1.Describe  the  mechanism  by  which  an  organism’s  genome  is  passed  on  to  the  next generation  of  cells.

a.  Define  somatic  cells,  and  relate  their  division  to  the  cell  cycle  and  mitosis.

- any cell of a living organism other than the reproductive cells.

### - Prophase Mitosis begins with prophase, during which chromosomes recruit condensin and begin to undergo a condensation process that will continue until metaphase. In most species, cohesin is largely removed from the arms of the sister chromatids during prophase, allowing the individual sister chromatids to be resolved. Cohesin is retained, however, at the most constricted part of the chromosome, the centromere (Figure 9). During prophase, the spindle also begins to form as the two pairs of centrioles move to opposite poles and microtubules begin to polymerize from the duplicated centrosomes.

Prometaphase

Prometaphase begins with the abrupt fragmentation of the nuclear envelope into many small vesicles that will eventually be divided between the future daughter cells. The breakdown of the nuclear membrane is an essential step for spindle assembly. Because the centrosomes are located outside the nucleus in animal cells, the microtubules of the developing spindle do not have access to the chromosomes until the nuclear membrane breaks apart.

Prometaphase is an extremely dynamic part of the cell cycle. Microtubules rapidly assemble and disassemble as they grow out of the centrosomes, seeking out attachment sites at chromosome kinetochores, which are complex platelike structures that assemble during prometaphase on one face of each sister chromatid at its [centromere](http://www.nature.com/scitable/topicpage/Chromosome-Segregation-in-Mitosis-The-Role-of-242). As prometaphase ensues, chromosomes are pulled and tugged in opposite directions by microtubules growing out from both poles of the spindle, until the pole-directed forces are finally balanced. Sister chromatids do not break apart during this tug-of-war because they are firmly attached to each other by the cohesin remaining at their centromeres. At the end of prometaphase, chromosomes have a bi-orientation, meaning that the kinetochores on sister chromatids are connected by microtubules to opposite poles of the spindle.

Metaphase Next, chromosomes assume their most compacted state during metaphase, when the centromeres of all the cell's chromosomes line up at the equator of the spindle. Metaphase is particularly useful in cytogenetics, because chromosomes can be most easily visualized at this stage. Furthermore, cells can be experimentally arrested at metaphase with mitotic poisons such as colchicine. Video microscopy shows that chromosomes temporarily stop moving during metaphase. A complex checkpoint mechanism determines whether the spindle is properly assembled, and for the most part, only cells with correctly assembled spindles enter anaphase.

Anaphase The progression of cells from metaphase into anaphase is marked by the abrupt separation of sister chromatids. A major reason for chromatid separation is the precipitous degradation of the cohesin molecules joining the sister chromatids by the protease separase.

Two separate classes of movements occur during anaphase. During the first part of anaphase, the kinetochore microtubules shorten, and the chromosomes move toward the spindle poles. During the second part of anaphase, the spindle poles separate as the non-kinetochore microtubules move past each other. These latter movements are currently thought to be catalyzed by motor proteins that connect microtubules with opposite polarity and then "walk" toward the end of the microtubules.

Telophase and Cytokinesis Mitosis ends with telophase, or the stage at which the chromosomes reach the poles. The nuclear membrane then reforms, and the chromosomes begin to decondense into their interphase conformations. Telophase is followed by cytokinesis, or the division of the cytoplasm into two daughter cells. The daughter cells that result from this process have identical genetic compositions.

b.  What  the  important  check  points  are  in  the  cell  cycle,  what  they  normally do and what  happens  if  they  are  nonfunctional.

## The cell cycle is controlled by three internal checkpoints that evaluate the condition of the genetic information.

#### Key Points

* A checkpoint is one of several points in the eukaryotic [cell](https://www.boundless.com/definition/cell/) cycle at which the progression of a cell to the next stage in the cycle can be halted until conditions are favorable.
* Damage to [DNA](https://www.boundless.com/definition/dna/) and other external factors are evaluated at the G1 checkpoint; if conditions are inadequate, the cell will not be allowed to continue to the S phase of [interphase](https://www.boundless.com/definition/interphase/).
* The G2 checkpoint ensures all of the [chromosomes](https://www.boundless.com/definition/chromosome/) have been replicated and that the replicated DNA is not damaged before cell enters [mitosis](https://www.boundless.com/definition/mitosis/).
* The M checkpoint determines whether all the sister [chromatids](https://www.boundless.com/definition/chromatid/) are correctly attached to the spindle [microtubules](https://www.boundless.com/definition/microtubule/) before the cell enters the irreversible anaphase stage.

#### Terms

* [spindle checkpoint](https://www.boundless.com/definition/spindle-checkpoint/) -(M checkpoint) prevents separation of the duplicated chromosomes until each chromosome is properly attached to the spindle apparatus
* [G2 checkpoint](https://www.boundless.com/definition/g2-checkpoint/) -ensures all of the chromosomes have been replicated and that the replicated DNA is not damaged
* [cyclin](https://www.boundless.com/definition/cyclin/) -any of a group of proteins that regulates the cell cycle by forming a complex with [kinases](https://www.boundless.com/definition/kinase/)
* [restriction point](https://www.boundless.com/definition/restriction-point/) - (G1 checkpoint) a point in the animal cell cycle at which the cell becomes "committed" to the cell cycle, which is determined by external factors and signals

## Regulation at Internal Checkpoints

It is essential that the daughter cells are exact duplicates of the parent cell. Mistakes in the duplication or distribution of the chromosomes lead to mutations that may be passed forward to every new cell produced from an abnormal cell. To prevent a compromised cell from continuing to divide, internal control mechanisms operate at three main cell cycle checkpoints. A checkpoint is one of several points in the [eukaryotic](https://www.boundless.com/definition/eukaryotic/) cell cycle at which the progression of a cell to the next stage in the cycle can be halted until conditions are favorable (e.g. the DNA is repaired). These checkpoints occur near the end of G1, at the G2/M transition, and during metaphase .

[Internal Checkpoints During the Cell Cycle](https://www.boundless.com/biology/textbooks/boundless-biology-textbook/cell-reproduction-10/control-of-the-cell-cycle-89/regulation-at-internal-checkpoints-398-11625/images/fig-ch10_03_01/)

The cell cycle is controlled at three checkpoints. The integrity of the DNA is assessed at the G1 checkpoint. Proper chromosome duplication is assessed at the [G2 checkpoint](https://www.boundless.com/definition/g2-checkpoint/). Attachment of each kinetochore to a spindle fiber is assessed at the M checkpoint.

## The G1 Checkpoint

The G1 checkpoint determines whether all conditions are favorable for cell division to proceed. The G1 checkpoint, also called the restriction point (in yeast), is a point at which the cell irreversibly commits to the cell division process. External influences, such as [growth factors](https://www.boundless.com/definition/growth-factor/), play a large role in carrying the cell past the G1 checkpoint. The cell will only pass the checkpoint if it is an appropriate size and has adequate [energy](https://www.boundless.com/definition/energy/) reserves. At this point, the cell also checks for DNA damage. A cell that does not meet all the requirements will not progress to the S phase. The cell can halt the cycle and attempt to remedy the problematic condition, or the cell can advance into G0 (inactive) phase and await further signals when conditions improve.

If a cell meets the requirements for the G1 checkpoint, the cell will enter S phase and begin DNA replication. This transition, as with all of the major checkpoint transitions in the cell cycle, is signaled by cyclins and [cyclin](https://www.boundless.com/definition/cyclin/) dependent kinases (CDKs). Cyclins are cell-signaling [molecules](https://www.boundless.com/definition/molecule/) that regulate the cell cycle.

## The G2 Checkpoint

The G2 checkpoint bars entry into the [mitotic phase](https://www.boundless.com/definition/mitotic-phase/) if certain conditions are not met. As with the G1 checkpoint, cell size and [protein](https://www.boundless.com/definition/protein/) reserves are assessed. However, the most important role of the G2 checkpoint is to ensure that all of the chromosomes have been accurately replicated without mistakes or damage. If the checkpoint mechanisms detect problems with the DNA, the cell cycle is halted and the cell attempts to either complete DNA replication or repair the damaged DNA. If the DNA has been correctly replicated, cyclin dependent kinases (CDKs) signal the beginning of mitotic cell division.

## The M Checkpoint

The M checkpoint occurs near the end of the metaphase stage of mitosis. The M checkpoint is also known as the spindle checkpoint because it determines whether all the [sister chromatids](https://www.boundless.com/definition/sister-chromatid/) are correctly attached to the spindle microtubules. Because the separation of the sister chromatids during anaphase is an irreversible step, the cycle will not proceed until the kinetochores of each pair of sister chromatids are firmly anchored to at least two spindle fibers arising from opposite poles of the cell.

2.  Describe the  molecular  anatomy  of  genes  and  genomes.

### Gene -DNA information unit that is able to perform a function

### Exons -Protein coding and untranslated regions (UTR)

### Introns-Splice acceptor and donor sites

### Non-coding genes -tRNA, rRNA, microRNA

### Other DNA elements -Transposable elements, repetitive DNA, "junk" DNA

### Semidiscontinuous DNA Replication -Both daughter strands are synthesized in their 5' to 3' direction. The leading strand is synthesized continuously, whereas the lagging strand is synthesized discontinuously. The lagging strand segments are known as Okazaki fragments

### Priming of DNA Synthesis by short RNA segments -Each Okazaki fragment consists of an RNA primer that has been extended by DNA polymerase. The RNA primer is later removed.

### Substrate requirements for DNA polymerase -Template: there must be a template strand to be copied. Primer: DNA polymerase I cannot initiate DNA synthesis by itself (de novo); it can only extend a preexisting chain. A 3' Hydroxyl End: The reaction mechanism requires that the primer must have a free 3' OH end

### DNA Polymerase Structure -The active site cleft of DNA polymerases resembles a partially closed right hand

### Palm domain -Beta-sheet. Primary elements of catalytic site. Binds two Mg2+ ions. Monitors accuracy

### Fingers -Binds to incoming dNTP. Folds over if correct base pair is made. Twists template so that only one base pair is in the active site.

### DNA Polymersae Function -Single active site. Exploits geometry of A=T and G=C base pairs. Kinetic selectivity. Distinguish between rNTPs and dNTPs

### The 3' to 5' exonuclease function of DNA polymerase I -This enzymatic activity excise mispaired nucleotides from the 3' end of the growing DNA strand

### Replication Initiation Requires Helicase and Primase - DNA helicases unwind DNA at the replication fork. DNA helicases are processive. DNA helicases must be "loaded" onto DNA

### The replication of DNA -The replisome, which contains two DNA polymerase III holoenzymes, synthesizes both the leading and lagging strands. The lagging strand template must loop around to permit the holoenzyme to extend the primed lagging strand. The holoenzyme releases the lagging strand template when it encounters the previously synthesized Okazaki fragment. This may signal the primosome to initiate synthesis of a lagging strand RNA primer. The holoenzyme rebinds the lagging strand template and extends the RNA primer to form a new Okazaki fragment.

### The leading and lagging strands are synthesized simultaneously -RNA primers are removed by Pol 1's 5' to 3' exonuclease function. Nicks are sealed by DNA ligase.

### Replication Terminates at specific sites -The TerC, TerB, TerF and TerG sites, in combination with Tus protein, allow a counterclockwise-moving replisome to pass but not a clockwise-moving replisome. The opposite is true of the TerA, TerD and TerE sites. Consequently, two replication forks that initiate bidirectional DNA replication at oriC will meet between the oppositely facing Ter sites

### Removal of RNA primers -RNase H1 excises all but the 5'-ribonucleotide of the RNA primer. FEN1, a 5' to 3' endonuclease, then removes the remaining ribonucleotide along with a segment of adjoining DNA if it contains mismatches. The excised nucleotides are replaced as DNA polymerase completes the synthesis of the next Okazaki fragment. The nick is eventually sealed by DNA ligase.

### Replication of a linear chromosome -Leading strand synthesis can proceed to the end of the chromosome. However, DNA polymerase cannot synthesize the extreme 5' end of the lagging strand because it can only extend an RNA primer that is paired to the 3' end of a template strand. Removal of the primer and degradation of the remaining single-stranded extension would cause the chromosome to shorten with each round of replication

### Telomerase extends chromosome ends -The telomere's 5'-ending strand is later extended by normal lagging strand synthesis

### Promoter -The DNA sequence at which the RNA polymerase (RNAP) binds

### 5' UTR -The untranslated sequence upstream from the coding region of an mRNA

### 3' UTR -The untranslated sequence downstream from the coding region of an mRNA.

### Splicing -One type of eukaryotic mRNA processing in which introns are removed from the primary transcript and exons are ligated together. Splicing of transcripts can be different in different tissues.

### Capping -mature mRNAs of eukaryotes have a modified guanosine covalently attached at the 5' end. occurs while pre-mRNA is being made by RNA polymerase, usually when the transcript is only 20 to 25 nucleotides in length.

### Polyadenylation -addition of a short sequence or a tail of adenine (poly A-tail) nucleotides to the 3' end of an mRNA molecule. happens during RNA spilcing in eukaryotes.

### Progressive unwinding of a negatively supercoiled DNA molecule -As the double helix in a negatively supercoiled circle (W < 0) is unwound without breaking covalent bonds (T decreases), W increases until it reaches 0. Further unwinding of the double helix then causes the DNA to supercoil in the opposite direction, yielding a positively coiled superhelix (W > 0)

### Type IA topoisomerase action -By cutting a single-stranded DNA, pasing a loop of a second strand through the break, and then resealing the break, a type IA topoisomerase can catenate two single-stranded circles or unwind duplex DNA by one turn

### Eukaryotic Chromosome Structure

Chromosomes - DNA + associated proteins  
- Compact  
- Protect DNA from damage  
- Ensures replicated DNA is properly segragated  
- Provides an overall organisation to DNA which facilitates recombination, and gene expression

### Nucleosome -DNA + histone proteins. Core of 8 histone proteins (H2A, H2B, H3, H4). DNA wrapped 1.65 x around outside. Linker DNA and histone H1 between

### Histone tails -Histone tails are not required for association. Histone tails are extensively modified by phosphorylation, acetylation and methylation of ser and lys. Core histones without N-terminal tailss cannot form 30-nm fibres

### Binding of histone H1 to the nucleosome - The two complete superhelical turns of the DNA enable H1 to bind to the DNA's two ends and its middle.

### Higher-order structures

- DNA double helix  
- Nucleosome supercoil  
- Chromatin filament

### Solenoid

- 6 nucleosomes/turn  
- stabilized by histone tails  
- weakened by acetylation

### Sanger Method (Dideoxynucleotide chain termination)

1. Obtain single polynucleotide strands  
2. Separate complementary DNA strands by heating, which breaks the hydrogen bonds between bases  
3. Generate polynucleotide fragments that terminate in positions corresponding to each of the four nucleotides  
4. Separate and detect fragments

### Limitations of Sanger Sequencing

Sequences can only be determined in approximately 400-800 base pair chunks known as "reads"

### 454 Sequencing

1. DNA library preparation  
2. DNA amplified on beads in microreactors  
2. DNA sequenced from each microreactor

### Transcriptome

All RNA molecules transcribed in a particular cell/cell line/tissue at a certain developmental stage and under certain conditions.

### Key steps in PCR

1. Isolate DNA  
2. Amplify DNA of fragment of interest  
- Denaturation step (heat for 2 min at 95C)  
- Primer annealing step (specific DNA primers bind to gene of interest, performed at about 60C)  
- Synthesis step (Taq polymerase in presence of deoxynucleotide triphosphates replicates DNA strands beginning at primers, done at 72C)

### Primer design rules

- Primers should be at least 15 base pairs long  
- Have at least 50% GC content  
- Anneal at a temperature in the range of 50-65 degrees C  
- Usually higher annealing temperatures are better (more specific for desired target)  
- Forward and reverse primer should bind at approximately the same temperature

### Primer problems

- Primers should flank the sequence of interest  
- Primer sequences should be unique - primers that match multiple sequences will give multiple products  
- Primers can have self-annealing regions within each primer (hairpin and foldback loops)  
- Pairs of primers can anneal to each other to form "primer dimers"

### Real-time PCR

- Detection of "PCR product fluorescence" at each cycle of PCR  
- No gel-based analysis at the end of the PCR cycle  
- Computer-based analysis of the cycle-fluorescene time course

### Comparative Sequence Analysis

Based on the fact that evolutionary related sequences will share sequence similarity and this provides a clue as to their role (eg related sequence might encode proteins with similar function)

a.  Recognize  that  a  given  gene  is  generally  situated  at  the  same  chromosomal

locus in a  species.

i. Differentiate  between  a  gene  and  an  allele.

A gene is a part of the [DNA](http://www.differencebetween.net/science/difference-between-dna-and-genes/). Alleles on the other hand refer to different versions of the same gene. There are other more subtle differences between the two and this is what we are going to explore on this page:

* Genes are the different parts of the [DNA](http://www.differencebetween.net/science/health/difference-between-dna-and-chromosome/) that decide the genetic traits a person is going to have. Alleles are the different sequences on the [DNA](http://www.differencebetween.net/science/difference-between-dna-and-rna/)-they determine a single characteristic in an individual.
* Another important difference between the two is that alleles occur in pairs. They are also differentiated into recessive and dominant categories. Genes do not have any such differentiation.
* An interesting difference between alleles and genes is that alleles produce opposite phenotypes that are contrasting by nature. When the two partners of a gene are homogeneous in nature, they are called homozygous. However, if the pair consists of different alleles, they are called heterozygous. In heterozygous alleles, the dominant allele gains an expression.
* The dominance of a gene is determined by whether the AA and Aa are alike phenotypically. It is easier to find dominants because they express themselves better when they are paired with either allele.
* Alleles are basically different types of the same gene. Let’s explain this to you in this way- If your eye color was decided by a single gene, the color blue would be carried by one allele and the color green by another. Fascinating, isn’t it?
* All of us inherit a pair of genes from each of our parents. These genes are exactly the same for each other. So what causes the differences between individuals? It is the result of the alleles.
* The difference between the two becomes more pronounced in the case of traits. A trait refers to what you see, so it is the physical expression of the genes themselves. Alleles determine the different versions of the genes that we see. A gene is like a machine that has been put together. However, how it will works will depend on the alleles.

Both alleles and genes play an all important role in the development of living forms. The difference is most colorfully manifest in humans of course! So next time you see the variety of hair color and eye color around you, take a moment and admire the phenomenal power of both the gene and the allele!

Summary:  
1. Genes are something we inherit from our parents- alleles determine how they are expressed in an individual.  
2. Alleles occur in pairs but there is no such pairing for genes.  
3. A pair of alleles produces opposing phenotypes. No such generalization can be assigned to genes.  
4. Alleles determine the traits we inherit.  
5. The genes we inherit are the same for all humans. However, how these manifest themselves is actually determined by alleles!

ii.  Diagram  a  typical  eukaryotic  chromosome  and  indicate  the  locations  of  the chromosome,  p  &  q  arms.

NOTE:  Each  chromosomes  has  a  p  and  q  arm;  p

(petit=  French  for  small)  is  the  short  arm  and  q  is  just  the  next  letter

in the alphabet  and  is  the  long  arm.

<http://www.iupui.edu/~wellsctr/MMIA/images/chromosome_graphic.jpg>

iii.  Differentiate  between  homologous  chromosomes  and  sister

chromatids

Homologous chromosomes are like the chromosomes an individual inherits from their parents. Like you receive an X from your mother and a Y from your father if you are a boy. The X and Y are homologous chromosomes because they code genes for similar traits though they code for different traits. Of your 46 chromosomes, they make 23 pairs--each of those pairs are homologs or homologous chromosomes.   
  
Sister chromatids are the chromosomes when a cell undergoes DNA replication. A chromosome will replicate and one sister chromatid will go to each daughter cell, resulting from the division. The DNA in sister chromatids are identical, assuming no crossing over and synapsis occurs.

b.  Explain  the functional  significance  of  packaging  DNA  into  chromosomes

and its impact  on  eukaryotic  chromosomes,  genetic  content  and  DNA   replication.

<https://www.inkling.com/read/alberts-essential-cell-biology-4th/chapter-5/the-structure-of-eukaryotic>

## Chromosome

A chromosome is an organized structure of DNA and protein that is found in nucleus of the cell. It is a single piece of coiled DNA containing many genes, regulatory elements and other nucleotide sequences. Chromosomes also contain DNA-bound proteins, which serve to package the DNA and control its functions. Chromosomes vary widely between different organisms. The DNA molecule may be circular or linear, and can be composed of 10,000 to 1,000,000,000 nucleotides in a long chain. Typically, eukaryotic cells (cells with nuclei) have large linear chromosomes and prokaryotic cells (cells without defined nuclei) have smaller circular chromosomes, although there are many exceptions to this rule. Also, cells may contain more than one type of chromosome; for example, mitochondria in most eukaryotes and chloroplasts in plants have their own small chromosomes.[[2]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-2)

In eukaryotes, nuclear chromosomes are packaged by proteins into a condensed structure called chromatin. This allows the very long DNA molecules to fit into the cell nucleus. The structure of chromosomes and chromatin varies through the cell cycle. Chromosomes are the essential unit for cellular division and must be replicated, divided, and passed successfully to their daughter cells so as to ensure the genetic diversity and survival of their progeny. Chromosomes may exist as either duplicated or unduplicated. Unduplicated chromosomes are single linear strands, whereas duplicated chromosomes (copied during synthesis phase) contain two copies joined by a centromere. Compaction of the duplicated chromosomes during mitosis and meiosis results in the classic four-arm structure (pictured to the right). Chromosomal recombination plays a vital role in genetic diversity. If these structures are manipulated incorrectly, through processes known as chromosomal instability and translocation, the cell may undergo mitotic catastrophe and die, or it may unexpectedly evade apoptosis leading to the progression of cancer. In practice "chromosome" is a rather loosely defined term.

In prokaryotes and viruses, the term genophore is more appropriate when no chromatin is present. However, a large body of work uses the term chromosome regardless of chromatin content. In prokaryotes, DNA is usually arranged as a circle, which is tightly coiled in on itself, sometimes accompanied by one or more smaller, circular DNA molecules called plasmids. These small circular genomes are also found in mitochondria and chloroplasts, reflecting their bacterial origins. The simplest genophores are found in viruses: these DNA or RNA molecules are short linear or circular genophores that often lack structural proteins. The word chromosome comes from the Greek χρῶμα (chroma, colour) and σῶμα (soma, body) due to their property of being very strongly stained by particular dyes.[[3]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-3)

### Chromatin

Chromatin is the combination of DNA, histone, and other proteins that make up chromosomes. It is found inside the nuclear envelope of eukaryotic cells. It is divided between heterochromatin (condensed) and euchromatin (extended) forms. The functions of chromatin are to package DNA into a smaller volume to fit in the cell, to strengthen the DNA to allow mitosis and meiosis, and to control gene expression and DNA replication. Changes in chromatin structure are affected by chemical modifications of histone proteins, such as methylation and acetylation, and by other DNA-binding proteins.

### Packaging of DNA in chromatin

Chromatin undergoes various forms of change in its structure. Histone proteins, the foundation blocks of chromatin, are modified by various post-translational modification to alter DNA packing. Acetylation results in the loosening of chromatin and lends itself to replication and transcription. When certain residues are methylated they hold DNA together strongly and restrict access to various enzymes. A recent study showed that there is a [bivalent](http://en.wikibooks.org/w/index.php?title=Bivalent_chromatin&action=edit&redlink=1) structure present in the chromatin: methylated lysine residues at location 4 and 27 on histone 3. It is thought that this may be involved in development; there is more methylation of lysine 27 in embryonic cells than in differentiated cells, whereas lysine 4 methylation positively regulates transcription by recruiting nucleosome remodeling enzymes and histone acetylases[[4]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-4).[[5]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-5)

Crick and Watson's famous structure of DNA (called B-DNA) is only one of three possible structural forms.

For the C-N bond between a base and its sugar there are two different conformations. The anti-conformation occurs in all A- and B-DNAs as well as in Z-DNA where a Cytosine is present. In case of a Guanine Z-DNA takes the syn-conformation. The periodic change between a purine and pyrimidine along the strand of a Z-DNA accomplishes the alternating syn-anti-conformation characteristic of the zigzag structure of the Z-DNA helix.

## Histone:The DNA binding protein

Histones are found in the nuclei of eukaryotic cells, and in certain Archaea, namely Euryarchaea, but not in bacteria. Archaeal histones may well resemble the evolutionary precursors to eukaryotic histones. Histone proteins are among the most highly conserved proteins in eukaryotes, emphasizing their important role in the biology of the nucleus.:939 In contrast mature sperm cells largely use protamines to package their genomic DNA, most likely because this allows them to achieve an even higher packaging ratio. Core histones are highly conserved proteins, that is, there are very few differences among the amino acid sequences of the histone proteins of different species. Linker histone usually has more than one form within a species and is also less conserved than the core histones. There are some variant forms in some of the major classes. They share amino acid sequence homology and core structural similarity to a specific class of major histones but also have their own feature that is distinct from the major histones. These minor histones usually carry out specific functions of the chromatin metabolism. For example, histone H3-like CenpA is a histone only associated with the centromere region of the chromosome. Histone H2A variant H2A.Z is associated with the promoters of actively transcribed genes and also involved in the prevention of the spread of silent heterochromatin. Another H2A variant H2A.X binds to the DNA with double strand breaks and marks the region undergoing DNA repair. Histone H3.3 is associated with the body of actively transcribed genes.[[8]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-8)[[9]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-9)

### The nucleosome and "beads-on-a-string"

The basic repeat element of chromatin is the nucleosome, interconnected by sections of linker DNA, a far shorter arrangement than pure DNA in solution.

In addition to the core histones, there is the linker histone, H1, which contacts the exit/entry of the DNA strand on the nucleosome. The nucleosome core particle, together with histone H1, is known as a chromatosome. Nucleosomes, with about 20 to 60 base pairs of linker DNA, can form, under non-physiological conditions, an approximately 10 nm "beads-on-a-string" fibre.

The nucleosomes bind DNA non-specifically, as required by their function in general DNA packaging. There are, however, large DNA sequence preferences that govern nucleosome positioning. This is due primarily to the varying physical properties of different DNA sequences: For instance, [adenosine](http://en.wikibooks.org/w/index.php?title=Adenosine&action=edit&redlink=1) and [thymine](http://en.wikibooks.org/w/index.php?title=Thymine&action=edit&redlink=1) are more favorably compressed into the inner minor grooves. This means nucleosomes can bind preferentially at one position approximately every 10 base pairs (the helical repeat of DNA)- where the DNA is rotated to maximise the number of A and T bases that will lie in the inner minor groove.

**What is a Nucleosome?** Nucleosomes are the basic unit of DNA packaging in eukaryotes, consisting of a segment of DNA wound around a histone protein core. This structure is often compared to thread wrapped around a spool.

Nucleosomes form the fundamental repeating units of eukaryotic chromatin, which is used to pack the large eukaryotic genomes into the nucleus while still ensuring appropriate access to it (in mammalian cells approximately 2 m of linear DNA have to be packed into a nucleus of roughly 10 µm diameter). Nucleosomes are folded through a series of successively higher order structures to eventually form a chromosome; this both compacts DNA and creates an added layer of regulatory control which ensures correct gene expression. Nucleosomes are thought to carry epigenetically inherited information in the form of covalent modifications of their core histones. The nucleosome hypothesis was proposed by Don and Ada Olins in 1974 and Roger Kornberg. The nucleosome core particle consists of approximately 147 base pairs of DNA wrapped in 1.67 left-handed superhelical turns around a histone octamer consisting of 2 copies each of the core histones H2A, H2B, H3, and H4. Core particles are connected by stretches of "linker DNA", which can be up to about 80 bp long. Technically, a nucleosome is defined as the core particle plus one of these linker regions; however the word is often synonymous with the core particle. Linker histones such as H1 and its isoforms are involved in chromatin compaction and sit at the base of the nucleosome near the DNA entry and exit binding to the linker region of the DNA. Non-condensed nucleosomes without the linker histone resemble "beads on a string of DNA" under an electron microscope. In contrast to most eukaryotic cells, mature sperm cells largely use protamines to package their genomic DNA, most likely to achieve an even higher packaging ratio.Histone equivalents and a simplified chromatin structure have also been found in Archea, proving that eukaryotes are not the only organisms that use nucleosomes.

### 30 nm chromatin fibres

With addition of H1, the "beads-on-a-string" structure in turn coils into a 30 nm diameter helical structure known as the 30 nm fibre or filament. The precise structure of the chromatin fibre in the cell is not known in detail, and there is still some debate over this.

This level of chromatin structure is thought to be the form of euchromatin, which contains actively transcribed genes. EM studies have demonstrated that the 30 nm fibre is highly dynamic such that it unfolds into a 10 nm fiber ("beads-on-a-string") structure when transversed by an RNA polymerase engaged in transcription.

The existing models commonly accept that the nucleosomes lie perpendicular to the axis of the fibre, with linker histones arranged internally. A stable 30 nm fibre relies on the regular positioning of nucleosomes along DNA. Linker DNA is relatively resistant to bending and rotation. This makes the length of linker DNA critical to the stability of the fibre, requiring nucleosomes to be separated by lengths that permit rotation and folding into the required orientation without excessive stress to the DNA. In this view, different length of the linker DNA should produce different folding topologies of the chromatin fiber. Recent theoretical work, based on electron-microscopy images[[10]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-10) of reconstituted fibers support this view.[[11]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-11)

### Spatial organization of chromatin in the cell nucleus

The layout of the [genome](http://en.wikibooks.org/w/index.php?title=Genome&action=edit&redlink=1) within the nucleus is not random - specific regions of the genome have a tendency to be found in certain spaces. Specific regions of the chromatin are enriched at the [nuclear membrane](http://en.wikibooks.org/w/index.php?title=Nuclear_membrane&action=edit&redlink=1), while other regions are bound together by protein complexes. The layout of this is not, however, well characterised apart from the compaction of one of the two X chromosomes in [mammalian](http://en.wikibooks.org/w/index.php?title=Mammal&action=edit&redlink=1) [females](http://en.wikibooks.org/w/index.php?title=Female&action=edit&redlink=1) into the [Barr body](http://en.wikibooks.org/w/index.php?title=Barr_body&action=edit&redlink=1). This serves the role of permanently deactivating these genes, which prevents females getting a '[double dose'](http://en.wikibooks.org/w/index.php?title=Dosage_compensation&action=edit&redlink=1) relative to [males](http://en.wikibooks.org/w/index.php?title=Male&action=edit&redlink=1). The extent to which the inactive X is actually compacted is a matter of some controversy.

### Human chromosomes

Chromosomes can be divided into two types—autosomes, and sex chromosomes. Certain genetic traits are linked to your sex, and are passed on through the sex chromosomes. The autosomes contain the rest of the genetic hereditary information. All act in the same way during cell division. Human cells have 23 pairs of large linear nuclear chromosomes, (22 pairs of autosomes and one pair of sex chromosomes) giving a total of 46 per cell. In addition to these, human cells have many hundreds of copies of the mitochondrial genome. [Sequencing](http://en.wikibooks.org/w/index.php?title=DNA_sequencing&action=edit&redlink=1) of the human genome has provided a great deal of information about each of the chromosomes. Below is a table compiling statistics for the chromosomes, based on the Sanger Institute's human genome information in the [Vertebrate Genome Annotation (VEGA) database](http://en.wikibooks.org/w/index.php?title=Vertebrate_and_Genome_Annotation_Project&action=edit&redlink=1).[[12]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-12) Number of genes is an estimate as it is in part based on [gene predictions](http://en.wikibooks.org/w/index.php?title=Gene_prediction&action=edit&redlink=1). Total chromosome length is an estimate as well, based on the estimated size of unsequenced heterochromatin regions.

An **autosome** is a [chromosome](http://en.wikibooks.org/w/index.php?title=Chromosome&action=edit&redlink=1) that is not a [sex chromosome](http://en.wikibooks.org/w/index.php?title=Sex_chromosome&action=edit&redlink=1); that is to say, there is an equal number of copies of the chromosome in males and females.[[13]](http://en.wikibooks.org/wiki/Principles_of_Biochemistry/Chromosome_and_its_structure#cite_note-13) For example, in [humans](http://en.wikibooks.org/w/index.php?title=Human&action=edit&redlink=1), there are 22 pairs of autosomes. In addition to autosomes, there are sex chromosomes, to be specific: X chromosome and Y chromosome. So, humans have 23 pairs of chromosomes.

**Sex chromosomes** The X chromosome is one of the two sex-determining chromosomes in many animal species, including mammals (the other is the Y chromosome). It is a part of the XY sex-determination system and X0 sex-determination system. The X chromosome was named for its unique properties by early researchers, which resulted in the naming of its counterpart Y chromosome, for the next letter in the alphabet, after it was discovered later.

The Y-chromosome is one of the two sex-determining chromosomes in most mammals, including humans. In mammals, it contains the gene SRY, which triggers testis development if present. The human Y-chromosome is composed of about 60 million base pairs. DNA in the Y-chromosome is passed from father to son, and Y-DNA analysis may thus be used in genealogy research.

i.  What  is  the  assumed  purpose  of  methylation  of  DNA  in  (a)

prokaryotes and  (b)  eukaryotes

 **DNA methylation** is a biochemical process where a methyl group is added to the cytosine or adenine **DNA** nucleotides.

A) The main function of DNA methylation in bacteria is to provide a mechanism, which protects the cell from the effect of foreign DNA introduction. Restriction endonucleases discriminate between endogenous and foreign DNA by its methylation pattern. Introduced DNA which is not protected by methylation is then eliminated by cleavage.

Another function of DNA methylation in prokaryotes is the involvement in the control of replication fidelity. During DNA replication the newly synthesised strand does not get methylated immediately, but analysed for mismatches by the mismatch repair system. When a mutation is found the correction takes place on the nonmethylated strand.

B) There are two basic types of normal methylation processes known in eukaryotic cells. First is de novo methylation which is involved in the rearrangement of methylation pattern during embryogenesis or differentiation processes in adult cells Recently a family of enzymes was described, containing two methyltransferases DNMT3a and DNMT3b which show the de novo methylation activity .The homologous genes were identified in mouse. Gene targeting experiments showed that both DNMT3a and DNMT3b are essential for de novo methylation and have no effect of maintenance methylation .

The second methylation activity in eukaryotic cell is the so-called maintenance methylation which is responsible for maintaining the methylation pattern once established. The first mouse maintenance methyltransferase DNMT1 was described by Bestor et al. The enzymes with high homology were found in human and chicken . The functional analysis of the enzyme showed that it has maintenance methylation activity and is vitally important for embryonic development in the mouse. The total homozygous knockout of mouse DNMT1 was lethal for the embryo. During DNA replication DNMT1 is located in the replication complex where it recognises the normally methylated CpG sites in the parent strand and catalyses the addition of the methyl group in the corresponding CpG site in the daughter strand. Active localisation of the enzyme to sites of DNA replication in dividing cells may facilitate a maintenance role of DNMT1. One more methyltransferase - DNMT2 with unclear function was identified by Yoder and Bestor. However already initial studies showed, that this enzyme is not essential for de novo methylation in eukaryotic cells.

To alter the established pattern of methylation there must be a mechanism responsible for the removal of existing methylation. There are two mechanisms known until now. First is a passive demethylation which occurs when DNMT1 fails to maintain the existing methylation pattern. Second is active demethylation which is performed by recently described demethylase.

c.  Cite  examples  of  chromosome  abnormalities  (aneuploidy  vs  polyploidy),

and explain  how  they  happen, why  it  affects  phenotype  and  why  alterations in chromosome  number  can  be  detrimental  or  beneficial.

**Aneuploidy** is a condition in which the [chromosome](http://en.wikipedia.org/wiki/Chromosome) number is not an exact [multiple](http://en.wikipedia.org/wiki/Multiple_%28mathematics%29) of the number characteristic of a particular species. An extra or missing chromosome is a common cause of [genetic disorders](http://en.wikipedia.org/wiki/Genetic_disorder) including human birth defects. Some cancer cells also have abnormal numbers of chromosomes.[[1]](http://en.wikipedia.org/wiki/Aneuploidy#cite_note-1) Aneuploidy originates during [cell division](http://en.wikipedia.org/wiki/Cell_division) when the chromosomes do not separate properly between the two cells. This generally happens when [cytokinesis](http://en.wikipedia.org/wiki/Cytokinesis) begins while [karyokinesis](http://en.wikipedia.org/wiki/Karyokinesis) is still under way.

Different species normally have [different numbers of chromosomes](http://en.wikipedia.org/wiki/List_of_number_of_chromosomes_of_various_organisms) from one another, and the term "aneuploidy" refers to the chromosome number being different from the usual number for that species.

Chromosome abnormalities occur in 1 of 160 live human births.[[*clarification needed*](http://en.wikipedia.org/wiki/Wikipedia:Please_clarify)] Apart from [sex chromosome disorders](http://en.wikipedia.org/wiki/Sex_chromosome_disorders), most cases of aneuploidy result in termination of the developing fetus; the most common extra [autosomal](http://en.wikipedia.org/wiki/Autosome) chromosomes among live births are [21](http://en.wikipedia.org/wiki/Chromosome_21), [18](http://en.wikipedia.org/wiki/Chromosome_18) and [13](http://en.wikipedia.org/wiki/Chromosome_13).

Most embryos cannot survive with a missing or extra [autosome](http://en.wikipedia.org/wiki/Autosome) (numbered chromosome) and are spontaneously aborted. The most frequent aneuploidy in humans is [trisomy 16](http://en.wikipedia.org/wiki/Trisomy_16), although fetuses affected with the full version of this chromosome abnormality do not survive to term (it is possible for surviving individuals to have the mosaic form, where trisomy 16 exists in some cells but not all). The most common aneuploidy that infants can survive with is trisomy 21, which is found in [Down syndrome](http://en.wikipedia.org/wiki/Down_syndrome#Trisomy_21), affecting 1 in 800 births. [Trisomy 18 (Edwards syndrome)](http://en.wikipedia.org/wiki/Edwards_syndrome) affects 1 in 6,000 births, and [trisomy 13 (Patau syndrome)](http://en.wikipedia.org/wiki/Trisomy_13) affects 1 in 10,000 births. 10% of infants with trisomy 18 or 13 reach 1 year of age.[[3]](http://en.wikipedia.org/wiki/Aneuploidy#cite_note-titleAneuploidy-3)

**Polyploid** [cells](http://en.wikipedia.org/wiki/Biological_cell) and [organisms](http://en.wikipedia.org/wiki/Organism) are those containing more than two paired ([homologous](http://en.wikipedia.org/wiki/Homologous_chromosome)) sets of [chromosomes](http://en.wikipedia.org/wiki/Chromosomes). Most species whose cells have [nuclei](http://en.wikipedia.org/wiki/Cell_nucleus) ([Eukaryotes](http://en.wikipedia.org/wiki/Eukaryotes)) are [diploid](http://en.wikipedia.org/wiki/Diploid), meaning they have two sets of chromosomes—one set inherited from each parent. However, **polyploidy** is found in some organisms and is especially common in plants. In addition, polyploidy also occurs in some tissues of animals that are otherwise diploid, such as human [muscle](http://en.wikipedia.org/wiki/Muscle) tissues.[[1]](http://en.wikipedia.org/wiki/Polyploid#cite_note-pmid19571289-1) This is known as **endopolyploidy**. Species whose cells do not have nuclei ([Prokaryotes](http://en.wikipedia.org/wiki/Prokaryotes)) are haploid organisms, with only a single chromosome in each cell. Most eukaryotes have diploid cells, but produce haploid [gametes](http://en.wikipedia.org/wiki/Gametes) (eggs and sperm) by [meiosis](http://en.wikipedia.org/wiki/Meiosis). In [plants](http://en.wikipedia.org/wiki/Plants) and multicellular [algae](http://en.wikipedia.org/wiki/Algae) the [gametophyte](http://en.wikipedia.org/wiki/Gametophyte) generation is haploid, and produces gametes by [mitosis](http://en.wikipedia.org/wiki/Mitosis). A [monoploid](http://en.wikipedia.org/wiki/Ploidy) has only one set of chromosomes, and the term is usually only applied to cells or organisms that are normally diploid. Male [bees](http://en.wikipedia.org/wiki/Bee) and other [Hymenoptera](http://en.wikipedia.org/wiki/Hymenoptera), for example, are monoploid.

Polyploidy refers to a numerical change in a whole set of chromosomes. Organisms in which a particular chromosome, or chromosome segment, is under- or overrepresented are said to be [aneuploid](http://en.wikipedia.org/wiki/Aneuploidy) (from the Greek words meaning "not", "good", and "fold"). Therefore the distinction between aneuploidy and polyploidy is that aneuploidy refers to a numerical change in part of the chromosome set, whereas polyploidy refers to a numerical change in the whole set of chromosomes.[[2]](http://en.wikipedia.org/wiki/Polyploid#cite_note-isbn0-7167-3520-2-2)

Polyploidy may occur due to abnormal [cell division](http://en.wikipedia.org/wiki/Cell_division), either during [mitosis](http://en.wikipedia.org/wiki/Mitosis), or commonly during [metaphase I](http://en.wikipedia.org/wiki/Meiosis#Metaphase_I) in [meiosis](http://en.wikipedia.org/wiki/Meiosis).

Polyploidy occurs in some [animals](http://en.wikipedia.org/wiki/Animal), such as [goldfish](http://en.wikipedia.org/wiki/Goldfish),[[3]](http://en.wikipedia.org/wiki/Polyploid#cite_note-3) [salmon](http://en.wikipedia.org/wiki/Salmon), and [salamanders](http://en.wikipedia.org/wiki/Salamander), but is especially common among [ferns](http://en.wikipedia.org/wiki/Fern) and flowering [plants](http://en.wikipedia.org/wiki/Plant) (see [*Hibiscus rosa-sinensis*](http://en.wikipedia.org/wiki/Hibiscus_rosa-sinensis)), including both wild and cultivated [species](http://en.wikipedia.org/wiki/Species). [Wheat](http://en.wikipedia.org/wiki/Wheat), for example, after millennia of [hybridization](http://en.wikipedia.org/wiki/Hybrid_%28biology%29) and modification by humans, has strains that are **diploid** (two sets of chromosomes), **tetraploid** (four sets of chromosomes) with the common name of [durum](http://en.wikipedia.org/wiki/Durum) or macaroni wheat, and **hexaploid** (six sets of chromosomes) with the common name of bread wheat. Many agriculturally important plants of the genus [*Brassica*](http://en.wikipedia.org/wiki/Brassica) are also tetraploids. Polyploidization is a mechanism of [sympatric speciation](http://en.wikipedia.org/wiki/Sympatric_speciation) because polyploids are usually unable to interbreed with their diploid ancestors.

Polyploidy can be induced in plants and [cell cultures](http://en.wikipedia.org/wiki/Cell_culture) by some chemicals: the best known is [colchicine](http://en.wikipedia.org/wiki/Colchicine), which can result in chromosome doubling, though its use may have other less obvious consequences as well. [Oryzalin](http://en.wikipedia.org/wiki/Oryzalin) will double the existing chromosome content, too.

3.  Justify  the  value  of  studying  genetics  in  organisms  other  than  humans.

a.  Explain  why  it  is  useful  to  investigate  functions  of  many  human  genes  by

studying simple  model  organisms  such  as  yeast,  nematode  worms,  and  fruit

flies.

b.  Describe  the  benefits  and  limitations  of  using  model  systems  to  study

human

diseases.

4.  Be  able  to explain

in  detail DNA  replication  process  in  E.  coli

<http://biowiki.ucdavis.edu/Genetics/Unit_II%3A_Replication,_Maintenance_and_Alteration_of_the_Genetic_Material/6._DNA_replication_II%3A_Start,_stop_and_control/Replication_landscape_in_E._coli>

a.    compare  and  contrast  differences  in  the    DNA  replication    process  in

prokaryotes  and  eukaryotes

b.  Know  the  importance  of  telomeres  and  what  would  be  the  consequences  if

the  telomerase  malfunctioned.

c.    Know  the  enzymes  and  their  functions  in  DNA  replication  including  repair

pathways

5.    Know  the  structure  of  DNA  molecules  and  the  primary,  secondary  and  tertiary  structures  and  their  functions

a.  Compare  and  contrast  purines  and  prymidines

b.  Under

stand  how  to  ‘read’  a  DNA  sequence  in  relationship  to  its  polarity

c.    Understand  the  process  of  DNA  synthesis  in  relation  to  its  structure

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