CHAPTER 2

Basic Principles

2.1 Plasma

Solid, liquid and gas are known as the matter of the world but almost all of the matter in the universe is in the plasma state of the star, nebular and the stellar. Normally, plasma is ionized gas but not all ionized gas can be called a plasma. Plasma is a gas of charged particles, a mixture of ions, free electrons and neutral gas atoms. We can find plasma in our everyday lives, such as in fluorescent tubes, neon signs, metal arc welding or the aurora polar. Producing plasma in laboratory was achieved by applied a potential to the gas. The electrons or charge particles present in the gas are accelerated by electric fields due to the background cosmic rays. The charged particles collide with an inelastic collision with each other atoms and knock their electrons off in the process. The charge separated between ions and electrons gives rise to electric fields, and charge particle flow gives rise to currents and magnetic fields. The molecule moves undisturbed until it makes a collision with another molecule, and these collisions control the particle's motion [42-45].

2.2 Collisions in Plasma

The collision can be classified to elastic and inelastic collision. Elastic collision has been exchanged kinetic energy during the collision. Inelastic collision is some of the kinetic energy transfer to the potential energy [46]. There are four inelastic processes in the laboratory plasma (Fig. 2.1): ionization, recombination, excitation and relaxation. The ionization is a primary electron knock the electron from the atom then two electrons will accelerated by the electric field. The recombination is inversed of ionization which an electron combined with a positive ion to an atom. Then a charge exchange collision results in exchanging an electron between the cold neutral atom or molecule and an energetic ion in plasma [47]. If the energy transfer is less than the ionization potential, the bound electron will jump to higher level in the excitation stage, called "excitation". The excited stage is unstable, then electron return to the lower

energy stage, called “relaxation”. The transition from a higher energy stage to lower energy stage causes the glow in plasma from the emission of a photon [48]. Then electron field was applied in the plasma to generated accelerators electrons to raise energy. The high energy electrons heat up to higher temperatures electron due to the fast moving electron collisions with slower atoms, but can transfer very small energy to the atom while ion motion is ignored. This makes only electrons hot while ions and neutrals remain at room temperature.

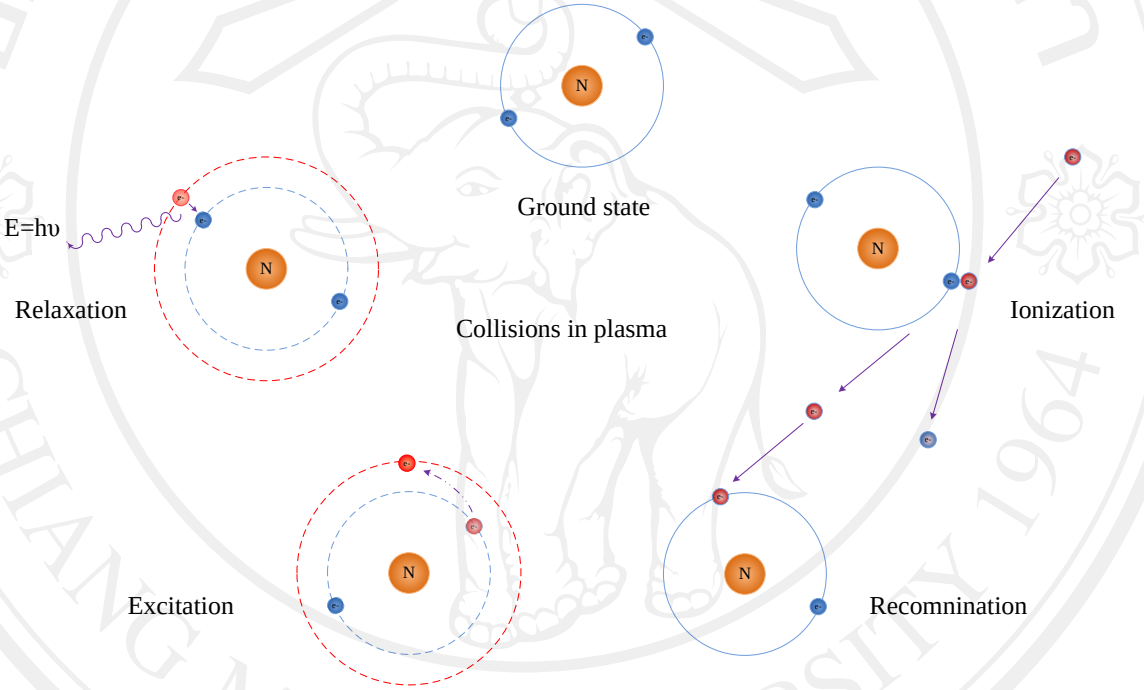


Figure 2.1 The four inelastic processes in laboratory plasma.

2.3 Plasma Parameters

There are three basic plasma parameters: density (*n*), temperature (T) and distribution functions these used to describe the plasma. The plasma density is a basic parameter that used. A host of subsidiary parameters such as Debye length, Larmor radius, plasma frequency, cyclotron frequency or thermal velocity can be derived from these fundamental parameters [49, 50]. For partially-ionized plasmas, the fractional

ionization and cross-sections of neutrals are also important. However, only a number of parameters was characterized during the experiment.

Plasma Density

The number of particles per unit volume is called "particle density". In a glow discharge plasma the gases atom was ionized only 0.01-0.1 %. However, for the ideal plasma, we consider a finite-temperature plasma in a statistically large number of electrons and ions and assume that the ion densities (n_i) and the electron densities (n_e) are initially equal and spatially uniform. There is no net charge in the bulk plasma. The electric fields tend to zero. The ions and electrons need be not in thermal equilibrium with each other and so the ions and electrons will have separate Maxwell-Boltzmann distributions with different temperatures by the ion temperature T_i and the electron temperature T_e. So, the electron density at position x is

$$, n_e = n_0 e^{(\frac{eV}{kT_e})} \quad (2.1)$$

and the ion density at position x is

$$, n_i = n_0(1-\frac{2eV}{MV_0^2})^{-1/2} \quad (2.2)$$

where e is magnitude of charge on electron (1.6022 x 10^{-19} C), ϕ is potential, k is Boltzmann constant (1.3807 x 10^{-23} J/K) [42].

The plasma has its ability to shield out electric potential that is applied to it. For the cold plasma, the electric field of electrode would be shielded. The plasma body would have no electric field but the edge of the cloud could escape. When electrons and ions hit the wall, they recombine or are lost then $n_i >> n_e$. Since electrons have much higher thermal velocities than ions, they are lost faster and leave the plasma with the positive charge, then a high electromagnetic field is formed. The plasma must then have a potential positive with respect to any surface such the wall or sample holder.

In the large area coating could be classified to consider plasma density in three levels; low (10^9-10^{10} cm^{-3}), high (10^{11}-10^{12} cm^{-3}) and very high (>10^{13} cm^{-3}). High

and very high density plasma tends to non-uniform result still depended on their objective.

Plasma Temperature

The temperature plasma is measured by representing the average particle kinetic energy. It is dependent on the particle energy distributions, both of the ions and electron motion. The particle temperature is defined by

$$T_x = \frac{2}{3}\frac{\langle E_x \rangle}{k}, \tag{2.3}$$

where T_x is the ion temperature T_i and the electron temperature T_e. $\langle E_x \rangle$ is the average particle kinetic energy. k is Boltzmann constant [42]. The electron temperature in glow discharge plasma is in the range of 1-10 eV while the ion temperature is around 0.03 eV.

Debye Length

The important property of the plasma is a quasineutral gas of charged and neutral particles, which can shield the electric field from the other charged particles inside the plasma and externally applied electric field [42, 48]. When the inner plasma is unbalanced charge, immediately the opposite charge will attract them. Additionally, in the case when an electric field is applied to the plasma-charged particle, it will find a way to shield and maintain equal density of both particles. They are totally shielded in the plasma body. However, at the edge of the wall could be escaped. The gap at the edge surrounding any object in contact with the plasma is called a sheath. The sheath thickness depends on the potential applied. The shielding distance or the thickness of the sheath is called the Debye length (λ_D) which can be found by

$$\lambda_D \equiv \left(\frac{\varepsilon_0 k T_e}{n e^2} \right)^{1/2}. \tag{2.4}$$

So, when the density increases, λ_D will decrease and when kT_e increases, λ_D will increase. So we can define λ_D from the electron temperature T_e because of the electrons being more mobile [51].

Plasma Sheath

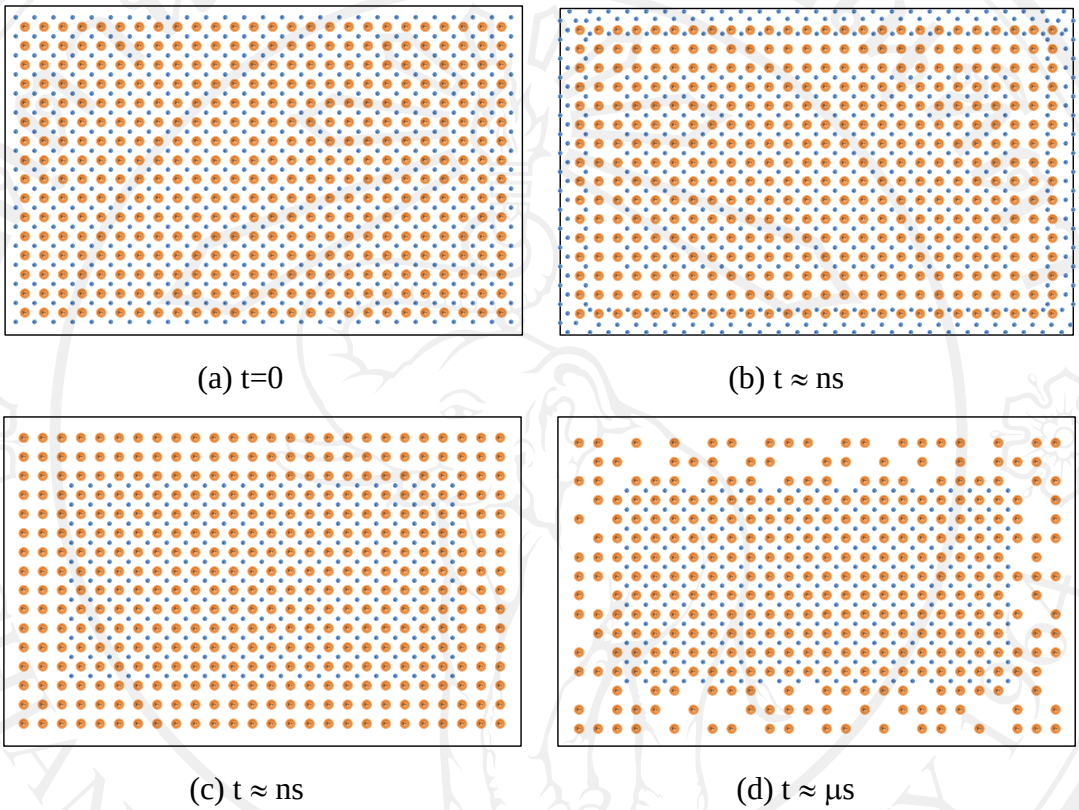
In uniform plasma $n_i \approx n_e$ which is quasineutral at the plasma body when that local, we can let the potential be zero there. However, at the edge of the plasma with the wall, when electrons and ions hit the wall, they recombine or are lost for a while $n_i >> n_e$. At that moment, electrons have much higher thermal velocities than ions; they are lost faster and leave the plasma with the positive charge. The plasma must then have a potential positive with respect to the wall; i.e., the wall or sample holder is potentially negative. When the region builds up a bridge between bulk plasma and boundary surface, plasma is joined to floating or low-voltage wall surfaces across thin positively charged layers called "sheaths". In the case of the floating substrate immersed in the plasma, it will have a sheath and will be negatively bias to the plasma. Then the floating substrate will be bombarded with ions from the plasma. When the acceleration of the ion passes through to the plasma sheath, the ion bombarded to the substrate or the wall chamber, the ion energy can be high to 1000 V. The speed of the electron and ion in the ionized gas discharge plasma is called Bohm's speed. It can be found by [42, 52]

$$\overline{C}_x = \sqrt{\frac{8kT_x}{\pi m_x}}\,, \tag{2.5}$$

where x is an electron or ion. The electron thermal velocity is at least 100 times the ion thermal velocity because of mass, so $T_e >> T_i$. The electrons move faster while ions move much more slowly. Therefore, the higher mobility of electrons caused the loss of electrons while raising the number of ions. These electric fields will push the ion loss to the adjacent surface through self-consistent particle motion until it reaches equilibriums or a steady state.

Fig. 2.2 shows the time evolution of the sheath in a cylindrical chamber geometry. In this case, we presume at the start the plasma was generated uniformly in the chamber as in Fig. 2.2-a. After few nanoseconds, the charged particle sees the wall as the ground; the potential is zero. Immediately, the light electrons that can move faster than the heavy ions hit to the chamber wall (Fig. 2.2-b). Then they leave the ions at the position (Fig. 2.2-c) that makes the matrix sheath and positive potential at the edge. The

sheath potential drives the positive charge accelerated to implant the wall. The sheath edge recedes and leaves a non-uniform charge for a while then the plasma will move through self-consistent particle motion and adjacent system to the equilibriums state.



(a) t=0 (b) t ≈ ns

(c) t ≈ ns (d) t ≈ μs

Figure 2.2 Shows the time evolution of the plasma boundary sheath in the chamber geometry [53].

These can be used as a model in the case of plasma surface treatment. When a worksheet is immerged in the uniform plasma chamber like a floating electrode. The worksheet was seen like the chamber wall and acted likewise, too. In addition, the plasma immersion ion implantation is operated by applying the negative charge to the worksheet. It is quite different because the electrons are driven away from the matrix sheath at the bias position. The accelerated ions are implanted into the worksheet. Then the surface collects more and more positive charges on the top of the surface. Afterward the sheath region is more expanded, and the ions are light and slowly move to implant. In consequence, this system solves by using the pulse voltage supply to leave the

positive potential off the worksheet. However, the worksheet is usually located at the uniform and high density of the plasma chamber, which is how its behavior was predicted.

Plasma Potential

The plasma or sheath potential (V_p) is the electric potential between the plasma and the surface (Fig. 2.3). This electric potential [53] can be found from the direct ion kinetic power density flux to surface (Γ) and ion Bohm's speed as following,

$$\Gamma = en_i \overline{C}_i V_p . \qquad (2.6)$$

This is an important process of plasma surface modification application, such etching, sputtering and deposition. The lost ion and electron recombination near the surface could be balanced in the discharge. The ion bombardment energy depends on the plasma density, plasma potential and electron temperature.

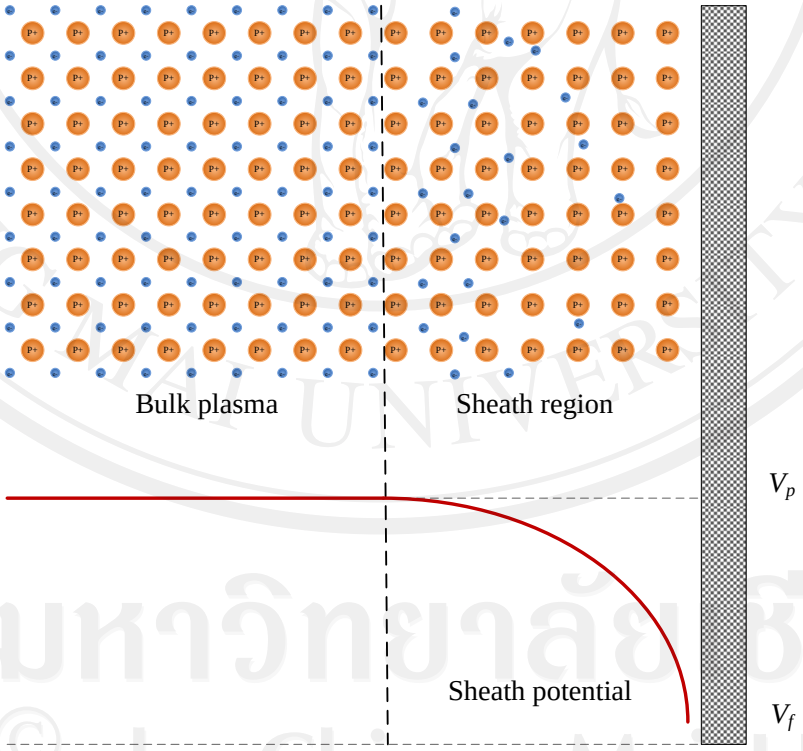


Figure 2.3 Plasma boundary sheath. Typical potential change in dependence on the distance from the surface.

2.4 Plasma Sources

The completely ionized plasma of heavy ions and electrons at high temperatures is called hot plasma, while the low ionization with low temperature plasma is called cold plasma or non-thermal plasma. Non-thermal plasma has been widely used to modify material surface properties. The success of plasma process to modified surfaces due to this technique only effect outer atomic layers of materials. Moreover, it is clean and friendly to the environment. There is having various plasma sources using in the surface modification fields such as microwave plasma, glowing discharge plasma, inductive coupled plasma, or atmospheric pressure plasma [54, 55].

Inductive Coupled RF Plasma (ICP)

Inductive coupled RF plasma is a simple type of high density plasma. The dielectric chamber is surrounded by the conduction coil. RF power applied to the coil induces an electric field to ionize the gas. There are several types of dielectric coil [53] can be as shown in Fig. 2.4. The dielectric chambers are most often made of glass, quartz or ceramic. The RF antenna coils were made from copper tube to which cool water was applied. Moreover, some ICP applications are operated at atmospheric pressure such as jet plasma.

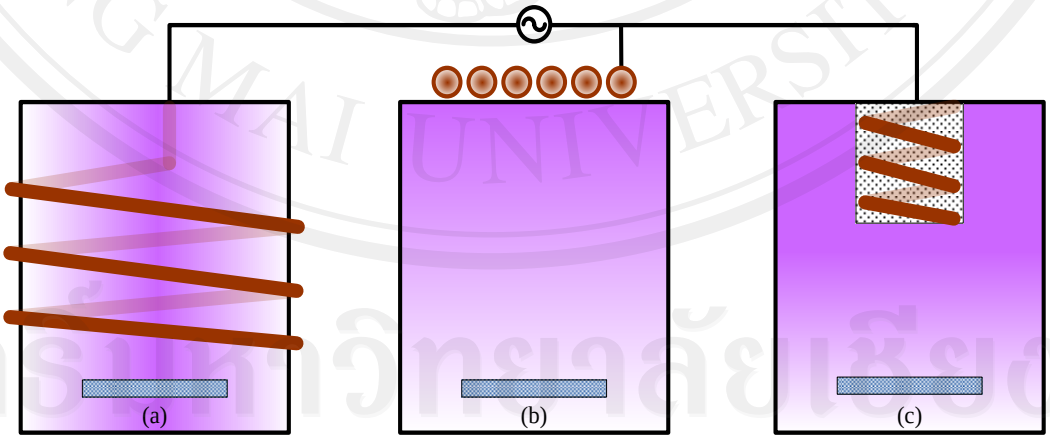


Figure 2.4 Some types of dielectric coil in the ICP system (a) outer the cylinder (b) one side of the cylinder and (c) inner the cylinder which outer the vacuum system.

The RF frequencies are in the range 0.1-100 MHz. However, 13.56 MHz is a popular choice. The RF power is coupled to the plasma through an oscillating magnetic field. When the RF power applied frequency high enough, electrons or ions are oscillate and traverse the sheath between the plasma and the electrodes. Accordingly, the plasma is interacting with the oscillating fields. Which the oscillating fields in the plasma such as the frequency of the oscillation, the electron plasma frequency and electron collision frequency are play an important role in determine. Especially, electron plasma frequency, ω_{pe} is a function of the electron density and it can be defined by equation as follows [47],

$$\omega_{pe}=2\pi\upsilon_{pe}=\sqrt{\frac{n_e e^2}{\varepsilon_0 m_e}} \quad . \tag{2.7}$$

Capacitive Coupled RF Plasma (CCP)

Capacitive coupled RF plasma sources are often used in the microelectronic industry to deposit the films and etch patterns on wafer. There are several types of different designs of the system. The CCP plasma source is heated by the oscillating electric field. The plasma generated by the conduction coil inside the chamber with an RF source which the electric field accelerates free electron collision with atom gas. These systems have the RF antenna and matching network to adjust the reflected power to zero.

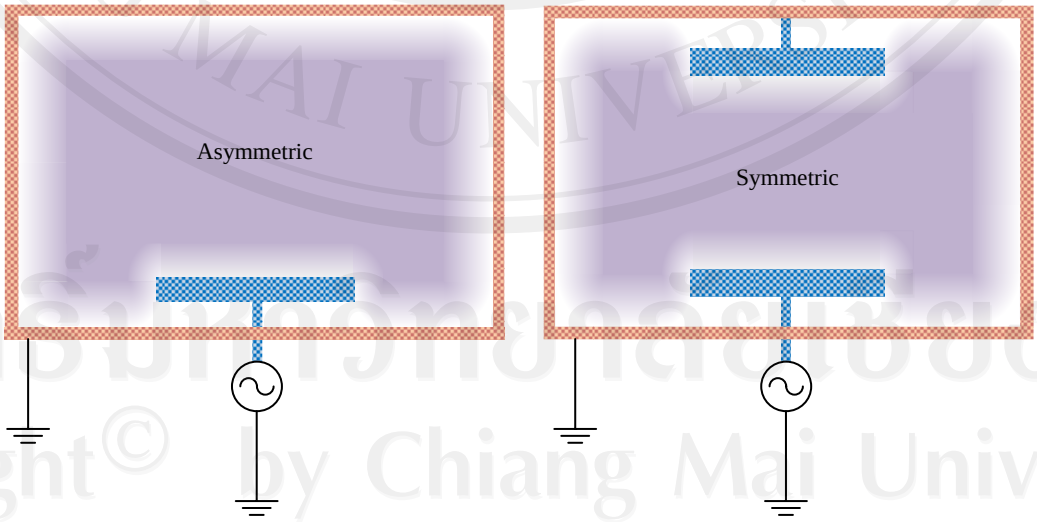


Figure 2.5 The schematic of the two types capacitive coupled RF plasma source.

The conduction coil inside the chamber has been seen in two types of asymmetric and symmetric conduction as shown in the Fig. 2.5. The RF parallel plate discharge can design for each plasma-processing application.

2.5 Interactions of Plasma with Polymers

Biodegradable polymers have increased in importance and use in biomedical fields and the packaging industry [56]. Its biodegradability is used for short term packaging and its biocompatibility in contact with living tissues is used in biomedical applications. PLA is one of the most extensively used biodegradable polymers which has found applications in drug delivery , artificial tissues, implants, sutures and food packaging, due to its biodegradability, biocompatibility, excellent shaping and molding properties.

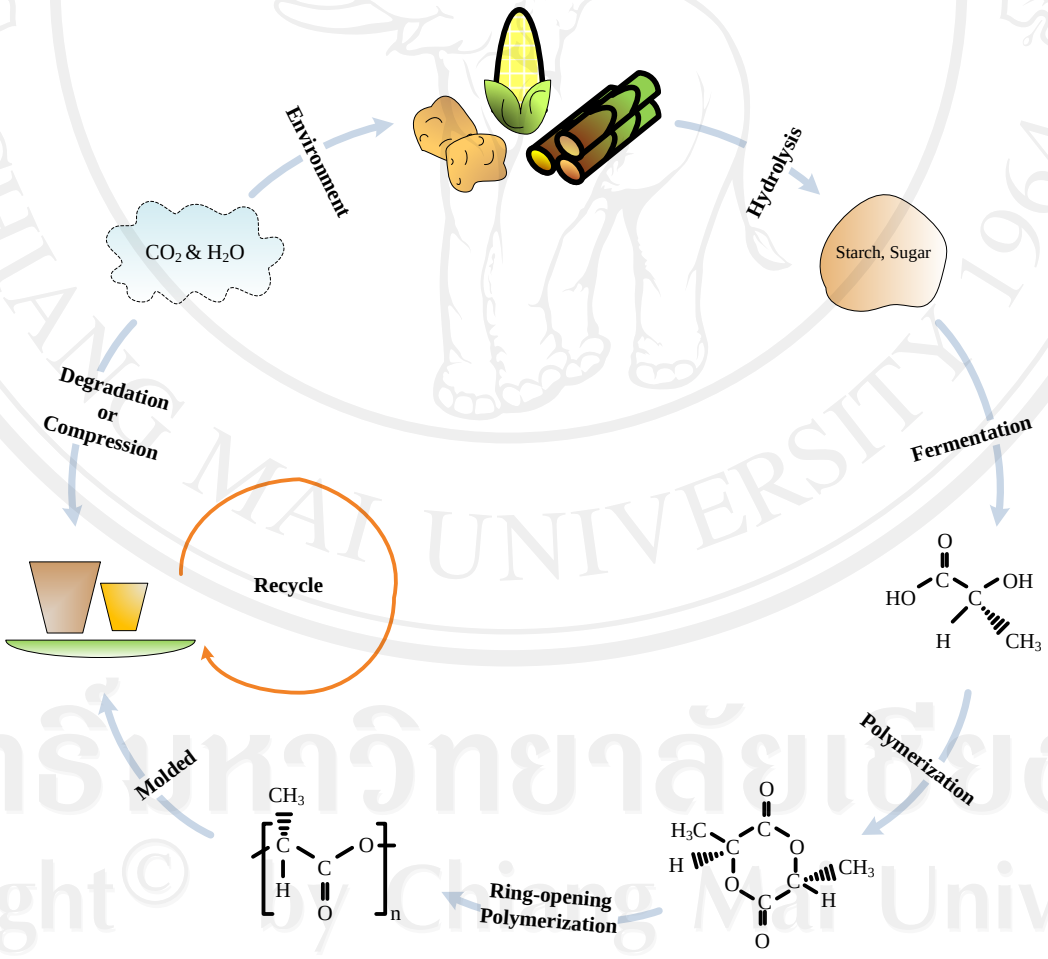


Figure 2.6 The life cycle of PLA.

PLA is made by a fermentation using 100 % annually renewable resources and it rapidly degrades in the environment which the by-products are non toxic to the environment. PLA can be processed in commercially available ways with a large number of techniques. Fig. 2.6 shows the cycle of PLA in process [18, 24, 27, 28, 57] which the basic start from renewable agricultural resources, such as corn, potato or beet sugar. Then it was hydrolyzed to the sugar or starch, the sources of sugars are glucose and maltose from corn or potato, the sucrose being from cane or beet sugar. Bacteria fermentation of these sugars produces lactic acid. The bacterium in varied species gives different types and yields of lactic acid. There is having the L, D or mixture of L and D lactic acid. These lactic acids in different ratios and conditions lead to formed lactides to three types of the stereoforms (Fig. 2.7) [58]. PLA synthesis is produces by the condensation polymerization of lactic acid or ring opening polymerization of lactide, the dimer of the lactic acids. The properties, such as surface energy, barrier or mechanical, of PLA depend on the crystalline structure [30]. Then polylactide resin is processed by injection molding, blow molding and fiber spinning to vary applications of products. After use, it can be recycled by hydrolyzation to get lactic acid or compression under right conditions to degrade in to carbon dioxide and water completing the life cycle [59, 60]

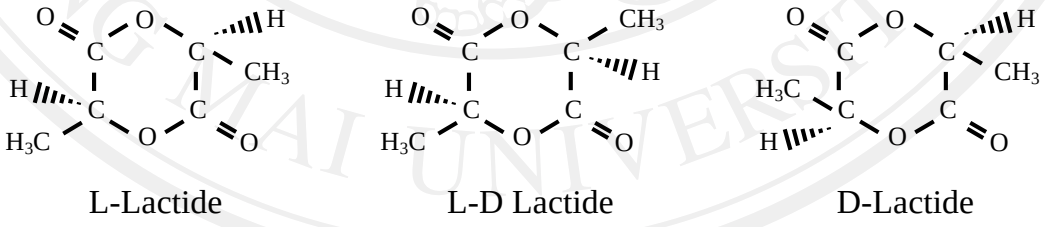


Figure 2.7 The chemical structure of lactic acid.

Therefore, polymer is a material which is made up of many molecules all strung together to form long chains. The polymer properties depend on the type of monomer. They are mainly distinguished by their degradation rate. Polymer molecules bond with covalent bonds. It can change conformation and diffuse with the neighbors. The polymer macromolecule is stable without external damage. When the external force

attacts a polymer, such as UV light, ion beam or plasma, some bonds dangle and a macromolecule is transformed into a free radical state. These generate a new structure of polymer, such as free radical molecules, crosslinks between macromolecules or induce additional structure changes. However, this process depends on photon excitation, electron stages and neighboring macromolecule fragments. There is the case of high energy ions colliding into macromolecules. The primary ions that can transport sheath potential bombarded to the polymer surface, the schematic of the physical process which occurs as in the Fig. 2.8. When the ion energy is higher, inelastic collision dominates. And when the ion energy is lower, elastic collision dominates. When a primary ion collides into a macromolecule, at the top of the surface, some electrons in the target may be emitted due to secondary electron emission. The elastic collisions between ions and the macromolecule may be back-scattered. When the ions impact with the macromolecule, the electrons may be excited and fall to the lower level, so it produces X-rays, visible light, UV and photon emissions. When the ions penetrate in the macromolecule, momentum and charge are transferred to the macromolecule.

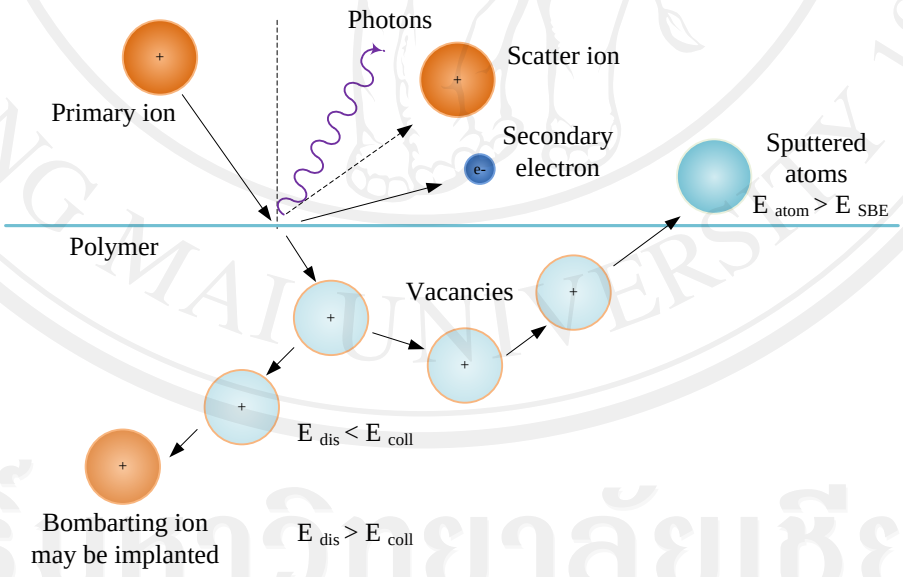


Figure 2.8 The schematic drawing of ion and polymer interactions.

If the collision energy is larger than the critical energy for displacement of the macromolecule, it is displaced. When an ion loses of kinetic energy, it will stops

between the polymer macromolecule [26, 61, 62]. The cross-linking occurs when the two free radicals of neighboring macromolecules meet. Moreover, the active species in the plasma interaction with the polymer etching surface causes roughness and may degrade the polymer with the scattering atoms. The free radicals at the surface induce the plasma functionalization and plasma polymerization. The free radicals survive for a long time. However the modified polymer is usually used in the air or the active environment. After the modified polymer is exposed to the air, a peroxide radical is started immediately. Fig. 2.9 shows the schematic diagram of the interactions of the plasma active species and polymer surface and oxidation on the polymer treated.

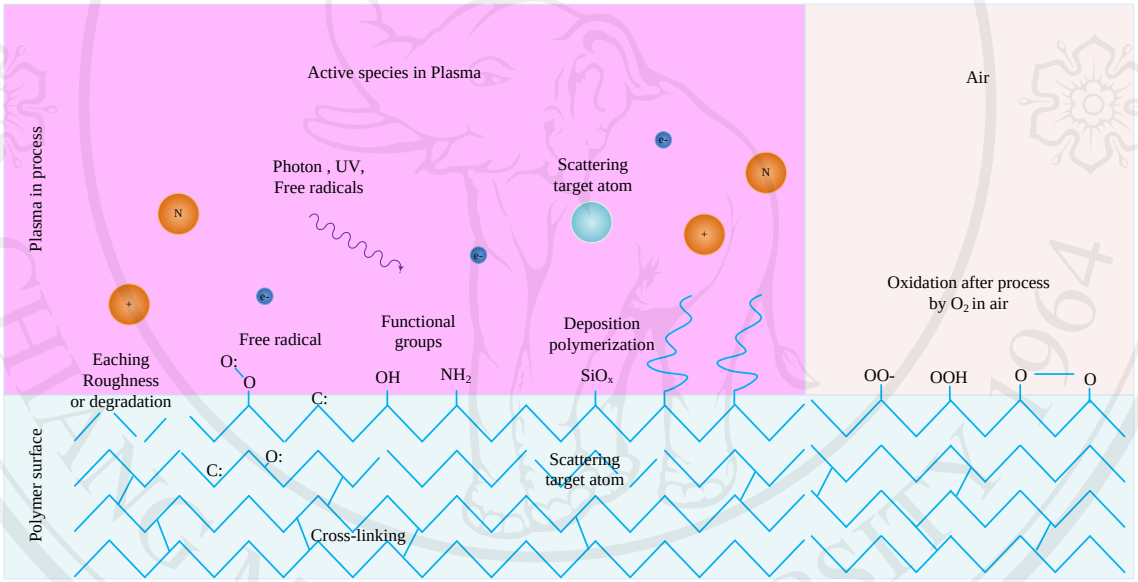


Figure 2.9 The Schematic drawing of the interactions of the plasma active species and polymer surface.

The degradation rate of polymers is important to its applications. Hence, controlling the degradation rate is critical to the assigned functions. Plasma is the choice to modify the polymers due to it developing the surfaces without changing the bulk properties of the polymers. The various applications of plasma treatments to plasma surface modification of polymer are surface cleaning or etching, improving the wettability, increasing the adhesion, reducing friction, improving cell attachment or protein adsorption. The plasma process is usually used for modification of the surface of

the polymer are the thin films deposition, etching, surface functional or plasma polymerization; these will be explained below.

The Thin Films Deposition

The plasma deposition process can be divided to sputter and enhance deposition from the characteristic of reaction when the films were formed. Sputter-deposition comprises with physical and reactive sputtering. For the physical sputtering, ions and atoms from plasma bombard the target or substrate then release molecules or atoms to form these materials. The reactive sputtering was name as such because the dissociated products are from the reactive gas. The positive ions bombard the target then the reactive gas combines with the sputter target materials and forms the films. The plasma-enhanced chemical vapor deposition formed chemical reactions in the plasma. The reactive gas with difference kinds of ions and radicals in the plasma is diffused and then deposits films to the substrate.

Etching

Plasma etching is the famous technique to remove the surface of the materials. The plasma source of etching can be found in a glowing discharges or plasma immersion ion implantation. The different types of plasma etching mechanisms, such as sputtering, ion enhanced energy, ion enhanced behavior and chemical etching depend on three important parameters; etched uniformity, anisotropy and selectivity. A number of gas-surface systems used in various purposes. For example, it used with the CC_4/Cl_2 discharge trench the aluminum surface or used F with Si. The etching as a result of the sputtering process, if the atom at the surface received enough energy, typically 2-5 eV [61] that it can break root from the surface potential then leave from the surface. The sputtering yield is defined as a number of surface atoms ejected per incident ions which depend on such an ion energy, target materials, incident ions and incident angles. The etching process is a spontaneous chemical reaction with Arrhenius relationship, the rate of reaction is given by [48]

$$ER_s = k_0 \, e^{\left(\frac{E_a}{kT}\right)} Q \qquad (2.8)$$

where Q is the flux of reactive species, T is the substrate temperature, k_0 is the preexponential factor and E_a is the activation energy.

Surface Active and Functionalization

Plasma surface modification of materials without affecting the bulk properties usually produces the reactive sites of the materials. These advantages can be used to desire the properties of the material, such as adhesion or wettability. The non-polymer forming plasma gas such as the inert gases, Ar, NH_3, N_2 or O_2 were used for activated surface for functional. The functional groups and cross-link are introduced at the surface of the polymer by the reactive gas species.

Plasma Polymerization

When the molecule inner the plasma form the polymer films on the surface is called plasma polymerization. Plasma polymerization is an important process for entry of new materials to modify the surface of polymer and other materials. However, the plasma polymerization is a complex process that is not well-understood. These polymers are not characterized by repeating units like normal polymers. The structure depends on the plasma parameters such as the reactor, monomer type and flow rate, substrate temperature, frequency and input power.

The main advantage of plasma polymerization is one step of coating process that conforms the thin films and pinholes free on the most substrate. Moreover, the properties of the films can be chosen by the monomers and plasma parameters. Most of the plasma polymerization studies focus on the high crosslink films by controling the high energy plasma conditions. Recently, synthesis of the specific functional groups was the trend. Various techniques were used to improve the chemical functional films. The pulse RF plasma has been successful in achieving this enhancement of the films chemical functional controll. This technique is more polymer-like with less cross link structure [63]. The application of plasma polymerization films are in the microelectronic, packaging industrial and the biomedical field. There are several organo-silicon precursors that are used for forming the plasma polymerized films. The

well-known precursor was used in the industries such as hexamethyldiiloxane (HMDSO), chlorotimethylsilane (CTMS), tetraethoxysilane (TEOS) and octamethylcyclotetrasiloxane (OMCTS) which OMCTS is a favorite one. A chemical formula of OMCTS is $Si_4O_4C_8H_{24}$. Fig. 2.10 shows the plasma polymerization of OMCTS with O_2 as a carrier gas which free electrons in the plasma collide with the macromolecule of the precursor into many fragments as below.

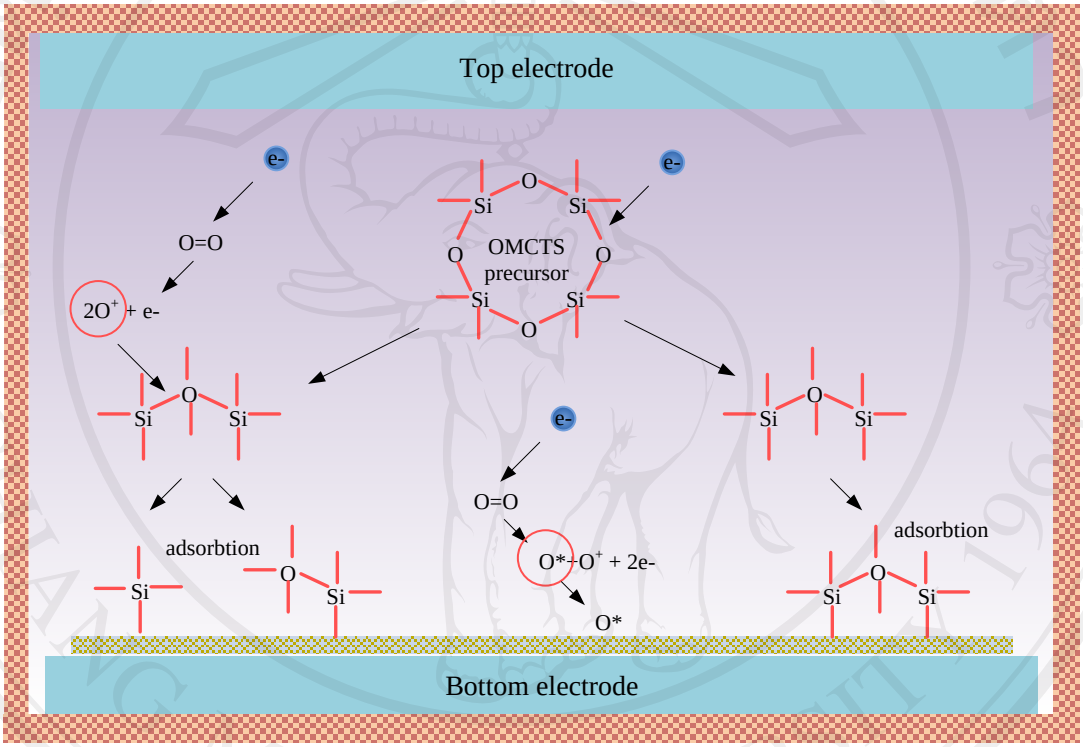


Figure 2.10 The Schematic of the plasma polymerization of OMCTS [64].

The small fragments are adsorbed onto the surface and released by product exposed to the plasma. Moreover, the radicals of oxygen are interact with the surface which leads to the increase in reactive surface benefits to the processing.

2.6 Plasma diagnostics and Surface analysis

Optical Emission Spectroscopy: OES

When plasma was generated the plasma diagnostic needed to be analyzed, one of these was the optical emission of plasma. The spectra could be used to analyze both

chemical species and its excited stage. The plasma emission occurred from the electrons colliding with other atoms. Then the energy transfer to the inner electrons was enough for exciting. The excited stage was not stable. Then the electrons released the photons and returned to the lower energy stage. These photons are a cause of spectra. The emission of atoms had a sharp spectra. However, the molecules had a broadening of emission energies due to the overlap of collisions and movement of the emission [48]. Normally, at higher pressures collisions broaden the emission energy that it is not usually observed in the low pressure plasma. The spectra of plasma radiation were collected by a lens that focused onto an optical fiber. The optical fiber took the spectra to the quartz window of the spectrometer. The spectrometer detected the spectra to prism, grating, filters and photodiode then CCDs analysed the photon and transfered energy to electrons in the light sensitive detector and jumped to the conduction band. The optical emission analysis was effective and quantitative when combined with the others.

Contact Angle

Increasing of the surface modification in the self-cleaning, nanofluidics or the electronic industrials lead to characteristic of the surface wettability which usually involved the measurement of the contact angle. Moreover, the contact angle lead to understanding of the surface functional groups or surface roughness. The contact angle is defined as the angle between a solid surface and the tangent of the liquid vapor interface of the liquid drop. The interface of three phase contact line where solid, liquid and vapor are located. The molecules of liquid were dropped on to the surface without neighboring molecules. Then they were pulled inward by the neighboring molecules form the internal pressure as shown in Fig. 2.11. Therefore, the surface area of the liquid-solid is maintained by the lowest surface free energy. The three major types of contact angle measurement [65] are static, advance and receding contact angle as shown in Fig. 2.12. The static contact angle can be found by measuring the angle of a tangent of dropped the liquid and the surface as the Fig. 2.12-a. The value of the contact angle is a result of competing tendencies between the energy of cohesion of liquid molecules and the energy of adhesion of the liquid-surface. When the work of cohesion of liquid

exceeds the work of adhesion of liquid-surface, a drop will be placed on the surface forming a finite contact angle. In the opposite way, if the work of cohesion of liquid loses the work of adhesion of liquid-surface then the spreading occurs. Then contact angles can be defined by Young's equation as follows [26, 66]

$$\gamma_{LV}\cos\theta = \gamma_{SV} - \gamma_{SL}, \qquad (2.9)$$

where γ_{LV} is the surface tension of the liquid in equilibrium with its saturated vapor, γ_{SV} the surface tension of the solid in equilibrium with the vapor, and γ_{SL} the interfacial tension between the solid and the liquid.

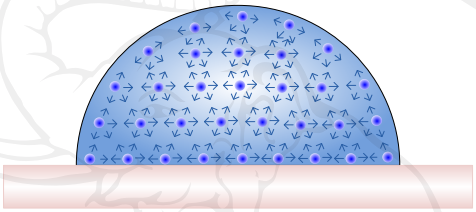


Figure 2.11 Surface tension is caused by the unbalanced forces of liquid molecules at the surface.

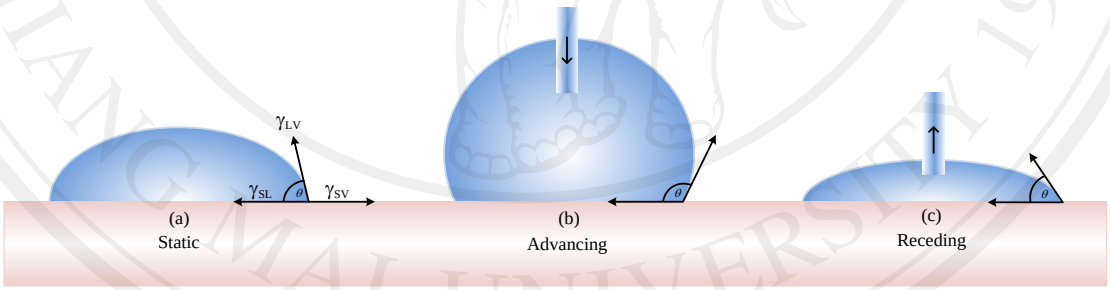


Figure 2.12 The schematic diagram of the measurement of the contact angle.

Normally, we class the wettability of water contact angle by the right angle. Fig. 2.13 shows the drop type of the contact angles. If the angle is lower it is called "wetting" or "hydrophilic" but the angle is higher it is called "hydrophobic". Moreover, the interesting part of the surface properties at the angle greater than 150 degree was called "super hydrophobic surface", it is the "lotus effect" from which its properties were used in the self-cleaning surface technique. The dynamic contact angle is measured by inserting a needle in the liquid, dropping it then measuring the contact

angle while the movement of addition of (advancing contact angle; Fig. 2.12-b) or removed of (receding contact angle; Fig. 2.12-c) the liquid.

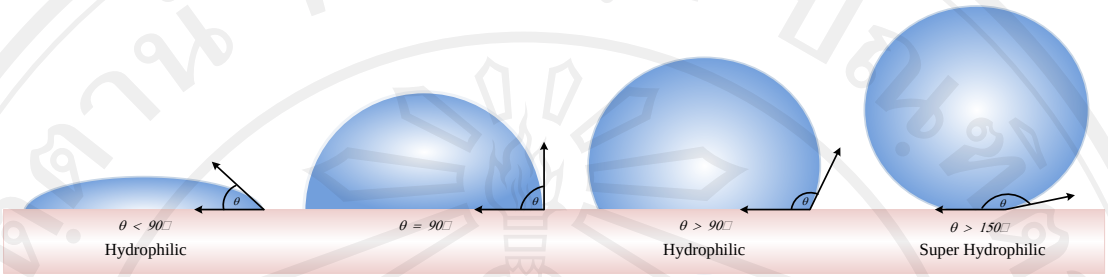


Figure 2.13 Illustration of the contact angle formed by the static liquid drop on the smooth solid surface.

Surface Free Energy

Characterization of surface free energy is critically important for these applications, such as printing, lubricant, coating, adhesion, self-cleaning, biochemistry and biomedicine. These properties used to forecast the new surface modified. The key to understanding the mechanisms of surface-based phenomena is surface-free energy components of solids which thermodynamic quantities are described in the stage of the equilibrium of atoms in the surface layer of materials. It shows the specific stage of unbalance of intermolecular interactions present at the phase boundary of two medium. Surface free energy and contact angle are often used to determine the energy properties of solids. The basic method to find out the surface free energy is Young equation Eq. 2.9 [66]. Moreover, the accuracy of the contact angle measurement depend on the liquid type, drop size, surface roughness, surface physical, surface chemical, surface impurity, Young's modulus, temperature and humidity.

There are no direct methods to resolve the surface free energy of solids. Various indirect methods are used. The Owens-Wendt method is the best one for these studies. The Owens-Wendt method is resolving the component of polar and dispersive component of surface free energy. Static contact angles were used to measure the contact angle and two liquids represented for measurement of the surface free energy,

polar: diiodomethane (CH_2I_2) and bipolar: de-ionised water. The surface energy was calculated using the Owens-Wendt equations [67, 68]:

$$\gamma_W(1+\cos\theta_w)=2\sqrt{\gamma_S^d\gamma_W^d}+2\sqrt{\gamma_S^p\gamma_W^p}, \quad (2.10)$$

$$\gamma_D(1+\cos\theta_D)=2\sqrt{\gamma_S^d\gamma_D^d}+2\sqrt{\gamma_S^p\gamma_D^p}, \quad (2.11)$$

where γ is the surface energy, the superscripts d and p represent the dispersive component and the polar component of the surface energy, respectively, the subscripts W, D and S are the water, diiodomethane and solid components, respectively, θ is the contact angle of the surface energy, θ_W is the contact angle of water, and θ_D is the contact angle of diiodomethane. For water, γ_W = 72.8 mJ/m^2, γ_W^d = 22.1 mJ/m^2, and γ_W^p = 50.7 mJ/m^2. For diiodomethane, γ_D = 50.8 mJ/m^2, γ_D^p = 44.1 mJ/m^2, and γ_D^d = 6.7 mJ/m^2 [69].

Profilometer

Profilometer is the surface profile measurement. This technique is not only used for quantifies the roughness but also wildly used for finding the thickness of the thin films coating. A diamond stylus is moved vertically in contact force on the surface. Fig. 2.14 shows the basic of the profilometer. The profilometer can be measured in the range of 10 nm to 1 μm in high and resolution in the range of 20 nm. It is easy to operate due to the sample is not necessary to prepare. Another advantage is this method is not sensitive to surface reflectance or color like the other light methods because the stylus is direct contact to the surface.

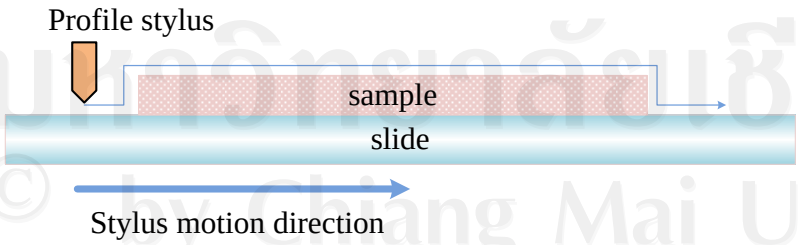


Figure 2.14 The scanning step of the profilometer.

Atomic Force Microscopy: AFM

Atomic force microscopy has been published in 1986 by Binnig, Quate and Gerber [65]. The three dimensional images of the surface can be presented in real time with very high resolution. AFM has been widely used in nanotechnology, biotechnology, biophysics, electrochemical, polymer science and material science. AFM is measured by the interaction of force between the very sharp tip and the surface with the very short distance. It can operate in various environments, such as air, liquid or vacuum. The sample was put on the piezoelectric scanner then scanned in both of X and Y direction by recording the force charge.

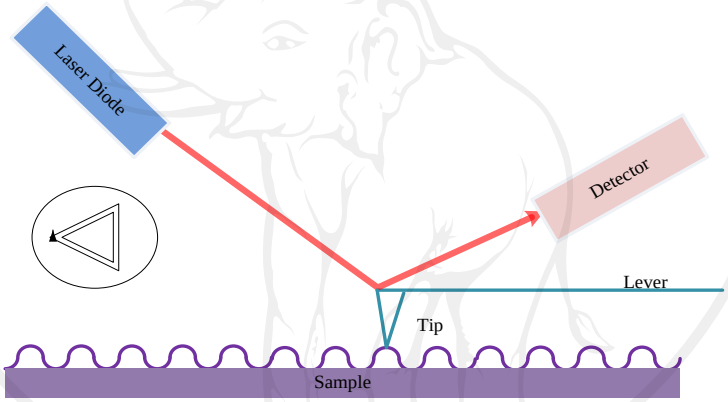


Figure 2.15 The schematic of AFM.

The schematic of AFM is shown in Fig. 2.15. Piezocrystals are ceramic that expand or contact when voltage is applied. The samples will move in three dimensions. The probes represent with a very sharp tip at one end which normally is made from silicon or silicon nitride. The scanning motion is detected by a reflection of the back scatter laser with the cantilever. The reflected laser was focused to the split photodiode which is used to control the height of the piezoelectric base. There are three image scanning modes. Contact mode is the highest resolution which is less than 0.5 nm. The tip scans at a constant low height above the surface while piezoelectric base was moved and recorded its position. This mode not only scans in highest speed and resolution but also damage the surface with tip sample interaction. Non-contact mode is operated in the attractive force region and tip sample interaction is minimized. The low force is exerted

on the surface. Then there is no damage to the sample but this causes low speed and resolution. Tapping mode is used to obtain soft samples, such as biolayers. This mode employs a cantilever with a high amplitude oscillator which once in the vibration period the tip contacted to the surface. The tip only intermittently taps on the surface. This causes less disturb once to the sample surface. The greatest advantage of the tapping mode is the high resolution without damage to the sample surface.

Fourior Transform Infrared Spectroscopy: FTIR

Fourior transform infrared spectroscopy has been used to find the chemical bonding and functional groups of the materials with the infrared adsorption process. The infrared spectra beam was applied to the sample surface. The matter atoms adsorbed the energy to vibrate, causing the chemical bonding and functional group inside. These molecule adsorption spectra related directly with its structure.

Attenuated total reflectance Fourior transform infrared spectroscopy (ATR-FTIR) is one of FTIR that effectivly characterize the biochemical molecules. This mode can be used to analyzed both quantitatively and qualitatively. The main advantage is a no sample preparation and it can analyzed the highly adsorption infrared materials such a polymer with the multiple inner reflections for increase the spectrum intensity (Fig. 2.16). These used only a basic principle of a Snell's law

$$n_1 \sin\theta_1 = n_2 \sin\theta_2, \qquad (2.12)$$

where $n_1$and n_2 are the optical density of each material. θ_1 and θ_2 are the angle of the incident and reflected light are represented. For the total internal reflection occurs when the incident angle is large enough and $n_1 > n_2$ none of the light in the first medium will enter the second medium. The incident angle of the critical angle so normally was 90 degree, which results in

$$\theta_c = \sin^{-1}(n_2/n_1). \qquad (2.13)$$

ATR-FTIR is very simple to operate by first placing the sample in close contact with an internal reflection element. Then the IR beam directly onto the crystal with high reflective index such as germanium, zinc sulfide, safire, diamond or cubic zirconia and the attenuation of the beam occurs due to a small fraction of the total internal reflected

beam penetrating into the lower index reflection medium (sample surface) in a small distance before it is reflected causing transition and longitudinal wave [70, 71].

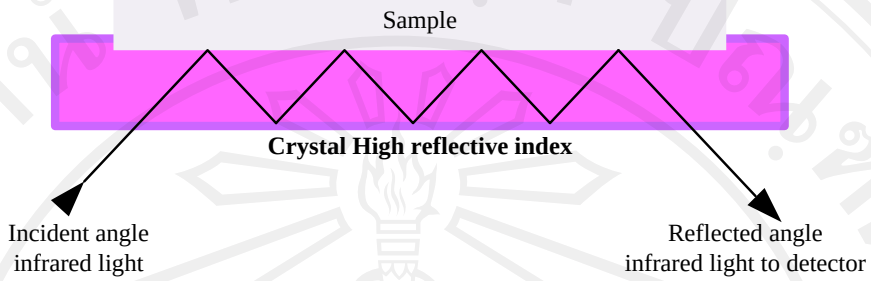


Figure 2.16 The multiple reflections of the highly adsorption infrared materials.

The internal reflectance creates an evanescent wave which extends beyond the surface of the crystal in to the sample (Fig 2.17). The light penetration produces an evanescent wave at the surface if a part of the evanescent wave was absorbed then the attenuation occurs. The evanescent wave and its theory is important because these are related with the penetration depth of the sample. Depth of penetration is defined as a required distance of sample penetration by evanescent waves, which penetration depth per reflection (d_p) is defined by [70, 71],

$$d_p = \frac{\lambda}{2\pi\left(n_1^2 \sin^2\theta - n_2^2\right)} \quad . \qquad (2.14)$$

The different substrates have a difference penetration depth.

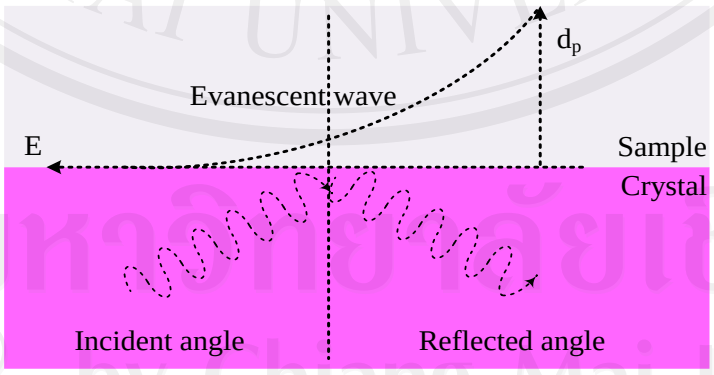


Figure 2.17 The internal reflectance creates an evanescent wave and penetration depth.

X-ray Photoelectron Spectroscopy: XPS

X-ray photoelectron spectroscopy is one of the widely used techniques to characterize the surface [72]. The basic principle is based on the irradiation of the sample surface with x-ray radiation. When the soft x-ray radiations such as Al K_α or Mg K_α impact the sample surface, the photon will transfer the energy directly to the core-level electron of atom of the materials. The detector collected the kinetic energy of emitted electrons to identify the binding energy of core electrons and chemical stage information from the binding energy of valence electrons. XPS can detect elements with an atomic mass more than 3 [53]. The schematic of XPS is shown in the Fig. 2.18. The kinetic energy (E_k) of a photoelectron is

$$E_k = h\upsilon - E_b, \qquad (2.15)$$

where $h\upsilon$ is the photon energy and E_b is the electron's binding energy of sample [65]. The binding energy of a particular shell of an atom can identify the element of matter. The x-ray fluorescence and the Auger electron emission related to the atomic number and quantum shell associated with the original vacancy. When the binding energy of the vacancy is 2 keV or less, an auger was produced. The kinetic energy of a photoelectron is related to atoms of the sample material.

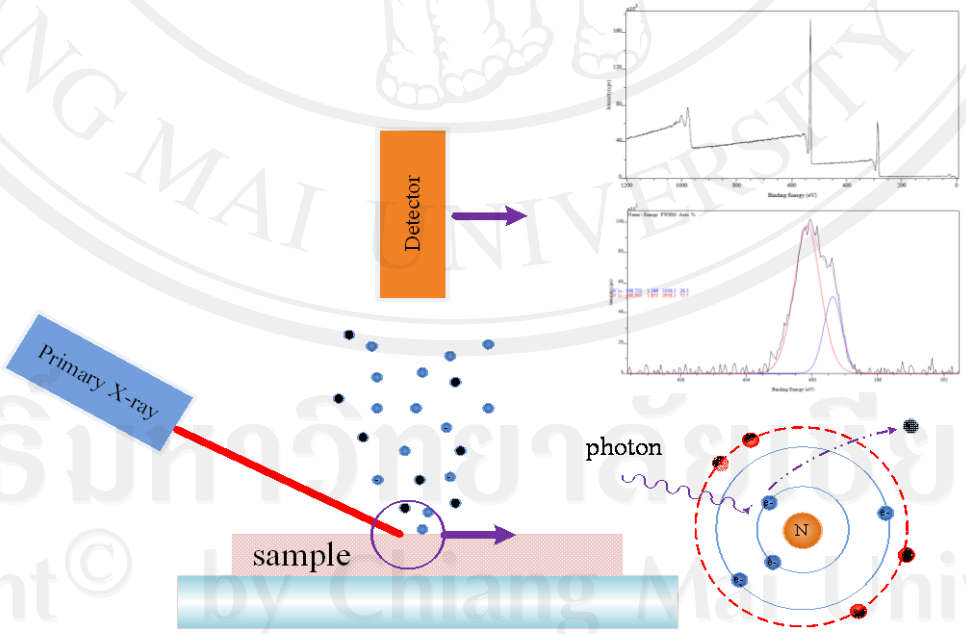


Figure 2.18 The schematic of the XPS.

2.7 Cell-Protein-Biomaterial Interaction

The use of biomaterials increase the trend to incorporate artificial devices into the human body which it has sharply focused attention only onto the compatibility of materials. Moreover, the increasing trend to predict the functions onto their surface is more effective [73]. Given its more function not only repaired damaged functions but also enhanced functions. Solving problems of how to design materials which are maximally compatible with living tissue is a major priority of bioengineering. Understanding of the mechanisms of the cell-protein-surface interaction needs to be studied.

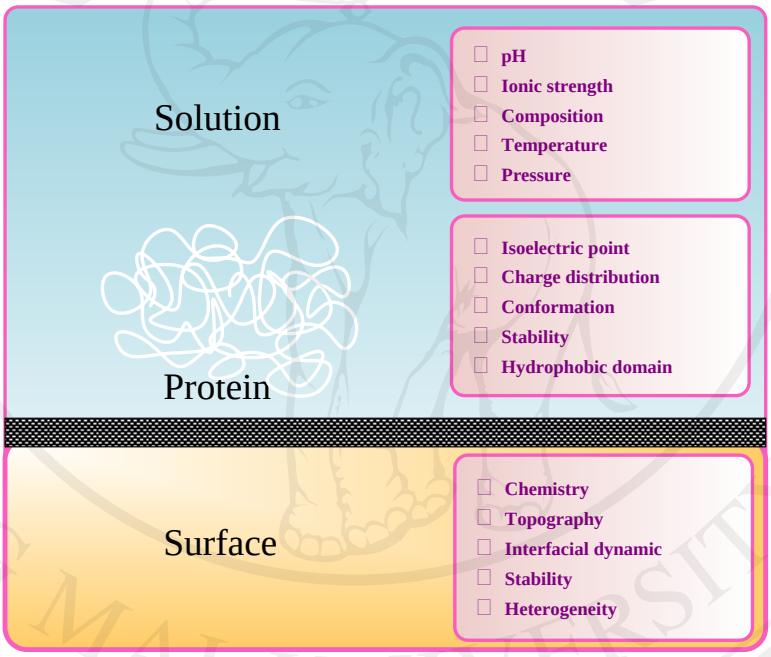


Figure 2.19 The diagram of some factor of the protein, solution and surface that affects the protein adsorption.

The environment of a biomaterial implant is a very complex medium containing various small molecules, ions and different kinds of polymers, such as protein. Moreover, the particular hydrogen bonding pattern of water will affect the other species molecules. The salty nature and warm aqueous give rise to corrosion and wear of materials leading to degradation [66]. In this study, we focus on the surface properties responses and concentrate on the protein-polymer interface due the biomaterials first contact with the blood plasma when it was implanted in to the human

body. Blood plasma is composed of three major proteins: human serum albumin, immunoglobulin and fibrinogen [12]. The proteins in the blood plasma will come in contact with the implanted materials; suddenly the proteins will get adsorbed to the surface. Then the cell attachment protein will take place [74]. After that the cell will attach on the proteins layers. As a result, the protein attachment is the first thing that takes place after biomaterial is implanted into the body. The nature and composition of the first adsorption protein layer is of major importance for the cellular response. This is the main reason for the development of the selective protein adsorption on the biomaterials. We need to understand the competitive protein adsorption. Some researchers studied research from blood plasma or mixture protein, but in this study we will focus on the interactions of albumin protein and biodegradable polymer. The protein adsorption is a very complex process and difficult to predict its quantity. The adsorption process depends on the nature of the protein, the solutions medium and the solid surface which each factor composes with the subsequent protein adsorption process. Fig. 2.19 shows some of factors [75] that affect to protein adsorption.

2.7.1 The Nature of Protein

Proteins are unbranched co-polymers of twenty-two different amino acids of varying hydrophobicity. The structure of protein comprises the polypeptide chain or amino acids sequence (Fig. 2.20). Some of the R groups of amino acid are acidic or basic conferring to the protein molecules an ambivalent character by reason of their differences in polarity; proteins are rendered surface active macromolecules of amphiphilic properties. The protein in three dimensional structures is a result of the interaction with the environment, so the shape of a protein is critical to its function due to the fact that it determines whether the protein can interact with other molecules.

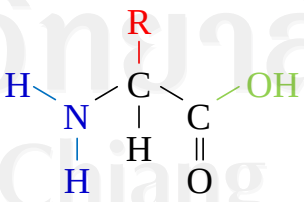


Figure 2.20 The amino acid monomer structure which R is the side chain; different in each amino acid.

As a result of the solution environment, protein folds with conformation change to a secondary structure which classes into globular and fibrous. Globular proteins are compactly folded and coiled and fibrous proteins are more filamentous. Consequently, one needs to understand the four levels of protein structure (Fig. 2.21); primary, secondary, tertiary, and quaternary to determine how the protein gets its final shape or conformation.

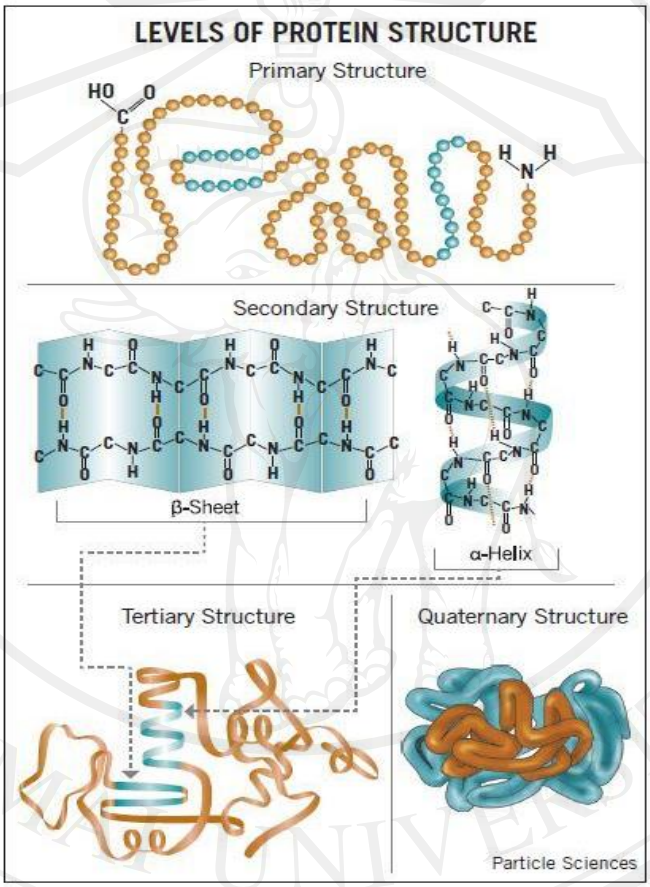


Figure 2.21 The four level of the protein structure [76].

Primary This level of protein structure is the polypeptide chain which forms peptide bonds of amino acids in the protein. The first step is the peptide bonds formed by dehydration reactions of the carboxyl group of one amino acid to the amino group so the polypeptide has a repetitive backbone.

Secondary or proteins conformations depend on hydrogen bonding. There are two main types of the secondary structure: the α-helix and the β-sheet. The α-helix is a

right-handed coiled strand. The side-chain of the amino acid groups in an α-helix that extends to the outside. Then the hydrogen bonds form between the oxygen of the C=O and the N-H group of each peptide bond in the strand of the peptide bond. The β-sheet conformation consists of pairs of strands lying side-by-side. The carbonyl oxygen bond hydrogen bonds with the amino with the adjacent strand; it can be either parallel or anti-parallel depending on the strand directions.

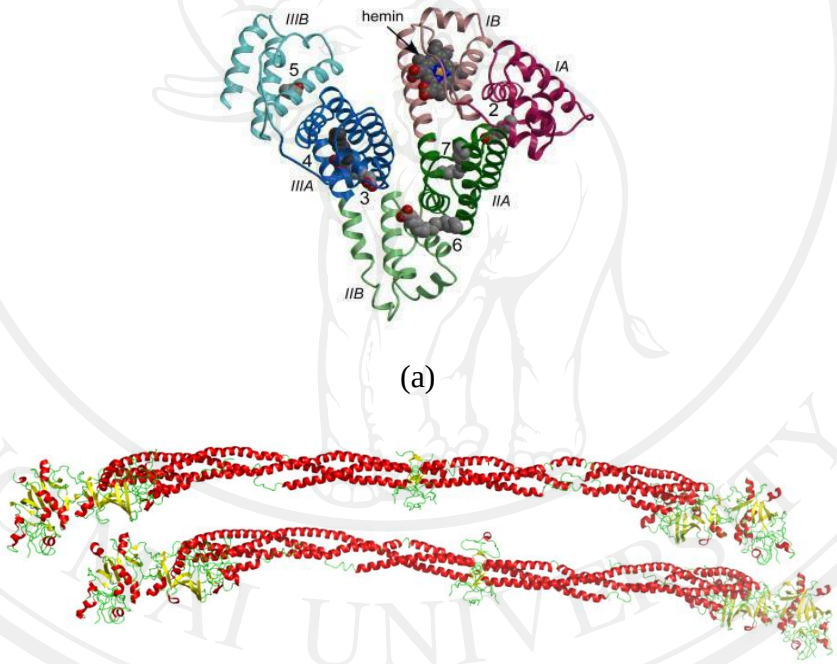
Tertiary The 3-dimensional structure of a protein's polypeptide chain may be locked in place by other stronger bonds. The protein molecule will bend and twist in such a way as to achieve maximum stability or lowest energy state. These bonds are formed between components of the -R groups of the amino acid residues. The types of bonds may include of hydrophobic, ionic, salt bridges, hydrogen or covalent interactions.

Quaternary The quaternary structure refers to how these protein subunits interact with each other and arrange themselves to form a larger aggregate protein complex. Not all proteins have a quaternary level of structure. A protein with a quaternary structure consists of more than one practically identical sub-unit. Its not joined by strong bonds, such as ionic or hydrogen bonds.

Human serum albumin (HSA) and Fibrinogen (Fib) are two of the most important human plasma proteins. HSA was used to study the Fib due to the fact that HSA is believed to act controversially to Fib. HSA is the first protein to contact the implant materials with the smallest and highest concentration in the blood plasma while Fib takes part in blood coagulation, adhesion and aggregation of platelets. HSA was used to block non-specific platelet adhesion and for hemocompatible coating surface [77]. These conditions lead to cell adhesion, which is the reason why these two proteins were selected for this study.

Albumin is the most abundant protein in the human blood serum due to its concentration and ability to bind with other molecules. HSA consists of a single polypeptide chain with contains 585 amino acids that compose a total molecular weight 66,439 Da. The crystalline structures consist of 69% α-helix and 23% β-sheet. HSA is a

globular and extra cellular protein with a heart-shape and is the smallest plasma protein with dimensions of 9.5 nm x 5 nm x5 nm (Fig. 2.22-a) [78]. Albumin has a highly polar nature and dissolves easily in water. HSA has Ip of 4.7-5.3 [12] which in the electrolyte solutions, the HSA molecule exhibits amphoteric properties. Its effective charge can be varied by pH on regular positive for pH < 4.7 and negative for pH > 5.3. Therefore, in blood plasma (pH 7.4), albumin has a negative charge; this gives a vast capacity for nonselective binding of other ligands. The HSA molecule exhibits quite an analogous chemical structure and composition to bovine serum albumin (BSA). As a reason, BSA was used as a model of HSA. BSA is in the heart shape with the molecular weight of 66,411 Da, Ip 5.1 and comprises of 583 amino acids [38].



(a)

(b)

Figure 2.22 The schematic of protein structure of (a) HSA [79] and (b) Fib [80].

Fib is the protein found in blood plasma which is formed by three different cross-link chains; α-helix, β-sheet and γ chain. They contain a domain of 225 amino acids polypeptide chain that composes a total molecular weight 340 kDa. Fib has an elongated shape (Fig. 2.22-b) and a larger size plasma protein with dimensions of 45 nm

x 9 nm x 6 nm [81] with the Ip 5.5-5.8 [12, 82]. Fib is an acute phase protein that is part of the coagulation cascade of proteins. The end result of the cascade is the production of thrombin. The insoluble fibrin aggregates and the aggregated platelets then block the damaged blood vessel and prevent further bleeding. However, these properties of both proteins may lead to unwanted effects, such as the irreversible protein adsorption which brings the biofouling of implantable biosensor, or the adhesion of clotting to promote or prevent the formation of thrombus at the site of the foreign.

Table 2.1 The properties of three main blood plasma protein [83].

Properties	*HSA*	*IgG*	*Fib*
Function	Carrier	Antibody	Clotting
MW (kDa)	66	160	340
% in blood	50-60	15-25	5
Shape	Heart shape	Y shape	Long fibrous
Secondary structure	Globular	Globular	Fibrous
Isoelectric point	5.4	6.1	5.5
Diffusion constant (cm^2/s)	6-8 x 10^{-7}	4 x 10^{-7}	3 x 10^{-7}
Protein type	Soft protein	Soft protein	Hard protein

2.7.2 The Theoretical Descriptions of Protein Adsorption

The adsorption of the protein onto the surface in an aqueous environment is crucial for biomaterial. The compactness of protein structure is the cause of hydrogen bonding, covalent bonding, ionic interactions, hydrophobic interaction and salt-bridges. The hydrophilic or charge polar is a charge at the side chains as acidic ($-COO^-$) and amino acid (NH_3^+). Charge groups are removed by water. The neutral polar is a side chain group, such as –OH, -SH, NH or C=O that can participate in hydrogen bonding with water molecules. Hydrophobic or non polar is hydrocarbons do not have any groups which can participate hydrogen bonding with water molecule. Fig. 2.23 shows

an ambivalent character of protein structure in an aqueous system, hence the structure comprises patches of hydrophilic, hydrophobic, positive charges and negative charges. Proteins carry electrostatic charges with both positive and negative on them.

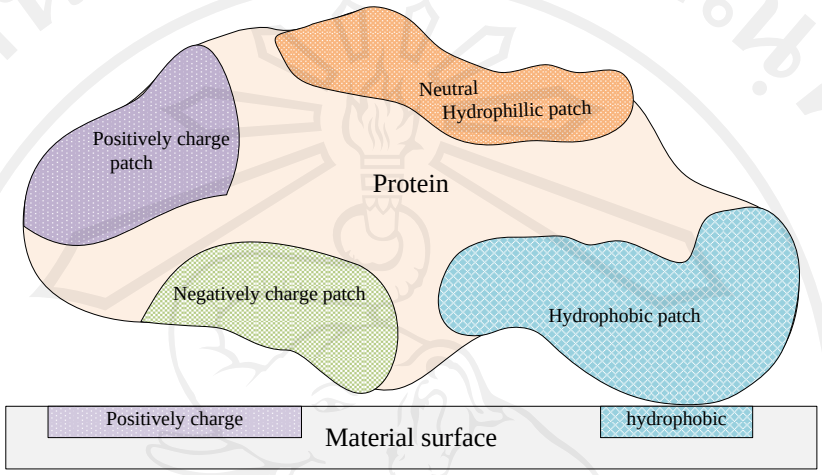


Figure 2.23 The protein adsorbed by different mechanisms on different surfaces properties via orientation and conformation.

The net charges of structure depend on the pH of the solution related to the isoelectric point (Ip) of each protein. These are directly related to the protein stability which each protein contains the difference of the amino acid protein. The proteins have a low internal stability that some call soft proteins and the others are called hard proteins. Consequently, the protein is adsorbed by different mechanisms on different surface properties via orientation and conformation [84, 85]. Some proteins adsorb with the protein net charge, charge distribution and decay length of electrostaticity between the protein and surface. Some proteins are less affected by electrostaticity than by hydrophobicity, the natural hydrophilic patch trends to be relatively weak with adsorption with reversible to the hydrophilic surface. On the other hand, the hydrophobic patch adsorbs on to the hydrophobic surface with the strong bond and is often partially irreversible [86]. The large conformational changes adsorption are soft proteins and hard proteins strongly affected by electrostatics. The general rule of thumb is the proteins prefer to adsorb onto the hydrophobic surface rather than the hydrophilic surface (Fig. 2.24) due to the former in that environment no or less electrostatic charge.

Some studies reported adsorbed BSA on the polymer surface that the protein adsorbed by the hydrophobic interaction and hydrogen bonding (ionic and Van der Waal interaction). Moreover, the other found that increasing hydrophobic lead to increasing BSA adsorption with the ionic strength.

Considering the protein adsorb with large affinity, the fact that it reflect the minimum free energy when adsorbed. Particularly, the adsorption process can be divided into three steps [87]. During the first step, molecules are transported from the liquid to the surface by convective motion. However, if the molecules are closer from the surface than 10 μm the diffusion motion will dominate. Hydrophilic force is the longest range which appearance the highly ramification hydrogen bonding network in liquid water under the typical length about 1 nm. The length depends on other effects on the surface roughness and solvent polarization.

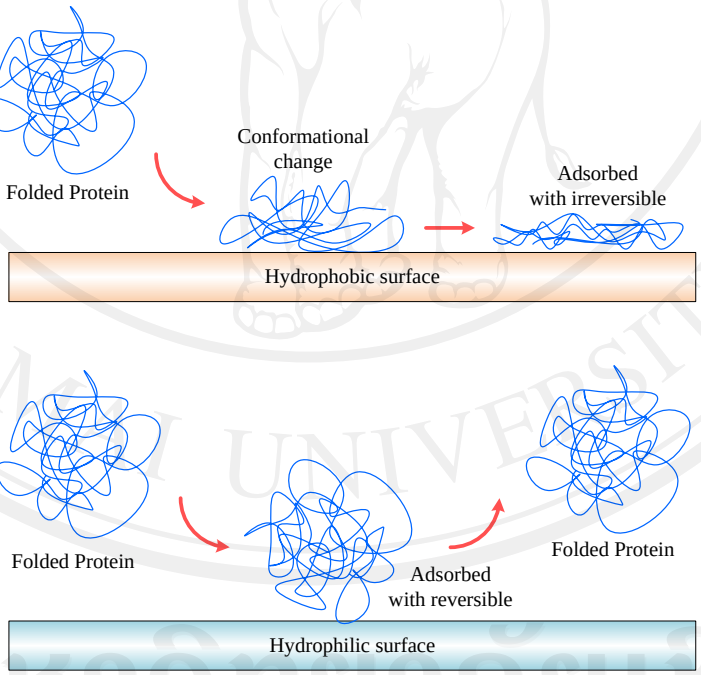


Figure 2.24 The effect of the protein adsorption on the different surfaces properties.

Next, the electrostatic force will be achieved. In the solution, the ions are present, after which the electrostatic force will be present with a characteristic length. The van der Waals interaction is even more short-ranged, which is very important in the

protein surface interaction. An initial of protein attachment occurs followed by a detachment or a relaxation process. The protein adsorption is often adsorb irreversibly but desorption can also occur. Relaxation processes occur after adsorption with following steps by diffusion, desorption and conformation change. Moreover, the adsorption may even lead to denaturation of the protein.

Finally, for complex solutions, such a blood plasma, the adsorption process will be more complicated; while the small and abundant molecules will be the first forming layer to be attached on the surface, over time, this layer may be displaced by other proteins, typically with a higher molecular weight. This phenomena is known as the Vroman effect [12, 74, 88], which was developed by Leo Vroman. "The physical reason behind it is the fact that the fastest diffusing proteins are not necessarily the ones with the highest affinity for the surface. Thus for longer times, slower diffusing proteins with higher affinity for the surface may arrive in the vicinity of the surface and replace the already adsorbed proteins" [87].

There are four classes of the interaction in the protein adsorption: ionic or electrostatic interaction, hydrogen bonding, hydrophobic interaction and interaction of charge transfer.

Interaction of Charge Transfer

Charge transfer interactions are important in protein stabilization and surface interaction. In aqueous media, the donor acceptor processes are donated to an electrophilic species, these interactions primarily due to pi orbital electron effects

Hydrogen Bonding

The hydrogen bond is a special case of dipole forces. A hydrogen bond is the attractive force between the hydrogen attached to an electronegative atom of one molecule and an electronegative atom of a different molecule. Usually the electronegative atom is oxygen, nitrogen, or fluorine. In addition, the hydrogen on one

molecule attached to O or N that is attracted to an O or N of a different molecule due to oxygen has two lone pairs and combinations with other.

Ionic or Electrostatic Interaction [89]

The net charges of the protein are the sum charges of its constituent. The charge of proteins is specified by the pKa of its amino acid side chains and the terminal amino acid and carboxylic acid. Groups with pHs above physiologic conditions have a positive charge and groups with the logarithmic constant pH below have a negative charge. These effects are short range due to the high dielectric constant of water. However, when the protein is close to a charged surface, electrostatic coupling becomes the dominant force. The ionic bonds are formed when positively and negatively charged ions are held together by electrostatic forces as well as the covalent bonding where electrons are shared equally. Therefore, partially ionic and partially covalent character bonds are called polar covalent bonds.

Hydrophobic Interaction

Hydrophobic interaction is the relation between water and low water soluble molecules or non-polar molecules. Hydrophobic interactions are basically on entropic interactions due to order or disorder phenomena in an aqueous medium. The hydrophilic groups on the outside of the molecule result in protein water solubility this phenomenon can be give explanation by hydrophobic relationships with interfacial free energy. As a result, the driving force of these interactions as the minimization of total interfacial free energy. The free energy related with minimizing interfacial areas is responsible for minimizing the surface area of water droplets and air bubbles in water. There is the same principle of hydrophobic amino acid side chains oriented away from water which minimizes their interaction with water [90, 91].

The Chemical and Physical Attributes of Biomaterial Surfaces

The simple idea of the protein adsorption is the chemical function of the protein interaction with surface. Other than that, the current debate is the positively

ionized groups, such as the amino group on the surface, should strongly adsorb protein with an excess, such as hydrophobic patches and aspartic acid residues [66]. When the protein is adsorbed onto the surface undergo with more or less drastic conformation changes. The hydrogen bonding is driving the protein exchange structure to bonding together to the surface. The adsorption is no significant change of enthalpy H but the exchange and conformation are increased the entropy S, according to the Eq. 2.16. The overall free energy of the adsorption ΔG will be negative.

$$\Delta G = \Delta H - T\Delta S \tag{2.16}$$

The potential interactions of the materials surface with their environment are determined by the energy. The interaction energy of the surface can be expressed by the surface tensions with the atom and molecule. The interfacial free energy [85] ΔG is the sum of cohesive energy of the liquid and their surface interaction, from which adsorption is the result of their energy as shown in Eq. 2.17. The energy of the material 1 was in the presence of the liquid medium 2 and the living mater 3. The ΔG of each term in the equation is summarized of the Lifshitz-van der Waals, electrostatic and Lewis acid base interaction. In the aqueous system, the dominant contributions of the hydrogen bonding demonstrated by the Lewis acid base interaction has the most effect on the total energy. Nevertheless, van der Waals interactions are ubiquitous but weak.

$$\Delta G_{123} = \Delta G_{13} + \Delta G_{22} - \Delta G_{23} - \Delta G_{12} \tag{2.17}$$

There are not only chemical effects to the protein adsorption, but also the physical attributes of the surface roughness are a response to protein and cell adsorption. The surface modification includes random roughness, gratings or isolated bumps in which the effect will be dependent on the interplay between the length scales characterizing the roughness and the adsorbing molecule. When the roughness is increased to a significant value two factors are important to consider. First is an increase in surface area that is related to the molecules size during the adsorption process. However, the conformational entropy plays a significant role for the adsorption. They are not solely controlled by energetic effects. Second, changing roughness may change the potentials of the surface such as the van der Waals interaction. This force is very

dependent on the geometry of the interacting entities. In the case of adsorption on a flat substrate, it can be described as a sphere interacting with an infinitely large plane to a good approximation other than the case of a rough film, which may be more appropriately described by the interaction of two spheres. In addition, the electrostatic force and the hydrophobic interaction will also depend on surface roughness. The changing of roughness will be concerned with chemical homogeneity and affect to the protein adsorption [87].

2.7.3 The Cell-Surface Interaction

Growing demand in biomaterials for tissue engineering is leading to new possibilities for design and fabrication of materials with tailored properties. Basically, biomaterials are designed to promote the organization, growth and differentiation of cells to forming functional tissue. The biodegradable polymer, such a PLA, is widely used in biomaterials due to its outstanding properties; however, the biocompatibility does not have enough biofunctionality to be of much interest. In the case of the implantation, the blood plasma proteins, small molecules and ions will come in contact with the implanted materials. Rapidly, the proteins will get adsorbed to the surface. Then for a longer time this layer will be displaced by a higher molecular weight. The cell adhesion peptides or extracellular matrix (ECM) proteins, such as collagen, selectins, integrins or fibronectin will be replaced on the surface. Finally, the cell will attach onto the protein layers, leading to proliferation and differentiation. That is why the nature and composition of the first adsorption protein layer is a major importance for the cellular response. The bioactive surface having optimal performance can provide high binding capacitive molecules, prevent denaturation and anti-biofouling. The background of the anti-biofouling are provided by the hydrophilic and bioinert [11]. An increased hydrophilicity of the polymer as a cell substrate leads to increased cell attachment and higher proliferation rates of the cultured cells. As a result, a characteristic of the substrate surface is the hydrophilicity or wettability.

For example, as shown in the Fig. 2.25, the blood plasma proteins can be adsorbed with irreversibly bound to a hydrophobic surface through the dehydration of

the interface and the undergo conformation changes on hydrophobic patch at the surface substrate. Then higher molecular weight proteins, such as integrins and ECM (fibronectin, vitronectin, collagen) cannot be replaced on the surface thus cell cannot attachment. On the other hand, the blood plasma proteins can be adsorbed with reversible bond onto the hydrophilic surface the cell adhesion proteins (higher molecular weight) can be replaced easily and enhance cells attachment and proliferation [17, 66, 90, 92].

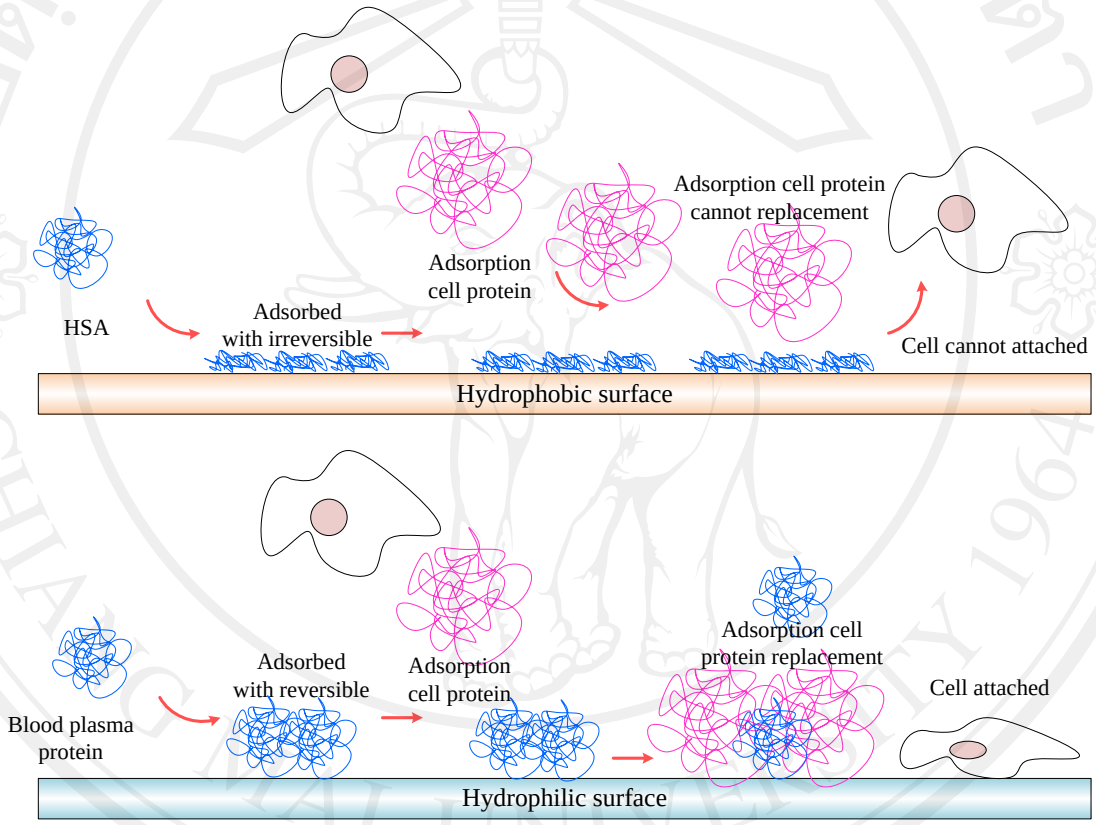


Figure 2.25 The protein and cell attached on the different surface.

Moreover, it has been found that the response of the cell is cell type specific and roughness dependent. The surface topography of the substrate can determine the response of cells which are typically 10-100 μm in diameter. In common, increased surface roughness is associated with decreased proliferation and increased differentiation of the cells. It was found that osteoblasts and bone marrow cells preferably attach onto and proliferate onto rougher surfaces while fibroblasts and epithelial cells prefer smoother and extremely smooth surfaces [4].