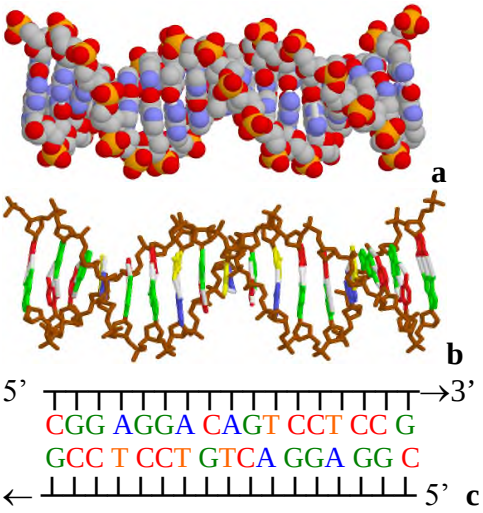
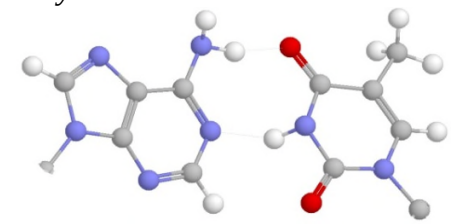
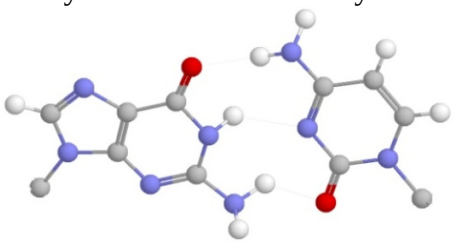
10. Nucleic acids DNA and RNA



23 Fig. ***a*** **DNA** *fragment of 17 nucleotide base pairs and paired bases* ***A***=***T*** *and* ***G***≡***C*** ***b*** *lie between polymer double stranded chains of phosphate deoxy riboses, which depicted with colored letters can draw code sequence on planar paper and* ***c****. Cytosine* ***C*** *is red, guanine* ***G*** *is green, adenine* ***A*** *is blue and thymine* ***T*** *is yellow.*



deoxy ribose **A**=**T** deoxy ribose



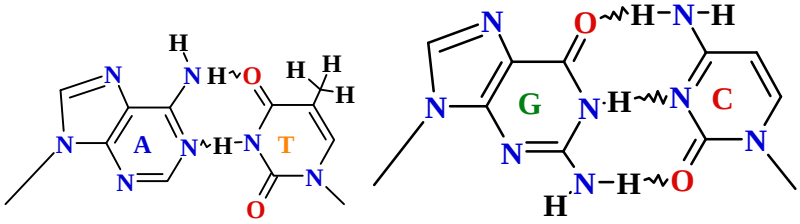
deoxy ribose **G**≡**C** deoxy ribose

24. Fig. Base pair adenine=thymine is bind with two hydrogen bonds. Base pair guanine≡cytosine is bind with three hydrogen bonds.

Aris Kaksis 2016. Year Riga Stradin’s University

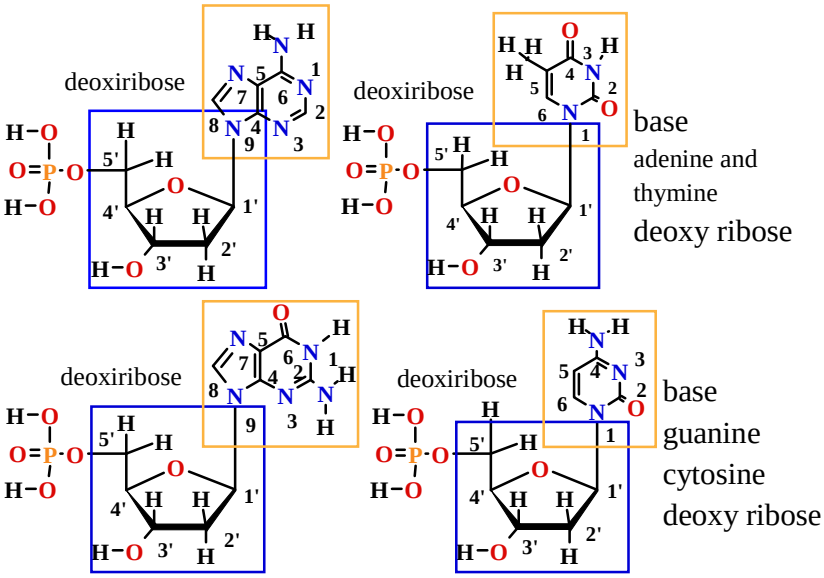
http://aris.gusc.lv/NutritionBioChem/38DNSLabEng310311.doc

Nucleic acids mass fraction of common mass in human body is small, remarkably smaller as 1%, because in each cell nucleus present just one **DNA** copy of molecule. For other molecules of cells copy numbers are millions and billions identical copies. Each cell can have just one active encoded gene set and that is written in unique alone **DNA** molecules. **DNA** molecule forms double stranded helix and consist of four type nucleotides composed two type base pairs adenine=thymine and guanine≡cytosine, where each base pair is genetic coding unit:



deoxy ribose **A**=**T** deoxy ribose **G**≡**C** deoxy ribose

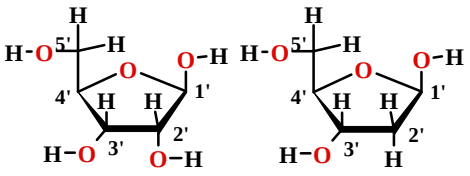
Base is bind with nitrogen atom to first carbon atom of deoxy ribose monosaccharide, but at monosaccharide deoxy riboses fifth carbon hydroxyl group is bind phosphoric acid ester.



Four nucleotides adenine, thymine, guanine and cytosine are encoding elements of genes on **DNA** chain double helix, which letter analogs are A T G C. Those letters original sequence is genetic code. **DNA** polymer chain in polycondensation reaction forms sequence phosphate 5’-deoxy ribose 3’- phosphate – 5’deoxy ribose 3’ – etc.

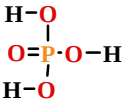
In experiments on 1944.year with bacteria was discovered, that gene information molecule is **nucleic acid**. Every cell of human has one copy of set **deoxyribonucleic acid** (**DNA**) , which comprise human genome, and is discovered since 2003 human genome mapping, as well **ribonucleic acid** (**RNS**) fragment contains genes for many viruses.

Nucleic acid is polymer, which structural unit, element, **nucleotide** Fig.28. (monomer molecule) makes polymer molecule.

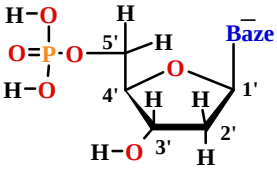


a **b**

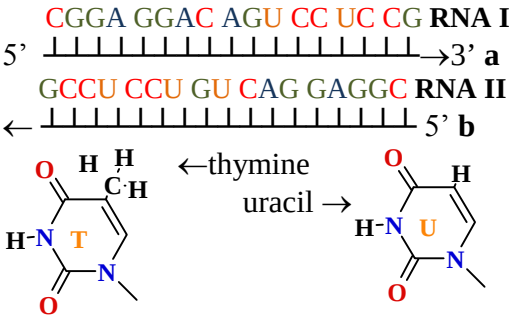
26 Fig. Ribose five carbon and **O** *atoms carbohydrate (sugar)* ***a****. Deoxy ribose five carbon atom carbohydrate (sugar)* ***b****, at 2' carbon atom is absent oxygen* **O** *atom 2'-deoxy-ribose.*



27. Fig. Phosphoric acid.



28. Fig. Nucleotide consist of phosphate, ribose and base as genetic code symbol **A**, **G**, **C**, **T**, **U** adenine, guanine, cytosine, thymine and uracil.



29. Fig. **RNA I** *17 bases chain fragment* **a** *and* **RNS II** *17 bases chain fragment* **b** *contains bases* ***A*** *adenines,* ***U*** *uracils,* ***G*** *guanines and* ***C*** *cytosines, which depicted with letters drawn on plane paper. In* **RNA** *thymine* ***c*** *replacing with uracil and deoxy ribose replacing with ribose assign to* **RNA** *molecules distinct properties from* **DNA** *molecules.* **DNA** *localizes and never leave self location site in nucleus of cell.* **DNA** *molecule forms two antiparallel nucleotide chains double helix. Whereas* **RNA** *molecules are mono thread polynucleotide chains and after transcription easy leave the nucleus of cell in cytosol perform its functions.*

Nucleotide structure make three smaller molecules: ◊ one of five bases, which cyclic molecule forms carbon and nitrogen atoms, ◊ carbohydrate 2-deoxyribose in **DNA** or ribose in **RNS** Fig.26., ◊ phosphoric acid esters of phosphate groups with 5' -**OH** group Fig.28. **Nucleotide** ribose and phosphate alternately forms long nucleic acid polymer chain, in which phosphoric acid second ester bond connects with next nucleotide on third carbon atom hydroxyl group -**OH**, which call one as three prim 3' carbon position on end of chain. **Nucleic acid** chain string direction determines starting from free phosphate ester group $H_2PO_4^-$ at ribose fives carbon atom Fig.28 , which call as five prim 5' on beginning of nucleic acid chain, to end of string, on which lies free spirit group -**OH** of ribose at carbon atom three prim 3'.

Five bases laterally bind to first prim 1' carbon atom of deoxy ribose (**DNA**) or of ribose (**RNA**) serve as genetic code elements and recover the encoded information sequence of genetic code about proteins. Human **deoxy ribonucleic acid DNA** has encoded 31078 proteins (Year 2003 Cellegan human genome mapping data).

That would safeguard the genetic information on alone **DNA** molecule from damages and accidental encoded information in genes erasing, **DNA** molecule forms double helix of two antiparallel polynucleotide chains in direction from 5' to 3' with base pairing between chains on antiparallel direction from 3' to 5' Fig.23.**c**.

Two intermolecular forces from five mentioned in former chapter 9 provide for high stability of **DNA**: **hydrogen bonds** and **hydrophobic bonds** in water medium press together base pair plates (Fig.23) in compact stock of base pair plates as **DNA** antiparallel double stranded helix shape.

Two differences are found in **DNA** and **RNS** molecules. First is sugar molecule, which is backbone member of nucleic acid, determines what's the name has. As sugar is ribose *26. Fig.* **a** , than nucleic acid name is **ribonucleic acid RNA**, if deoxy ribose *26. Fig.* **b**, than nucleic acid name is **deoxy ribonucleic acid DNA**. Second: uracil bases in **RNA** molecule replace position of thymine bases from **DNA** molecule 29 Fig. .

Genetic code from **DNA** molecule to ribosome brings **RNA** polymer chain. **RNA** products of hydrolyze content is similar: adenine, uracil, guanine, cytosine, phosphate and ribose. Ribose at second carbon atom has hydroxyl group —**OH**, but uracil instead thymine methyl group —$\mathbf{CH_3}$ has hydrogen atom —**H**. **RNA** polymer chain is phosphate-5'ribose 3'-phosphate– 5'ribose 3'- phosphate –5'ribose 3'– etc.

Biological differences in **DNA** and **RNA** molecules cause two chemical distinctions: deoxy ribose and ribose; thymine and uracil:

1. **DNA** molecules have antiparallel polynucleotide chains, which form double helixes, and locate only in nucleus of human cells. Also influence or HIV viruses entrancing in cytosol of cell synthesize its **DNA** fragment, which after immediately integrates in **DNA** genome of cell nucleus and never more can leave outside of cell nucleus back to cytosol.

2. **RNA** molecules are mono thread polynucleotide chains and never make long double helixes. **RNA** molecules form both in nucleus of cell and outside cell nucleus. In **RNA** molecule encoded genetic information enzymes transcribe from **DNA** molecule code.

Nucleus of animal, plant and human cells has one **DNA.** **DNA** is as instruction set, what regulates all cell functions. Cells reproduce dividing, etc. parent cell divides in two identical new cells and each new with own original parent nucleus copy.

Before cell division, that biological proliferation, under government of enzymes **DNA** double helix rewinds and new **DNA** copy synthesis process of replication begins, that each new cell in division process would get original parent **DNA** copy.

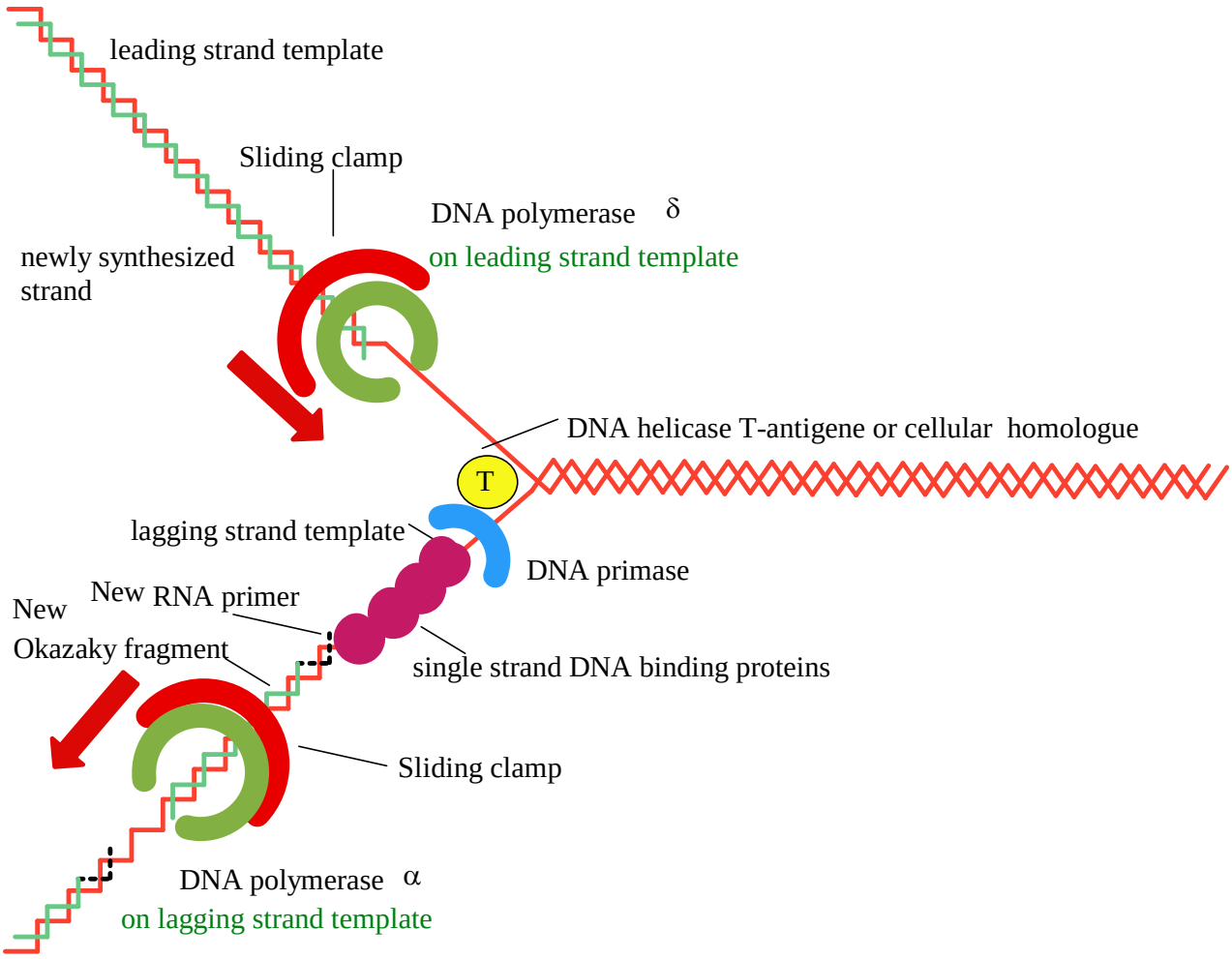
Replication enzymes read nucleotide original sequences and copy over information to two new **DNA** molecules, which receive each divided cell as original copy.

Segment of **DNA** molecule (approximately 300÷34000 nucleotides), what encodes one protein synthesis in ribosome, calls one about **gene**. All in chromosomes being genes compendium calls one about **genome**.

RNA molecule is synthesized in nucleus of cell, because enzymes unwind **DNA** double helix. **RNA** polymerases enzyme reads nucleotide sequence and copy it on messenger **RNA** molecule, which gets out from cell nucleus. Organic bases sequence of messenger **mRNA** molecule calls about **gene**, which contains information about amino acid sequence on protein chain. Synthesized messenger **mRNA** molecule binds to ribosome and initiates protein synthesis reaction. Protein synthesizes in ribosomes reading nucleotide sequence from messenger **mRNA** molecule**.**

20 amino acids transportation to ribosomes carry out 64 transport **tRNA** molecules. Each transport **tRNA** molecule chain thread backbone form 76 nucleotides with ester bonds between phosphate - 5'ribose3'- phosphate – 5'ribose3'- -phosphate – 5'ribose3' – etc. Ribosome enzymes with polycondensation reactions translate to synthesized protein chain amino acids in correct sequence from encoded messenger **mRNA gene** sequence of organic bases set.

Translation process in ribosomes start with amino acid methionine Met[M].

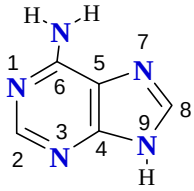


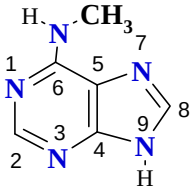
30. Fig. **DNA** *replication (reproduction)*

DNA methylation – adenine, cytosine methyl-transferases

*epigenetics, **DNA methyl**ation, **DNMT1**, **DNMT3**, restriction modification system*

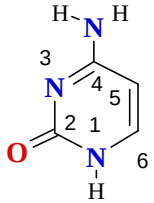
There are three classes of methyltransferases. Two of the classes methylate exocyclic **nitrogens** to convert: 1) **adenine** to **N6**-methyl**adenine** and 3) The third class methylates the fifth **cytosine** carbon **C5** to convert it to **C5**-methyl**cytosine**; this class is referred to as **m5C**-methyltransferases.

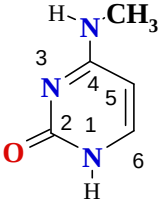




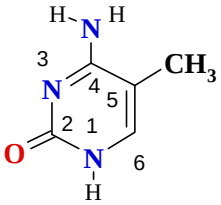
adenine (**A**), **N6**-methyl-**adenine**

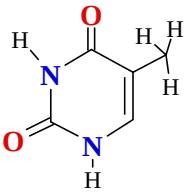
2) **cytosine** to **N4**-methyl**cytosine**.





cytosine (**C**), **N4**-methyl**cytosine**





m5C **cytosine** (**C**) thymine (**T**)

All family members of m5c-methyltransferases are built upon a common architecture of ten conserved motifs (conserved blocks of amino acids). The majority of these conserved, structural motifs are located on the surface of the binding cleft of the molecule to **DNA**.

Your body is built of skin cells, nerve cells, bone cells, and many other different types of cells which are different shapes and sizes, and each type of cell builds a characteristic collection of proteins that are needed for its function. However, every cell in your body contains the same genetic information, encoded in strands of **DNA**. How does each cell decide which genes to use and which ones to ignore?

Genetics and Epigenetics Scientists have discovered that the information in **DNA** does not end at the simple genetic sequence of bases. Cells layer additional forms of control on top of the genetic code, creating "epigenetic" information that modifies the use of particular genes. In some cases, this control is performed by the positioning of nucleosomes. In other cases, bases in the **DNA** are **methyl**ated, modifying how they are read during protein synthesis.

Clean Slate In the first minutes of life, when we are composed of a single cell, this epigenetic information has been wiped clean. In the fertilized egg, the **methyl** groups have been removed and every gene is like all the others. Then, as cells divide in the embryo, they have to make choices about what they are going to do-becoming skin cells or nerve cells or their particular fate. At this point, **DNA methyl**transferases come into play, and they add **methyl** groups to genes, shutting off some and activating others. The **DNA methyl**transferase **DNMT3**, shown here from PDB entry **2QRV**, performs this important job, creating the proper epigenetic coding of **methyl** groups throughout the genome.

Methyl Maintenance Once each cell has decided its fate, this epigenetic code must be maintained for the rest of the life of the organism. When a cell divides, the information must be transmitted to each of the new cells. The **DNA methyl**transferase **DNMT1**, shown here from PDB entry **3PT6**, performs this job. As **DNA** is being replicated, it adds the proper **methyl** groups to the new **DNA** strands.

Notice that both strands have a **Cytosine**, so in a **methyl**ated region of **DNA**, both strands will have a **methyl** group. When the **DNA** is replicated, each of the new **DNA** double helices will have one old strand, complete with **methyl** groups, and one new strand, which is not **methyl**ated. So, **DNMT1** just needs to look for CG base steps where only one strand has a **methyl** group.

Restrictive Bacteria Bacteria also use **DNA methyl**ation, but they use it to protect themselves from viruses. They build **restriction enzymes** that cut **DNA** at specific sequences. Then, they build specific **DNA methyl**transferases, such as the one shown here from PDB entry **1MHT**, that add **methyl** groups to these sequences. The **methyl** groups block the restriction enzyme, but still allow proper reading of the bases during transcription and replication. So, the restriction enzyme floats around the cell with nothing to do, until a virus infects the cell. The **DNA** from the virus typically does not contain any **methyl** groups, so the restriction enzyme quickly chops it into pieces.