DNA and Chromosomes

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eLearning in Studienbereichen – MNF – Universität Potsdam

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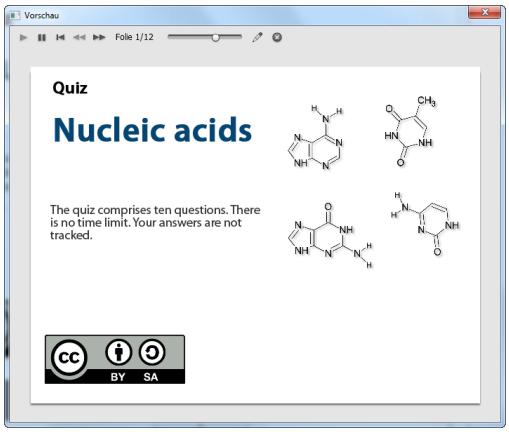
Letzte Überarbeitung: **Oktober 2014**.

Quiz

Start this chapter with the quiz to test for your mastery. You may reattempt the quiz later to check your progress.



Quiz 1. Nucleic acids. Click to play - HTML or Flash (opens new window in your standard web browser).

Chromosomes

Each human cell contains about 2 m of DNA. However, the cell nucleus is only 5-10 µm in diameter. The long DNA molecules are packaged into structures called chromosomes.

The DNA of a chromosome contains many genes, regulatory elements and other intervening nucleotide sequences. Chromosomes also include the DNA-bound proteins which serve to package and manage the DNA. Although the DNA is compacted it remains accessible to all the proteins that replicate it and repair it and which use it for RNA synthesis.

Diploid organisms have two sets of chromosomes (molecules of DNA). For example, human cells have 46 chromosomes: two of the chromosomes 1 through 22 (present in two copies), plus two sex chromosomes – two X chromosomes in a female, one X and one Y chromosome in a male.

The complete set of chromosomes is termed the **karyotype**. Another term for the entire set of chromosomes is **genome**.

For further details on DNA structure, karyotypes and genomes see:

B. Alberts, A. Johnson, J. Lewis et al. (2002) Molecular Biology of the Cell. 4th edition. Garland Science: http://www.ncbi.nlm.nih.gov/books/NBK26909/#A100

C. 'Connor (2008) Karyotyping for chromosolam abnormalities. Nature Education 1: 27

NCBI (2014) Information on genomes including sequences, maps, chromosomes, assemblies, and annotations

Scitable by Nature Education (2014) DNA Is a structure that encodes biological information

A **gene** is usually defined as a segment of DNA that contains instructions for making a protein (i.e. the regulatory sequences such as a promoter and the sequence that is used as a template for mRNA synthesis).

However, some genes direct the synthesis of an RNA molecule as their final product, and RNA can have structural, enzymatic, and regulatory functions (like a protein). Thus, a gene may not necessarily encode a protein, and a better definition may be "molecular unit of heredity".

A gene may vary slightly in its DNA sequence. These variants are called **alleles**. Each gene resides at a particular location on the chromosome. This is more formally called a genetic **locus**.

DNA has two strands of nucleic acid, and RNA has only one strand. The sequence of RNA is determined by the sequence of the DNA. In many, but not in all cases, the RNA in turn is used to direct production of a protein. This flow of information from DNA to RNA (transcription) and from RNA to protein (translation) occurs in all living cells (Figure 1).

Bacteria carry their genes on a single, circular DNA molecule. This molecule is also associated with proteins, but these proteins differ from the ones that package eukaryotic DNA. Thus, the structures of prokaryotic and eukaryotic chromosomes differ in many aspects.

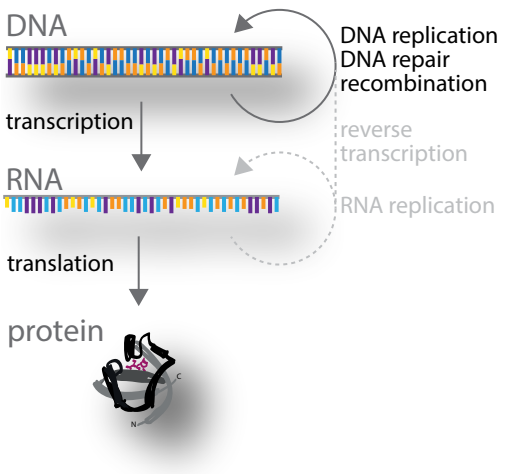


Figure 1. Transfer of information in cells. The information flows from DNA to RNA to protein. This scheme corresponds to the "central dogma of molecular biology" (Crick, 1970). The central dogma, however, is somewhat outdated (Shapiro, 2009). Transfer from RNA to DNA and RNA to RNA occurs in special circumstances. The synthesis of DNA using RNA as template takes place in retroviruses such as HIV. These viruses are single-stranded RNA viruses that use an enzyme termed reverse transcriptase to produce DNA from its RNA genome. RNA viruses use RNA-dependent RNA polymerases to copy their RNA genome.

Cell cycle (eukaryotic cells)

Chromosomes exist in different states throughout the cell cycle.

The cell cycle consists of four distinct phases: G1, S, G2 (collectively known as **interphase**) and M phase (Figure 2). Activation of each phase is dependent on the proper progression and completion of the previous one.

The **M phase** is the period when cells prepare for and then undergo cytokinesis. M phase stands for mitotic phase or mitosis. M phase is itself composed of two tightly coupled processes: **mitosis**, in which the cell's chromosomes are divided between the two daughter cells, and **cytokinesis**, in which the cell's cytoplasm divides forming distinct cells.

During mitosis the chromosomes are paired and then divided prior to cell division. The events in this stage of the cell cycle leading to cell division are prophase, metaphase, anaphase and telophase.

After M phase, the daughter cells begin interphase of a new cycle. The G1, S, and G2 phase of the cell cycle has a distinct set of specialized biochemical processes that prepare the cell for initiation of cell division.

The first phase within interphase is called **G1** (G indicating gap or growth). G1 phase corresponds to the gap in the cell cycle that occurs following cytokinesis. During G1 cells begin synthesizing all the cellular components needed in order to generate two identically compliment-ed daughter cells. As a result the size of cells begins to increase during G1.

Alternatively, cells can exit the cell cycle here and become quiescent or terminally differentiated. Terminal differentiation of a cell is identified as a non-dividing state. Quiescent and terminally differentiated cells are identified as being in **G0** phase.

S phase is the phase of the cell cycle during which the DNA is replicated. This is the DNA synthesis phase. During this phase, the amount of DNA in the cell has effectively doubled. Each chromosome has two (sister) chromatids. Additionally, some specialized proteins are synthesized during S phase, particularly the histones.

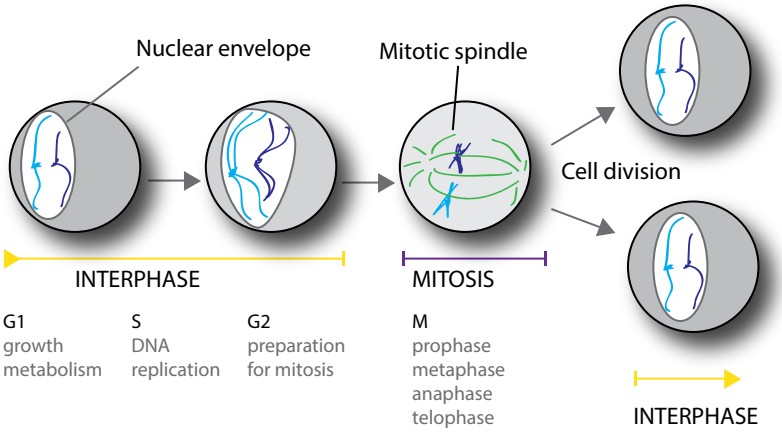


Figure 2. Replication of chromosomes occurs through an ordered cell cycle.

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The cell then enters the **G2** phase, which lasts until the cell enters the next round of mitosis. Significant protein synthesis occurs during this phase, mainly involving the production of microtubules, which are required during the process of mitosis.

Nucleotides

The basic building block of nucleic acids is the **nucleotide**. Nucleotides are the monomers of nucleic acids.

In addition, nucleotides are the structural units of several cofactors and molecules such CoA, flavin adenine dinucleotide, flavin mononucleotide, adenosine triphosphate and nicotinamide adenine dinucleotide phosphate.

Nucleotides have three components:

- a heterocyclic base (Figure 3)
- a sugar
- and a phosphate.

The purine and pyrimidine ring compounds in nucleic acids are known as "**bases**", even though some of them have almost no basic character. The base is linked to position 1 on sugar by a glycosidic bond from N_1 of pyrimidines or N_9 of purines.

Each nucleic acid contains 4 types of bases. The same two purines, adenine and guanine, are present in both DNA and RNA. The two pyrimidines in DNA are cytosine and thymine. In RNA uracil is found instead of thymine. The only difference between uracil and thymine is the presence of a methyl substituent at position C_5.

The bases are usually referred to by their initial letters. DNA contains A, G, C, T, while RNA contains A, G, C, U. The purine and pyrimidine bases are the "side chains" of the nucleic acids.

Nucleic acids are named for the type of sugar: DNA has **2'-deoxyribose**, whereas RNA has **ribose**. The difference is that the sugar in RNA has an OH group at the 2' position of the pentose ring.

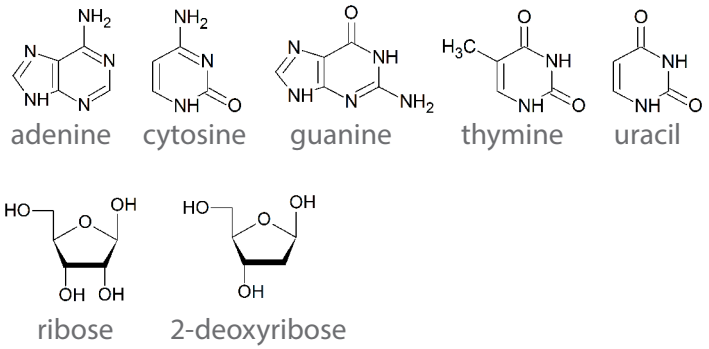

Figure 3. Nitrogen-containing bases and sugars (pentoses) in DNA and RNA. Adenine and guanine are termed **purines**. Cytosine, thymine and uracil are termed **pyrimidines**.

To avoid ambiguity between the numbering systems of the heterocyclic rings and the sugar, positions on the pentose are given a prime (').

RNA but not DNA is susceptible to base-catalyzed cleavage (hydrolysis). Therefore, 2-deoxyribose gives a stable backbone, ribose does not. DNA, which lacks the 2'-OH groups, is resistant to base-catalyzed hydrolysis and is therefore much more chemically stable than RNA.

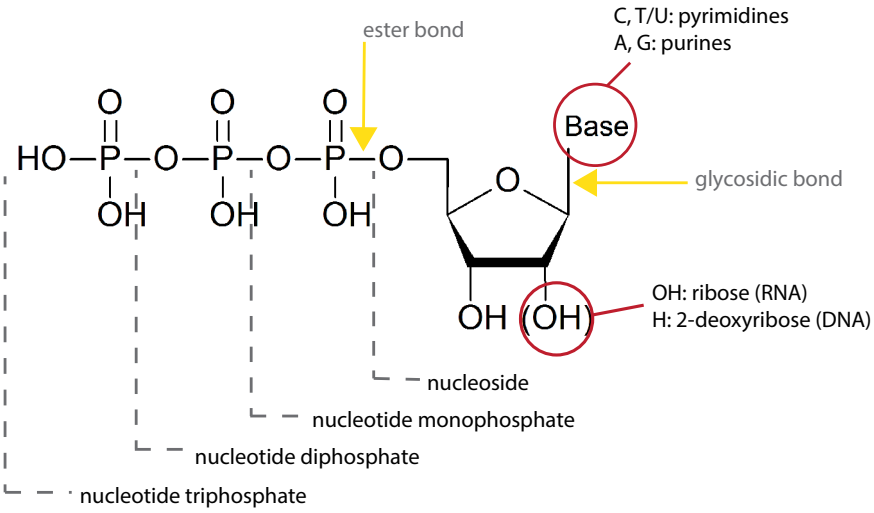

Figure 4. Structure of nucleosides and nucleotides.

Furthermore, a 2'→5' linkage is possible for RNA. This linkage is important in the removal of introns and the joining of exons for the formation of mature RNA.

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This is probably why DNA rather than RNA evolved to be the cellular genetic archive.

Nucleotides are phosphate esters of **nucleosides**. Nucleosides are the N-glycosyl derivates of the bases with ribose or 2-deoxyribose (Figure 4).

The polar groups

- C=O (carboxyl group)
- NH (N-atoms in rings)
- NH_2 (amino group)

present in the bases can form hydrogen bonds to other nucleic acid chains, e.g., in the base pairs of the DNA double helix, and also to proteins.

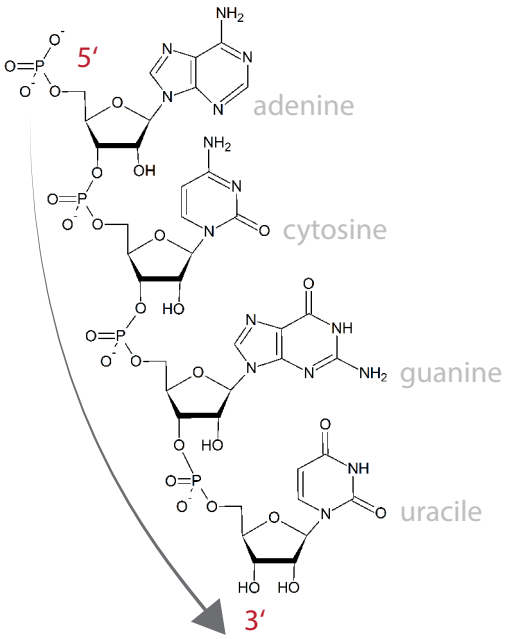

Figure 5. A short length of RNA. The chemical linkage between nucleotides in RNA is the same as that in DNA.

Nucleic acids

A nucleic acid consists of a long chain of nucleotides. The backbone of the polynucleotide chain consists of an alternating series of pentose (sugar) and phosphate residues (Figure 5, Figure 6).

The **sugar-phosphate backbone** consists of 5′-3′ phosphodiester linkages. Each phosphodiester bridge has a negative charge. This negative charge repels nucleophilic species such as hydroxide ions; consequently, phosphodiester linkages are much less susceptible to hydrolytic attack than are other esters.

Whereas the backbone is constant in DNA and RNA, the bases vary from one monomer to the next. The bases stick out from the backbone.

The sugars in nucleic acids are linked to one another by phosphodiester bridges. This is constructed by linking the 5′ position of one pentose ring to the 3′ position of the next pentose ring via a phosphate group.

Double-stranded DNA has equal numbers of adenine and thymine residues (A=T) and equal numbers of guanine and cytosine residues (G=C) (**Chargaff's rule**).

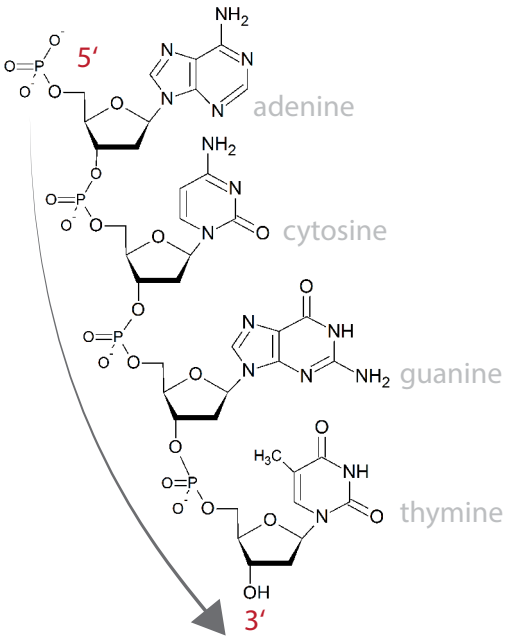

Figure 6. A short length of single stranded DNA.

A DNA chain has **polarity**. The terminal nucleotide at one end of the chain has a free 5′ group, the terminal nucleotide at the other end has a free 3′ group, neither of which is linked to another nucleotide.

It is conventional to write nucleic acid sequences in the 5′→3′ direction – that is, from the 5′ terminus at the left to the 3′ terminus at the right.

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Double helix

The **B form** of DNA is thought to approximate that of most DNA in cells (Figure 7). The double helix is stabilized by hydrogen bonds and hydrophobic interactions.

The **features of the Watson - Crick model** of DNA are:

1. Two helical polynucleotide chains are coiled around a common axis. The chains run in opposite directions.

2. The sugar-phosphate backbones are on the outside and, therefore, the purine and pyrimidine bases lie on the inside of the helix. The bases occupy the core of the helix and sugar-phosphate chains are coiled about its periphery, thereby minimizing the repulsions between charged phosphate groups.

3. The bases are nearly perpendicular to the helix axis, and adjacent bases are separated by 3.4 Å. The helical structure repeats every 34 Å, so there are 10 bases (= 34 Å per repeat/3.4 Å per base) per turn of helix. There is a rotation of 36 degrees per base (360 degrees per full turn/10 bases per turn).

4. The diameter of the helix is 20 Å (2.0 nm).

5. G can be paired with C and A with T to form base pairs that have essentially the same shape (thus, DNA can accommodate an arbitrary sequence of bases) (Figure 8). The Watson-Crick structure can accommodate any sequence of bases on one polynucleotide strand if the opposite strand has the complementary base sequence. This immediately accounts for Chargaff's rule.

6. Base pairs are held together by specific hydrogen bonds. Each base is hydrogen bonded to a base on the opposite strand to form a planar base pair.

7. Adjacent base pairs attract one another through van der Waals forces.

8. Double helix is stabilized by the hydrophobic effect: base stacking, or hydrophobic interactions between the bases, results in the exposure of the more polar surfaces to the surrounding water.

This arrangement is reminiscent of protein folding, where hydrophobic amino acids are interior in the protein and hydrophilic residues are exterior.

On the outside of the DNA molecule are many oxygen atoms, some negatively charged, which are able to form strong hydrogen bonds with water or with proteins that surround the DNA.

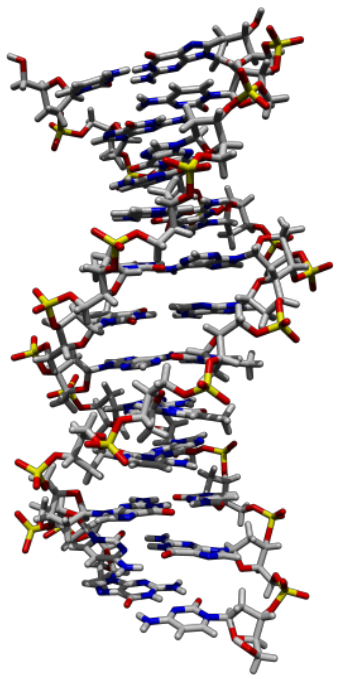

Figure 7. DNA double helix. The model shows a B-DNA dodecamer (drawn from Protein Data Bank 1BNA using YASARA; Drew et al., 1981).

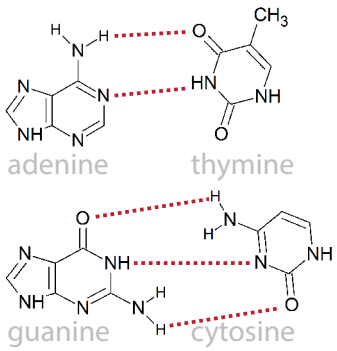

Figure 8. A - T and G - C base pairing. Uracil has the same base-pairing properties as thymine (not shown).

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Semiconservative replication

DNA replication produces two complete double helices from the original DNA molecule. The DNA is the template for its self-replication. The double-helical model of DNA suggested how the genetic material replicates.

The sequence of bases of one strand of the double helix precisely determines the sequence of the other strand. Thus, separation of a double helix into its two component chains would yield two single-stranded templates onto which new double helices could be constructed, each of which would have the same sequence of bases as the parent double helix.

According to the semiconservative replication model the two original DNA strands (i.e., the two complementary halves of the double helix) separate during replication; each strand then serves as a template for a new DNA strand, which means that each newly synthesized double helix is a combination of one old (or original) and one new DNA strand. This distribution of parental atoms is achieved by semiconservative replication.

Meselson and Stahl carried out a critical test of this hypothesis. See web resources:

D.E. Sadava et al. (2008) The Science of Biology. The Meselson-Stahl expperiment. Sinauer Associates, W.H. Freeman & Co, and Sumanas, Inc.

L. Pray (2008) Semi-conservative DNA replication: Meselson and Stahl. Nature Education 1: 98

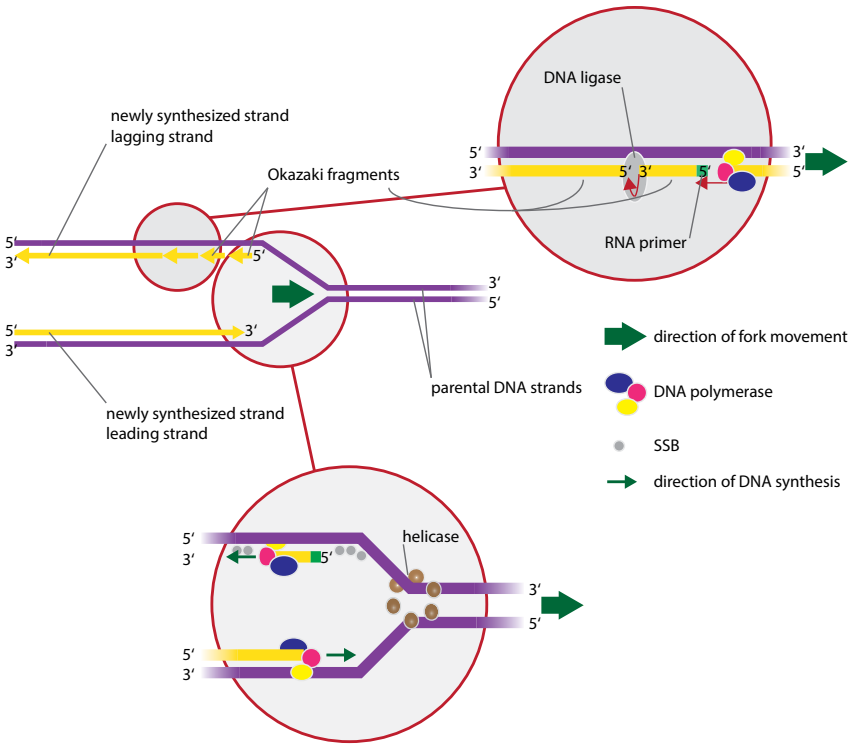

Figure 9. Replication fork. The leading and lagging strand are synthesized in a coordinated fashion. Several proteins act together as a replication machine.

Initiation of DNA replication commits the cell (prokaryotic or eukaryotic) to a further division. Replication is controlled at the stage of initiation. Once replication has started, it continues until the entire genome has been replicated. The completion of replication may provide a trigger for cell division. Then the duplicate genomes are segregated one to each daughter cell.

Replication of duplex DNA takes place by synthesis of two new strands that are complementary to the parental strands. Each parental strand is a template. The point at which replication is occurring is called the replication fork (Figure 9). The double helix is opened up and the two strands are separated to expose unpaired bases (Figure 10).

The most common form of replication is bidirectional, with two replication forks setting out from the origin in opposite directions.

A **replicon** is a region of DNA that replicates from a single origin of replication. In other words: The unit of DNA in which

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an individual act of replication occurs is called the replicon.

DNA replication involves the stages of initiation, elongation, and termination:

Initiation

Initiation involves recognition of an **origin** by a complex of proteins (ORC: origin recognition complex). An origin is a sequence of DNA from which DNA replication is initiated. Before DNA synthesis begins, the parental strands must be separated. Then synthesis of daughter strands can be initiated at the replication fork (Figure 10).

Prokaryotes typically have a single circular chromosome. The initiation of replication is a single event involving a unique site on the bacterial chromosome.

Thus, initiation at a **single origin** sponsors replication of the entire genome.

- A genome of a prokaryotic cell constitutes a single replicon.
- The bacterial chromosome is replicated bidirectionally as a single unit from ***oriC***.
- Two replication forks initiate at *oriC* and move around the genome (at approximately the same speed) to a meeting point.

Eukaryotes possess multiple large linear chromosomes (contained in the cell's nucleus).

- In eukaryotic cells, the replication of DNA is confined to part of the cell cycle, the S phase.
- Eukaryotic chromosomes contain **many replicons**.
- Individual replicons are activated at characteristic times during S phase.
- Regional activation patterns suggest that replicons near one another are activated at the same time.

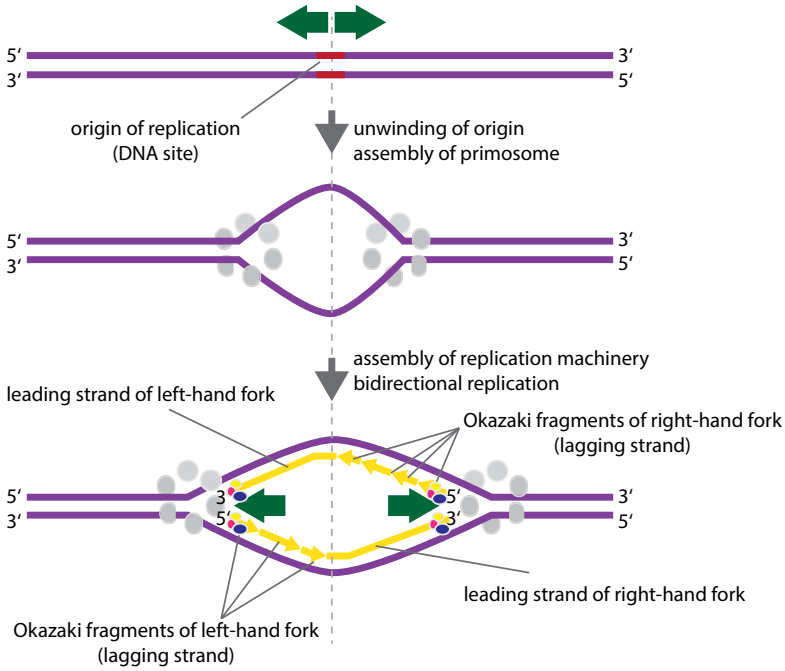

Figure 10. Initiation of DNA replication and formation of a replicon in *E. coli*. During the initiation stage of DNA replication, double-stranded DNA is melted at the origin or replication (*oriC*), a specific DNA sequence. The primosome and finally the replisome (including DNA polymerase) assembles. Usually replication is bidirectional. Thus, two replication forks move in opposite directions. Each fork has a **leading strand**, which is synthesized continuously, and a **lagging strand**, which is discontinuously synthesized in small DNA pieces termed **Okazaki fragments**. These fragments are later joined together for form a continuous strand.

Elongation

Elongation is undertaken by another complex of proteins. The **replisome** exists only as a protein complex associated with DNA during DNA replication, it does not exist as an independent unit (for example, analogous to the ribosome).

The antiparallel structure of the two strands of duplex DNA poses a problem for replication. As the replication fork advances, daughter strands must be synthesized on both of the exposed parental single strands. The fork moves in the direction from 5′ to 3′ on one strand, and in the direction from 3′ to 5′ on the other strand. However, nucleic acids are synthesized only from a 5′ end toward a 3′ end.

On the leading strand DNA synthesis can proceed continuously in the 5′ to 3′

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direction as the parental duplex is unwound.

On the lagging strand a stretch of single-stranded parental DNA must be exposed, and then a segment is synthesized. A series of these fragments are synthesized, each 5′ - 3′; then they are joined together to create an intact lagging strand in a reaction catalyzed by the enzyme DNA ligase.

So the lagging strand is synthesized discontinuously and the leading strand is synthesized continuously. This is called **semidiscontinuous replication**.

Termination

At the end of the replicon, joining and/or termination reactions are necessary. Following termination, the duplicate chromosomes must be separated from one another.

In prokaryotes, termination occurs in a discrete region. Sequences that cause termination are called *ter* sites.

Enzymes involved in DNA replication

Replication of duplex DNA is a complex process involving a variety of enzyme activities.

Different activities are involved in the stages of initiation, elongation, and termination.

- **Topoisomerase** unwinds the helix in front of the "unzip".
- **DNA helicase** "unzips" the DNA at the hydrogen bonds. Helicases facilitate strand separation and use the energy of ATP hydrolysis to move progressively along the DNA and increase strand separation.
- **SSB**s (single strand binding proteins) bind single stranded DNA to prevent premature reannealing.
- **RNA primase** lays down RNA nucleotide "primers" on the template. Synthesis of the new strand can only start from a pre-existing 3′-OH end. The 3′-OH end is called a primer. A sequence of RNA is synthesized on the template, so that the free 3′-OH end of the RNA chain is extended by the DNA polymerase. An enzyme called primase catalyzes the actual priming reaction. Thus, primase is a special RNA polymerase.
- **DNA polymerases** add new dATP, dTTP, dGTP and dCTP to the growing strand. These enzymes utilize single-stranded DNA as templates on which to catalyze the synthesis of the complementary strand from the appropriate deoxynucleoside triphosphates. DNA polymerases catalyze the step-by-step addition of deoxyribonucleotide units to a DNA chain.

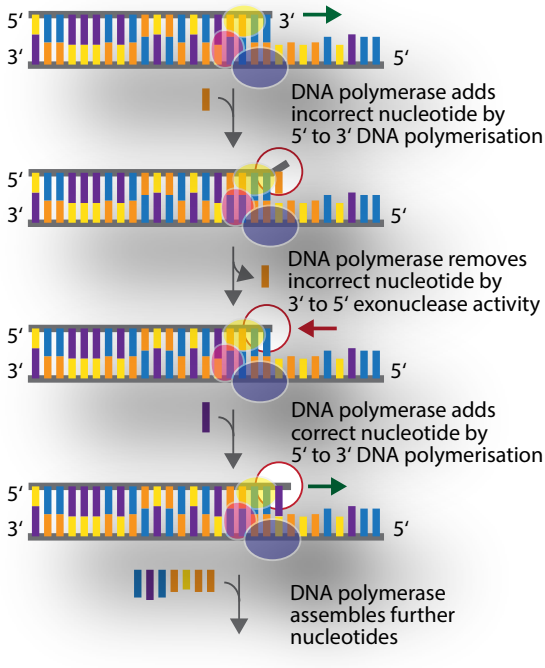

Figure 11. DNA polymerase combines DNA polymerisation activity and proofreading activity. DNA synthesis in the 5′ to 3′ direction is a need for proofreading. In contrast to a (hypothetical) 3′ to 5′ synthesis, incoming nucleotides (rather than the synthesized DNA strand) carry the energy (i.e., two energy-rich phosphoanhydride bonds) required for formation of the sugar-phosphate DNA backbone.

Deoxynucleoside triphosphates are coupled to DNA in a reaction that occurs through the nucleophilic attack of the growing DNA chain's 3′-OH group on the α-phosphoryl of an incoming nucleoside triphosphate. The incoming

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nucleotides are selected by their ability to form Watson-Crick base pairs with the template DNA so that the newly synthesized DNA strand forms a double helix with the template strand. The reaction is driven by the resulting elimination of PP_i and its hydrolysis by pyrophosphatase. DNA polymerase is able to correct DNA mismatches produced during replication (Figure 11).

- **DNA ligase** joins the fragments on the lagging strand. DNA ligase makes the bond that connects the 3′ end of one Okazaki fragment to the 5′ beginning of the next fragment.

For further details on the enzymes involved in DNA replication see:

S. Tintori et al. (2011) CreatureCast - untangling DNA. Vimeo

D. Goodsell & The Protein Data Bank (2013) DNA helicase. RCSB PDB

D. Goodsell & The Protein Data Bank (2004) DNA ligase. RCSB PDB

Scitable by Nature Education (2014) Primase and DNA polymerase

Chromatin

Chromosomes carry the genes (Figure 12). The total number of genes in humans is about 25,000. Nuclear chromosomes (i.e., eukaryotic chromosomes) are packaged by proteins (particularly histones) into chromatin to fit the massive molecules into the nucleus.

Chromatin can be divided into two types. In most regions, the fibers are much less densely packed than in the mitotic chromosome. This material is called **euchromatin**. Euchromatin occupies most of the nuclear region.

Some regions of chromatin are very densely packed, displaying a condition comparable to that of the chromosome at mitosis. This material is called **heterochromatin**. It passes through the cell cycle with little change in its degree of condensation.

The structural condition of the genetic material is correlated with its activity.

Heterochromatin is

- permanently condensed
- often consists of repeats of simple sequences
- density of genes is very much reduced compared with euchromatin, and genes are often inactivated.

Location in euchromatin is necessary for gene expression, but is not sufficient for it.

Chromatin is the complex of DNA and protein found in the eukaryotic nucleus. The structure of chromatin varies through the cell cycle (see page 3), and is responsible for the compaction of DNA into the classic four-arm structure during mitosis and meiosis.

For more details on DNA packaging see:

A.T. Annunziato (2008) DNA packaging: nucleosomes and chromatin. Nature Education 1: 26

Cold Spring Harbor Laboratory (2014) DNA molecule: how DNA is packaged. DNA Learning Center

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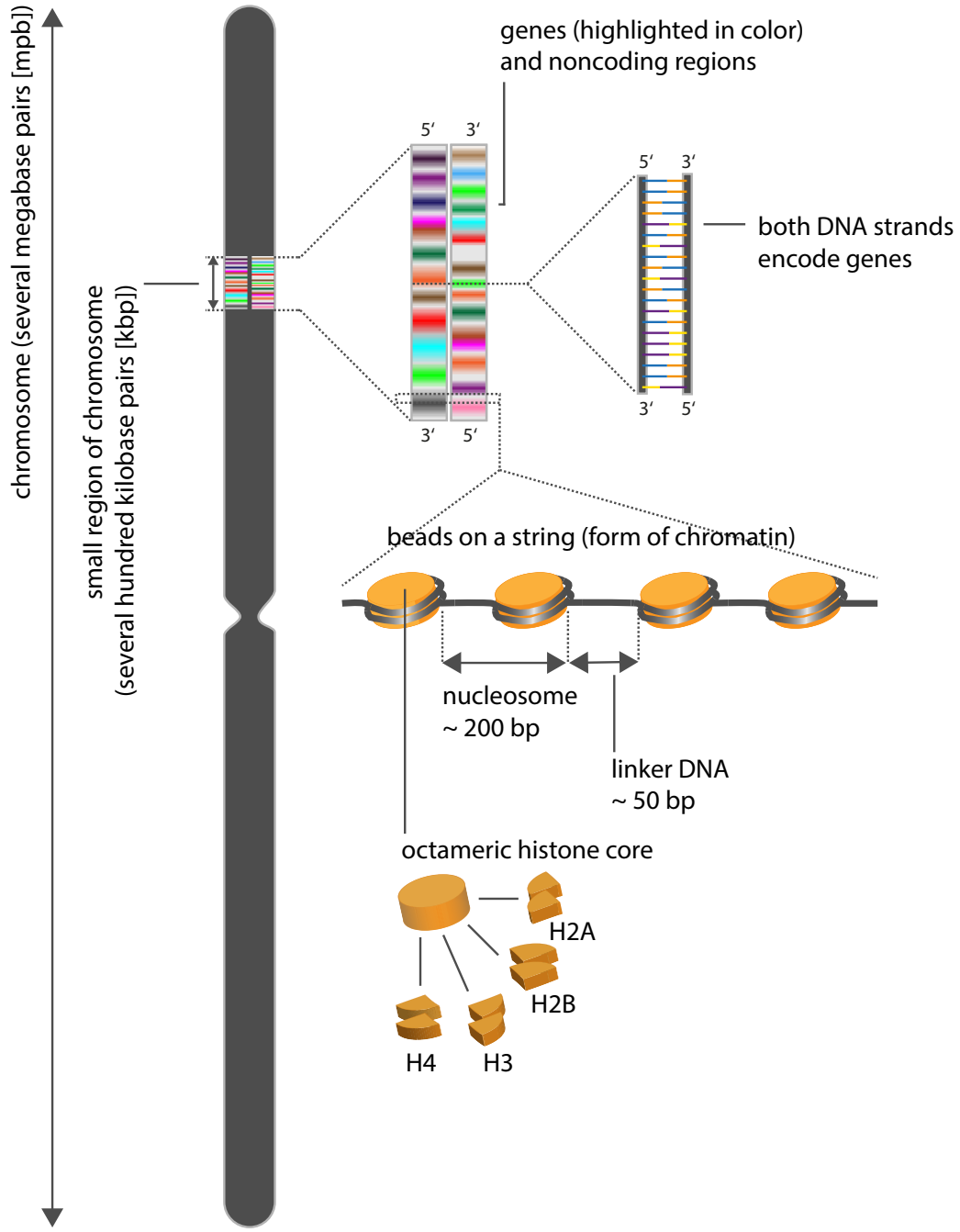

Figure 12. Chromosome structure. Genes are arranged along the chromosomes. Both strands encode genes. Genes vary in length (average length in humans is several kbp). The DNA double strand is wrapped around the **histone core**. 146 nucleotide pairs are wrapped almost twice around the histone core. Histone cores are connected by linker DNA and an additional linker histone, histone H1 (not shown).

Nucleosomes

The fundamental subunit of chromatin – the nucleosome – has the same type of design in all eukaryotes.

Nucleosomes serve two major purposes within the cell nucleus. First, they provide the lowest level of compaction which is required to fit dsDNA (double-stranded DNA) into the cell nucleus. Secondly, they are important in the regulation of transcription by preventing RNA polymerase from unnecessarily accessing the promoter regions of genes which are not needed by the cell.

Nucleosomes are an invariant component of both euchromatin (active chromatin) and heterochromatin (inactive chromatin).

The nucleosome contains ~200 bp of DNA, organized by an octamer of small, basic proteins (**histones**) into a bead-like structure. Thus, nucleosomes look like a

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series of "**beads on a string**". The string is DNA, and each bead is a nucleosome.

A nucleosome contains 2 copies of each histone (H2A, H2B, H3, and H4), and 1 copy of H1. The **core histones** form an interior core; the DNA lies on the surface of the particle. H2A, H2B, H3, and H4 are known as the core histones (Figure 13).

Each of the core histones has a globular body that contributes to the central protein mass of the nucleosome. Each histone also has a flexible N-terminal tail.

The positions of the tails, which account for about one quarter of the protein mass, are not so well defined, and extend out of the nucleosome.

- The N-terminal tails of histones are modified by methylation, acetylation, and phosphorylation.
- These modifications have important effects on the structure of chromatin and in controlling gene expression. In fact, they carry information and represent the **histone code**.

The role of **histone H1** is different from the core histones. It can be extracted more readily from chromatin.

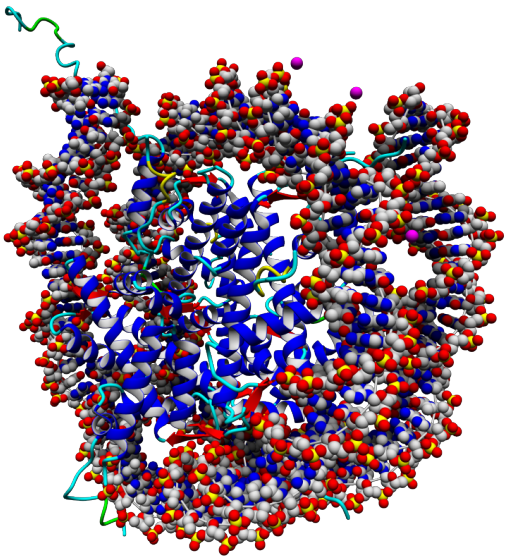

Figure 13. Structure of the nucleosome core particle. 146 bp of DNA are wrapped around the histone protein octamer (drawn from 1AOI.pdb using YASARA; Luger et al., 1997).

The H1 can be removed without affecting the structure of the nucleosome, which suggests that its location is external to the particle. H1 is associated with **linker DNA** which joins adjacent nucleosomes.

30 nm fiber

Chromosome packing occurs on multiple levels.

The current understanding is that repeating nucleosomes with intervening linker DNA form a **10 nm fiber**, known as "**beads on a string**" and have a packing ratio of ~6. The 10 nm fiber is essentially a continuous string of nucleosomes.

A chain of nucleosomes can be arranged in a 30 nm fiber with a packing ratio of ~ 40. The linker histone H1 helps to pull nucleosomes together.

The **30 nm fiber** has a coiled structure. The most likely arrangement is the **solenoid** (a coiled coil structure in which the nucleosomes turn in a helical array).

The 30 nm fiber is folded into loops, and these loops are further condensed to produce the interphase chromosome. This string of loops is further condensed to form the mitotic chromosome. The mechanisms are not yet known in detail.

Functional compartmentalization of the nucleus

Advantages of compartmentalization are:

1. Concentration of the necessary regulatory, structural, and enzymatic components.

2. More opportunities for regulation compared to a freely diffusible state.

Nucleolus

The nucleolus (plural: nucleoli) is a dis-

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crete region of the nucleus where ribosomal RNA is produced (Shaw 2005).

The nucleolus is the **ribosome factory** of the cell where transcription of ribosomal genes (rDNAs), maturation/processing of ribosomal RNAs (rRNSs), and assembly of rRNAs with ribosomal proteins takes place.

Nucleoli assemble at the exit from mitosis, they are functionally active throughout interphase, and they disassemble at the beginning of mitosis.

Speckles

Speckles (**interchromatin granules**) are sites at which the splicing machinery accumulates together with intron containing pre-mRNA and polyadenylated mRNA (Spector and Lamond, 2011).

Speckles potentially represent sites of pre-mRNA processing and of mature mRNA accumulation in the nucleus. Speckles are dynamic structures, their constituents can exchange continuously with the nucleoplasm and active transcription sites.

Chromosomal territories

Chromosomes occupy discrete territories in the cell nucleus and represent highly differentiated structures. The gene's position in the nucleus can impact its transcriptional activity. Active genes in the nucleus are predominantly found within the nuclear interior (Misteli, 2008).

Further Readings

References

B. Alberts, D. Bray, K. Hopkin, A. Johnson, J. Lewis, M. Raff, K. Roberts and P. Walter (2009) Essential Cell Biology, 3rd edition. Garland Science

J.M. Berg, J.L. Tymoczko, L. Stryer (2012) Biochemistry, 7th edition. W.H. Freeman

H.M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T.N. Bhat, H. Weissig, I.N. Shindyalov, and P.E. Bourne (2000) The Protein Data Bank. Nucleic Acids Res. 28: 235-242

T.A. Brown (2002) Genomes. 2nd edition Garland Science: http://www.ncbi.nlm.nih.gov/books/NBK21128/

F. Crick (1970) Central Dogma of Molecular Biology. Nature 227: 561-563

H.R. Drew, R.M. Wing, T. Takano, C. Broka, S. Tanaka, K. Itakura, and R.E. Dickerson (1981) Structure of a B-DNA dodecamer: conformation and dynamics. Proc. Natl. Acad. Sci. USA 78: 2179-2183

E. Krieger and G. Vriend (2014) YASARA View - molecular graphics for all devices - from smartphones to workstations. Bioinformatics doi:10.1093/bioinformatics/btu426

J. Krebs, E.S. Goldstein and S.T. Kilpatrick (2012) Lewin's GENES XI. 11th edition. Jones & Bartlett Learning

K. Luger, A. W. Mäder, R.K. Richmond, D.F. Sargent, and T.J. Richmond (1997) Crystal structure of the nucleosome core particle at 2.8 Å resolution. Nature 389: 251-260

T. Misteli (2008) Chromosome territories: The arrangement of chromosomes in the nucleus. Nature Education 1: 167

J.A. Shapiro (2009) Revisiting the Central Dogma in the 21st century. Ann. N. Y. Acad. Sci. 1178: 6-28

P.J. Shaw (2005) Nucleolus. Encyclopedia of Life Sciences

D.L. Spector and A.I. Lamond (2011) Nuclear Speckles. Cold Spring Harb. Perspect. Biol. 3:a000646

CC BY SA

OER and OCW

Cold Spring Harbor Laboratory (2011) DNA from the beginning

C. O'Connor (editor) (2014) Chromosomes and Cytogenetics. Scitable by Nature Education

G.M. Cooper and M.A. Sunderland (2000) The eukaryotic cell cycle. In: The Cell: A molecular approach, 2nd edition: http://www.ncbi.nlm.nih.gov/books/NBK9876/

OpenLearn (2014) Nucleic acids and chromatin. The Open University

Scitable by Nature Education (2014) Essentials of Cell biology. How do cells know when to divide?

University of Arizona (2004) The cell cycle & mitosis tutorial. In: The Biology Project

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