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PG AND RESEARCH DEPARTMENT OF BIOCHEMISTRY

E-NOTES

SUBJECT NAME: CHEMISTYY OF BIOMOLECULES

SUBJECT CODE: GBC12

Unit-IV Nucleic acids

Nucleotides- structure and properties, physicochemical properties of nucleicacids, cleavage of nucleic acids by enzymatic methods, non – enzymatic transformation of nucleotides and nucleic acids, methylation, Sequencing, chemical synthesis of DNA. Three dimensional structure of DNA. Different forms of DNA – circular DNA and Supercoiling. Types of RNA mRNA,tRNA, rRNA, Sn RNA,Si RNA,Hn RNA. Structure of t-RNA. Nucleotides as source of energy, component of coenzymes, second messengers.

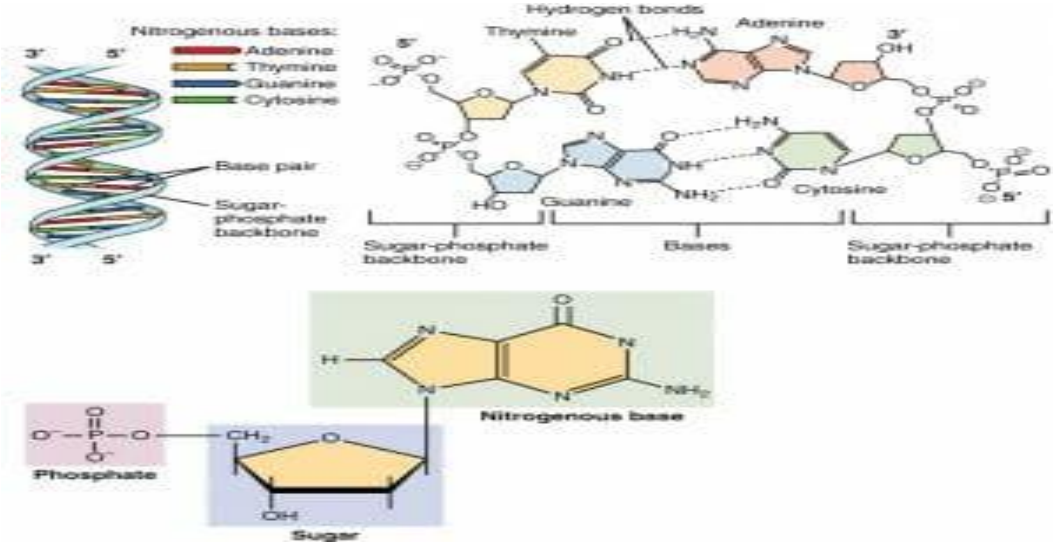
Nucleotide Definition

A nucleotide is an organic molecule that is the building block of DNA and RNA. They also have functions related to cell signaling, metabolism, and enzyme reactions. A nucleotide is made up of three parts: a phosphate group, a 5-carbon sugar, and a nitrogenous base. The four nitrogenous bases in DNA are adenine, cytosine, guanine, and thymine. RNA contains uracil, instead of thymine. A nucleotide within a chain makes up the genetic material of all known living things. They also serve a number of function outside of genetic information storage, as messengers and energy moving molecules.

A series of three nucleotides within the DNA is known as a *codon*, and directs the proteins within the cell to attach a specific protein to a series specified by the rest of the DNA. Special codons even specify to the machinery where to stop and start the process. *DNA translation*, as it is known, converts the information from DNA into the language of proteins. This chain of amino acids can then be properly folded, and provide one of many functions within the cell.

Nucleotide Structure

Nucleotide structure is simple, but the structure they can form together is complex. Below is an image of DNA. This molecule consists of two strands which wrap around each other, forming *hydrogen bonds* in the middle of the structure for support. Each nucleotide within has a specific structure which enables this formation.



Nitrogenous base

The nitrogenous base is the central information carrying part of the nucleotide structure. These molecules, which have different exposed functional groups, have differing abilities to interact with each other. As in the image, the idea arrangement is the maximum amount of hydrogen bonds between nucleotides involved. Because of the structure of the nucleotide, only a certain nucleotide can interact with other. The image above shows thymine bonding to adenine, and guanine bonding to cytosine. This is the proper and typical arrangement.

This even formation causes a twist in the structure, and is smooth if there are no errors. One of the ways proteins are able to repair damaged DNA is that they can bind to uneven spots within the structure. Uneven spots are created when hydrogen bonding does not occur between the opposing nucleotide molecules. The protein will cut out one nucleotide, and replace it with another. The duplicate nature of the genetic strands ensures that errors like this can be corrected with a high degree of accuracy.

Sugar

The second portion of the nucleotide is the sugar. Regardless of the nucleotide, the sugar is always the same. The difference is between DNA and RNA. In DNA, the 5-carbon sugar is deoxyribose, while in RNA, the 5-carbon sugar is ribose. This gives genetic molecules their names; the full name of DNA is deoxyribonucleic acid, and RNA is ribonucleic acid.

The sugar, with its exposed oxygen, can bond with the phosphate group of the next molecule. They then form a bond, which becomes the *sugar-phosphate backbone*. This structure adds rigidity to the structure, as the *covalent* bonds they form are much stronger than the hydrogen bonds between the two strands. When proteins come to process and *transpose* the DNA, they do so by separating the strands and reading only one side. When they pass on, the strands of genetic material comes back together, driven by the attraction between the opposing nucleotide bases. The sugar-phosphate backbone stays connected the whole time.

Phosphate Group

The last part of nucleotide structure, the phosphate group, is probably familiar from another important molecule *ATP*. Adenosine triphosphate, or ATP, is the energy molecule that most life on Earth relies upon to store and transfer energy between reactions. ATP contains three phosphate groups, which can store a lot of energy in their bonds. Unlike ATP, the bonds formed within a nucleotide are known as *phosphodiester bonds*, because they happen between the phosphate group and the sugar molecule.

During DNA replication, an enzyme known as *DNA polymerase* assembles the correct nucleotide bases, and begins organizing them against the chain it is reading. Another protein, *DNA ligase*, finished the job by creating the phosphodiester bond between the sugar molecule of one base and the phosphate group of the next. This creates the backbone of a new genetic molecule, able to be passed to the next generation. DNA and RNA contain all the genetic information necessary for cells to function.

Nucleotide Examples

Adenine

Adenine is a purine, which is one of two families of nitrogenous bases. Purines have a double-ringed structure. In DNA, adenine bonds with thymine. In RNA, adenine bonds with uracil. Adenosine triphosphate, as discussed earlier, uses the nucleotide adenine as a base. From there, three phosphate groups can be attached. This allows a great deal of energy to be stored in the bonds. For the same reason that the sugar-phosphate backbone is so strong, the bonds in ATP are as well. When combined with special enzymes which have formed to release the energy, it can be transferred to other reactions and molecules.

Guanine

Like adenine, guanine is a purine nucleotide; it has a double ring. It bonds with cytosine in both DNA and RNA. As seen in the image above, guanine binds to cytosine through three hydrogen

bonds. This makes the cytosine-guanine bond slightly stronger than the thymine-adenine bond, which only forms two hydrogen bonds.

Cytosine

Pyrimidines are the other class of nucleotide. Cytosine is a pyrimidine nucleotide; it has only one ring in its structure. Cytosine bonds with guanine in both DNA and RNA. Bonding with the nucleotide guanine, the two make a strong pair.

Thymine

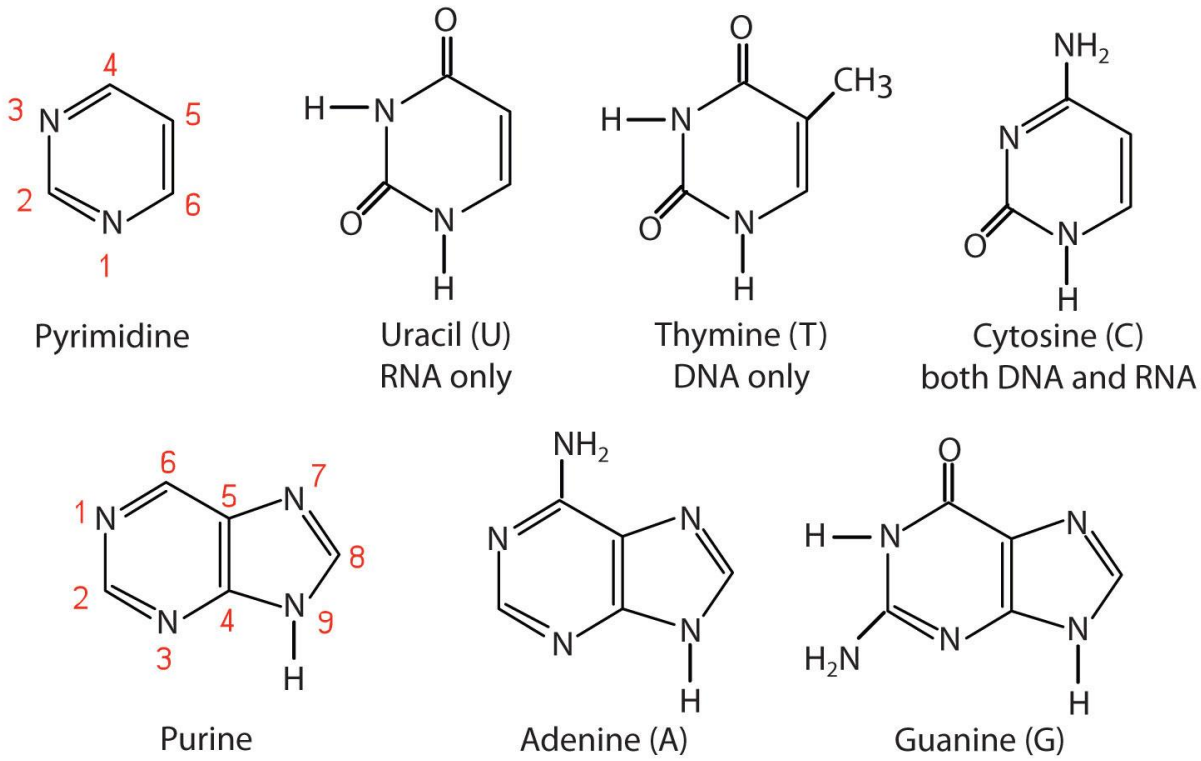
Like the nucleotide cytosine, thymine is a pyrimidine nucleotide and has one ring. It bonds with adenine in DNA. Thymine is not found in RNA. In DNA, it forms only two hydrogen bonds with adenine, making them the weaker pair.

Uracil

Uracil is also a pyrimidine. During transcription from DNA to RNA, uracil is placed everywhere a thymine would normally go. The reason for this is not entirely understood, though uracil has some distinct advantages and disadvantages. Most creatures do not use uracil within the DNA because it is short lived, and can degrade into cytosine. However, in RNA uracil is the preferred nucleotide because RNA is also a short lived molecule.

Nucleotide Function

Besides being the basic unit of genetic material for all living things, a nucleotide can have other functions as well. A nucleotide can be a base in another molecule, such as adenosine triphosphate (ATP), which is the main energy molecule of the cell. They are also found in coenzymes like NAD and NADP, which come from ADP; these molecules are used in many chemical reactions that play roles in metabolism. Another molecule that contains a nucleotide is cyclic AMP (cAMP), a messenger molecule that is important in many processes including the regulation of metabolism and transporting chemical signals to cells. Nucleotides not only make up the building blocks of life, but also form many different molecules that function to make life possible.



DNA Sequencing Definition

DNA sequencing is the process of determining the sequence of nucleotides within a DNA molecule. Every organism's DNA consists of a unique sequence of nucleotides. Determining the sequence can help scientists compare DNA between organisms, which can help show how the organisms are related.

DNA Sequencing Overview

This means that by sequencing a stretch of DNA, it will be possible to know the order in which the four nucleotide bases – **adenine, guanine, cytosine, and thymine** – occur within that nucleic acid molecule.

The necessity of DNA sequencing was first made obvious by Francis Crick's theory that the sequence of nucleotides within a DNA molecule directly influenced the amino acid sequences of proteins. At the time, the belief was that a completely sequenced genome would lead to a quantum leap in understanding the biochemistry of cells and organisms.

Modern DNA sequencing consists of high-throughput methods which allow entire DNA sequences to be discovered in a matter of hours. This technology has allowed many companies to start offering at-home DNA testing. Many of the "results" found by these tests are simply correlations found between a genetic variant and a certain condition. However, technology has also allowed scientists to test the DNA of many organisms to better understand evolutionary relationships.

DNA Sequencing Example

Though DNA sequencing used to take years, it can now be done in hours. **Further, the first full sequence of human DNA took around 3 billion dollars.** Now, certain companies will sequence your entire genome for less than $1,000. The most advanced tests will analyze every nucleotide within your genome. However, many companies now offer *single-nucleotide polymorphism* tests.

These tests focus on individual nucleotides within genes that can signify certain genetic variants. **These SNPs, as they are known, have been correlated to certain conditions and can help predict how your genes may influence your life.** Some SNPs are related to various diseases, while others are related to your metabolism and how your body processes nutrients. Thousands of different correlations have been found, and DNA sequencing can be used to figure out how your genome affects your life.

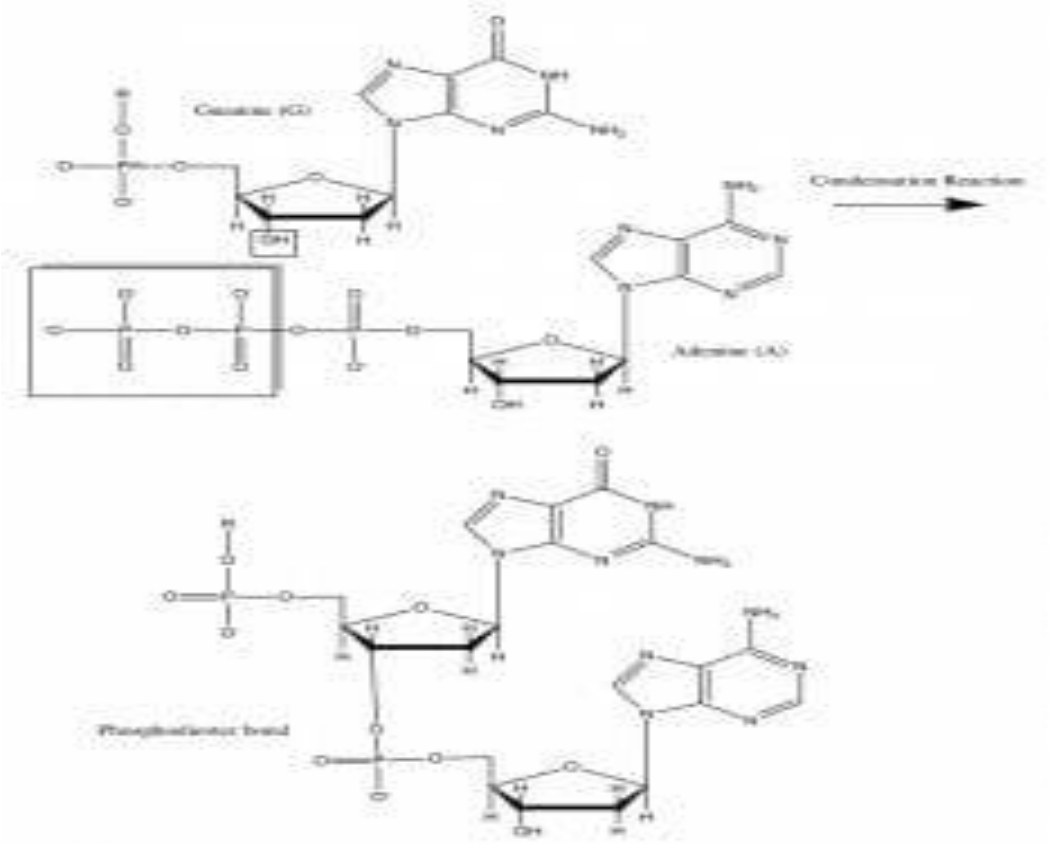
DNA Sequencing Methods

There are two main types of DNA sequencing. **The older, classical chain termination method is also called the Sanger method.** Newer methods that can process a large number of DNA molecules quickly are collectively called High-Throughput Sequencing (HTS) techniques or Next-Generation Sequencing (NGS) methods.

Sanger Sequencing

The Sanger method relies on a **primer that binds to a denatured DNA molecule** and initiates the synthesis of a single-stranded polynucleotide in the presence of a DNA polymerase enzyme,

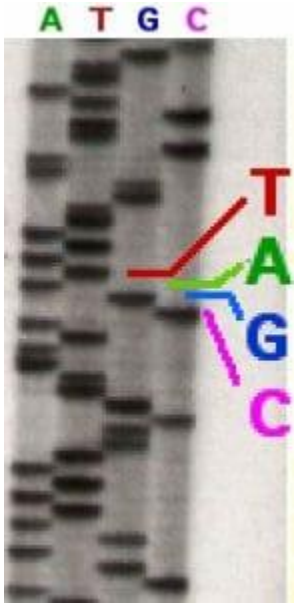
using the denatured DNA as a template. In most circumstances, the enzyme catalyzes the addition of a nucleotide. A covalent bond, therefore, forms between the 3′ carbon atom of the deoxyribose sugar molecule in one nucleotide and the 5′ carbon atom of the next. This image below shows how this bond is formed.



A sequencing reaction mixture, however, would have a small proportion of modified nucleotides that cannot form this covalent bond due to the absence of a reactive hydroxyl group, giving rise to the term ‘dideoxyribonucleotides’, i.e., they do not have a 2’ or 3’ oxygen atom when compared to the corresponding ribonucleotide. This would terminate the DNA polymerization reaction prematurely. **At the end of multiple rounds of such polymerizations, a mixture of molecules of varying lengths would be created.**

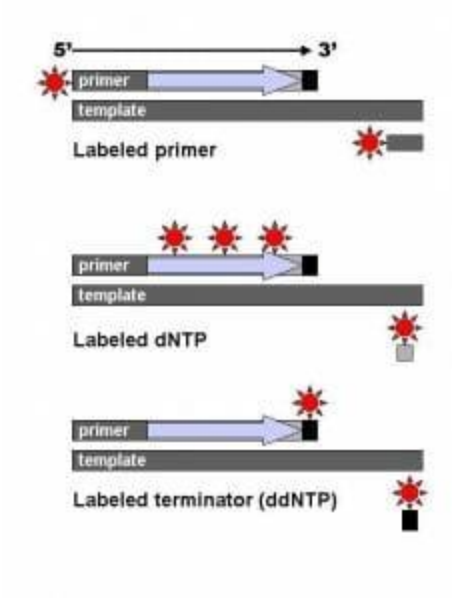
In the earliest attempts at using the Sanger method, the DNA molecule was first amplified using a labeled primer and then split into four test tubes, each having only one type of ddNTP. That is, each reaction mixture would have only one type of modified nucleotide that could cause chain

termination. After the four reactions were completed, the mixture of DNA molecules created by chain termination would undergo electrophoresis on a polyacrylamide gel, and get separated according to their length.

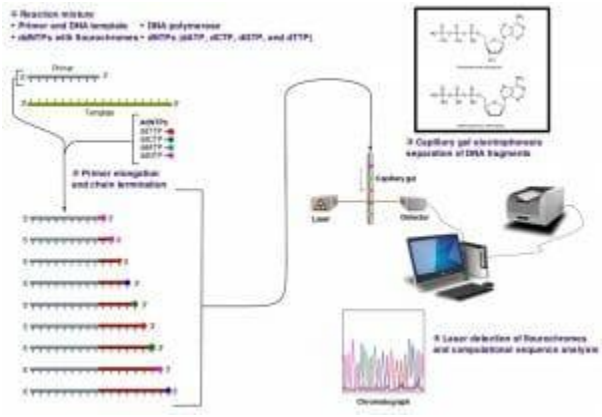


In the image above, a sequencing reaction with ddATP was electrophoresed through the first column. Each line represents a DNA molecule of a particular length, the result of a polymerization reaction that was terminated by the addition of a ddATP nucleotide. The second, third and fourth columns contained ddTTP, ddGTP, and ddCTP respectively.

With time, this method was modified so that each ddNTP had a different fluorescent label. The primer was no longer the source of the radiolabel or fluorescent tag. Also known as dye-terminator sequencing, this method used four dyes with non-overlapping emission spectra, one for each ddNTP.



The image shows the difference between labeled primers, labeled dNTPs and dyed terminator NTPs.



The image above shows a schematic representation of dye-terminator sequencing. There is a single reaction mixture carrying all the elements needed for DNA elongation. The reaction mixture also contains small concentrations of four ddNTPs, each with a different fluorescent tag. The completed reaction is run on a capillary gel. The results are obtained through an analysis of the emission spectra from each DNA band on the gel. A software program then analyzes the spectra and presents the sequence of the DNA molecule.

High Throughput Sequencing

Sanger sequencing continues to be useful for determining the sequences of relatively long stretches of DNA, especially at low volumes. **However, it can become expensive and laborious when a large number of molecules need to be sequenced quickly.** Ironically, though the traditional dye-terminator method is useful when the DNA molecule is longer, high-throughput methods have become more widely used, especially when entire genomes need to be sequenced.

There are three major changes compared to the Sanger method. The first was the development of a cell-free system for cloning DNA fragments. Traditionally, the stretch of DNA that needed to be sequenced was first cloned into a prokaryotic plasmid and amplified within bacteria before being extracted and purified. High throughput sequencing or next-generation sequencing technologies no longer relied on this labor-intensive and time-intensive procedure.

Secondly, these methods created space to run millions of sequencing reactions in parallel. **This was a huge step forward from the initial methods where eight different reaction mixtures were needed to produce a single reliable nucleotide sequence.** Finally, there is no separation between the elongation and detection steps. The bases are identified as the sequencing reaction proceeds. While HTS decreased cost and time, their 'reads' were relatively short. That is, in order to assemble an entire genome, intense computation is necessary.

The advent of HTS has vastly expanded the applications for genomics. DNA sequencing has now become an integral part of basic science, translational research, medical diagnostics, and forensics.

Uses of DNA Sequencing

Traditional, chain-termination technology and HTS methods are used for different applications today. **Sanger sequencing is now used mostly for *de novo* initial sequencing of a DNA molecule to obtain the primary sequence data for an organism or gene.** The relatively short 'reads' coming off an HTS reaction (30-400 base pairs compared to the nearly a thousand base pair 'reads' from Sanger sequencing methods) make it difficult to create the entire genome of an

organism from HTS methods alone. Occasionally, Sanger sequencing is also needed to validate the results of HTS.

On the other hand, **HTS allows the use of DNA sequencing to understand single-nucleotide polymorphisms – among the most common types of genetic variation within a population.** This becomes important in evolutionary biology as well as in the detection of mutated genes that can result in disease. For instance, sequence variations in samples from lung adenocarcinoma allowed the detection of rare mutations associated with the disease. The chromatin binding sites for specific nuclear proteins can also be accurately identified using these methods

Overall, DNA sequencing is becoming an integral part of many different applications.

Diagnostics

Genome sequencing is particularly useful for identifying the causes of rare genetic disorders. **While more than 7800 diseases are associated with a Mendelian inheritance pattern, less than 4000 of those diseases have been definitively linked to a specific gene or mutation.** Early analysis of the exon-genome, or exome, consisting of all the expressed genes of an organism, showed promise in identifying the causal alleles for many inherited illnesses. In one particular case, sequencing the genome of a child suffering from a severe form of inflammatory bowel disease connected the illness to a mutation in a gene associated with inflammation – XIAP. While the patient initially showed multiple symptoms suggestive of an immune deficiency, a bone marrow transplant was recommended based on the results of DNA sequencing. The child subsequently recovered from the ailment.

In addition, HTS has been an important player in developing a greater understanding of tumors and cancers. Understanding the genetic basis of a tumor or cancer enables doctors to have an extra tool in their kit for making diagnostic decisions. **The Cancer Genome Atlas and International Cancer Genome Consortium have sequenced a large number of tumors and demonstrated that these growths can vary vastly in terms of their mutational landscape.** This has also given a better understanding of the kind of treatment options that are ideal for each patient. For instance, the sequencing of the breast cancer genome identified two genes – BRCA1 and BRCA2 – whose pathogenic variants have an enormous impact on the likelihood of

developing breast cancer. People with some pathogenic alleles even choose to have preventive surgeries such as double mastectomies.

Molecular Biology

DNA sequencing is now an integral part of most biological laboratories. It is used to verify the results of cloning exercises to understand the effect of particular genes. **HTS technologies are used to study variations in the genetic compositions of plasmids, bacteria, yeast, nematodes or even mammals used in laboratory experiments.** For instance, a cell line derived from breast cancer tissue, called HeLa, is used in many laboratories around the world and was earlier considered as a reliable cell line representing human breast tissue. Recent sequencing results have demonstrated large variations in the genome of HeLa cells from different sources, thereby reducing their utility in cell and molecular biology.

DNA sequencing gives insight into the regulatory elements within the genome of every cell, and the variations in their activity in different cell types and individuals. **For instance, a particular gene may be permanently turned off in some tissues, while being constitutively expressed in others.** Similarly, those with susceptibility for a specific ailment may regulate a gene differently from those who are immune. These differences in the regulatory regions of DNA can be demonstrated through sequencing and can give insight into the basis for a phenotype.

Recent advances have even allowed individual laboratories to study structural variations in the human genome – an undertaking that needed global collaboration two decades ago.

Forensics

The ability to use low concentrations of DNA to obtain reliable sequencing reads has been extremely useful to the forensic scientist. In particular, the potential to sequence every DNA within a sample is attractive, especially since a crime scene often contains genetic material from multiple people. **HTS is slowly being adopted in many forensics labs for human identification.** In addition, recent advances allow forensic scientists to sequence the exome of a person after death, especially to determine the cause of death. For instance, death due to poisoning will show changes to the exome in affected organs. On the other hand, DNA

sequencing can also determine that the deceased had a preexisting genetic ailment or predisposition. The challenges in this field include the development of extremely reliable analysis software, especially since the results of HTS cannot be manually examined.

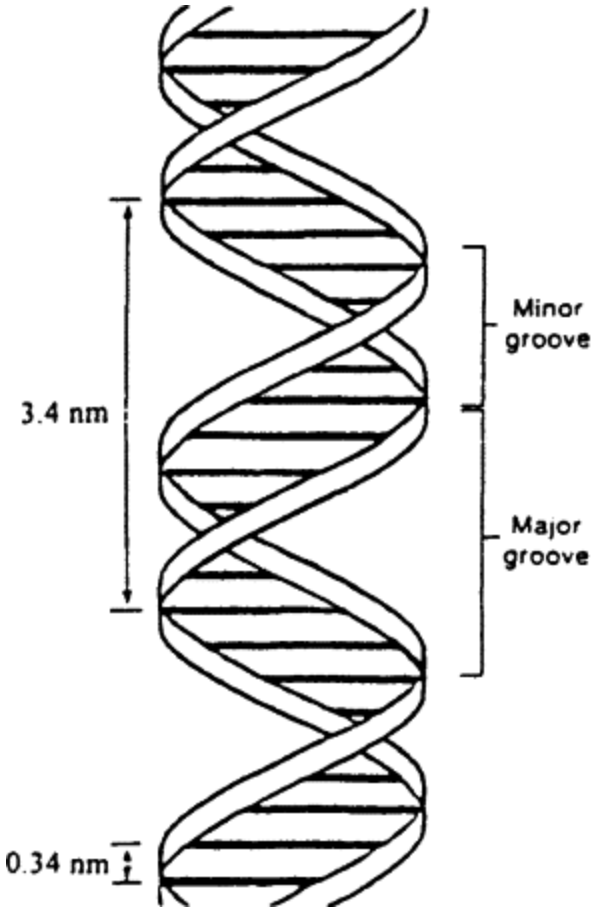
DNA Double-Helix Structure

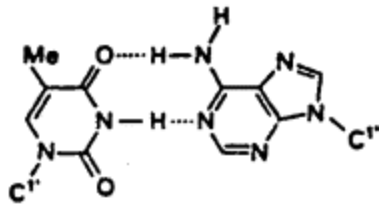
DNA is an antiparallel double helix. The phosphate backbone (the curvy lines) is on the outside, and the bases are on the inside. Each base interacts with a base from the opposing strand. (credit: Jerome Walker/Dennis Myts)

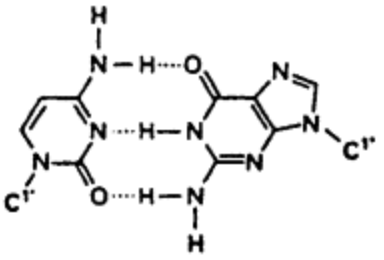
DNA has a double-helix structure . The sugar and phosphate lie on the outside of the helix, forming the backbone of the DNA. The nitrogenous bases are stacked in the interior, like the steps of a staircase, in pairs; the pairs are bound to each other by hydrogen bonds. Every base pair in the double helix is separated from the next base pair by 0.34 nm.

The two strands of the helix run in opposite directions, meaning that the 5′ carbon end of one strand will face the 3′ carbon end of its matching strand. (This is referred to as antiparallel orientation and is important to DNA replication and in many nucleic acid interactions.)

Only certain types of base pairing are allowed. For example, a certain purine can only pair with a certain pyrimidine. This means A can pair with T, and G can pair with C, as shown in Figure 3. This is known as the base complementary rule. In other words, the DNA strands are complementary to each other. If the sequence of one strand is AATTGGCC, the complementary strand would have the sequence TTAACCGG. During DNA replication, each strand is copied, resulting in a daughter DNA double helix containing one parental DNA strand and a newly synthesized strand.







Functions

Nucleic acid is an important class of macromolecules found in all cells and viruses. The functions of nucleic acids have to do with the **storage** and expression of genetic information. Deoxyribonucleic acid (DNA) encodes the information the **cell** needs to make **proteins**

Types of DNA

A-form DNA

A-DNA is a right-handed double helix made up of deoxyribonucleotides. It appears when the relative humidity of the environment is less than 75%, which means that it is rarely present in normal physiological condition. The two strands of A-DNA are anti-parallel with each other and

not symmetrical. The molecule is asymmetrical is because the glycosidic bonds of a base pair are not diametrically opposite to each other. Therefore, major grooves and minor grooves can be observed in each turn. One turn of the helix consists of 11 base pairs with a length of 2.86nm. The backbone of A-DNA is formed by sugar phosphates that are linked continuous using phosphodiester bonds. All the nitrogenous bases are at the core centre of the helix. Hydrogen bonds between nitrogenous bases allow the molecule to exhibit the double helix structure. The helix width of A-DNA is 2.3nm. Overall, A-DNA is wider than the more commonly found B-DNA.

B-form DNA

B-form DNA is a right-handed double helix, which was discovered by Watson and Crick based on the X-ray diffraction patterns. It is the common form of DNA exists under normal physiological condition. The double strands of B-DNA run in opposite directions. The structure is asymmetrical with major grooves and minor grooves present alternatively. The molecule is asymmetrical is because the glycosidic bonds of a base pair are not diametrically opposite to each other. In one turn, there are 10 base pairs with a length of 3.4nm. The distance between adjacent deoxyribonucleotides is 0.34nm. Same as A-DNA, the backbone of B-DNA is formed by sugar phosphates that are linked continuous using phosphodiester bonds and the core region consists of nitrogenous bases. The two strands are held together by hydrogen bonds between nitrogenous bases. The helix width of B-DNA is 2nm. B-DNA is narrower than A-DNA.

Z-form DNA

Z-form DNA is a left-handed double helix. It has a very different structure when compared with A-DNA and B-DNA. The zigzag appearance of backbone allows it to be distinguished from other forms of DNA. The helix width is 1.8nm, which is the narrowest among the three types. The structure consists of major and minor grooves. One turn of Z-DNA has 12 base pairs and the length is 4.56nm. The distance between two adjacent deoxyribonucleotides is 0.37nm. Same as the other forms of DNA, hydrogen bond is present to hold the two strands together. Z-DNA is difficult to be observed since it is unstable. It may take part in expression regulation of some

genes or in genetic recombination. It can be found in bacteria, eukaryotes and viruses. In some viruses, they require Z-DNA binding proteins for pathogenesis.

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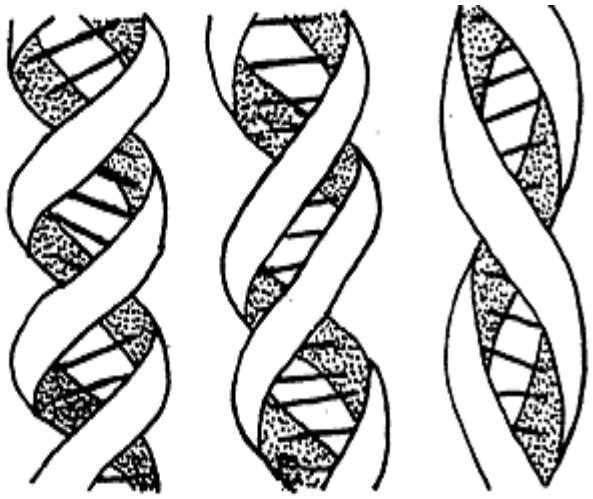

Form	A	B	Z
helical twist	right	right	left
base pairs per turn	11	10	12
occurrence	RNA, DNA	DNA	DNA

Parameter	A-DNA	B-DNA	Z-DNA
Orientation	Right-handed	Right-handed	Left-handed
Helix diameter (Å)	26	20	18
Rise (Å)	2.56	3.38	3.70
Pitch (Å)	28.2	33.8	44.5
Base pairs/turn	11	10	12
Helix twist (°)	32.7	36.0	−30.0
Major groove width[a] (Å)	2.7	11.7	2.0
Minor groove width[a] (Å)	11.0	5.7	8.8

[a] Groove width is the perpendicular separation of helix strands drawn through phosphate groups, added by 5.8 Å to account for van der Waals radii of phosphate groups.

RNA or ribonucleic acid

RNA or ribonucleic acid is a polymer of nucleotides that is made up of a ribose sugar, a phosphate, and bases such as adenine, guanine, cytosine, and uracil. It plays a crucial role in gene expression by acting as the intermediate between the genetic information encoded by DNA and proteins.

RNA has a structure very similar to that of DNA. The key difference in RNA structure is that the ribose sugar in RNA possesses a hydroxyl (-OH) group that is absent in DNA.

Types of RNA

In both prokaryotes and eukaryotes, there are three main types of RNA – messenger RNA (mRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA). These 3 types of RNA are discussed below.

Messenger RNA (mRNA)

mRNA accounts for just 5% of the total RNA in the cell. mRNA is the most heterogeneous of the 3 types of RNA in terms of both base sequence and size. It carries complimentary genetic code copied, from DNA during transcription, in the form of triplets of nucleotides called codons.

Each codon specifies a particular amino acid, though one amino acid may be coded for by many different codons. Although there are 64 possible codons or triplet bases in the genetic code, only 20 of them represent amino acids. There are also 3 stop codons, which indicate that ribosomes should cease protein generation by translation.

As part of post-transcriptional processing in eukaryotes, the 5' end of mRNA is capped with a guanosine triphosphate nucleotide, which helps in mRNA recognition during translation or protein synthesis. Similarly, the 3' end of an mRNA has a poly-A tail or multiple adenylate residues added to it, which prevents enzymatic degradation of mRNA. Both the 5' and 3' end of an mRNA imparts stability to the mRNA.

Ribosomal RNA (rRNA)

rRNAs are found in the ribosomes and account for 80% of the total RNA present in the cell. Ribosomes are composed of a large subunit called the 50S and a small subunit called the 30S, each of which is made up of its own specific rRNA molecules. Different rRNAs present in the ribosomes include small rRNAs and large rRNAs, which belong to the small and large subunits of the ribosome, respectively.

rRNAs combine with proteins and enzymes in the cytoplasm to form ribosomes, which act as the site of protein synthesis. These complex structures travel along the mRNA molecule during translation and facilitate the assembly of amino acids to form a polypeptide chain. They interact with tRNAs and other molecules that are crucial to protein synthesis.

In bacteria, the small and large rRNAs contain about 1500 and 3000 nucleotides, respectively, whereas in humans, they have about 1800 and 5000 nucleotides, respectively. However, the structure and function of ribosomes is largely similar across all species.

Transfer RNA (tRNA)

tRNA is the smallest of the 3 types of RNA, possessing around 75-95 nucleotides. tRNAs are an essential component of translation, where their main function is the transfer of amino acids during protein synthesis. Therefore, they are called transfer RNAs.

Each of the 20 amino acids has a specific tRNA that binds with it and transfers it to the growing polypeptide chain. tRNAs also act as adapters in the translation of the genetic sequence of mRNA into proteins. Thus, they are also called adapter molecules.

tRNAs have a cloverleaf structure which is stabilized by strong hydrogen bonds between the nucleotides. They normally contain some unusual bases in addition to the usual 4, which are formed by methylation of the usual bases. Methyl guanine and methylcytosine are two examples of methylated bases.

Other types of RNA

Beyond the primary role of RNA in protein synthesis, several varieties of RNA exist that are involved in post-transcriptional modification, DNA replication, and gene regulation. Some forms of RNA are only found in particular forms of life, such as in eukaryotes or bacteria.

Small nuclear RNA (snRNA)

snRNA is involved in the processing of pre-messenger RNA (pre-mRNA) into mature mRNA. They are very short, with an average length of only 150 nucleotides.

Regulatory RNAs

A number of types of RNA are involved in regulation of gene expression, including micro RNA (miRNA), small interfering RNA (siRNA) and antisense RNA (aRNA).

miRNA (21-22 nt) is found in eukaryotes, and acts through RNA interference (RNAi). miRNA can break down mRNA that it is complementary to, with the aid of enzymes. This can block the mRNA from being translated, or accelerate its degradation.

siRNA (20-25 nt) are often produced by breakdown of viral RNA, though there are also endogenous sources of siRNAs. They act similarly to miRNA. An mRNA may contain regulatory elements itself, such as riboswitches, in the 5' untranslated region or 3' untranslated region; these cis-regulatory elements regulate the activity of that mRNA.

Transfer-messenger RNA (tmRNA)

Found in many bacteria and plastids. tmRNA tag the proteins encoded by mRNAs that lack stop codons for degradation, and prevents the ribosome from stalling due to the missing stop codon.

Ribozymes (RNA enzymes)

RNAs are now known to adopt complex tertiary structures and act as biological catalysts. Such RNA enzymes are known as ribozymes, and they exhibit many of the features of a classical enzyme, such as an active site, a binding site for a substrate and a binding site for a cofactor, such as a metal ion.

One of the first ribozymes to be discovered was RNase P, a ribonuclease that is involved in generating tRNA molecules from larger, precursor RNAs. RNase P is composed of both RNA and protein; however, the RNA moiety alone is the catalyst.

Double-stranded RNA (dsRNA)

This type of RNA has two strands bound together, as with double-stranded DNA. dsRNA forms the genetic material of some viruses.