An Introduction to Carbohydrates

- Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones.
- Monosaccharides also known as simple sugars, are the simplest carbohydrates containing 3-7 carbon atoms.
- sugar containing an aldehydes is known as an aldose.
- sugar containing a ketones is known as a ketose.

- The number of carbon atoms in an aldose or ketose may be specified as by tri, tetr, pent, hex, or hept. For example, glucose is aldohexose and fructose is ketohexose.
- Monosaccharides react with each other to form disaccharides and polysaccharides.
- Monosaccharides are chiral molecules and exist mainly in cyclic forms rather than the straight chain.

Carbohydrate



Check https://www.youtube.com/watch?v=LeOUIXbFyqk

















• Anomers: Cyclic sugars that differs only in positions of substituents at the hemiacetal carbon; the α -form has the –OH group on the opposite side from the –CH₂OH; the β -form the –OH group on the same side as the –CH₂OH group.



 α -D-Galactose



β-D-Galactose

Some Important Monosaccharides

Monosaccharides are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents. Most monosaccharides are sweet tasting, digestible, and nontoxic.









Some Common Disaccharides







Polysaccharides





Cell-Surface Carbohydrates Involved in Molecular Recognition



Lectin

Lectins are sugar-binding proteins which are highly specific for their sugar moieties. They typically play a role in biological recognition phenomena involving cells and proteins. For example, some bacteria use lectins to attach themselves to the cells of the host organism during infection.







Blood Type







The Nobel Prize in Chemistry 2022

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry 2022 to

Carolyn R. Bertozzi

Morten Meldal

K. Barry Sharpless

Stanford University, CA, USA Howard Hughes Medical Institute, USA University of Copenhagen, Denmark

Scripps Research, La Jolla, CA, USA

"for the development of click chemistry and bioorthogonal chemistry"



Figure 6: Copper-catalysed reactions from a) **Meldal** and coworkers,^{15,16} and b) **Sharpless** and coworkers;¹⁷ F: phenylalanine, G: glycine, filled circle: solid support, THF: tetrahydrofuran, ^tBuOH: *tert*-butanol.



Figure 7: Strain-promoted azide-alkyne cycloaddition (SPAAC).

Click Chemistry

The click reaction that changed chemistry

Azides and alkynes react very efficiently when copper ions are added. This reaction is now used globally to link molecules together in a simple manner.







Figure 8: Cell labelling using metabolic engineering. N-levulinoyl mannosamine or N-azidoacetylmannosamine is fed to cells, converted into functionalized sialic acids, and expressed in glycans at the cell surface.²⁴

Bioorthogonal chemistry illuminates the cell



Glycobiology

Glycobiology is the scientific study of glycomes, which are the entire complement of sugars, whether free or present in more complex molecules, of an organism. This field encompasses the structure, biochemistry, and biology of carbohydrates (sugars and their derivatives) and glycoconjugates (molecules that contain sugar residues attached to another structure, such as proteins or lipids).

Carbohydrates are crucial components of all living organisms and are involved in a variety of biological processes, including cell-cell recognition, cell adhesion, immune response, and inflammation. They play key roles in the structure and function of many proteins and lipids, which are modified by the addition of sugar molecules in a process known as glycosylation.

Glycobiology integrates various disciplines, including biochemistry, molecular biology, cell biology, and biotechnology, to understand the roles of carbohydrates in biology and to utilize this knowledge in applications ranging from biomedicine to bioenergy. This research has significant implications for understanding diseases, developing new vaccines and therapeutics, and advancing biotechnological applications.

Carbohydrates are essential biomolecules that play numerous vital roles in biological systems, impacting both the structure and function of organisms. Here are some key aspects of their importance:

Energy Source: Carbohydrates are a primary energy source for most organisms. Glucose, a simple sugar, is a crucial energy substrate in cells and is central to cellular respiration and ATP production, which fuels various biological processes.

Energy Storage: Carbohydrates also serve as energy storage molecules. Plants store energy in the form of starch, while animals store energy as glycogen in the liver and muscles, which can be rapidly mobilized to meet energy demands.

Structural Components: Certain carbohydrates are integral to the structural integrity of cells and organisms. For example, cellulose, a polysaccharide found in plant cell walls, provides structural support to plants. In animals, chitin, a component of the exoskeletons of insects and other arthropods, serves a similar structural role.

Cell Recognition and Signaling: Carbohydrates on the surfaces of cells play key roles in cell-cell recognition and signaling. They are involved in various biological processes, including immune responses, where they help in the identification of foreign substances and pathogens.

Biological Lubrication: Mucins, which are glycoproteins, rely on their carbohydrate components to maintain viscosity and lubrication in biological tissues, crucial for the proper functioning of respiratory, digestive, and reproductive systems.

Glycosylation of Proteins and Lipids: Many proteins and lipids undergo glycosylation, where carbohydrates are covalently attached. This modification can affect the molecules' stability, activity, and localization, impacting various physiological processes.

Dietary Fiber: Some carbohydrates, particularly those that are indigestible by humans like dietary fiber, play important roles in maintaining gut health. They support bowel regularity and can influence the composition of gut microbiota, which is crucial for overall health.

Understanding these roles of carbohydrates is fundamental not only in biochemistry and cell biology but also in fields like nutrition, medicine, and biotechnology, showcasing their broad impact on life and health. Bioorthogonal chemistry refers to chemical reactions that can occur inside living systems without interfering with native biochemical processes. This concept is crucial in the fields of chemical biology and drug development, as it allows scientists to introduce and track synthetic molecules within biological systems without affecting their normal functions.

In practical terms, bioorthogonal reactions are highly selective and fast under physiological conditions. They do not cross-react with biological molecules, thereby enabling researchers to label, visualize, or manipulate biomolecules in real-time, in living organisms. Some common bioorthogonal reactions include the copper-catalyzed azide-alkyne cycloaddition (though copper-free versions are preferred in biological contexts to avoid toxicity) and the strain-promoted alkyne-azide cycloaddition.

Overall, bioorthogonal chemistry offers a powerful set of tools for studying biological processes at the molecular level, with applications ranging from imaging specific proteins in cells to targeted drug delivery.

Glycan and Glycomic



https://www.youtube.com/watch?v=NqEgrAYN2Bc

Glycan







Glycan Binding in Ilmmune Cells





Main classes of glycans modulating cancer hallmarks. **N-glycans**, whose biosynthesis starts in the endoplasmic reticulum (ER) with the addition of an oligosaccharide chain to an asparagine (Asn) residue, experience further structural maturation in the golgi apparatus (GA) to yield complex bisected and branched structures. **O-GaINAc** glycans, initiated in the GA by the attachment of a GaINAc to the hydroxyl groups of serine (Ser) or threonine (Thr) residues, forming the simplest **O-glycan** Tn antigen (GaINAcα-Ser/Thr), may be further elongated into different core structures that serve as scaffolds for more complex O-GaINAc glycans. Both O- and N-glycan chains are generally branched and/or elongated and may present sialic acids, Lewis blood group related antigens and/or their sialylated counterparts as terminal structures. The figure highlights the structures of some of the most relevant glycans and glycoconjugates driving cancer hallmarks.





Lipid

- Lipids are naturally occurring molecules from plants or animals that are soluble in nonpolar organic solvents.
- Lipid molecules contain large hydrocarbon portion and not many polar functional group, which accounts for their solubility behavior.







A cis unsaturated fatty acid (linolenic acid)



Stearic acid, an 18-carbon saturated fatty acid



Lipid



https://www.youtube.com/watch?v=ebScOnAJdu0

Lipid



https://www.youtube.com/watch?v=bUaJFg10nkc












A sphingomyelin



Polar head (hydrophilic)

Nonpolar tail (hydrophobic)

Membrane lipid



Lipid bilayer





Properties of cell membranes:

- Cell membranes are composed of a fluid like phospholipid bilayer.
- The bilayer incorporates cholesterol, proteins, and glycolipids.
- Small nonpolar molecules cross by diffusion through the lipid bilayer.
- Small ions and polar molecules diffuse through the aqueous media in protein pores.
- Glucose and certain other substances cross with the aid of proteins without energy input.
- Na⁺, K⁺, and other substances that maintain concentration gradients inside and outside the cell cross with expenditure of energy and the aid of proteins.

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Lipids play several crucial and diverse roles in cells, influencing both their structure and function.

Structural Components of Membranes: Lipids, particularly phospholipids, are fundamental constituents of cellular membranes. They form bilayers that provide the basic structure of the plasma membrane and the membranes of various organelles within the cell. These lipid bilayers are fluid and dynamic, allowing for membrane fluidity and flexibility, which are essential for various cellular processes.

Energy Storage: Lipids serve as an important source of energy.

Signaling Molecules: Various lipids act as signaling molecules or precursors to signaling molecules. For instance, steroid hormones, which are derived from cholesterol, are crucial signaling molecules that regulate a wide range of physiological processes

Coenzymes and Vitamins: Certain lipids act as coenzymes or essential components of coenzymes. For example, the lipid-soluble vitamins A, D, E, and K are critical for various biological functions, including vision, bone metabolism, antioxidant protection, and blood coagulation.

Anchoring Membrane Proteins: Lipids can covalently attach to proteins to anchor them within the cell membrane. This lipid modification is crucial for the localization, function, and signaling of membrane proteins.

Insulation and Protection: In multicellular organisms, lipids provide insulation and protection. Subcutaneous fat serves as an insulator, reducing heat loss, and provides mechanical cushioning to protect internal organs.

Cell Recognition and Communication: Lipids are involved in cell recognition and communication processes. For example, glycolipids, which are lipids with carbohydrate chains, are present on the cell surface and play roles in cell-cell interactions, recognition, and immune responses.

Modulating Membrane Fluidity: The composition of lipids in membranes can influence their fluidity, which in turn affects various membrane-associated functions such as vesicle formation, fusion, and the activity of membrane-bound enzymes and receptors. For instance, cholesterol in animal cell membranes modulates fluidity and permeability.





EXTRACELLULAR FLUID









The major classes of lipids found in cells are phospholipids, glycolipids, cholesterol, and triglycerides. Each of these classes plays essential roles in cellular structure and function:

Phospholipids: These are the most abundant lipids in cell membranes. Phospholipids are amphipathic molecules, meaning they have both hydrophilic (water-attracting) and hydrophobic (water-repelling) regions.

Glycolipids: Comprised of a lipid moiety and one or more sugar residues, glycolipids are primarily found on the extracellular surface of cell membranes. They play crucial roles in cell recognition, communication, and immune responses. The sugar moieties of glycolipids interact with specific molecules and cells in the organism's environment, facilitating cellular interactions and signaling.

Cholesterol: Though often associated with health risks when present in excess in the bloodstream, cholesterol is a vital component of animal cell membranes. It modulates the fluidity and permeability of the membrane and is involved in the formation of lipid rafts—specialized membrane domains that serve as organizing centers for the assembly of signaling molecules. Cholesterol is also a precursor for the synthesis of steroid hormones, bile acids, and vitamin D.

Triglycerides (Triacylglycerols): These are the main form of stored energy in many types of cells, particularly adipocytes (fat cells). Triglycerides consist of three fatty acids linked to a glycerol backbone. They are stored in lipid droplets within cells and are metabolized to provide energy when needed. Although not components of cell membranes, triglycerides play a critical role in energy metabolism and homeostasis.

Lipids on Cell Membranes





Cholesterol



Liposome Preparation



https://www.youtube.com/watch?v=7UvUm2lrZk4

Liposome Preparation by Microfluidics



https://www.youtube.com/watch?v=DmJrsvCLR5w

Liquid-Liquid Phase Separation

Liquid-liquid phase separations in cells refer to the process where biomolecules undergo demixing from a homogenous solution into two distinct liquid phases, resulting in the formation of membrane-less organelles or biomolecular condensates. These phase transitions play crucial roles in cellular organization, function, and regulation:

Compartmentalization: Liquid-liquid phase separation (LLPS) allows cells to organize their intracellular environment without the need for membrane-bound organelles. This compartmentalization facilitates the concentration and sequestration of specific proteins and nucleic acids, enhancing biochemical reactions and processes.

Regulation of Biochemical Reactions: By concentrating specific enzymes and substrates within phase-separated droplets, cells can enhance or regulate the rates of biochemical reactions. This mechanism allows for the spatial and temporal control of metabolic pathways and signaling cascades.

Response to Environmental Stimuli: The dynamics of phase-separated droplets can change rapidly in response to environmental cues, such as changes in temperature, pH, or ion concentration. This responsiveness enables cells to adapt quickly to environmental changes, modulating cellular processes accordingly.

Stress Response: Under stress conditions, cells can form stress granules through LLPS. These granules sequester and protect mRNA and proteins, preventing their aggregation and facilitating their rapid reactivation when stress conditions abate. This process is crucial for cell survival under adverse conditions.

Signal Transduction: Phase-separated compartments can concentrate signaling molecules, enhancing signal transduction pathways. By bringing together key components of a signaling pathway, LLPS can increase the efficiency and specificity of signal transmission.

RNA Processing and Transport: LLPS plays a role in the formation of nuclear speckles and other nuclear bodies that are involved in RNA splicing, processing, and transport. These condensates can regulate gene expression by influencing RNA metabolism and dynamics.

Protein Folding and Stability: By providing a unique microenvironment, phaseseparated droplets can influence protein folding and stability. This environment can prevent protein aggregation and assist in the proper folding of proteins, which is essential for their function and longevity.

Membrane Dynamics: LLPS can also influence the organization and dynamics of cellular membranes. For example, the clustering of signaling receptors and other membrane proteins into lipid rafts can be driven by phase separation processes, affecting membrane fluidity and signaling.

In summary, liquid-liquid phase transitions are fundamental for cellular organization, enabling cells to create dynamic, membrane-less compartments that regulate and facilitate a myriad of biochemical processes essential for life.

Liquid-Liquid Phase Separation



Liquid-Liquid Phase Separation



Factors Regulate LLPS



LLPS in Diseases



LLPS in Cancer



Surface to Volume Ratio





Surface Energy

One face surface energy: γ 27 cube: 27 x 6 γ 3 x 9 cube line: 114 γ 3 x (3x3) square: 90 γ 3 x 3 x 3 cube: 54 γ











Electron Sea





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$$m \frac{d^2 \delta x}{dt^2} = e E_x = -m \omega_p^2 \, \delta x,$$

$$\omega_p^2 = \frac{n e^2}{\epsilon_0 m},$$



Surface Plasmonon



$$\varepsilon_m = 1 - \frac{\omega_p^2}{\omega^2}$$

Contact Angle





Young's Equation

$\gamma_{\rm SL} + \gamma_{\rm LV} \cos \theta_{\rm c} = \gamma_{\rm SV}$





Surfactant





DLVO Theory

 $V_T = V_A + V_R + V_S$

 $V_A = -A/(12 \ \pi \ D^2)$

A is the Hamaker constant and D is the particle separation

 V_R = 2 π ε a ξ^2 exp(- κD)

a is the particle radius, π is the solvent permeability, κ is a function of the ionic composition and ξ is the zeta potential



$$\begin{split} &\omega = \omega_{el} + \omega_{vdW} \\ &\omega = 64RTc_{\infty}\gamma_{0}^{2}\frac{1}{\kappa}e^{-\kappa d} - \frac{A}{12\pi d^{2}} \\ &\omega = 64RTc_{\infty}\gamma_{0}^{2}\sqrt{\frac{RT\varepsilon}{F^{2}\sum z^{2}c_{\infty}}}e^{-\sqrt{\frac{F^{2}\sum z^{2}c_{\infty}}{RT\varepsilon}}d} - \frac{A}{12\pi d^{2}} \end{split}$$



DLVO Theory









Two main mechanisms are shown here: **a**, coalescence sintering, and **b**, Ostwald ripening sintering. Coalescence sintering occurs when two clusters touch or collide and merge to form one bigger cluster. In contrast, Ostwald ripening sintering occurs by evaporation of atoms from one cluster, which then transfer to another. This is a dynamic process — both clusters exchange atoms, but the rate of loss from the smaller cluster is higher, because of the lower average coordination of atoms at the surface and their relative ease of removal. Thus big clusters get bigger at the expense of smaller clusters, which shrink and eventually disappear. The latter process is the usual form of sintering for metal clusters on a supported surface that are well spaced apart, although coalescence can occur for a high density of clusters. In general, the presence of the surface results in SMORS (surface-mediated Ostwald ripening sintering) in which material is transferred from one cluster to another by diffusion across the surface, and not through the gas phase.

Nanoparticles for Biomedical Applications

Nanoparticles have been extensively explored for various biomedical applications, ranging from drug delivery and diagnostic imaging to therapy and regenerative medicine. The diversity in their composition, size, shape, and surface properties allows for their tailored application in different biomedical fields. Here are some of the key types of nanoparticles used in biomedical applications:

Metal Nanoparticles:

Silver nanoparticles, Gold nanoparticles, Iron oxide nanoparticles:. Quantum Dots:

Lipid-Based Nanoparticles:

Liposomes

Polymeric Nanoparticles:

Dendrimers:

Carbon-Based Nanoparticles:

Carbon nanotubes and graphene:

Nanodiamond

Carbon dot

Silica Nanoparticles:

Porous Nanoparticles