

# Plasma Irradiation of Polymers: Surface to Biological Mitigation



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**Abstract** Development in science and technology has made human life much simpler, but evolution and progress of time as well as increasing human demand have generated problems related to energy, health [1], etc. Progress in science and technology is trying to solve these issues to make the human life more comfortable. Growing requirement of biomedical devices, replacement of body parts after their failure, body implants [2, 3], bio-separation, sterilizations [4, 5], biosensors, etc. [6, 7], have shown need of development of advance smart materials (biomaterials). The choice of any material to be used as biomaterial/biomedical applications [8] depends on physical, chemical, surface, and biological properties, i.e., the presence of functional groups, surface free energy, hydrophilicity, surface morphology affects use of any material as biomaterial [9]. In other words, materials having high bio-adoptability and biocompatibility can only be used as biomaterials [10, 11]. Polymers arise as a suitable alternative of conventional biomaterial from last few decades, for synthesis of important biomaterials in modern manufacturing processes as they offer wide varieties of physical, chemical, biological, mechanical, and elastic properties with good processability. None of the normally available polymers possess surface and chemical properties required for many of biomedical applications. Nanomaterials and low-temperature plasma processing offer a novel route for surface and chemical modification in controlled manner without affecting their bulk properties [12]. Plasma processing can be utilized in various pathways to control the desired properties of modified materials, makes plasma so important that we can say “Plasma will future: Plasma for mankind.” Present work shows efficient

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and relevant route for synthesis of nanobiomaterials using nanotechnology and plasma processing to fabricate biomedical devices for biomedical applications [13].

**Keywords** Plasma irradiation • Polymers • Biomaterials • Biomedical applications

## 1 Biomaterials

Any substance/material (other than a drug) or a combination of substances/materials, synthetic [14] or natural [15] in origin that can be used for any period of time, as a whole or part of a system which treats, augments, or replaces any tissue, organ, or function of the body is known as biomaterials [16]. They are nonviable materials used in biomedical devices, intended to interact with biological systems [17, 18]. If the word “nonviable” is removed from the definition, it becomes even more general and can address tissue engineering and hybrid artificial organ applications where living cells are used [19]. These materials can be classified into several categories on basis of their use. Most common classification consists of two parts: body implants and medical devices [20].

Body implants are generally made from one or more biomaterials that are intentionally placed as a substitute for biological system within the body, totally or partially buried beneath the surface and usually intended to remain there for a significant period of time like artificial skin, lenses for eye, bone cement, intraocular lenses, contact lenses, dentures, adhesives, artificial hearts, hip joint, knee joint [21]. While medical devices refer instruments, apparatus, implement, machine, contrivance, in vitro reagent, other similar or related articles intended for use in diagnosis, cure, mitigation or treatment of disease or other conditions do not depend on being metabolized or being part of chemical action within or on the body [22–26]. In other words, medical devices generally involve materials, tools, or devices that are not directly used in biological systems but are equally important in many of biomedical applications like fabrication of blood storage bags, tubes for various catheters, blood pumps, syringes, arterial tubules, surgical sutures [27]. Figure 1 shows various parts of the human body. Artificial materials that simply are in contact with the skin, such as hearing aids and wearable artificial limbs are not included in our definition of biomaterials since the skin acts as a barrier with the external world. So biomaterial can be internal or external material; but the subject cannot be explored without considering biomedical devices and the biological response to them, i.e., for both cases, materials must be bio-adoptable and bio-

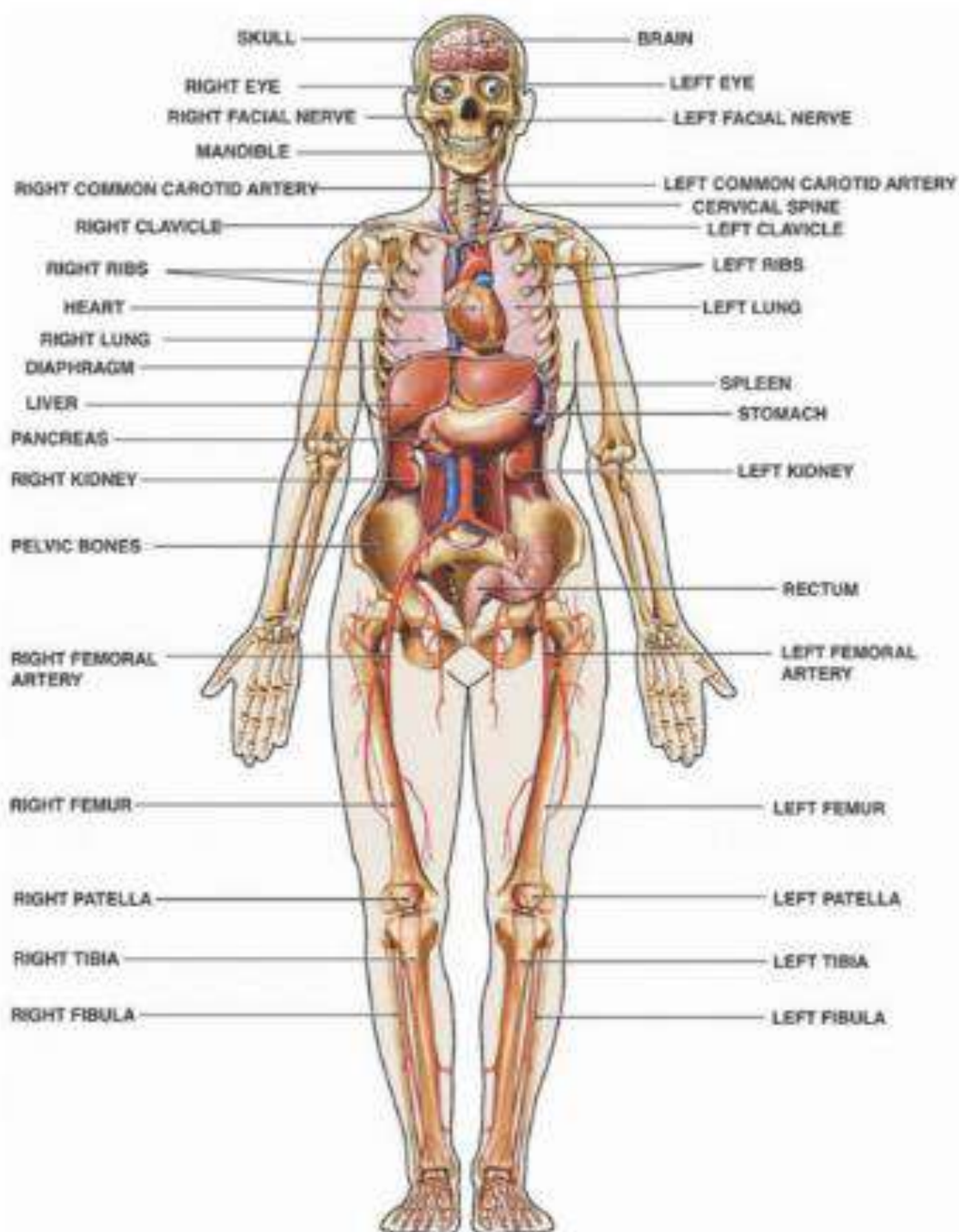


Fig. 1 Schematic representation of various parts of the human body and implants

surfaces with proteins and cells are also important. Control of surface properties and chemistry not only modulates cell attachment but also cell spreading, which is important as it affects cell division [30].

## 2 Polymers

Exciting chemical, mechanical, elastic properties, lightweight, flexibility, and easy processability that can be varied drastically in various polymers had made them widely useable materials in modern manufacturing processes [31]. These vast ranges of properties of various polymers are increasing their applicability in numerous fields starting from fabrication of materials used in daily life to some advanced applications like gas filtration [32], bactericidal properties [33], electrical [34], optical [35], mechanical applications [36], organic solar cells formations [37], biomaterial, and implant fabrications [38]. During the last 20 years', polymers have received fabulous interest for synthesis of biomedical devices and continuously replacing all conventionally available biomaterials, as physicochemical properties of the surface of polymers (like surface free energy, hydrophilicity, and surface morphology) influence cell-polymer interactions that make them widely useable material for synthesis of advance biomaterials, bio-devices, and biosensors.

Thousands of natural and synthetic polymers are available around the world, and polymer reaction engineering makes it very easy to synthesize various kinds of polymers with desired physicochemical properties [43, 44]. Depending on the properties, mechanical strength and chemical structure/functionality, these polymers can be used for synthesis of various biomaterials and implants (Table 1).

**Table 1** Polymers and their applications for fabrication of biomaterials and implants [14, 39–41]

Polymers	Biomedical applications
Polyethylene	Tubes for various catheters, hip joint, knee joint prostheses
Polypropylene	Suture materials, hemodialysis, blood transfusion bags
Polytetrafluoroethylene	Vascular and auditory prostheses, catheters, tubes
Polycarbonates	Hard tissue replacement

## 2.1 Polymethyl methacrylate (PMMA)

Poly(methyl methacrylate) (PMMA)/methyl methacrylate resin/polymethyl 2-methylpropenoate (IUPAC name) is a transparent thermoplastic polymer normally used as a shatter-resistant alternative to glass. It is also well known as acrylic glass ACRYLITE<sup>®</sup>, Lucite, Perspex, Optix (Plaskolite), Oroglas, Altuglas in scientific community based on its properties and uses. Chemically, it is the synthetic polymer of methyl methacrylate. Industrial production of PMMA is carried out by emulsion polymerization, solution polymerization, or bulk polymerization techniques. A bisphenol group available in PMMA also makes it an economical alternative to polycarbonate (PC) with high degree of flexibility [45, 46].

Excellent properties, easy handling and processing, low cost, high impact strength, more prone to scratching make them suitable in various applications. Various modifications applied to PMMA through polymer reaction engineering offer very high scratch and impact resistance to PMMA for ex. addition of butyl acrylate or plasticizers in very small amount and improve its impact strength [47].

Various physical and chemical properties of PMMA are listed in Table 2, and its chemical structure is shown in Fig. 2 [48]. It allows 92% transmission of visible light with only 4% reflections. Its refractive index is 1.4914 at 587.6 nm and can also filter ultraviolet (UV) light at wavelengths below 300 nm (similar to ordinary window glass). Adding/coatings with various organic and inorganic additive

**Table 2.** Chemical and physical properties of PMMA [47]

Molecular formula	$(C_5O_2H_8)_n$
Molar mass	Varies
Density	1.18 g/cm <sup>3</sup>
Melting point	160 °C (320 °F)
Refractive index (nD)	1.4914 at 587.6 nm
Reflectance	$R = 0.03890$ at 587.6 nm
Brewster's angle	$\theta_B = 56.158^\circ$
Molecular weight (MW)	100 g/mol
Glass transition temperature ( $T_g$ )	105 °C (221 °F) [varies from 85 to 165 °C (185–329 °F)]
Coefficient of thermal expansion	$(5-10) \times 10^{-5} K^{-1}$

At these scales, materials show completely different properties compared to their bulk counterparts [51], even intrinsic properties of material such as band gap, color, crystal structure, mechanical, catalytic, optical, chemical, and magnetic properties of materials get modifies. Field and scope of nanotechnology include all branches of science even in day-to-day life of living beings. Nanoparticles, can be called building blocks of nanotechnology, are of great scientific interest as they effectively bridge between bulk materials and atomic or molecular structures. Nanoparticles exhibit remarkably improved physical, chemical, and biological activity that enhances their uses in various applications. Also, biomaterials in contact with biological body have optimal combination of mechanical properties and surface characteristics that result superior performance in biological environment [52–54]. Nanomaterials can be used for biological/biomedical applications for fabrication of biomaterials, having superior surface properties like low surface energy, hydrophilicity, specific surface morphology, higher cell/protein adhesion, and antibacterial activity. Many of these properties are directly used or being explored for their possible application in the synthesis of advanced biological materials, biomedical devices and implants such as artificial skin diaphragm, valves for heart, kidney, lenses for eye, and other biomedical fields so that they can positively/negatively affect cell to material interactions.

From past ten years', various metal and metal oxide nanoparticles (NPs) are used or being explored for biomedical applications such as gold NPs for cancer treatment, Cu NPs as good antibacterial agent, ZnO NPs for protection from UV light, Ag NPs for affecting growth mechanism of plants, TiO<sub>2</sub> NPs for degradation of biomass. In present study, we have used Ag (Fig. 4) and TiO<sub>2</sub> NPs for enhancement of properties and applications of biomaterials [19, 55–90].

## 4 Polymer—Nanocomposite

Nanocomposites are combinations of materials in which at least one of the phases having dimension in nanometer range. They can, in principle, be formed from clays and organoclays in a number of traditional methods including various in situ polymerization [91], solution and latex [92] methods, mechanical agitation, ball milling, ultrasonic vibration, shear mixing, non-contact mixing, [34]. Investigations performed on these materials have indicated that they exhibit improved and sometimes new possessions that are not displayed by the separate phases or conventional composite complements [93]. Incorporation of nanomaterials/

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nanocomposite. Since last few years, polymer nanocomposites give new alternative to conventional filled polymers and materials for synthesis of biomaterials.

## 5 Plasma Surface Modification

Plasma, the fourth state of matter, is known as ionized gases having neutrals with almost equal number of ions and electrons. A more precise definition is that plasma is a quasi-neutral gas of charged and neutral particles exhibiting collective behavior. It is the most wonderful fact about the plasma that the stars and the tenuous space between them of the visible universe make up more than 99% with plasma and perhaps most of which is not visible, even not fully explored. The plasma contains energetic species like atoms, molecules, ions, radicals, electrons, neutrals, dust/charge particles, and photons. Hence, interaction of plasma with various materials leads to interaction/bombardment of energetic particles on to the materials. These bombardments stimulate the productions of outgoing fluxes of neutrals, ions, electrons, radicals, and photons leading to modification/irradiation/treatment/etching of surface layer for modulation of physical, chemical, and biological characteristic that becomes basis for plasma-enabled material processing [117–121]. Figure 5 shows the PMMA surface after plasma treatment.

Plasma-based processing of materials becomes widely acceptable in all branches of science and technology [111, 122–124]. Wide range of dynamic applications of the technique starting from fabrication to processing makes it most powerful



technique even some time it is neither purely physical nor chemical. It offers desired pathway for materials processing depending on the application of material. The plasma modulation technique precedes a number of subtractive and additive processes in a selective manner for highly controlled nanomachining, uniformity, surface quality, and profile control. Based on modification techniques, it also has variety of advantages such as fewer disposal problems, modifications carried without use of chemicals/rinsing, less corrosion and material failure, less undercutting, high-speed fabrication, cleaner resulting surfaces [125].

Plasma can be produced by electron separation/ionization from atoms/molecules in the gaseous state. When an atom/molecule gains enough energy (higher than ionization energy) from any source that makes interaction (collisions) with another atom/molecule, ionization occurs. Under favorable conditions, these ionizations can be enhanced to produce sufficient breakdown to satisfy the plasma conditions. Based on the conditions to create breakdown, many kinds of plasma sources are available commonly known as gaseous, metallic, sputtering, dry etching, and laser-based plasma sources. The sources used for plasma productions for material processing and applications have characteristic difference in plasma parameters such as electron temperature, ion temperature, electron/ion density, electron/ion energy, state and uniformity. These plasma parameters can be modulate/controlled or depend on gas pressure, type of gas, gas composition, gas flow rate, type of plasma (DC/RF), particle density, electric field strength, electron velocity, electron current, strength of magnetic field, and distance between anode and cathode. Each of these experimental conditions can drastically affect the plasma parameter to be used in various plasma-based processing by ion and electrons such as reflection, physico-absorption, surface migration, surface damage, heating, material ejection, sputtering, ion etching, ion implantation, doping. These various plasma parameters and experimental conditions for creating and maintaining plasma make its nature very amazing. Below we have listed several other regions which can further increase superiority of plasma and their effects that can be used in plasma-based processing and applications:

1. Electrons in plasma can extract energy form electric and magnetic fields.
  2. Kinetic energy of electrons can be converted into space charge electric field and thermal energy [126].
  3. Plasma-based processing does not require any type of confinement even some
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and other gas ions. Due to inert nature of Ne gas, they cannot produce any type of chemical reaction on the material surface but Ne ions have sufficient energy to produce ion etching or sputtering totally controlled by impact of incident ions. The process is inherently non-selective due to widespread in ion energies compared with different surface bond energies and chemical reactivity. The modification (based on inert ion) is generally slow compared to other gases used for modification (with the etch rate of few ten angstroms to few hundred angstroms per minute). These types of modifications are used to form facets, ditches, hourglass-shaped trenches, removing of various damage, device complexity, and re-deposit materials with high aspect ratio. When ions of sufficient energy are used, they can produce high sputtering rate of materials and weight loss. Such weight loss is generally restricted to the topmost layers of the polymer, without affecting the inner layer. Ne gas plasma can create new surface morphology and improve the hydrophilicity and wettability on polymer surfaces.

### ***6.3 Reactive Gas Nitrogen ( $N_2$ ) and Its Properties as a Source of Plasma***

Nitrogen is diatomic, colorless, odorless gas with high reactivity at standard temperature and pressure. It is a common element of solar system and most abundant in atmospheric gases. It has atomic number 7, atomic weight 14.007 amu, electronic configuration [He]  $2s^2 2p^3$ , melting point 63.15 K, boiling point 77.35 K, hexagonal crystal structure, and density 1.251 g/L. Its first, second, and third ionization energies are 1402.3, 2856, 4578.1 kJ mol<sup>-1</sup>, respectively. It is used to make many industrially important compounds such as ammonia, nitric acid, fertilizers, and organic nitrates. Organic nitrates such as nitroglycerin and nitroprusside are used to control blood pressure by metabolization. Chemically it shows high electronegativity in reactions and makes strong bonds. It is also found in various organisms primarily in form of amino acids, proteins, and nucleic acids (DNA and RNA). A human body contains about 3% nitrogen by mass (fourth most abundant element in body after oxygen, carbon, and hydrogen). It is considered as a great source of energy production at Sun/stars in form of carbon nitrogen cycle.

For plasma processing of materials, nitrogen is extensively used for more than four decades, due to its easy availability and relatively easier plasma production ability. First application of nitrogen plasma was nitriding of high-carbon steels, titanium, aluminum, and molybdenum. This is a process where nitrogen will diffuse inside the materials in form of ions to form their nitrides that prevent material

further absorbed there to react with the surface material and end reaction products leave surface by desorption if it is volatile. From the listed steps those occurs in gas phase are termed as homogeneous reactions while those occurs at the surface of material are termed as heterogeneous reactions. Radical-based modifications are generally chemical in nature; hence, they are also selective for different materials or gas used for processing. As oxygen plasma removes photoresists by oxidizing hydrocarbon material, fluorine is used for silicon etching. Aluminum makes volatile chlorides while aluminum fluorides are nonvolatile. If plasma is used for processing of polymeric material using  $F$  radicals,  $F/C$  ratio controls the type of processing, as for  $F/C > 3$  etching is dominant and for  $F/C < 2$  polymerization takes place.

## 7 Biocompatibility and Bio-adoptability (in General and Properties Required)

In past few decades, advancements in science and technology focused on animal health and related issue to make it more and more comfortable. In this consequence, huge scientific efforts and interdisciplinary research are going on for development and fabrication of advanced materials those can be used for replacement of body parts after their failure. The synthesized materials have to be used for various applications like fabrication of body implants, biomedical devices, bio-separation, sterilizations, biosensors; hence, they must have specific surface and bulk properties that should not produce any deleterious effects, failure of material, or formation of unusual tissues. It must be noted that the synthesized materials are foreign materials to biological body, and normally, biological bodies do not accept foreign materials very easily till they shows superior biological response. Material that has to be used as biomaterial must show superior biocompatibility and bio-adoptability while retaining high-performance physical, chemical, and mechanical properties to fulfill other requirements [13, 128, 153].

Phenomena of biocompatibility and bio-adoptability are very similar to each other. Biocompatibility defines ability of a material to perform appropriate host response in a specific situation or in contact with biological system [157]. Hence, biocompatibility phenomena investigation involves the process where biological response of materials is tested using various components (like blood, DNA, protein)

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compatibility with overall system must show high porosity). Hence, any material and its property that may be suitable for synthesis of one class of biomedical devices/implants may not be suitable for other applications and produce challenge in the field of biomedical devices fabrication. Below is the list of few class and group of properties those are generally required for all kind of biomaterials in various forms (low/high/positive/negative effect) other than normal physical, mechanical, and chemical properties, as decided by international biological, medical boards, and scientific communities [65, 158–164]:

- Antibacterial and antimicrobial properties
- Toxicity
- Ecofriendly nature
- Wettability
- Micro-patterning
- Biological response to foreign materials
- Strong adsorption of proteins by surface
- Chemical functionality
- Cross-linked films formation irrespective of surface energy and geometries
- Adhesion
- Porosity
- Cell/tissue adhesion and compatibility
- Blood compatibility.

It is very easy to find a material with appropriate chemical, physical, and mechanical properties required for fabrication of biomedical devices/implants, but in general no natural/synthetic material or polymer possesses the surface interface and biological properties needed for various biomedical applications or in other words "any material/polymer do not have inherent properties (like surface energy, hydrophilicity, surface morphology, chemical functionality, antibacterial and antimicrobial properties, adhesion, peeling strength, and blood compatibility) required for synthesis of biomaterials". These drawbacks/requirements and growing need of biomaterials have drawn marvelous interest of scientific community in past decades in this area [20, 128].

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## **1 Biomaterials**

Any substance/material (other than a drug) or a combination of substances/materials, synthetic[14] or natural[15] in origin that can be used for any period of time, as a whole or part of a system which treats, augments or replaces any tissue, organ or function of the body are known as biomaterials[16]. They are non-viable materials used in biomedical devices, intended to interact with biological systems[17, 18]. If the word “nonviable” is removed from the definition, it becomes even more general and can address tissue engineering and hybrid artificial organ applications where living cells are used[19]. These materials can be classified in several categories on basis of their use. Most common classification consist two parts: body implants and medical devices[20].

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meanwhile having bulk properties to meet other physical, chemical and mechanical requirements[29].

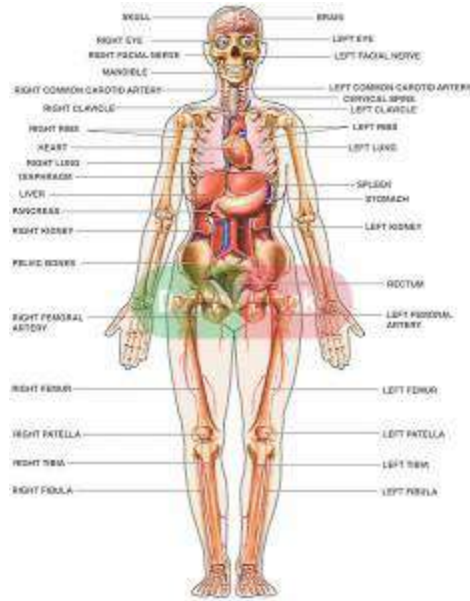


Figure 1: Schematic representation of various parts of the human body and implants.

2000 years ago Romans used gold in dentistry as first generation ad-hoc implants. Since then extensive research has been performed on many metals, compounds and alloys for their possible use as biomaterials. From 1960 onwards a new era has started for biomaterials fabrication processes when first time polyethylene was used for hip implants[30]. Since then many polymers has been thoroughly investigated for their possible use for synthesis of biomaterials with relatively great success.

Polymer nanocomposites (PNC) comprise polymer or copolymer having nanomaterials dispersed in polymer matrix [10]. Polymer nanocomposites (PNC) has demonstrated advanced applications in composite reinforcement, solar cell [12], gas sensor, bio medical sensors, fuel cell, chromatography, optical information technology, sensors, heterogeneous catalysis, filter applications, optoelectronics, optical computing devices and synthesis of the biomaterials [1]. PNC are being used for fabrication of various biological implants like ear replacement [15], tendon & knee prosthesis, hip prosthesis, ocular prosthesis, artificial heart & lungs, synthetic skin, cardiac valve, tube for Neuron regeneration, catheters, blood storage bags, skin, bone, cartilage, blood vessels and other organs etc [4-8].

From most of the biomaterials available do have acceptable bulk and mechanical properties but does not possess required bioactivity as implants tissue interfaces have very complex phenomenon. Hence success of designed devices depends on controlled healing, normal wound healing, interfacial layer, cell attachment and matrix [13]. Also the chemical functionality of the surfaces greatly affects the response of the biomaterials. But biocompatibility is measure issue with biomaterials to use in specific application [3]. Many materials can meet their bulk biocompatibility requirements but does not possess ideal surface properties like topography, surface energy, wettability, surface mobility, crystallinity, heterogeneity, chemical composition etc[8]. This shows the need for controlling surface properties depending on specific applications [6].

Researchers working in the area using chemical modification/oxidation, plasma modification, irradiation, ion implantation, graft copolymerization, self-assembled monolayers, morphological methods, biomolecule immobilization, plasma surface treatment for modulation of surface properties of polymer surface [18]. But numerous parameters involved and produced variation on material processing by modulation of experimental condition makes plasma treatment very useful technique for advanced applications [31]. Number of experimental investigations has been performed to identify effect of plasma treatment on surface, chemical, physical, biological and mechanical properties. These investigations show that plasma treatment can modulate wettability, antibacterial properties, roughness, smoothness, crosslinking, chemical functionality, blood compatibility, surface energy, perm-selectivity, conductivity, adhesion, cleaning of organic contaminations, micro-etching, cross-linking etc. It can also produce etching, remove surface contaminants, substitute chemical groups and produce induced grafting /polymerization [7-12].

These modified materials have various applications in automobiles, microelectronics, chemical and biological industry. Biomaterials in contact with biological systems need optimal combinations of mechanical properties and surface properties that can lead to superior performance in biological systems. Various investigations performed in the field of plasma surface modification of polymers/polymer nanocomposite has shown enhancement/increase in hydrophilicity and cell adhesion by helium plasma, gas sensor, antibacterial properties, immobilization of thrombomodulin to inhibits coagulation applicable in improved drug adhesion in intra uterine devices, adhesion of metals, in vitro activation of artificial surfaces, small



diameter vascular grafts, blood vessel, blood borne tissue generation, vascular prosthetic grafts, cardiopulmonary bypass with heparin-coated circuits etc [17-21].

Such as various combinations of polymer, plasma parameter and processing conditions have been explored by many researchers around the world like pre-irradiation of PTFE-styrene produces improved adhesion, cation exchange membrane & grafting mechanism while pre-irradiation of PTFE in presence of vinyl acetate improves the grafting conditions [21-28]. Simultaneous of PTFE with DMAA produces improve blood compatibility [28] while simultaneous of ePTFE with AAc improve bone-bonding ability [29]. Methacryloyloxyethyl phosphate (MOEP)/high density polyethylene has been used for surface modification of biopolymers for orthopaedic applications [30]. Studies performed by Garbassi and Occhiello shows that plasma treatments can enhance adhesion as well as decrease adhesion. Shenton et al. describe the use of atmospheric plasma treatment improves adhesion for LDPE and (PET) [12]. Also atmospheric plasma treatment is potential tool for modifying tribological, toughness, hardness, optical, electronic properties of polymers [6]. Reactive gases plasma treatment of polymers can produce branching, crosslinking, etching and functionalization of surface groups [9]. Fakes et. al and Li et. al has shown that plasma treatment can render polymer surfaces hydrophilic as well as hydrophobic depending on plasma gases [10]. Inert gas (argon and helium) plasmas modify the surface through cross-linking, chain scission, branching, surface roughening, and wettability by inducing surface charge via polarization which changes during storage and storage conditions [11]. Surface with very good wettability, high roughness and high surface energy favors cell attachment, platelet adhesion, thrombus formation and proliferation while reactive plasmas have potential ability to chemically etch polymers depending on dose and volatility of products produced. Few modified polymers like Poly-dimethyl siloxane (PDMS) and Poly-methyl methacrylate (PMMA) is also used as structural material for fabrication of microfluidic devices, routinely patterned with the hot-embossing technique [2], diagnostic tests, chemical sensing and detection experiments [30].

Hence these plasma-based approach for surface modification have received considerable interest for formation of surfaces designed to be in contact with biological systems/interfaces [31]. In last few decays various studies have been reported using various processing parameters and process gases. Recently, the majority of studies in the area have been focus on the applicability of plasma for processing of polymers, but, to use plasma-treated surfaces or plasma

polymers as interfacial bonding layers for subsequent immobilization of molecules designed to elicit specific biological responses [31]. Now the design of plasma treatment methods for biomaterial/biomedical applications is based on understanding of requirements of the bio-interface/device. Definitions of ‘biocompatibility’ [7–9] are, unfortunately, vague in terms of what chemical composition a biocompatible surface should possess. Endothelial seeding [9] and pre-adsorbing fibronectin for endothelialization [10] are approaches for blood compatibility, but design rules do not exist for plasma surfaces that are to promote these effects. Interactions of plasma surfaces with proteins and cells are also important. Control of surface properties & chemistry not only modulates cell attachment but also cell spreading, which is important as it affects cell division [30].

## 2 Polymers

Exciting chemical, mechanical, elastic properties, lightweight, flexibility and easy process-ability that can be varied drastically, in various polymers had made them widely useable materials in modern manufacturing processes[31]. These vast range of properties of various polymers are increasing their applicability in numerous fields starting from fabrication of materials used in daily life to some advanced applications like gas filtration [32], bactericidal properties [33], electrical [34], optical [35], mechanical applications [36], organic solar cells formations [37], biomaterial and implants fabrications [38] etc. During the last 20 years polymers have received fabulous interest for synthesis of biomedical devices and continuously replacing all conventionally available biomaterials, as physico-chemical properties of the surface of polymers (like surface free energy, hydrophilicity and surface morphology) influence cell-polymer interactions that make them widely useable material for synthesis of advance biomaterials, bio-devices and bio-sensors.

Table 1 Polymers and their applications for fabrication of biomaterials and implants[14, 39-41]

<b>Polymers</b>	<b>Biomedical applications</b>
Polyethylene	Tubes for various catheters, hip joint, knee joint prostheses
Polypropylene	Suture materials, hemodialysis, blood transfusion bags
Poly Tetrafluroethylene	Vascular and auditory prostheses, catheters, tubes
Polyacetals	Hard tissue replacement
Polycarbonate	Syringes, arterial tubules, hard tissue replacement,

	hemodialyzers, blood pumps, oxygenators
PET	Vascular, laryngeal, esophageal prostheses, surgical sutures, knitted vascular prostheses
Biodegradable polymers	Sutures, drug delivery matrix, adhesives, temporary scaffolding, temporary barrier
Polyurethane	Adhesives, dental materials, blood pumps, artificial hearts & skin, blood contacting devices[42]
PMMA	Bone cement, intraocular lenses, contact lenses, fixation of articular prostheses, dentures, adhesives, artificial hearts and ski, blood contacting devices[42], various catheters

Thousands of natural and synthetic polymers are available around the world and polymer reaction engineering makes it very easy to synthesis of various kinds of polymers with desired physico-chemical properties[43, 44]. Depending on the properties, mechanical strength and chemical structure/functionality, these polymers can be used for synthesis of various biomaterials and implants (table 1)

### ***2.1 Polymethyl Methacrylate (PMMA)***

Poly (methyl methacrylate) (PMMA)/ methyl methacrylate resin / poly-methyl 2-methylpropenoate (IUPAC name) is a transparent thermoplastic polymer normally used as a shatter-resistant alternative to glass. It is also well known as acrylic glass ACRYLITE®, Lucite, Perspex, Optix (Plaskolite), Oroglas, Altuglas in scientific community based on its properties and uses. Chemically, it is the synthetic polymer of methyl methacrylate. Industrial production of PMMA is carried out by emulsion polymerization, solution polymerization or bulk polymerization techniques. A bisphenol group available in PMMA also makes it an economical alternative to polycarbonate (PC) with high degree of flexibility[45, 46].

Excellent properties, easy handling & processing, low cost, high impact strength, more prone to scratching makes them suitable in various applications. Various modifications applied to PMMA through polymer reaction engineering offers very high scratch and impact resistance to PMMA for ex. addition of butyl acrylate or plasticizers in very small amount, improves its impact strength[47].

Various physical and chemical properties of PMMA are listed in table 2, and its chemical structure is shown in figure 2 [48]. It allows 92% transmission of visible light with only 4% reflections. Its refractive index is 1.4914 at 587.6 nm and can also filters ultraviolet (UV) light at wavelengths below 300 nm (similar to ordinary window glass). Adding/coatings with various

organic and inorganic additive materials to PMMA improve absorption in the 300–400 nm range. It shows similar behavior in case of IR light, where it transmit IR light of up to 2800 nm and blocks IR of longer wavelengths up to 25000 nm. Hence its color composite or colored PMMA is used in remote control and heat sensor applications where they allow specific IR wavelengths to pass while blocking visible light. PMMA swells and easily dissolves in many organic solvents on account of its easily hydrolyzed ester groups. Environmental stability of PMMA is superior to most other plastics such as polystyrene and polyethylene which makes it material of choice for outdoor and biomedical applications. Its maximum water absorption ratio (0.3–0.4% by weight) is lower relative to other conventional polymers. Tensile strength decreases with increased water absorption. It ignites at 460 °C (860 °F) and burns to produce carbon dioxide, water, carbon monoxide, low-molecular-weight compounds and formaldehyde[47].

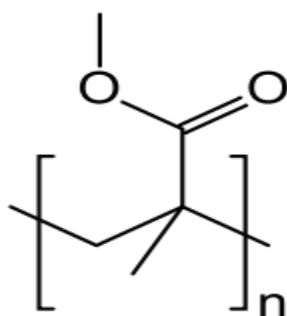


Figure 2: Chemical structure of PMMA [48].

Table 2: Chemical and Physical properties of PMMA[47]

Molecular formula	(C <sub>5</sub> O <sub>2</sub> H <sub>8</sub> ) <sub>n</sub>
Molar mass	Varies
Density	1.18 g/cm <sup>3</sup>
Melting point	160 °C (320 °F)
Refractive index (n <sub>D</sub> )	1.4914 at 587.6 nm
Reflectance	$R = 0.03890$ at 587.6 nm
Brewster's angle	$\theta_B = 56.158^\circ$
Molecular weight (MW)	100 g/mol
Glass transition temperature (T <sub>g</sub> )	105 °C (221 °F) [varies from 85 to 165 °C (185 to 329 °F)]
Coefficient of thermal expansion	(5–10)×10 <sup>-5</sup> K <sup>-1</sup>

These exciting properties of PMMA makes it suitable for various mechanical, optical and biomedical applications[49] including synthesis of bone cement, intraocular lenses, contact lenses, fixation of articular prostheses, dentures, adhesives, artificial hearts & skin, blood contacting devices[42], various catheters [38] etc. Figure 3 show polymerization process of polymers.

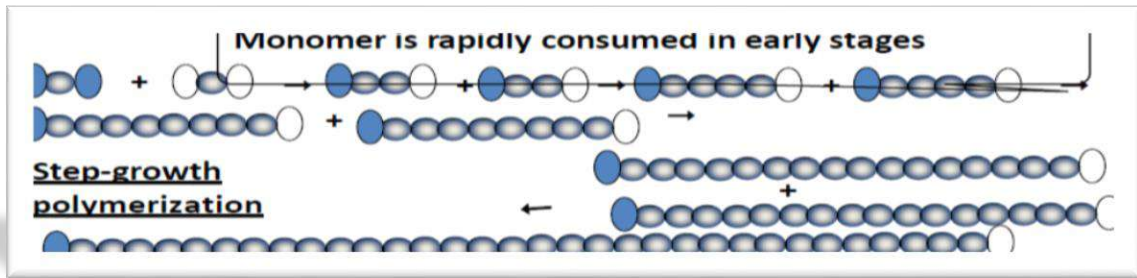


Figure 3  
Schematic representation

on of polymerization process in various polymers.

### 3 Nanotechnology and Nanomaterials

Nanotechnology and nanoscience are the study of materials having at least one dimension in nanometer and their applications across various fields of science and technology including chemistry, biology, physics, materials science, medical science and engineering to make human life more simple, comfortable and advance. The literal meaning of ‘Nano’ is “dwarf” (Greek term), while Technology “τέχνη” in Greek is an art/skill for making, modification, usage, visualize, characterize and production of tools, machines, systems and methods in order to solve problems, improve a pre-existing solution to a problem and ability to control and adapt natural environment[50]. Nanotechnology also includes fabrication and uses of structures that have novel properties because of their size in nano range. It is a multidisciplinary science that looks at how matter can be manipulated and controlled at molecular and atomic level and hence dramatic improvements in their properties. At these scales materials show completely different properties compared to their bulk counterparts [51], even intrinsic properties of material such as band gap, color, crystal structure, mechanical, catalytic, optical, chemical and magnetic properties of materials get modifies. Field and scope of nanotechnology includes all branches of science even in day to day life of living beings. Nanoparticles, can be called building blocks of nanotechnology, are of great scientific interest as they effectively bridge between bulk materials and atomic or molecular structures. Nanoparticles exhibits remarkably improved physical,

chemical and biological activity that enhances their uses in various applications. Also biomaterials in contact with biological body have optimal combination of mechanical properties and surface characteristics that results superior performance in biological environment[52-54]. Nanomaterials can be used for biological/biomedical applications for fabrication of biomaterials, having superior surface properties like low surface energy, hydrophilicity, specific surface morphology, higher cell/protein adhesion and antibacterial activity. Many of these properties are directly used or being explored for their possible application in the synthesis of advanced biological materials, biomedical devices and implants such as artificial skin diaphragm, valves for heart, kidney, lenses for eye and other biomedical fields so that they can positively/negatively affect cell to material interactions.

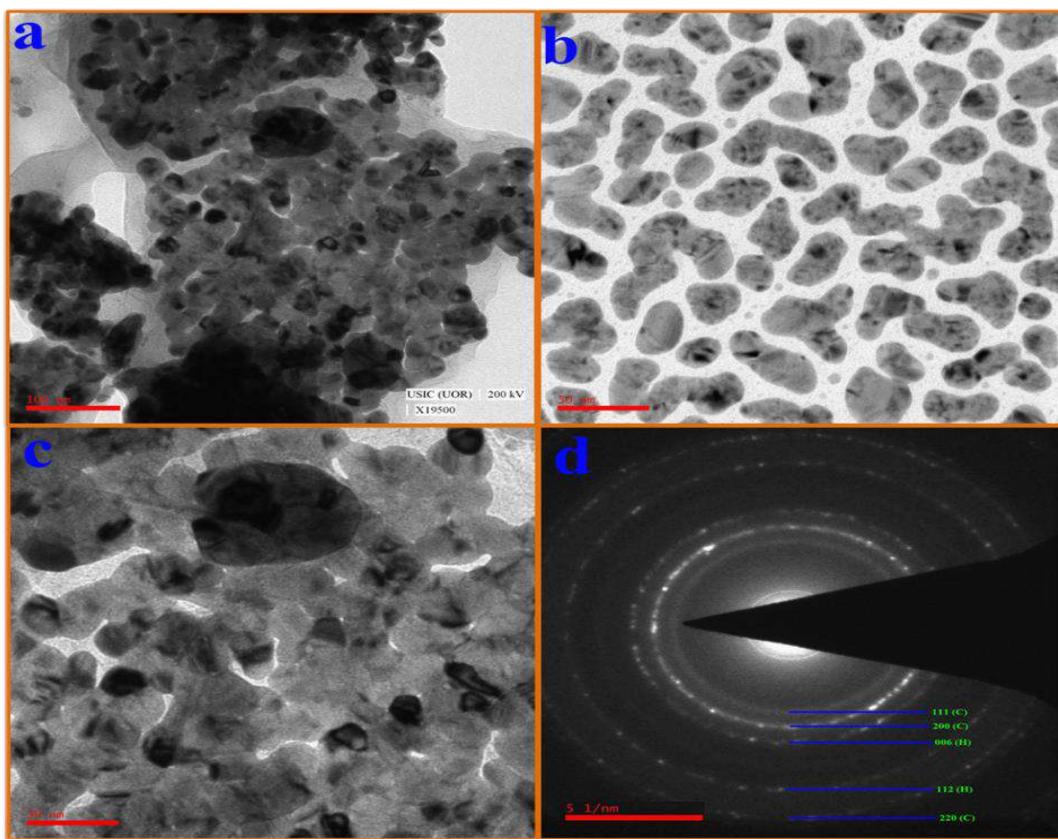


Figure 4. TEM images and diffraction pattern of synthesized silver nanoparticles.

From past ten years various metal and metal oxide nanoparticles (NPs) are used or being explored for biomedical applications such as gold NPs for cancer treatment, Cu NPs as good antibacterial agent, ZnO NPs for protection from UV light, Ag NPs for affecting growth

mechanism of plants, TiO<sub>2</sub> NPs for degradation of biomass etc. In present study we have used Ag (figure 4) and TiO<sub>2</sub> NPs for enhancement of properties and applications of biomaterials [55-91].

#### **4 Polymer - Nanocomposite**

Nanocomposites are combinations of materials in which at least one of the phases having dimension in nanometer range. They can in principle be formed from clays and organoclays in a number of traditional methods including various in situ polymerization [92], solution and latex [93] methods, mechanical agitation, ball milling, ultrasonic vibration, shear mixing, non-contact mixing etc [34]. Investigations performed on these materials have indicated that they exhibit improved and sometimes new possessions that are not displayed by the separate phases or conventional composite complements [94]. Incorporation of nanomaterials/nanoreinforcements such as nanoparticles, layered silicate clays, nanotubes, nanofibers into polymers leads to formations of polymer nanocomposite (PNC) with ominously enhanced physicochemical, thermomechanical, mechanical, thermal, dynamic mechanical and barrier properties along with significant improvements in adhesion, rheological and processing behavior[95]. Even a very small amount of nano-particles has the potential to radically transform properties of the host polymer [96, 97]. As Smaller/ nano size of the filler material provides more surface area for interaction with polymer matrix [61, 98].

Interaction area between filler & polymer matrix is used for controlling properties of PNC, which make these polymer nano-composite materials special for use in particular applications. Polymer nanocomposites have many diverse applications like composite reinforcement [99], flame resistance[53], self-assembled polymer films [100], conducting properties [101], barrier properties [102], dye-sensitized solar cells [64], gas sensor [103], nanomedicine[104], cosmetic applications [105], information storage[106], electronics[107], sensors, structural components, catalysis[108], flammability resistance, polymer blend compatibilization[109], bound catalysts [110], miniemulsion particles [111], fuel cell electrode polymer[112, 113], high performance fabrics, ballistic protection [114], actuators, diffusion barriers [115], refractive index tuning, corrosion & scratch resistant, layer-by-layer self-assembled polymer films [116], polymer blends [117], nanocomposite etc. Since last few years

polymer nanocomposites gives new alternative to conventional filled polymers and materials for synthesis of biomaterials.

## 5 Plasma Surface Modification

Plasma, the fourth state of matter, is known as ionized gases having neutrals with almost equal number of ions and electrons. A more precise definition is that: plasma is a quasineutral gas of charged and neutral particles exhibiting collective behavior. It's a most wonderful fact about the plasma, that the stars and the tenuous space between them of the visible universe make up more than 99% with plasma and perhaps most of which is not visible, even not fully explored. The plasma contains energetic species like atoms, molecules, ions, radicals, electrons, neutrals, dust/charge particles and photons. Hence interaction of plasma with various materials leads to interaction/bombardment of energetic particles on to the materials. These bombardments stimulates the productions of outgoing fluxes of neutrals, ions, electrons, radicals and photons leading to modification/irradiation/treatment/etching of surface layer for modulation of physical, chemical and biological characteristic that becomes basis for plasma-enabled material processing [118-122]. Figure 5 shows the PMMA surface after plasma treatment.

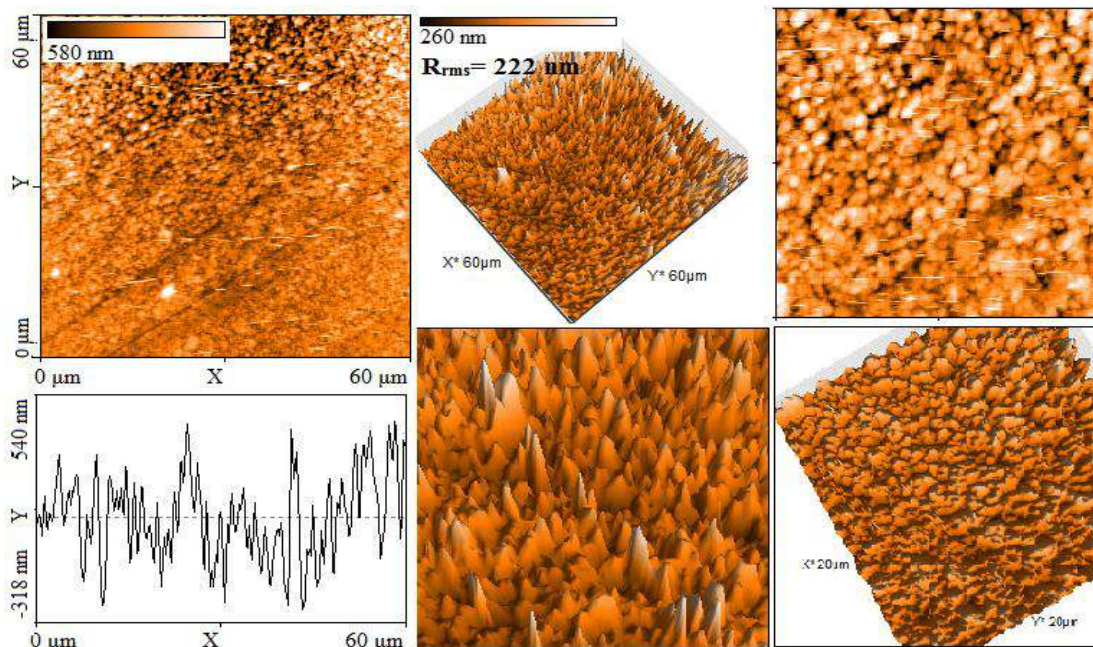


Figure 5 Atomic Force Microscopy image of PMMA after plasma treatment (2D & 3D view).



Plasma based processing of materials become widely acceptable in all branches of science and technology[112, 123-125]. Wide range of dynamic applications of the technique starting from fabrication to processing makes it most powerful technique even some time it is neither purely physical nor chemical. It offers desired path way for materials processing depending on the application of material. The plasma modulation technique precedes a number of subtractive and additive processes in a selective manner for highly controlled nanomachining, uniformity, surface quality and profile control. Based on modification techniques it also has variety of advantages such as fewer disposal problems, modifications carried without use of chemicals/rinsing, less corrosion & material failure, less undercutting, high speed fabrication, cleaner resulting surfaces[126] etc.

Plasma can be produced by electron separation/ionization from atoms/ molecules in the gaseous state. When an atom/molecule gains enough energy (higher than ionization energy) from any source make interaction (collisions) with another atom/molecule, ionization occurs. Under favorable conditions these ionizations can be enhanced to produce sufficient breakdown to satisfy the plasma conditions. Based on the conditions to create breakdown, many kinds of plasma sources are available commonly known as gaseous, metallic, sputtering, dry etching and laser-based plasma sources. The sources used for plasma productions for material processing and applications have characteristic difference in plasma parameters such as electron temperature, ion temperature, electron/ion density, electron/ion energy, state and uniformity. These plasma parameters can be modulate/controlled or depends on gas pressure, type of gas, gas composition, gas flow rate, type of plasma (DC/RF), particle density, electric field strength, electron velocity, electron current, strength of magnetic field and distance between anode and cathode. Each of these experimental conditions can drastically affect the plasma parameter to be used in various plasma based processing by ion and electrons such as reflection, physico-absorption, surface migration, surface damage, heating, material ejection, sputtering, ion etching, ion implantation, doping etc. These various plasma parameters and experimental conditions for creating and maintaining plasma, makes its nature very amazing. Below we have listed several other regions which can further increase superiority of plasma and their affects that can be used in plasma based processing and applications:

1. Electrons in plasma can extract energy form electric and magnetic fields.

2. Kinetic energy of electrons can be converted into space charge electric field and thermal energy[127].
3. Plasma based processing does not require any type of confinement even some times deconfinement is required, as the output of processing depends only on flux of ions and electrons[128].
4. Plasma generation, gas phase chemistry & transportation, material interactions depend on plasma parameter and conditions. Each of these requires input from plasma and material science[129].
5. Plasma has tendency to shield & localize externally applied electric potential for creating intense electric field regions called sheath or double layers through which ions/electrons can be accelerated.
6. Plasma can of the type of momentum transfer type between energetic ion (usually inert) and substrate surface causes bond breakage or ballistic material ejection.
7. Natural chemical species such as chlorine/fluorine atoms generated in the plasma diffuse to the substrate to from volatile products[130].
8. Creation of chemically active species from neutrals by collision with energetic electrons and ions.
9. Creation of ion damage on surfaces, including highly reactive chemical reactions on surface with plasma neutrals, ion/electron beam bombardment[107, 131].
10. Background energetic radiations in plasma produced either by atomic processes or by interactions with electromagnetic field.
11. Plasma process can be carried out in DC field (0 Hz), AC field (50 kHz), RF field (13.6-27 MHz) and Microwave field (300 MHz -10 GHz).
12. During plasma processing various events can occur based on the kinetic energy of incoming particle, such as particles having energy between 3-5 eV can either be reflected or physisorbed, 4-10 eV energetic particles induced surface migration or surface damage, 5-5000 eV can create substrate heating, surface damage and material ejection i. e. sputtering or ion etching and for further higher energies more than 10,000 eV ion implantation or doping can occur.
13. Plasma usually offers small etching rate typically of the order of hundred to few hundred angstroms per minute.

14. Ions/energetic particles may implant, bounce, absorbed or reflected during plasma processing, while sputtered material can redeposit and undergo backscattering.
15. Ion Plasma processing of any materials is controlled by (1) neutral atom and free radical concentration, (2) ion concentrations (3) ion energies.
16. Respective contribution of chemical and physical action in plasma processing can be controlled by varying voltage and gas pressure.
17. Plasma can also work as a source of heat; by conversion of electrical energy into ionization and heating of the feedstock gas
18. Plasma can be a chemical catalyst by formation of species of required chemical reactivity or other properties.
19. Plasma can work as a source of sputtered particles.
20. Transport of energy, momentum and mass to the process region of boundaries including transport to the electrodes.
21. Quenching/termination of reaction at an appropriate time and removal of products.

The plasma normally used for polymer processing can be divided into two groups thermodynamically balanced and unbalanced. Thermodynamically balanced plasma is characterized by very high temperature of heavy particles (often about 11, 000 K) and are not suitable for plasma treatment of polymeric materials, as high temperature can cause thermal degradation. In thermodynamically unbalanced plasma gas temperature is significantly lower, as it is composed of low temperature heavy particles (charged and neutral molecular and atomic species) and very high temperature electrons (often about 50 000K). Such plasma exposure causes following main effects that occur during the plasma modification process itself: (i) surface cleaning, (ii) surface ablation or etching, (iii) cross-linking and (iv) modification of chemical properties.

Plasma based surface processing of materials generally works in the region where incident ions have energies 4-10 eV that can induce surface migration or surface damage. When organic polymers lead to surface modification by plasma, the interaction between plasma and polymer produce two competitive processes, namely modification and degradation [132]. When modification is significant, properties of the polymer get modified due to ion beam interaction, plasma-graft co-polymerization and plasma polymerization while for degradation processes

etching takes place on the polymer surface[133, 134]. Other than these plasma technique sometimes especially useful for functionalization of surfaces as it is possible to modify outermost surface layer by this technique. Ions from plasma have sufficient energy to induce cleavage of the chemical bonds in the polymer to form macromolecule radicals, which subsequently initiate graft copolymerization[135]. During plasma processing of materials, plasma exposure not only causes surface modification but also leaves active sites on the surface which is subjected to post-reaction [136]. For polymer surface, plasma has been recognized as a valuable tool to significantly improve adhesion properties. Plasma can also work as a source for removing weak boundary layers and surface contaminants during modification[53, 137, 138]. For sufficient plasma density and treatment time many functionalities created on surface leads to cross-linked polymer chain formation. In these plasma implantation processes, hydrogen is first removed from polymer chains to create radicals in polymer chains that recombine with simple radicals created by the plasma gas to form oxygen or nitrogen functionalities. Radical species, rather than ion species, that are created in the plasma zone play an important role in implantation process. Plasma-material processing scheme [34] in figure 6 shows modulation in surface properties of polymers by low pressure plasma treatment such as formation of macromolecule radicals, increase in chemical reactivity, formation of sputtered particles and creation of active sites followed by graft copolymerization.

Research based on plasma surface modification of polymers for biomaterials synthesis mainly focuses on argon plasma exposure of polymers. This creates an etching/degradation reaction at surface of the polymers; even a small exposure to inert gas plasma can cause etching of polymers and rate of weight loss is strongly dependent on the nature of polymer as well as energy of the plasma. Polymers having oxygen functionalities in form of ether carboxylic acid or ester groups show high plasma susceptibility while polyolefin with no substituents show low plasma susceptibility[139, 140]. Interestingly, polymers subjected to the plasma modification process possess similar chemical and physical properties as original polymers since technique only modifies outermost layer of polymers. The elemental composition, chemical structure, degree of polymerization and crystallinity of the bulk polymers are hardly altered. Etching processes sometimes cause smaller weight loss due to bond scission of polymers and reactions of the radicals generated in the polymer chains upon plasma exposure [141, 142]. Normally polymers are hydrophobic and conversion of these polymers from hydrophobic to hydrophilic

depends on their surface characteristic. Plasma can modulate surface properties in controlled manner to improve adhesion strength, biocompatibility and other pertinent properties[118-122, 143, 144].

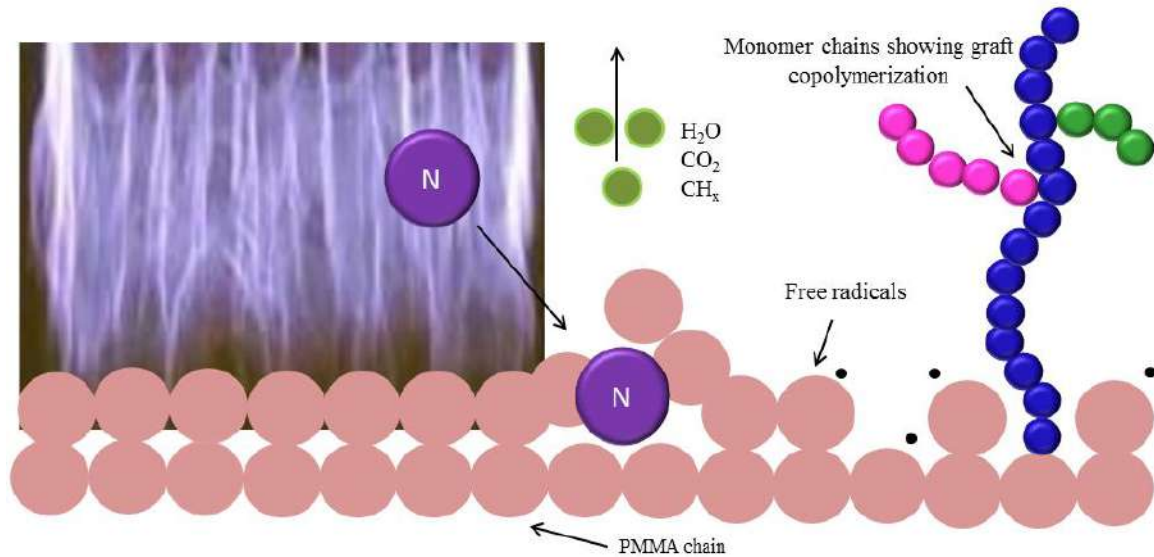


Figure 6: Schematic representation of polymer surface modulation induced by low pressure plasma treatment

Below is list of other affect that can be obtained by plasma based material processing:

#### ***Surface Modification***[136, 145, 146]

- ❖ Alters surface properties of material without affecting their bulk properties
- ❖ Surface modification in a controlled fashion
- ❖ Surface properties (Roughness and Smoothness)
- ❖ Advantageous for design, development and manufacture
- ❖ Surface interaction

#### ***Chemical Modification***[48, 147, 148]

- ❖ Eco-friendly nature
- ❖ No water and chemicals required
- ❖ Selection of desired chemical path ways
- ❖ Hydrophobicity & Hydrophilicity

- ❖ Chemical structure
- ❖ Chemical catalyst: Increased surface area
- ❖ Highly cross-linked films irrespective of the surface geometries

***Physical Modification[121, 149-151]***

- ❖ Formation of multilayer films
- ❖ Prospect of scaling up
- ❖ Smooth, pin hole free ultra-thin film
- ❖ Minimization of thermal degradation and rapid treatment
- ❖ Conductivity
- ❖ Surface tuning
- ❖ Adhesion
- ❖ Low friction coefficient

***Bio-Induced Modification[38, 152-155]***

- ❖ Influence cell adhesion
- ❖ Biocompatible polymers
- ❖ Hindering bacterial adhesion
- ❖ Antimicrobial coatings.
- ❖ Bio-adoptability: Selective Bacterial Growth

**6 Plasma Gases**

Various plasma parameters and experimental conditions such as gas pressure & flow rate, type of plasma (DC/RF), particle density, electric field strength, ion/electron velocity, ion/electron energy, type of gas, gas composition and distance between anode & cathode can significantly affect the plasma processing. Keeping all others parameters constant if only the gas will change it will affect the polymer property dramatically[129, 138, 156]. As a gas used may increase surface energy while other gas will reduce the same. Almost similar effect can observe on hydrophilicity, surface morphology, chemical functionality, antibacterial & antimicrobial properties and adhesion strength of processed material. Hence the role of gas used and its composition can most significantly affect the processing. Even a very small variation in gas composition can produce completely different property to the material that can be used for novel

applications. The different surface properties obtained via using different gases as source of plasma are very important for biomaterial fabrication processes in desired path-way, as oxygen plasma used for modification can generate oxygen functionalities and hydrophobic nature to polymer while other compound gases such as carbon dioxide, carbon monoxide, nitrogen dioxide and nitric oxide can make the polymer surface hydrophilic. Chlorine functionalities can contribute to increase in the hydrophilicity when  $\text{CF}_2\text{C}$  and  $\text{CCl}_4$  plasmas were used while hydrophobic properties of polymer can be enhanced using higher-degree fluorinated compound gases such as  $\text{SF}_6$ ,  $\text{CF}_4$ , and  $\text{C}_2\text{F}_6$ [157, 158]. Table 3 list the affect and applications of different gases used as a source for plasma surface modification.

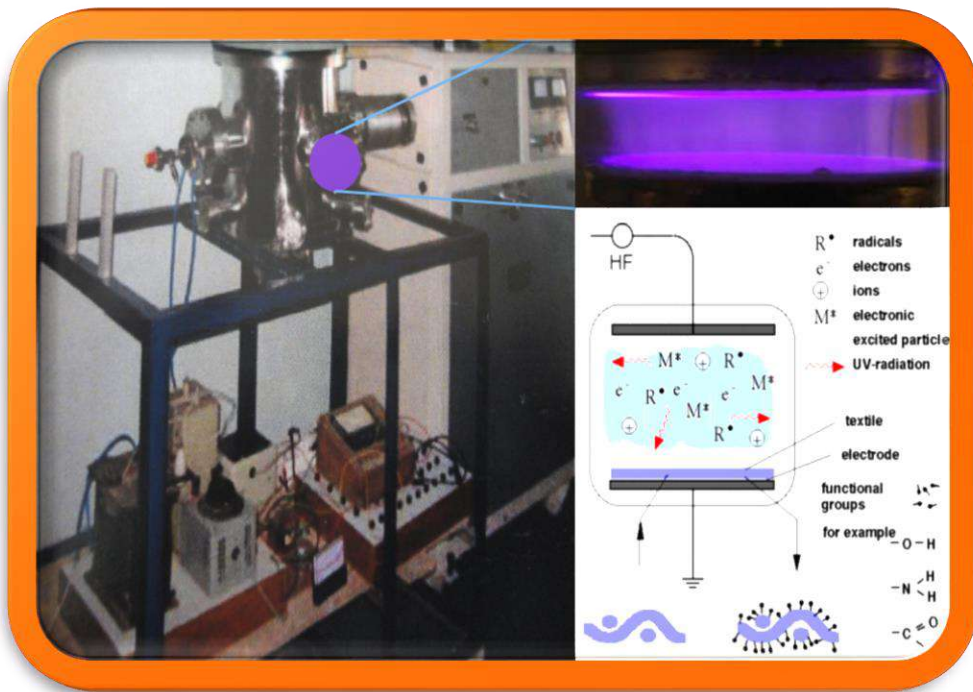


Figure 7:

Experimental set up used for production of DC plasma.

Table 3: Different plasma gases, their affect and applications on material processing

Plasma gases	Effect and applications in plasma processing
Reducing gases( $\text{H}_2$ , mixtures of $\text{H}_2$ )	Replacement of F or O on surfaces, removal of oxidation sensitive materials, conversion of contaminants to low molecular weight species.
Oxidizing gases( $\text{O}_2$ , air, $\text{H}_2\text{O}$ )	Removal of organics and to leave oxygen species.
Nitrogen ( $\text{N}_2$ )	Removal of organic sand to leave $\text{N}_2$ species, removingoxide layers, surface Cleaning, surface smoothening.

Noble gases (He, Ne, Ar etc.)	To generate free radicals on surfaces to cause crosslinking or to generate active sites for further reaction.
Active gases(NH <sub>3</sub> )	Functionalization of materials through amino groups.
Fluorinated gases (SF <sub>6</sub> )	To make the surface inert and hydrophobic.
Polymerizing gases	Polymerization of layers on substrates by direct polymerization or by grafting on Ar/He processed polymer surface.

In this study Air, N<sub>2</sub>, Ne and SF<sub>6</sub> gases were used for controlled modification of surface properties and a detailed investigation has been performed to identify their effect on property enhancement of nano-biomaterials. DC plasma surface modification instrument (fig 7).

### ***6.1 Air and its properties as a source of plasma:***

Air is the atmosphere of Earth or layer of gases surrounding the Earth retained by its gravity. Role of Air is very important to protect life of all leaving beings, absorbing ultraviolet solar radiation and production of greenhouse effect, with normal constitution by volume is nitrogen (78.09%), oxygen (20.95%), argon (0.93%), carbon dioxide (0.039%) and rest is several other gases like neon, helium, methane, krypton, hydrogen, nitrous oxide, carbon monoxide, xenon etc. It also contains a variable amount of water vapor ranging around 1%.

Air is not only important for animals to survive but also plays a critical role in plasma generation and processing as thundering of clouds is an example of production of natural plasma. Many of the plasma physics experiments and applications works at atmospheric pressure or at little reduced pressure like high power laser, MEMS electronic switches, EM absorbers/reflectors, remediation of gaseous pollutants/waste systems, sterilization, decontaminations and advanced plasma processing applications including plasma treatment of human skin. In all above listed applications the air plasma can significantly affect material properties that make the role of air composition very critical for plasma production and processing. Still very few efforts has been performed by researcher & industry for biomaterial production using air as a source of plasma except plasma treatment/healing of human skin. This shows need of detailed investigation of the properties and applications of air plasma in materials processing, as this offers low cost processing of materials without any damage[159].

### ***6.2 Inert gas Neon (Ne) and its properties as a source of plasma:***



Neon is a monatomic, colorless, odorless, inert gas at standard temperature and pressure having two-third density of air. It shows bright orange-red emission spectra under high electric field. It has atomic number 10, atomic weight 20.1797 amu, electronic configuration [He]  $2s^2 2p^6$ , melting point 24.56 K, boiling point 27.10 K, FCC crystal structure and density 0.9002 g/L. Its first, second and third ionization energies are 2080.7, 3952.3, 6122  $\text{kJ}\cdot\text{mol}^{-1}$  respectively. Interestingly it is fifth most cosmic abundant element in universe and solar system after hydrogen, helium, oxygen and carbon, but it is rare on Earth (18.2 ppm by volume). Air is only source for production/separation of neon, which makes it more costly even than He (helium gas) and limits its industrial applications in plasma tube and refrigerant.

When inert gas (He, Ne and Ar gas) plasma is used to modify the surface of material, they can undergo physical etching, ion etching or sputtering of the substrate material. Mostly researcher are using Ar and He plasma for materials due to their easy availability, but Ne exhibits similar chemical behavior with different physical characteristic like smaller atomic size and weight compared to argon can produce different mechanism and results during processing. To best of our knowledge no efforts have been performed for Ne based plasma processing especially for biomaterials productions. Ne ions can be extracted from glow discharge region and accelerated in electrical field towards the substrate similar to argon and other gas ions. Due to inert nature of Ne gas they cannot produce any type of chemical reaction on the material surface but Ne ions have sufficient energy to produce ion etching or sputtering totally controlled by impact of incident ions. The process is inherently nonselective due to wide spread in ion energies compared with different surface bond energies and chemical reactivity. The modification (based on inert ion) are generally slow compared to other gases used for modification (with the etch rate of few ten angstroms to few hundred angstroms per minute). These types of modifications are used to form facets, ditches, hourglass shaped trenches, removing of various damage, device complexity and redeposit materials with high aspect ratio. When ions of sufficient energy are used they can produce high sputtering rate of materials and weight loss. Such weight loss is generally restricted to the topmost layers of the polymer, without affecting the inner layer. Ne gas plasma can create new surface morphology, improve the hydrophilicity and wettability on polymer surfaces

### ***6.3 Reactive gas Nitrogen ( $N_2$ ) and its properties as a source of plasma:***

Nitrogen is diatomic, colorless, odorless gas with high reactivity at standard temperature and pressure. It is a common element of Solar system and most abundant in atmospheric gases. It has atomic number 7, atomic weight 14.007 amu, electronic configuration [He]  $2s^2 2p^3$ , melting point 63.15 K, boiling point 77.35 K, hexagonal crystal structure and density 1.251 g/L. Its first, second and third ionization energies are 1402.3, 2856, 4578.1  $\text{kJ}\cdot\text{mol}^{-1}$  respectively. It is used to make many industrially important compounds such as ammonia, nitric acid, fertilizers and organic nitrates. Organic nitrates such as nitroglycerin and nitroprusside are used to control blood pressure by metabolization. Chemically it shows high electronegativity in reactions and makes strong bonds. It is also found in various organisms primarily in form of amino acids, proteins and nucleic acids (DNA and RNA). A human body contains about 3% nitrogen by mass (fourth most abundant element in body after oxygen, carbon and hydrogen). It is considered as a great source of energy production at Sun/stars in form of carbon nitrogen cycle.

For plasma processing of materials nitrogen is extensively used for more than four decades, due to its easy availability and relatively easier plasma production ability. First application of nitrogen plasma was nitriding of high-carbon steels, titanium, aluminum and molybdenum. This is a process where nitrogen will diffuse inside the materials in form of ions to form their nitrides that prevents material rusting/corroding and makes them suitable for various applications like gears, crankshafts, injectors, camshafts, extrusion dies, valve parts, die-casting tools, forging dies and firearm components. Later nitrogen glow discharge plasma has shown its potential applications in various material fabrication processes. Nitrogen ions also work as good reducing agent and hence oxide layers can be removed very easily from surface by transferring sufficient energy to substrate during bombardment of energetic particles. It can also remove various organics from material surface to leave  $\text{N}_2$  species. Comprehensively nitrogen plasma is used for surface cleaning, surface smoothening and also enhances fatigue strength, surface hardness, wear and corrosion resistance of materials. Based on chemical functionality of materials nitrogen plasma can leave active sites on materials surface that can further cause post reaction. These properties of nitrogen ion plasma highlight their use for various materials fabrication and processing processes especially for biomedical applications.

#### ***6.4 Sulfur hexafluoride ( $\text{SF}_6$ ) and its properties as a source of plasma:***

Sulfur hexafluoride ( $\text{SF}_6$ ) is colorless, non-flammable, odorless, inorganic and extremely potent greenhouse gas. It is also an excellent electrical insulator, it has molar mass 146.06 g/mol, density 6.17 g/L (that is very high in comparison to air (1.225 g/L)), boiling point 209 K, slightly soluble in water but possess good solubility in ethanol, hexane, benzene and orthorhombic crystal structure. Most significantly it is used as gaseous dielectric medium in electrical industry.

Use of  $\text{SF}_6$  gas plasma has been first started in semiconductor industry as an etchant and making their surface hydrophobic. Depending on plasma parameters and processing conditions  $\text{SF}_6$  breaks down into sulfur and fluorine under plasma and the fluorine plasma is further used for material processing.

When  $\text{SF}_6$  gas is used for surface modification of materials, the processing is sometime known as radical etching or reactive ion etching. Surface modifications are generally carried out by reactive, neutral or chemical species such as fluorine atoms and molecular species instead of ions as done by other plasmas. The radicals are not as much reactive as ions but they are more abundant in plasma because they can be generated at lower threshold ( $< 8$  eV) and have high generation rate with longer lifetime compared to ions. Here used radicals from  $\text{SF}_6$  gas plasma (fluorine) produce volatile products with layer to be removed hence they are more useful for surface cleaning of materials or generation of specific surface functionality where plasma works to supply reactive gas etchant to materials. Using  $\text{SF}_6$  as a source gas for plasma, a dry physico-chemical modifications regime can be established by operating at various voltages, impingement of high energetic ions, various chemical reactions etc.

The process of modification can be divided into five steps: In glow discharge  $\text{SF}_6$  dissociates in various components or reactive species (like  $\text{SF}_5^+$ ,  $\text{SF}_4$ , F ion or radical) by bombardment of energetic particles (having energy distribution between 1- 10 eV). These radicals and other neutrals reach to the surface by diffusion while ions are accelerated by field. Here most of the species does not undergo spontaneous reaction with the material. These species then diffuse into material, further absorbed there to react with the surface material and end reaction products leave surface by desorption if it is volatile. From the listed steps those occurs in gas phase are termed as homogeneous reactions while those occurs at the surface of material are termed as heterogeneous reactions. Radical based modifications are generally chemical in nature hence they are also selective for different materials or gas used for processing. As oxygen

plasma removes photoresists by oxidizing hydrocarbon material, fluorine is used for silicon etching. Aluminum makes volatile chlorides while aluminum fluorides are nonvolatile. If plasma is used for processing of polymeric material using F radicals, F/C ratio controls the type of processing, as for  $F/C > 3$  etching is dominant and for  $F/C < 2$  polymerization takes place.

## **7 Biocompatibility and Bio-adoptability (In general and properties required)**

In past few decades advancements in science and technology focused on animal health and related issue to make it more and more comfortable. In this consequence, huge scientific efforts and inter-disciplinary research are going on for development and fabrication of advanced materials those can be used for replacement of body parts after their failure. The synthesized materials have to be used for various applications like fabrication of body implants, biomedical devices, bio-separation, sterilizations, biosensors etc., hence they must have specific surface and bulk properties that should not produce any deleterious effects, failure of material or formation of unusual tissues. It must be noted that the synthesized materials are foreign materials to biological body and normally biological bodies do not accept foreign materials very easily till they shows superior biological response. Material that has to be used as biomaterial must show superior biocompatibility and bio-adoptability while retaining high performance physical, chemical and mechanical properties to fulfil other requirements[13, 133, 156].

Phenomena of biocompatibility and bio-adoptability are very similar to each other. Biocompatibility defines ability of a material to perform appropriate host response in a specific situation or in contact with biological system[160]. Hence biocompatibility phenomena investigation involves the process where biological response of materials is tested using various components (like blood, DNA, protine etc.) of any biological system, while bio-adoptability involves identification of biological response of any material with respect to any living biological body such as virus, bacteria or any other. Both biocompatibility and bio-adoptability can be considered as in-vitro and in-vivo investigation of materials. It is very difficult to say that a material is biocompatible/bio-adoptable or not, as different biomaterials require different properties to be used in particular applications for ex. contact lenses and bones requires very high wettability while artificial teeth requires low wettability. Even though sometimes situations become more critical for ex. artificial skin (its inner part must be blood compatible while outer part must show low blood compatibility with overall system must show high porosity). Hence

any material and its property that may be suitable for synthesis of one class of biomedical devices/implants may not be suitable for other applications, produces challenge in the field of biomedical devices fabrication. Below is the list of few class and group of properties those are generally required for all kind of biomaterials in various forms (low/high/positive/negative effect) other than normal physical, mechanical and chemical properties, as decided by international biological, medical boards and scientific communities [161-168]:

- Antibacterial & antimicrobial properties
- Toxicity
- Ecofriendly nature
- Wettability
- Micro patterning
- Biological response to foreign materials
- Strong adsorption of proteins by surface
- Chemical functionality
- Cross-linked films formation irrespective of surface energy and geometries
- Adhesion
- Porosity
- Cell/tissue adhesion and compatibility
- Blood compatibility

It is very easy to find a material with appropriate chemical, physical and mechanical properties required for fabrication of biomedical devices/implants, but in general no natural/synthetic material or polymer possess the surface-interface and biological properties needed for various biomedical applications or in other words “any material/polymer do not have inherent properties (like surface energy, hydrophilicity, surface morphology, chemical functionality, antibacterial & antimicrobial properties, adhesion, peeling strength and blood compatibility) required for synthesis of biomaterials. These drawbacks/requirements and growing need of biomaterials have drawn marvelous interest of scientific community in past decades in this area[20, 133].

## **8 Role of Nanotechnology for enhancement of biocompatibility & bio-adoptability**

Based on large investigation done by various scientific groups through-out the world and available literature it can be easily concluded that most of the properties required for biomaterial synthesis are surface properties of the material[169]. Hence techniques are required that can

modulate the surface properties of materials in desired pathways to produce desired bio-response.

Nanotechnology/nanomaterials gains amazing interest for material fabrication processes due to their large surface to volume ratio that can be directly applicable for biomedical application. Recently Agarwal et. al 2014 [48, 140] and several other groups shown nanotechnology based innovative approach for modulation of biological responses and surface properties of polymers with enhancement of normal physical, chemical and mechanical properties of polymers using nanostructured materials in polymer matrix. These new class of materials are known as Nano-biomaterials. They have shown that casting of various nanomaterials/nanoparticles in polymer matrix not only improves physical and chemical properties of polymers but also drastically modifies the biological response of these polymer based on properties of selected nanostructured materials [170]. Nanomaterial exhibits unique surface properties due to their smaller size and high surface to volume ratio. When these nanomaterials are mixed/incorporated in polymer, they homogeneously distribute in polymer matrix, but for the apt amount incorporation nanoparticles there are sufficient NPs on the surface of polymer leads to modification of surface properties of polymer-nanocomposite in desired path-way. Also attractive forces between polymeric chains and tendency of polymerization could provide them unique qualities while reinforcing them by organic [171] & inorganic nanoparticles that leads to enhancement of wettability, surface energy, geometries, blood compatibility & antibacterial properties, toxicity, surface tuning [172], abrasion [173], cross-linking [174] and modification of chemical properties [175] in controlled manner. Advancement shown here for synthesis of Nano-biomaterials will surely be future of biomedical devices/implants fabrications.

## **9 Role of Plasma Treatment in enhancement of biocompatibility and bio-adoptability**

Forming and removing are the fundamental processes in nanoscale manufacturing processes or modulation of properties of materials. Removing is process that destroys cohesion among particles while formation creates an original shape from molten mass, gaseous/solution states, plasma or solid particles. During formation process, cohesions are created among particles. The formation/removing can be done by wet chemical etching, thermal/mechanical energy based removing, electrical discharge, traditional mechanical turning, laser drilling, plastic molding, thin film deposition by evaporation/sputtering, electrochemical deposition, dry etching,

ion etching, plasma based etching and irradiation etc[176-181]. From the above listed techniques plasma based etching and irradiations are most powerful techniques as they can be used for both formation and removing in controlled way as per requirement in various applications. Plasma based processing can be controlled precisely using various plasma parameter and experimental conditions involved in processing that can lead desired path-way for material modification due to various process involved in processing like nanomachining, uniformity, profile & surface quality, less corrosion & material failure, less undercutting, high speed fabrication, physisorbed, surface migration, surface damage, substrate heating, sputtering, material ejection, ion etching, ion implantation, doping etc.

Using various plasma parameters, processing methods and their combinations, one can provide new property to the material in desired path way that may be useful for fabrication of different class of biomaterials. Number of experimental investigations performed in this field has shown that plasma treatment is sufficient to modify wettability, surface characteristic, surface energy, antibacterial property, hydrophilicity, blood coagulation, toxicity, blood cell adhesion patterns, defense systems[182], hemocompatibility characteristics, blood anticoagulation, metabolic functions[22, 183], thrombogenesis[184], tissue engineering[185] etc. These modifications are responsible for biological response of biomedical devices and implants in the biological systems such as vascular grafts[186], artificial devices used for extracorporeal circulation [187], blood cells and postoperative morbidity [188], pediatric cardiac operations [189], antithrombogenicity by urokinase immobilization[190] etc. In short plasma treatment can significantly affect the biocompatibility and bio-adoptability of materials in desired pathways.

## **10 Influence of plasma processing and Nanomaterial casting on biocompatibility and bio-adoptability of biomaterials**

Recent advancement in nanotechnology show various applications in all fields of science where nano size materials are receiving great interest for further improving the materials properties and plasma is a widely acceptable technique for improving the material properties[191-193]. The role of nanotechnology and plasma processing for controlling biological response of materials is described separately. Few doped materials have been investigated to identify the influence of plasma treatment and doping by Zhang et. al. 2013 [194]. They had demonstrated that Cl based plasma can be used to etch lightly doped P/N type silicon

anisotropically while isotropically for heavily doped n type silicon. Schwartz et. al. 2007 [195, 196] shown that more than  $10^{19} \text{ cm}^{-3}$  dopant concentration gives higher performance during processing. Figure 8 shows experimental study of blood cell attachment on various plasma treated PMMA surfaces.

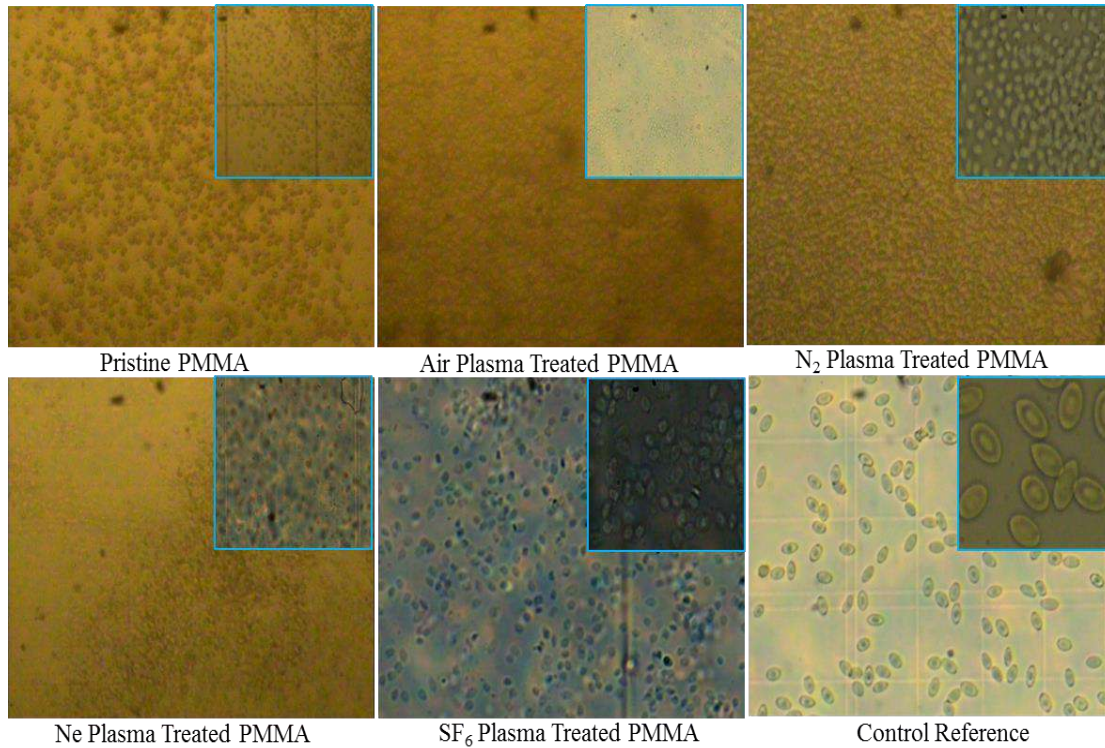


Figure 8 Blood cell attachment on various plasma treated surfaces.

Presence of nanoparticles, filler dispersed nano-composites exhibit remarkably improved properties, compared to pure polymers or their traditional composites[197]. When nanoparticles are incorporated into the polymer in apt amount, especially for smaller/nano size of the filler material provides more area for interaction with polymer matrix that provides very high surface concentration of NPs to give them superior performance as biomaterials[61]. If these polymer nanocomposite materials will further processed by the ion plasma, more superior effect can be induced via processing on surface properties depending on plasma parameters and processing conditions, those lead to increase in surface amount of NPs if polymer is selectively etched out, porosity will increase if NPs are selectively etched out, relative surface smoothness increases if both NPs and polymer is equally etched out, if NPs are more potent to bacteria their surface exposure can enhance the antibacterial efficiency of nanocomposite, blood homo-compatibility



of material will increase if used NPs show higher compatibility, exposure of NPs on the surface can influence the cell and DNA attachment to biomaterials etc[198-200]. Figure 9 Optical micrograph of various plasma treated nanocomposite surfaces.

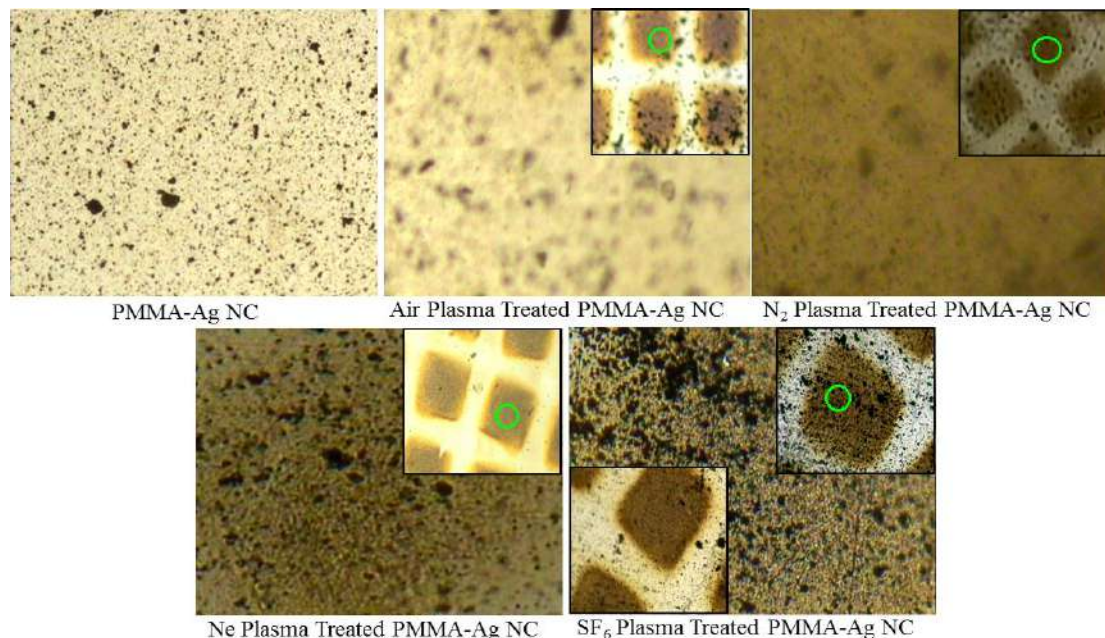


Figure 9 Micrograph of plasma treated PMMA- Ag Nanocomposites.

## 11 Nano-biomaterials

Polymers exhibit many interesting properties that have increased their use in modern manufacture process. Number of experimental investigations performed on plasma treatment of polymers show controlled improvement in biological properties of polymers while retaining their bulk properties[201]. Recent advancement in the field of nano-science and nanotechnology shows their potential to influence biological response of materials[202]. If combination of Nanotechnology i. e. nanomaterials/polymer nanocomposites and plasma treatment will used to modify surface properties of materials that can produces superior biological response (biocompatibility and bio-adaptability) in more controlled fashion via chemical functionalization, highly cross-linked films formation, scaling up the antibacterial & antimicrobial properties in ecofriendly nature, high adhesion & peeling strength, blood compatibility etc[203]. These new materials are known as Nano-biomaterials [33, 140,204] (Plasma treated polymer nanocomposite materials), extremely suitable for biomedical applications (fabrication of biomedical devices/implants) and nano-biomaterial synthesis.

## *Summary, Conclusions & Scope for Future Work*

Growing requirement of advance materials has been realized in last couple of decades for fabrication of biomedical devices and implants. These advance smart materials are called biomaterials. The choice of any material to use as biomaterial depends on their physical, chemical surface and biological properties. The surface characteristics play a vital role in the performance of biomaterials. The fate of implants are determined by interactions – to a large extent cell-specific [98] between the biomaterial and tissues. Polymeric materials do not always possess the specific bioactivity required to promote suitable interaction with cells, thus methods to enhance biocompatibility are required [102]. Polymers are receiving great interest for fabrication of biomaterials in last few decades, but normally no polymer have suitable property required to be used as biomaterials. Nanotechnology and low temperature plasma based approaches offered unique route to modify the surface and chemical properties of materials, due to their wide range of dynamic applications starting from fabrication to processing. Surface properties may be altered by plasma treatment techniques. The modulation of the effects obtained is possible through control of operational parameters, including the gas used, reaction conditions (power, pressure and exposure time) and the reactor geometry [196]. Plasma technique is a convenient method to modify the surface properties of polymeric materials, keeping intact their bulk properties. Hence this chapter explored the use of nanotechnology and plasma treatment for enhancement of bio-adoptability and biocompatibility of polymers/polymer nanocomposites by plasma treatment.

Further polymers can be subjected to modifications with various ion plasma but there are several other parameters of plasma like ion energy, ion temperature, ion flux, electron flux, type of plasma etc. that can significantly affect the processing conditions hence the behavior of materials, so one can also explore the effect of these parameters on plasma based processing.

1. air, nitrogen, Ne and SF<sub>6</sub> plasma were used but it is possible to modulate properties of material by combination of these and several other gases that can provide both positive and negative effect on processing even more various monomers or liquids with high evaporation rate can be used/explored for their effect on plasma treatment of materials. Further after processing one can try to attach various functional groups on plasma treated polymer surface to increase their surface properties and efficiency.

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