NBL 355-655 Module 3 Review Q&A

1. *What does “organic” mean (in chemistry)? What are four categories of cellular building blocks and what units/polymers does each form? What are two other important components of cells?*

In chemistry, organic means a molecule contains carbon. Building blocks form polymers: sugars form polysaccharides; amino acids form proteins; nucleotides (and deoxynucleotides) form nucleic acids (RNA and DNA) and fatty acids form fats, lipids, and lipid bilayers. The other important components of cells are water and ions.

1. *What is an ion? Define anion, cation, polyatomic/molecular ion, inorganic ion, organic ion, monovalent ion and divalent ion. Name six important ions in cells.*

Ions are charged atoms and molecules. Ions can contain only one atom (monoatomic) or contain two or more atoms (polyatomic or molecular). Ions can contain carbon (organic) or no carbon (inorganic). Ions can have a positive charge (cation) or a negative charge (anion). Ions can contain one charge (monovalent) or two charges (divalent) or more (polyvalent). The calcium ion (Ca2+) is an example of a monoatomic inorganic divalent cation. The bicarbonate ion (HCO3-) is an example of a polyatomic (molecular) organic monovalent anion. Some other important cellular ions include the chloride ion (Cl-), the sodium ion (Na+), the potassium ion (K+), the magnesium ion (Mg2+), the iron ion (Fe+3), and the phosphate ion (PO43-).

1. *In what three important ways is CSF different from blood?*

Under normal conditions (no disease, disorder or injury) CSF does not contain nearly as many proteins as blood (the concentration of proteins in CSF is much lower than in blood), CSF does not contain red blood cells, and CSF contains only a few white blood cells (mainly T cells). Blood contains lots of red and white blood cells.

1. *Define a chemical bond. What is a covalent bond? How are polar and nonpolar molecules different? What do hydrophilic and hydrophobic mean? Why is this important in cells? (Where do nonpolar and polar molecules go/form in a cell?)*

A chemical bond is formed when two or more atoms have an attraction to one another. In cells, there are two main types of bonds between atoms: covalent bonds and non-covalent bonds.

Covalent bonds involve the sharing of electrons and can be either polar or nonpolar. Molecules are formed by covalent bonding between atoms. A molecule is stable under aqueous physiological conditions meaning that the molecule does not break apart (dissociate) into smaller molecules or atoms. In polar bonds, there is unequal sharing of the electrons, leading to a separation of charge, called a dipole, where there is a concentration of positive charge on one side and a concentration of negative charge on anther side of the molecule. Water is a polar molecule. Polar molecules are soluble in water, and are called hydrophilic.

In nonpolar bonds, the electrons are shared equally between or among the atoms. (Also some molecules can be nonpolar if there is a symmetrical arrangement of polar bonds in a more complex molecule, such as CO2). For both, the nonpolar molecule does not have a permanent dipole. Most nonpolar molecules are not soluble in water, and are called hydrophobic. Covalent bonds are strong bonds that ensure the stable primary sequence of polymers such as proteins, DNA and polysaccharides and keep them intact in cells. Polar molecules are found in the cytoplasm and inside organelles. Nonpolar molecules form lipid bilayers in biological membranes around and within cells.

1. *What is a noncovalent bond and what are the four main types? Why are noncovalent bonds important? (Which polymers involve non-covalent bonds?)*

In a noncovalent bond, the atoms do not share electrons. Instead, the atoms are attracted to each other. There are several types of noncovalent bonds/interactions. Noncovalent bonds are weaker bonds than covalent bonds and in aqueous solution an individual noncovalent bond can be broken apart (dissociate) fairly easily. The four types of noncovalent bonds are ionic, hydrogen, Van der Waals, and hydrophobic.

In an ionic bond, a positively charged ion (a cation) is attracted to a negatively charged ion (an anion). Hydrogen bonds form between a hydrogen atom in one polar molecule that is attracted to a more electronegative atom such as oxygen or nitrogen, in another polar molecule. Hydrogen bonds form between water molecules and are found in lots of other polymers in cells, including proteins and DNA. Van der Waals attractions occur for a very short time period when electrons from two atoms are positioned so that the slightly more negative side of one atom attracts the slightly more positive side of another atom. Hydrophobic bonds form between nonpolar molecules, and as we will discuss in the next modules, are in fact driven to form by the nonpolar molecules being repulsed by water.

Noncovalent bonds are much weaker than covalent bonds. However, noncovalent bonds are important because they give water many of its characteristics. And importantly, they allow for the secondary and tertiary structures of proteins and DNA to ensure the packing and three dimensional structure and function of these molecules. Even though individual non-covalent bonds are fairly weak, since a protein (or DNA) contains tens to hundreds to thousands of noncovalent bonds, its three dimensional structure is stable in aqueous solution. Hydrophobic bonds are essential in forming the lipid bilayers in biological membranes, which are essential for cells and signaling.

1. *Define the two types of metabolism. How does ATP link the two?*

Catabolism breaks down biological macromolecules/polymers into individual subunits (building blocks) and can release energy (that can be used to form ATP). Anabolism creates/synthesizes biological macromolecules/polymers and consumes energy (usually ATP) and individual subunits (building blocks.)

1. *Most catabolic reactions are exergonic and “spontaneous,” but (on their own) don’t occur at any significant rate at physiological conditions in cells (low temperature and pressure and low substrate/reactant concentrations). Most anabolic reactions are endergonic, nonspontaneous and require an energy input (usually from ATP hydrolysis). In cells, both catabolic/exergonic and anabolic/endergonic reactions require enzymes. What does an enzyme do, and what effect does that have on the rate of a reaction? How do enzymes affect the change in Gibbs free energy (delta G) of a reaction?*

Most catabolic reactions are exergonic. Exergonic reactions can release energy (sometimes in the form of high energy substrates). For exergonic reactions, the change in free energy (delta G- which is the energy of the products minus the energy of the reactants) is less than 0, it is negative. Exergonic reactions are technically spontaneous, but in a cell under physiological conditions (low temperature, low pressure and low substrate concentrations), they proceed at an extremely slow rate because there is an activation energy for the reaction. Hence they require an enzyme to lower the activation energy to speed up the rate of the reaction.

Most anabolic reactions are endergonic. Endergonic reactions require an input of energy, and often the energy source is ATP. For endergonic reactions the delta G is greater than 0, it is positive. Endergonic reactions are not spontaneous (since they require an energy input). In addition, they also require an enzyme to overcome the activation energy of the reaction, because in a cell under physiological conditions (low temperature and pressure and low substrate concentrations), the rate of the reaction (even with an energy input) is very slow. Therefore, in cells, both endergonic and exergonic reactions require enzymes. Enzymes decrease the activation energy for the reactions and thus speed up the rate of both types of reactions. Enzymes act as catalysts for reactions. Enzymes have no effect on the delta G of the reaction.

1. *Enzymes are proteins. By what three mechanisms can enzymes function as catalysts to enhance reaction rates?*

For both endergonic (En) and exergonic (Ex) reactions at physiological temperatures and pressure, the thermal energy of molecules is too low, and the concentrations of reactants are too low, for reactions to occur at any appreciable rate in cells. Hence both En and Ex reactions have an activation energy. An enzyme can lower the activation energy by (A) binding the substrate(s)/reactants. If it’s an En reaction, this can increase the effective concentration of the reactants, which will speed the reaction rate. In addition, by binding the reactants, it can (B) orient the reactants in the right conformation, stabilizing the transition state, so they can form a new bond, in a type of En reaction. Or an enzyme can bind reactants and strain a bond and make it more accessible to, for example water, (stabilize the transition state) so that can help to break the bond in the case of an Ex reaction. Finally, enzymes provide active site molecules such as nucleophiles (example is OH-) that assist in forming or breaking bonds or other reactions. **Enzymes do not, on their own, provide the energy that is required for En reactions to proceed, but provide a physical platform for the reaction to occur, and so act as catalysts.** For En reactions, the energy required for the reaction is often supplied by ATP hydrolysis.

1. *What type of chemical bond is formed during protein synthesis (translation) and where does translation occur?*

During protein synthesis (translation), amino acids form peptide bonds, which are a special type of covalent bond that defines proteins. Translation occurs on ribosomes located in either the cytoplasm (free polyribosomes) for cytoplasmic/cytosolic proteins or associated with the endoplasmic reticulum (ER), forming the rough ER (RER), for transmembrane/integral membrane proteins.

1. *What are the three main categories of amino acid side chains (R groups)? How else do L-amino acids function in neurons?*

The three chemical types of R groups on amino acids are “nonpolar,” polar uncharged (often called just “polar”), and “polar charged.” Polar/uncharged and polar/charged amino acids are hydrophilic while nonpolar amino acids are hydrophobic.

Nonpolar-a molecule may be nonpolar either when there is an equal sharing of electrons between the two atoms of a diatomic molecule or because of the symmetrical arrangement of polar bonds in a more complex molecule (such as CO2). Nonpolar molecules do not have a permanent dipole, cannot participate in hydrogen bonding, are not very soluble in water, and are hydrophobic; they group together in aqueous solution.

A polar amino acid R group has a permanent dipole, since its atoms do not share the electrons equally, and contain one or more bonds in which one atom has a higher density of negative charge and the other has a higher density of positive charge. Polar charged amino acids contain an ionic group, in which atoms of the molecule have at least one electron in excess (negative charge) or is missing one electron (positive charge). Polar and polar charged amino acids are soluble in water (hydrophilic).

Some L-amino acids, for example L-glutamate and L-glycine also function as neurotransmitters. Some other L-amino acids such as L-tyrosine and L-tryptophan are substrates for the synthesis of the biogenic amine neurotransmitters.

1. *Define a gene, a codon, the genetic code and the primary amino acid sequence.*

Replication is the synthesis of a new DNA molecule (chromosome) from a DNA template and occurs during cell division. A gene is a region of DNA that usually codes for a specific protein. A codon is a three-nucleotide series in DNA (or RNA) that codes for a specific amino acid. The genetic code encodes for each amino acid that will be inserted into the primary amino acid sequence of a protein. The primary amino acid sequence is the sequence of amino acids that forms the backbone of the protein, since the amino acids are covalently bonded to each other during translation. Replication and transcription occur in the nucleus. Following transcription, the transcribed mRNA is exported out of the nucleus and translation (protein synthesis) takes place in the cytoplasm, either by ribosomes attached to the ER for producing membrane or secreted proteins; or free polyribosomes in the cytoplasm to produce cytosolic proteins.

1. *What types of chemical bonds mediate interactions to form the primary, secondary, tertiary and quaternary protein structures? What is the function of these higher order structures?*

The primary amino acid sequence is formed by covalent/peptide bonds. But as the protein backbone (primary sequence) is being synthesized, the carbons, hydrogens and nitrogens will interact with each other to form noncovalent bonds and first produce secondary structures and then tertiary structures. The two most common types of secondary structures are the alpha-helix and beta-sheet. Both are secondary structures formed by hydrogen bonds between the amino hydrogen and carbonyl oxygen of two amino acids of the backbone of the peptide chain (not the side chain R groups). The protein tertiary structure occurs through the noncovalent bonding between the R groups (side chains) on the amino acids. The non-covalent interactions include hydrogen bonding, ionic interactions, hydrophobic interactions, and van der Waals attractions. Quaternary structures are derived from individual protein subunits bonding together to form larger proteins – these also use hydrogen bonds, ionic bonds, hydrophobic bonds, and van der Waals attractions. Secondary, tertiary and quaternary structures ensure the three dimensional structure of a protein, which is essential for proteins to perform their functions correctly.

1. *What are the ten main functional categories of proteins?*

Functional categories of proteins: enzymes, transcription factors, translation factors, cytoskeletal proteins, motor proteins, ion channels, ion transporters, receptors, cell adhesion proteins, and signaling ligands.

1. *What is the definition of the genotype and the cellular phenotype? What determines the cellular phenotype?*

The genotype is the genetic makeup (chromosomal DNA) contained in the nucleus of a eukaryotic cell. The cellular phenotype includes the features/characteristics of a cell such as its morphology, biochemistry, physiology, and function. The cellular phenotype is determined by the genotype and gene expression. The genotype and gene expression control the types and levels of proteins expressed by that cell. Hence the cellular phenotype is determined by the types and levels of proteins expressed in the cell.

1. *What is the definition of gene expression? In what seven ways can gene expression be controlled? In what two ways can transcription be controlled?*

From Wikipedia, “a gene is the basic physical and functional unit of heredity.” Genes, which are composed of DNA, act as instructions for producing proteins. There are thought to be about 20,000 protein-coding genes in the human genome. From Wikipedia, “gene expression is the process by which information from a gene is used in the synthesis of a functional gene product, usually a protein.”

Gene expression controls the types (which ones) and levels (how much) of the proteins that are synthesized in the cell. Since all the activities of the cell are dependent on and carried out by proteins, the types and levels of proteins a cell expresses will determine its phenotype and function. From Wikipedia: [“Regulation of gene expression] gives the cell control over structure and function, and is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism. Gene regulation may also serve as a substrate for evolutionary change, since control of the timing, location, and amount of gene expression can have a profound effect on the functions (actions) of the gene in a cell or in a multicellular organism.”

Gene expression can be controlled by 1) transcription, 2) RNA processing, 3) RNA export from the nucleus and localization, 4) translation, 5) RNA degradation, and 6) protein activity control (protein activation/inhibition) and 7) protein degradation.

1. *What occurs during transcription? In what two ways can transcription be controlled? What is the definition of epigenetics? What can be modified in epigenetic modifications?*

Transcription is the process of synthesis of an RNA molecule based on a DNA template. One type of RNA, mRNA is then used to synthesize proteins in translation. Transcription is regulated by transcription factors and epigenetics. Binding of transcription factors to the promotor region in the DNA, can activate or inhibit the transcription process. Epigenetics is the covalent modification of DNA and DNA binding proteins (histones), which can enhance or inhibit the access of the DNA to transcription factors and the transcription machinery. Two of the most important mechanisms that provide epigenetic control over gene expression are DNA methylation and covalent modification (such as acetylation) of the histone proteins.

1. *What is the definition of the “cytoplasm” and the “cytosol?” What are cellular “organelles?”*

The cytoplasm is everything inside the cell except the nucleus. The cytosol is everything except the nucleus and organelles. The cytosol is the aqueous part of the cell, filled with soluble proteins, amino acids, sugars, nucleotides, etc. Cellular organelles are specialized structures in cells, and the majority (but not all) are enclosed within a membrane, that carry out various and specific functions within a cell. For example, mitochondria, which are separated from the cytosol by two membranes, perform the TCA cycle, electron transport and oxidative phosphorylation to produce ATP. The nucleus, which is also separated from the cytosol by two membranes, is where the chromosomal DNA is located and replicated during cell proliferation, and where transcription (synthesis of RNA) occurs. In the cytoplasm, soluble proteins (which comprise about half of all proteins) are synthesized by free ribosomes, which often form together in long chains, each producing the same protein and are called polyribosomes. The other half of proteins are integral membrane proteins, which are synthesized in the rough endoplasmic reticulum (RER).

1. *Describe the organelles in a eukaryotic cell and each of their functions.*

See <https://www.thoughtco.com/organelles-meaning-373368>; understand the functions of the plasma membrane, nucleus, mitochondria, smooth endoplasmic reticulum, rough endoplasmic reticulum, Golgi complex, vesicles, lysosomes, proteosomes, polyribosomes, and cytoskeletal proteins.

1. *Where and what are the two pathways/mechanisms that produce ATP in cells? What is the glucose-lactate shuttle and why is it important?*

Glycolysis occurs in the cytoplasm and converts one glucose molecule into two pyruvates, with the net production of two molecules of ATP and two molecules of NADH. Glycolysis does not require oxygen.

Mitochondria involve three processes, called the Krebs cycle (also called the citric acid cycle or TCA cycle), electron transport chain, and oxidative phosphorylation, to produce ATP from pyruvates and NADH. (This is sometimes called cellular respiration or aerobic respiration and depends on oxygen.)

For each glucose, during glycolysis in the cytoplasm, there is initially a net of two ATP molecules, two NADH and two pyruvates produced. From glycolysis, the two pyruvates and two NADH are shuttled into mitochondria where an additional net 30 molecules of ATP are produced. (You don’t need to memorize the numbers for this course.) This means that typically, for one molecule of glucose, through glycolysis (anaerobic) and aerobic metabolism in mitochondria the net ATP production is ~32 molecules. Note that although there is a theoretical yield of 38 ATP molecules per glucose during cellular respiration, which is often shown in Biology texts, such conditions are generally not realized because of the cost (use of ATP/energy) of moving pyruvate (from glycolysis), phosphate, and ADP (substrates for ATP synthesis) into the mitochondria.

The glucose-lactate shuttle occurs in astrocytes. Astrocytes (specifically their end feet) take up (transport) glucose (and other nutrients) from the extracellular fluid around the vascular endothelial cells, into the astrocyte cytoplasm. Astrocytes can then release the glucose and other nutrients into the extracellular fluid (ECF). In addition, in the cytoplasm, through the process of glycolysis, in astrocytes the glucose is converted to pyruvate. Then, the pyruvate is converted to lactate by the enzyme lactate dehydrogenase (LDH). That lactate is transported out of the astrocyte and into the ECF around the astrocyte. Lactate in the ECF is taken up by neurons, converted to pyruvate by LDH in the neuron, and then the pyruvate is shuttled into mitochondria where it is used to produce ATP by the Kreb’s cycle, electron transport chain and oxidative phosphorylation (aerobic respiration). Note that the interconversion of pyruvate and lactate is an unusual reaction in cells in that the delta G is close to 0, meaning that the reactant and product have very similar energies, and so it is a reversible reaction. The enzyme LDH catalyzes both reactions: pyruvate to lactate and lactate to pyruvate. The neurons, their axons and other glial cells such as oligodendrocytes can take up the glucose and lactate that the astrocytes provide to the ECF.

1. *Why do neurons rely on oxygen for production of ATP? Where are mitochondria located in neurons?*

The brain comprises about 2% of the total body mass but uses about 20% of the body’s total energy and oxygen. Neurons have low levels of glycogen (glucose stores) and also have low levels of glycolytic enzymes. Hence they can’t make much ATP by glycolysis. They express LDH so when they take up lactate (that the astrocytes provided to the ECF), they can convert the lactate to pyruvate by LDH, and shuttle the pyruvate into mitochondria for aerobic respiration, which depends on oxygen. Hence neurons depend almost exclusively on mitochondria and oxygen for aerobic respiration and ATP production. In neurons, mitochondria are located in the presynaptic axon, cell body/soma, and in dendrites.

1. *What are the other functions of mitochondria in neurons?*

In addition to containing the Kreb’s cycle and forming ATP by oxidative phosphorylation, mitochondria are also involved in Ca2+ uptake and Ca2+ buffering and are involved in triggering apoptosis (a type of cell death.) And, in addition to forming the intermediates involved in ATP synthesis, the Kreb’s cycle also provides intermediates for amino acid, pyrimidine and porphyrin (precursor of heme) synthesis. Mitochondria have their own small genome and ribosomes, and synthesize (by translation) some, but not all mitochondrial proteins. Some mitochondrial proteins are encoded by the nuclear DNA and so those proteins have to be imported into the mitochondria.

1. *What are the functions of the cytoskeleton in cells? Cytoskeletal filaments are formed by protein monomers that interact by noncovalent bonds. What does it mean that the cytoskeleton is dynamic? Why is this important for the cytoskeleton?*

From Wiki, the cytoskeleton “is a complex network of interlinking filaments and protein tubules that extend throughout the cytoplasm, from the nucleus to the plasma membrane.

In neurons, the cytoskeleton has important roles in maintaining the shape and structure of neurons, in development during neuronal and glial cell migration, axonal/dendritic outgrowth, and synaptogenesis, in fast axonal transport and in dendritic plasticity. The cytoskeleton is dynamic because each cytoskeletal filament is composed of many monomer protein subunits, which polymerize via protein-protein interactions (noncovalent bonds) to form the polymers. They can depolymerize as well, and depolymerized (disassemble). In neurons this is important in axonal and dendritic outgrowth so these processes can grow out in the developing neuron. It is also important so that dendrites can change shape and volume depending on activity.

1. *Where are the intermediate filament proteins called neurofilaments found in neurons and what is their function?*

The neuronal intermediate filaments are called neurofilaments and are localized mainly to the axon. The main function for neurofilaments is to provide strength and stability for the axon, and to ensure the axon maintains a fairly constant diameter along its length. (The diameter of the axon is important in conduction of the action potential.) Neurofilaments are not nearly as dynamic as the microtubules and actin microfilaments. Neurofilaments remain more stable and don’t polymerize and depolymerize as dynamically as the other two types of filaments.

1. *Where are microtubules found in neurons and what are their functions? What is the role of microtubule based motors? What are microtubule associated proteins (MAPs)?*

The largest filaments, microtubules are found in the axon, cell body and dendrites. In the axon, microtubules form the tracks for fast axonal transport (FAT). FAT requires microtubules and microtubule based motors (kinesins to move cargoes from the cell body to the terminus, and dyneins to move cargoes from the terminus to the cell body). The cargoes include transport vesicles, secretory vesicles, large cytoskeletal complexes, scaffolding proteins, and mitochondria, which are transported from the cell body to the axon terminal (in anterograde FAT) and from the axon terminal back to the cell body (in retrograde FAT). FAT requires ATP (since the motor proteins kinesin and dynein use the hydrolysis of ATP to provide the energy to move the cargoes along the MT). We’ll discuss later in the synaptic transmission section that FAT transports secretory granules containing neuropeptides, and the lipid and transmembrane components of synaptic vesicles. Microtubules and its motors kinesin and dynein, are also used in dendrites to transport the same types of cargoes (as well as mRNA) along the dendrites. There are microtubule associated proteins (MAPs) which bind the microtubule and regulate its stability, polymerization and depolymerization. An important MAP is tau, a protein that has been implicated in Alzheimer’s Disease and fronto-temporal dementia (FTD).

1. *Where are actin microfilaments found in neurons and what are their functions? What is the role of microfilament based motors?*

The smallest filaments are actin filaments (I’ll call them actin microfilaments) are found in the axon, cell body and dendrites. Actin microfilaments are important during growth cone outgrowth and guidance, and they are also an important cytoskeletal protein found in dendritic spines. Dendritic spines are small protrusions from the dendrites. Spine are the region where the majority of excitatory synapses form in neurons in the CNS and therefore are the place where the majority of excitatory synaptic transmission occurs in the CNS. Dendritic spines are motile (they can move), and they can get bigger or smaller. It is proposed that reorganization of the actin cytoskeleton is a key aspect of dendritic spine and synaptic plasticity. Many proteins can bind actin and regulate actin polymerization, depolymerization, formation of bundles, and localization. Myosin is the most abundant actin based motor protein, which in neurons moves cargoes (vesicles and organelles) along the actin cytoskeleton. (Actin and myosin is also involved in cell movement/migration in non-muscle cells.) You’ve likely learned about actin and myosin in skeletal muscle contraction. In non-muscle cells such as neurons, different isoforms/genes of actin and myosin are expressed, which have different characteristics so they don’t form myofibrils.