1.12:
Explain the progress from serial to batch to beyond batch manufacturing (R2R).

Answer:
In serial manufacturing, a manufacturing station produces one product at the time. As an example for serial machining consider focused ion beam milling (FIB), a mechanical removing technique. In batch fabrication, a "group" or "batch" of identical products is produced in one single machining step. Batch fabrication techniques lend themselves to economies of scale that are unavailable with serial techniques. The use of batch processes is widespread throughout the manufacturing industry, producing a diverse range of products including ICs, pharmaceuticals, polymers, biochemicals, food products, and specialty chemicals. Most nontraditional micromachining carried out today, like IC fabrication, relies on batch fabrication; that is, repetitive features are simultaneously defined on a workpiece. In the case of IC fabrication, an array pattern is photolithographically defined on a silicon wafer, and many wafers are then processed further to fabricate desired structures. Beyond batch manufacturing, the ultimate in automation of manufacturing is continuous or web-based manufacturing with a web moving from supply roll to take-up roll (also called R2R manufacturing) with visions of low cost photovoltaics, thin-film transistors (TFTs), large area organic light emitting diode (OLED) lighting, flexible displays, low-cost sensors, RFID tags, etc. Today polymer films and stainless steel are the two flexible substrates of choice. R2R manufacturing dramatically increases throughput with a significant reduction of capital and device costs.

1.13:
Characterize objects made by laser machining, mechanical machining, E-beam machining, and plastic molding using the following criteria:
- Projected versus 3D
- Serial, batch, or continuous manufacturing
- Top-down or bottom-up machining

Answer:
- Laser machining: projected, serial, top-down
- Mechanical machining: 3D, serial, top-down
- E-beam: projected, serial, top-down
- Plastic molding: 3D, batch, top-down

Chapter 2: Nature as an Engineering Guide: Biomimetics

2.1:
Immunoassays are based on the specific binding of antibodies with antigens.
(a) Describe an ELISA.
(b) Explain how nonspecific binding can produce unwanted signals in both immunoassays and in DNA assays. (Nonspecific binding refers to the binding of adsorption of molecules onto the surface without any preference or selectivity.)

Answer:

(a) Enzyme-Linked Immunosorbent Assay (ELISA) is a useful and powerful method for estimating ng/ml to pg/ml amounts of antigens (Ag) or antibodies (Ab) in solutions, such as serum, urine, and culture supernatant. The basic principle of an ELISA is to use an enzyme to detect the binding of an Ag with an Ab. The enzyme converts a colorless substrate (chromogen) to a colored product, indicating the presence of Ag:Ab complexes. An ELISA can be used to detect either the presence of antibodies or of antigens, depending on how the test is designed.

(b) Typically, the identification process with DNA probes or immunosensors first involves immobilizing a molecular probe, DNA, or antibody on the sensor surface. Next, target molecules are captured onto the surface via specific DNA (probe)-DNA (target) hybridization or antibody (probe)-antigen (target) binding. Secondary probes modified with either fluorescence or enzyme labels to bind the target molecules for either optical or electrical signal detection are then applied to the surface. The non-binding probes falsely contribute to the signal. So non-binding molecules (probes, enzyme, or substrate) are washed away to reduce noise. Incomplete washing is one of the main sources of non-specific signal noise and ultimately influence on the sensitivity of the assay.

2.2:

With the aid of diagrams, describe
(a) A competitive immunoassay
(b) A sandwich immunoassay

Answer:

(a) In a competitive assay the solid phase is coated with purified specific antigen: native, recombinant, or synthetic peptide. Sample and conjugate, comprising enzyme-labelled specific antibody, are added simultaneously. The conjugate and any specific antibody in the sample then compete for the immobilized antigen binding sites, the specific antibody binding preferentially. The specific antibody concentration in the conjugate is carefully set so that the concentration of specific antibody in any sample will nearly always be significantly greater than that in the conjugate and therefore compete successfully for the antigen binding sites. If there is no specific antibody in the sample, the antigen sites will all be filled by conjugate, while if there is specific antibody in the sample the antigen sites will all be filled by that antibody. When substrate is added, any enzyme present will cause the chromogen to change from colorless to colored, but in this case a positive result is indicated by little or no color, the antibody in the sample has prevented the conjugate from binding; a negative result is indicated by color. Figure 2.2.1 illustrates a competitive assay.

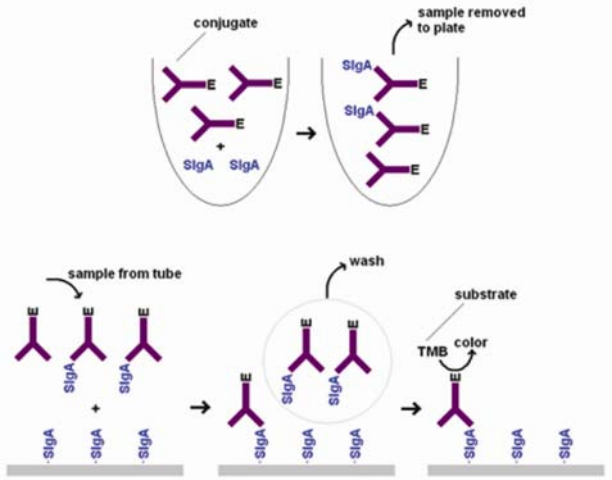


FIGURE 2.2.1: A competitive immunoassay

(b) In a sandwich assay the solid phase is coated with purified specific antigen: native, recombinant, or synthetic peptide; or with purified specific antibody: polyclonal or monoclonal. Any specific antibody or antigen in the sample binds to the immobilized antigen or antibody. Bound antibody or antigen is detected by adding a conjugate comprising enzyme-labelled specific antibody or antigen. When substrate is added, any enzyme present will cause the chromogen to change from colorless to colored. If this type of assay is used in an antigen assay, e.g. HBsAg, and if a pair of monoclonal antibodies are used, one immobilized and the other as the conjugate, which recognize different epitopes on the antigen, the sample and conjugate can be added simultaneously, as the immobilized and free antibodies will not compete for the same binding sites. This can decrease the assay time and increase the sensitivity. Figure 2.2.2 illustrates a typical sandwich assay.

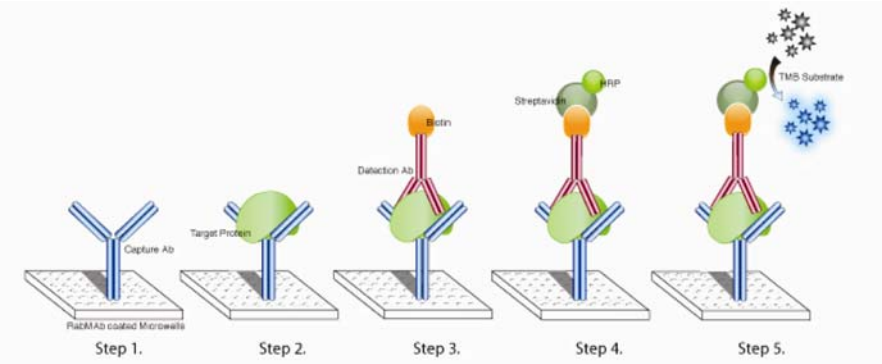


FIGURE 2.2.2: A sandwich immunoassay

2.3:
Why are living systems, at first glance, violating the second law of thermodynamics?

Answer:
The second law of thermodynamics states that in any spontaneous process there is always an increase in entropy. Living creatures have spontaneously developed into more ordered and sophisticated systems through evolution with accompanying entropy (ΔS) decrease. This apparent violation of the second law of thermodynamics is easily explained if one recognizes that the evolutionary process takes place within the broader context of a universe in which chaos keeps on increasing. Every single chemical and biological reaction in the entire history of life has worked in accordance with the second law. This obviously includes the processes to which evolution is ascribed, such as mutation and natural selection. It also includes all other processes which produce an increase of complexity, such as the development from embryo to adult. Creatures are not closed systems. They eat, excrete, use sunlight, and/or feed off the chemicals of thermal vents. Nor is Earth an isolated system. It receives light from this sun, without which most of evolution would not have been possible. A tally of the entropy of the entire solar system would show that it has increased during the evolution of life. Local variations in entropy are not precluded by the second law.

2.4:
Briefly discuss the "who was on first" dilemma: DNA, RNA, or proteins?

Answer:
Researchers working out the understanding of the machinery of life wondered: which came first, DNA, RNA, or protein? The first information molecule must have been able to reproduce itself and carry out tasks similar to those done by proteins today. Proteins were obviously important, since so many cellular functions depended on them; but proteins are even bigger and more complicated than DNA and can't make copies of themselves without DNA and RNA. The chemicals making up DNA include parts of RNA, so proteins and DNA were out. That left RNA. The "RNA World," in which primitive RNA molecules assembled themselves randomly from building blocks and accomplished some very simple chemical chores, won over many scientists, when two biochemists, Sidney Altman and Thomas Cech, discovered independently a kind of RNA that could edit out unnecessary parts of the message it carried before delivering it to the ribosome. Since RNA (ribonucleic acid) was acting like a type of protein known as an enzyme, Cech called his discovery a ribozyme.

2.5:
What models are complexity and communication sciences contributing to the biogenesis question?

Answer:
Complexity Theory: Complexity scientists suggest that life is an "emergent" or "self-organizational" property that arises spontaneously when a large set of chemicals reaches a certain level of complexity. The background here is quite profound: mankind is reasonably capable of calculating behavior of inorganic materials and the structures built from them, but we have had much less success with the more complex organic

systems. This is where the science of complexity comes in; just like scaling and artificial life, complexity is a subdiscipline of biomathematics and represents a general attempt to elucidate fundamental biological principles.

Belgian Nobelist Ilya Prigogine models complex systems that are far removed from thermodynamic equilibrium and describes their self-organizing properties. These self-organizing properties have a tendency to reach critical "bifurcation" or "indecision points" where their behavior may leap into chaos or greater complexity stability. The latter scenario, Prigogine envisions, is how life might have started; that is, on the precipice between order and chaos.

Sceptics not only point at the simplification and arbitrariness of the rules of complexity theory, but they also point out that life is actually not an example of self-organization but one of genetically directed or specified organization. In other words, in life there is a software code directing the organization that emerges from complexity; in the complexity theory, on the other hand, there is no underlying software. In complexity theory, the physical boundaries of the system lead to the emergence of organization.

Communication theory: Another way of looking at the emergence of life comes from the theory of information and communication. Considering that DNA stores the information needed to construct and operate an organism, noise, a form of disorder, may then be regarded as the encroaching entropy. Mutations in this model generate noise, and it is the environment, via natural selection, that selects which information out of noise ends up in a genetic message. The ultimate question in this model is: from where did the information content of the universe come? The above considerations can be expressed in some simple mathematical formulations. There is a direct connection between information content (I) in a system and its entropy (S); an increase in entropy implies a decrease of information, and vice versa. Boltzmann linked entropy, S, to the computed probability of sorting objects into bins—a set of N into subsets of sizes n_i as:

$$S = -k\sum_i p_i \log p_i$$

where p_i is n_i/N and k is the Boltzmann constant. One of the classic equations of information derived by Claude Shanon in the 1940s is formally similar to the above equation:

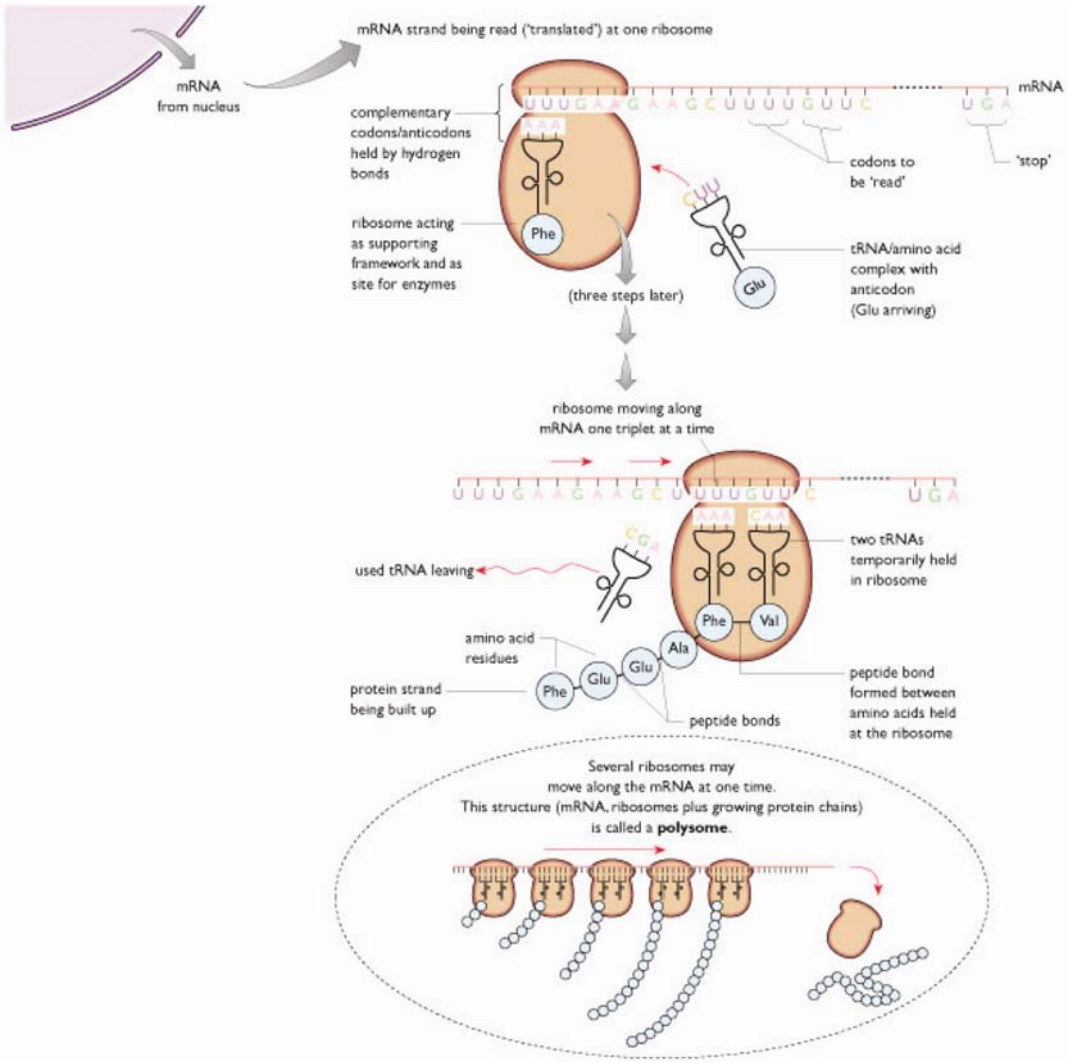
$$I = \Sigma\, p_i \log_2 p_i$$

Information, I, is a dimensionless entity, but its partner entity, entropy, has a dimension; comparing these two equations, one notices that S and I have opposite signs and otherwise only differ by their scaling factors, and to convert from one to other expression, one may write $S = -(k\ln 2)$, or an entropy unit equals $-k\ln 2$ bits. Information is thus a concept equivalent to entropy, and "life" can be described in terms of one or the other.

2.6:

Draw a diagram to illustrate how proteins are manufactured.

Answer:



2.7:
List examples of emergent properties of complex systems.

Answer:
Example #1: Surface Tension
Surface tension is "nothing but" water molecules, but it is not a property of individual water molecules. Rather, it is a property of their properties in relation to one another.
Example #2: The Human Brain
Psychological properties are irreducibly distinct from the physical and biological conditions in which they occur (i.e., consciousness is unpredictable and inexplicable in terms of its physical constitution).
Example #3: An Ecosystem
Other examples of emergent behavior are honey bee hives, ant or termite colonies, cities, and human economies. All exhibit the same set of underlying conditions; all have

a critical mass, or number of participants, below which the emergent property suddenly disappears.

2.8:
Find some examples of man-made materials that feature self-repair.

Answer:
-The repair of microdamage in polymer matrix composites can be accomplished by incorporating an appropriate number of repair fibers in which repair chemicals are entrapped [Dry C, *"Procedures developed for self-repair of polymer matrix composite materials,"* Composite Struct 35 (3): 263–269 Jul 1996].
-Self-repairing elastomeric materials which incorporate microcapsules filled with a monomer resin and a small amount of a polymerization catalyst. Upon damage to the material, some of the capsules burst and release the monomer, becoming polymerized after making contact with the embedded catalyst and thus effecting repair of the damage [http://www.techbriefs.com/component/content/article/5004].

2.9:
Which of the following statements regarding GFP is True/False?

____ The excitation maxima of GFP are at 395 and 470 nm.
____ GFP is extracted from *A. victoria* jellyfish.
____ GFP has a highly unstable molecular structure.
____ GFP emits light at high intensity but with a very low quantum efficiency.
____ GFP gets activated by red or infrared light.

Answer:
T ____ The excitation maxima of GFP are at 395 and 470 nm.
T ____ GFP is extracted from *A. victoria* jellyfish.
F ____ GFP has a highly unstable molecular structure.
F ____ GFP emits light at high intensity but with a very low quantum efficiency.
F ____ GFP gets activated by red or infrared light.

Thanks to Mr. Youssef Farhat, UC Irvine.

2.10:
What are DNA microarrays? What are their applications?

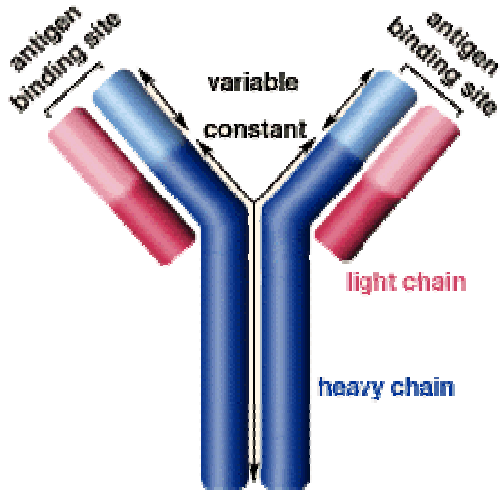
Answer:
DNA microarrays consist of an arrayed series of thousands of microscopic spots of DNA oligonucleotides, each containing picomoles of a specific DNA sequence (called DNA probes). This can either be a short section of a gene or other DNA element that is used as a probe to hybridize a cDNA or cRNA sample (called target) under high-stringency conditions. Probe-target hybridization is usually detected and quantified by

detection of fluorophore-, silver-, or chemiluminescence-labeled targets to determine relative abundance of nucleic acid sequences in the target. DNA microarrays can be used to measure changes in expression levels, to detect single nucleotide polymorphisms (SNPs), in genotyping, or in resequencing mutant genomes.

2.11:

Define what an antigen and an antibody are. What class of proteins are antibodies? Sketch an antibody, and illustrate where the antigen binds to the antibody. Explain what forces contribute to the antigen-antibody interaction.

Answer:



Antibodies are globular glycoproteins from the immunoglobulin family (IgG, IgA, IgM, IgE, IgD) that are produced by the B-cells of the immune system in response to the presence of a foreign substance and to neutralize it. This foreign substance is termed an antigen. Antigens are molecules capable of eliciting an immune response in animals. Antibodies are large proteins, ~150,000 Da, and have a Y shape. Each antibody consists of four polypeptides linked by disulfide bridges, namely two heavy chains, VH, and two light chains, VL, joined to form a "Y"-shaped molecule. They have two distinct regions, the variable region or Fab where the antibody binds to its specific antigen and the constant region or Fc with no antigenic specificity. An antibody is made up of two light chains and two heavy chains. The amino acid sequence in the Fab regions, (tips of the Y) varies greatly among different antibodies. This variable region, composed of 110–130 amino acids, gives the antibody its specificity for binding antigen. The variable region includes the ends of the light and heavy chains. The binding mechanism of the antibody to its antigen occurs in the Fab portion of the antibody and it happens through a series of H-bonding interactions and also through other weak interactions such as van der Waals forces, hydrophobic interactions, and electrostatic forces that improve the binding specificity between antibody and antigen. It is a key-lock type mechanism, which can endow the antibody-antigen interaction with a high binding constant and specificity.

2.12:

Explain the error catastrophe in gene copying.

Answer:

Higher organisms have about thirty thousand genes capable of storing about one hundred million bits of information, each of which may be subject to copying errors. Too many copying errors can cause the reproduction machine itself to come to a halt. The German biochemist Eigen called this the *error catastrophe* and introduced a simple mathematical formulation for characterizing this error catastrophe. He assumed that a self-replicating system is specified by N bits of information and that each time a single

bit is replicated from parent to offspring the probability of making and error is given by ε. He also accepted that natural selection penalizes copying errors by a selection factor S. In other words, an error-free replication has a selective advantage of S over a system with one error, and so on. Then according to Eigen the criterion for survival of a replicating organism is:

$$N\varepsilon < \log S$$

The greater the number of genes an organism possesses, the lower the error rate must be to avoid error catastrophe. Human beings accumulate about 100 mutations per generation, with N of the order of 10^8, to satisfy the above equation, ε must be of the order of 10^{-8}. In other words to avoid error catastrophe, the copying error in human DNA should be less than one in a hundred million per replication. In human cells, an editing process weeds out errors, and the remaining error rate is actually one in a billion.

2.13:

Explain the difference between DNA cloning, reproductive cloning, and biomedical or therapeutic cloning.

Answer:

The term "DNA cloning" denotes the process by which genetic material from one species is transferred to a self-replicating genetic element, such as a bacterial plasmid or a virus. A plasmid is an extra-chromosomal circular piece of DNA distinct from the normal bacterial genome that contains genes and that is capable of producing multiples copies of itself when introduced into a host organism (i.e., bacteria, yeast, or mammalian or plant cells). The process of reproductive cloning is different from DNA cloning as described above. Its goal is to create an animal from the nuclear DNA of an existing one. The principle of this method involves the removal of the nucleus of an egg containing all the DNA of the cell, and replacing it with that from another cell. In the laboratory, the newly created egg is then treated with chemicals or electrical stimulation so it can divide. Once the embryo reaches a certain cellular stage it is inserted into the uterus of a female host or "surrogate mother" where it grows and develops until birth. The goal of therapeutic cloning is to produce an artificial organ or tissue that can be transplanted back into the individual who supplied the original DNA. The procedure, in its first stages, is almost identical to that of reproductive cloning, and involves first removing the nucleus of an egg, then replacing the genetic material by inserting the nuclear DNA of the individual for whom a new organ or tissue is needed. The egg is allowed to develop until it has produced a large number of stem cells. After that, the stem cells are harvested from the embryo. This procedure results in the destruction of the embryo. The stem cells are allowed to reproduce *in vitro* and are chemically treated so as to develop in different types of stem cells that will give rise to the desired organ or tissue type. Once the artificial tissue or organ has been produced, it can be implanted into the patient.

2.14:

PCR is a very important analytical methodology to amplify genetic material. Briefly

describe how it works and the merits/problems miniaturization of PCR entails.

Answer:

Polymerase chain reaction (PCR) is a process by which a small strand of DNA (usually less than 3000 bp) can be replicated more than a million times. The principle of PCR is based on an iterative process which consists of repeating the following steps (the following answer comes from Roche Diagnostics, PCR explained. http://molecular.roche.com/roche_pcr/roche_pcr_process.html):

1. Denaturation: Double-stranded DNA is heated up to temperatures higher than 90ºC which breaks the hydrogen bonds keeping the two strands together.
2. Annealing: Annealing usually takes place at temperatures around 50ºC. Two specific primers are introduced in the solution and allowed to bind with their specific complementary location on each branch of the two single-stranded DNA. This process is normally diffusion driven. The nature of these primers will determine which section part of the initial DNA strand will be amplified.
3. Extension: This step occurs at around 72ºC where in the presence of Taq DNA polymerase the synthesis process at the region marked by the primers begins. It synthesizes new double-stranded DNA molecules, both identical to the original double-stranded target DNA region, by facilitating the binding and joining of the complementary nucleotides that are present in solution.

At the end of the first cycle, the number of DNA sample doubles. The thermocycling is then repeated back again until a sufficient amount of DNA is available. The amplification factor being 2^n, where n is the number of cycles.

Miniaturization in this case has its merits in that the heat cycling can be done very efficiently (very fast heating/cooling cycles) and in a very controlled fashion given that the thermal mass of small structures (microfluidics) is very small. Also smaller amounts of reactants are needed given the high confinement of the reaction. On the other hand the high evaporation rate of the sample solution (due to its large surface to volume ratio) makes the mixture very volatile and thus hard to control, especially during the high-temperature denaturation step of the PCR.

2.15:

Contrast human manufacturing techniques with nature's methods.

Answer:

Human and natural mechanical designs are two individually well-integrated technologies but within very separate contexts. Each might be uniquely integrated by its own elements of internal harmony and consistency, but an impressive aspect of one may have little relevance to the other. A prominent example is metallurgy. In human technology, metals enable stamping, forging, casting, grounding, slicing, and sawing. No known organism uses pieces of pure metal for any mechanical purpose; they make stiff materials into artifacts by internal growth and surface deposition. So man's diverse array of metal manufacturing techniques is of no value in nature. Nature, on the other hand, does not use steel, nor does it favor the production of flat surfaces and sharp corners—all very useful in human manufacturing. Nature builds with proteins and produces mostly curved surfaces and rounded corners, resulting in such masterfully engineered objects as biological cells. Both natural and human manufacturing approaches have their merits within their own proper frame of reference.

In the nano world, nature is way ahead of human engineering, as it works with much smaller, more versatile building blocks and has mastered the self-assembly and multi-parallel construction of those building blocks to create large hierarchically arranged organisms that are much more complex than even the most complex human machines. Today, using human engineering techniques such as MEMS and NEMS, we are not able to build a single micromachine displaying anywhere near the complexity of even the simplest biological cell.

The reason why nature is leading in nanotechnology may be sought in the fact that evolution has worked much longer on developing a single biological cell (3.5 billion years for the first life-forms to evolve) than on the larger life-forms (Homo sapiens only first appeared about 120,000 years ago). In other words many designs were experimented with over a much longer period of time to come to the optimally designed single cell life-forms than for the larger living creatures like trees and humans. It will perhaps be through nanochemistry that mankind can aspire to reach the same level of sophistication in the manufacture of nanostructures as nature does. Moreover, the flight of birds did inspire the Wright brothers' first successful fixed wing aircraft. But, as we are cautioned to do, the Wright brothers did not blindly mimic nature: they used fixed wing aircraft not the flapping bird wings of Icarus. That is, one should learn from nature's manufacturing techniques and adapt them to human/societal needs, rather than blindly mimic nature's approaches. After all, nature's manufacturing techniques are geared towards maximizing procreation, not to be the fastest and most efficient product manufacturing techniques in a modern human societal context.

2.16:

What does the term "binding constant" refer to in antibody chemistry? What is the value of a typical binding constant between an antigen and an antibody? What does the term "cross-reactivity" mean?

Answer:

Binding constant refers to the affinity between an antigen and an antibody. It is commonly reported as the "off rate" or dissociation constant (K_d) of the equilibrium of the reaction between the antigen and the antibody. Typical dissociation constants are in the $K_d = 10^{-10}$-10^{-9} M range.

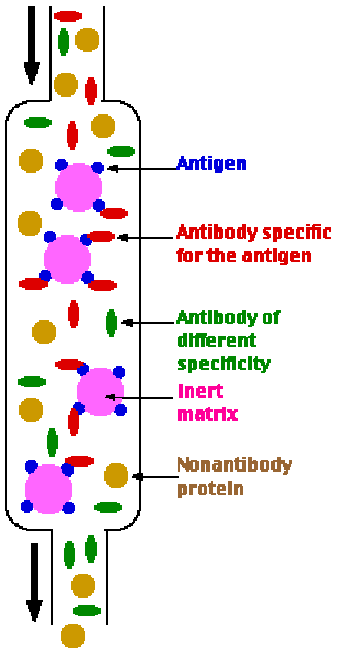
Cross-reactivity refers to the ability of a given antibody to bind different compounds with regard to its antigen. It is a measure of how specific the binding of an antibody toward its antigen is. It is expressed in %. The higher the % cross reactivity, the higher the ability of the antibody to bind to a compound with regard to its antigen, and thus, the higher the interference of the compound with regard to the antigen-antibody interaction.

2.17:

What is the difference between polyclonal and monoclonal antibodies? Briefly discuss the advantages and/or disadvantages of monoclonal vs. polyclonal antibodies.

Answer:

Polyclonal antibodies are produced as a result of an antigenic response to a foreign substance (i.e., an antigen) in an animal. The animal produces a series of antibodies against the different epitopes of the antigen and these antibodies bind to the antigen with different binding constants. This natural mixture of antibodies found in serum is known as polyclonal antibodies. The binding constant reported for a polyclonal antibody is the average of those of the different antibodies against the antigen. A



monoclonal antibody is one produced in a hybridoma cell line. B-cells from the spleen or lymph nodes of an animal that has been challenged several times with the antigen of interest are fused with myeloma tumor cells that can grow indefinitely in a culture and that have lost the ability to produce antibodies. The fused hybrid cells, hybridomas, multiply rapidly and indefinitely. Large amounts of antibodies can therefore be produced. The antibodies from the different clones are then tested for their ability to bind to the antigen by ELISA or immunoblotting, etc. Then the monoclonal antibody with the highest binding constant is isolated and produced in large amounts. Because it is produced in cell lines it is always identical and there is only one antibody.

An advantage of monoclonal antibodies is that in general they have a higher binding constant for the antigen than polyclonal antibodies. They constitute a homogeneous population when produced and therefore when used in bioanalytical applications they result in more reproducible methods. A disadvantage is that they are more difficult to produce and are more expensive. An advantage of polyclonal antibodies is that they can be produced for almost any antigen. They are thus easier to produce than monoclonal antibodies, and are thus cheaper. A disadvantage of polyclonal antibodies is that given their heterogeneity they result in less reproducible methods when employed in bioanalysis.

2.18:

The antigen-antibody interaction is used in a good number of bioanalytical techniques. One such example is affinity chromatography. Describe the principle of affinity chromatography and give one example where you would need to use affinity chromatography.

Answer:

Affinity chromatography is a method that allows for the purification of a target biomolecule analyte by taking advantage of a specific interaction between the target analyte and another molecule, namely its affinity pair (also known as binding pair). The affinity pair is covalently immobilized onto a solid surface, usually a chromatographic column. The sample containing the target analyte to be purified is then passed through the column so that it is specifically and reversibly interacts with its affinity pair on the solid phase. The sample is applied to the column under favorable conditions for the specific binding of the target analyte to its affinity pair. In this manner the target analyte is consequently bound to the column while unbound substances are washed away. Elution of the target analyte from the column is achieved by changing the experimental conditions to favor disruption of the interaction between the target analyte and its affinity pair.

An example of an affinity chromatography process is that involving a metal affinity column that can be used to separate proteins containing a metal binding site, such as an engineered His-tag. Others are those based on antigen-antibody interactions, ligand-binding protein interactions, etc. See schematic on the left.

2.19:
Match the following terms with the appropriate definitions:

(1) Fluorophore	(a) Crystals composed of materials from periodic groups II-VI, III-V, or IV-VI and can be conjugated to biomolecules
(2) Stokes shift	(b) Method used to measure the ability of a molecule to move around in a cell over time
(3) FRAP	(c) Intense fluorescent probe used in many biological studies
(4) Quantum dots	(d) Difference in wavelength between fluorescence excitation maximum and the fluorescence emission maximum
(5) Green fluorescent protein	(e) Molecule that can be excited by light to emit fluorescence

Thanks to Youssef Farhat, UC Irvine.

Answer:
1-E, 2-D, 3-B, 4-A, 5-C

2.20:
What is a biosensor? Draw a schematic of a typical biosensor with its components and explain its operation with an example.

Answer:
A biosensor is an analytical device that incorporates a biological recognition component (e.g., microorganisms, receptors, enzymes, antibodies, nucleic acids, etc.), intimately associated with or integrated within a physicochemical transducer, which may be optical, electrochemical, thermometric, piezoelectric, or magnetic (see Figure 2.20.1).

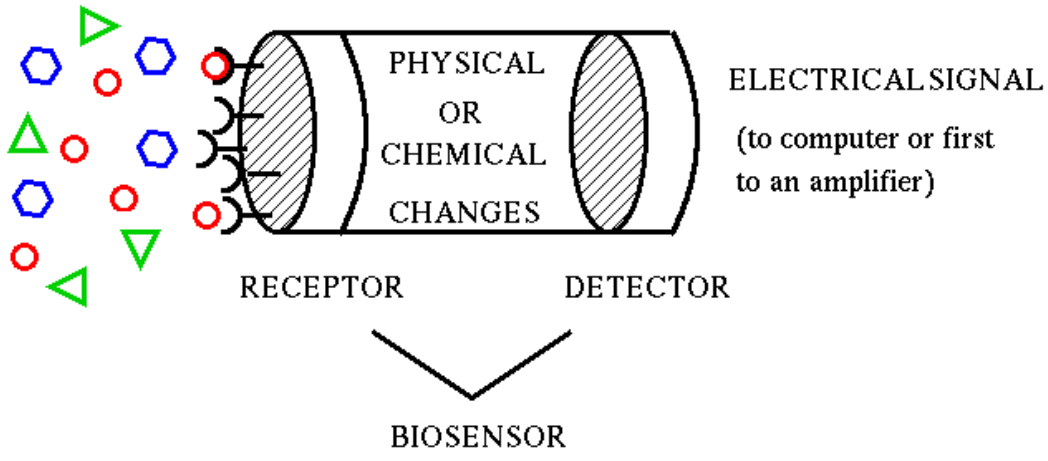


FIGURE 2.20.1 Biosensor example: Glucose biosensor that incorporates the enzyme glucose oxidase as the biological recognition element and an electrode as a transducer.