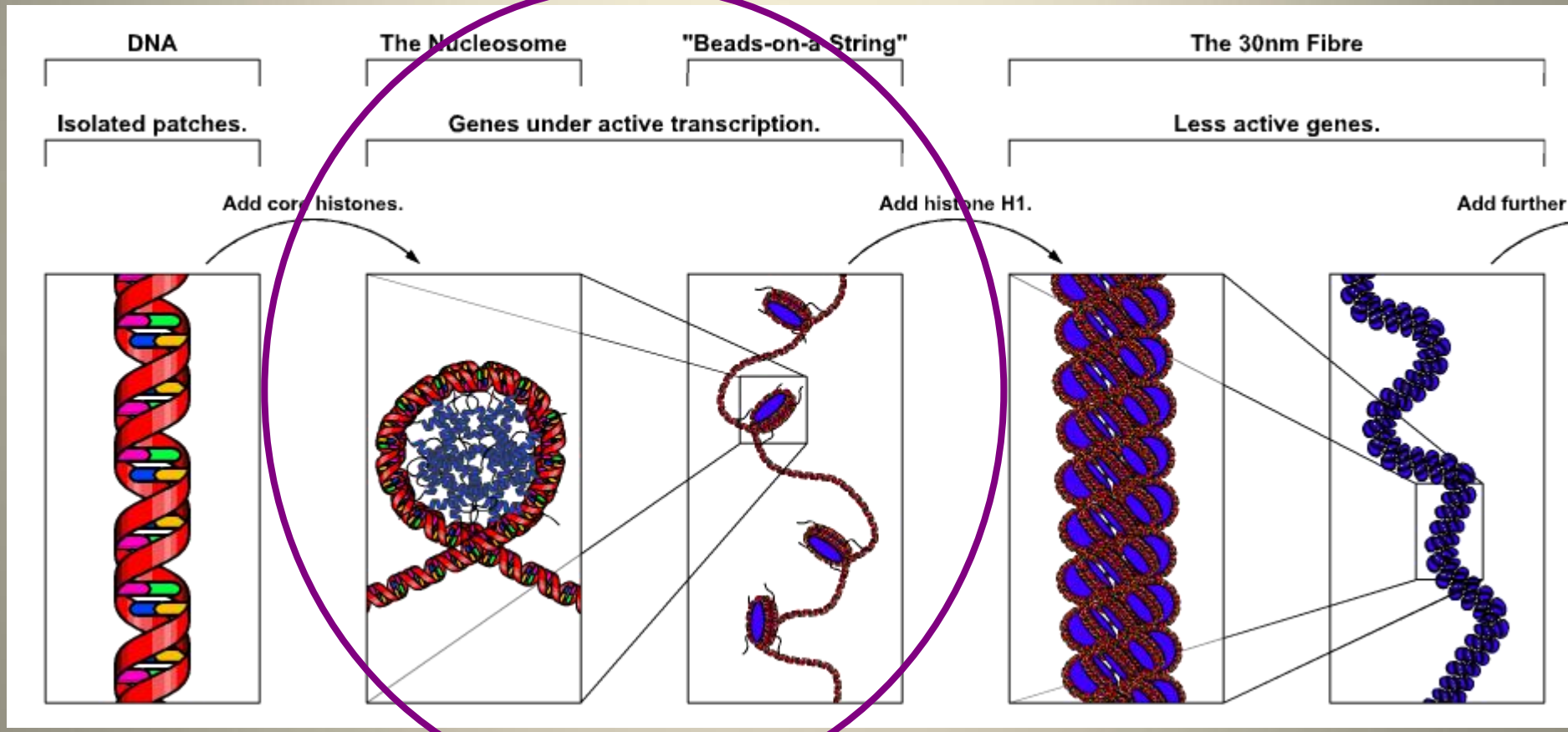
# Interphase Chromatin

- Different levels of packing on various regions of the same chromosome
- **Euchromatin**: loosely packed region on chromatin, active transcription (light stain)
- **Heterochromatin**: densely packed region on chromatin, inactivated (dark stain)

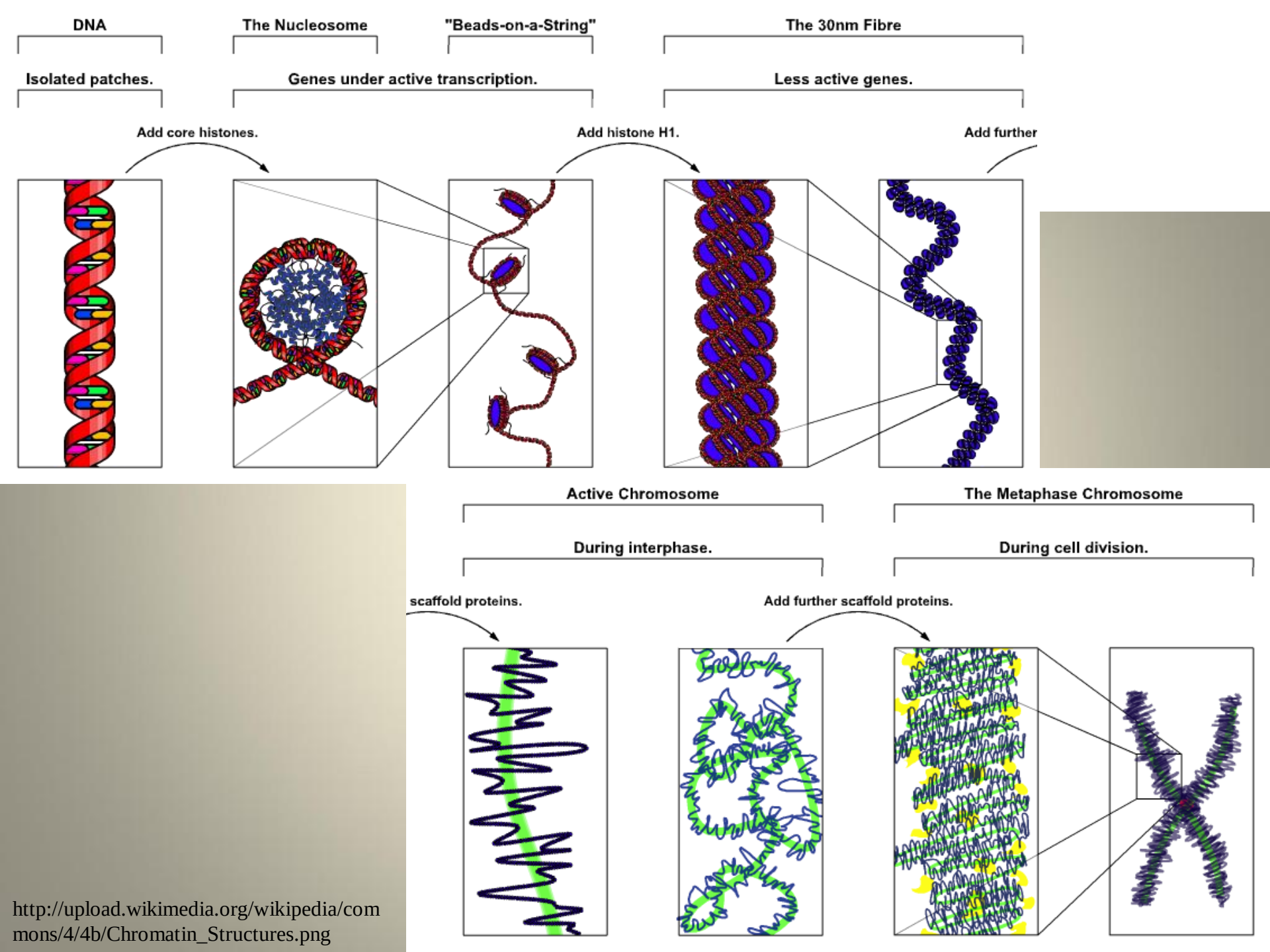



Eu = true; Hetero = different

# Chromatin Structure during Transcription

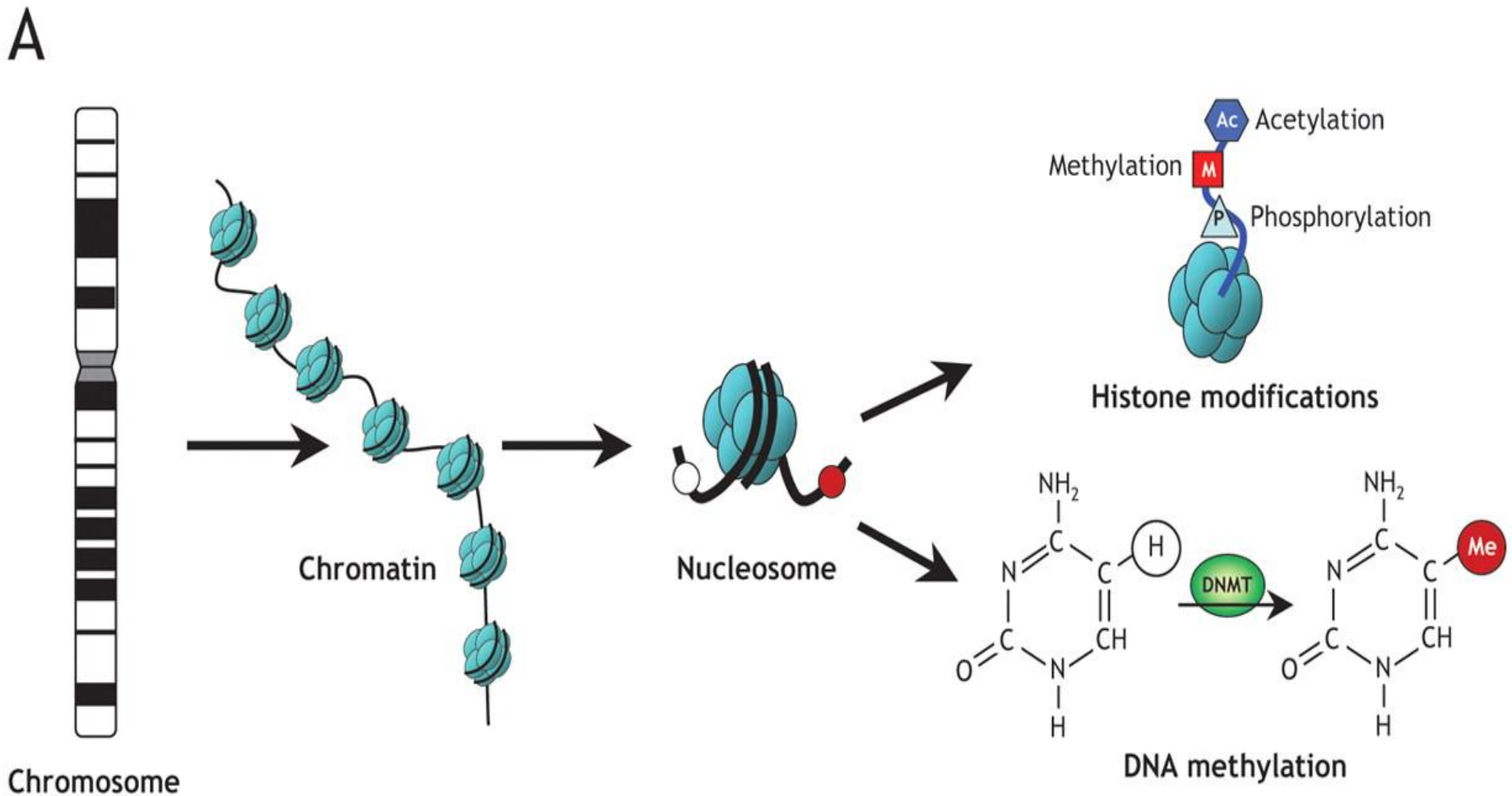



http://upload.wikimedia.org/wikipedia/commons/4/4b/Chromatin_Structures.png



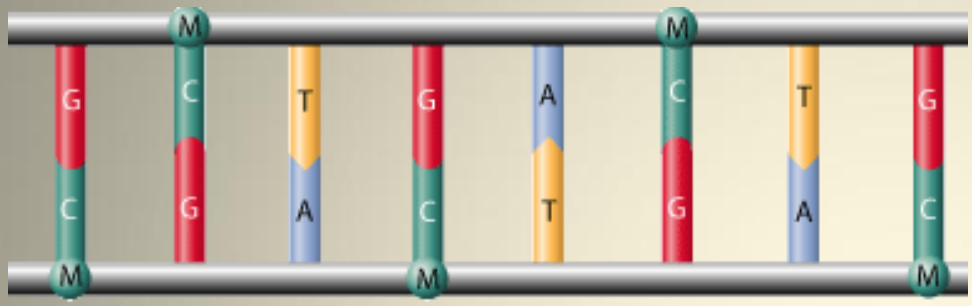

http://upload.wikimedia.org/wikipedia/commons/4/4b/Chromatin_Structures.png

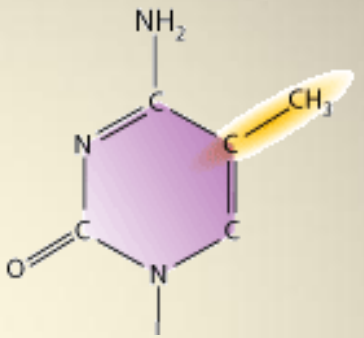
# Chromatin Modifications Affecting Gene Expression




http://cnx.org/content/m26565/latest/graphics35.jpg

# Methylation




DNA methylation is the addition of a methyl group (M) to the DNA base cytosine (C).

- Attachment of methyl groups (-$CH_3$) to DNA bases, usually at cytosine
- Occurs after DNA is replicated (S-phase)
- In general, methylation occurs on genes that are not expressed
  - Methylation suppresses gene expression
  - Removing methylation turns genes “on”

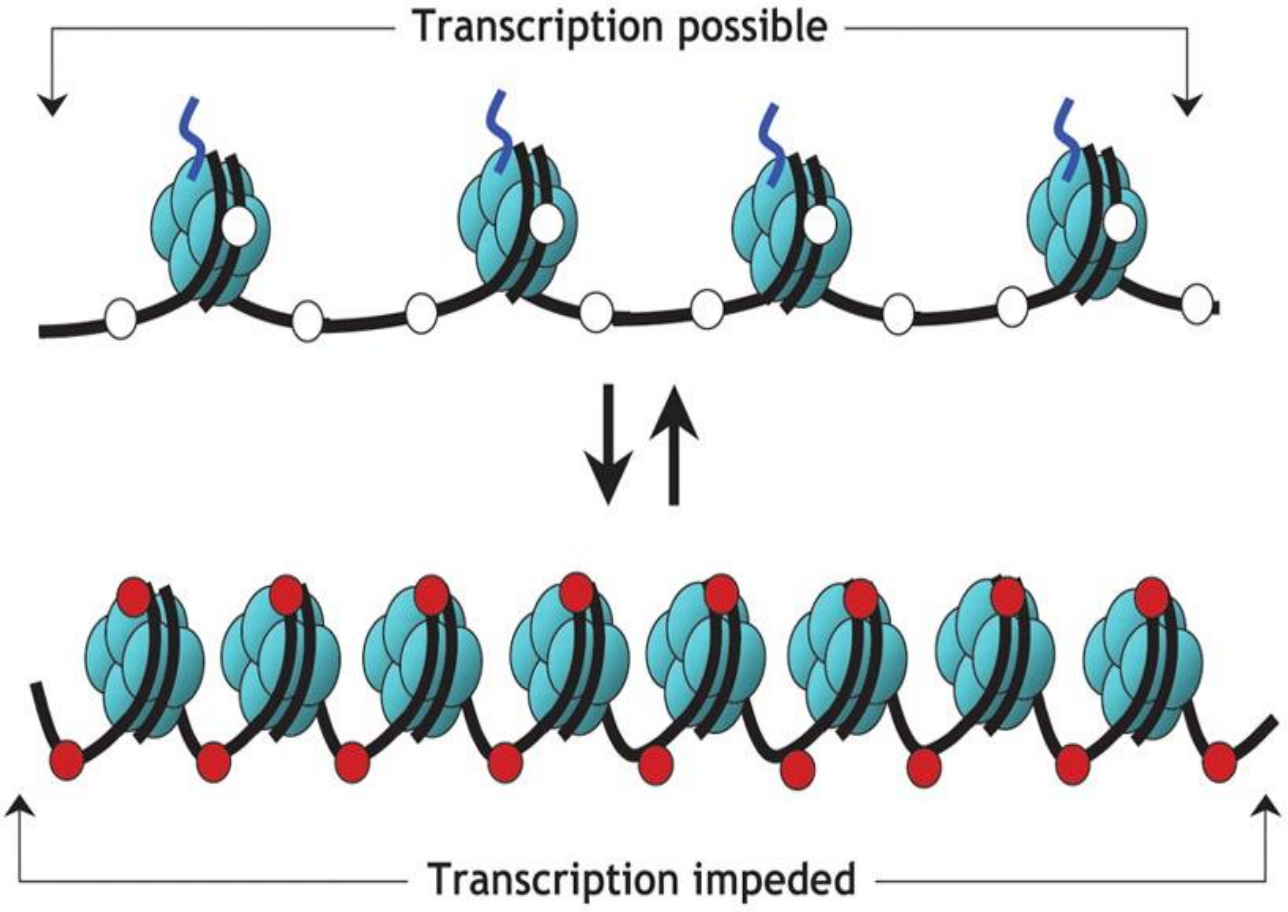
# Histone Acetylation

- Attachment of acetyl group (-$COCH_3$) to histones
- Acetylation changes histone shape reducing its grip on the DNA
- Results in more loosely packed DNA, available for transcription
  - Acetylation activates gene expression
  - Deacetylation suppresses gene expression

# Chromatin Modifications

B

**Gene "switched on"**
- Active (open) chromatin
- Unmethylated cytosines (white circles)
- Acetylated histones




**Gene "switched off"**
- Silent (condensed) chromatin
- Methylated cytosines (red circles)
- Deacetylated histones

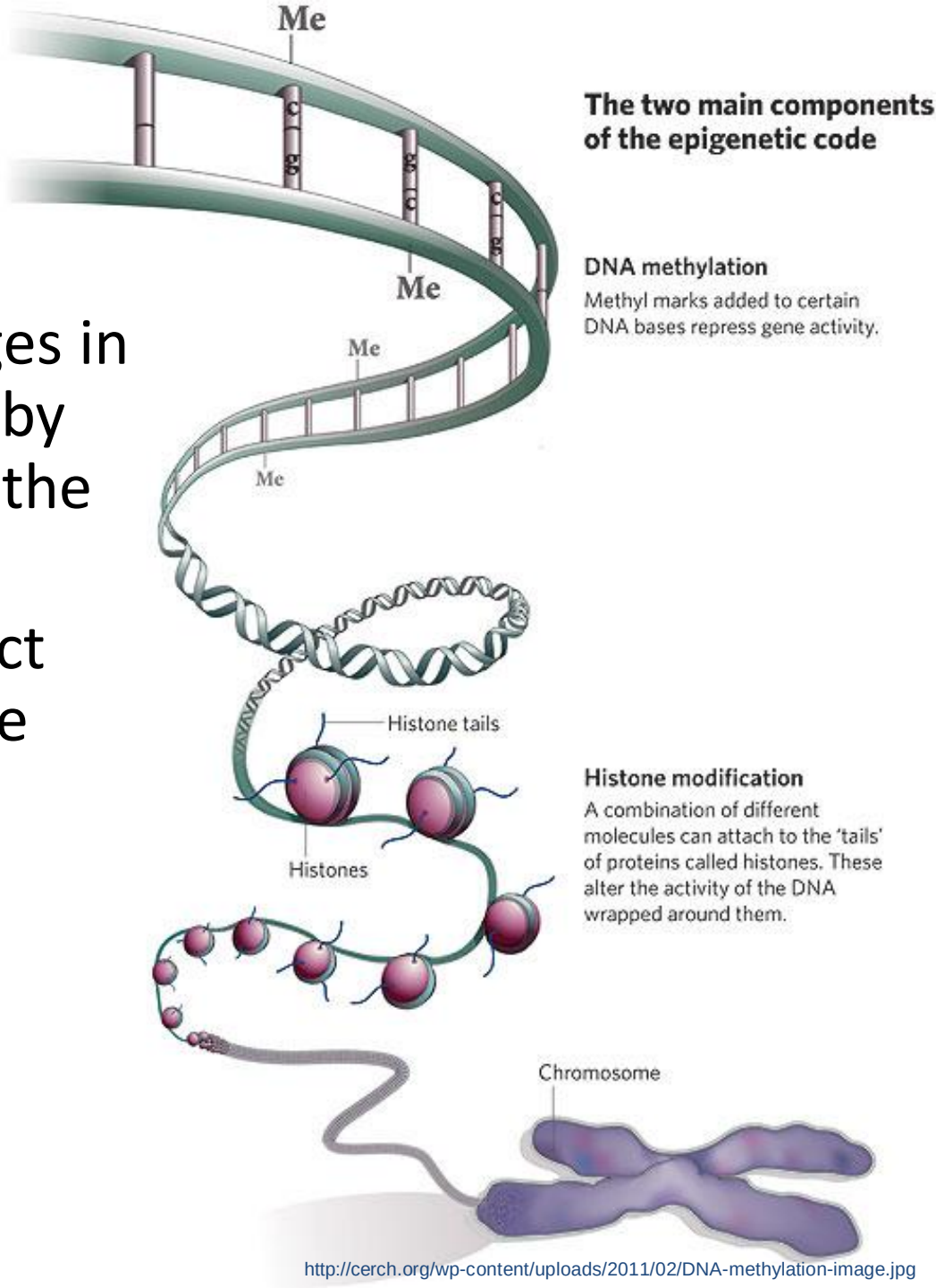
http://cnx.org/content/m26565/latest/graphics35.jpg

# MaCS only

- The following sections are for the MaCS grade 12 biology class only

# Epigenetics

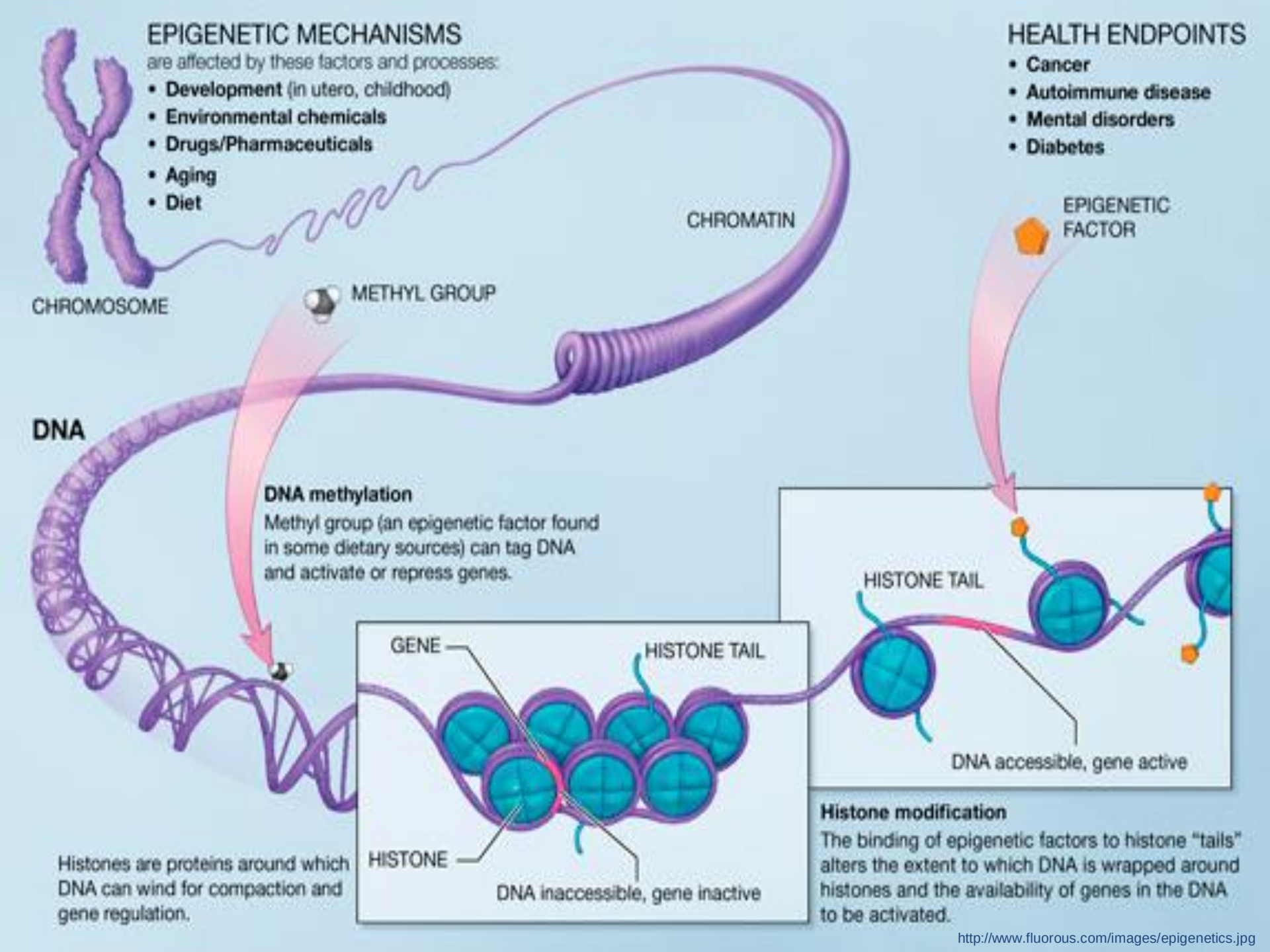
- Study of heritable changes in gene expression caused by mechanisms other than the DNA sequence
- Modifications often affect both chromatin structure and gene regulation
- Modifications include:
  - DNA methylation
  - Histone acetylation




http://cerch.org/wp-content/uploads/2011/02/DNA-methylation-image.jpg

# Genomic Imprinting

- Imprinting: suppression of genes so that only 1 allele is expressed
  - Established in germline cells
  - Maintained in all somatic cells derived from the parent cell
- Most genes are not imprinted: both alleles are expressed
- Imprinted genes:
  - Expressions regulated by epigenetic factors
  - Inactivated gene can be either maternal or paternal
  - Genes are expressed from the non-imprinted allele




http://www.fluorous.com/images/epigenetics.jpg

# Epigenetics Videos

- BeginBeforeBirth “What makes us who we are?” (4:11)
  http://www.youtube.com/watch?v=9AfBsTAQ8zs

- Watch the two videos below and answer the associated questions on the worksheets (download from website)
- PBS NOVA Now “Epigenetics” (13:03)
  http://www.youtube.com/watch?v=7WEHoCA1hpo
- BBC Horizon “The Ghost in Your Genes” (49:06)
  http://www.youtube.com/watch?v=dibpxvU4ml0