IUPAC Recommendations

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Terminology of bioanalytical methods (IUPAC Recommendations 2018)

https://doi.org/10.1515/pac-2016-1120
Received November 21, 2016; accepted February 1, 2018

Abstract: Recommendations are given concerning the terminology of methods of bioanalytical chemistry. With respect to dynamic development particularly in the analysis and investigation of biomacromolecules, terms related to bioanalytical samples, enzymatic methods, immunoanalytical methods, methods used in genomics and nucleic acid analysis, proteomics, metabolomics, glycomics, lipidomics, and biomolecules interaction studies are introduced.

Keywords: bioanalytical samples; biomolecule interaction studies; enzymatic methods; genomics; glycomics; immunoanalytical methods; lipidomics; metabolomics; nucleic acid analysis; proteomics.

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Article note: This work was started under project 2011-047-1-500: Recent advances in bioanalytical chemistry: characterization and classification, with membership of Jan Labuda, Günter Gauglitz, Pier Giorgio Righetti, Frantisek Foret, Frank-Michael Matysik, Boris Mizaikoff, and D. Brynn Hibbert.

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1 Preface

The recommendations contained in this document complete the terminology of bioanalytical chemistry in general and of the analysis of biomacromolecules in particular. The previous IUPAC recommendation, published in 1994, mostly covers analytical terminology related to body fluids, enzymology, and immunology [1]. Elsewhere, selected terms related to bioanalysis are included within the recommendations and reports devoted to the unit "katal" [2], biotechnology [3], clinical chemistry [4], toxicology [5, 6], medicinal chemistry [7, 8], proteomics [9], electrochemical biosensors [10, 11], and physical organic chemistry [12]. The definitions of some terms have been updated here with respect to new reports and considerations and a number of new terms have been introduced, particularly on the topics of "–omics", DNA analysis, and studies of the interactions between biomolecules.

These recommendations will become part of a chapter in the revised Orange Book (Compendium of Terminology in Analytical Chemistry, 4th edition).

2 Introduction

Bioanalytical chemistry is a branch of science that represents large and dynamic areas of research and practical analytical activities, from human health screening (medical, clinical, food, and pharmaceutical analysis) to forensic analysis and from basic biochemistry studies to special apparatus development.

Bioanalytical chemistry and biochemical analysis often require special methods for sampling and sample preparation and for handling biomolecules, including isolation, purification, separation, and fragmentation. Special attention is paid to apparatus and to techniques with immobilised bioreceptors (biosensors, bioarrays). The methods of analysis and identification of biomacromolecules are radically different from those used to analyse relatively small organic molecules. Most "classical" analytical methods are not suitable for the analysis of biomacromolecules or are suitable only to a limited extent.

There is no complete vocabulary on this topic. With respect to the terminological broadness of the methods used in bioanalysis, the approach taken here is to offer complete and informative definitions specific to bioanalysis without covering definitions utilised generally in branches of analytical chemistry but also widely used in bioanalysis, such as separation methods, mass spectrometry, and others.

Note that "Source: [xx]" indicates a previously published definition with no changes made; "Source: [xx] with minor changes" means that the intent of the existing definition is unchanged but that wording or grammar has been updated; and "Source: Adapted from [xx]" indicates that changes to the definition have been made.

2.1 bioanalytical chemistry

Sub-field of analytical chemistry dealing with analysis of *biomolecules*.

Note: Bioanalytical chemistry covers the identification (identity, sequence), characterization (properties such as polarity and charge, structure, folding, intermolecular interactions), and quantification and monitoring (stability, dynamics, fragmentation, degradation, metabolism, and others).

Source: [13]

2.2 biomolecule

Molecule of biological origin.

Note 1: Most biomolecules are organic compounds present in living organisms. They may also include exogenous molecules modified by metabolism. Some typical biomolecules representing subjects of bioanalytical chemistry are amino acids, peptides, polypeptides, proteins, nucleotides, nucleic acids, carbohydrates, glycoconjugates, lipids, antibodies, haptenes, and receptors, as well as primary and secondary metabolites.

Note 2: Modern bioanalytical chemistry shifts its attention to the analysis and investigation of biomacromolecules, such as nucleic acids, proteins, polysaccharides, and others.

2.3 biomacromolecule

biological macromolecule

Macromolecule (including proteins, nucleic acids, and polysaccharides) formed by living organisms.

Note 1: From a biological standpoint, a biomacromolecule can also be defined as a biomolecule of high relative molecular mass.

Note 2: Non-natural biomacromolecule-like synthetic molecules, such as poly(lactic acid), and nucleic acid analogues, such as peptide nucleic acid or locked nucleic acid, are also used in bioanalysis.

Source: [14], term 28 with added notes. See also [3, 15].

2.4 biopolymer

Substance composed of one type of *biomacromolecules*.

Note 1: Modified from the definition given in [16] in order to avoid confusion between polymer and macromolecule in the fields of proteins, polysaccharides, polynucleotides, and bacterial aliphatic polyesters.

Note 2: The use of the term "biomacromolecule" is recommended when molecular characteristics are considered.

Example: Substances with a periodic repetition of their biomacromolecular subunits (*e.g.* polysaccharides such as glycogen, starch and cellulose, polypeptides and polynucleotides).

Source: [14], term 32 with added example.

3 Bioanalytical samples

3.1 amniotic fluid

Fluid that surrounds the foetus in the amniotic sac.

Note: A specimen is obtained by a technique called amniocentesis, in which a long needle is inserted into the amniotic sac through the abdominal wall, through which fluid is withdrawn.

Source: [1]

3.2 blood

Fluid that circulates through the heart, arteries, capillaries, and veins.

Note: Circulating blood is a heterogeneous fluid consisting of a clear, slightly yellow liquid (native *plasma*) and three groups of suspended, formed elements: red *blood cells*, or erythrocytes (about 99 % of the blood cells), white blood cells, or leukocytes, and blood platelets, or thrombocytes. When no anticoagulant is added, normal blood withdrawn from the circulation forms a clot due the polymerization of fibrinogen to fibrin. On standing, the clot retracts, expressing serum which differs from plasma chiefly in that it contains no fibrinogen.

Source: [1]

3.3 blood cell

hematocyte
hemocyte
haematopoietic cell

Any cellular element of the *blood*, including erythrocytes, leucocytes, and platelets.

Note: A blood cell is produced by hematopoiesis and is normally found in blood. In mammals, these fall into three general categories: red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes).

Source: [1]

3.4 blood cell count

Number of red *blood cells* and white *blood cells* per unit volume in a specimen of venous *blood*.

Source: [1]

3.5 blood group

Red cell phenotypes classified by their antigenic structural characteristics, which are under the control of various allelic genes.

Note: The cell membrane properties that provide the specific antigenicity of the blood groups are called agglutinogens, as they agglutinate or clump in the presence of their specific antibody.

Example: 0, A, B

Source: [1]

3.6 body fluids

Liquids originating from the bodies of living or dead humans, animals, and other organisms.

Note: They include fluids that are excreted or secreted from the body.

3.7 cerebrospinal fluid (CSF)

Clear, colourless fluid that fills spaces within and around the central nervous system.

Note: CSF originates from *plasma* by a biological ultrafiltration process. Specimens are obtained by a lumbar puncture (*i.e.* a spinal tap).
Source: [1]

3.8 cord blood

Blood contained in the vessels of the umbilical cord at the time of birth.

Note: Cord blood contains stem cells.
Source: [1]

3.9 lymph

Yellowish, slightly basic fluid circulating through the lymphatic system.

Note: Lymph is similar to *plasma* and contains *white blood cells*.
Source: [1]

3.10 occult blood

Blood present in such small amounts that its presence can be ascertained only by chemical analysis or by spectroscopic or microscopic examination; particularly the blood found in stools.

Source: [1]

3.11 peripheral blood

Blood obtained from parts of the body that are located at some distance from the heart.

Example: Blood drawn from the earlobe, fingertip, or heel pad.
Source: [1]

3.12 plasma

Fluid portion of *blood* in which the *blood cells* and platelets are suspended.

Note 1: Plasma is obtained by centrifuging whole blood with anticoagulant addition.
Note 2: Plasma from which fibrinogen and related coagulation proteins have been removed is called *serum*.
Source: Adapted from [1, 6]

3.13 protein-free filtrate

Sample of *blood*, *serum*, or *plasma* from which all *proteins* have been removed by chemical or physical denaturation, dialysis, ultrafiltration, or solvent extraction.

Source: [1]

3.14 saliva

Clear, viscous secretion from the parotid, submaxillary, sublingual, and smaller mucous glands in the cavity of the mouth.

Note: Saliva contains many important substances, including electrolytes, mucus, antibacterial compounds and various enzymes.

Source: [1]

3.15 serum

Watery proteinaceous portion of the *blood* that remains after clotting. Serum closely resembles *plasma* except for the absence of some coagulation factors.

Note: Serum contains hydrophilic proteins and electrolytes, *antibodies*, *antigens*, hormones, and exogenous substances.

Source: Adapted from [1, 6]

3.16 skin

Soft outer covering of vertebrates.

3.17 sperm

Seminal fluid containing male reproductive cells.

3.18 sweat

Fluid excreted by the sweat glands in the skin of mammals during perspiration.

3.19 tears

Clear salty liquid that is secreted by the lachrymal gland of the eye to lubricate the surface between the eyeball and eyelid and to wash away irritants.

3.20 tissue

Group of biological cells that perform a specific function.

Note: A cellular organizational level intermediate between cells and complete organs.

3.21 urine

Fluid containing metabolic products that is excreted by the kidneys, stored in the bladder, and normally discharged by way of the urethra.

Source: [1]

4 Analysis of biomolecules

4.1 General Terms

4.1.1 assay

Set of operations for the identification of a component or the measurement of a quantity in analytical chemistry.

Note 1: Assay is an historical term, now largely obsolete, used as a synonym for the metrological terms examination or measurement. It is still used in compound terms, *e.g. immunoassay*, *bioassay*.

Source: [17] with minor changes.

4.1.2 assay kit

Set of components (reagents, solutions, and other necessary materials) and procedural instructions needed to perform an *assay*.

Source: [17] with minor changes.

4.1.3 bioassay

Assay in which an effect on an organism, tissue, cell, enzyme, or receptor is compared with the effect of a reference material.

Note 1: The analyte may be of biological origin (*e.g.* vitamin, hormone, plant growth factor, antibiotic drug, enzyme).

Source: Adapted from [3, 7, 14]

4.1.4 bioinformatics

Discipline encompassing the development and utilisation of computational tools to store, analyse, and interpret biological data.

Note: Among the most important bioinformatics tools are specialised databases with genetic and protein sequences accompanied by related data (biological function, cell localisation, *etc.*) and including search, alignment, and sorting algorithms or graphical modelling.

Source: [8]

4.1.5 biological recognition element

biochemical receptor

biocomponent, at a biosensor

Component of biological origin that translates information from the physicochemical domain into an *indication* [VIM 4.1] with a defined *selectivity* [VIM 4.13].

Note 1: The main purpose of the biological recognition element is to provide a *biosensor* or other system with a high degree of selectivity for the kind of quantity to be measured.

Note 2: Typical biological recognition elements include biocatalysts, immune receptors, nucleic acids, and others. Biologically-derived recognition elements, such as oligopeptides, oligosaccharides, and peptide nucleic acids are also of great interest.

Note 3: A biocatalytic recognition element is based on a biocatalytic reaction. Five types of biocatalyst are commonly used: (a) Enzyme (mono-or multi-enzyme): the most common and well-developed recognition system; (b) whole cells (micro-organisms, such as bacteria, fungi, eukaryotic cells or yeast) or cell organelles or particles (mitochondria, cell walls); and (c) tissue (plant or animal tissue slice). (d) Ribozymes, and (e) DNAzymes.

Note 4: A biocomplexing or bioaffinity recognition element is based on the binding interaction of the analyte with macromolecules or organised molecular assemblies that have either been isolated from their original biological environment or engineered.

Source: [10]

4.1.6 biomarker

marker

Molecule, specifically related to a particular state of a biological system, used to provide information about an organ function, disease, or other aspect of health.

Note 1: Biomarkers are traceable substances that are either introduced into an organism or formed in the body.

Note 2: The molecule signals an event or condition in a biological system or sample and gives a measure of exposure, effect, or susceptibility.

Examples: Protein or peptide, nucleic acid, metabolite, hormones, *etc.*

Source: Adapted from [8]

4.1.7 biosensor

Measuring instrument [VIM 3.1] requiring no additional reagents and providing *selective* qualitative and/or quantitative analytical information using a *biological recognition element*, which is retained in direct spatial contact with a transduction element *(transducer)*.

Note 1: The biological recognition system, mediated by isolated *enzymes*, immunosystems, tissues, organelles, whole cells, or others, translates information from the biochemical domain, usually an analyte concentration, into a chemical or physical (electrical, thermal or optical) output signal with a defined sensitivity.

Note 2: As a biosensor is a self-contained integrated *receptor– transducer* device, it should be clearly distinguished from an analytical system that incorporates additional separation steps, such as high performance liquid chromatography (HPLC) or additional hardware and/or sample processing, such as specific reagent introduction, *e.g.* flow injection analysis (FIA). Thus, a biosensor should be a reagentless analytical device, although the presence of ambient cosubstrates, such as water for hydrolases or oxygen for oxidoreductases, may be required for the analyte determination. HPLC or FIA system may incorporate a biosensor as a detecting device.

Note 3: It is necessary to distinguish strictly between biosensor (*e.g.* nucleic acid-based biosensors) and biosensing or *bioassay* (*e.g.* nucleic acid sensing).

Note 4: The variation of a biosensor response depending on the method of preparation and operational conditions is called the biosensor stability. Storage stability and working stability are typically distinguished.

Example: The detection of complementary oligonucleotide sequences by DNA sensors represents selective qualitative information.

Source: Adapted from [3, 10]

4.1.8 enzymatic decomposition

Decomposition of organic materials (*e.g.* starch, sugars, proteins, lignin, hemicelluloses, *etc.*) with specific *enzymes* or microbes in which the enzyme converts a high relative molecular mass compound into lower relative molecular mass species.

Example: Enzyme-catalysed hydrolytic degradation of biomolecules.
Source: [18]

4.1.9 Hansch analysis

Investigation of the quantitative relationship between the biological and physicochemical activity of compounds and global parameters representing hydrophobic, electric, steric, and/or other effects using multiple regression correlation.

Note: Hansch analysis is a type of regression analysis used for quantitative structure-activity relationship (QSAR).

Source: [7]

4.1.10 hydrolase

Enzyme that catalyses the cleavage of C–O, C–N, and other bonds by a reaction involving water.

See *enzymatic decomposition*

Source: Adapted from [3]

4.1.11 immobilization (at bioassay and biosensors)

Procedure or state when the *biological recognition element* is fixed in a thin layer at the *transducer*.

Source: Adapted from [3, 10]

4.1.12 label
tracer

Species covalently bound to a *biomolecule* and used for its detection.

Note: The analytical signal is either a measurable property of the *label* or is produced by the *label*.

Example: In an *enzyme immunoassay* (EIA) the label is an enzyme, in a *fluorescence immunoassay* (FIA) the label is a fluorescent chemical, and in a *radioimmunoassay* (RIA) the label is a radionuclide.

4.1.13 ligand (in bioanalysis)

Ion, group, or molecule that binds to a specific *receptor*.

Example: Ion or molecule-like hormone that binds to a biomolecular target to elicit, block, or attenuate a biological response, or to produce a specific analytical signal.
Source: [8, 12]

4.1.14 lysis

Breaking down of a cell.

Note 1: Lysis may be caused by physical, (bio)chemical, or biological means.
Note 2: A fluid containing the contents of lysed cells is called a "lysate".
Source: Adapted from [3]

4.1.15 microarray

Two-dimensional arrangement of a device for analysis of sub-microlitre sample volume.

Note 1: This screening format is a direct offshoot of genomic microarray technologies and makes use of ultra-low-volume miniaturization provided by nanodispensing technologies.
Note 2: A collection of molecules spatially addressed on a surface within features that have micrometer dimensions. Planar device (flat plane) used for off-line determination and identification of biocompounds.
Example: As a multiplex lab-on-a-chip, it can be used as an analytical device to measure the mRNA abundance (gene expression) of thousands of genes in one experiment binding the immobilised DNA fragments.

Source: Adapted from [8]

4.1.16 receptor

Molecular structure in or on a cell that specifically recognises and binds to a compound and acts as a physiological signal transducer or as the mediator of an effect.

Note: A receptor can also be immobilised onto a surface used in *immunoassays*, *biosensors*, and microchip separation devices.
Source: [19]

4.1.17 response time (of biosensor)

Time interval after an introduction of the detected analyte at which a signal of the *biosensor* (the measuring instrument) appears.

Note 1: Steady-state response time is, by convention, the time necessary to reach 90 % of the steady-state response value.
Note 2: Step response time is the duration between the instant when a signal of the biosensor is subjected to a change (due to a detected analyte) and the instant when a corresponding indication settles within specified limits around its final steady value.
Note 3: Transient response time is the time necessary for the first derivative of the output signal R to reach its maximum value $(\mathrm{d}R/\mathrm{d}t)_{\max}$ following the addition of an *analyte*.

Source: Adapted from [VIM 4.23], [10]

4.1.18 sample quality control

Test of the purity of the sample that will be subjected to detailed biochemical analysis.

Note: *Microelectrophoresis* belongs to methods used for sample quality testing.
Example: DNA or protein analysis.

4.1.19 sequence

The order of neighbouring amino acids in a *protein*, or of the *nucleotides* in DNA or RNA.

Source: Adapted from [20]

4.1.20 sequencing

Analytical procedures for the determination of the *sequence* of amino acids in a *polypeptide* chain (*primary structure of a protein)* or of *nucleotides* in DNA or RNA (primary structure of nucleic acid).

Source: Adapted from [3]

4.1.21 steady-state response time (of biosensor)

See *response time (of biosensor)*

4.1.22 transducer (at biosensor)

Part of a *biosensor* that converts a detected physical or chemical change at the level of the *biological recognition element* into an observable (usually electronic) signal.

Example: Electrode in voltammetric/amperometric or potentiometric mode, optical fiber, *etc*.
Source: Adapted from [10]

4.1.23 transient response time (of biosensor)

See *response time (of biosensor)*

4.2 Enzymatic Methods

4.2.1 activator (in protein binding)

See *effector*

4.2.2 allostery
allosteric regulation

Phenomenon where the conformation of an *enzyme* or other *protein* is altered by combination, at a site other than the substrate-binding site, with a small molecule, referred to as an *effector*, which results in either increased or decreased activity by the enzyme.

Source: [1]

4.2.3 apoenzyme

Protein part of an *enzyme* without the *cofactor* necessary for catalysis.

Note: The cofactors can be a metal ion (*e.g.* Cu^{2+}, Cu^{+}, Co^{2+}, Fe^{3+}, Fe^{2+}, Zn^{2+}, Mn^{2+}), an organic molecule (*e.g.* a coenzyme or prosthetic group), or a combination of both.
Source: [1]

4.2.4 catalytic activity (in enzymology)

enzyme activity
enzyme catalytic activity

Property of an *enzyme* as a biocatalyst, expressed as the rate of the catalysed conversion of a specified chemical reaction produced in a specified assay system.

Note 1: The SI unit of enzyme *catalytic activity, a*, is the katal, the enzyme activity that converts one mole of substrate per second under specified reaction conditions. "katal", $kat = 1\ mol\ s^{-1}$.
Note 2: The International Unit (U) was defined as the amount of enzyme that catalyses the conversion of one micromole of substrate per minute under the specified conditions of the assay method ($1\ U = 1\ \mu mol\ min^{-1} \approx 16.67$ nkat). This unit of enzyme catalytic activity was originally proposed by the International Union of Biochemistry in 1964 and is no longer recommended, because the minute is not the SI base unit of time.
Note 3: Quantities derived from the *enzyme activity* lead to the following pairs of kind-of-quantity and coherent SI unit:
specific enzyme activity, $a_s = a/m$, with the unit katal per kilogram ($kat\ kg^{-1}$);
molar catalytic activity, $a_m = a/n_E$, equal to the turnover number, where n_E is the amount of enzyme E, with the unit katal per mole of enzyme ($kat\ mol^{-1}$).
Source: Adapted from [1, 2, 4]

4.2.5 catalytic activity concentration

catalytic concentration

Catalytic activity divided by the volume of the system.

Note 1: In clinical chemistry the component is usually an *enzyme*.
Note 2: The term catalytic concentration is accepted for use in clinical chemistry.
Note 3: Use of the term "level" as a synonym for concentration is deprecated.
Note 4: In describing a quantity, concentration must be clearly distinguished from amount of substance.
Source: Adapted from [1, 4]

4.2.6 catalytic activity content

Catalytic activity divided by the mass of the system.

Note 1: The term catalytic content is accepted for use in clinical chemistry.
Source: [4] page 964

4.2.7 catalytic activity fraction

Quotient of the *catalytic activity* of a particular form of an *enzyme*, such as isozyme, and the catalytic activity of all the isozymes of the same enzyme in the system.

Note 1: The term catalytic fraction is accepted for use in clinical chemistry.
Note 2: The definition also applies to other multiple forms of an enzyme that are not isoenzymes.
Source: [4]

4.2.8 coenzyme

Organic molecule that is required by a certain *enzyme* to carry out catalysis.

Note 1: This low relative molecular mass and active group of an enzyme is an intermediate carrier of chemically active groups, specific atoms, and/or electrons. A coenzyme binds with its associated protein (*apoenzyme*) to form the active enzyme (*holoenzyme*).
Note 2: Coenzymes may be dissociable or covalently bound. In the latter case they are called prosthetic groups.
Example: The most common is NADH.
Source: Adapted from [1]

4.2.9 denaturation of protein

Partial or total alteration of the structure of a *protein*, without change in covalent structure, by the action of certain physical procedures (heating, agitation) or chemical agents (alcohols, tensides, foaming agents).

Note 1: Denaturation is the result of the disruption of tertiary bonding, which causes the opening of the folded structure of a protein and the loss of characteristic physiologic, enzymatic, or physicochemical properties.
Note 2: Denaturation can be either reversible or irreversible.
Source: Adapted from [1]

4.2.10 Eadie-Hofstee plot

See *Lineweaver-Burk plot*

4.2.11 effector

Small molecule which increases (activator) or decreases (*inhibitor*) the activity of an (*allosteric*) protein by binding to the protein at the regulatory site

Note: The regulatory site is different from the substrate-binding catalytic site.
Source: [3]

4.2.12 enzyme

Macromolecule, usually a *protein* that functions as a *catalyst*.

Note: In general, an enzyme catalyses only one reaction type (reaction selectivity) and operates on only one type of *substrate* (substrate selectivity). Substrate molecules are transformed at the same site (region selectivity); often only one enantiomer of a chiral substrate is transformed.

Source: Adapted from [1, 7, 8]

4.2.13 Hanes–Woolf plot

See *Lineweaver-Burk plot*

4.2.14 holoenzyme

Active enzyme consisting of the *apoenzyme* and *coenzyme* (cofactor).

Source: [1]

4.2.15 inhibitor

Substance that diminishes the rate of a biochemical reaction.

Note: The process is called inhibition.

See also *effector*
Source: Adapted from [1]

4.2.16 isoenzymes

Related *enzymes* catalysing the same reaction but having different molecular structure.

Note: Isoenzymes are characterised by different physical, biochemical, or immunological properties.
Source: [1]

4.2.17 Lineweaver-Burk plot

Plot of the reciprocal of initial velocity of an *enzyme-catalysed reaction* (ordinate) versus the reciprocal of initial substrate concentration (abscissa).

Note 1: The plot is used to graphically define the maximum velocity, V, of an enzyme-catalysed reaction and the Michaelis constant for the enzyme.
Note 2: Eadie-Hofstee plot is an alternative using a linear plot of initial velocity versus the ratio of initial velocity and initial substrate concentration.
Note 3: *Hanes–Woolf plot* is another graphical representation of enzyme kinetics which uses a plot of the ratio of the initial substrate concentration $[S]_0$ to the reaction velocity v_0 versus $[S]_0$.

See *Michaelis-Menten equation*
Source: Adapted from [1].

4.2.18 Michaelis-Menten equation

The relationship between the initial rate (velocity) of an *enzyme-catalysed reaction* v_0 and the initial substrate concentration $[S]_0$ in the form

$$v_0 = V[S]_0 / (K_M + [S]_0)$$

where V (the limiting rate) and K_M (the Michaelis constant) are independent of the initial substrate concentration and constant at a given temperature and a given enzyme concentration. The reaction is then said to display Michaelis-Menten kinetics.

Note 1: The term 'hyperbolic kinetics' is also sometimes used, because a plot of v_0 against $[S]_0$ has the form of a rectangular hyperbola through the origin with asymptotes $v_0 = V$ and $[S]_0 = -K_M$. This term, and others that imply the use of particular kinds of plot, should be used with care to avoid ambiguity, as they can be misleading if used out of context.

Note 2: The symbol V_{max} and the names "maximum rate" and "maximum velocity" are also in widespread use, although in general and under normal circumstances there is no finite substrate concentration at which $v_0 = V$. Hence, there is no maximum in the mathematical sense.
The alternative name Michaelis concentration for K_M may also be used and has the advantage of emphasizing that the quantity concerned has the dimension of a concentration and is not, in general, an equilibrium constant. The Michaelis constant is the substrate concentration at which $v_0 = V/2$.
Source: Adapted from [1, 21–23]

4.2.19 molar catalytic activity

See *catalytic activity, in enzymology*

4.2.20 specific enzyme activity

See *catalytic activity, in enzymology*

4.3 Immunoanalytical Methods

4.3.1 adjuvant

Material introduced with an *antigen* to augment its immunogenicity.

Note: A substance that helps and enhances the effect of a drug, treatment, or biological system.
Source: [1]

4.3.2 affinity (in immunology)
binding affinity

Strength of association between a single *antibody* and a single *epitope* of *antigen*.

Note 1: Affinity of the immunochemical reaction:
Antibody + Antigen = Antibody-Antigen
is characterised by the affinity (binding, association) constant
K_A = [Antibody-Antigen]/[Antibody][Antigen]
Note 2: The average binding constant reflects a population of *antibody* molecules (polyclonal antibody).
Source: Adapted from [1]

4.3.3 agglutination

Immunospecific aggregation of particulate biological matter or synthetic particles.

Immunochemical specific reaction leading to the aggregation of particulate biological matter or synthetic particles.

Note 1: The biological matter can be bacteria, erythrocytes, or other cells, and the synthetic particles can be polymer beads coated with *antigens* or *antibodies*.
Note 2: Such aggregation is usually primarily dependent on surface reactions mediated by either antigens or antibodies. Physically or chemically, they are attached to the particulate surfaces; agglutination or clumping of the particles follows as a secondary immune reaction.

Source: Adapted from [1, 3]

4.3.4 agglutination inhibition

Type of *agglutination* in which particulate and soluble *antigen* compete for soluble *antibody*.

Note: Typically, it is soluble *antigen* in the test medium which reacts first with the soluble antibody, inhibiting the agglutination of indicator particles. With viral hemagglutination inhibition *assays*, host *antibodies* resulting from a specific infection are the most common forms of agglutination inhibition assays. In this case, viral-specific antibodies block the sites on the virus that agglutinate erythrocytes.

Source: [1]

4.3.5 antibody (Ab)

Protein produced by the immune system of an organism in response to exposure to a foreign molecule (*antigen*).

Note 1: These *proteins* are *immunoglobulins* and bind by means of specific binding sites to a specific antigenic determinant.

Note 2: An antibody molecule is, by definition, monospecific, but might also be "idiospecific," "heterospecific," "polyspecific," or of "unwanted specificity." It cannot be "nonspecific", except in the sense of nonimmunochemical binding.

Source: Adapted from [1, 3]

4.3.6 antigen (Ag)

Substance that stimulates the immune system to produce a set of specific *antibodie*s in a suitable host and will combine with such generated antibodies through its antibody-binding sites (*antigenic determinants*, *epitopes*).

Source: Adapted from [1, 3]

4.3.7 antigenic determinant
epitope

Part of the structure of an *antigen* molecule that is responsible for specific interaction with *antibody* molecules evoked by the same or a similar *antigen*.

Source: [1]

4.3.8 antiserum

A *serum* containing *antibodies*.

Source: [1]

4.3.9 avidity

Net *affinity* of all binding sites of all *antibodies* in the *antiserum* under specified physicochemical reaction conditions.

Source: Adapted from [1]

4.3.10 binding capacity

Amount of a *ligand* that binds to a *receptor* expressed in operational units.

Note 1: Operational units are defined in contrast to the quantitative mass units of the *affinity* constant.
Note 2: Binding capacity is determined by saturating the receptor and then measuring the amount of complex forming ligand. Parameters like pH and ionic strength influence the capacity value, which will be changed depending on the experimental conditions.

Source: Adapted from [1]

4.3.11 blocking

Coating of an immunospecific surface (*e.g. serum*, *tissues*, cells, *biological macromolecules*, *biosensor* surface) to form an active cover with selectivity or an inert layer.

Note: Blocking is a pre-treatment method with blocking agents (*e.g.* monovalent Fab fragment, *i.e.* the antigen-binding fragment of an immunoglobulin molecule; mono or divalent antibodies; organic ligands; metals).

4.3.12 bound/free ratio (in immunoassay) (B/F)

Amount-of-substance ratio of bound to free-labelled analyte.

Source: Adapted from [1]

4.3.13 carrier protein

(1) *Protein* to which a specific *ligand* or *hapten* is conjugated.
(2) Unlabelled *protein*, introduced into an *assay* at relatively high concentrations, which distributes in a fractionation process in the same manner as a labelled protein analyte present in very low concentrations.
(3) *Protein* added to prevent nonspecific interaction of reagents with surfaces, sample components, and each other.

Source: [1]

4.3.14 complement (in immunology)

Array of serum *proteins* (some of which are *enzymes*) that become sequentially activated after the first member of the series is activated by either *antigen-antibody* complexes or microbial products.

Source: [1]

4.3.15 conjugate

Material produced by attaching two or more substances together.

Note: Conjugates of *antibody* with fluorochromes, radioactive isotopes, or enzymes are often used in immunoassays.

Source: [1]

4.3.16 cross reactivity (in immunology)

Reaction of an *antibody* with an *antigen* other than that which elicited the formation due to the presence of related *antigenic determinants*.

Note: Cross reactivity is due to not ideal *selectivity* of the antibody.
Source: Adapted from [1]

4.3.17 enzyme conjugate

Conjugate that has an *enzyme* bound covalently.

Example: Various reporter enzymes, such as horseradish peroxidase (HRP), alkaline phosphatase (AP), and many others can be attached to antibodies. Key substance in ELISA *immunoassay*.
Source: Adapted from [1]

4.3.18 epitope

See *antigenic determinant*

4.3.19 hapten

Low relative molecular mass molecule that contains an *antigenic determinant* but which is not itself antigenic unless combined with an antigenic carrier.

Note 1: The carrier may be one that also does not elicit an immune response by itself. It interacts with specific antibody-combining sites of an *antibody* molecule but is not immunogenic by itself.
Source: Adapted from [1, 7]

4.3.20 hemagglutination

Agglutination reactions in which the particles used are *erythrocytes*.

Note: Hemagglutination may be either direct, in which erythrocyte antigens are reactants, or indirect (passive) for coated *antigen* or, in the case of reverse (passive) assays, coated *antibody*. One of the most common uses of hemagglutination is to quantitate the number of hemagglutinating viruses (*cf.* influenza) or their soluble hemagglutinating surface subunits. It can also be used for blood typing.

4.3.21 immune response

Selective reaction of the body to substances that are foreign to it, or that the immune system identifies as foreign, shown by the production of *antibodies* and antibody-bearing cells, or by a cell-mediated hypersensitivity reaction.

Source: [5]

4.3.22 immunoassay

Ligand-binding *assay* that uses a specific *antigen* or *antibody* capable of binding to the analyte.

Note 1: The antibody can be linked to a radiosotope (radioimmunoassay, RIA), to an enzyme which catalyses an easily monitored reaction (enzyme immunoassay, enzyme-linked immunosorbent assay, ELISA), or to a highly fluorescent compound by which the location of an antigen can be visualised (immunofluorescene, fluorescence immunoassay, chemiluminescent immunoassay).

Type of immunoassay	Ligand/label	Physical/chemical phenomenon observed
radioimmunoassay, RIA, immunoradiometric assay	radioactive nuclide	radioactivity
enzyme immunoassay, EIA, and	enzyme like horseradish peroxidase	catalytic activity of a specific enzyme conjugate
enzyme-linked immunosorbent assay, ELISA (heterogeneous EIA when antigen or antibody is firmly attached to a solid support)	enzyme like horseradish peroxidase	catalytic activity of a specific enzyme conjugate
fluorescence immunoassay	fluorescent compound	fluorescence
chemiluminescent immunoassay	chemiluminescent system	chemiluminiscence
light-scattering immunoassay	none	changes in turbidity (*turbidimetry*) or light scattering (*nephelometry*)

Note 2: In general, immunoassays fall into two broad categories: competitive and non-competitive. In a competitive assay, analyte (antigen) in a sample competes with a constant amount of labelled analyte for a limited amount of antibody. For instance, a radioligand assay is a type of radioimmunoassay in which unlabelled and radioactive-labelled molecules of the same analyte compete for a limited number of binding sites on a specific binding protein (an *antibody*, transport protein, hormone receptor in radioreceptor assay, or any other cell associated receptor or tissue component). A non-competitive immunoassay involves the capture of all the analyte in the sample by excess antibody, usually immobilised on a solid phase.

Note 3: Sandwich immunoassay is immunoassay using the chemical or immunochemical binding of *analyte* to a solid phase and the immunochemical binding of a second (typically labelled) reagent to the analyte. This is one of the most common assays in clinical practice.

Examples: Fluorescent excitation transfer immunoassay, fluorescence polarization immunoassay, solid-phase "dipstick" immunoassay, solid-phase microbead fluorescence immunoassay, substrate-labelled fluorescence immunoassay, fluorescence immunoassays using *e.g.* internal reflectance spectroscopy.

Source: Adapted from [1, 3, 17, 24]

4.3.23 immunoblotting

Technique that uses *antibodies* (or other specific ligands in related techniques) to identify target *proteins* among a number of unrelated protein species.

Note: The techniques allow the detection of proteins from complex mixtures separated by gel chromatography and then transferred to a membrane. After incubation of the attached product from membrane with labelled antibody, the target proteins become visible.

4.3.24 immunochemical specificity
specificity

The extent to which the *immunoassay* responds only to (all subsets of) a specific analyte and not to other substances of similar structure that are present in the sample.

Source**:** Adapted from [5]

4.3.25 immunochemistry

Study of biochemical and molecular aspects of immunology, especially the nature of *antibodies*, *antigens*, and their interactions.

Source**:** Adapted from [5]

4.3.26 immunocomplex

Product of an *antigen-antibody* reaction that may also contain components of the complement system.

Note 1: Formation of the immunocomplex is characterised by the binding constant
Source**:** Adapted from [5]
See *affinity*

4.3.27 immunogen

Substance that elicits a cellular immune response and/or *antibody* production (cf. *antigen*).

Source: [1, 3]

4.3.28 immunoglobulin (Ig)

Antibody which is a large Y-shape *protein* produced by plasma cells.

Note 1: As glycoprotein is found in serum or other body fluids and possesses antibody activity.
Note 2: An individual Ig molecule is built up from two light (L) and two heavy (H) polypeptide chains linked together by disulfide bonds. Igs are divided into five classes based on antigenic and structural differences in the H chains. Ig is used by the immune system to identify and neutralise foreign objects such as bacteria and viruses. It is a protein of the globulin-type structure which is found in serum or in other body fluids that possesses antibody activity.
Note 3: It denotes also the family of closely related glycoproteins.

Source: Adapted from [1, 3, 5]

4.3.29 immunoglobulin class

Classification of *immunoglobulins* based on antigenic and structural differences of the heavy peptide chain.

Note 1: There are five classes: IgG, IgA, IgM, IgD, and IgE.
Note 2: Immunoglobulin subclass (isotype) represents the subdivision of an *immunoglobulin class* based on structural and antigenic differences in the heavy peptide chain. Four human IgG subclasses and two IgA subclasses have currently been recognised; IgM subclasses have been postulated; IgD and IgE subclasses are unknown.

Source: Adapted from [1]

4.3.30 immunoprecipitation

Isolation and concentration of an *antigen* by forming a precipitate with an *antibody*.

Note: Immunoprecipitation requires that the antibody be coupled to a solid substrate at some point in the procedure.
Source: Adapted from [1]

4.3.31 immunoreactivity

Kinetic property of the immune reaction caused by an *antigen*.

Note: Reactivity is defined in [25] page 1159.

4.3.32 immunosensor

Biosensor where one of the immunointeracting partners (an *antibody* or an *antigen* as the analyte) is immobilised on the surface of a physicochemical *transducer*.

Note: The generated signal either directly reflects the amount of formed *immunocomplex* or corresponds to the amount of *label*.

4.3.33 indirect agglutination
passive agglutination

Agglutination in which *antigen* is first immobilised artificially onto the particulate surfaces, either by physical adsorption or by chemical and/or immunochemical linkers.

Note: Antigen-loaded particles can be used to detect the presence of the corresponding specific agglutinins in sample. Agglutination results by cross-linking of the antigen-bearing particles onto an extensive antigen-antibody lattice (*i.e.* in detectable agglutination of the particles).

4.3.34 lateral flow test

Migration of the sample zone driven by capillary forces in a porous carrier strip.

Note 1: During migration the dissolved tracer becomes distributed between capture and control zones with immobilised *antibodies*.
Note 2: The amount of the label compound in both zones depends on the concentration of the compound in the studied sample.
Example: The most common test of this type is the one for pregnancy.

4.3.35 monoclonal

Arising from a single clone of cells.

Note 1: In the case of immunoglobulin, 'monoclonal' refers to its origin.
Note 2: Usually, the monoclonal *antibody* is of a single immunoglobulin class containing only one light chain type of either the K or L variety. It also refers to all antibody molecules having identical physical-chemical characteristics and antibody specificity. Monoclonal antibodies have very restricted structural diversity and they are homogeneous compared with polyclonal antibodies.

Source: Adapted from [1]

4.3.36 monospecificity

Immunoreactivity of an antiserum with its designated antigen

Note: In practice, true monospecificity to naturally occurring antigens does not occur in antisera produced by the immunization of the intact animal. An attempt is made to reduce the level of unwanted specificities below that which will interfere with the intended use of a particular immunochemical test.
Example: Reaction of an antiserum with antihuman IgG.
Source: [1]
See also *immunochemical specificity*

4.3.37 polyclonal

Arising from multiple, different clones.

Note: Polyclonal *antibodies* (pAbs) are antibodies that are secreted by different B cell lineages within the body. They are a collection of immunoglobulin molecules that react against a specific antigen, each identifying a different epitope.
Example: A typical antiserum obtained from a conventional immunization is polyclonal.
Source: Adapted from [1]

4.3.38 reverse passive agglutination

Modification of the indirect agglutination assay, where the particles are coated with *antibody*.

Note: These antibody-laden particles become probes for detecting specific antigens in the sample material. The presence of the relevant *antigen* will result in the *agglutination* of particles.

4.3.39 sandwich immunoassay
two-site, noncompetitive immunoassay

Immunoassay using chemical or immunochemical binding of *analyte* to a solid phase carrying *antibody* and the immunochemical binding of a second (labelled) reagent to the analyte.

Note: This is one of the most common assays in clinical practice.
Source: Adapted from [1]

4.4 Genomics and Nucleic Acid Analysis

4.4.1 amplification of DNA

Process of producing multiple copies of a DNA sequence by the repeated copying of a DNA segment.

4.4.2 aptamer

See *nucleic acid aptamer*

4.4.3 base pair (bp)

Pair of two *nucleobases*, consisting of one purine and one pyrimidine base, held together by hydrogen bonds.

Note: In DNA, guanine typically pairs with cytosine and adenine typically pairs with thymine. In *RNA*, adenine typically pairs with uracil.

4.4.4 base sequence

See *nucleotide sequence*

4.4.5 base sequence analysis

Method for determining the *nucleotide sequence*.

4.4.6 basic local alignment search tool (BLAST)

Computer algorithm that finds regions of local similarity between DNA or protein sequences.

4.4.7 chromosome

Organised, defined structure of DNA and *proteins* found in cells. In its *nucleotide sequence*, it bears the linear array of genes.

4.4.8 clone

Exact copy of biological material.

Example: The biological material can be a DNA segment, whole cell, or complete organism.

4.4.9 cloning

Specialised DNA technology for the production of multiple exact copies of a single gene or another segment of DNA.

4.4.10 cloning vector

DNA molecule into which another DNA fragment of appropriate size can be integrated without the loss of its capacity for self-replication.

4.4.11 complementary DNA (cDNA)

Artificial DNA that is synthesised in the laboratory from a messenger RNA template.

4.4.12 complementary sequence

Nucleotide sequence that can form a double-stranded structure with another DNA sequence by following base-pairing (see *base pair*) rules.

4.4.13 complete genome sequence

High-quality, low-error, gap-free DNA sequence of an entire *genome* of an organism.

4.4.14 damage to DNA
damage

Alteration in the DNA chemical structure resulting from interactions with physical or chemical agents occurring in the environment, generated in the organisms as by-products of metabolism, or used as therapeutics.

Note 1: The main types of DNA damage include the interruption of the sugar-phosphate backbone (strand breaks) or the release of bases due to hydrolysis of N-glycosidic bonds (resulting in abasic sites), inter- and intra-strand crosslinks (such as pyrimidine dimers), and a variety of nucleobase lesions (adducts) resulting from reactions of DNA with a broad range of oxidants, alkylating compounds, and other agents.

Note 2: Terms "(product of) DNA damage" (lesion, adduct) and "mutation" should not be intermingled. Mutations refer to hereditable changes in DNA sequence—substitutions, deletions, or insertions of (one or more) standard base pair(s) and are not synonyms to "base mismatches". Importantly, DNA damage and its repair can promote the occurrence of mutations.

Source: [11]

4.4.15 deletion

Loss of a part (one or more base pairs) of DNA.

4.4.16 deoxyribonucleotide

See *nucleotide*

4.4.17 deoxyribose

Type of pentose sugar that is incorporated in the structure of DNA.

4.4.18 deoxyribonucleic acid (DNA)

High relative molecular mass linear *biological macromolecule* composed of *nucleotides* containing 2-deoxy-D-*ribose* and linked by phosphodiester bonds. DNA contains the genetic information of organisms.

Note 1: DNA is a polyanionic macromolecule consisting of chains of nucleotides linked with phosphate bridges (phosphodiester bonds) at the 3′ and 5′ positions of neighbouring sugar (2-deoxy-D-ribose) units (single stranded, ssDNA). Complementary base pairing results in the specific association of two polynucleotide chains that wind around a common helical axis to form a *double helix* (double stranded DNA, dsDNA). Supercoiled DNA represents a contortion of circular DNA into more complex

conformations in which the DNA helices fold around each other. DNA supercoiling is important to assist with DNA packaging within all cells.

Note 2: DNA contains the genetic information of organisms.

See *nucleic acid*
Source: Adapted from [3]

4.4.19 DNA fragmentation

Breaking and/or separation of large DNA molecules into smaller pieces (fragments).

Note 1: DNA fragmentation is usually achieved via cleavage with restriction *endonucleases* at specific sites or non-specifically by, for example, sonication.

Note 2: DNA fragmentation is also a consequence of damage to DNA.

4.4.20 DNA fragmentation index (DFI)

Fraction of DNA having fragmented DNA.

Example: Results of sperm DNA damage are generally reported as the percentage of sperm having fragmented DNA, what is called the sperm DNA fragmentation index.

4.4.21 DNA integrity index

Ratio of longer fragments to shorter DNA.

Note 1: Integrity index may be clinically usefully used as surrogate for detection of tumours.

Note 2: DNA strand integrity is measured by *quantitative PCR* (QPCR) using a real-time system.

4.4.22 DNA mismatch

Defect in the double stranded DNA structure in which the DNA *double helix* contains one (or more) non-standard *base pairs*.

Note: One mismatch is known as a single mismatch. Multiple mismatches are called multi-base mismatches.

Example: Guanine paired with thymine instead of cytosine, or adenine with cytosine instead of thymine.

4.4.23 DNA profiling

Identification of individuals by matching characteristics of their *genome* DNA sequence.

Note 1: DNA profiles are at a lower resolution than a full genome DNA sequence, but this is adequate for forensic purposes, such as in parental testing and criminal investigations.

Note 2: Characteristics used include the frequency (or size) of tandem repeats in the genome.

4.4.24 DNA replication

Synthesis of new DNA strands using existing DNA as a template.

4.4.25 DNA sequencing

Determination of *nucleotide sequence* (the DNA primary structure).

Note: Next-generation sequencing refers to non-Sanger-based high-throughput DNA sequencing technologies where millions of DNA strands can be sequenced in parallel.

4.4.26 double helix

The twisted shape of two complementary DNA strands.

Note 1: The complementary chains are held together by hydrogen bonds between pairs of the complementary *nucleobases*. The helical conformation is promoted by several relatively weak interactions, including hydrophobic (stacking) ones between the bases.

Note 2: The double helix is the most frequent DNA structure formed by two complementary DNA strands. It can also be formed by two complementary RNA strands, one DNA and one RNA strand, as well of any of these with synthetic nucleic acids analogues, such as locked nucleic acid, LNA, or *peptide nucleic acid*, PNA.

4.4.27 endonuclease

Enzyme that cleaves nucleic acids by hydrolysing phosphodiester bonds between nucleotides within a nucleic acid molecule.

4.4.28 exogenous DNA

DNA molecule of foreign origin that has been introduced into an organism.

4.4.29 exonuclease

Enzyme that cleaves nucleotides from free ends of a linear nucleic acid molecule.

4.4.30 gene

Molecular unit of heredity of a living organism that encodes a specific feature, usually a *protein*.

Note 1: The gene includes, however, regions preceding and following the coding region (leader and trailer) as well as (in eukaryotes) intervening sequences (introns) between individual coding segments (exons).

Note 2: Functionally, the gene is defined by the cis-trans test that determines whether independent mutations of the same phenotype occur within a single gene or in several genes involved in the same function.

Source: [3]

4.4.31 gene expression

Process for converting a gene's coded information into biomolecules present and operating in the cell.

4.4.32 genome

Complete set of chromosomal and extrachromosomal *genes* of an organism, a cell, an organelle or a virus; the complete DNA component of an organism.

Source: [3, 7]

4.4.33 genomics

Complex and comprehensive study of *genome* structure and function.

Note 1: Also, specifically refers to the science of using DNA- and RNA-based technologies to demonstrate alterations in gene expression.
Note 2: Functional genomics represents a branch of methods to study the sequencing data for description of the gene functions and interactions.
Source: Adapted from [8, 19]

4.4.34 genotype

Genetic constitution of an organism as revealed by genetic or molecular analysis.

Source: http://goldbook.iupac.org/D01597.html [3]

4.4.35 insertion

Incorporation of a *nucleotide sequence* of DNA into a *genome*.

4.4.36 multi-base mismatch

See *DNA mismatch*

4.4.37 mutagen

Agent that causes a permanent genetic change in a cell.

Source: [7]

4.4.38 mutation

Alterations in the genomic *nucleotide sequence*, such as substitutions, insertion, or deletions of single *base pairs* or of longer DNA stretches.

Source: [11]

4.4.39 Northern blot

Technique involving nucleic acids *hybridization* used to study *gene expression* at the level of RNA.

Note: The Northern blot approach is opposed to *Southern* (and other) blots.

4.4.40 nucleic acid

Large biomolecule composed of *nucleotide* subunits.

Note: The major organic matter of the nuclei of a biological cell. It can be hydrolysed into certain *pyrimidine* or *purine* bases (usually adenine, cytosine, guanine, thymine, and uracil), D-ribose or 2-deoxy-D-ribose, and phosphoric acid.

Examples: Ribonucleic acid and deoxyribonucleic acid.

Source: Adapted from [3, 7, 26]

4.4.41 nucleic acid aptamers

Single stranded (ss) *oligonucleotides* (mainly DNA or RNA) originating from *in vitro* selection, which, starting from random sequence libraries, optimise the nucleic acids for high-affinity binding to a given target.

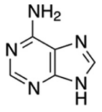
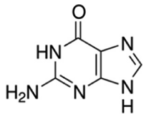
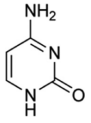
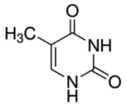
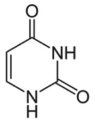
Note 1: *In vitro* selection is an iterative method mainly known as Systematic Evolution of Ligands by EXponential enrichment (SELEX).

Source: [11]

4.4.42 nucleobase

Purine or *pyrimidine* nitrogenous base occurring in DNA or RNA.

Example: Purine and pyrimidine bases of ribo- and deoxyribonucleotides.

Purine bases	
Adenine (A)	
Guanine (G)	
Pyrimidine bases	
Cytosine (C)	
Thymine (T)[b]	
Uracil (U)[a]	

[a] Uracil is normally found in RNA but not in DNA.

[b] Thymine is usually found in DNA but not in RNA.

4.4.43 nucleobase lesion

Product of chemical modification of a *nucleobase*.

Example: Products of oxidation (*e.g.* 8-oxoguanine), alkylation (*e.g.* O6-alkyl guanine), or deamination (*e.g.* uracil as a product of cytosine deamination).

See also *damage to DNA*

4.4.44 nucleoside

Compound in which a *purine* or *pyrimidine* base is bound via a N-atom to C-1, replacing the hydroxy group of either 2-deoxy-D-ribose or D-ribose, but without any phosphate groups attached to the sugar.

Note: The common nucleosides in biological systems are adenosine, guanosine, cytidine, and uridine, which contain ribose; as well as deoxyadenosine, deoxyguanosine, deoxycytidine, and thymidine, which contain deoxyribose.

Source: [7, 26]

4.4.45 nucleotide

Nucleoside in which the primary hydroxy group of either 2-deoxy-D-ribose or of D-ribose is esterified by orthophosphoric acid.

Note 1: Compounds formally obtained by esterification of the 3- or 5-hydroxy group of nucleosides with phosphoric acid.
Note 2: Nucleotides are the subunits of nucleic acids.
Note 3: Nucleotides can be obtained from nucleic acids by *hydrolytic cleavage*.

Source: [7]

4.4.46 nucleotide sequence

Order of *nucleotides* in a DNA or RNA molecule.

4.4.47 oligonucleotide

Short nucleic acid typically consisting of up to 50 bases resulting from a linear sequence of *nucleotides*.

Source: [7]

4.4.48 open reading frame (ORF)

Sequence of DNA or RNA *nucleotides*, located between the start-code sequence (initiation codon) and the stop-code sequence (termination codon), which is transcribed and translated to generate a *protein*.

4.4.49 peptide nucleic acid (PNA)

Synthetic DNA mimic, which contains 2-aminoethylglycine linkages instead of the negatively charged phosphodiesteric backbone of oligonucleotides.

Note: The PNA probes are particularly convenient for the detection of single-base *mismatches* (*point mutations*, SNPs), because the stability of DNA-PNA duplexes is strongly influenced by a single-base *mismatch*.

Source: [11]

4.4.50 plasmid

Autonomously replicating extra-chromosomal circular DNA molecule.

Source: Adapted from [3]

4.4.51 polymerase chain reaction (PCR)

Laboratory technique for rapid amplification and pre-determination of regions of double-stranded DNA using DNA *polymerase*.

See *quantitative PCR*, *real-time PCR*

Source: [20]

4.4.52 polymerase, DNA or RNA

Enzyme that catalyses the synthesis of nucleic acids on pre-existing *nucleic acid* templates.

4.4.53 primer

Short pre-existing polynucleotide chain attached to a complementary stretch in template DNA to which new deoxyribonucleotides can be added by DNA *polymerase*.

4.4.54 probe, in genomics

Single-stranded DNA or RNA molecule used to determine the *nucleotide sequence*.

Note: Typically, a probe is either immobilised at a surface to capture the complementary target sequence from a sample (*capture probe*) or labelled, radioactively or immunologically, by fluorescent, electroactive, or other species) to produce a specific signal upon hybridization (*signalling or reporter probe*).

4.4.55 purine

Nitrogen-containing, double-ring, basic compound that occurs in nucleic acids.

See *nucleobase*

4.4.56 pyrimidine

Nitrogen-containing, single-ring, basic compound that occurs in nucleic acids.

See *nucleobase*

4.4.57 quantitative PCR (qPCR)

Polymerase chain reaction to quantify target nucleotide sequences of interest.

4.4.58 real-time PCR

Polymerase chain reaction where data are collected and monitored in real-time as the reaction proceeds.

Note: Digital PCR is a new alternate method to conventional real-time PCR and *quantitative PCR* for absolute quantification and rare allele detection. Digital PCR works by partitioning a sample of DNA or cDNA into many individual, parallel PCR reactions; some of these reactions contain the target molecule (complementary DNA, positive) while others do not (negative). A single molecule can be amplified a million-fold or more.

4.4.59 recombinant DNA

DNA molecules joined together using *recombinant DNA technology*.

4.4.60 recombinant DNA technology

Procedure used to join together different DNA segments (sequences).

Note: Recombinant DNA technology can include integration of DNA into the genome of a cell.

4.4.61 recombination

Process by which genetic material is broken and joined to other genetic material, which can lead to a rearrangement of genetic sequences.

4.4.62 replication

Process by which *DNA polymerase* generates two identical copies of DNA from one original DNA molecule.

Note: Different processes of replication have been identified, though cells typically use semi-conservative replication, in which each strand of the original DNA molecule serves as a template for the production of a new strand containing a complementary DNA sequence.

4.4.63 restriction enzyme
restriction endonuclease

Protein that recognises specific short *nucleotide sequences* (restriction site) and hydrolyses the DNA backbone at the sequences, generating one (or more) fragments from the DNA molecule.

4.4.64 restriction fragment length polymorphism (RFLP)

Variation between individuals in DNA fragment sizes cut by specific *restriction enzymes*.

4.4.65 reverse transcriptase

Enzyme used to form a complementary DNA sequence (cDNA) from a RNA template.

4.4.66 ribonucleic acid (RNA)

High relative molecular mass linear *biological macromolecule* composed of *nucleotides* containing D-ribose as the sugar and linked by phosphodiester bonds.

Note 1: RNA molecules play important roles in protein synthesis and other chemical activities of the cell.
Note 2: Classes of RNA molecules include messenger RNA (mRNA), transfer RNA (tRNA), ribosomal RNA (rRNA), and other types of non-coding RNA with diverse regulatory functions.
See *nucleic acid*

4.4.67 ribonucleotide

See *nucleotide*

4.4.68 ribosomal RNA (rRNA)

Single-stranded molecule found in the catalytic core of the ribosome.

4.4.69 ribosome

Small cellular component capable of performing protein synthesis and composed of specialised ribosomal RNA and protein.

4.4.70 Sanger sequencing

Method for determining nucleotide sequence of DNA based on incorporating chain-terminating dideoxynucleotides.

Note: The method is named after Frederick Sanger (1918–2013, awarded the Nobel Prize in 1958 and 1980).

4.4.71 shotgun method

Method used for determining the order of bases in long DNA using *sequencing* of DNA broken up randomly into numerous small segments.

4.4.72 single mismatch

See *DNA mismatch*

4.4.73 single nucleotide polymorphisms (SNPs)
point mutations

Variant of *nucleotide sequence* of DNA in which the *purine* or *pyrimidine* base of a single *nucleotide* is replaced by another such base.

Note 1: SNP is the most common type of change in DNA.
Note 2: SNPs occur normally throughout a human DNA once in every 300 nucleotides on average, which means there are roughly 10 million SNPs in any typical human genome. They can act as biological (diagnostic) markers.

4.4.74 Southern blot

Technique based on DNA *hybridization* used for the detection of a DNA fragment of specific *nucleotide sequence*.

4.4.75 strand break

Interruption of the sugar-phosphate backbone of a polynucleotide chain.

4.4.76 tandem repeat sequence

Multiple consecutive copies of the same *nucleotide sequence* on a *chromosome*.

Note: Tandem repeat sequences can be used as markers in physical mapping *e.g.* by *DNA profiling*.

4.4.77 telomerase

Enzyme that directs the replication of *telomeres*.

4.4.78 telomere

Repetitive *nucleotide* sequences present at the ends of a *chromosome* that protect the chromosome from deterioration.

Note: In polymer sciences, an oligomer obtained by telomerization is often termed a telomer.

Source: [15], term 23.

4.4.79 yeast artificial chromosome (YAC)

Vector used to clone large DNA fragments.

See *cloning vector*

General references: [27–31]

4.5 Proteomics

4.5.1 alternative splicing

Process occurring during gene expression that allows the generation of multiple protein molecules from one gene. It generally involves the processing of mRNA via elimination of introns.

Source: [32] page 69

4.5.2 bottom-up proteomics

Approach to identify *proteins* and characterise their amino acid sequences or post-translational modifications by sequential combination of *proteolysis* (*enzymatic proteolysis* and *chemical proteolysis*) prior to mass spectrometric analysis of the resulting *proteolytic peptides*.

Note: In shotgun proteomics, the proteins in a mixture are digested, usually by a specific enzyme, and the resulting peptides are separated by liquid chromatography and identified by tandem mass spectrometry.

Source: [33, 34]

See *top-down proteomics*

4.5.3 C-terminal analysis

Chemical method for C-terminal sequencing of proteins and peptides starting at their C-terminus.

Source: [35, 36]
See *C-terminus*

4.5.4 C-terminus

The end of an amino acid chain (*protein* or *polypeptide*), terminated by a carboxylic group.

Source: [36]

4.5.5 collision-induced dissociation (CID) (in proteomics)

Ion fragmentation technique in mass spectrometry-driven proteomics used to generate peptide fragment ions from proteins in peptide sequencing by tandem mass spectrometry.

Source: [37]

4.5.6 database searching (in proteomics)

Bioinformatics analysis of proteomic mass spectrometric data used in order to identify a protein or its post-translational modification. It results in a list of candidates presented mostly in order of the decreasing statistical significance of the hit.

4.5.7 difference gel electrophoresis (DIGE) (in proteomics)

Mode of *two-dimensional gel electrophoresis* used to study protein expression regulation by the differential staining of multiple gels representing different states of a *proteome*, preferably with fluorescent dyes (*e.g.* Cy3, Cy5, Cy2).

Note: The resulting stained gels are analysed using 2D image analysis.
Source: [38]

4.5.8 differential proteomics

See *expression proteomics*

4.5.9 disulfide bond cleavage

Chemical reduction of protein disulfide bonds.

Note: Reductants, such as tributylphosphine (TBP), 2-sulfanylethan-1-ol (BME), or dithiothreitol (DTT) are used.
Source: [36] page 101

4.5.10 Edman degradation

Method of N-terminal analysis in which the N-terminal amino acid residue is labelled and cleaved from the peptide without affecting other peptide bonds in the peptide chain.

Note: The method is named after Pehr Victor Edman (1916–1977).
Source: [39]

4.5.11 electron-transfer dissociation (ETD) (in proteomics)

Ion fragmentation technique in mass spectrometry-driven proteomics based on the transfer of low energy electrons to the molecules selected for fragmentation.

Note: ETD is particularly effective for analysis of post-translational modification.

Source: [37]

4.5.12 electron-transfer/higher-energy collision dissociation (EthcD) (in proteomics)

Ion fragmentation technique in mass spectrometry-driven proteomics that is a combination of electron-transfer dissociation (ETD) and higher-energy collision dissociation (HCD) in orbitrap instruments.

Note: The dual fragmentation allows generation of rich MS/MS spectra for peptide sequencing and PTM analysis.
Source: [40]

4.5.13 electrospray ionisation (ESI) (in proteomics)

Soft ionisation technique in mass spectrometry-driven proteomics.

Note: Electrospray ionisation is optimal for ionising liquid eluates from separation methods, as well as for the direct introduction of liquid samples to fragmentation in MS. Ionisation is made by positive or negative mode, depending on the ability of the molecules to form cations or anions. During the ionisation process, a *biomacromolecule* obtains a number of charges roughly proportional to its relative molecular mass. Also, non-covalent protein complexes may be ionised with ESI.

Source: [37]

4.5.14 expression proteomics

Field of study in proteomics that deals with the determination of changes in protein expression and regulation in response to different stimuli, internal or external. It also includes the analysis of post-translational modifications (*e.g.* phosphorylation, glycosylation, *etc.*), their identification, and their localisation.

Source: [41]

4.5.15 functional proteomics

Field of study in *proteomics* studying protein interactions on different levels: protein-protein interactions (*interactomics*), the formation of protein complexes, and the interaction of proteins with other *biomolecules*.

Source: [42]

4.5.16 gel electrophoresis (1D PAGE) (in proteomics)

Separation technique used to separate or fractionate proteins and larger peptides according to their relative molecular mass using an electric field in polyacrylamide gel (PAGE).

Note 1: 1D PAGE has two basic modes: a denaturing (or SDS) PAGE to estimate relative molecular masses and a native PAGE to separate proteins as their native structures.

Source: [32] page 592

4.5.17 higher-energy collision dissociation (HCD) (in proteomics)

Ion fragmentation technique in mass spectrometry-driven proteomics used mostly at orbitrap instruments. It does not have low mass cut-off of collision-induced dissociation (CID) and therefore is used for the tandem mass tag of stable isotope labels.

Source: [43]

4.5.18 isoelectric focusing (IEF) (in proteomics)

Separation technique used to separate or fractionate proteins and peptides in a gel (or similar type of media) according to their isoelectric point.

Note: IEF is typically the first dimension of two-dimensional *gel electrophoresis*.

Source: [44]

4.5.19 mass fingerprinting (in proteomics)

peptide mass fingerprinting
mass mapping

Protein analysis where an unknown protein is chemically or enzymatically cleaved into peptide fragments whose masses are determined by mass spectrometry. The peptide masses are compared to peptide masses calculated for known proteins in a database and analysed statistically to determine the best match.

Source: [37]

4.5.20 MS/MS data based identification (in proteomics)

Mass spectrometric method used for protein/peptide identification based on *protein sequencing*.

Note: Using peptide ion fragments, the peptide sequence is read and a list of hit candidates is obtained in combination with *database searching*.

Source: [45]

4.5.21 multi-dimensional protein identification technology (MudPIT)

Non-gel step-wise multi-dimensional technique for separating and identifying individual components of complex protein and peptide mixtures. It combines fractionation of proteolytic peptides in steps on a strong cation exchanger (SAX) using ion exchange chromatography (IEC); each step uses higher elution force. Then, each fraction is separated on reversed phase liquid chromatography and analysed using mass spectrometry.

Source: [37]

4.5.22 N-terminal analysis

Chemical method for N-terminal sequencing of proteins and peptides starting at their N-terminus.

See *N-terminus* and *Edman degradation*

Source: [36, 46] page 102

4.5.23 N-terminus

The end of an amino acid chain (*protein* or *polypeptide*), terminating in a free primary amine group.

Source: [36] page 71

4.5.24 off-gel isoelectric focusing (OFFGEL™)

Separation technique used to fractionate proteins and peptides into discrete liquid fractions according to their isoelectric point.

Source: [47]

4.5.25 off peptide product ions

Protein/peptide sequencing approach using overlapping complementary information on a sequence acquired using proteolysis in bottom-up proteomic analysis by at least two different proteolytic approaches.

Source: [13]

4.5.26 peptide

Amide derived from two or more amino acid molecules (whether of the same or of different molecules) by the formation of a covalent bond from the carbonyl carbon of one to the nitrogen atom of another with formal loss of water (peptide bond).

Note 1: The term is usually applied to structures formed from α-amino acids, but it includes those derived from any amino acid.

Note 2: Usually, when the number is higher than ten, the peptide is expressed using the term *polypeptide*. An oligopeptide consists of between 2 and 20 amino acids.

Source: [26]

4.5.27 peptide *de novo* sequencing

Analytical process that derives an amino acid *sequence* of a peptide from its tandem mass spectrum without the assistance of a sequence database.

Note: It is defined in contrast to protein/peptide identification using a database search. An advantage of *de novo* sequencing is its applicability to both known and novel peptides from organisms with unsequenced genome.

Source: [48]

4.5.28 peptide fragment ion

Product ion which originates in a *peptide precursor ion* fragmentation process.

Note: Peptide fragment ions are generated in pairs according to the kind of mechanism that dissociates the chemical bonds around the peptide bond.

Source: [49] page 243, [50]

4.5.29 peptide fragmentation technique

Mass spectrometric technique that serves to generate *peptide fragment ions* through the fragmentation of *peptide precursor ions* via different physicochemical processes in an ion source.

Note: This approach based on the *top-down proteomics* is an alternative to *bottom-up proteomics*. The main advantages include the potential for 100 % sequence coverage of the protein and improved detection of post-translational modifications.

Source: [49] pages 251–258, [50]

4.5.30 peptide precursor ion

Peptide ion generated during the ionisation of peptides in an ion source or during *tandem mass spectrometry* of an intact protein in *top-down proteomic* analysis, selected for further analysis by means of tandem mass spectrometry.

Note: Once generated, a peptide fragment ion may become a precursor ion for tandem mass spectrometry of higher orders (MS^n, $n = 3$).
Source [49] page 243, [50]

4.5.31 peptidomics

Study of the set of *peptides* in an organism, its peptidome.

Note: It uses similar approaches and methods as *proteomics*.
Source: [51]

4.5.32 phenotype

Set of observable organismal characteristics.

Note 1: The characteristics can be morphological, developmental, biochemical, or physiological properties, or behaviour.
Note 2: The diversity of the phenotype is driven by a combination of the gene expression, social, and environmental factors. *Proteome* plays an important role in the transformation of *genotype* into phenotype.
Source: [32] page 1477

4.5.33 polypeptide

Peptide containing ten or more amino acid residues.

Source: [32] page 1359

4.5.34 primary structure of a protein

Amino acid *sequence* of the *polypeptide* chain(s) without regard to spatial arrangement (apart from configuration at the α-carbon atom).

Note: This definition does not include the positions of disulfide bonds and is therefore not identical with 'covalent structure'.
Source: [32] page 1579, [52]

4.5.35 protein

Naturally occurring or synthetic *polypeptide* having a relative molecular mass greater than about 10 000.

Source: [26]

4.5.36 protein complex

Ensemble of two or more different associated proteins, each with a specific function, linked by non-covalent protein-protein interactions.

Note 1: Protein complexes are required for most biological processes. Together they form molecular machines that perform biological functions.
Note 2: Proteins with *quaternary structure* are not considered as protein complexes.
Example Anaphase promoting complex.
Source: [32] page 1572

4.5.37 protein complex purification

Set of methods serving to purify the intact *protein complex* for further analysis.

Note: The methods used may employ single step affinity purification or tandem affinity purification (two affinity purification steps). These approaches include the direct application of an epitope on a bait protein for immunopurification or the genetic insertion of an affinity tag to bait protein, both used to co-purify the prey components of the protein complex.
Source: [49] page 273, [50]

4.5.38 protein database

Collection of *protein sequences* from several sources, including translations from annotated genetic coding regions, as well as original protein and peptide sequences.

Note: A protein database is fundamental for the determination of protein structure and function via bioinformatics.
Source: [36] page 109

4.5.39 protein folding

Physicochemical process by which a *polypeptid*e folds into its characteristic and functional three-dimensional structure from a random coil.

Source: [32] page 1574

4.5.40 protein fractionation
protein separation

Methodical approach to simplify a complex mixture of proteomic sample.

Note: Target compounds can either be separated into individual protein/peptides or fractionated into groups with similar physicochemical properties (polarity, charge, relative molecular mass, *etc*.). Different analytical separation methods are deployed to achieve this effect: liquid chromatography, gel electrophoresis, isoelectric focusing, affinity chromatography, *etc*.
Source: [44]

4.5.41 protein fragmentation

Process which happens during *tandem mass spectrometry* of intact proteins.

Note: This process is used in *top-down proteomics*. It generates specific *peptide fragment ions* from a selected protein precursor ion.
Source: [49] page 242, [50]

4.5.42 protein identification

Analytical approach leading to the identity of a *protein*.

Note: The identity of the protein is given in respect to the proteoform by its primary structure, post-translational modification, or tertiary structure.
Source: [53] page 14

4.5.43 protein machine

Supramolecular interacting system, such as a metabolic circuit, intracellular signal transduction, or cell-to-cell communication.

Note: These systems are operated under process control strategies involving integrated feedback control. The input and output of the circuits or modules are coordinated to assure the normal or adaptive function of the cell or organism.
Source: [54]

4.5.44 protein primary structure

Sequence of the amino acids in the *polypeptide* chain.

Note: The primary structure of a protein is crucial information for further proteomics analyses.
Source: [32] page 1579

4.5.45 protein purification

Series of processes conducted to isolate either the whole proteome or a subset from a biological sample.

Note: Protein purification involves many different methods, such as chromatography, immunopurification, precipitation, *etc.*
Source: [44]

4.5.46 protein quantitation Analytical methods and related techniques to measure the *protein* content.

Note 1: Basic analytical methods used in proteomics to quantitate protein content are gel electrophoresis, immunoanalysis (see *Western blotting*), densitometry of differential staining and mass spectrometry. Mass spectrometry especially offers many particular techniques based on either stable isotope labelling or label-free approaches.

Note 2: Absolute quantitation of proteins (AQUA) is performed via measurements on constituent proteolytic peptides using chemically synthesised isotope-labelled peptides as surrogate internal standards for mass spectrometry.

Source: [55]

4.5.47 protein sequencer

Equipment designed for the automatic determination of amino acid sequences of peptides using a method of N-terminal analysis.

See *Edman degradation*.

4.5.48 protein sequencing

Determination of the *primary structure of a protein*.

Source: [44]

4.5.49 protein staining

Technique used to visualise *proteins* separated on electrophoretic slab gels.

Note: Typically, three types of staining are commonly used: silver staining, which is highly sensitive and non-quantitative; Coommassie Brilliant Blue staining, which is less sensitive than silver staining and quantitative; and fluorescent dye staining, which is highly sensitive and quantitative.

Source: [9]

4.5.50 proteoform

All of the different molecular forms in which the protein product of a single *gene* can be found, including changes due to genetic variations, alternatively spliced RNA transcripts, and post-translational modifications.

Source: [56]

4.5.51 proteogenomics

Field of biological research in-between *proteomics* and *genomics* using proteomic information (mostly derived from mass spectrometry) to improve *gene* annotations.

Source: [57]

4.5.52 proteolysis

Protein cleavage to generate *proteolytic peptides* for *bottom-up proteomic* analysis, either enzymatic or chemical.

Note: Both enzymatic and chemical proteolysis may be sequence-specific or unspecific. Proteolysis is specific where cleavage appears at a few specific sequence motives (*e.g.* proteolysis by trypsin), or unspecific, being connected to wide range of sequence motives (*e.g.* proteolysis by chymotrypsin).

Source: [32] page 1586, [36] page 103, [58] pages 78–86

4.5.53 proteolytic digestion

Exposure of a sample to proteolytic reactions.

See *proteolysis*

4.5.54 proteolytic enzyme

Group of enzymes that cleave the *polypeptide* into shorter oligopeptides (peptides) and amino acids.

Source: [32] page 1570

4.5.55 proteolytic peptide

Peptide generated via proteolysis.

Source: [49] page 144, [50]

4.5.56 proteome

Complete set of proteins and their modifications in an organismal compartment (organelle, cell, tissue or organism).

Note 1: The proteome is an analogue of the *genome*.
Note 2: Proteome may be viewed as an actual proteome, as a set given by the actual level of protein expression (depending on conditions of growth), or as an overall proteome, a set of all potentially possible proteins expressed according to a given genome.
Source: [32] page 1586

4.5.57 proteomics

Complex and comprehensive study of *proteomes*, particularly *proteins*, and the way they are expressed, modified, involved in metabolism, as well as of their interactions.

Source: [32] page 1587

4.5.58 quaternary structure of a protein

Arrangement of subunits of a *protein* molecule in space and the ensemble of its intersubunit contacts and interactions, without regard to the internal geometry of the subunits.

Note: A protein molecule not made up of at least potentially separable subunits (not connected by covalent bonds) possesses no quaternary structure. Examples of proteins without quaternary structure are ribonuclease (one chain) and chymotrypsin (three chains).

Source: [32, 52], page 1579

4.5.59 relative quantification (in proteomics)

Type of protein/peptide quantitation, where the relative quantities of one protein in different samples is determined, *i.e.* the ratio of the content of a protein/peptide in sample 1 to sample 2.

Source: [55] page 184

4.5.60 secondary structure of a protein

Local spatial arrangement of main-chain atoms of a segment of *polypeptide* chain without regard to the conformation of its side chains or to its relationship with other segments.

Note: Regular sub-structures favoured by specific groups of *amino acid* sequences; examples include α-helix and β-sheet.

Source: [32] page 1579, [52]

4.5.61 stable isotope labelling (in proteomics)

Techniques which serve to quantify *protein* content by means of mass spectrometry. The principle lies in the introduction of a mass tag to an internal standard protein/peptide containing different stable isotopes than the protein/peptide in the sample. Mass resolved signals originating in the internal standard and the sample are read individually and evaluated.

Note: In the case of a complex sample, the use of multiple reaction monitoring allows for the resolution of multiple overlapping signals.

Source: [59]

4.5.62 structural proteomics

Field in *proteomics* which focuses on higher orders of the *protein* structure, mainly tertiary or quaternary.

Source: [60]

4.5.63 targeted proteomics

Approach in *proteomics* focused on the selected *proteins* of a sample.

Note 1: In a targeted analysis, the mass spectrometer is programmed to analyse a preselected group of proteins. This can be achieved using a technology called selected reaction monitoring (SRM; also referred to as multiple reaction monitoring, MRM), whereby assays are developed on a triple quadrupole instrument to detect fragment-ion signals arising from unique diagnostic peptides representing each of the targeted proteins.

Note 2: Targeted proteomics achieves the highest sensitivity and throughput for hundreds or thousands of samples in regard to the intended aspect (namely target fragments).

Source: [61]

4.5.64 tertiary structure of a protein

Arrangement of all atoms of a *protein* molecule or a subunit of a protein molecule in space, without regard to its relationship with neighbouring molecules or subunits.

Note: The tertiary structure represents a three-dimensional fold/organisation of a *polypeptide* chain, one containing specific arrangements of secondary structures (See *secondary structure of a protein*).

Source: [32] page 1579, [52]

4.5.65 top-down proteomics

Approach to identify *proteins* and characterise their *amino acid* sequences or post-translational modifications either by direct mass spectrometric analysis of an ionised protein molecule or by sequential combination of protein/*peptide* fragmentation in the ion source or mass analyser with ion trapping mass spectrometers.

Source: [33, 62]

See *bottom-up proteomics*

4.5.66 trypsin (in proteomics)

Serine protease with highly specific primary endoproteolytic activity that serves to generate proteolytic peptides in *bottom-up proteomics* analysis.

Note: It may be modified by reductive methylation or glycosylation to increase its thermal stability.

Source: [32] page 2041

4.5.67 two-dimensional gel electrophoresis (2D PAGE) (in proteomics)

Technique used to separate proteins using *isoelectric focusing* in a gel. The proteins are then further separated in the second dimension using *denaturing PAGE*.

Note: 2D PAGE greatly enhances the capacity of the separation and facilitates further analysis, such as the *difference gel electrophoresis* or the mass spectrometric analysis of gel separated proteins.

Source: [63]

4.5.68 Western blot

Immunoanalytical technique for the identification of polypeptides separated using gel electrophoresis. The polypeptide is transferred by blotting to a membrane, where it undergoes specific interaction with primary antibody that is specific to the protein of interest. The peptides are detected as complexes by a *label* and/or enzymatic reaction, which may be conjugated to the primary antibody directly or via a separate (secondary) antibody.

Source: [32] page 2101

General References: [9, 32, 64]

4.6 Metabolomics

4.6.1 cultivation (in metabolomics)

Sample pretreatment to degrade complex metabolites in the presence of oxygen; a method for amplifying the concentration of native metabolites in solution.

4.6.2 design of experiment (in metabolomics)

Metabolomic workflow composed of sampling, metabolism quenching, metabolite extraction, metabolite analyses, data analysis, and interpretation.

Source: [65]

4.6.3 endometabolome

Complete set of metabolites inside a cell (intracellular metabolites).

4.6.4 excretion

Process removing compounds and their metabolites from the body, usually through the kidneys (via urine) or in the feces. Unless excretion is complete, the accumulation of foreign substances can adversely affect normal metabolism.

4.6.5 exometabolome

Complete set of metabolites outside the cell (extracellular environment).

4.6.6 fermentation (in metabolomics)

Degradation of the sample compounds in the absence of oxygen; this produces metabolites for intracellular metabolic profile characterization.

4.6.7 fingerprinting (in metabolomics)

Qualitative analysis of the *endometabolome*.

Example: Profiling and screening the matrix profile with known standards.

Source: [65]

4.6.8 fluxomics

In vivo measurements of metabolic fluxes and integration of the results into stoichiometric network models.

Source: [66]

4.6.9 footprinting (in metabolomics)

Qualitative analysis of the *exometabolome*.

Source: [65]

4.6.10 glucuronide

Glycoside of glucuronic acid.

Note: Glucuronides of xenobiotics (such as drugs, toxic substances, *etc.*) are formed to *excrete* them from the organism.
Example: Drug glucuronides and sulfate conjugates are identified in excreted fluids.

4.6.11 metabolic pathway

All metabolic products of the main compound (*e.g.* phase 1 and phase 2 metabolites) with the routes of metabolism and the excreted metabolites in body fluids, *e.g.* in urine or blood.

Source: [7]

4.6.12 metabolism

Set of continuous life-sustaining chemical processes within cells that can be divided into two categories: in catabolism, some substances are broken down to yield energy for vital processes and provide the precursors for biosynthesis, whereas in anabolism, part of this energy and the precursors formed are used to construct new cell components.

Note 1: Metabolism means the continuously progressive physical and chemical processes involved in the maintenance and reproduction of life in which nutrients are broken down to generate energy and to produce simpler molecules (catabolism), which by themselves may be used to form more complex molecules (anabolism). In the case of heterotrophic organisms, the energy evolving from catabolic processes is made available for use by the organism.
Note 2: In medicinal chemistry, the term metabolism refers to the biotransformation of xenobiotics and particularly drugs.
Source: Adapted from [7]

4.6.13 metabolism quenching

Physical or chemical methodology used for rapidly breaking all biochemical processes in *metabolomic* samples.

Source: [65]

4.6.14 metabolite

Any chemical compound of the biological system that is not genetically encoded and is a substrate, intermediate, or product of metabolism; is consumed from the external environment; or comes from co-habiting microorganisms, such as gut microflora.

Source: Adapted from [7]

4.6.15 metabolite fingerprinting and footprinting

Unique pattern characterizing the metabolism in a given living phase that does not attempt to identify or quantify all the metabolites.

See *fingerprinting* and *footprinting*

4.6.16 metabolite profiling

Strategy to identify and quantify a particular set of metabolites belonging to a specific metabolic pathway or class of compounds.

Source: [65]

4.6.17 metabolome

Complete quantitative set of organic or inorganic low relative molecular mass compounds (from 50 to 1000) – *metabolites* – present in the cell or organism and which participate in the metabolic reactions required for growth, maintenance, and normal functioning.

Note: The metabolome forms a large network of metabolic reactions where outputs from one enzymatic chemical reaction are inputs to other chemical reactions.

Source: [67]

4.6.18 metabolomics

Complex and comprehensive study of *metabolome;* identification and quantification of the small molecule metabolic products of a biological system (cell, tissue, organ, biological fluid, or organism) at a specific point in time.

Note: An essential part of systems biology in addition to genomics, transcriptomics, proteomics, interactomics, and fluxomics.

Source: [68, 69]

4.6.19 metabonomics

Measurement of the dynamic multiparametric metabolic response of a living system to pathophysiological stimuli or genetic modification.

Note: This term is sometime misapplied to refer to the whole of "metabolomics".

Source: [70]

4.6.20 primary metabolites

Metabolites directly involved in the normal life processes of each cell.

Examples: alcohols, amino acids, monosaccharides, nucleotides, organic acids.

Source: [7]

4.6.21 secondary metabolites

Metabolites not required for the survival of the corresponding organism, but which have other important functions.

Examples: antibiotics, pigments, attractants, flavours, drugs, biomarkers.

Source: Adapted from https://doi.org/10.1351/goldbook.D01597 [7]

General References: [7, 69, 71–73]

4.7 Glycomics

4.7.1 activated nucleotide sugar

Activated form of *monosaccharide* linked to a *nucleotide* to be available in a high-energy state for *glycosyl* transfer.

Source: [74, 75]

4.7.2 aglycon

The non-sugar compound remaining after the replacement of the glycosyl group from a *glycoside* by a hydrogen atom. Non-carbohydrate part of a *glycoconjugate* or a *glycoside*.

Note: The alternative spelling aglycone is discouraged because it suggests a ketonic structure.
Source: [26, 74–76]

4.7.3 aldose

Monosaccharide with an aldehydic carbonyl or potential aldehydic carbonyl group.

Note: The term potential aldehydic carbonyl group refers to the hemiacetal group arising from ring closure.
Example: D-glucose
Source: [26, 74, 76]

4.7.4 anomeric hydroxy(l) group
glycosidic hydroxy group

Hydroxy(l) group that originates from the aldehydic or ketonic group of a *monosaccharide* after ring closure.

Note: A functional group in one of two stereoisomers of a cyclic saccharide that differs only in its configuration at the hemiacetal or hemiketal carbon, which is also called the anomeric carbon. An anomer is a special type of epimer.

See *hemiacetal* and *hemiketal*
Source: [74]

4.7.5 carbohydrate

Monosaccharides, *oligosaccharides* and *polysaccharides*, as well as substances derived from monosaccharides by reduction of the carbonyl group (alditols), by oxidation, including the oxidation of one or more terminal groups to carboxylic acids, or by replacement of one or more hydroxy groups by a hydrogen atom, an amino group, a thiol group, or by similar heteroatomic groups. This term also includes derivatives of these compounds.

Note: The term carbohydrate was applied originally to monosaccharides, in recognition of the fact that their empirical composition can be expressed as $C_m(H_2O)_n$. However, the term is now used generically in a wider sense.

Source: [76]

4.7.6 carbohydrate-binding protein

See *glycan-binding protein*

4.7.7 comparative glycoproteomics

Field of *glycoproteomics* that studies that the changes in the structures and expression levels of *glycoproteins* under different conditions.

4.7.8 comparative proteoglycomics

Field of *proteoglycomics* that studies the changes in the structures and expression levels of *proteoglycans* under different conditions.

Source: [77]

4.7.9 glycan

The term includes *oligosaccharides* and *polysaccharides*, either free or bound to other chemical entities (*glycoconjugates*).

See *polysaccharides*

Source: Adapted from [26, 75, 78].

4.7.10 glycan microarray

Glycans attached to a surface of a *microarray*.

Note 1: Glycan microarrays are used for the characterization of *lectins* and other glycan-binding proteins via specific interactions with labelled glycan-binding proteins.

Note 2: Specific lectin–glycan interactions are also used for the characterization of glycans in the opposite set-up (see lectin microarray, glycan profiling).

Source: [74, 75, 79]

4.7.11 glycan profiling

Determination of the diversity of *glycan* structures expressed on *glycoconjugates* or cells.

See *lectin microarray*
Source: [75]

4.7.12 glycan-binding protein
carbohydrate-binding protein

Protein that recognises and binds to specific *glycans* and mediates their biological function.

See *lectin*
Source: [74, 75]

4.7.13 glycoconjugate

Compound in which *glycan* is covalently bound to other chemical species.

Note: The glycan part of a glycoconjugate is called glycone. The non-sugar part is called aglycon.

Example: glycoprotein, glycolipid

Source: [74, 75]

4.7.14 glycoform

Specific form of a *glycoprotein* containing a distinct *glycan* structure per glycosylation site.

Note: Natural glycoprotein consists of a population of glycoforms resulting from variable glycan structure and/or glycan attachment site occupancy.

Source: [74, 75]

4.7.15 glycogene

Gene encoding an enzyme or other functional protein for *glycan* synthesis.

Note 1: The term should not be confused with *glycogen* (an energy-storage glucose polysacharide in animals and fungi).
Note 2: Proteins for glycan synthesis include glycosyltransferases, sugar-nucleotide synthases, sugar-nucleotide transporters, and sulfotransferases (see glycosylation, activated nucleotide sugars).
Source: [75]

4.7.16 glycolipid

Compound containing a *glycan* covalently linked to a lipid *aglycon*.

Note: The term “lipid” comprises several types of compounds. Therefore, different classes of glycolipides are described. For example, typical glycolipids in higher organisms are glycosphingolipids.
Source: [74]

4.7.17 glycome

Complete set of *glycans* and *glycoconjugates* produced by a species, tissue, or cell in a specified time, space, and environment.

Note 1: Glycome is an analogue of the terms *genome*, *proteome*, and transcriptome.
Note 2: The terms, as for example "sialome", are sometimes used for the specific subclasses of the glycome.
Source: [74, 75, 80]

4.7.18 glycomics

Complex and comprehensive study of the *glycome*.

Note: An analogue of the terms *genomics* or *proteomics*. The terms, as for example "fucanomics" or "galactanomics", are sometimes used for the specialised fields of glycomics.
Source: [75, 81]

4.7.19 glycone

Carbohydrate part of a *glycoconjugate* or a *glycoside*.

Source: [74, 76]

4.7.20 glycoprotein

Protein with one or more covalently bound *glycans*.

See *lectin*
Source: [74]

4.7.21 glycoproteomics

Comprehensive analysis of *glycoproteins*.

Note: Glycoproteomics studies the glycosylated subset of the proteome, including sites of glycosylation and glycan structures.
Source: [74]

4.7.22 glycosaminoglycan (GAG)

Long, linear, highly-charged polysaccharide composed of disaccharide repeating units, each containing hexose or hexuronic acid and *N*-acetylated or substitution-free hexosamine.

Note: GAG could be a free complex polysaccharide or be covalently linked to a protein core.

See *proteoglycan*
Source: [74, 75]

4.7.23 glycosidase

Enzyme that catalyses the hydrolysis of *glycosidic linkages*.

Note: Endoglycosidase hydrolyses internal glycosidic linkages, while exoglycosidase removes terminal monosaccharide from the non-reducing end of a glycoside.

Source: [74, 75]

4.7.24 glycoside

Mixed acetal formally arising by the elimination of water between the *hemiacetal* or *hemiketal* hydroxy group of a sugar and a hydroxy group of a second compound. *Glycan* containing at least one *glycosidic linkage* to another glycan or an *aglycon*.

Note: The bond between the two components is called a glycosidic bond.

Source: [74, 76]

4.7.25 glycosidic linkage
glycosidic bond

Linkage of a monosaccharide to another residue via the anomeric hydroxy(l) group.

Source: [74, 75]

4.7.26 glycosidic hydroxy group

See *anomeric hydroxy(l) group*

4.7.27 glycosyl

Monosaccharide ring without the anomeric oxygen.

Source: Adapted from [75]

4.7.28 glycosylation

Covalent attachment of a *saccharide* to a *protein*, *lipid*, *polynucleotide*, *saccharide*, or other organic compound, generally catalysed by enzymes *glycosyltransferases*.

Source: [74]

4.7.29 glycosyltransferase

Enzyme that catalyses the transfer of a *saccharide* from a nucleotide di(mono)phosphate-activated *sugar* to an acceptor molecule.

See *activated nucleotide sugars, glycosylation*

Source: [74, 75]

4.7.30 hemiacetal

Compound having the general formula RCH(OH)(OR′) (R′ ≠ H).

Note: A hemiacetal results from the nucleophilic addition of a hydroxy group to a carbonyl functionality of an aldehyde, as in ring closure of an *aldose*.

See *anomeric hydroxy(l) group*, *hemiketal*
Source: Adapted from [26, 74]

4.7.31 hemiketal

Compound having the general formula $R_2C(OH)OR'$ (R′ ≠ H).

Note: A hemiketal results from the nucleophilic addition of a hydroxy group to a carbonyl functionality of a ketone, as in ring closure of a *ketose*.

Source: Adapted from [26, 74]. See *hemiacetal*.

4.7.32 ketose

Monosaccharide with a ketonic carbonyl or a potential ketonic carbonyl group.

Example: D-fructose
Source: [26, 74, 76]

4.7.33 lectin

Saccharide binding *protein* of non-immune origin.

Note 1: Some lectins participate in immune system processes, but they are not products of primary immune response. Lectins also do not display catalytic activity towards their ligands; the binding of carbohydrate is reversible and highly specific.

See *glycoprotein*
Source: Adapted from [82]

4.7.34 lectin microarray

Lectins with distinct *saccharide*-binding specificity arranged on a *microarra*y platform.

Note 1: Lectin microarray is used for the characterization of glycans (see: *glycan profiling*) via specific interactions with labelled *glycans*.
Note 2: The specific lectin–glycan interactions are also used for the characterization of lectins in the opposite set-up (see: glycan microarray).
Source: [75]

4.7.35 monosaccharide

Polyhydroxy aldehyde H-$[CHOH]_n$-CHO or polyhydroxy ketone H-$[CHOH]_n$-CO-$[CHOH]_m$-H, with at least with three or more carbon atoms, respectively.

Note 1: The generic term monosaccharide (as opposed to *oligosaccharide* or *polysaccharide*) denotes a single unit without glycosidic connection to other such units.
Note 2: Most monosaccharides exist as cyclic *hemiacetals* or *hemiketals*.
Examples: *Aldoses*, dialdoses, aldoketoses, *ketoses*, diketoses, as well as deoxy sugars and amino sugars, and their derivatives, provided that the compound has a (potential) carbonyl group.
Source: Adapted from [74, 76]

4.7.36 nucleotide sugar

See *activated nucleotide sugar*

4.7.37 oligosaccharide

Compound in which *monosaccharide* units are joined by *glycosidic linkages*.

Note: Oligosaccharides are called disaccharides, trisaccharides, tetrasaccharides, pentasaccharides, *etc.*, according to their number of units.

Source: Adapted from [76]

4.7.38 polysaccharide

Biomacromolecule consisting of a large number of *monosaccharide* (glycose) residues joined to each other by *glycosidic linkages*.

See *glycan*
Source: [76]

4.7.39 proteoglycan

Compound consisting of a protein core to which one or more *glycosaminoglycan* chains are covalently attached.

Source: [74, 75]

4.7.40 proteoglycomics

Systematic study of the structure, expression, and function of *proteoglycans*.

Source: [77]

4.7.41 saccharide

The generic term applied to *monosaccharides*, *oligosaccharides*, and *polysaccharides*.

Source: [76]

4.7.42 sugar

The term frequently applied to *monosaccharides* and lower *oligosaccharides*.

Source: [76]

General References: [80–83]

4.8 Lipidomics

4.8.1 alkaline degradation (in lipidomics)
alkaline hydrolysis

Treatment with alkaline solution (*e.g.* hydrazine, KOH, NaOH) useful for the cleavage of *fatty acids*.

Note: The resulting (partially or fully) O-deacylated and (fully) N-deacylated products enable the determination of the fatty acid substitution positions by mass spectrometry.

Source: Adapted from [84]

4.8.2 core oligosaccharide

Intermediate structural region between the O-polysaccharide and *lipid A* moiety of *lipopolysaccharides* (LPS).

Source: [85, 86]

4.8.3 eicosanoids

See *icosanoids*

4.8.4 fatty acids

Aliphatic rnonocarboxylic acids derived from or contained in esterified form in an animal or vegetable fat, oil, or wax.

Note: Fatty acids are building blocks of the majority of complex cellular lipids, such as phospholipids, sphingolipids, triacylglycerols, and sterylesters.

Source: Adapted from [26]

4.8.5 fatty acyls (FA)

Diverse group of lipid molecules synthesised by chain elongation of an acetyl-CoA primer with malonyl-CoA (or methylmalonyl-CoA) groups.

Note 1: The fatty acyl category is further divided into multiple subclasses, including *fatty acids* and conjugates, *icosanoid*, fatty alcohols and esters, *glycans*, and others.

Examples: Palmitic acid, oleic acid, octanedioic acid, prostaglandin A_1, leukotriene B_4.

Source: Adapted from [26]

4.8.6 glycerolipids (GL)

Esters, ethers, and other *O*-derivatives of glycerol with alkyls or alkenyls, including mono-, di-, and tri-substituted glycerols.

Examples: 1-dodecanoyl-*sn*-glycerol (monoacylglycerol), 1-dodecanoyl-2-hexadecanoyl-3-octadecanoyl-*sn*-glycerol (triacylglycerol).

4.8.7 glycerophospholipids (GP)

phospholipids

Lipids with glycerol backbone esterified with one or two fatty acids in position C-1 and/or C-2 and with phosphoric acid at position C-3. The phosphate group is usually esterified with an alcohol (choline, ethanolamine, serine, inositol, glycerol) to form the "lipid head group".

Note: GP are ubiquitous in nature and are key components of the membrane lipid bilayers of cells.
Examples: phosphatidyl choline, phosphatidyl ethanolamine, plasmalogens.

4.8.8 icosanoids

Unsaturated C_{20} *fatty acids* and skeletally related compounds. Biologically active lipid mediators, including prostaglandins, thromboxanes, leukotrienes, and other oxygenated derivatives, which are produced primarily by three classes of enzymes, cyclooxygenases (COX-1 and COX-2), lipoxygenases (LOX) and cytochrome P450 mono-oxygenases.

Note: The spelling icosanoids is preferred over the spelling eicosanoids for consistency with icosanoic acid.
Source: [26, 87]

4.8.9 lipid A

Glycolipid component of *lipopolysaccharides* (LPSs) that is integrated into the bacterial cell wall and is responsible for the beneficial (immunostimulatory) or toxic (immunopathological) effects of the molecule.

Note: The archetypical (*Enterobacteriaceae*) structure of lipid A consists of a β-1,6-linked D-glucosamine (GlcN) or 2,3-diamino-2,3-dideoxy-D-glucose (GlcN3N) disaccharide (or a mixture of them), which is acylated by varying numbers (usually four to seven) of ester- and amide-linked acyl groups (often termed primary and secondary fatty acids). Phosphate groups and other glycosyl substituents may be linked at the C-1 and C-4′ positions. Lipid A is linked to the core oligosaccharide at the C-6′ position of the distal sugar unit of lipid A.
Source: Adapted from [84, 85, 88]

4.8.10 lipid droplets

lipid particles
lipid bodies
adiposomes
oleosomes
oil bodies

Round-shaped intracellular inclusions consisting of hydrophobic cores (mainly triacylglycerols, sterol esters, occasionally free fatty acids or squalene) covered by a phospholipid monolayer containing a specific set of proteins.

Note: Originally considered as lipid storage compartments, lipid droplets are currently recognised as organelles with high metabolic activity. The defective formation and/or function of lipid droplets is involved in various pathogenic conditions, such as obesity, cardiovascular diseases, type 2 diabetes, or metabolic syndrome.

Source: [89]

4.8.11 lipid extraction

Isolation of *lipids* in their native state from samples of different origin.

Note: Usually based on the use of organic solvents (methanol, chloroform) to facilitate lipid partitioning between aqueous and organic phases.

4.8.12 lipid profiling

Lipidomics technique conferring unbiased information about total *lipids* within a particular cell type, tissue, or body fluid.

4.8.13 lipid remodelling

Changes in the lipid molecules composition after completion of their biosynthesis.

Note 1: In glycerophospholipids, remodelling includes changes in the composition of fatty acids (for example by acyl chain exchange catalysed by transacylases) or the introduction of unsaturated double bonds (catalysed by desaturases), or by the synthesis of new lipid species or degradation of existing ones. In phosphoinositides, it can involve phosphorylation/dephosphorylation processes.

Note 2: Lipid remodelling is important for the adaptation of biological membranes to changing environmental conditions and physiological demands.

4.8.14 lipidome

Complete set of lipid species and their metabolites present within a particular cell type, tissue, or body fluid.

Note: It is estimated that lipidome of a eukaryotic cell may contain over 100 000 individual molecular species of various lipids.

Source: [90]

4.8.15 lipidomics

Systematic and comprehensive study aimed at the identification, profiling, and quantification of *lipidome*.

Note 1: In a broader context, lipidomics includes system-level analysis of subcellular localization and the biological activities of individual lipids.

Note 2: Lipidomics is a lipid-targeted *metabolomics* approach aimed at a comprehensive analysis of lipids in biological systems.

Source: [90, 91]

4.8.16 lipids

Small, biologically active molecules of variable structure, commonly defined by their solubility in non-polar solvents. Hydrophobic or amphipathic small molecules that may originate, entirely or in part, by the carbanion-based condensations of thioesters (fatty acyls, glycerolipids, glycerophospholipids, sphingolipids, saccharolipids, and polyketides) and/or by carbocation-based condensations of isoprene units (prenol lipids and sterol lipids).

Source: Adapted from [92, 93]

4.8.17 lipooligosaccharide (LOS)

Lipopolysaccharides produced by specific wild-type bacteria that give a smooth-colony appearance when cultured on agar plates.

Note 1: LOSs are composed of *lipid A* and a *saccharide* moiety, limited to an *oligosaccharide* core only.
Note 2: The lack of O-polysaccharide chains in LOS structures is an inherent property of bacteria.
Source: Adapted from [88, 94]

4.8.18 lipopolysaccharide (LPS)

Principal structural component of the outer leaflet of the outer membrane of gram-negative bacteria and cyanobacteria. It forms a tight permeability barrier that prevents the passage of cell-damaging agents (detergents, bile salts, hydrophobic antibiotics) into the cell.

Note 1: The chemical structure of an LPS molecule is divided into three covalently linked segments: the *O-polysaccharide*, the *core oligosaccharide* (featuring an inner and outer region), and the *lipid A* moiety.
Note 2: The biological activity of LPS, LOS, or lipid A molecules as endotoxins in terms of host-mediated responses to LPSs or related compounds is called endotoxic activity (endotoxicity).
Note 3: Beyond this general structure, there are variations in all parts of LPS, depending on the bacterial strain from which the LPS originate.
Source: Adapted from [84, 85, 88]

4.8.19 lipopolysaccharidomics

Study of the structure-activity relationship of bacterial *lipopolysaccharides*.

4.8.20 membrane bilayer

Planar structure spontaneously formed by amphipathic *lipids* in a polar (aqueous) environment.

Note: Formation of a lipid bilayer is driven by the interaction of the polar heads of lipids with water molecules while minimizing the exposure of the hydrophobic parts of lipids to water. Lipid bilayers represent the basic structure of biological membranes.

4.8.21 membrane rafts

Dynamic, nanometre-sized, highly ordered, membrane domains enriched in sterols and sphingolipids. They contain specific sets of membrane proteins that are sorted into rafts by their specific physical properties and specific lipid-protein interactions.

Note: In functional terms, membrane rafts represent highly specialised membrane domains involved in various cellular processes, such as transmembrane transport, membrane trafficking, cell signalling, or virus assembly.

Source: [95]

4.8.22 molecular shape of lipids

Specific structure of lipid molecules (*glycerophospholipids*) in aqueous environments and membranes as a function of the ratio between the cross-sections of their polar heads and hydrophobic tails.

Note 1: Lipids' ability to self-assemble in dynamic macrostructures in an aqueous medium is driven by the amphiphilic nature of lipid molecules, which tend to aggregate so that the hydrophobic (tails) and the hydrophilic (heads) parts of the lipid are well separated and the area of the dividing surface is held by the hydrophobic effect.

Note 2: The shape of a membrane lipid depends on the relative size of its polar headgroup and apolar tails. In cases in which the headgroup and lipid backbone have similar cross-sectional areas, the molecule has a cylindrical shape (phosphatidylcholine and phosphatidylserine). Lipids with a small headgroup, such as phosphatidylethanolamine, are conical shaped. By contrast, when the hydrophobic part occupies a relatively smaller surface area, the molecule has the shape of an inverted cone (lysophosphatidylcholine and, to some extent, sphingomyelin).

4.8.23 O-polysaccharide

Part of *lipopolysaccharide* that consists of a *polysaccharide* chain extending outwards from the bacterial cell surface.

Source: Adapted from [85, 88]

4.8.24 plasma lipoproteins

Assemblies of *lipids* and *proteins* in blood *plasma* transporting lipids between tissues.

Note: They are structurally very similar to intracellular lipid droplets. They are classified according to their size and buoyant density into five types with different functions: chylomicrons, very low density lipoproteins (VLDL), intermediate lipoproteins (IDL), low density lipoproteins (LDL), and high density lipoproteins (HDL).

Source: [96]

4.8.25 polyketides (PK)

Heterogeneous group of compounds assembled from simple acyl building blocks made up of polyethers, polyenes, polyphenols, macrolides, and enediynes.

Note: Many polyketides are cyclic molecules whose backbones are often further modified by glycosylation, methylation, hydroxylation, oxidation, and/or other processes.
Examples: erythromycin, nystatin, tetracyclines.
Source: [97]

4.8.26 polyunsaturated fatty acids (PUFA)

Fatty acids with more than one double bond.

Note: The double bonds usually have *cis* (*Z*) configuration and are methylene-interrupted.
Example: linoleic and arachidonic acids.

4.8.27 prenol lipids (PR)

Lipids containing a linear chain of isoprenoid groups.

Note: Prenol lipids are synthesised from the five-carbon precursors isopentenyl diphosphate and dimethylallyl diphosphate. Both precursors are produced mainly via the mevalonic acid pathway.
Example: vitamin A, vitamin E, vitamin K, ubiquinone, β-carotene.

4.8.28 proteolipids

Proteins with covalently linked lipids, *e.g.* fatty acid or glycophosphatidylinositol (GPI).

Note: The term 'lipoprotein' is also occasionally used to describe such compounds, but to avoid confusion this might be better reserved for the non-covalently linked lipid-protein complexes of the type found in plasma (*plasma lipoproteins*).

4.8.29 saccharolipids (SL)

Biomolecules where *fatty acids* are directly bound to a *saccharide* backbone, thus forming structures similar to glycerolipids or glycerophospholipids, with *saccharide* substituting for the glycerol.

Examples: lipid X (diacylaminosugar), Kdo_2LipidA (acylaminosugar glycan).

4.8.30 shotgun lipidomics

Methodological approach based on the direct analysis of the total lipid extracts from cells or tissues without an online chromatographic separation.

Source: [98]

4.8.31 signalling lipids
lipid mediators

Lipid molecules involved in intracellular signalling and the regulation of cell death, immune response, or inflammation.

Note 1: Signalling lipids include diacylglycerol, phosphatidic acid, phosphatidylinositol-4,5-bisphosphate (the source of polyphosphorylated inositols), arachidonic acid-derived mediators (icosanoids,

prostaglandins and leukotrienes), sphingolipid-derived mediators (ceramides, sphingosine, sphingosine-1-phosphate), or cholesterol-derived steroid hormones (androgens, estrogens, progestogens, mineralocorticoids, glucocorticoids).

Note 2: Broadly defined term referring to any lipid messenger that binds a protein target, such as a receptor, kinase or phosphatase, which in turn mediates the effects of these lipids on specific cellular responses.

Source: [99]

4.8.32 sphingolipids (SP)

A complex family of *lipids* that contain a sphingoid base backbone and a fatty acyl chain.

Note: Together with glycerophospholipids and sterols, sphingolipids are the major lipid components of cellular membranes.

Examples: Subclasses are represented by ceramides, gangliosides, sphingosines, sphingomyelines.

4.8.33 sterol lipids (ST)

Structural derivatives of tetracyclic alcohols with a hydroxyl group in the position C-3 and an aliphatic side chain in the position C-17.

Note: This category primarily comprises sterols: polycyclic compounds of isoprenoid origin and their various derivatives, including steroids, bile acids, and sterol esters. Sterols, along with glycerophospholipids and sphingolipids, are important constituents of cellular membranes. In addition, sterol lipids act as hormones (steroids) or fat emulsifiers (bile acids).

Examples: Subclasses are represented by cholesterol, ergosterol, taurocholic acid, glucuronides.

4.8.34 structural lipids

Lipids (mainly glycerophospholipids, sterols and sphingolipids) involved in the formation of biological membranes.

4.8.35 targeted lipidomics

Analytical technique focusing on the quantification of specific *lipids* of interest.

4.8.36 unsaturation index (UI)

A number indicating the proportion of double bonds in *fatty acids* moieties of phospholipids.

Note: UI is indicative of membrane physical properties (*e.g.* fluidity, curvature, or flexibility).

General References: [83, 90, 100].

5 Studies of the interactions between biomolecules

5.1 capture probe

Specifically-designed single-stranded *nucleic acid* with a defined (known) *nucleotide sequence* immobilised on a surface.

Note 1: Capture probes are utilised as a recognition element to test the nucleotide sequence of target DNA or RNA in the sample solution by using DNA or RNA hybridization.

Note 2: An analogous principle, based on immobilised nucleic acid probes, has been applied in studies of the interactions of nucleic acids with proteins or other targets. See also *nucleic acid aptamers*.

Examples: Nucleic acids: ssDNA (alternatively, RNA or a synthetic nucleic acid analogue, such as LNA or PNA). Surfaces: microarray, magnetic, or other micro/nanoparticle, a transducer of the biosensor.

Source: [11]

5.2 chromatin immunoprecipitation

Method for studying DNA–protein and/or protein–protein interactions in the context of chromatin, suitable for the identification of binding sites of proteins in genome DNA, *etc*. This method combines chemical cross-linking, the isolation of specific protein conjugates by immunoprecipitation, and PCR amplification of co-precipitated DNA.

5.3 cross-linking (in biomolecules)

Formation of a covalent bridge between two *biomacromolecules* or between two segments of the same *biomacromolecule* using reactive substances (*e.g.* formaldehyde, bifunctional aldehydes such as glutaraldehyde, or cisplatin) or photochemical processes.

Note: Cross-linking is used to study protein oligomerization, as well as protein–protein and nucleic acid–protein interactions

See *chromatin immunoprecipitation*

5.4 fluorescent *in situ* hybridization (FISH)

Cytogenetic technique used to detect and localise the presence or absence of specific DNA sequences on chromosomes. It uses fluorescent probes that only bind to those parts of the chromosome with which they show a high degree of sequence complementarity.

Note: FISH is often used for finding specific features in DNA for use in genetic counselling, medicine, and species identification. FISH can also be used to detect and localise specific RNA targets (mRNA, lncRNA and miRNA) in cells, circulating tumour cells, and tissue samples. In this context, it can help define the spatial-temporal patterns of gene expression within cells and tissues.

Source: [101, 102]

5.5 groove binding (in DNA)

Process in which molecules are bound within a minor or major groove of the DNA *double helix*.

Source: [11]

5.6 hybridization (nucleic acids)

Process of forming a double-stranded molecule from two strands of DNA, RNA or synthetic nucleic acids analogues (*e.g.* PNA, LNA) with *complementary sequence*.

Example: DNA hybridization as a chemical interaction based on the ability of ssDNA to form a DNA double helix (dsDNA) with a counterpart molecule consisting of a complementary nucleotide sequence.

Source: [11]

5.7 hybridization assay

Assay with specifically designed single-stranded DNA probe with a defined (known) *nucleotide sequence* usually immobilised on a surface (in such a case, the nucleic acid probe is called the *capture probe*).

Note: The probe is used as a recognition element to test for the nucleotide sequence within the target DNA in the sample solution. If target DNA contains a sequence complementary to the probe, a hybrid dsDNA is formed.

Source: [11]

5.8 interactome

Virtual map depicting protein–protein interactions.

Note: The interactome is the most visible outcome of *functional proteomics*.

Source: Adapted from [103]

5.9 interactomics

Complex and comprehensive study of the interactions between various proteins and between protein and other molecules within a cell, such as nucleic acids and metabolites, as well as the consequences of these interactions.

Source: [104]

5.10 intercalation (in biomolecules)

Thermodynamically favourable, reversible inclusion of a molecule (or group) between two other molecules (or groups).

Example: An insertion of guest molecules between the stacked base pairs of the DNA double helix (double stranded DNA) structure. It typically occurs with compounds of a planar structure with 3–4 condensed aromatic rings. To accommodate an intercalating molecule, the DNA double helix must lengthen and unwind slightly.

Source: [8, 11]

5.11 intermolecular interactions (in biomacromolecules)

Interactions between (parts of) two *biomolecule* chains (*e.g.* base pairing in DNA double helix, or the interactions between two polypeptide chains, or between a DNA and a protein molecule).

5.12 intramolecular interactions (in biomacromolecules)

Interactions between (neighbouring or distant) segments within the same *biomolecule* chain (*e.g.* base pairing in hairpin or monomolecular tetraplex structures of DNA or RNA, the interactions stabilizing the secondary or tertiary structures of proteins, *etc.*).

5.13 non-covalent interactions (in biomolecules)

Interactions between *biomolecules* or within a *biomolecule* (*e.g.* hydrogen bonds, electrostatic interactions, and van der Waals forces) taking part in the stabilization of proper biomolecule structure and *intermolecular interactions*.

5.14 non-specific binding (in DNA-protein interactions)

Binding of a *protein* to DNA independent of the *nucleotide sequence* or the conformation of the DNA, often with a strong contribution of electrostatic interaction between the negatively charged sugar-phosphate backbone of the DNA and basic amino acid residues of the protein.

5.15 nucleic acid–protein interaction

Formation of specific or non-specific complexes between DNA or RNA and proteins, mediated and stabilised by a network of *non-covalent interactions*.

Note: Nucleic acid–protein interactions are critical for basic cellular functions such as replication, transcription, translation, recombination, DNA repair *etc.* as well as for fine regulation of them. Proteins may bind more tightly to specific sequences in the nucleic acid or non-specifically, in which case their affinity is independent of sequence.

5.16 protein–protein interaction (PPI)

Association of one protein with one or more other proteins to form either homo- or heteromeric proteins or protein complexes.

Note: Such associations are common in biological systems and are responsible for the regulation of numerous cellular functions in addition to the mediation of disease morphology, where aberrant interactions play a significant role.

Source: [8]

5.17 pull-down assay

Approach used for studying *protein–protein interactions* analogous to immunoprecipitation, using (instead of antibody) one of the interacting proteins (the "bait") immobilised at a surface to capture the other protein (the "prey").

5.18 reporter (signalling) probe

Specifically-designed ssDNA (alternatively, RNA or a synthetic nucleic acid analogue, such as LNA or PNA) with a defined (known) *nucleotide sequence* used to detect complementary DNA or RNA sequence in a sample.

Note 1: Reporter probe is usually labelled (radioactively, immunologically, or by fluorescent, electroactive, or other species to produce a specific signal upon hybridization).
Note 2: Similar to capture probes, nucleic acid signalling probes (or nucleic acid aptamers) can be applied in studies of nucleic acid interactions with proteins and other ligands.

5.19 specific binding (in DNA-protein interactions)

Binding of *proteins* to specific sites in DNA based on the precise recognition of *nucleotide sequence* and/or conformation of the DNA.

Note: Sequence-specific DNA binding is typical for restriction enzymes, transcription factors and other proteins involved in cellular regulation, *etc*.

5.20 stacking interactions

Attractive interaction between planar aromatic rings, in *nucleic acids* being one of the critical forces stabilizing double- and multistranded structures.

Note: Stacking interactions are involved in binding of intercalators to DNA.

5.21 TUNEL test

Method for the determination of *strand breaks* and *DNA fragmentation* in cells based on labelling and quantification of free 3′-OH ends of DNA.

Note: The abbreviation is for terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL).

5.22 two hybrid system

A molecular biology method for studying protein–protein or protein–DNA interactions in cellular (yeast or bacterial) milieu.

Note: This method involves a transcription factor split into two separate domains (DNA binding and transcription activating), one of which is fused with one of the tested proteins (the “bait”) and the other with another tested protein (the “prey”), as well as with a reporter gene construct. Only upon physical interaction between bait and prey is the expression of the reporter gene observed.

General References: [7, 11]

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Funding: International Union of Pure and Applied Chemistry, Funder Id: 10.13039/100006987, Grant Number: 2011-047-1-500: Recent advances in bioanalytical chemistry: characterization and classification.

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