Cambridge University Press 978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt More information

# Part I

Introduction to non-equilibrium plasma, cell biology, and contamination

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

More information

Cambridge University Press 978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt More information

# 1

### Introduction

MOUNIR LAROUSSI

For millennia, engineering-based solutions/technologies have played key roles in healthcare. Humankind figured out long ago that fire/heat can be used to coagulate blood and help a wound to heal. Medical pioneers in the middle ages developed specialized instruments to conduct surgery and treat wounded soldiers (Ramen, 2006). In modern times, more advanced tools and diagnostics, such as lasers and sophisticated computer imaging techniques, are used on a daily basis by healthcare practitioners to help them overcome medical challenges that were thought to be insurmountable not too long ago. Recently, plasmas (ionized gases) have been under investigation as a medium on which a new, promising medical technology can be developed (Laroussi, 2005; Stoffels, 2006; Laroussi & Fridman, 2008; Fridman et al., 2008; Laroussi, 2009; Kong et al., 2009; Weltmann et al., 2010). Plasma technology played a key role in revolutionizing semiconductor manufacturing in the 1960s and 1970s. Today, it is poised to usher in a new revolution in the healthcare industry.

There are three states of matter that are prevalent on our planet. These are the solid, the liquid, and the gaseous states. However, there is a fourth state, which is much more ubiquitous than the previous three throughout our universe, and that is the "plasma" state. If a gas is heated or subjected to high electrical stresses, seed electrons are accelerated to acquire high kinetic energies. When these electrons collide with the atoms and molecules of the background gas they are able to knock off and free other electrons, creating positively charged atomic and molecular ions. The newly freed electrons are instantaneously accelerated by the applied electrical field and in their turn enter into ionizing collisions with other atoms and molecules. The mixture of neutral atoms and molecules, ions, and electrons is what is referred to as "plasma". Depending on the operating conditions and the power applied to create

*Plasma Medicine*, eds M. Laroussi, M. Kong, G. Morfill, and W. Stolz. Published by Cambridge University Press. © Cambridge University Press 2012.

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

More information

#### 4

### Plasma Medicine

the plasma, the different particles constituting plasma can achieve an energetic equilibrium or can exhibit different energies. Thermal or high-temperature (hot) plasmas are of the equilibrium type, having all their particles sharing the same energy. Non-equilibrium or low-temperature (cold) plasmas have electrons that are much more energetic than the neutrals or the ions. Hot plasmas are used in various applications, including energy production research and welding. Cold plasmas are used in semiconductor manufacturing (computer chips), television screens, and in lighting (neon tubes), to name just a few. Since the early 2000s, research efforts on the application of low-temperature plasmas in medicine have intensified and today low-temperature plasmas are poised to revolutionize healthcare. Researchers have found ways whereby plasmas can be applied in direct contact with living tissues to deactivate pathogens, to stop bleeding with no damage to healthy tissue, to disinfect wounds and accelerate wound healing, and to selectively kill some types of cancer cells. These research activities constitute the basis of a new approach to healthcare and are the foundation of new field of research, collectively referred to as "plasma medicine".

Plasmas produce chemically reactive species such as hydroxyl (OH) and atomic oxygen (O), which exhibit strong oxidative properties. For example, oxidation of the lipids and proteins that constitute the membrane of biological cells leads to the loss of their function and in some cases can lead to the complete disruption of the membrane. Bacteria were found not to be able to cope with the environment created by plasma and die in large numbers in a matter of minutes or even seconds, depending on how robust the bacterial strain is (Laroussi, 2002). Therefore, reactive plasma species generated by plasmas and sustained at near room temperature can rapidly inactivate bacteria, virus, and fungus deposited on the surfaces of surgical instruments and medical devices, including those made of heat-sensitive polymeric materials.

Plasma can be an effective method to control the proliferation of biofilms (Becker et al., 2005; Laroussi, 2005). A biofilm is a highly organized, three-dimensional bacterial community, which enables micro-organisms to communicate, maximize resources, and protect the integrity of the community. Biofilms can be found on solid surfaces and in pores in contact with aqueous solutions or as films floating on liquid surfaces. Because cells in a biofilm closely interact with each other within the protective environment of the film, they exhibit different characteristics from those of free-floating planktonic cells. Biofilms are very resistant to chemicals found in detergents and even to antibiotics. Therefore, if not controlled, biofilms can represent serious health hazards. In addition, biofilms can cause damage, such as corrosion, to the surfaces of the materials they attach to, adding an economic cost to their health risk.

More information

Cambridge University Press

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

Introduction

Dental plaque is an oral biofilm and the primary etiologic agent responsible for dental caries and periodontal diseases. An example of caries-causing bacteria is *Streptococcus mutans*. There are also a large number of bacteria that cause periodontal diseases such as gingivitis (inflammation of the gum tissues) and periodontitis (inflammation of the periodontium, the tissue that supports the teeth, which if left untreated leads to teeth loss). Plasma has been shown to be able to inactivate many of the bacteria that cause such diseases. Plasma has also been applied to dentin, the calcified tissue structure underneath the tooth enamel, and was found to reduce the infection there and even potentially remove the infected tissue in the tooth cavity, ultimately replacing the universally feared dentist drill. These recent developments indicate that not too far in the future plasma-based devices could be at the disposal of dentists, allowing them to effectively treat oral-borne diseases with little pain to their patients (Morris et al., 2009).

Low-temperature plasmas, under some conditions, appear to cause little damage to living animal and plant tissues. Having different structures and morphologies, bacterial and mammalian cells are known to exhibit different responses to physical and chemical stresses. For example, skin fibroblast cells are found to remain viable under plasma conditions that can be lethal to bacterial cells. Cold plasmas have also been shown to induce apoptosis, or programmed cell death, opening the possibility of using plasma technology to fight some type of cancers by halting the proliferation of cancer cells.

Preliminary work by various groups showed that plasma enhances the proliferation of fibroblasts. Proliferation of this type of cell is an important step in the wound healing process, known as the "proliferative phase". The ability of plasma to kill bacteria cells and to accelerate the proliferation of specific tissue cells is the concept on which the application of plasma in wound care is based (Fridman et al., 2008; Laroussi, 2009; Kong et al., 2009). Tens of thousands of amputations occur every year in the US because of the inability of present medical methods to heal chronic wounds, such as diabetic ulcers. The application of plasma-based technology in wound care is still in the research phase, but preliminary tests show signs of successful treatments.

Since the field of plasma medicine is cross-disciplinary, covering plasma physics, plasma chemistry, biochemistry, cell biology, and medicine, it is out of the reach of a single individual to write an entire authoritative book about the subject. For this reason the editors of this book called on a team of experts, each contributing sections related to his/her own discipline. It is important to note that all these experts are actively involved in ongoing research on plasma medicine. They present the latest state of knowledge in this still-emerging field. To convey both background knowledge as well as the state-of-the-art, the book is divided into two parts. The first

5

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

More information

6

Plasma Medicine

introduces basic plasma and electrical discharge concepts, as well as fundamental background in cell biology and contamination. The second part consists of seven chapters which discuss today's healthcare challenges, plasma–cell interactions (this includes prokaryotic cells and eukaryotic cells), plasma-based wound care, and plasma-based surgery (including dental applications).

#### References

Becker K., Koutsospyros A., Yin S. M., Christodoulatos C., Abramzon N., Joaquin J. C., and Brelles-Mariño G. *Plasma Phys. Control. Fusion* **47**, B513 (2005).

- Fridman G., Friedman G., Gutsol A., Shekhter A. B., Vasilets V. N., and Fridman A. Plasma Proc. Polym. 5, 503 (2008).
- Kong M. G., Kroesen G., Morfill G., Nosenko T., Shimizu T., van Dijk J., and Zimmermann J. L. *New J. Physics* **11**, 115012 (2009).
- Laroussi M. IEEE Trans. Plasma Sci. 30, 1409 (2002).
- Laroussi M. Plasma Proc. Polym. 2, 391 (2005).
- Laroussi M. IEEE Trans. Plasma Sci. 37, 714 (2009).
- Laroussi M. and Fridman A., Plasma Proc. Polym. 5, 501 (2008).
- Morris A. D., McCombs G. B., Akan T., Hynes W., Laroussi M., and Tolle S. L. J. Dental Hygiene 83, 55 (2009).

Ramen F. Albucasis (Abu Al-Qasim Al-Zahrawi): Renowned Muslim Surgeon of the Tenth Century. Rosen Publishing Group, NY (2006).

Stoffels E. J. Phys. D: Appl. Phys. **39** (2006).

Weltmann K-D., Kindel E., von Woedtke T., Hahnel M., Stieber M., and Brandenburg R. *Pure Appl. Chem.* 82, 1223 (2010).

# 2

# Fundamentals of non-equilibrium plasmas

MARK KUSHNER AND MICHAEL KONG

### 2.1 Introduction

Generation of gas plasmas is associated with production of energetic particles (e.g. electrons, ions, and photons), chemical reactive species (e.g. free radicals and metastables), and a myriad of transient fields (e.g. heat, shock and acoustic wave, electrostatic and electromagnetic fields). This is a highly coupled process of complexity and dynamics. For example, through Poisson's equation, a nonuniform or non-neutral spatial distribution of charged particles can set up a local electrostatic field and its role near the electrodes can outweigh the contributions of the externally applied electric field. Photons and some charged particles (e.g. superoxide  $O_2^-$ ) are also chemically reactive. In fact, production of different plasma agents and fields is closely coupled and it is usually not possible for one plasma agent to be produced without many other agents also being produced. When used for treating and processing materials, and biological materials in particular, these plasma agents and electric fields tend to work synergistically in their interaction with, and their effects on, the material that is brought in contact with the gas plasma. The synergistic effect is distinct in the extent and the richness of physiochemical functionalities facilitated and is not usually accessible with other techniques for materials treatment. This is an important aspect of gas plasmas from an application standpoint, and a key reason why gas plasmas have been used widely in our society, as discussed in Chapter 1. Yet it also brings with it the challenge of unraveling the associated complexity in plasma-material interactions in order to improve and optimize the efficiency of the material-processing application. Fortunately, the development of microelectronics industry since the 1970s has resulted in a considerable understanding of how plasma agents and fields interact with materials.

*Plasma Medicine*, eds M. Laroussi, M. Kong, G. Morfill, and W. Stolz. Published by Cambridge University Press. © Cambridge University Press 2012.

More information

Cambridge University Press

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

8

### Plasma Medicine

Despite their close coupling and synergy, it is desirable to categorize the numerous plasma agents and fields in order to reach a broad clarity and consensus when gas plasmas sources are developed and designed for a given application. In many ways, particles and fields resulting from plasma generation may be regarded as media that carry energy of different kinds (e.g. chemical energy, wave energy, and particle kinetic and mechanical energy). When a gas plasma source is brought in contact with a material, the former releases its many forms of energy thus facilitating many different changes in the latter. These can range from physical changes, such as material destruction and etching, to chemical changes, such as modification of polymeric surface functionality. The length scale of these effects can vary by up to 10 orders of magnitude, ranging from tens of meters (e.g. magnetic fusion) to a few nanometers (e.g. nanostructure fabrication). A key reason why vastly different plasma effects are facilitated in different scenarios is that different forms of energy are preferentially produced and released. For applications that favor physical forces, substantial energy coupled into plasma is often necessary and its consequent conversion into mechanical and wave energy is also common in the resulting plasma. For low-temperature applications, such as treatment of semiconductors, polymers, colloids, and indeed living tissues, chemical energy is preferred and macroscopic physical forces such as heat and shock waves often need to be mitigated. Therefore, the development and design of appropriate gas plasma sources for any specific application are concerned with selective production of some forms of energy at the expense of the others. The degree to which such selectivity can be achieved and controlled is critically dependent on the underpinning scientific understanding. For plasma medicine, this is aided by a vast body of scientific understanding and know how in terms of the choice of many key parameters, such as the plasma-forming gas, excitation voltage properties (e.g. excitation frequency or pulsing parameters), input energy coupling (e.g. electrode design), and precursor chemistries.

It is therefore clear that a key objective of plasma science is to understand how the externally supplied electrical power is coupled into different energy forms and how the energy couple can be controlled preferentially. For the vast majority of applications in medicine and healthcare, chemical energy of gas plasmas is critical and its delivery should preferably be at relatively low-temperature. For example, skin disinfection requires a thermally gentle delivery of appropriate reactive plasma species to the skin surface at a temperature below 60°C in order to avoid permanent thermal damage to skin tissue (Leach et al., 1943). In general, ideal plasma properties include: (1) a mean electron energy around one electron volt (equivalent to about 11 000 Kelvin) to facilitate chemical dissociation, excitation, and ionization; and simultaneously (2) a gas temperature not exceeding 100°C (or 373 Kelvin) for treatment of plastics and living tissues. This implies that the electron kinetic energy is much higher than the thermal energy of the plasma, or they are not in thermodynamic equilibrium. Gas plasmas with such non-equilibrium energy

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

Fundamentals of non-equilibrium plasmas

More information



Fig. 2.1 Schematic energy level diagram of n = 1, 2, 3, 4, and 5 states of helium showing radiative transitions between n = 4 to lower levels. Some of the radiative transitions between states are shown by the dotted lines.

distribution are commonly known as non-equilibrium plasmas. Given their dominance in medical applications, this chapter provides a basic understanding of non-equilibrium plasmas.

### 2.2 Plasma ignition and sustainment

Without the influence of an electrical discharge, gases are electrically neutral and gas atoms have a balanced population of protons and electrons. The protons are contained in the nucleus of an atom and the electrons are confined in orbitals and move around the nucleus. The electron confinement is achieved by means of the balance between two forces, namely the electrostatic attraction force to the protons and the centrifugal force of the orbiting electrons around the nucleus. The total charge of all electrons in an atom is equal to that of all protons in the atom's nucleus, and therefore an atom is electrically neutral when not ionized. For any given type of gas atom (e.g. helium, argon, or oxygen), there exists a set of discrete electron orbits, each characterized by a specific energy level with the lowest energy associated with the orbit closest to the nucleus. As an example, the energy level diagram for helium is shown in Figure 2.1. Helium is a particularly simple atom

9

978-1-107-00643-0 - Plasma Medicine: Applications of Low-temperature Gas Plasmas in Medicine and Biology Edited by M. Laroussi, M. Kong, G. Morfill and W. Stolz Excerpt

More information

10

### Plasma Medicine

because it has only two electrons in orbit around the nucleus, and so the variety of interactions between the electrons and nucleus produces a relatively small number of atomic states, only a subset of which are shown in Figure 2.1. However, even this simple atom has a complex atomic-level structure, which must obey quantum mechanical selection rules. For example, singlet states cannot transition to lower triplet states by emitting a photon – states also cannot transition to lower states having the same orbital angular momentum. As a result, there are certain states that are metastable, which means these states do not radiatively relax to a lower state of the atom. Since these metastable states do not radiatively relax to the ground state, they store energy for long periods of time and so are more likely to be available for chemical reactions. The He(2<sup>3</sup>S) state, having an energy of 19.8 eV, is an example of such a metastable state that is important for producing reactions in other atoms and molecules. Other examples of metastable states that are important to air plasmas are  $O_2(^1\Delta)$ , with about 1 eV of stored energy, and  $N_2(A)$ , with about 6 eV of stored energy.

Normally, most electrons rotate in the lowest-energy orbit and their move to a higher-energy orbit, called an excited state, requires an electron gaining adequate energy from an external source. In electric discharges, this energy is transferred to the orbital electron by a collision with an unbound, free electron moving through the gas. The free electron gains its energy from an applied (or internally generated) electric field. Since a high-energy orbit has a larger radius than a low-energy one, an electron moves further away from the nucleus as it gains energy from the external source to join a higher energy orbit. Eventually, it reaches an energy threshold above which the electron can escape the electrostatic confinement of the nucleus and becomes "unbound" to the atom. The gas atom now becomes positively charged by virtue of the loss of an electron, or an ion, and is now said to be ionized. From this point onwards, both the electron and the ion are accelerated by the externally applied electric field. As an ion is much heavier than an electron, the ion is less mobile.

Once released from a gas atom, an unbound electron is subsequently accelerated by the externally applied high electric field. With the kinetic energy thus gained, the electron can, on collision with other gas atoms, release additional electrons from these gas atoms. This process repeats itself as the original electron and the new electrons released so far are accelerated from the cathode to the anode, thus supporting an electron multiplication process. It is essential for a gas discharge to be ignited. However, it is not a sufficient condition since electrons released from the external electric field can also be lost and thus become unavailable for sustaining the development of electron multiplication. There are a number of electron loss mechanisms, for instance electron–ion recombination and electron absorption or attachment to a solid object such as an electrode. For gas ionization to be triggered