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Low Temperature Plasma Interaction with Biological Matter

Topic: Plasma Atomic Physics and the Interface with Chemistry and Biology

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Author cannot attend the Town Hall meeting but would like to participate in future planned workshops.

Historical Perspective

Following a few preliminary works on the inactivation of bacteria by low temperature plasma (LTP) reported in mid to late 1990's [1]-[3] AFOSR established a small funded program aiming to evaluate the effects of plasma on biological cells. This program was managed by the Electronics and Physics Directorate of the US Air Force Office of Scientific Research (AFOSR). This program had two main aims: 1. the investigation of the efficacy of low temperature atmospheric pressure plasma to destroy pathogenic bacteria; 2. the investigation of the possibility of these plasmas to be applied to a wound in order to disinfect it and facilitate the healing process. The initial AFOSR goals were the decontamination of tools and gear (from biological warfare agents, for example) and acquiring a technology that can be used in forward deployed field hospitals to treat wounded soldiers. The latter application is particularly important for temporarily set-up military hospitals since stocking, storing, and preserving perishable medication is a tough logistical challenge. However, by using plasma as a disinfectant these logistical problems completely disappear.

Unfortunately, after this pioneering AFOSR program came to a close interest in funding this research waned and no government agency seemed to be interested in continuing or sustaining this kind of work in the United States. Nevertheless, research work continued in a few US labs and more scientific knowledge and applications were created. On the other hand, by the mid-2000s interest in this multidisciplinary field (which came to be known as "Plasma Medicine" [4]) grew sharply in Europe and Asia. Several well-funded programs were subsequently established in Germany, France, Japan, South Korea, etc. In addition, in Germany, Japan, and South Korea research centers entirely dedicated to advancing the field are in operation today. This situation has put US researchers at a severe disadvantage in a plasma application field with great scientific and economical promise and greater societal impact.

Advancing the Frontier in the Field of Plasma Medicine

The interaction of LTP with biological cells and tissues involves complex biochemical pathways. To make the situation even more daunting is the fact that biological targets are usually surrounded by matter in the liquid phase (biological fluids). Therefore, one has to deal with plasma-driven chemistry in the gaseous, liquid, and solid phases. In addition, the resulting mechanisms span wide ranges both in space and in time, from the micrometers (cells) to the centimeters/meters (experimental dimensions) and from the nanoseconds (chemical reactions and plasma dynamics) to hours (cells response). Therefore to advance the scientific knowledge in this field, investigators have to elucidate intricate and interlinked chemical and biochemical mechanisms occurring at the four known states of matter (plasma, gas, liquid, and solid). Figure 1 illustrates this paradigm.

The effect on biological cells involves various biochemical pathways that enter into play on the cellular and sub-cellular levels. It has been shown that plasma-generated reactive species, such as reactive oxygen species (ROS) and nitrogen reactive species (RNS) are the main actors. Therefore in order to understand the biological outcomes resulting from LTP application, investigators have to elucidate the effects of these species on cell membranes, mitochondria, DNA and other cell organelles. In addition, these chemical species can trigger cell signaling which can impact the cells in a fundamental way. For example, in the application of LTP to kill cancer cells [5], it has been shown that LTP can activate caspases which lead to a chain of events that result in cell death by apoptosis [6]. Also, LTP has been

shown to selectively target the S-phase of the cell replication cycle and therefore is more likely to kill cancer cells than healthy ones [7]. All this work is preliminary and needs further in-depth investigations to yield a complete picture of the effects of LTP on biological cells.

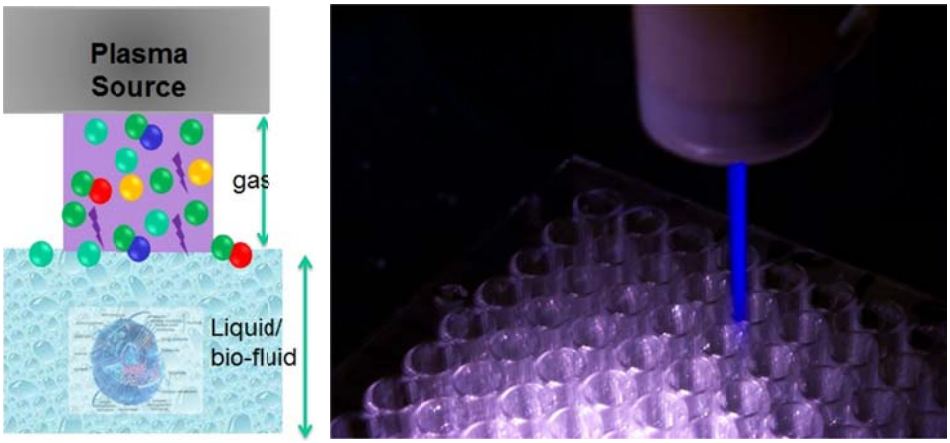

Fig. 1 Illustration of the complex interactions between plasma and biological targets (left), and a photograph of the application of the plasma pencil to biological media in vitro.

Impact of this Research

The interaction of LTP with biological cells and tissues is an interdisciplinary field that involves expertise in plasma physics, chemistry, and engineering, in biochemistry, microbiology, and medicine. The scientific issues are yet to be resolved and well understood. However, the scientific impact is undeniably far-reaching and the possibility that LTP can potentially introduce a paradigm shift in medicine and in the healthcare arena in general is palpable. LTP could one day be used to kill antibiotic resistant pathogens, treat chronic wounds such as diabetic ulcers, and kill cancer cells without the serious side effects of radiation and chemotherapy. Society stands to greatly benefit from the results of such scientific endeavor.

References

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