

Biomolecular Applications for bioMEMS

Primary Knowledge Participant Guide

Description and Estimated Time to Complete

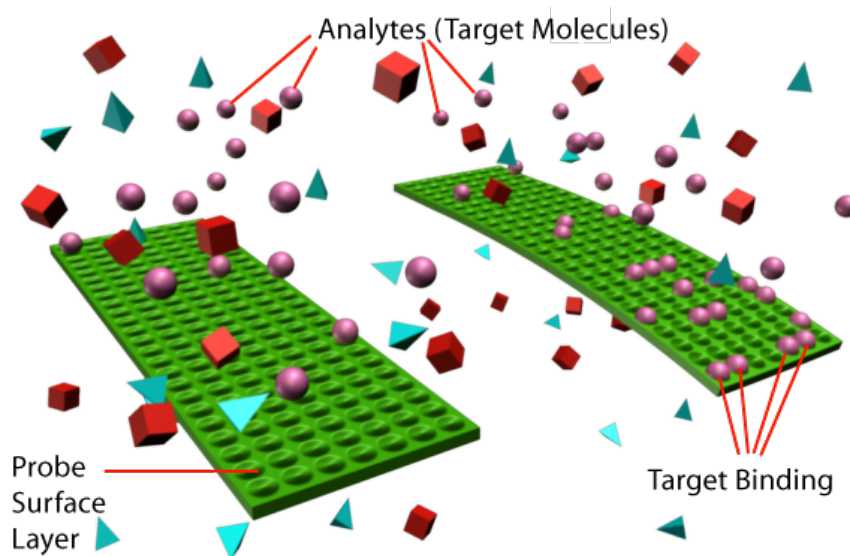
This learning module is an overview of biomolecules, what are they, types of biomolecules, and how microtechnology is using biomolecules or exploiting their functions for micro and nano-sized transducers, sensors and actuators. Activities provide the opportunity to better understand the function of biomolecules, their scale and why they are so important for micro and nanotechnologies.

This unit discusses the characteristics and phenomena of biomolecules that make them attractive components for bioMEMS devices. It provides information that helps you understand how biological molecules can be used as working devices within bioMEMS.

Estimated Time to Complete

Allow at least 30 minutes to complete.

Introduction



A MEMS cantilever coated with a monolayer of biological molecules (probe surface layer) can bind with and capture other molecules (analytes) of complementary shapes

As MEMS devices become smaller and smaller, the use of biomolecules as a MEMS component becomes more attractive. But how can biomolecules be used as a MEMS component?

- Biomolecules can self-assemble into predictable and precise structures in the nano range. This offers a vast new repertoire of structures and functions to MEMS devices.
- Many of these molecules' functions in living organisms can be harnessed to perform the same functions in a bioMEMS device. This provides a wealth of materials and applications that can be applied to bioMEMS design.

To understand how biomolecules can be used in bioMEMS, it is useful to learn about the types of biomolecules and how they associate with each other in functional units. The following information gives a brief overview of the possible applications of biological molecules in the design of bioMEMS. It describes some of the properties that make biological molecules assemble and function.

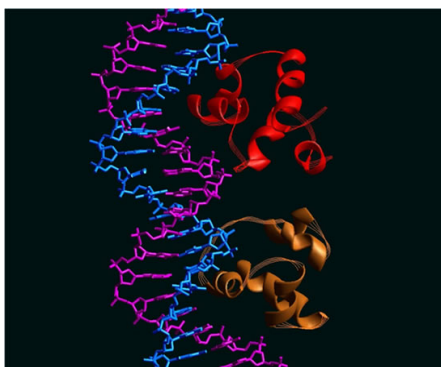
Learning Module Objectives

- State the types of biological structures that are useful in bioMEMS.
- Describe at least three (3) types of functions that biological structures can provide in bioMEMS design.
- Describe two applications of biological components being used in bioMEMS.

Key Terms (Definitions of key terms are in the glossary at the end of this unit)

Analyte
Antibody
Antigen
Biosensor
Cantilever
Cell surface receptor
Collagen
Complementary DNA sequence
DNA hybridization
Drug delivery
Enzyme
Flagella
Gene technology
Hydrogen bonding
Hydrophilic effect
Hydrophobic effect
Lab-on-a-chip devices
Ligand
Liposome
Macromolecule
Microfilament
Microtubule
Nanoparticles
Nucleotides
Organelle
Oxidation
Phospholipid
Protein
Reduction
Scaffold
Self-assembly
Solvent
Supramolecular structure
Vesicles

What are biomolecules?



Biomolecules – DNA and Proteins

[Image source: Swiss Institute of Bioinformatics (SIB) gallery]

A molecule is the smallest form of a substance that contains all the properties of that substance. A molecule is made from atoms. For example, a single H_2O molecule is the smallest form of water. You break it up and you have two atoms of hydrogen and one atom of oxygen.

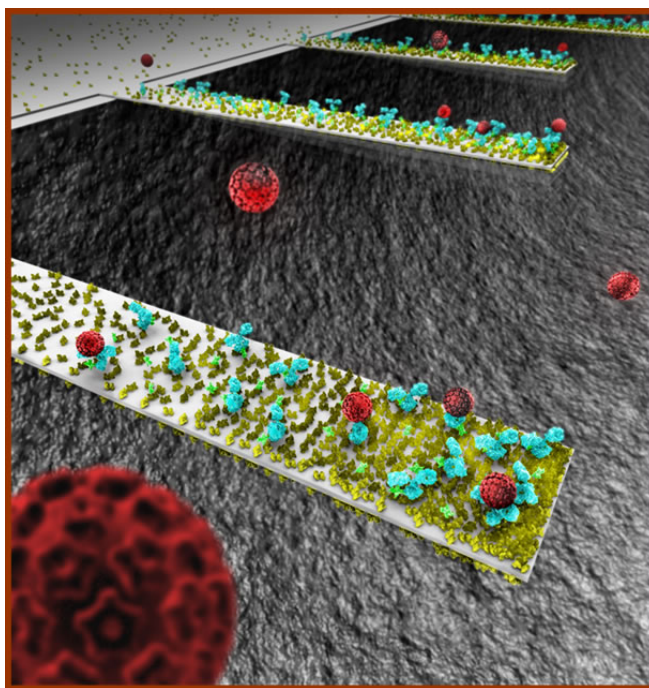
Biomolecules are the molecules of life. All known forms of life are comprised solely of biomolecules. Biomolecules are formed by the self-assembly of atoms (primarily carbon and hydrogen). Once formed, biomolecules continue to self-assemble into larger structures such as larger molecules, compounds, organelles and cells. It is the structure, the three-dimensional shape and the conformation that determines the role a biomolecule plays in the complex chemical processes of life.

There are four types of biomolecules that are abundant in all cells: carbohydrates, nucleic acids, proteins and lipids.

Biomolecule	Types and functions of biomolecules
Carbohydrates	Carbohydrates have both structural and energy storage abilities. Monosaccharides (simple sugars such as glucose) Disaccharides (lactose, maltose and sucrose) Polysaccharides (cellulose, glycogen, and starch)
Nucleic Acids	DNA (The main constituent of genes. DNA passes hereditary characteristics from one generation to the next.) RNA (Triggers the manufacture of specific proteins. Involved in the transmission of DNA's genetic information.)
Proteins	Enzymes (Catalyze or accelerate cellular reactions) Collagen, keratin, and elastin (Structural or support proteins) Hemoglobin (Transport proteins) Casein, ovalbumin (Nutrient proteins) Antibodies (Necessary for immunity) Hormones (Regulate metabolism) Actin and myosin (Perform mechanical functions such as muscle contraction)
Lipids (fats and oils)	Triglycerides (A form of stored energy) Phospholipids (The major components of the biological cell membrane. Able to limit the passage of water and other water-soluble compounds through the membrane.)

Table 1: Types of Biological Molecules

Biomolecules in MEMS Devices



*Nanocantilevers coated with antibodies that capture viruses (red spheres)
[Image generated and printed with permission by Seyet, LLC]*

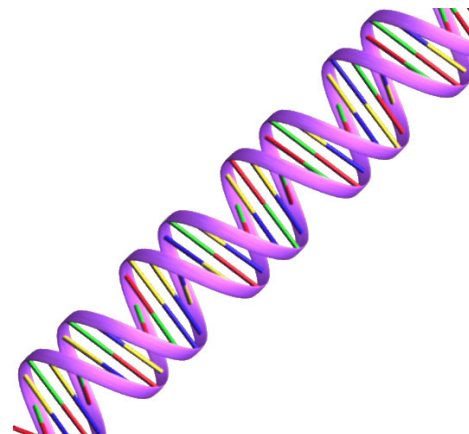
Biomolecules offer bioMEMS engineers a multitude of structures and functional applications. These molecules come in all sizes and shapes within the nano-size range of dimensions. Biomolecules assemble themselves from solutions into biomolecular structures. Their designs have evolved to perform quite specific tasks; tasks which can be applied to a bioMEMS function. Here are examples of some of these tasks and functions:

- Biomolecules have the ability to specifically recognize and bind to a particular molecule in a complex solution. This can be applied to a biosensor function.
- Some enzyme-catalyzed (accelerated) reactions can be used as a biosensor where the catalyzed reaction is detected rather than the binding process itself.
- Some enzyme-catalyzed reactions are used by living cells to generate energy from small molecules readily available in body fluids. These same enzymes can be used in implantable devices to replace the need for batteries.
- Other proteins are used by cells to move particles within the cell, or to move the cell itself around in its environment. These same proteins can be used as actuators in a bioMEMS device.

Biomolecules used in bioMEMS

Three types of biomolecules are being used and studied for bioMEMS interfaces:

- Nucleic acids, such as DNA - These are the molecules that cells use to carry genetic information.
- Proteins, such as enzymes, fibers, molecular motors, channels and pores, vesicles - These molecules are often referred to as the "work horses" of the cell because they perform so many of the jobs of cellular metabolism.
- Lipids, such as phospholipid vesicles and membranes - These are relatively small molecules that self-assemble into very thin membranes in order to make separate compartments in the cell. They also provide a membrane barrier on the outside of all cells.



Double-stranded DNA molecule (a nucleic acid)

What will you explore in this unit?

In the following discussion,

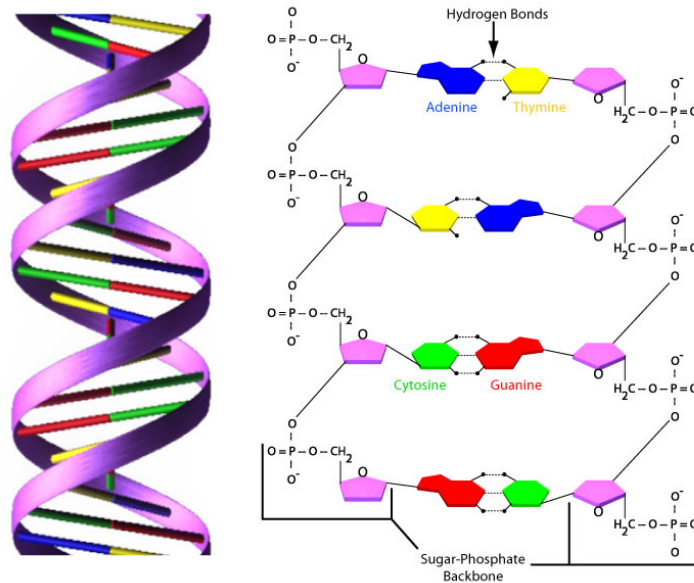
- You will explore how nucleic acids, proteins, and lipids self-assemble into structures that have a functional application in bioMEMS devices.
- You will discover how some of the functions of biomolecules provide the specific recognition properties required in a biosensor-type application.
- You will explore some interesting applications of biomolecules based on their structure
- You will see how some biological molecular motors move within the nanoscale.

Biomolecular Self-Assembly

A unique property of biological molecules is the ability to recognize each other's molecular surfaces in order to bind and assemble into a complex structure. This ability to self-assemble is like having a 3-dimensional jigsaw puzzle solve itself. Each piece would find its own nearest neighbors from all the other pieces, assemble, and then continue until the entire puzzle is solved. This amazing process of self-assembly relies on the continuous motion of molecules in a solution and the resulting collisions. The molecules collide with each other until they encounter molecules to which they can bind. Their unique shape and surface chemistry define how they assemble in solution. This complex process is what takes place when you perform the simple task of blowing a bubble.



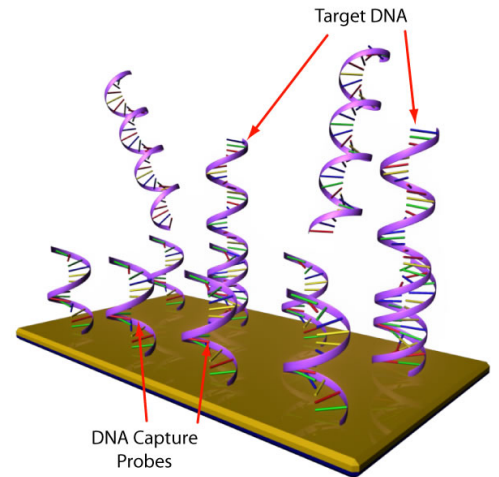
DNA Self-Assembly



Double-stranded DNA

A DNA molecule is a double-stranded helix. Sugar and phosphate groups form the ladder. Nucleotide bases form the steps of the ladder. DNA self-assembly is when two single strands of DNA assemble into a double helix (*see graphic of Double-stranded DNA*). This occurs if the nucleotide bases in each strand of DNA have complementary sequences where the bases pair off with the correct hydrogen bond between them. The cumulative effect of large numbers of hydrogen bonds in a long DNA molecule stabilizes the double helical structure. Only high temperatures can overcome the hydrogen bonding and split the double helix into separate strands. (*For more information on DNA and DNA replication, read SCME's DNA Overview*)

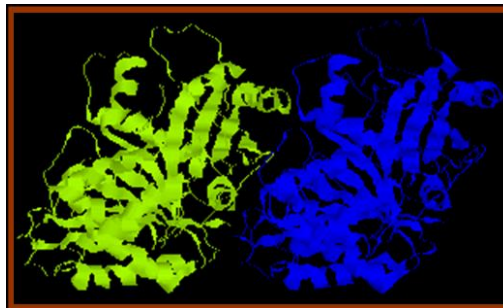
In a type of biosensor (see above graphic) that contains genetic information, a single strand of DNA can "capture" or detect its complementary strand of DNA (the "target"). This selective binding of a molecule is the basis of DNA microarrays, or gene chips. The binding of target DNA can be detected in many ways, depending on the technique used in the MEMS design.



There are many applications of DNA microarrays in medicine. DNA microarrays can be used to detect infectious agents or genetic disease. Applications in public health include detection of contamination in food and water.

A DNA molecule of a specific sequence ("target DNA") can be detected on a DNA microarray by binding to a single-stranded DNA strand ("probe") that has a sequence that is complementary to it.

Protein Self-Assembly



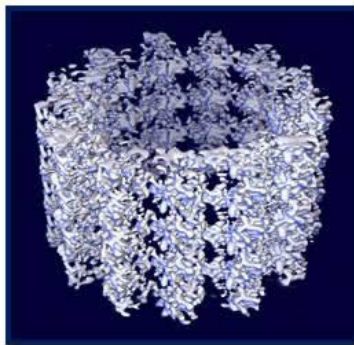
Ribbon diagrams of quaternary protein structures

[Image source: Research Collaboratory for Structural Bioinformatics Protein Data Bank]

Similar to DNA self-assembly, certain proteins will associate with other specific proteins that complement the shape and chemistry of their surfaces. This causes proteins to coordinate with each other in what is referred to as quaternary protein structures (*see figure*).

These protein structures assemble into superstructures using an instruction manual that has become internally "hardwired" through the evolution of cells and organisms. Inside the cells, newly assembled proteins in the cytoplasm are constantly moving, vibrating, rotating, and gliding in solution, bouncing off each other like dancers in a discotheque. When a protein happens to bump into a "partner" protein that has a complementary surface shape and chemistry, the two subunits "plug into" each other and continue their dancing motion as a functional pair. This continues until all the protein subunits have been found and assembled into the final functional structure. At that point, the work of self-assembly is finished.

Example of Protein Self-Assembly



Microtubule

[Image Courtesy of Lawrence Berkeley National Laboratory]

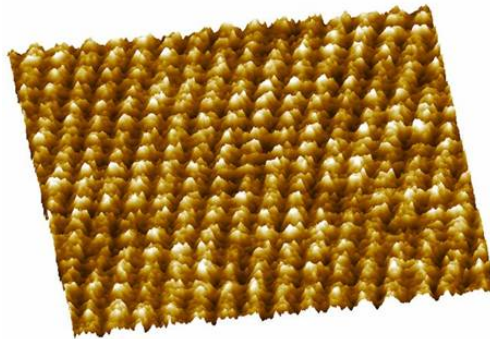
This image shows a microtubule, a principal component of the cell's skeleton. This microtubule is formed by the self-assembly of tubulin dimers (a type of protein molecule). Each tubulin dimer binds to other tubulin dimers in order to "grow" this large spiral microtubule. The association of hundreds to thousands of tubulin dimers into a long microtubule spiral then into a microtubule is an example of a supramolecular structure. Keep in mind that this microtubule is a nanostructure, approximately 20 - 30 nanometers in diameter.

Applications of Biomolecular Self-Assembly

Because of their size, biomolecules provide a convenient means to further miniaturize MEMS devices. The highly predictable and unique nanoscale structures created by biomolecules range in size from sub-nanometer to micrometer, and in some cases millimeter, depending on the type of biomolecule.

The ability of biomolecules to self-assemble provides a faster, cheaper, and more reliable means of generating a 2-dimensional pattern or a 3-dimensional architecture on a bioMEMS surface. The structures formed through self-assembly can be used as templates or scaffolding for deposition of other organic or inorganic molecules. Such supramolecular structures form useful nanoscale particles or fibers such as nanowires or nanotubes.

A Biomolecular Filter

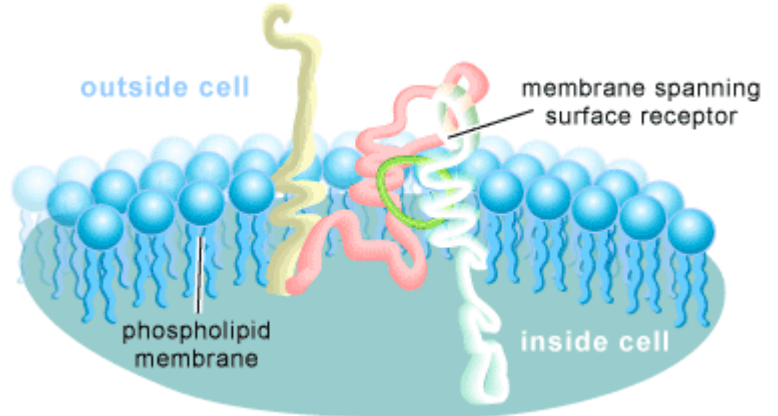


*AFM image of bacterial cell S-layer proteins (Scan size 250 nm x 250 nm)
[Agilent Technologies. Image Courtesy of T.Hopson]*

Crystalline bacterial cell surface layer (S-layer) proteins (*see figure*) are building blocks of one of the simplest self-assembly systems. S-layer proteins form the outer most cell envelope of bacteria by building a monolayer lattice generally 5 – 10 nm thick. . These monolayers find analytical application through their ability to separate and identify molecules, thus acting as a filter. Such nanofilters offer new approaches to water purification and environmental cleanup.

The Function of Cell Surface Receptors

Proteins play many roles in the cell. One role is as a cell surface receptor: A protein embedded in the plasma membrane of a cell is directly concerned with cell communications (getting information from outside the cell to the inside of the cell). The information transferred comes from signal molecules. This cell surface receptor protein has a very hydrophobic site to anchor itself into a surface membrane. It has another site for binding to a signal molecule. The signal molecule binding site has the exact shape and chemistry required for binding to a specific protein. This binding is referred to as a lock and key model, where the protein is the lock that fits one exact key. Only a signal molecule of the correct shape and position will bind and become "locked to" the protein. All other molecules are rejected as "imposters".³



*Cell Surface Receptor – Transfers the information from a protein outside the cell, to the interior of the cell.
[Image courtesy of "The Science Creative Quarterly" (scq.ubc.ca). Illustrator: Jane Wang]*

The Function of Enzymes

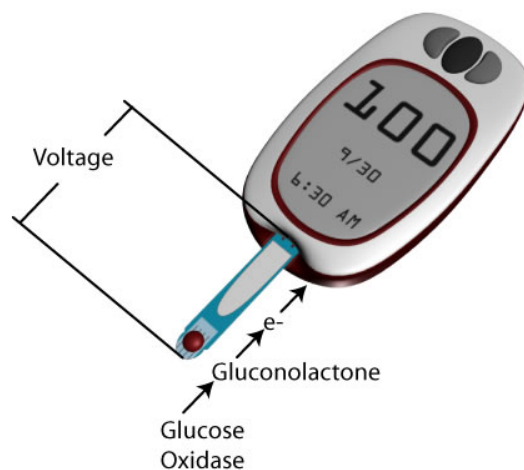
Like receptor proteins, enzymes can also recognize specific molecules and bind to them. Like a cell surface receptor, an enzyme active site has a shape and surface chemistry that allows for recognition and binding of specific or complementary molecules. The binding process is through multiple weak intermolecular interactions (such as hydrogen bonds).

Unlike cell surface receptors, once a target molecule binds to a capture molecule on the enzyme active site, the enzyme catalyzes a chemical reaction to form products that leave the enzyme. This leaves the active site open to catalyze reactions again and again between target and capture molecules. Enzyme active sites generate a "signal" as a result of the binding of molecules and the catalyzed reactions. This signal is monitored in enzyme biosensors.

Enzymes as Biosensors

An example of an enzyme biosensor is the glucose monitor (*see graphic – Glucose monitor*). The glucose monitor is the most common diagnostic bioMEMS on the market.¹⁰ It uses the enzyme "glucose oxidase" from a blood sample (red dot) to recognize and transform glucose molecules. Glucose molecules are oxidized to gluconolactone molecules, releasing electrons (e^-) that can be detected at an electrode.

Glucose Monitor (biosensor)

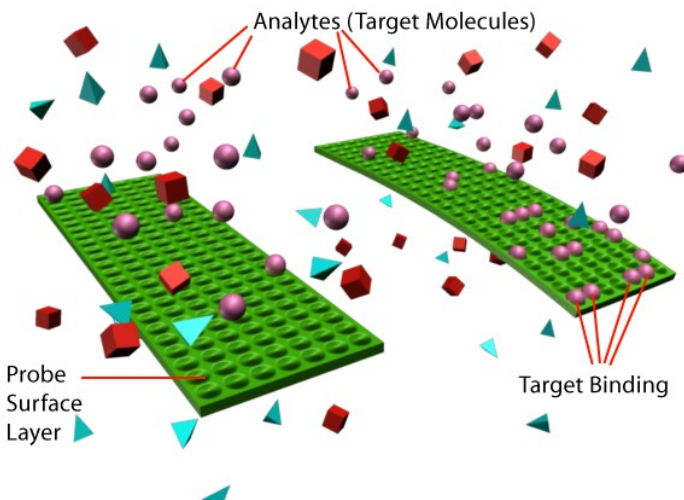


Energy Generation by Enzymes

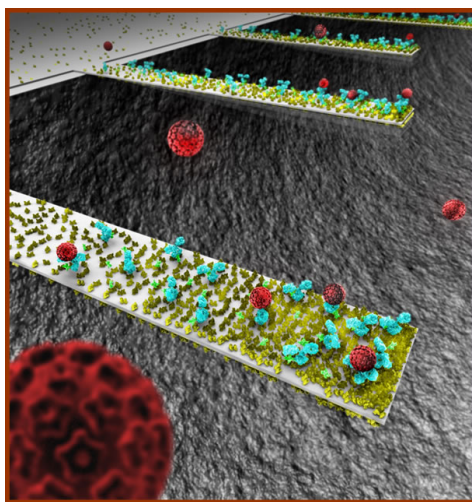
Another attractive property of certain enzymes for bioMEMS applications is their ability to generate energy in response to an environmental change. For example, an enzyme called ATP synthase responds to a change in pH on one side of a membrane, generating ATP (adenosine triphosphate) on the other side of the membrane. The generation of ATP molecules is important in that these molecules transport the chemical energy within cells that is used for metabolism. There are other enzymes that convert the energy of high-energy molecules into ATP. For bioMEMS, this energy-producing property of enzymes can be useful in replacing the bulky battery packs of implantable devices.

MEMS Biosensors

This ability of a cell surface receptor to recognize an exact molecule in chemically complex body fluids can be simulated in a MEMS biosensor. In the biosensor in the graphic to the right, the surfaces of the sensors (cantilevers) are coated with the "capture" molecule. A capture molecule binds to a "target" molecule. When a target molecule binds to a capture molecule, a bioMEMS device detects the binding and sends a signal to a detector.



The Function of Antibodies



Nanocantilevers coated with antibodies that capture viruses (red spheres)

[Image generated by Seyet, LLC]

Antibodies are proteins made and secreted by immune cells. Antibodies bind to specific molecules that are foreign to the body. In laboratory research, these foreign molecules, called antigens, are used to induce an immune reaction in a laboratory animal. Once the animal becomes "immunized" by antigen injections, the animal's immune cells secrete antibodies. Those antibodies that recognize the injected antigen are isolated from the animal's blood. Monoclonal antibodies are identical antibodies that are produced by one type of immune cell. This immune cell and its clones can be isolated and extracted from the lab animal. Using this process a bioMEMS engineer can generate cell cultures that produce monoclonal antibodies that bind to specific target molecules.

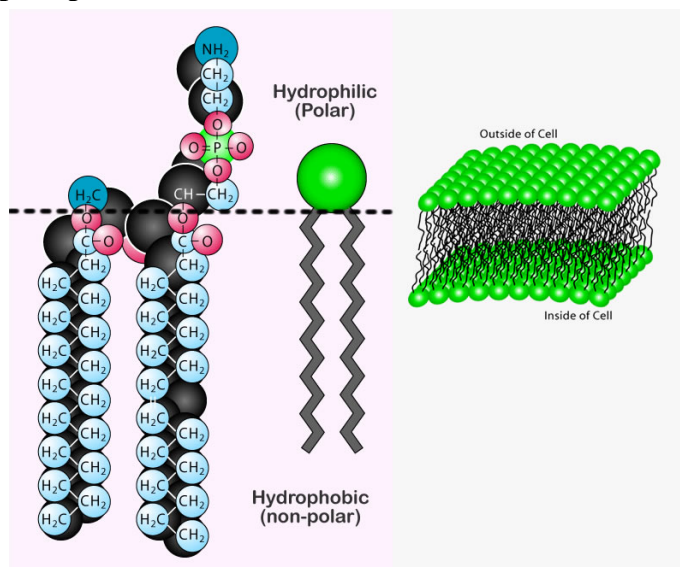
Common applications of monoclonal antibodies in bioMEMS devices are protein microarrays (*see graphic*). Similar to the process of DNA microarrays, protein microarrays use thousands of different monoclonal antibody "capture" molecules as the surface of a biosensor. When a capture molecule binds with a target molecule, the chemical reaction that takes place is detected.

This graphic illustrates the function of a protein microarray. This microarray consists of nanocantilevers coated with a monolayer of antibodies to be used as the "capture" molecules. The "target" molecules are viruses. Notice how "target" molecules (red spheres) bind to the antibodies on the surface of the cantilever. Such an array could also have a different antibody monolayer on each nanocantilever. This would allow the capture of different target molecules within the same solution or sample.

Future medical application of a protein arrays include the following:

- A diagnostic for diseases that create an imbalance in proteins found in cells or body fluids.
- A protein array coupled to a drug delivery device could target a specific cell type. For example, an antibody that recognizes a cancer antigen can be used to seek out and target cancer cells.

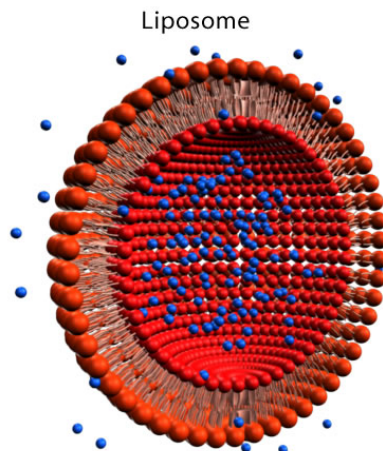
The Function of Phospholipids



Phospholipid and Bilayer Membrane

Phospholipids are very small lipid molecules that are a major component of all biological membranes. Phospholipids self-assemble into membranes, mainly through hydrophobic and hydrophilic interactions. The graphic above shows a phospholipid with its hydrophobic tail and hydrophilic head. To form a bilayer membrane, the hydrophobic tails associate with each other and the hydrophilic heads line up together on either side of the membrane. The graphic on the right shows a bilayer membrane (the hydrophilic heads in green and the hydrophobic tails in black). This membrane serves as a very thin, but very effective barrier. Polar or charged molecules cannot cross a phospholipid membrane. These bilayer membranes, in combination with membrane proteins, form the natural barriers surrounding all living cells, providing a structural and barrier function.

The Liposome Drug Delivery System

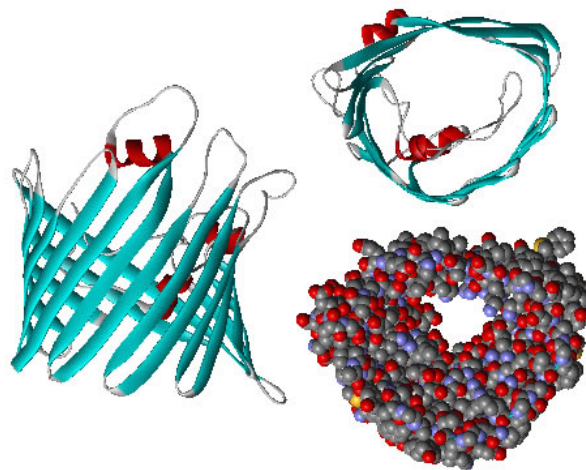


Liposome (red) with drug (blue) in cavity

This graphic shows a liposome (a spherical vesicle composed of a phospholipid bilayer membrane with an aqueous solution in the core). Can you identify the phospholipid heads and tails in this graphic?

In bioMEMS design liposomes are being used for drug delivery systems. The bilayer membrane can sequester drugs within the liposome core (*drugs shown in blue*). The drug carrying liposomes can be injected into the bloodstream where they are carried to the target area (such as a tumor). The proteins in the membrane utilize the "lock and key" process to lock on to a target molecule (cancerous tumor cell). The liposome fuses to the membrane of the target molecule. The drug inside the liposome slowly travels through the membrane and into the cancerous cell (like a timed-release capsule).

The Function of Porin Proteins



*(Left) Ribbon diagram of a porin. (Right) Top view of the same porin molecule in a ribbon diagram (top) and atomic detail (bottom). Notice the pore through the middle of the structure.
[Image source: Tulane University, BioChemistry/ RCSB Protein Databank]*

Porin proteins are a class of outer membrane proteins found in bacteria. Porins are barrel proteins that cross a cell's membrane and act as "nanopores" through which molecules can diffuse. These nanopores act as channels that are specific to different types of molecules.

In bioMEMS design, nanopores are being studied and engineered for various applications:

- Molecule separation - To separate molecules based on size, charge, and hydrophobicity
- "Gating" channels– To control when a molecule is allowed to pass through the membrane.
- Analyte detection – To selectively bind with specific analytes passing through the nanopore, thereby partially blocking the channel. By measuring the conductance of ions through channel, analyte concentration can be directly detected.

The Function of Molecular Motors

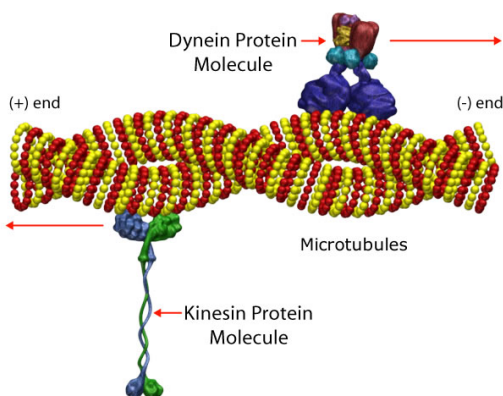
Strictly speaking, all cellular receptors and enzymes are molecular machines because they all have moving parts. Internal movement within protein and enzymes occurs when the capture molecules bind with the target molecules. This binding process results in a change in shape or re-arrangement of the atoms that make up the protein. The range of motion of this rearrangement is generally very small and subtle, on the order of nanometers. However, the movement is large enough to be detected with the right microsensor.

In contrast, protein molecules or “motors” within cells produce relatively large movements. One function of a protein motor is to move "cargo" around in the cell. Other protein motors are responsible for providing locomotion for the cell, or for transporting particles within the cell. Some of these motors have a linear motion, while others have a rotary motion. In bioMEMS devices, such motors can be used for similar functions as their macroequivalents.

Linear Motion Molecular Motors

Molecular motors that have linear motion move along microtubules or microfilaments within the cell. Three such motors are the kinesin, dynein, and the myosin protein molecules. They all transport cargo that includes other proteins, membrane vesicles and organelles.

Kinesin and Dynein Linear motors

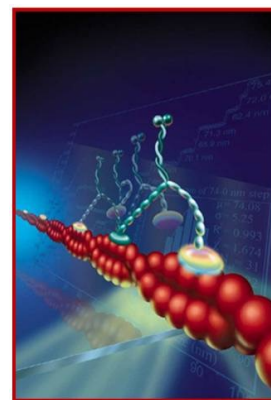


Kinesin and Dynein Protein Molecules (Molecular linear motors)

Kinesin and Dynein (*shown in the figure above*) are protein molecules that exist in the living cells of all plants and animals. These molecules can "walk" along tube-like material called microtubules. They crawl "hand-over-hand", using two "heads" like feet to move forward. This action allows these molecules to transport material within cells. Kinesin proteins travel toward the positive end of the microtubule while dynein proteins travel toward the negative end. Some viruses such as herpes and smallpox use kinesin molecules to move within an infected cell.

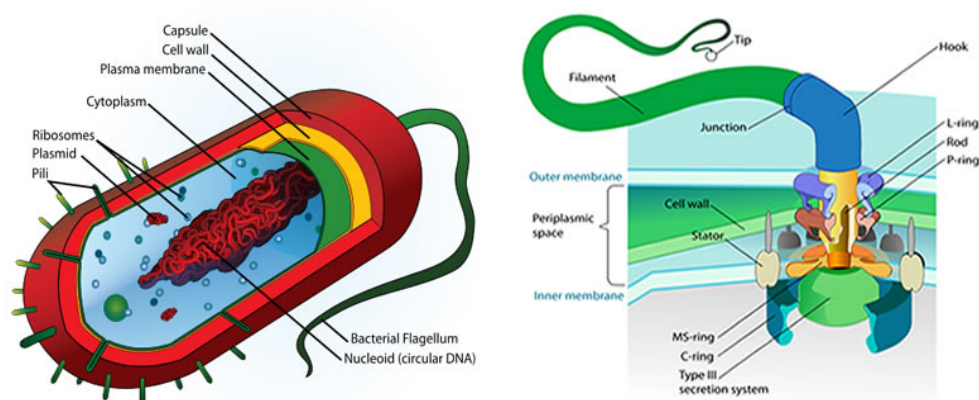
Myosin Linear Motor

Another linear motor is myosin protein, which travels along a microfilament in muscle cells causing muscle contraction. The figure shows a myosin (green) "walking" in nano-size steps along a microfilament (red). As the myosin molecule walks it pulls on the microfilament causing the muscle cells to contract.



Myosin Protein Molecule (A molecular linear motor)
[Illustration by PrecisionGraphics.com. Printed with permission by the University of Illinois]

Bacterial Flagellar Rotary Motor



Bacterium Cell (left) and Bacterial Flagellar Motor (right)
[Graphics courtesy of Mariana Ruiz Villarreal]

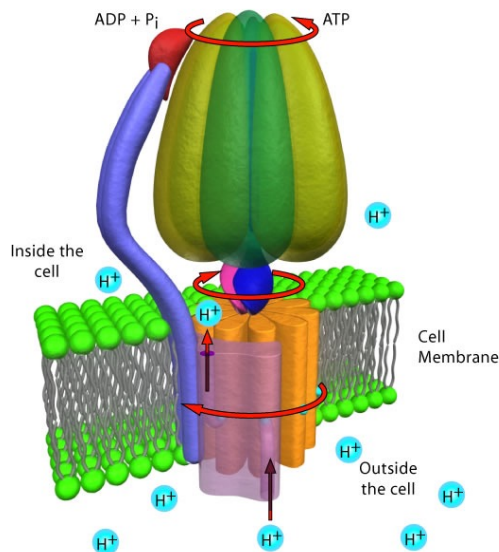
Two types of molecular rotary motors are the bacterial flagellar motor and the enzyme ATP synthase.

The bacterial flagellar motor (shown above) is responsible for the locomotion of bacterial cells. A flagellum is a long, slender tail or tube that projects from a bacterium cell (*figure-left*). The detail in the right figure illustrates the flagellum as an assemblage of rotor, stator and filament. A bacterium can have several flagella. The concentrated whip-like motion of the filaments causes the rotors to turn. This propels the bacterium through its medium.

The ATP synthase rotary motor

The ATP synthase motor is an enzyme embedded in a cell membrane. This enzyme is responsible for generating ATP (adenosine triphosphate), a high-energy molecule that is the universal fuel of cells.. As the ATP synthase motor spins, ATP is created.

The ATP synthase motor (*see figure*) is powered by incoming protons (H^+) that cause a difference in electro-chemical potential to occur across its rotor membrane (*as illustrated in the figure*). The energy from this potential difference is transduced to mechanical energy that spins the motor. As the motor spins, the rotor inside the cell generates ATP.



Other molecular motors use this ATP as fuel. For example, each molecule of ATP that a linear motion kinesin motor encounters triggers precisely one, 8 nm step along its microtubule.

All of these molecular motors enable MEMS engineers to integrate the functions of macromotors into micro and nanoscale devices.

Food For Thought

1. What types of biomolecules are being investigated for use in bioMEMS designs?
2. How can the specific types of structures and functions of biomolecules be used to do the work in bioMEMS designs?
3. On what scale are the sizes of the biomolecules being used in bioMEMS?

Summary

- Biomolecules have precise recognition properties that can provide self-assembling structures for bioMEMS surfaces. This property is also useful for biosensing and separations in bioMEMS design.
- The use of simple biological subunits that can assemble in complex 3-D structures provides a simpler, faster, and less expensive route to nanoscale structures than do most top-down types of fabrication. Useful 3-D structures include channels and pores that can discriminate according to size or chemical properties, providing a means for chemical separations.
- The active site recognition of enzymes and other binding proteins can discriminate between small differences at the atomic scale. This is very useful in biosensor designs.
- DNA microarrays can be used to capture or detect complementary strands of DNA. These microarrays can be used in a biosensor for analyzing genetic information.

Summary Table

The following table summarizes types of biomolecules and their function in bioMEMS devices.

Biomolecule	Example	Function in a bioMEMS device	An example of an application
Nucleic acids	DNA	Recognition of a DNA sequence by selective binding sites	DNA microarrays
Proteins	Receptors and antibodies	Biosensing an analyte by capture (binding) to a target molecule (analyte)	Protein microarrays
	Enzymes	Biosensing an analyte by catalyzing a specific chemical reaction	Monitoring blood glucose levels with glucose oxidase
	Channels & pores	Separation of molecules by size	Membrane embedded with bacterial porin proteins for molecular separations by size differences
	Molecular motors	Moving particles	Actuators
	Filters	Identify and separate molecules	Nanofilters for water purification
Lipids	Phospholipids	Sequester solutions into membrane-coated compartments	Storage compartments for drug delivery devices

Table 2: Biomolecules and their functions in bioMEMS devices

References

1. "BioMEMS: State-of-the-art in Detection, Opportunities and Prospects." Bashir, R. Advanced Drug Delivery Reviews (2004)
2. Biomolecules: DNA and Proteins Image: Swiss Institute of Bioinformatics (SIC). Publication: Gasteiger E., Gattiker A., Hoogland C., Ivanyi I., Appel R.D., Bairoch A. ExPASy: the Proteomics server for in-depth protein knowledge and analysis Nucleic Acids Res. 31:3784-3788(2003).
3. "Cell Surface Receptors: A Biological Conduit for Information Transfer". David Secko. The Science Creative Quarterly. Issue 3. <http://www.scq.ubc.ca/cell-surface-receptors-a-biological-conduit-for-information-transfer/>
4. "Molecular Motors". Bates, Karl Leif. Michigan Today. University of Michigan. 2004.
5. "Single living cell encapsulation in nano-organized polyelectrolyte shells." Diaspro, A. D. Silano, S. Krol, O. Cavalleri, & A. Gliozzi. Langmuir. 18:5047-5050. (2002)
6. "Bioengineered flagella protein nanotubes with cysteine loops: self-assembly and manipulation in an optical trap." Kamura, T., N. Srividya, S. Muralidharan, & B.C. Tripp. Nano Letters. 6:2121-2129 (2006)
7. "Toward intelligent molecular machines: directed motions of biological and artificial molecules and assemblies." Kinbara, K. & T. Aida. Chem. Rev. 105:1377-1400. (2005)
8. "Nanostructuring by deposition of protein channels formed on carbon surfaces." Niederweis, M, C. Heinz, K. Janik & S.H. Bossmann. Nano Letters. 2:1263-1268 (2002)
9. Nanobiotechnology: Concepts, Applications and Perspectives. Niemeyer, C.M. & C.A. Mirkin (Eds). Wiley-VCH (2005)
10. Fundamentals of BioMEMS and Medical Microdevices. Saliterman, S.S. Wiley-Interscience. (2005)
11. "Patterned assembly of genetically modified viral nanotemplates via nucleic acid hybridization." Yi, H., S. Nisar, S-Y. Lee, M.A. Powers, W.E. Bentley, G.F. Payne, R. Ghodssi, G.W. Rubloff, M.T. Harris, & J.N. Culver. Nano Letters. 5:1931-1936. (2005)
12. "Fabrication of novel biomaterials through molecular self-assembly." Zhang, S. Nat. Biotech. 21:1171-1178. (2003)
13. "Third-generation biosensors based on the direct electron transfer of proteins." Zhang, W. & G. Li. Anal. Sci. 20:603-609. (2004)
14. Biotechnology glossary
<http://biotechterms.org/sourcebook/savegotcategory.php3?firstchar=A>
15. "The Use of Microtechnology and Nanotechnology in Fabricating Vascularized Tissues". Raquel Obregon, Javier Ramon-Azcon, Samad Ahadian. Journal of Nanoscience and Nanotechnology. Vol. 14, 487-500, 2014. <http://bit.ly/2vMHxMS>
16. "Biotechnology and Biomolecules". Matis – Icelandic Food and Biotech R&D Institute. <http://old.matis.is/english/emphasis/biotechnology-and-biomolecules/>
17. Biomolecular Engineering. Wikipedia.
https://en.wikipedia.org/wiki/Biomolecular_engineering

Glossary

Actin microfilament -- A 2-stranded helical polymer of the protein actin that form the thin filaments of muscle and the cytoskeleton of cells where they are highly concentrated just below the plasma membrane.

Amphipathic -- Describing a molecule, such as a phospholipid, that contains both hydrophobic (i.e. nonpolar) and hydrophilic (i.e. polar) parts.

Analyte -- A component to be measured in an assay or test.

Antibody -- A protein that is capable of binding noncovalently, reversibly, and in a specific manner with a corresponding antigen. They are produced in higher animals by cells of the immune system in direct response to the introduction of immunogens (antigens), and circulate in the blood.

Antigen -- Any agent that, when introduced into an immunocompetent animal, stimulates the production of a specific antibody or antibodies that can bind to the antigen.

ATP synthase - A general term for an enzyme that can synthesize adenosine triphosphate (ATP) from adenosine diphosphate (ADP) and inorganic phosphate by utilizing some form of energy.

Biosensor – A sensor that can detect specific biological compounds present in a gas or liquid. Receptor biomolecules, such as antibodies, are attached to a sensor device that can detect a mechanical change (such as an increased mass on a cantilever), a change in conductivity (such as an enzyme that carries out a oxidation or reduction reaction), or an optical change (such as an analyte that carries a fluorescent molecule tag).

Cell surface receptor -- A protein embedded in the plasma membrane of a cell that undergoes binding with a hormone, neurotransmitter, drug, or intracellular messenger molecule to initiate a change in cell function. Receptors are concerned directly and specifically with cell communications that involve signal molecules.

Collagen -- A group of fibrous proteins of very high tensile strength that form the main component of connective tissue in animals.

Complementary DNA sequence -- Sequence of nucleotide bases that are complementary to each other, forming the hydrogen bonds of base pairs in a double helix.

Cytoskeletal elements – Filamentous proteins within the cytoplasm of cells that provide structural stability of cell shape and have roles in cellular movement and movement of particles through the cytoplasm. Includes intermediate filaments, microfilaments, and microtubules.

DNA hybridization -- The process of forming a hybrid DNA double strand between single-stranded DNA polymers that have sequences that are complementary to each other, allowing formation of the hydrogen bonding of complementary base pairs.

Drug delivery - The use of physical, chemical, and biological components to deliver controlled amounts of a therapeutic agent.

Enzyme – A macromolecular substance composed wholly or largely of protein, that catalyzes one specific biochemical reactions. The substances upon which they act are known as substrates, for which the enzyme possesses a specific binding or active site.

Enzyme substrate – The molecule that binds to an enzyme active site under catalysis of a chemical transformation.

Flagella -- (singular, flagellum) A fibrous protein assembly that forms the specialized locomotive appendage of bacteria. It is commonly 3-20 μm long and 12-25 nm in diameter, is built up of several (often 3) longitudinally arranged chains of flagellum protein subunits, often assembled in a long spiral. A basal body anchors it to the cell envelope, where a flagellum motor molecule imparts rotary motion to it.

Gene technology - Techniques that allow experimenters to manipulate specific genes within an organism and determine the effect this has on the functioning of the organism.

Hydrogen bonding - The interaction of a hydrogen atom with another atom, influencing the physical properties and three-dimensional structure of a chemical substance. Hydrogen bonding generally occurs between atoms of hydrogen and nitrogen, oxygen, or fluorine. An important example of a hydrogen bonding is the formation of the DNA double helix.

Hydrophilic effect -- Having an affinity for, attracting, adsorbing, or absorbing water. Hydrophilic effect occurs when a liquid comes in contact with another phase — typically a solid substrate that attracts the liquid molecules — causing the liquid to attain a relatively large contact area with the substrate.

Hydrophobic effect -- Lacking an affinity for, repelling, or failing to adsorb or absorb water. Hydrophobic effect occurs when a liquid comes in contact with another phase — typically a solid substrate, that exerts a repulsive force onto the liquid — causing the liquid to retract from the surface, with relatively little contact area between liquid and substrate.

Intermediate filament -- A type of protein filament that contributes to the cytoskeleton of cells. Composed of heterogeneous subunit proteins, they are involved in mechanically integrating the cytoplasm of the cell with the cell membrane.

Ion channel - A protein-coated pore in a cell membrane that selectively regulates the diffusion of ions into and out of the cell, allowing only certain ion species to pass through the membrane.

Lab-on-a-chip (LOC) devices - Miniaturized analytical systems that integrate a chemical laboratory on a chip. Lab-on-a-chip technology enables portable devices for point-of-care (or on-site) medical diagnostics and environmental monitoring.

Ligand -- A molecule that is bound selectively to one or more specific sites on another molecule (as in the combination of antigen with antibody, of hormone with receptor protein, of enzyme substrate with enzyme active site, etc)

Liposome - A type of nanoparticle made from fat molecules surrounding a core of water. Liposomes were the first nanoparticles used to create unique therapeutic agents.

Microfilament -- A type of actin filament that contributes to the cytoskeleton of cells. The major component of a cell's contractile machinery, used for cell movement and muscle contraction.

Macromolecule - A very large molecule composed of hundreds or thousands of atoms, built from connecting a large number of simple subunits such as nucleotide (for nucleic acids) or amino acids (for proteins).

Microtubule -- A long, generally straight, narrow protein filament consisting of a supramolecular structure of tubulin proteins arranged in a helical pattern. Microtubules exist in equilibrium with a pool of tubulin monomers in the cell cytoplasm and can be rapidly assembled and disassembled in response to various physiological stimuli. They play a role in the cell cytoskeleton, providing a tract for motor proteins to move cargo around the cell.

Monomer - A small molecule that may become chemically bonded to other monomers to form a polymer; from Greek mono "one" and meros "part". The subunits used to make polymers or macromolecules.

Nanoparticles - Particles ranging from 1 to 100 nanometers in diameter. Semiconductor nanoparticles up to 20 nanometers in diameter.

Noncovalent interactions - Interactions first recognized by J. D. van der Waals in the nineteenth century. In contrast to the covalent interactions, noncovalent interactions are weak interactions that bind together different kinds of building blocks into supramolecular entities. Also referred to as van der Waals interactions.

Nucleotides -- Building blocks used to make nucleic acids (DNA, RNA). There are 4 nucleotide bases found in the synthesis of DNA (guanine, cytosine, adenine, and thymine) and 4 nucleotide bases found in the synthesis of RNA (guanine, cytosine, adenine, and uracil).

Oxidation - Chemical reaction in which a molecule loses one or more electrons to another component of the process.

Phospholipid -- Any lipid comprised of a glycerol bound to a phosphate group and two fatty acids by ester bonding. The phosphate group can have various charged or polar groups attached, while the fatty acids can vary in size and degree of unsaturation. Phospholipids are ubiquitous components of all biological membranes.

Protein - Large organic molecules involved in all aspects of cell structure and function, synthesized by ribosomes from amino acid building blocks.

Reduction - In chemistry, reduction refers to the reaction of hydrogen with another substance or the chemical reaction in which an element gains an electron.

Scaffold - Three-dimensional biodegradable polymers engineered for cell growth.

Self-assembly - At the molecular level, the spontaneous gathering of molecules into well-defined, stable, structures that are held together by intermolecular forces. In chemical solutions, self-assembly (also called Brownian assembly) results from the random motion of molecules and the affinity of their binding sites for one another. Self-assembly also refers to the joining of complementary surfaces in nanomolecular interaction. Developing simple, efficient methods to organize molecules and molecular clusters into precise, pre-determined structures is an important area of nanotechnology exploration.

Solvent -- A liquid that dissolves other molecular components to form a stable and homogeneous solution. In biological systems, the solvent is water.

Solute -- A molecule or ion that can be dissolved in a solvent to form a solution. In general, hydrophobic (nonpolar) molecules dissolve in hydrophobic (nonpolar) solvents, and hydrophilic (polar) molecules dissolve in hydrophilic (polar) solvents.

Supramolecular structure -- Complex assemblies of multiple structures, such as multienzyme complexes, microtubules, biological membranes, viral envelopes, cell walls, and other cellular structures.

Vesicles - In cell biology, a relatively small and enclosed compartment, separated from the cytosol by at least one lipid bilayer. Cellular vesicles store, transport, or digest cellular products and wastes.

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