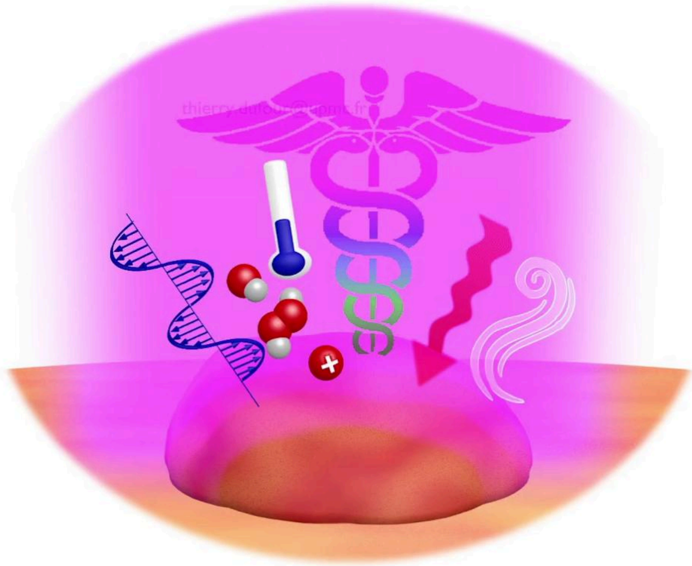
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

PLAS@PAR Plasmas à Paris

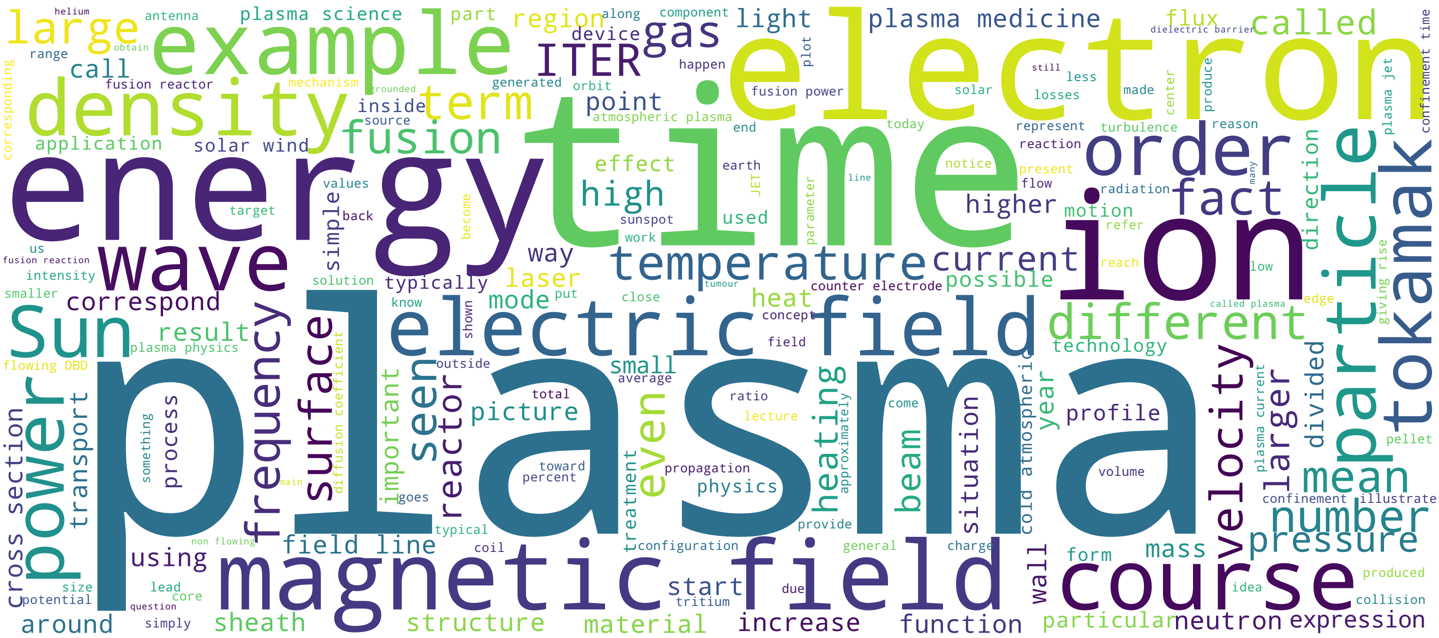
PLASMA MEDICINE



Introduction

Lecture 5F

Thierry Dufour



EPFL

Outlines

I. MEDICAL CONTEXT

II. PLASMA MEDICINE: FROM ORIGINS TO AWAKENING

III. BASICS OF COLD PLASMA SCIENCE & TECHNOLOGY

Plasma

Welcome to this first MOOC, which is an introduction to plasma medicine. It will help students in biology and medicine to discover what are called plasma. It will also help students in plasma science and technology to better understand the potential of cold plasma as an innovative approach for biomedical applications. The outlines of these introductions are as follow. First, the medical context will be set. Second, we will discover how plasma medicine was born and how it is now applied. And third, the basics of cold plasma science and technology will be reminded. First, let's start with the medical context.

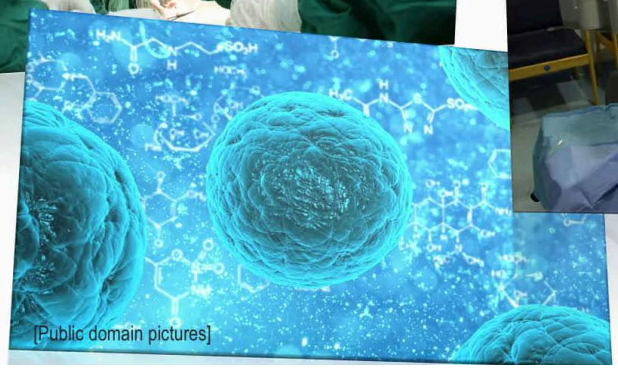
Notes

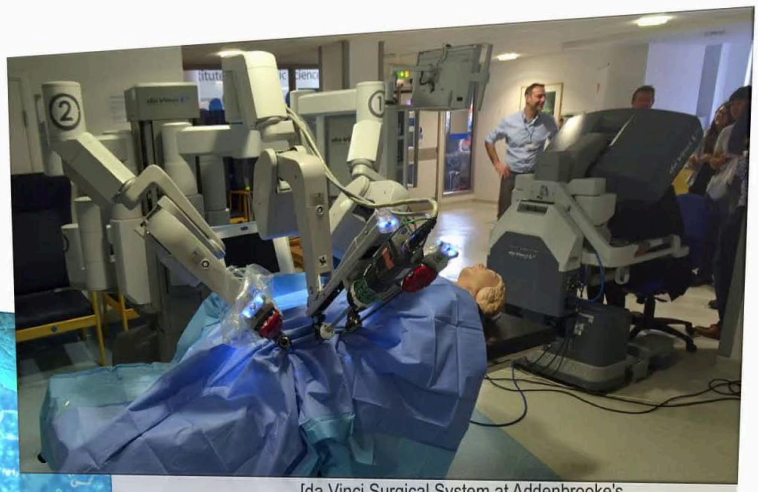
Summary

0m 05s

I. Medical context


[© CMSRC]


[Public domain pictures]


[da Vinci Surgical System at Addenbrooke's Treatment Centre, commons.wikimedia.org]

Plasma

Organ transplantation, cell therapy, surgical robots, medicine surpluses itself to save and extend human life or simply improve our quality of life. However, even up to now, medicine faces major limitations to cure legions of diseases and troubles.

Notes

Summary

0m 44s

I. Medical context

I.1. Head & Neck cancer

- 6th cancer the most frequent worldwide
- Squameous carcinomas from the upper aerodigestive tract

[S. Islam et al., 2011, ANZ J. of Surgery, letters to the editor, 949]

- Almost 540 000 new cases per year
- Problems
  - Frequent relapse (35-55% over 2 years)
  - Severe prognosis (survival rate<20% on 10 years)

1.2. Foot ulcers in the diabetic patient

- Origin: peripheral neuropathy
- Consequences
  - Impairment of nerves
  - Foot hydration is reduced

[H. Mohamed. 2015;27(4):103-114]

- Preventive solutions
  - Daily feet examination (cuts, blisters, bruises, color changes, swelling, open wounds)
  - Wearing appropriate shoes
  - Cutting nails properly

Plasma

To illustrate these limitations, let us espouse on two blatant examples. First example is head and neck cancer. It is the sixth most frequent cancer worldwide, which corresponds to squameous carcinomas from the upper aerodigestive tract. It represents almost 540,000 new cases per year, and even if there exists therapies combining ablative surgery, radiotherapy and chemotherapy, problems still persist. We have frequent relapse between 35 and 55 percent over two years and severe prognosis since the survival rate is less than 20 percent in 10 years. So new therapies are highly expected. Another examples are foot ulcers in the diabetic patient. The destruction of the foot tissues can be caused by peripheral neuropathy. The consequences are an impairment of nerves, which induces loss of foot sensitivity and then a higher risk of accidental injury, and also foot hydration that is reduced, inducing dryness cracks and calluses. So there exists some preventive solutions combining daily feet examinations, wearing appropriate shoes or cutting nails properly. But all those solutions only improve life quality, but they cannot be considered as curative treatments.

Notes

Summary

1m 04s

1.3. LIMITATIONS

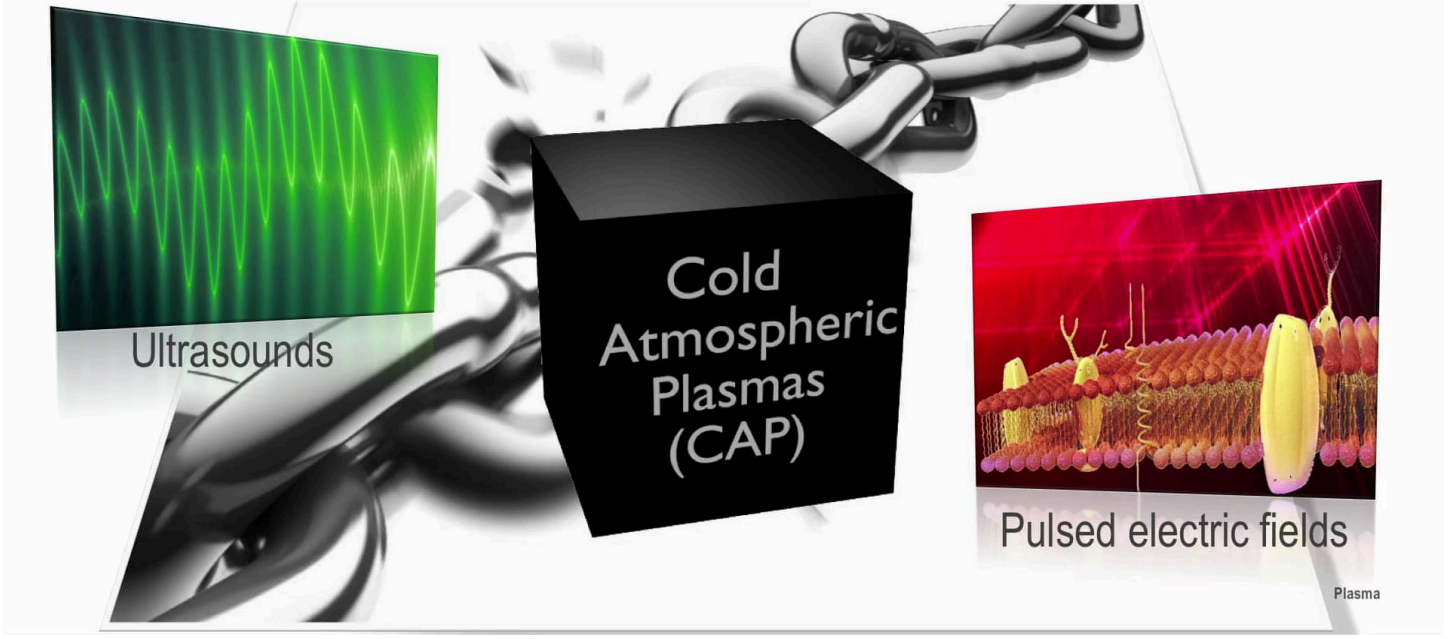
Those two examples merely illustrate the fact that the conventional therapies even if combined remain limited and therefore new therapies are highly expected, in particular, innovative approaches at the interface of physics and chemistry.

Notes

Summary

2m 23s

1.3. LIMITATIONS



On that purpose, approaches such as PEF, Pulsed Electric Fields, and therapeutic ultrasound techniques are studied for several years and even decades. But more recently, another approach shows the promising potential which is the science of plasma and more specifically, cold atmospheric plasmas.

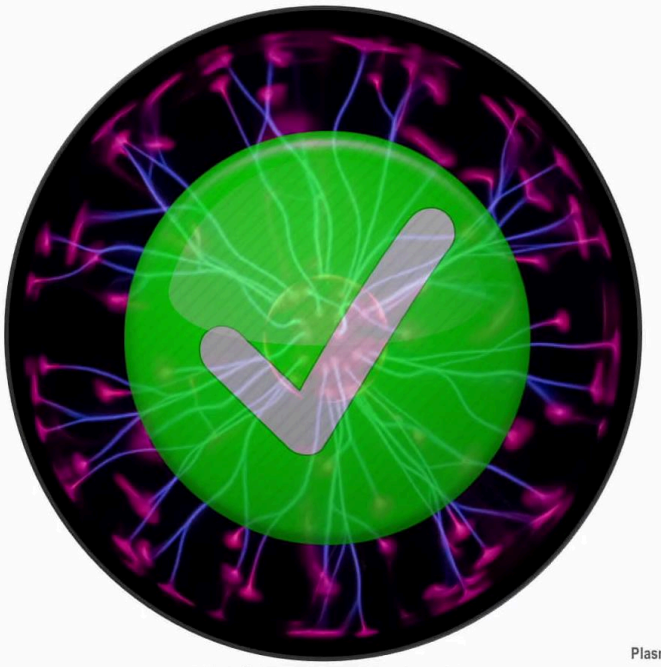
Notes

Summary

2m 39s

I. Medical context

[© Avery Dennison, PR082]



Plasma

[© L. Viatour / www.Lucnix.be]

Here the term plasma does not refer to the liquid component of blood which acts like an extracellular matrix to hold red and white blood cells. Here, plasma refers to a very specific state of matter, distinct from the well known solid liquid and gas state.

Notes

Summary

2m 57s

Outlines

I. MEDICAL CONTEXT

II. PLASMA MEDICINE: FROM ORIGINS TO AWAKENING

III. BASICS OF COLD PLASMA SCIENCE & TECHNOLOGY

Plasma

Before understanding the basics of plasma science and technology, let's introduce how medicine and plasma science have met to allow the emergence of a new research area called plasma medicine.

Notes

Summary

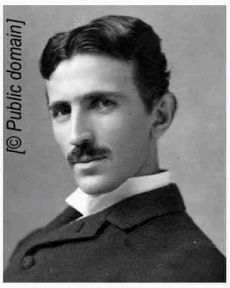
3m 16s

II. Plasma medicine: from origins to awakening

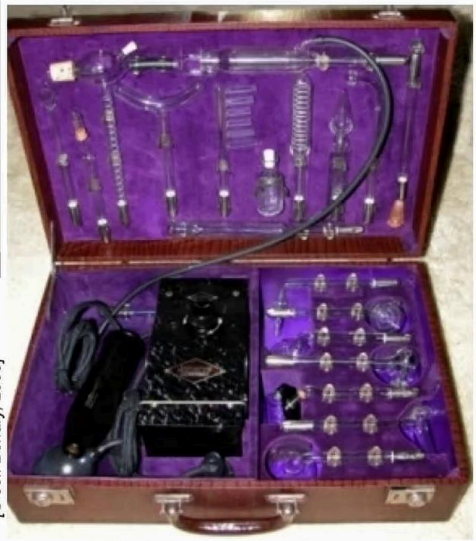
II.1. … From nebulous origins


[© Public domain]

1893, World's Columbian Exposition at Chicago


[© Public domain]

N. Tesla


[© Jeff Behary, 2008]

Violet ray device

Plasma

The utilisation of plasma for therapeutic purposes is quite old. In 1893, during the World's Columbian Exposition at Chicago, Nikola Tesla presented the first prototype of its Violet Ray medical appliance. Then the invention aroused the curiosity of manufacturers and found its first domestic utilisation at the [inaudible 00:03:49] sanctuary.

Notes

Summary

3m 28s

II. Plasma medicine: from origins to awakening

II.1. … From nebulous origins

- The device was equipped with a variety of glass applicators
- Applications: nervous, dermatological or muscular diseases and troubles

[© electrotherapymuseum]

Plasma

It was equipped with a variety of glass applicators where plasma could be generated and applied on the body to treat nervous, dermatological, or muscular diseases and troubles. However, the success story stopped for two reasons. First because of misuse by some people and second, because of the Second World War conflict, which compelled manufacturers to reorient their activity to equip the US military forces.

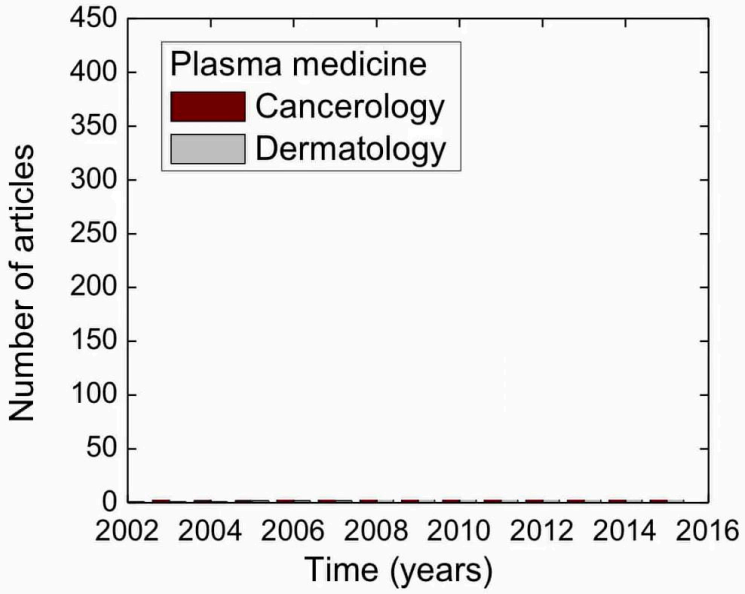
Notes

Summary

3m 51s

II. Plasma medicine: from origins to awakening

II.2. … TO A WELL STRUCTURED AND EMERGING RESEARCH FIELD



Plasma

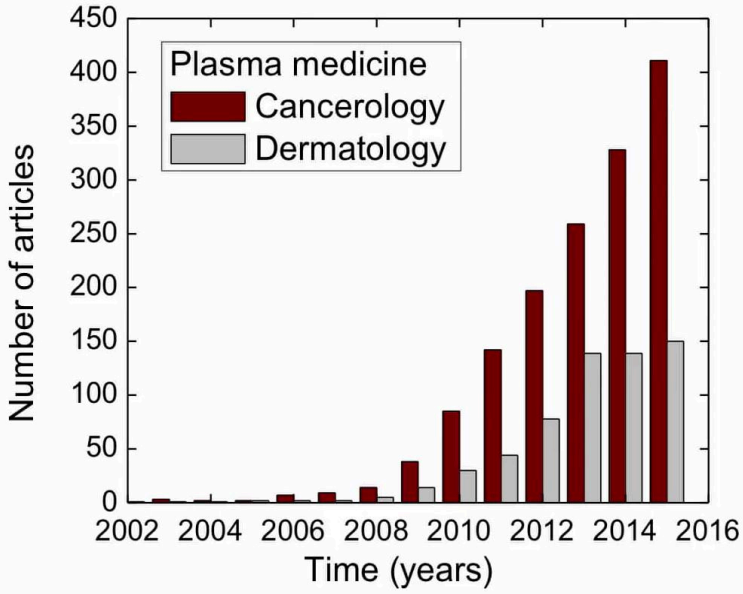
At the early of the 21st century, cold atmospheric plasma, now a second birth to answer medical issues under the form of an academic discipline called Plasma Medicine. One can have an idea of its emerging nature by visiting the Google Scholar search engine and typing sentences like plasma medicine plus cancer or plasma medicine plus dermatology.

Notes

Summary

4m 18s

II.2. … TO A WELL STRUCTURED AND EMERGING RESEARCH FIELD



Plasma medicine can be considered as an emergent / exploratory research field

Plasma

Then the annual number of articles published per year on these research activities can be measured. On this graph, we clearly observe that plasma medicine has started around 2006 and that the research works in cancerology and in dermatology have continued to grow inexorably. For this reason, the academic research in plasma medicine can be considered as emergent or exploratory.

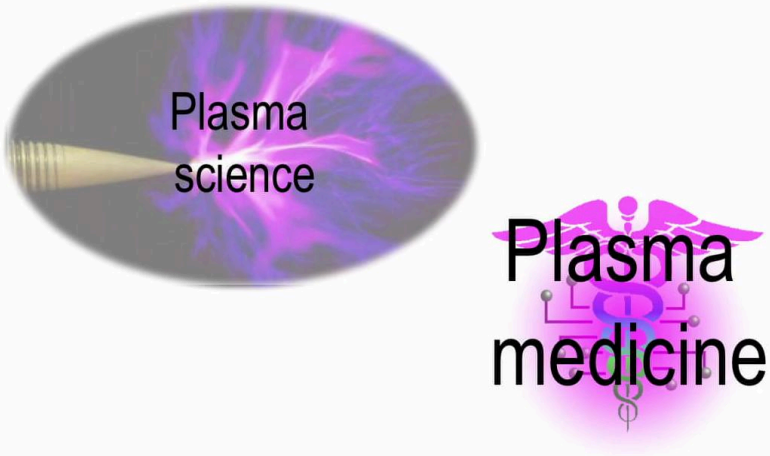
Notes

Summary

4m 39s

II. Plasma medicine: from origins to awakening

II.3. A MULTIDISCIPLINARY RESEARCH FIELD



Plasma

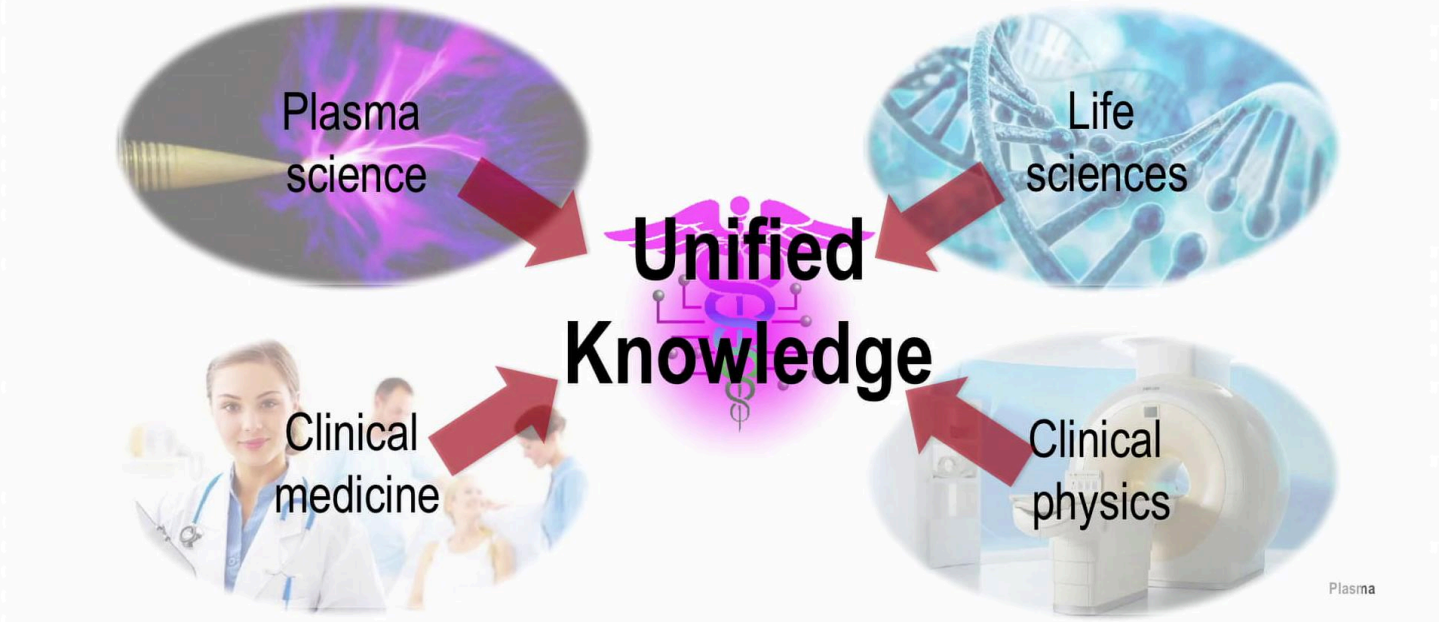
Plasma medicine is also highly multidisciplinary.

Notes

Summary

5m 04s

II.3. A MULTIDISCIPLINARY RESEARCH FIELD



Today, it is at the interface of plasma science, life sciences such as biology, clinical physics and clinical medicine The convergence of these competencies is a mandatory to build a unified knowledge.

Notes

Summary

5m 12s

Outlines

I. MEDICAL CONTEXT

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III. BASICS OF COLD PLASMA SCIENCE & TECHNOLOGY

Plasma

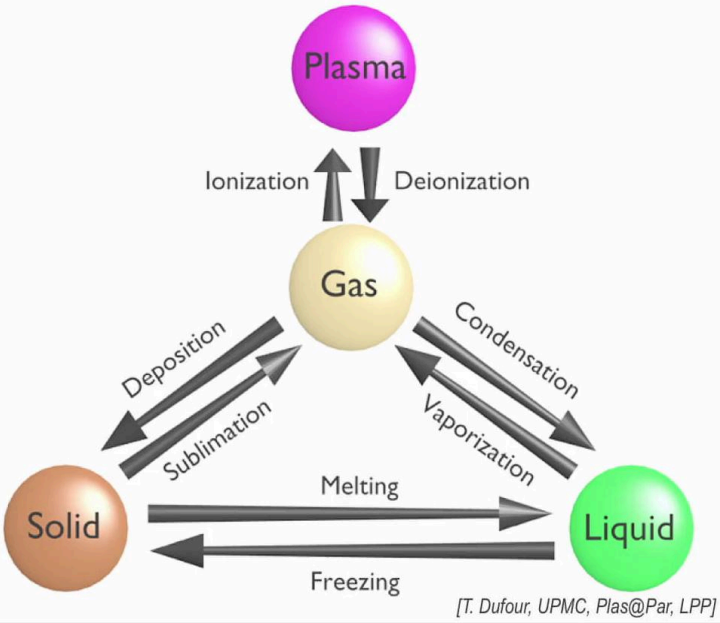
So now it is time to focus on one of the four disciplines taking part to this unified knowledge, plasma science and technology.

Notes

Summary

5m 27s

III.2. States of matter



The three basic states of matter commonly described in introductory chemistry texts are solid, a liquid, and gas. However, such a representation is incomplete since a fourth state of matter exists under the name of 'plasma'.

Notes

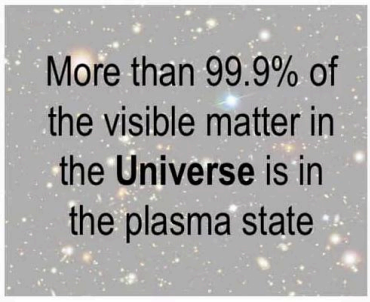
Summary

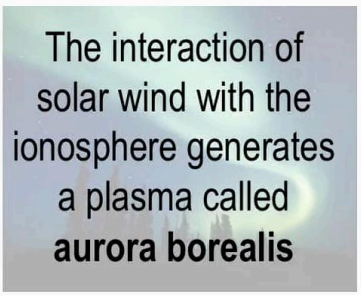
5m 36s

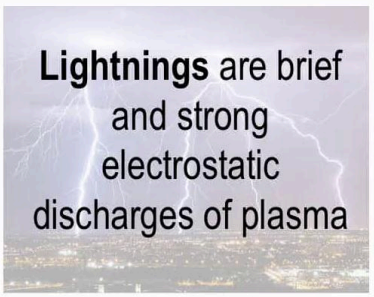
III. Basics of cold plasma science & technology

III.1. NATURAL PLASMAS AND ARTIFICIAL PLASMAS: EXAMPLES

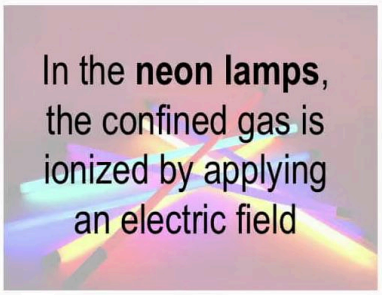
Natural plasmas

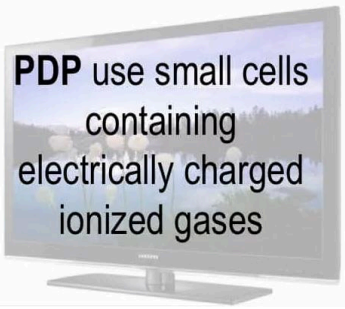


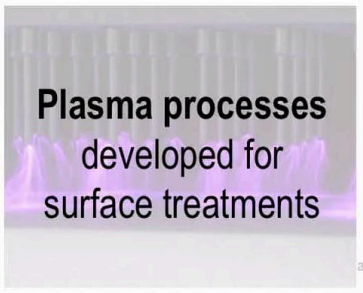




Artificial plasmas







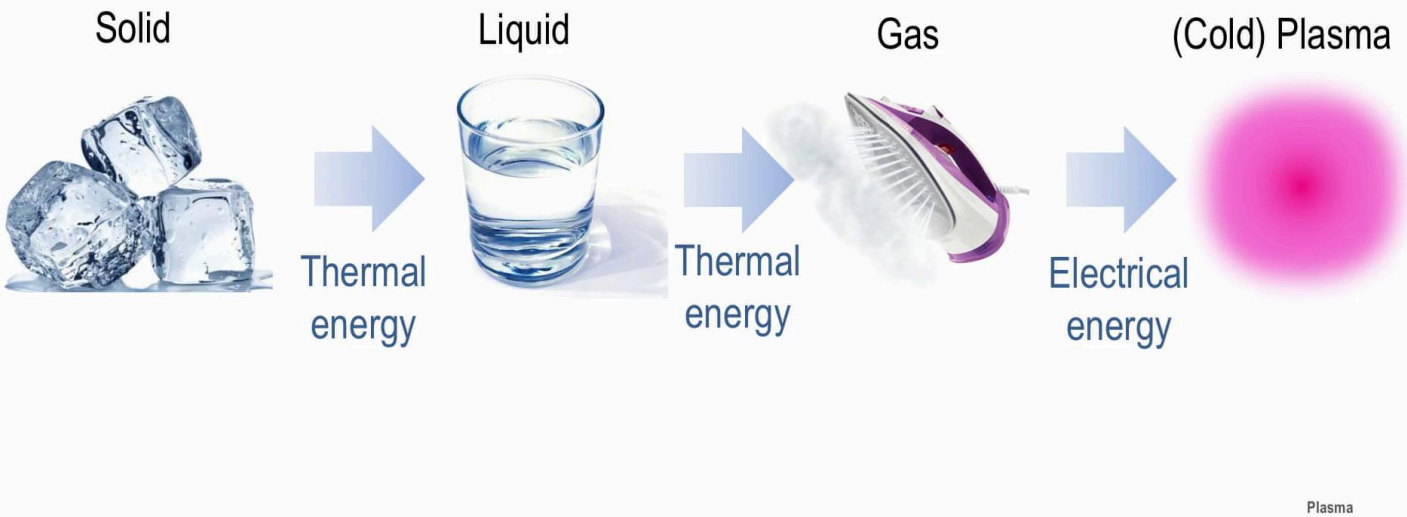
Plasma can be classified into two main families, natural plasmas and artificial plasmas. In the natural plasmas, the first example that can be mentioned is the universe. More than 99.9 percent of the visible matter in the universe is in the plasma state. The solar wind is a plasma which passes through the magnetosphere tail. It interacts with ionosphere gases giving rise to the aurora borealis. Other examples are lightnings that result from electrically conducting plasma channels giving rise to a brief but strong electrostatic discharge. Among the artificial plasmas, neon lamps figure among the most basic examples. The gas is contained in a tube and ionised by applying an electric field. Also, plasma display panels use small cells containing electrically charged ionised gases. And plasma processes are developed for surface treatments using, for example, metrics of coronary discharges.

Notes

Summary

5m 51s

III.2. States of matter



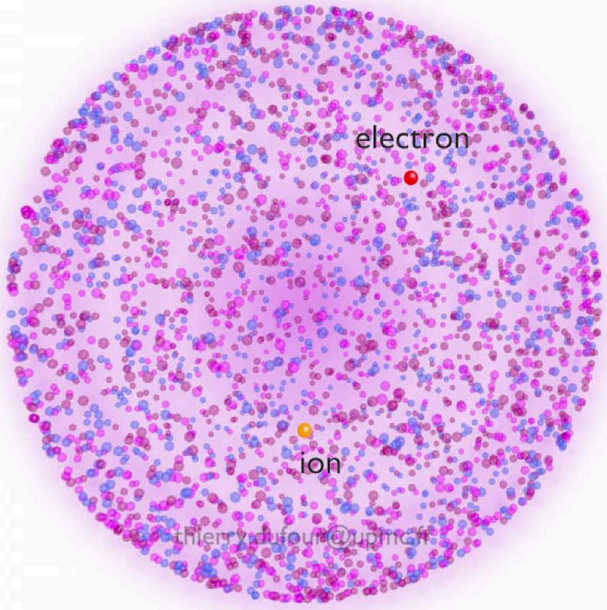
To understand very simply what is a plasma let's consider a system solely composed of water molecules. If the temperature is very low, then water is under the solid state. It corresponds to the ice cubes that you put in your soda. If you increase the thermal energy of these ice cubes, then they transit from solid to a liquid state. This is the water you daily drink. If you increase again the thermal energy of this liquid, then it can transit to its gaseous state. It is the water vapour emitted, for example by an iron. Finally, if electrical energy is injected into this gas, for example, by applying an electric field, then a plasma can be generated.

Notes

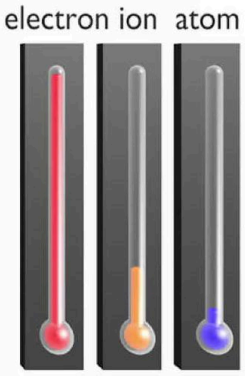
Summary

6m 48s

III.3. Expected characteristics of a cold plasma



- Weakly ionized gas (1 electron & 1 ion for 1 billion of neutral species)
- Atmospheric pressure
- Gas temperature close to body temperature



To be used in medicine. Plasmas must meet specifications based on practical and medical considerations. If the plasma has to interplay directly with biological tissues, then it has to be weakly ionised. This means that for roughly one billion of neutral species, less than 100 are electrons and ions. The plasma has to operate also at atmospheric pressure, and the gas temperature of the plasma must be close to the temperature of the human body. Since the plasma is in a thermodynamic disequilibrium electron temperature is much higher than the ion temperature, which in turn is also much more higher than the temperature of the neutrals.

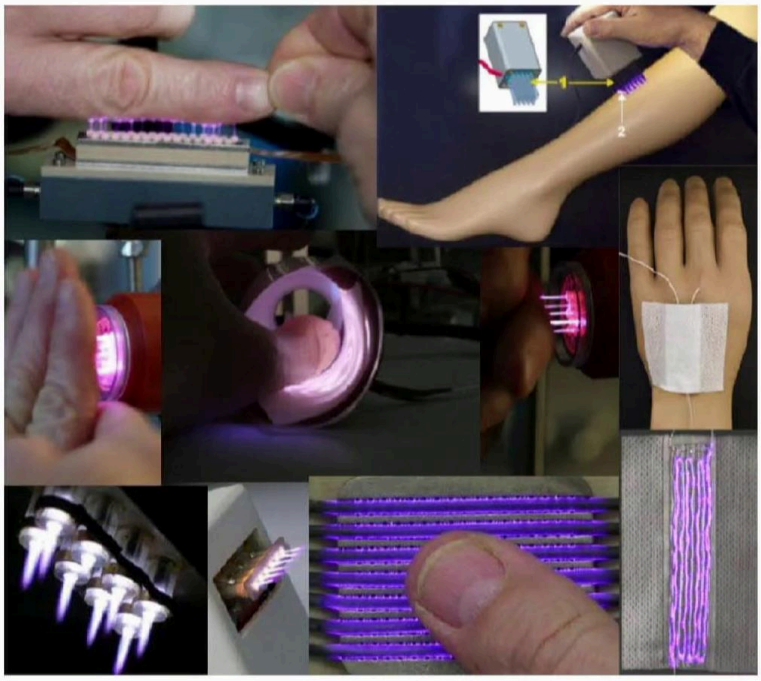
Notes

Summary

7m 29s

III.4. PLASMA SOURCES FOR THE TREATMENT OF LIVING SYSTEMS

- Plasma sources
  - Plasma jets & plasma guns
  - Surface DBD & Volume DBD
- Treatments
  - Large areas
  - Very localized regions
  - Complex structures/geometries



[K.-D. Weltmann et al., Contrib. Plasma Phys. 52(7)7, 644–654 (2012)]

Now let's talk about the plasma sources for the treatment of living systems. Plasma jets, Surface DBD and Volume DBD have already been employed for the treatment of large areas, or on the contrary of very localised regions, and even for the treatment of complex structures and geometries.

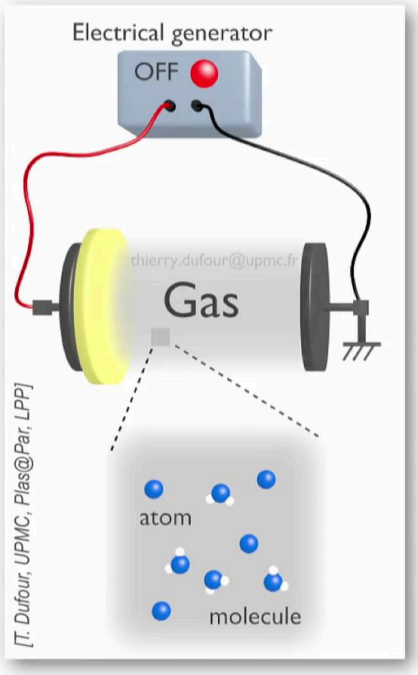
Notes

Summary

8m 12s

III.4. Plasma sources for the treatment of living systems

- Gas confined in a two electrodes configuration



Plasma

Usually, a cold atmospheric plasma is generated by mediating a gas between two electrodes. One of the electrode is connected to the electrical generator while the other is grounded. The resulting voltage applied along the inter-electrode distance allows the generation of an electric field, which, if it is strong enough, can ionise the gas thus giving rise to a plasma.

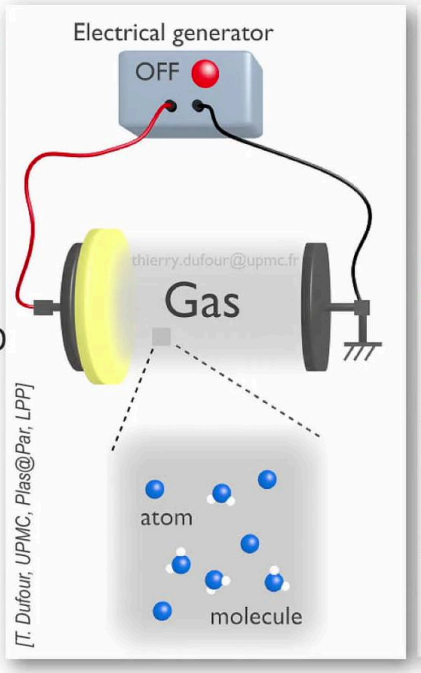
Notes

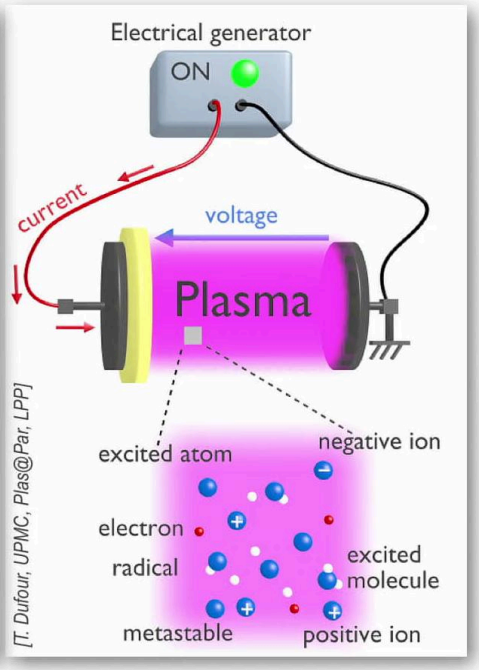
Summary

8m 30s

III.4. PLASMA SOURCES FOR THE TREATMENT OF LIVING SYSTEMS

- Gas confined in a two electrodes configuration
- The reduced electrical field has to be high enough to ionize the gas
- Production of electrons, +/- ions, chemical radicals, energetic, metastable species, …





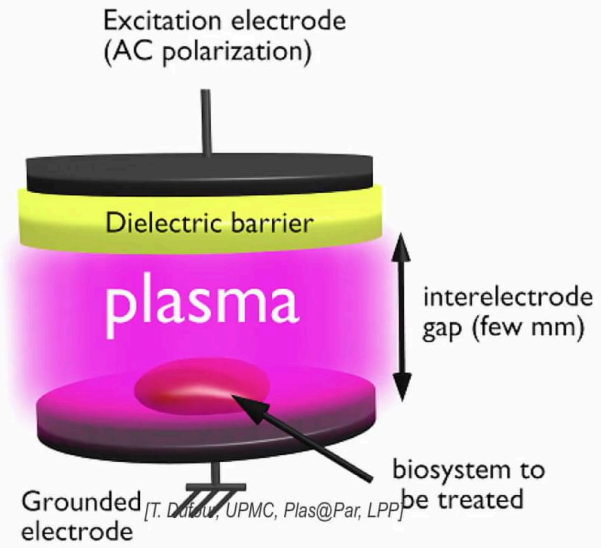
This plasma contains atoms and molecules excited to different energetic levels, positive ions and electrons and eventually negative ions, chemical radicals, and metastable species.

Notes

Summary

8m 52s

III.4. PLASMA SOURCES FOR THE TREATMENT OF LIVING SYSTEMS



A. The non flowing DBD

- Structure
  - Excitation electrode: AC voltage
  - Dielectric barrier: no arc formation
  - Gap region: plasma & biosystem
  - Counter electrode: grounded

Plasma

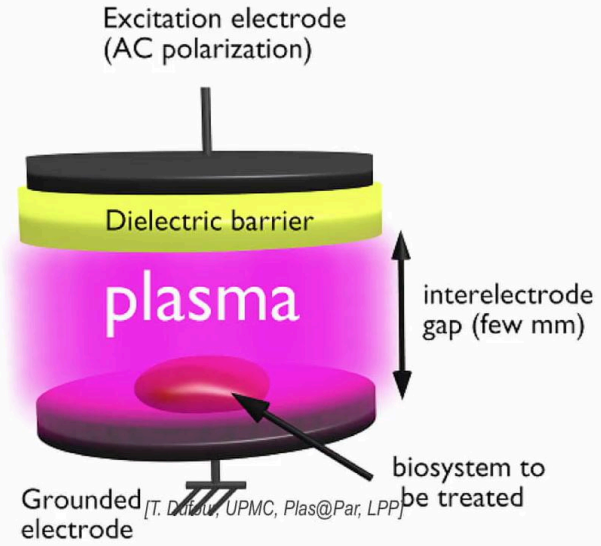
Most of the plasma sources rely on the same configuration, two electrodes separated by a dielectric barrier. Such discharges are called dielectric barrier discharges. Two main types of DBD can be distinguished. The non-flowing DBD and the flowing DBD, also called plasma jet. So let's first consider the non-flowing DBD.

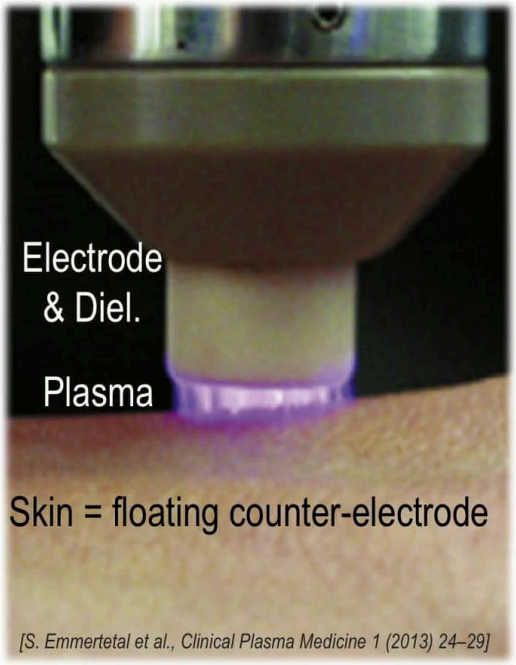
Notes

Summary

9m 05s

III.4. PLASMA SOURCES FOR THE TREATMENT OF LIVING SYSTEMS





Plasma

The structure of the non-flowing DBD is as follows; an excitation electrode, a dielectric barrier, a gap region where a gas can be ionised, and the counter electrode. The excitation electrode is polarised to an AC [inaudible 00:09:41] voltage while the counter electrode is grounded. Hence, an alternative electric field applied in the gap region can generate a cold plasma. The dielectric barrier is of major importance since it prevents any thermal arc formation. The electrical advantages are amplified, giving rise to plasma micro discharges developing at a nanosecond timescale. The main limitation of this device is the interelectrode distance that has to be less than one centimetre. As you can observe in this picture, the human skin here plays the role of the counter electrode whose potential is not grounded, but floating.

Notes

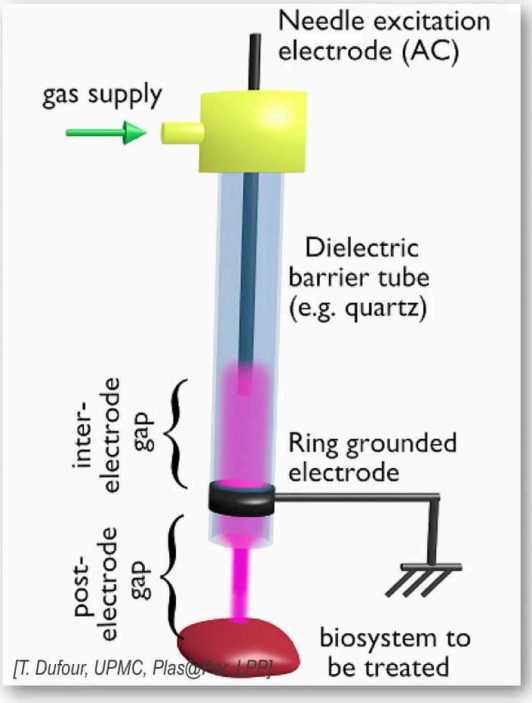
Summary

9m 32s

III.4. Plasma sources for the treatment of living systems

B. The flowing DBD = Plasma jet

- Configuration very close to the non flowing DBD
- A gas is delivered upstream the interelectrode region
  - Plasmagen gas: helium or argon
  - Admixture of reactive gases (O_2, …)
  - The gas flow allows to extend plasma beyond the interelectrode region ⇒ A plasma plume can easily develop on several centimeters



The configuration of the plasma jets now is very close from the structure of the non-flowing DBD. In the kinetics, the voltage is delivered by an inner needle electrode while the outer-ring electrode is grounded.

Notes

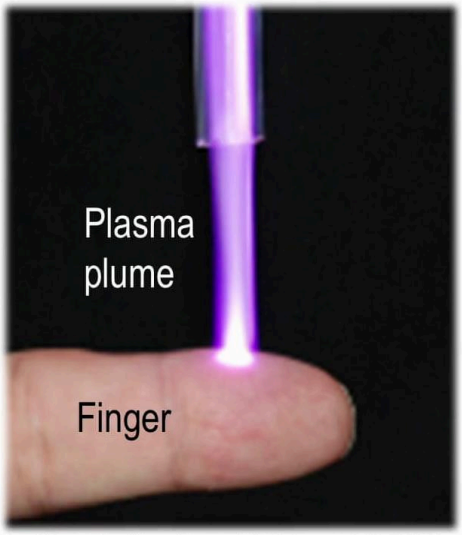
Summary

10m 20s

III.4. PLASMA SOURCES FOR THE TREATMENT OF LIVING SYSTEMS

B. The flowing DBD = Plasma jet

- Advantages
  - Hollow cavities are accessible as well as very localized areas
  - Huge 3D tumors can be treated
  - Cooling effect induced by the gas flow



[© K. Kitano, https://www.jst.go.jp/tt/EN/cips_details/pdf_2/7-9.pdf]

Plasma

The electric barrier separates these two electrodes. Inside this tube, a gas is delivered upstream of the interactive region. Usually this gas is helium or argon, but it can be mixed with other reactive gases such as oxygen. The input gas allows to extend plasma beyond the interelectrode region, and therefore a plasma plume can easily be developed on several centimetres. Several advantages are noteworthy. First, hollow cavities are accessible as well as very localised areas. The treatment of 3D biosystems and also the lowering of the heating of the biosystem. The plasma can be applied on tissue located several centimetres away from the plasma jet and without inducing thermal damages as can be observed here on this picture where a finger is directly exposed to this plasma plume.

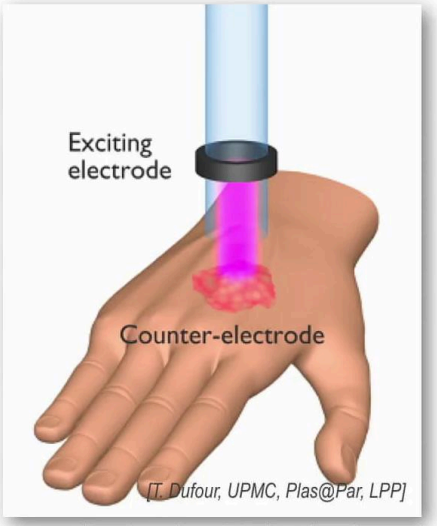
Notes

Summary

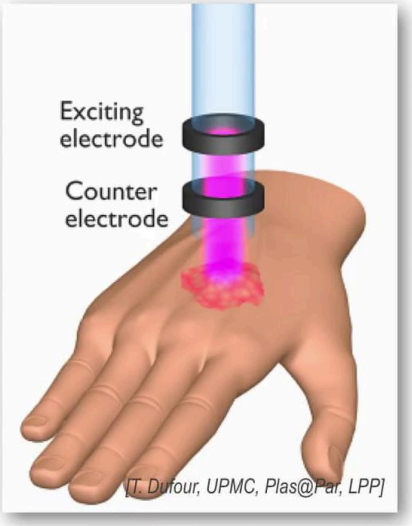
10m 34s

III.5. APPROACHES

A. Direct contact approaches



Counter-electrode: biological system



Counter-electrode: metal

Plasma

These plasma sources can be used following direct and indirect contact approaches. In the direct contact approaches, the biological tissues or tumour is directly exposed to the plasma. One can distinguish the case where the biological system constitutes the counter electrode and the other case where the counter electrode is integrated to the DBD device.

Notes

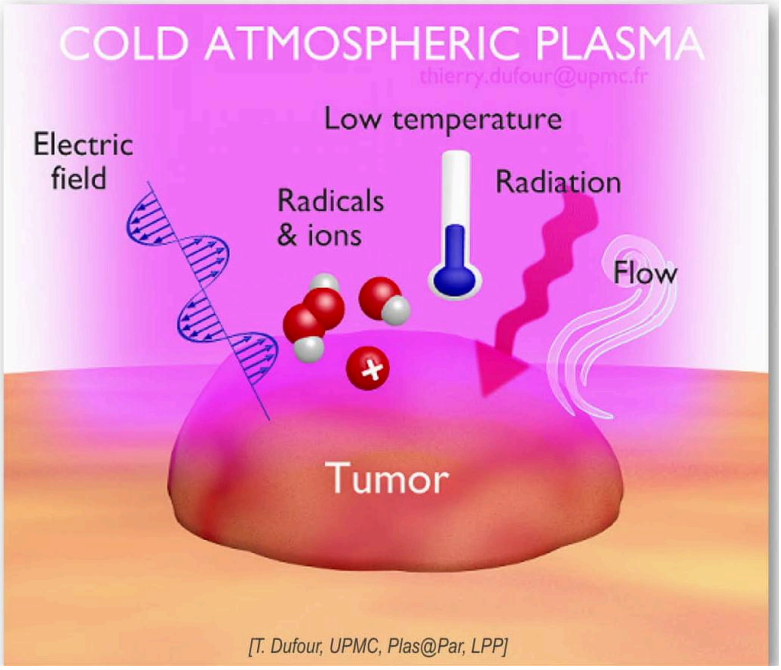
Summary

11m 26s

III.5. Approaches

A. Direct contact approaches

- Here, several properties of the plasma can present a therapeutic plus-value:
  - Electrical field
  - Chemical species (radicals & ions)
  - Temperature
  - Radiation
  - Gas flowing
- Depending on their range in intensity, some of these properties could present competitive or synergetic effects



Here several properties of the plasma can present a therapeutic plus-value. The electric field, chemical species, radicals and ions, the gas temperature, radiation, the gas flowing and depending on the range in amplitude in intensity, some of these properties could present competitive or synergetic effects.

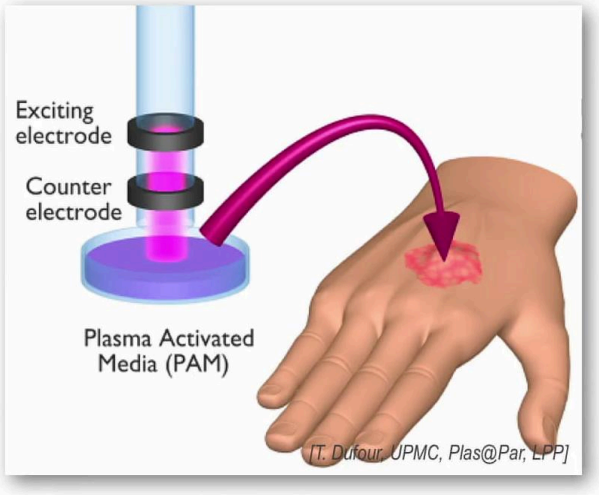
Notes

Summary

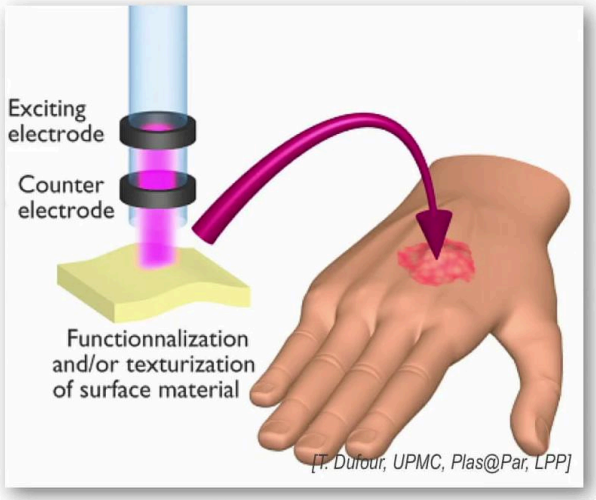
11m 48s

III.5. APPROACHES

B. Indirect contact approaches



Liquid/wet process



Dry process

Plasma

The indirect conduct approach can be performed via liquid or dry intermediate media. First, a liquid can be plasma-activated during several minutes and subsequently injected into tumour. Second, a therapeutic material or substance can be treated by plasma or subsequently set on the tumour. In this indirect approach, only long live radical species can have a therapeutic plus-value. The potential therapeutic effect of electric field or short lifetime radicals such as OH are absent.

Notes

Summary

12m 10s

Conclusion

- Most of the time, they are generated using DBD devices, in particular plasma jets
- They can be utilized following 2 approaches:
  - Direct contact (short lifetime species and transient physical phenomena can have a direct therapeutic impact on the system to be treated)
  - Indirect contact (PAM, i.e. plasma activated medium, is synthesized and then interplays with the system to be treated)

Plasma

So as a conclusion, we have to keep in mind that cold atmospheric plasma are investigated as an innovative approach for the treatment of diseases where conventional therapists fail. Cold atmospheric plasma are weakly organised gases characterised by several properties; electric fields, chemical reactive species energetic species, controlled heating, flowing and radiation. Also, most of the time they are generated using DBD devices in particular, plasmajets. They can be used following two approaches. The direct contact or short lifetime species as well as transient physical phenomena can have a direct therapeutic impact on the system to be treated. And indirect contact, where PAM, plasma-activated medium is synthesised and then interplays with the system to treat.

Notes

Summary

12m 41s