Chemistry of protein and amino acids metabolism

Second Stage

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Medical Biochemistry

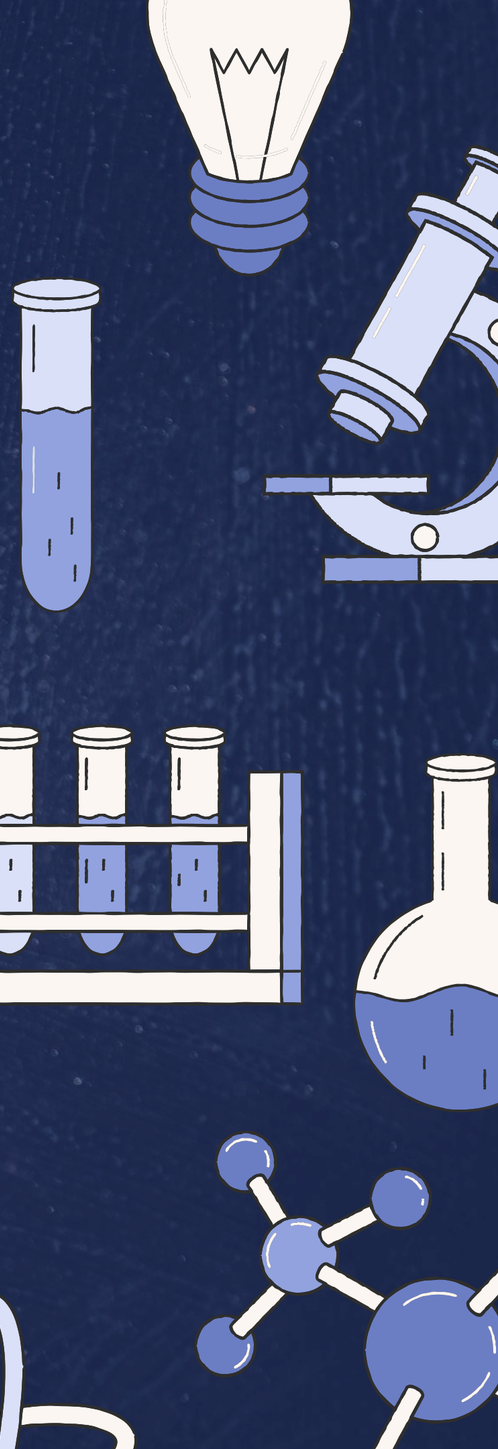
AMINO ACIDS AND PROTEIN STRUCTURE

amino acids: although over 300 amino acids exist in nature, only 20 standard amino acids

are encoded by DNA and commonly found in mammalian proteins. these amino acids

consist of a carboxyl group, an amino group, and a distinctive side chain, which

determines their properties and roles in proteins.



amino acids with nonpolar side chains:

the amino acids in this category have nonpolar side chains that do not participate in hydrogen or ionic bonds, promoting hydrophobic interactions.

location in proteins: in polar environments, nonpolar amino acid side chains cluster in the protein's interior due to the hydrophobic effect

helping to stabilize its three-dimensional structure. in hydrophobic
environments, nonpolar R groups of proteins are located on the surface, interacting with lipids to stabilize protein structure.

classification of the 20 standard amino acids:

nonpolar (neutral): GLYCINE (GLY), ALANINE (ALA), VALINE (VAL), LEUCINE (LEU), ISOLEUCINE (ILE), METHIONINE (MET), PROLINE (PRO).

polar (neutral): SERINE (SER), THREONINE (THR), CYSTEINE (CYS), ASPARAGINE (ASN), GLUTAMINE (GLN).

acidic (negatively charged): ASPARTIC ACID (ASP), GLUTAMIC ACID (GLU).

sickle cell anemia:

SICKLE cel anemia, a disease that causes red blood cels to become sickle shaped rather than disc

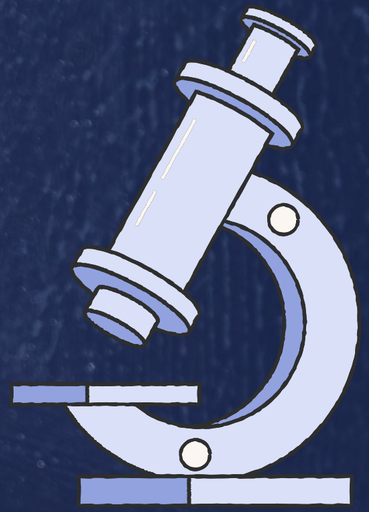
shaped, results from the replacement of polar

GLUTAMATE with nonpolar VALINE at the sixth position in the β subunit of hemoglobin A.

amino acids with uncharged polar side chains:

unique features of proline: PROLINE, an imino acid with a rigid five-membered ring has a
secondary amino group that influences

collagen structure and disrupts α-helices
in globular proteins. B. amino acids with uncharged polar side chains: at physiologic PH



of 7.4, amino acids like serine, threonine, and tyrosine can form hydrogen bonds due to their polar hydroxyl groups, while asparagine and

glutamine can do so through their carbonyl and amide groups.

disulfide bond formation:
CYSTEINE'S sulfhydryl group (-SH) can form disulfide bonds (-S-S-) between two residues, creating cystine, which is crucial in enzyme active sites. 2. side

chains as attachment sites for other compounds: the hydroxyl groups of serine, threonine, and tyrosine allow for phosphorylation by kinases, affecting

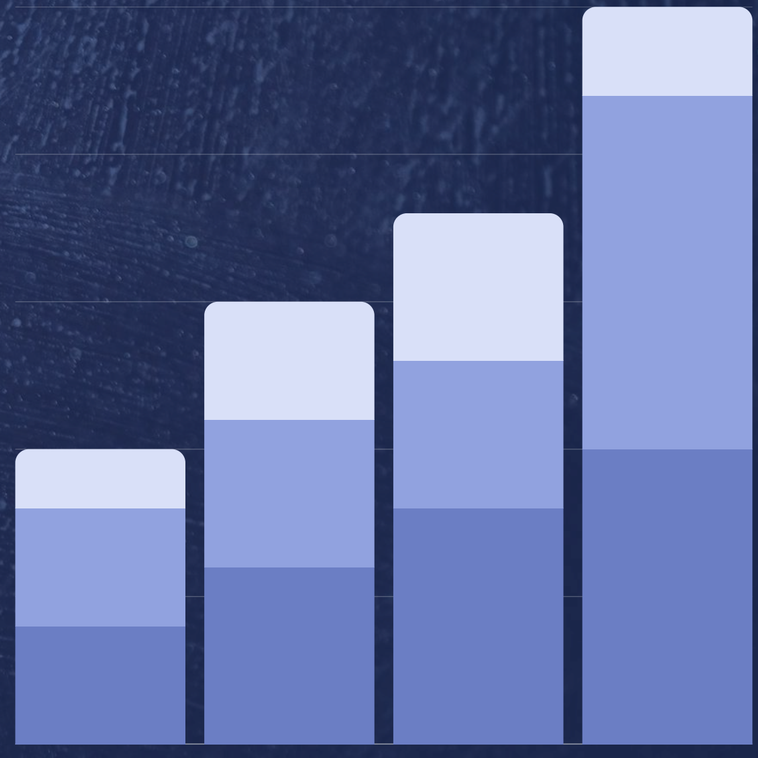
enzyme activity, while asparagine, serine, and threonine can also attach oligosaccharide chains in glycoproteins.

amino acids with acidic side chains:

ASPARTIC acid and GLUTAMIC acid act as proton donors, existing as

negatively charged carboxylate ions (aspartate and glutamate) at

physiological PH.



ACIDIC AND BASIC PROPERTIES :

amino acids in solution can act as buffers due to their weakly acidic **α**-carboxyl groups, weakly basic **α**-amino

groups, and ionizable side chains. A. PH: the concentration of protons ([H+]) in aqueous solution is

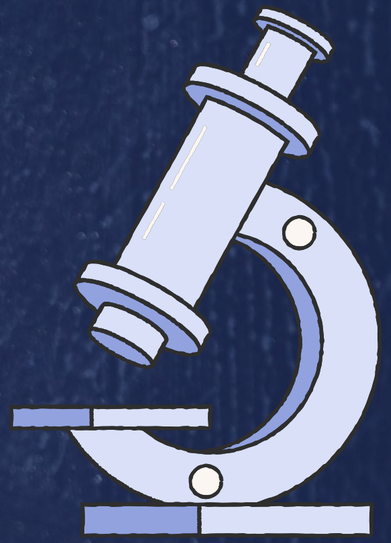
expressed as PH. PH = log 1/ [H+] or -log [H+]. B. 1. dissociation constants: the dissociation constant (KA)

indicates acid strength, with larger values signifying stronger acids due to greater dissociation into H+ and A-.

HENDERSON-HASSELBALCH equation:

the HENDERSON-HASSELBALCH equation, PH = PKA + log [A-] [HA], relates the PH of a solution to the

concentrations of a weak acid and its conjugate base. B. buffers: a buffer solution, created by mixing a weak acid



(HA) with its conjugate base (A-), resists PH changes upon the addition of acids or bases, with maximum buffering

capacity at PH equal to PKA and effective buffering wit
hin ±1 PH unit. for instance, a solution of acetic acid and

acetate, with a PKA of 4.8, maintains PH stability between 3.8 and 5.8, where the protonated form predominates below

PKA and the deprotonated form above it.

dissociation of the carboxyl group:

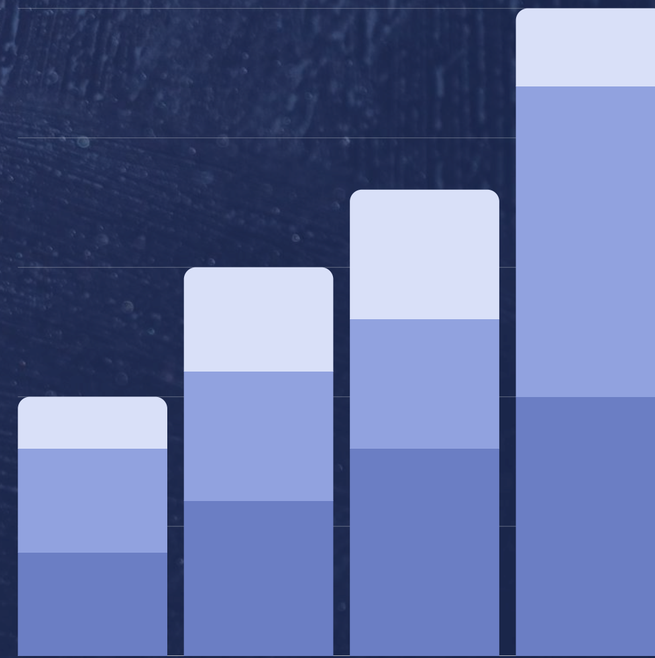
the dissociation constant for the carboxyl group of an amino acid is referred to as

K1 due to the presence of a second titratable group, and the HENDERSONHASSELBALCH

equation can be applied to analyze alanine's dissociation, resulting in the relationship

PH = PK1 + log [II] / [I], where [I] represents the fully protonated form and

[II] the isoelectric form of alanine.

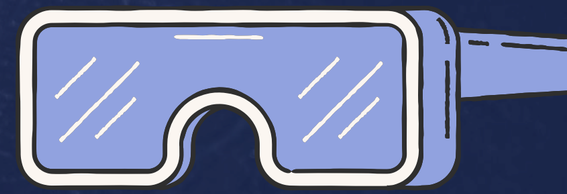


amino group dissociation:

the amino (-NH3+) group in alanine is a weaker acid than the carboxyl

group, resulting in a smaller dissociation constant (K2) and

higher PKA, with H+ release leading to the fully deprotonated form, form III.



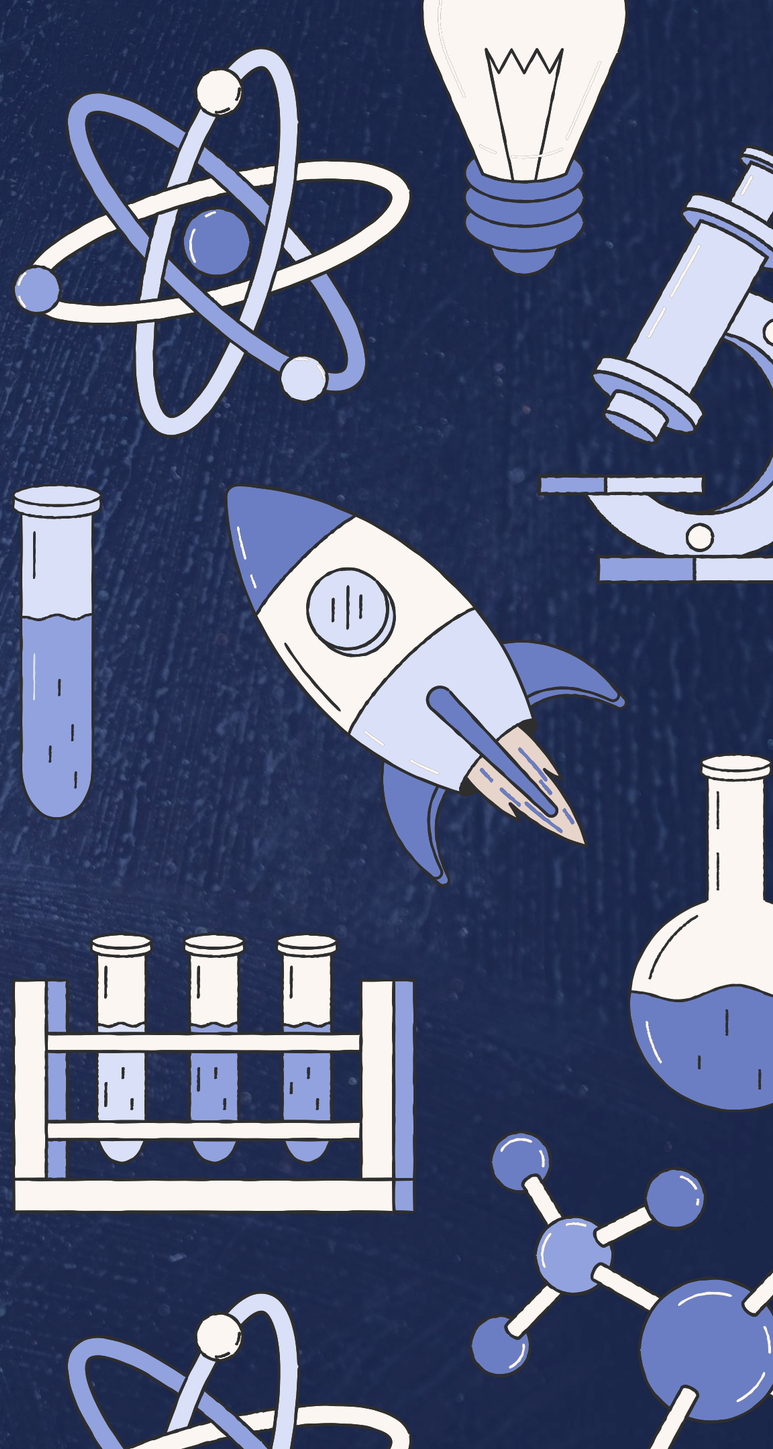
PKS and sequential dissociation: the sequential dissociation of H+ from

alanine's carboxyl and amino groups, characterized by PKA values of ~2

and ~9, respectively, can be analyzed using the HENDERSON-HASSELBALCH equation to generate

a complete titration curve illustrating PH changes during the transition from the fully

protonated to the fully deprotonated form.



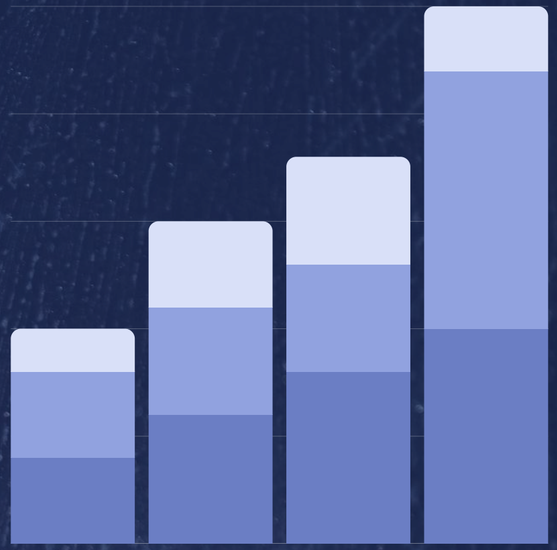
buffer pairs: the -COOH/-COO- pair can serve as a buffer in the PH region around PK1

and the -NH3+/-NH2 pair can buffer in the region around PK2.
b. when PH = PK: when

the PH is equal to PK1 (2.3), equal amounts of forms I and II of alanine exist in solution

when the PH is equal to PK2 (9.1), equal amounts of forms II and III are present in solution.

ISOELECTRIC POINT PI:



at neutral PH, alanine predominantly exists as the dipolar form II, with an isoelectric point (PI) of 5.7,

calculated as the average of PK1 (2.3) and PK2 (9.1), where the net charge is zero and equal amounts of

the charged forms I and III are present.

acidic and basic properties (separation):

in the laboratory, separation of plasma proteins by charge is typically done at a PH

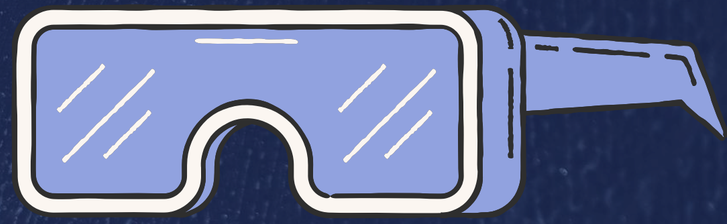
above the PI of the major proteins. therefore, at a high PH (alkaline) the charge on the

proteins is negative. in an electric field, the proteins will move toward the positive

electrode at a rate determined by their net negative charge. variations in the mobility

pattern are suggestive of certain diseases.

net charge at neutral PH: at physiological PH, amino acids possess both negatively charged



(COO-) and positively charged(NH3+) groups, with some

, like glutamate and lysine, having additional charged side chains,

making them amphoteric substances that can act as either acids or bases.

buffering the blood, the bicarbonate buffer system:

the bicarbonate buffer system maintains blood PH in the slightly alkaline range of 7.35

to 7.45, with optimal protein function at this PH, while the lungs and kidneys play crucial

roles in regulating acid-base balance by managing CO_2 and bicarbonate levels.

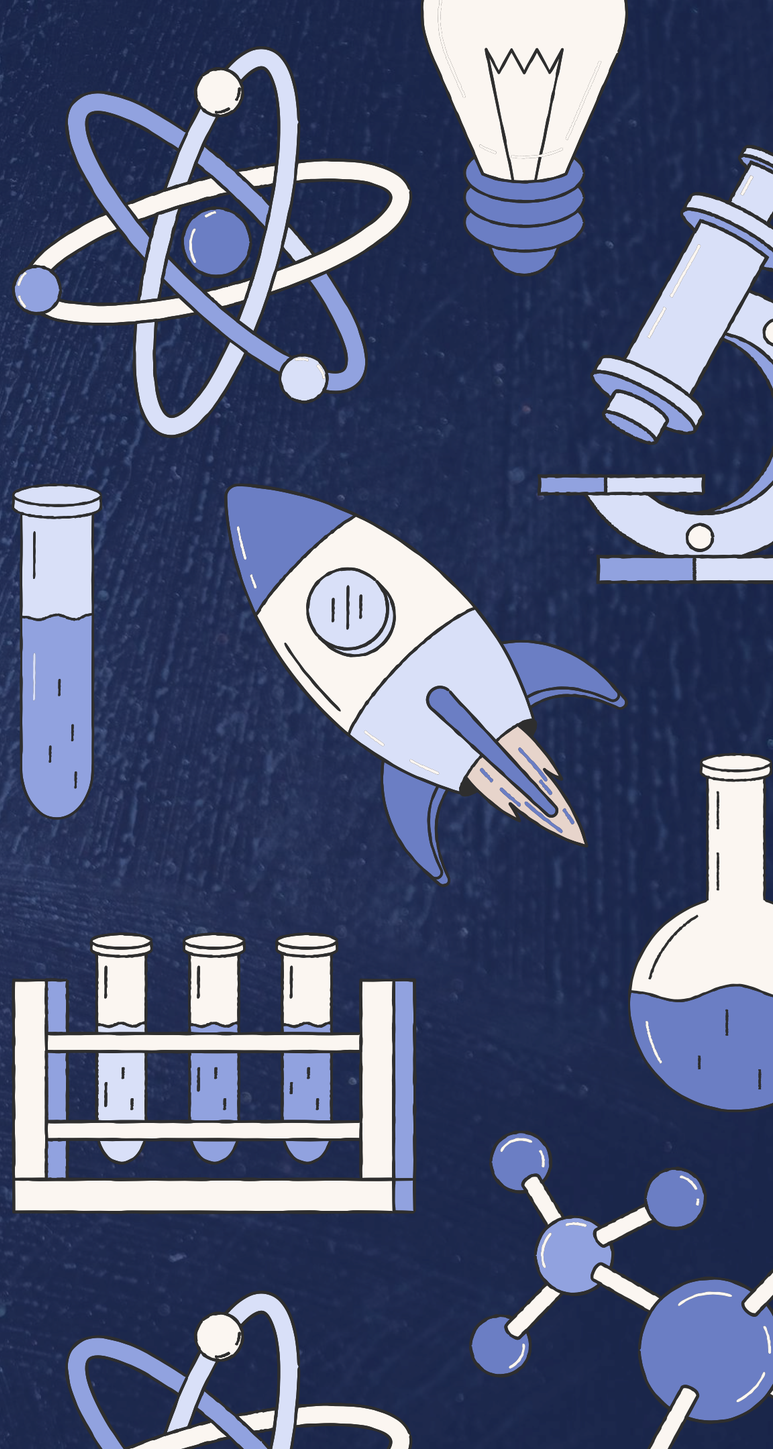
PROTEIN STRUCTURE:

primary structure: the primary structure of a protein, defined by its linear amino acid sequence

can be altered in genetic diseases, leading to improper folding and function, and studying these sequences can aid in diagnosis and research.

peptide bond: adjacent amino acids in proteins are linked by peptide bonds, formed between the α-carboxyl and α-amino groups, which are stable

under denaturing conditions but require strong acids or bases at high temperatures for nonenzymatic cleavage.



peptide bond characteristics: the peptide bond has partial double bond character, making it rigid and planar with

restricted rotation, while the bonds between α-carbons allow for free rotation, enabling diverse conformations,

and peptide bonds typically adopt a trans configuration due to steric interference of side chains

. peptide bond polarity: peptide bonds are uncharged and do not accept or release protons across a PH range of 2 to

12, but their polar carbonyl (-C=O) and amine (-NH) groups can form hydrogen bonds, contributing to

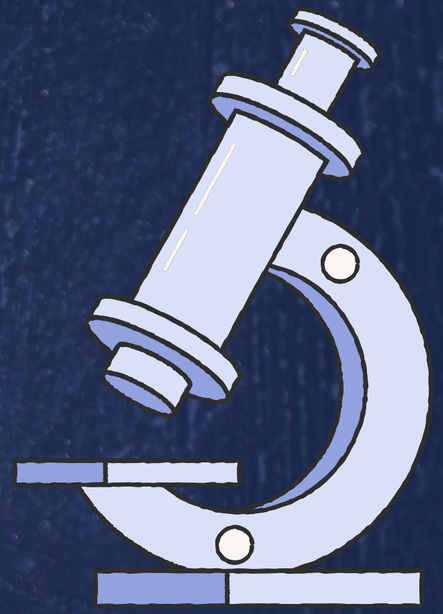
secondary structures like α-helices and β-sheets.

determining the amino acid composition of a polypeptide:

to determine a polypeptide's primary structure, it is hydrolyzed to release amino acids, which are then separated and

quantified using cation-exchange chromatography and an amino acid analyzer. C. sequencing the peptide from its N-

terminal end: sequencing is a methodical process for identifying the specific amino acids in a peptide chain from the N-terminal end, typically performed using automated.



cleaving the polypeptide into smaller fragments:

large molecules cannot be sequenced end-to-end directly; instead, they are cleaved at specific sites

using peptidases or proteases, with exopeptidases cutting at the ends and endopeptidases cleaving

within the protein.

METABOLISM OF PROTEINS AND AMINO ACIDS:

OVERVIEW: unlike fats and carbohydrates, amino acids are not stored in the body and must be obtained from the diet or synthesize

d; their catabolism involves the removal of α-amino groups to form ammonia and α-keto

acids, with excess nitrogen primarily excreted as urea, while the carbon skeletons are

metabolized into energy-producing intermediates. II.

OVERALL NITROGEN METABOLISM:

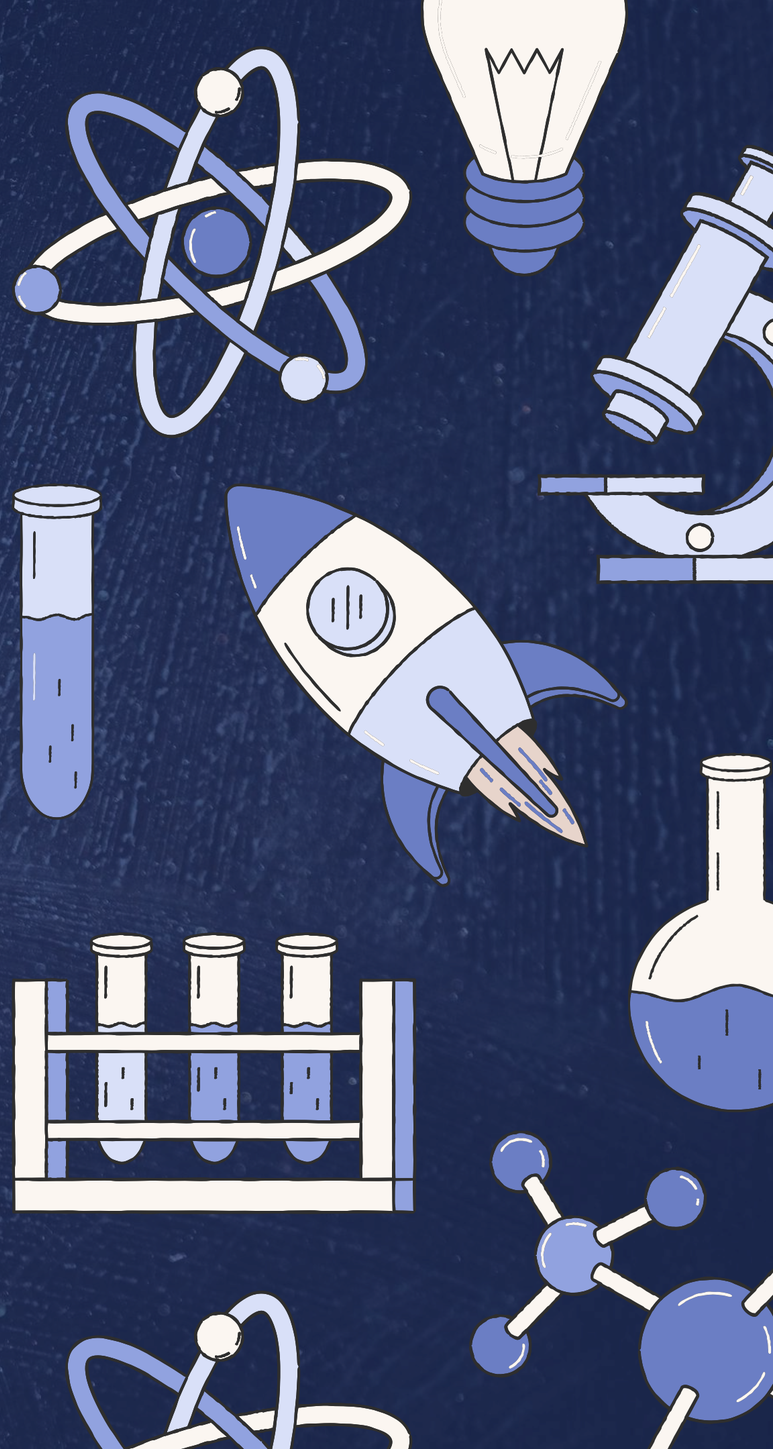
amino acid catabolism is integral to nitrogen metabolism, where nitrogen from dietary proteins is excreted as urea and ammonia, and involves concepts like the amino acid pool and protein turnover.

amino acid pool

Consisting of free amino acids in the body, is maintained by the degradation of body proteins, dietary proteins, and synthesis of

nonessential amino acids, while it is depleted through protein synthesis, conversion to small nitrogen-containing molecules, and metabolic transformations.

protein turnover: most body proteins undergo constant synthesis and degradation, with synthesis primarily regulating protein concentration in cells, while some proteins are maintained at constant levels through selective degradation.



rate: in healthy adults, protein turnover maintains constant body protein levels, with daily hydrolysis and resynthesis of

300 to 400 g, varying widely in rate and half-lives from minutes for short-lived proteins to months or years for stable

structural proteins. 2. protein degradation: two major enzyme systems degrade proteins: the ATP-dependent ubiquitin-

proteasome system, which selectively targets damaged or short-lived proteins, and the ATP-independent lysosomal

system, which nonselectively degrades both intracellular and extracellular proteins.

ubiquitin-proteasome system: proteins destined for degradation by the ubiquitin-proteasome system are marked with ubiquitin through a three-step,

ATP-dependent process, forming polyubiquitin chains that signal recognition and degradation by the proteasome, which then breaks the proteins into

fragments for further degradation. b. degradation signals: protein degradation is influenced by structural signals recognized by E3 enzymes, with

the N-terminal residue affecting half-life—destabilizing residues like arginine lead to rapid degradation, while sequences rich in proline,

glutamate, serine, and threonine (PEST sequences) also result in short half-lives.

GENOME, HISTONES, AND TRANSCRIPTION:

DNA to protein (length): DNA length per cell: each human cell contains approximately 2 meters of DNA when fully extended. total cells: the human body is

estimated to contain about 37.2 trillion cells (37.2 x 10^12). total length of DNA in all cells: approximately 74.4 trillion meters (or about 74.4 million kilometers).

genome: a genome is the complete set of genetic material in an organism, encompassing all of its DNA, including genes and non-coding sequences.

1. definition: the genome contains the entire hereditary information necessary for the growth, development, and functioning of an organism.

2. components: genes: segments of DNA that encode proteins or functional RNAs. non-coding DNA: regions that do not code for proteins but can have regulatory or other functions. 3. structure: in humans, the genome consists of 23 pairs of chromosomes (46 total), housed in the cell nucleus.

mitochondrial DNA is also part of the genome, located in mitochondria.

4. size: the human genome contains about 3 billion base pairs, which are the building blocks of DNA.

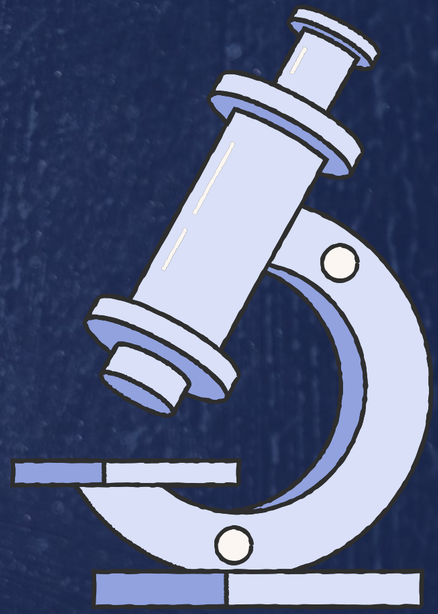
5. functionality: the genome dictates various biological traits and processes. it is also crucial for heredity, as it is passed from parents to offspring.

6. variation: genomes vary between individuals, contributing to genetic diversity within populations and affecting susceptibility to diseases, physical traits, and more.

7. applications: understanding the genome has significant implications in fields like genetics, medicine (e.g., personalized medicine), evolutionary biology, and biotechnology.

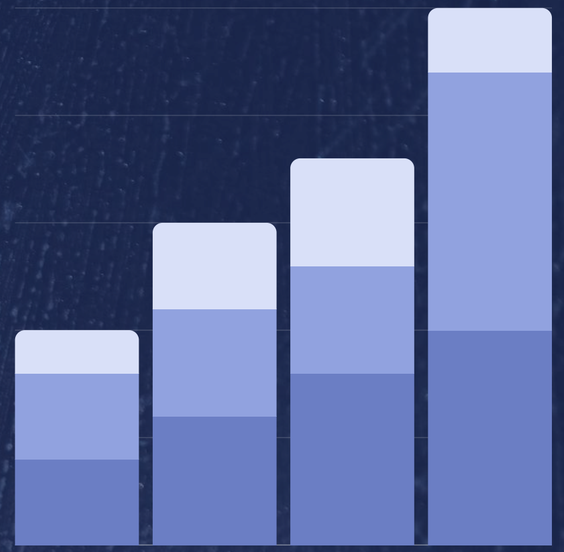
histones: histones are essential proteins that play a key role in the packaging and regulation of DNA within the cell.

there are five main types of histones: H1: linker histone that helps package DNA between nucleosomes; H2A, H2B, H3, H4: core histones that form the nucleosome structure.



nucleosome formation: histones bind to DNA to form nucleosomes, where approximately 146 base pairs of DNA wrap around a core of eight histone proteins.

function of histones:

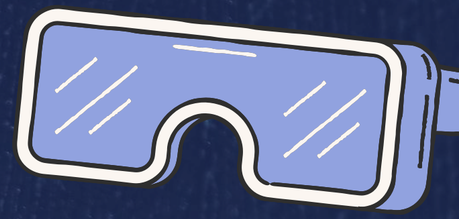


1. DNA packaging: histones condense DNA into a compact, organized structure called chromatin, enabling it to fit within the nucleus of a cell.

2. gene regulation: histones influence gene expression by altering the accessibility of DNA. modifications to histones (e.g., acetylation, methylation) can either promote or inhibit transcription.

3. chromatin structure: depending on modifications, chromatin can exist in two forms: euchromatin: loosely packed, active in gene expression; heterochromatin: densely packed, generally inactive in transcription.

transcription:



transcription is the process by which the information in a gene's DNA sequence is copied into a complementary RNA molecule.

steps:

1. initiation: RNA polymerase binds to the promoter.

2. elongation: RNA polymerase synthesizes a single strand of RNA by adding complementary RNA nucleotides in the 5' to 3' direction.

3. termination: reaches a termination signal and the RNA molecule (pre-mRNA) detaches.

messenger RNA (MRNA):

MRNA is a vital molecule in the process of gene expression and protein synthesis. structure of MRNA:

1. sugar-bases: MRNA is typically a single strand of nucleotides, made up of four bases: adenine (A), uracil (U), cytosine (C), and guanine (G).

2. 5' cap: a modified guanine nucleotide is added to the 5' end, which helps protect the MRNA from degradation and assists in ribosome binding during translation.

3. poly-A tail: a string of adenine nucleotides (the poly-A tail) is added to the 3' end, which also enhances stability and facilitates the export of the MRNA from the nucleus.

4. coding sequence: the sequence of nucleotides in MRNA corresponds to the amino acid sequence of the protein it encodes.

ribosomes:

ribosomes are essential cellular structures responsible for protein synthesis.
structure of ribosomes:

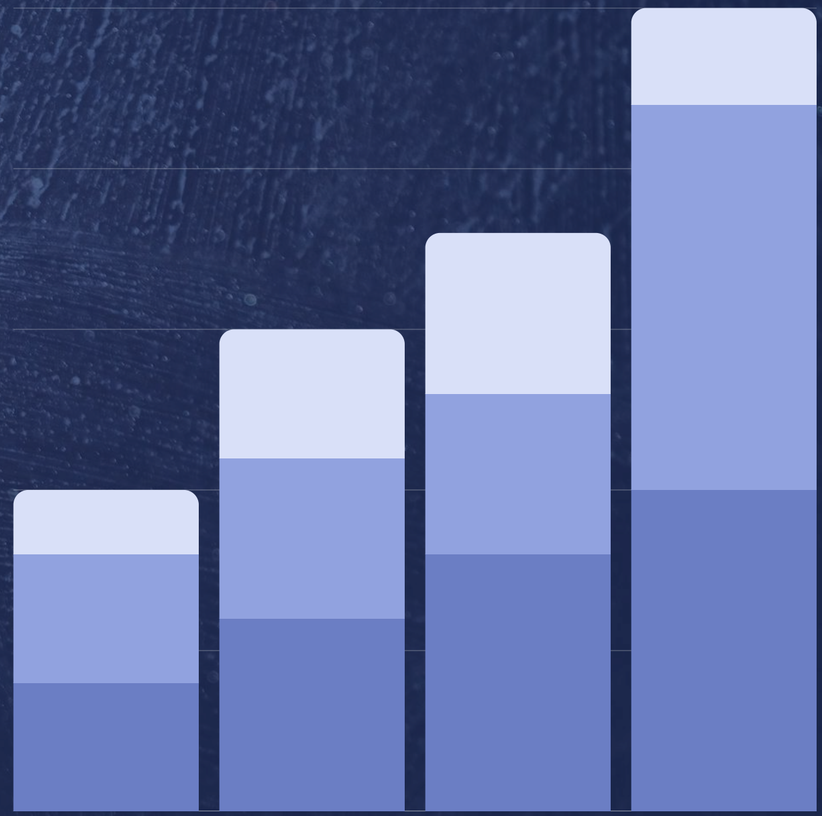
1. composition: ribosomes are composed of ribosomal RNA (RRNA) and proteins. they consist of two subunits: large subunit: facilitates the formation of peptide bonds between amino acids.

small subunit: binds to MRNA and is responsible for reading the MRNA sequence.

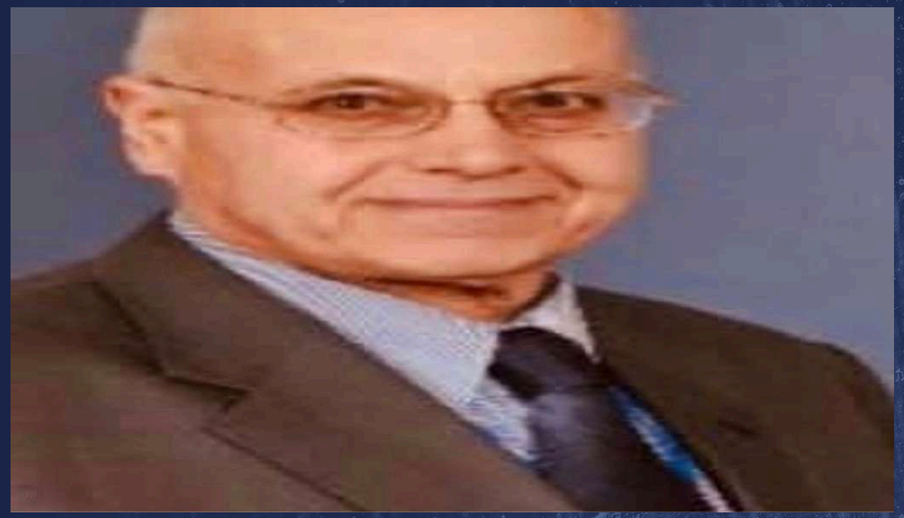
2. size: ribosomes vary in size and density between prokaryotes (70S) and eukaryotes (80S).

prokaryotic ribosomes: 70S (composed of 50S and 30S subunits). eukaryotic ribosomes: 80S (composed of 60S and 40S subunits).

3. location: ribosomes can be found free-floating in the cytoplasm or attached to the endoplasmic reticulum (forming rough ER).



الدكتور عبد المجيد عبد الحميد السلماسي



استشاري أمراض القلب في لندن وخريج كلية طب بغداد ١٩٧١ مسؤولا عن الامتحان العملي للكلية الملكية الطبية في لندن الدكتور سلماسي هو محاصر إكلينيكي كبير في المعهد الوطني للقلب والرئة والقيادة السريرية للملحق الإكلينيكي الثاني في كلية إمبريال لندن. هو استشاري أمراض القلب في لندن شمال غرب الرعاية الصحية، ومستشفيات رويال بروميتون وها ريفيلد. لغة الصحة الوطنية.

في عام 1979 حصل على درجة الدكتوراه في الطب من كلية الطب في مستشفى سانت ماري حاليا كلية إمبريال لندن) وواصل تدريبه في طب القلب في مستشفى سانت ماري لندن يعود اهتمامه بتصوير صدى القلب والموجات فوق الصوتية دوبلر إلى عام 1980 في عام 1982 نشر أول تقرير عن استخدام الموجات فوق الصوتية دوبار اثناء التمرين التخصيص وظيفة البطين الأيسر جنبا إلى جنب مع البروفيسور ميريل سبنسر من سيائل، كان مؤسسا مشاركة لجمعية دوبئر القلب الدولية في عام 1983 وأصبح نائب رئيسها الأول قام بتحرير أربعة كتب دراسية عليا في أمراض القلب ونشر حتى الآن 52 مقالة أصلية في مجال القلب والأوعية الدموية كما نشر بعض المقالات الأصلية حول قائدة تمرين الأيزومتري . مترى الدراسة وظائف البطين الأيسر الانبطاطي لدى المرضى الذين يعانون من أمراض الشريان التاجي ومرضى السكري وفقر الدم.

وهو زميل في الكلية الملكية للأطباء (لندن)، وزميل الجمعية الأوروبية الأمراض القلب، وزميل الكلية الأمريكية الأمراض القلب وزميل الجمعية البريطانية لارتفاع ضغط الدم وزميل كلية الصحة العامة في الكلية الملكية الأطباء لندن. اهتمامه البحثي الرئيسي هو فرط البطين الأيسر والعلاقة بين ارتفاع ضغط الدم وعدم تحمل الجلوكوز وسرعة نبض الشرايي والامتثال والرجفان الأذيني وتغيرات القلب والأوعية الدموية في أمراض المناعة الذاتية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