+Article type: Review paper

Title: Translation of plasma technology from the lab to the food industry

P.J. Cullen*[1,2], James Lalor[2], Laurence Scally[2], D. Boehm[2], V. Milosavljević[2], P. Bourke[3] and K. Keener[4]

---

1. Prof. Patrick Cullen
   Department of Chemical and Environmental Engineering, University of Nottingham,
   Nottingham, NG7 2RD
   E-mail: pjcullen@dit.ie
2. Mr James Lalor, Mr Laurence Scally, Dr. Daniela Boehm, Dr. V. Milosavljević,
   BioPlasma group, Dublin Institute of Technology, Marlborough Street, Dublin, Ireland
3. Dr. Paula Bourke
   School of Food Science and Environmental Health, Dublin Institute of Technology,
   Marlborough Street, Dublin, Ireland
4. Prof. Kevin Keener
   Center for Crop Utilization Research, Iowa State University, Ames, IA, 50011, USA

Keywords: atmospheric pressure glow discharges (APGD); biomaterials; dielectric barrier discharges (DBD); food packaging; non-thermal plasma

Abstract

The potential of cold plasma as a food processing aid has been demonstrated for a range of processes and products. The potential applications of plasma technology are extensive and include: microbial decontamination, pest control, toxin elimination, food and package functionalisation and many others. However, studies reported to date have principally been at laboratory scale. This paper discusses the status and challenges of transferring the technology to the industry. The major challenges discussed for adoption of atmospheric plasma as a food processing tool by industry are: 1) demonstration of product/process specific efficacies; 2) development of process compatible technology designs and scale-up; 3) effective process control and validation; 4) regulatory approval and 5) consumer acceptance.

1 Introduction

The food industry continually seeks innovative technologies and approaches to improve both food production and processing methods. Apart from the competitive advantages such innovation may bring, the industry faces a global challenge of ensuring food security for a rapidly growing population. Food by its nature and production means is prone to microbial and/or pest contamination. Consequently, the industry relies on a range of intervention strategies where processing steps are employed at points along the food chain to control contaminants to ensure both product safety and/or extend shelf-life. Thermal processing of food has been a cornerstone of processing along with drying, freezing, chemical agents and protective packaging. A noticeable development in food processing over the past decade has been increased demand for ‘minimally processed’ or ‘natural’ foods by consumers which has resulted in reduced demand for technologies which induce notable changes in the physical, nutritional or taste properties of foods such as freezing, drying etc. Consequently alternative approaches which confer antimicrobial or ‘pesticidal’ effects yet retain the product’s quality attributes close to that of its ‘fresh’ state are currently under active research. One grouping of technologies, collectively referred to as ‘non-thermal’ technologies aim to offer antimicrobial efficacies similar to those found with thermal pasteurisation, these include the use of high hydrostatic pressures, pulsed electric fields, radiofrequency waves and UV light to mention a few.[1] Recently cold plasma has been added to this list. The potential and adoption of non-thermal treatments has been further expanded by regulatory agencies increasingly acknowledging their demonstrated efficacies. Of note here is the expansion of the definition of pasteurization beyond solely a thermal treatment by the NACMCF (the US National Advisory Committee on Microbiological Criteria for Foods Adopted August 27, 2004 Washington, DC) to include any treatments which can “reduce the most resistant microorganism(s) of public health significance to a level that is not likely to present a public health risk under normal conditions of distribution and storage”.

Nonthermal plasmas are considered to be in a state of nonthermal equilibrium. This imbalance may occur because the ion temperature is different from the electron temperature, or because the velocity distribution of one of the species does not follow a Maxwell–Boltzmann distribution. Although they contain high temperature electrons, critically the neutrals, ions, and radicals remain close to room temperature and as such they are considered “cold” plasmas. Within the physics and engineering domains, the descriptors of low temperature plasmas may operate at temperatures of hundreds or thousands of degrees above ambient. Consequently, the term ‘cold plasma’ has recently been coined to distinguish one-atmosphere, near room temperature plasma discharges from other non-thermal plasmas.[2] Cold plasma discharges may be obtained artificially by many means of electromagnetic wave disturbances resulting from the application of direct current, alternating current, or ionization radiation in such a way that a measureable charge is created in the gas and the gas temperature remains near ambient. Examples of these cold plasma devices include DC glow discharge, radio frequency (RF) discharge, dielectric barrier discharge (DBD), atmospheric pressure plasma jet (APPJ), microwave discharge and pulsed power discharge.[3] A wide variation of discharges in the form of corona, spark or arc can be formed in gas or liquid media using pulsed power with various kinds of reactor configurations; all with important technological wide applications.[4]

The potential applications of plasma technology are extensive and include: microbial decontamination, pest control, toxin elimination, food and package functionalisation and many others. Research to-date has particularly focused on fresh produce, grains and meats. Successful demonstration of these many applications have caught the attention of the scientific community and industry alike, with demonstrated efficacies for a range of applications and products. Potential drivers of the technology for the food industry have been identified by Keener and Misra: [5] 1) potential extension of product shelf-life - lower consumer food waste; 2) maximum retention of food quality - lower food processing and storage losses; 3) low energy requirement - more green than current technology; 4) low operational and maintenance costs - simple systems with minimal maintenance and sanitation requirements; 5) enhanced chemical safety of foods – plasma inactivation and removal of pesticide and chemical residues; and 6) green technology and environmental sustainability – only need air and electricity to create an effective plasma. A growing number of publications including several recent reviews are found on the topic of plasma in food, particularly focused on antimicrobial efficacy,[6,7] food applications,[8,9] functional properties,[10] and food packaging.[11] However the reported studies to date are almost exclusively at lab scale. Commercial advances at processing scale in atmospheric plasma technology have focused on food contact surfaces, packaging and modification of material for improved labelling with food grade inks. [5] The major challenges for adoption of atmospheric plasma as a food processing tool by industry are: 1) demonstration of product/process specific efficacies; 2) development of process compatible technology designs and scale-up; 3) effective process control and validation; 4) regulatory approval and 5) consumer acceptance. The objective of this paper is to review the status and discuss the challenges of translating plasma technology from the laboratory to industrial use. For detailed discussions of the plasma interactions with microbiology, food properties or packaging the reader is referred to the papers above.

2 Plasma sources and delivery approaches for foods

2.1 Plasma sources

Plasma generation at atmospheric pressure is of interest to the food processing sector because it compatible with typical manufacturing conditions. The ability to generate cold plasma discharges at atmospheric pressure makes integration of the decontamination or treatment process easier and less expensive. [12] For food and bio-medical applications, the plasma needs to be truly non-thermal in its operation, at least at the point of interaction with heat sensitive bio-materials. Due to the complex physical and chemical processes inside a low temperature plasma, a multiplicity of different biologically active agents are produced with dependence on the adjusted parameters, such as gas chemistry, flow rate, moisture, temperature and excitation properties. Table 1 provides a summary of the design variables and current techniques employed in the generation of cold atmospheric pressure plasmas. All these parameters offer a significant operational space which can be optimised and exploited to meet the processing challenges found within the food industry.

2.2 Inducer gases

A plasma can be formed in any gas once sufficient energy is supplied in the correct manner. The first studies using plasma as a food disinfection technology employed plasma jet configurations designed for surface modification and consequently employed common carrier gases of argon and helium. However, for discharges to open air atmospheres reactive oxygen and nitrogen species will be generated even if the operating gas does not contain either gas.[13] Numerous studies have examined the role of inducer gases with the addition of various amounts of oxygen and many contemporary studies continue to employ helium,[12] and argon.[14] However, ROS (Reactive Oxygen Species) and RNS (Reactive Nitrogen Species) are often cited for their roles in the observed anti-microbial effects. The feasibility of using air as the plasma source gas offers a cheap processing aid for food applications which is practically essential given the large scales of production and the typically low value added nature of food processing. However, one important limiting factor is the dielectric strength of air, which is about 3×10^6 V/m, meaning that high voltages or small discharge gaps are required for breakdown under atmospheric conditions. Examination of the rapidly expanding literature shows a clear trend towards the use of air as the operational gas of choice. [15]

2.2.1 Relative Humidity (RH)

The RH of the inducer gas has been showed to significantly influence the anti-microbial efficacy of plasma. Given that many foods have a high water content the surrounding air is often of high RH. Patil *et al.* explored the role of RH for a range of gases on the inactivation of *Bacillus atrophaeus* spores contained within a sealed package.[16] This work reported that humidity influences ozone generation which is important for the analysis of plasma chemistry (as the presence of water leads to lower O_2 dissociation levels and promotes formation of OH radicals that can quench O_3 generation). The resultant plasma chemistry at different RH levels indicated generation of numerous reactive species such as N_2O_5, H_2O_2, HNO_4, and OH radicals in addition to O_3, with increasing concentrations of these species recorded at high RH levels. The study also examined direct plasma exposure and indirect exposure to the contained plasma afterglow which is relevant given the complex structural nature of many foods and the associated difficulty in obtaining complete surface exposure. Based upon these and other[17] findings RH is likely to be a critical control parameter for many food decontamination applications and consequently the influence of environmental RH on the plasma induced chemistries and their resultant effects on the target should be understood.

2.2.2 Modified Atmosphere Packaging (MAP)

A feasible alternative to using air is to employ gases currently used by the food industry to control the product's environment. MAP is the practice of controlling the composition of the internal atmosphere of a food package to improve the shelf life of perishable products including; meat, fish, fruits and vegetables. The modification process often lowers the concentration of oxygen, generally close to 0%, resulting in a slow down the growth of aerobic organisms and prevention of oxidation reactions. Conversely, high levels of oxygen (70–80%) have also been used in MAP to reduce microbial growth in packages. Common replacement gases employed include nitrogen and carbon dioxide. Typically, fresh red meat packaging use 70% O2 + 30% CO2 for MAP and cooked meats are stored in 70% N_2 + 30% CO_2. For fruit and vegetables low oxygen/high nitrogen (10% O_2 + 90% N_2) MAP are preferred, to inhibit respiration and undesirable colour changes. Han *et al*. investigated the effect of plasma discharges in sealed MAP gas mixtures on the reactive species generated (ROS and RNS), their efficacy and mechanism of inactivation against *Escherichia coli*, *Listeria monocytogenes* and *Staphylococcus aureus*.[18] The study examined three MAP gas mixtures of, 70% N_2 + 30% CO_2, 90% N_2 + 10% O_2 and 70% O_2 + 30% CO_2 along with reference to atmospheric air. While the capacity for ROS generation was mainly dependent on the oxygen content of the gases, RNS formation was governed by both the nitrogen content and the presence of oxygen. In a comparable study on microbial decontamination of strawberries inside sealed packages with two different gas mixtures (65 % O_2 + 16 % N_2 + 19 % CO_2 and 90 % N_2 + 10 % O_2), Misra *et al*. showed that background micro-flora could be significantly reduced (~3.0 log cycles) for both gas mixes.[19] However, strawberries treated and stored in the high oxygen gas mixture showed favourable quality results with similar respiration rates and an 11 % higher firmness than the control. These studies demonstrate that microbial inactivation can be achieved with common MAP gases coupled with the positive effects on product shelf-life from the MAP process.

2.3 Plasma Activated Water (PAW)

A relatively new approach for the delivery of plasma generated species to biological targets is to 'activate' water or other liquids through exposure to plasma discharges. PAW provides a number of advantages over direct plasma treatment for biological applications; these include ease of application, defined dose, storability and off-site generation. The approach is similar to ozone containing water, where the ozone molecule is dissolved typically through bubbling ozone through water. The resulting water displays, for a period of time, reactive properties which may be used for either disinfection of the water itself or as a wash agent for contact or food surfaces. Current research in PAW is examining the efficacy and mechanisms of action of the approach as an antimicrobial agent for foods. An advantage of the technology is the potential to develop a window of activity after which the PAW returns to stability and possible self-sanitation of the wash water. PAW allows for a more controllable 'dose' from the perspective of application to a food's surface.

Many foods have a high water content which may act as a barrier between the product and plasma discharges or reactive species and consequently the reaction chemistry observed with PAW is often present for direct plasma treatment of such foods. The reactive species generated in the liquid phase act as mediators for reactions with these biological targets and have been shown to possess anti-microbial and/or cytotoxic activity indicating that these solutions retain their biological activity post-plasma exposure. [20] Thus, these solutions are of interest as novel anti-microbial agents for decontamination of food contact surfaces and food products. The exposure of aqueous solutions to atmospheric plasmas results in the generation of relatively long-lived secondary products such as hydrogen peroxide, nitrates and nitrites which may react to form further cell toxic compounds such as peroxynitrous acid.[21,22]

Conventional methods of decontamination and cleaning of fresh produce such as vegetables are based on rinsing with water containing concentrations of chlorine, chlorine dioxide or ozone. Technology limitations with chlorine relate to poor stability and the association with a possible formation of carcinogenic chlorinated compounds in water, which have brought the use of chlorine in food processing applications into question.[23] The formation of plasma discharges in air admixed with microliquid particles in the form of mist is another approach for targeted delivery of reactive species to a surface.[24] The approach is particularly suited where full emersion of food products into a solution is not feasible, such as animal carcasses.

Solutions exposed to plasma discharges could provide a novel resource which can be tailored to a range of applications in food processing environments. However, a holistic insight into the mechanisms governing the liquid-mediated effects of plasma exposure is required to discover the full potential of this technology, to develop known potential applications and to inform policy and regulation related safety considerations with regard to long-term effects of exposure to both direct plasma and plasma activated liquid. This currently forms an active and exciting area of research.

3. Food Applications

Plasma has a number of potential applications in the food industry each with different efficacies and challenges. Applications which do not have direct contact with foods such as food packaging and food contact surfaces typically offer relatively homogenous and smooth surfaces, facilitating ease of treatment and a well-defined pathway for regulatory acceptance. Conversely, direct food contact with cold plasma is intended for human/animal consumption and typically has a more complex interaction and therefore presents a higher regulatory challenge. Given the vast diversity of foods and the potential food-plasma-package interactions, the regulatory approval process will likely require a product-process-package regulatory review and approval data needed will likely differ for each product-process-package combination.[25]

3.1. Packaging and contact surfaces

Plasma discharges have been successfully applied for both surface modification and sterilisation of food packaging material.[11,26] Recent plasma designs also show promise for sanitation of food processing surfaces such as conveyor belts through intermittent disinfection cycles. In a similar fashion the technology can be used to disinfect food containers prior to product filling. Given the fact that plasma is widely employed for surface and packaging modification in other industries its transfer to the food sector for such purposes is relatively straightforward. Such surfaces are typically smooth which supports sanitation efficacy, rapid treatment times and process validation. Recently, active packaging has been developed by surface coating antimicrobials onto polymer packaging using a plasma discharge process.[27] The process resulted in reductions in the microbial loads for beef products with significant increases in product shelf-life.

3.2. Food decontamination

The multi-species nature of plasma provides a distinct advantage due to the difficulty for bacteria to offer or develop resistance.[6] Consequently, a significant body of research over the past few years has focused on food decontamination. However, given the diversity of food products available, the findings are almost equally as diverse. Pignata *et al*. compiled a recent survey of plasma disinfection of food products and reported that 40% of the reported literature over the past decade used cold plasma on fresh fruits and vegetables, 21% on dry fruits, nuts and seeds, 19% on protein foods such as meat and cold cuts, 10% on spices, 6% on liquids and 4% on the eggshells.[15] Product properties such as surface roughness, moisture content and chemistry are found to govern both process efficacy and technology suitability. Vast differences, both in terms of technological challenges and process acceptability, are likely to be observed between applying plasma as a disinfection technique for egg shell by comparison with nuts or leafy greens or cooked meats. Indeed even the definitions and metrics of food decontamination are very broad with significant differences between pasteurization, sterilization, disinfection, etc. Each term has a specific definition or multiple definitions depending on the regulatory agency, country, and product. Given the diversity of food products there is no universal technology for product disinfection and consequently an array of technologies are employed each offering advantages for specific commodities. It is likely that plasma too will prove to be suitable for select products and unsuitable for others. Food decontamination offers the greatest impact for plasma in the food industry, however it also offers the greatest challenges in terms of process efficacy and regulatory acceptance.

3.3. Food properties modification

A growing area of research is the use of plasma for the modification of food properties where novel and desirable functional properties are induced or improved by plasma treatment. Thirumdas *et al*. presents a review of plasma treatment of native starch with the objective of enhancing its functional properties.[10] The alteration in the properties is mainly due to depolymerization and cross linking of amylose and amylopectin side chains. Plasma treatment is reported to decrease molecular weight, viscosity, and gelatinization temperatures. Plasma etching also increases surface energy and enhances the hydrophilicity of the starch granules.[10] The treatment of flour can have positive effects on the bulk mechanical properties of resultant doughs. Misra *et al*. reported that the rheological properties of treated wheat flour revealed an improvement in the dough strength and optimum mixing time.[28] Plasma was found to induce changes in the secondary structure of the flour's proteins. The results indicated that atmospheric plasma can be exploited as a means to modulate functionality of wheat flour. Yepez and Keener induced a cold plasma discharge within a contained hydrogen gas atmosphere to partially hydrogenate soybean oil without the formation of trans-fatty acids.[29] This study demonstrated that plasma could be an alternative processing technology to traditional catalytic hydrogenation.

Misra *et al*. demonstrated the potential of plasma to enhance the surface hydrophobicity of baked biscuits facilitating increased spreading of vegetable oil.[30] The effect allows retention of the functionality of the oil but with less oil or fat required due to the increased spread leading to healthier products. Functionalisation of food properties using plasma could have different technical and regulatory barriers than those of food disinfection.

4. Scale-up

Common approaches for plasma generation at atmospheric pressure include corona discharge, Radio-Frequency Plasma (RFP), gliding arc discharge and Dielectric Barrier Discharge (DBD). Atmospheric-pressure plasma sources have gained increased attention for food applications, yet the issue of scaling discharges up to larger areas without compromising the plasma uniformity remains a major challenge.

4.1. Multiple plasma sources

The growth in the number of applications of non-equilibrium plasmas for materials processing during the last quarter century has created a demand for developing novel plasma-generation technology, such that it is becoming possible to realise uniform plasmas of higher density in larger volumes.[24] One approach to scaling is to use multiple sources or reactors.

Cao *et al.* challenged the efficacy of a linear jet array with a complex three-dimensional substrate and reported excellent jet-to-jet uniformity both in time and in space.[31] The spatial uniformity was found to be four times better than a comparable single jet. Conversely, Cao *et al.* [32] and Kim *et al.* [12] reported that when atmospheric jets were arranged in 2-D arrays, mutual electric and hydrodynamic interactions occur, which result in divergent or extinguishing of the individual jets or merging of the individual jets into a single jet much smaller than the diameter of the jet array system. Placing plasma jets adjacent to one another may result in amplified jet intensities where the charged particles affect each other due to the nature of their collective behaviour. Furmanski *et al.* reported on a honeycomb design for plasma jet-to-jet coupling and the formation of an intense plasma jet at atmospheric pressure.[33] Such research demonstrates the variability and potential of innovative array designs on the scale-up process.

When using a system that requires a gas flow, a plasma jet for example, one must consider at what ratios of gas mixtures and flow rates would be the most efficient. If the distance between the sample surface and the plasma plume are increased to accommodate a bulk amount of sample or prevention of detrimental thermal effects, then the mixtures and flow rates that were used on the lab-scale must be changed accordingly. The challenge with this is that some efficiency may be lost in the generation of the plasma and also may reduce the amount of specific reactive species to interact with the sample surface and thus cause an adverse effect on the sample treatment. The increase of flow rates of certain gases has been shown to decrease the amount of other reactive species formed within the plasma. **Figure 1** shows a large (450mm diameter) multi-jet array designed for continuous treatment of food products by employing a conveyor belt and a surrounding wall to help retain the reactive species.

In order to secure a method that can secure uniform plasma discharge when scaling up, there must be thought put into the changes of system volume, sample surface interactions, plasma density, samples residence time, sample-to-source distances, power and current supply, and the relative cost effectiveness of such systems. Three-dimensional modelling and simulations can assist with regard to assembly, fluid dynamics, thermal, and electric field behaviour. Ideally this would be carried out in conjunction of experimental work on complex samples such as food.

4.2. Microplasma arrays

Microplasma are plasmas which are confined in a cavity of small dimensions typically ranging from tens to thousands of micrometers. The design can provide stable discharges at atmospheric pressure, operate in open air and as such are a good candidate for biological processing.

Microplasma designs may allow for effective scale-up as they can be flexible in both their geometrical design and packing density, coupled with their ability to operate under low voltages at atmospheric pressure.[34,35] Microdischarge devices which operate at atmospheric pressure are gaining increased attention, primarily due to the significant cost reduction for processing compared with their low pressure counterparts.[35] Such designs may also suit scale-up for large volume food treatments through homogeneous large area treatment and could be particularly suited for continuous processing conditions. However, micro-plasma array structures can have significant fluxuations compared to the discharges generated by larger and more confining structures. This is due to the high surface-to-volume ratio of micro-plasma array systems. Boettner *et al*. investigated a microplasma array consisting of a large number (50x50) of single microplasma discharges and reported on the designs suitability for a variety of applications.[36]

4.3. Surface & Coplanar dielectric barrier discharges.

Another design which has been highlighted as a promising design for scale-up is the Surface Barrier Discharge (SBD). For SBD both electrodes are in direct contact with the barrier with the plasma is formed in the gas at the exposed surface electrode.[37] Recent scale-up efforts at the University of Liverpool aimed directly at *in-situ* decontamination of food and food-processing equipment have been reported.[38] Bauer *et al* reported on the system’s design features and its anti-microbial efficacy for treating food packaging films.[39] The DBD design uses metallic mesh electrodes adherent to a quartz dielectric surface and a metallic sheet on the opposing side of the quartz to form counter electrodes (**Figure 2a**). The surface DBD electrode unit was capable of generating an air plasma over the 80×80 mm area of the hexagonal mesh electrode.[38] An enclosure covering the treatment zone facilitates retention of the generated long-lived species. For coplanar discharges both electrodes are embedded in the dielectric material with the discharge forming in the gas above the dielectric surface.[37] This design is particularly suited to food applications as the electrodes can be completely sealed off from any food/water contact. It is also compatible with scale-up.

4.4. Retention of plasma species

After the role of key long-lived species in the observed antimicrobial effects were identified, it became apparent that techniques which could prevent their loss to the surrounding environment would significantly reduce the processing times required. A number of approaches have been tested to date including the use of containment reactors, process tunnels and sealed packages. The SBD design detailed in **Figure 2(a)** employs such an enclosure to control species retention. Such designs are compatible with conveyor belts and comparable in design to continuous processing approaches commonly employed by the food industry such as tunnel ovens, dryers and freezers. With regards to sealed packages, researchers at Purdue University and the Dublin Institute of Technology began investigating the potential of large gap DBD designs which could facilitate the insertion of packages within the discharge gap. To achieve plasma discharges in these large gaps, much larger voltages (up to 130 kV) and use of tailored dielectric barrier materials and designs are needed. **Figure 3** shows a schematic of this discharge process within the confines of a food package. The gas type/mixture, gas density (n_g), electron density (n_e) temperature (T_g) are key parameters governing the plasma formed and the observed process efficacy. Electron-Ion recombination can occur with third body collisions within the gas volume or with the package walls and food surfaces. A key area of research is the ‘reaction products’ due to plasma species interaction with a food’s surface and its microflora over the extended exposure periods. Advantages of the approach include; (1) rapid processing due to the retention and continued action of the contained species post treatment, (2) prevention of possible recontamination events due to the sealed environment and (3) compatibility with MAP and continuous processing.

The first reported application of the design was by Klockow and Keener describing the approach and reporting its efficacy for eliminating *E. coli* O157:H7 on spinach leaves.[40] The EU funded 'SAFE-BAG' project developed a continuous DBD design through which packaged food could be conveyed. The design could operate an open discharge in ambient air conditions for an adjustable electrode gap of up to 45mm over an electrode length of 1m. The design allowed for several flexible packages (from 4 to 10, depending on the package size) to be treated simultaneously as they are conveyed through the discharge zone. A description of the technology and its efficacy under processing conditions for fresh produce is reported by Ziuzina *et al*. [41]

Anacail Limited (UK) also markets an in-package ozone treatment technology aimed at the preservation of perishable foods.[42] Although the technology is marketed as an “ozone” generation device, their patent reveals that the technology is based on a plasma co-axial “surface” generator operating with voltages between 5 and 20 kV, which creates a hemispherical plasma field that passes through food packaging films.[5]

5. Process control and validation

Process validation and process control are critical operations for product assurance of high risk products such as food. Process validation for heat treatments is relatively straightforward through temperature profiling of the heated products. Additional challenges arise with the use of non-thermal technologies such as those employing electrical fields (pulsed electric fields, radio frequency electric fields and plasma discharges). One of the often promoted advantages of plasma is its multi-modal stresses and associated mechanisms of action for bacteria. The question then emerges what factors should be controlled in terms of the plasma source, the discharge and the reactive species.

Real-time plasma control for surface modification of any material is a challenging problem. The process is multivariate, multi-time scale, time varying, and nonlinear. The most likely process control approaches for plasma processes at industrial level are electrical and optical measurements. Electrical techniques commonly monitor electron density, ion species or power input by measuring a current or potential change related to the plasma discharge. Electrical diagnostics include Langmuir probes, electric-field and magnetic-field probes that are inserted into the plasma. Invasive probes are not desirable for most food processing conditions and probes such the Langmuir are generally not effective for atmospheric conditions. Alternative electrical measurements, like current/voltage characterisation, are non-intrusive and can be used for process control. For example, a plasma impedance monitoring system could be used to measure the amplitude and phase of the few Fourier components (harmonics) of the plasma voltage and current of AC plasma process reactors. In this case, electrical probes used are *ex situ* and can be integrated into the electrical circuit.

Optical techniques rely on either the optical emission from the plasma or an external light source such as a lamp or laser to probe the plasma species. In many cases, optical measurements attempt to characterise a specific species since optical emission (absorption) wavelengths are unique to a given atom or molecule. This diagnostics approach does not affect the process, i.e. does not perturb plasma conditions and is very sensitive, permitting measurement of very low densities of many gas-phase species. The optical measurements can also provide the desired temporal and spatial resolutions.

Most plasma systems, operating at atmospheric pressure, involve ambient air chemistry, i.e. nitrogen, oxygen and water vapour. Therefore, the diagnostic techniques listed above, would involve: O I, O_2, O_3, N_2, N_2+, OH and H I. In addition, depending on the plasma system's chemistry, it may also be possible to observe noble gas atomic emission. Most studies in the literature on plasma treatment of food report some electrical and/or optical characterisation of the plasma discharge and/or species. However there are very significant challenges to move from such diagnostics to process control or process validation.

6. Toxicology and dose

A number of recent publications have reported on the cytotoxic activity of plasma treated liquids such as plasma-activated water or more complex solutions such as plasma-activated medium (PAM) on eukaryotic cells. [43,44] Such findings emphasize that cell toxic effects must be considered from a safety perspective for the application of plasma for food and food production processes. Hydrogen peroxide has been implicated as a key cytotoxic species in plasma activated liquids but studies have shown that it is not the sole toxic mediator.[45,46] This is of relevance both for the applications of PAW in the food industry as well as the direct plasma exposure of food products with moisture content, where similar reactive species will be generated. Plasma exposure can induce a range of chemical changes to food components including the oxidation of sugars to organic acids, the modification of amino acid residues in proteins, and the peroxidation of lipids, which can result in the generation of toxic metabolites such as short chain aldehydes. [47,48] Cytotoxic and mutagenic effects have been demonstrated for long-term exposure of cell lines to complex plasma-treated protein models, [45] while other studies did not observe mutagenic potential of plasma-treated media, [49,50,51] highlighting the differences with regards to plasma devices, treatment regimens and target composition. It will be important to establish minimal concentrations and exposure times at which an increased rate of toxic or mutagenic effects can occur and to define safe doses dependent on the application or food target in question. *In vivo* toxicological studies are lacking to date and will be needed to evaluate the safety of long-term exposures along with more detailed elucidation of the plasma-induced modifications occurring in various target substrates. In particular, comparative studies on cytotoxicity and mutagenicity of cold plasma compared with currently approved disinfectants, sanitizers, and sterilants are needed.

The issue of a measureable or controllable plasma dose for food materials is another challenge and one similarly faced by the field of 'plasma medicine'. Given the diversity of sources and species employed in the induced effects, it is challenging to select one or a number or parameters to define a plasma treatment dose. The alternative of a measuring the dose absorbed by the target which is suitable for medical applications is not compatible with food analysis given their diverse product range.

7. Regulatory and consumer acceptance

7.1: Food regulation

To our knowledge no legislation or regulatory guidance specific to plasma treatment of food currently exists from any of the regulatory bodies globally. As a novel technology this is to be expected with regulatory responses typically emerging as a response to either industry usage (due to a lack of any regulation) or industry seeking guidance or specific approval of a process. The sparse data available on toxicity of plasma treated foods needs to be addressed for any likely regulatory approval. The approval of comparative technologies such as ozone as a direct additive to food by the US FDA can be referenced as a potential successful regulatory approval approach. Indeed, some plasma devices are currently marketed as ozone systems for food applications. Only employing long lived species may simplify somewhat regulatory processes however the regulation around key metastables (O_3, CO, H_2O_2) for foods is also in a state of flux depending on country and/or product and of course a plasma afterglow typically contains many other species. Regulatory approval for PAW may be a somewhat easier path as the key species, chemical pathways, product reactions and dose should be easier to measure, control and reproduce. Only metastables will be present in PAW post treatment, and although still highly dynamic in nature it is comparably less so than direct plasma exposure (no electric fields, UV etc). The approach is also more controllable in terms of application, ie exposure to complex surfaces (cracks, folds, pores etc) via immersion of the product or product spraying. As previously mentioned, food product or food application specific cases are more likely for plasma than in the case of the US FDA approval of ozone which was classified as as a direct additive to food. It is important for expert groups to start forming to begin collating data and providing opinions on the use of plasma in food applications. Some such opinions have started to emerge such as that of the Senate Commission on Food Safety (SKLM) part of the German Research Foundation (DFG).[52] The authors point to a number of key recommendations for plasma adoption for food processing, including;

1. Products or product groups must be subjected to a case-by-case assessment.
2. The plasma process must be described with respect to its technical parameters, including the working gas, degree of ionization, treatment geometry, exposure time, temperature, pH value, system layout, etc.
3. A profile as comprehensive as possible of the plasma-induced physical/chemical/biochemical/microbiological changes in the food is required.
4. The requirement for studies on whether toxic compounds are formed as a result of plasma treatment.
5. The impact on microbiological safety must also be taken into account in order to achieve an adequate health evaluation.

Some advancement has been made since this report with a number of studies reporting on biochemical changes, microbiological responses/mutagenicity and toxicity.

7.2. Consumer acceptance:

Consumers are not only concerned about the nutrition, origins and safety of the food they consume but also the processes and practices which are employed along the production and processing chain. Paradoxically, consumers are demanding foods which are minimally processed, meet their nutritional and taste desires yet require minimal preparation.[53] For successful adoption and acceptance of a novel process technology within the food industry an understanding of consumer views, their understanding of the technology and concerns is critical. Research suggests that acceptance of new technologies is based to a great extent on public perceptions of the associated risks, and that perceptions of risk are influenced by trust in information and the source which provides it.[53] However consumer research studies have consistently shown that consumers have poor knowledge and awareness levels towards most novel food-processing techniques, which has resulted in potential technologies been effectively lost or their adoption restricted. Early and effective communication of the technologies, applications, potential benefits and risks is important to gain consumer acceptance. If a novel technology allows the introduction of new products with tangible benefits or provides a safer product/process over existing technologies, consumers are most likely to accept it. Whilst there are many studies examining the societal and consumer acceptance of novel technologies, to our knowledge no study has specifically elucidated the consumer understanding or potential acceptance of plasma technology for foods. Ultimately critical product factors such as taste and sensory properties govern consumer purchase of food products. The principal driver for industrial adoption of any processing technology is to meet consumers' demands for improved taste and nutrition at the time of consumption. However, limited data is available on the sensory properties of plasma treated food with studies to date examining instrumental analysis techniques such as colour, texture and odour.[54] Future studies should address this lack of data.

8. Conclusion

The translation of plasma technology from the laboratory to the food industry is characterized by significant challenges and opportunities. Novel designs for targeted species delivery and treatment of various food products are emerging including; atmospheric air discharges, plasma active water and sprays and in-package technology. The diverse range of processes and products found in the food industry, from batch to continuous processing, from dry to wet processing from fine granular matter to large carcasses will require a range of plasma treatment designs.

The scientific community is responding to these challenges by linking the disciplines of plasma physics, plasma engineering, microbiology and food science. Areas of research which are lacking include toxicology, sensory and consumer acceptance studies.

Acknowledgements: Science Foundation Ireland Grant No 14/IA/2626

Received: ((will be filled in by the editorial staff)); Revised: ((will be filled in by the editorial staff)); Published online: ((please add journal code and manuscript number, e.g., DOI: 10.1002/ppap.201100001))

References:

[1] F. Chemat, N. Rombaut, A. Meullemiestre, M. Turk, S. Perino, A. Fabiano-Tixier, M. Abert-Vian, Innov. Food Sci. Emerg. Technol. 2017, 41, 357–377

[2] N. Misra, O. Schlüter, P. Cullen, in *Cold Plasma in Food and Agriculture: Fundamentals and Applications*. (Eds: NN Misra, O. Schlüter, P.J. Cullen), Elsevier, Amsterdam, Netherlands **2016**, Ch. 1.

[3] P. Lu, K. Ostrikov, P. Cullen, in *Cold Plasma Sources. In Cold Plasma in Food and Agriculture: Fundamentals and Applications*. (Eds: NN Misra, O. Schlüter, P.J. Cullen), Elsevier, Amsterdam, Netherlands **2016**, Ch. 4.

[4] P. Lu, D. Boehm, P. Bourke, P. Cullen, Plasma Process Polym. **2017,** DOI:10.1002/ppap.201600207

[5] K. Keener, N.N. Misra, in *Cold Plasma in Food and Agriculture: Fundamentals and Applications*. (Eds: NN Misra, O. Schlüter, P.J. Cullen), Elsevier, Amsterdam, Netherlands **2016**, Ch. 14.

[6] P. Bourke, D. Ziuzina, L. Han, P. Cullen, B. Gilmore. B. *J Appl. Microbiol.* **2017**, DOI: 10.1111/jam.13429

[7] N. Misra, B. Tiwari, K. Raghavarao, P. Cullen, *Food Eng. Rev*. **2011**, 3, 159-170.

[8] B. Niemira, *Annu. Rev. Food Sci. Tech*. **2012**, 3, 125-142

[9] S.A. Mir, M.A. Shah, M.M. Mir, *Food Bioprocess Technol*. **2016**, 9, 734.

[10] R. Thirumdas, D. Kadam, U. Annapure, *Food Biophysics*. **2017**, 12, 129–139

[11] S. Pankaj, C. Bueno-Ferrer, N. Misra, V. Milosavljević, C. O'Donnell, P. Bourke, K. Keener, P. Cullen, *Trends Food Sci Technol*. **2014**, 35, 5–17

[12] J.E. Kim, Y.J. Oh, M.Y. Won, K.-S. Lee, S.C. Min, *Food Microbiol*. **2017**, 62, 112-123

[13] R. Brandenburg, J. Ehlbeck, M. Stieber, T. von Woedtke, J. Zeymer, O. Schlüter, K. Weltmann, *Contrib. Plasma Physics*. **2007**, 47, 72–79

[14] M. Moritz, C. Wiacek, M. Koethe, P.G. Braun, *Int J Food Microbiol*. **2017**, 245, 22-28

[15] C. Pignata, D. D'Angelo, E. Fea, G. Gilli, *J Appl Microbiol*. **2017**. DOI: 10.1111/jam.13412

[16] S. Patil, T. Moiseev, N. Misra, P. Cullen, J. Mosnier, K. Keener, P. Bourke, *J Hosp Infect*. **2014**. 88, 162–169

[17] F. Pasquali, A. Stratakos, A. Koidis, A. Berardinelli, C. Cevoli, L. Ragni, R. Mancusi, Food Control. 2016, 60, 552-559

[18] L. Han, D. Boehm, E. Amias, V. Milosavljević, P. Cullen, P. Bourke, *Innov. Food Sci. Emerg. Technol*. **2016**, 38, 384–392

[19] N.N. Misra, T. Moiseev, S. Patil, S.K. Pankaj, P. Bourke, J.P. Mosnier, K.M. Keener, P.J. Cullen, *Food Bioprocess Tech*. **2014**. 7, 3045-3054

[20] Q. Zhang, Y. Liang, H. Feng, R. Ma, Y. Tian, J. Zhang, J. Fang, *Appl. Phys. Lett*. **2013,** 102, 203701

[21] M. Naïtali, G. Kamgang-Youbi, J. Herry, M. Bellon-Fontaine, J. Brisset, *Appl Environ Microbiol*. **2010,** 76, 7662-7664

[22] M. Traylor, M. Traylor, M. Pavlovich, S. Karim, P. Hait, Y.Sakiyama, D. Clark, D. Graves, Long-term antibacterial efficacy of air plasma-activated water. *J Phys D: Appl Phys*. **2011**, 44, 472001

[23] D. Rico, A. Martín-Diana, J. Barat, C. Barry-Ryan, *Trends Food Sci. Technol*., **2007**, 18, 373.

[24] K. Tachibana, *Pure Appl. Chem*. **2010**, *82*, 1189–1199.

[25] J.H. Han, in Packaging for Nonthermal Processing of Food. (Ed: J.H. Han), Wiley-Blackwell, Oxford, UK 2007. Ch.1.

[26] V. Scholtz, J. Pazlarová, H. Soušková, J. Khun, J. Julák, *Biotechnol Adv*. **2015**, 33, 1108–1119.

[27] D. Clarke, A. Tyuftin, M. Cruz-Romero, D. Bolton, S. Fanning, S. Pankaj, C. Bueno-Ferrer, P. Cullen, J. Kerry, *Food Microbiol*. **2017**, 62, 196–201

[28] N. Misra, S. Kaur, B. Tiwari, A. Kaur, N. Singh, P. Cullen, *Food Hydrocoll*. **2015**, 44, 115–121

[29] X. Yepeza, K. Keener, *Innov. Food Sci. Emerg. Technol*, **2016**, 38, 169–174

[30] N. Misra, C. Sullivan, S. Pankaj, L. Alvarez-Jubete, R. Cama, F. Jacoby, P. Cullen, *Innov. Food Sci. Emerg. Technol*, **2014**, 26, 456–461

[31] Z. Cao, J. Walsh, M. Kong, *Appl. Phys. Lett*. **2009**, 94, 021501.

[32] Z. Cao, Q. Nie, D. Bayliss, J. Walsh, C. Ren, D. Wang, M. Kong, *Plasma Sources Sci*. Technol. **2010**, 19, 025003

[33] J. Furmanski, J. Kim, S. Kim, *IEEE T Plasma Sci*. **2011**, 39, 2338-2339

[34] K. Becker, K. Schoenbach, J. Eden, *J. Phys. D: Appl. Phys*. **2006**, 39, R55–R70

[35] J. Eden, S. Park, *Plasma Phys. Control. Fusion,* **2005,** 47, B83–B92

[36] H. Boettner, J. Waskoenig, D. O'Connell, T. Kim, P. Tchertchian, J. Winter, V. Schulz-von der Gathen, *J. Phys. D: Appl. Phys*. **2010,** *43*, 124010

[37] R. Brandenburg, *Plasma Sources Sci. Technol*. **2017**, 26, 5

[38] J. Walsh,. *IAFP's European Symposium on Food Safety*, Brussels, Belgium 3, **2017**

[39] A. Bauer, Y. Ni, S. Bauer, P. Paulsen, M. Modic, J. Walsh, F. Smulders, *Meat Sci*, **2017**, 128, 77–87

[40] P. Klockow, K. Keener, *Food sci. technol.* **2009**, 42, 1047-1053

[41] D. Ziuzina, N. Misra, P. Cullen, K. Keener, J. Mosnier, I. Vilaró, E. Gaston, P. Bourke, *Plasma Med*. **2017**, DOI: 10.1615/PlasmaMed.2017019498

[42] H. Potts, D. Diver (Anacail), USA, US20160263262 A1, 2014.

[43] T. Adachi, H. Tanaka, S. Nonomura, H. Hara, S. Kondo, M. Hori. *Free Radic Biol Med*, **2014,** 79c, 28-44.

[44] Z. Chen, L. Lin, X. Cheng, E. Gjika, M. Keidar, *Plasma Process Polym.* **2016**, 13, 1151-1156.

[45] D. Boehm, C. Heslin, P. Cullen, P. Bourke, *Sci. Rep*l. **2016,** 6, 21464

[46] J. Winter, H. Tresp, M. Hammer, S. Iseni, S. Kupsch, A. Schmidt-Bleker, K. Wende, M. Dünnbier, K. Masur, K-D. Weltmann, S Reuter. *J. Phys. D: Appl. Phys,* **2014**, 47, 285401.

[47] J. Park, N. Kumar, H. Uhm, W. Lee, E. Choi, P. Attri. *RSC Adv.* **2015**, 5, 47300-47308.

[48] Q. Zhang, Y. Liang, H. Feng, R. Ma, Y. Tian, J. Zhang, J. Fang, *Appl. Phys. Lett.* **2013**, 102, 203701

[49] V. Boxhammer, Y. Li, J. Köritzer, T, Shimizu, T. Maisch, H. Thomas, J. Schlegel, G. Morfill, J. Zimmermann, *Mutat Res Genet Toxicol Environ Mutagen*. **2013**, 753, 23-28.

[50] S. Kalghatgi, C. Kelly, E. Cerchar, B. Torabi, O. Alekseev, A. Fridman, G. Friedman, J. Azizkhan-Clifford, *PLOS ONE*, 6, e16270.

[51] K. Wende, S. Bekeschus, A. Schmidt, L. Jatsch, S. Hasse, K. Weltmann, K. Masur, T. von Woedtke, *Mutat Res Genet Toxicol Environ Mutagen*. **2016**, 798, 48-54.

[52] O. Schlüter, J. Ehlbeck, C. Hertel, M. Habermeyer, A. Roth, K. Engel, T. Holzhauser, D. Knorr, G. Eisenbran, *Mol Nutr Food Res.* **2013**, 57, 920–927

[53] P. Cullen, B. Tiwari, V. Valdramidis. in *Novel thermal and Nonthermal Technologies for Fluid Foods* (Eds: P.J. Cullen, B.K.Tiwari, V. Valdramidis), Elsevier, Amsterdam, Netherlands **2011**, Ch. 1.

[54] U. Schnabel, R. Niquet, M. Andrasch, M. Jakobs, O. Schlüter, K. Katroschan, K. Weltmann, J. Ehlbeck, *Plasma Med*, **2017**, DOI: 10.1615/PlasmaMed.2017019033

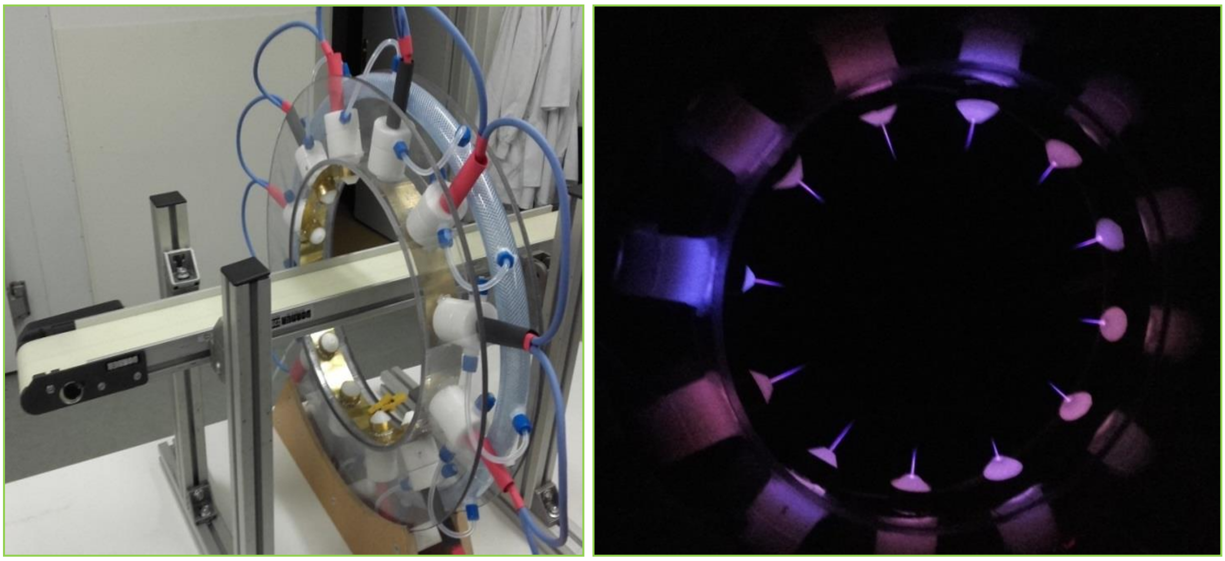

Figure 1. Multi-jet Atmospheric Pressure Plasma discharges designed for food decontamination (DIT BioPlasma Lab)

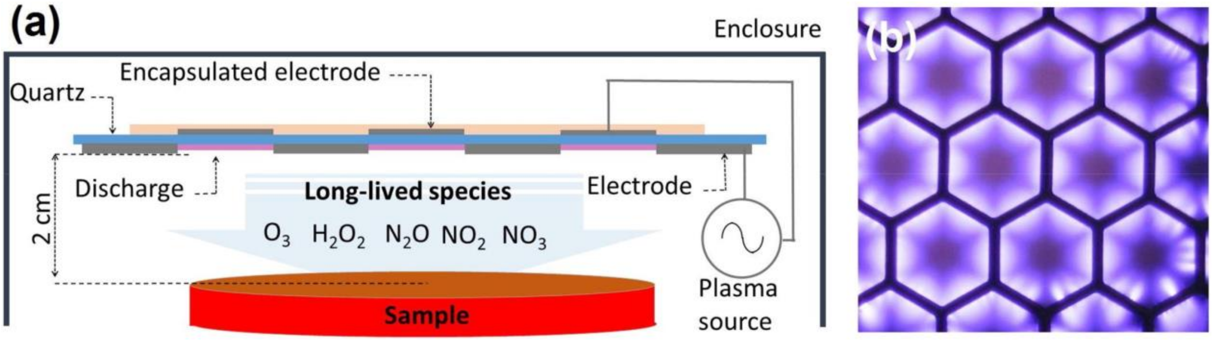

Figure 2. (a) Schematic showing surface DBD electrode and sample position, (b) Photograph showing plasma formed on hexagonal mesh electrode at a discharge power of 0.67 W/cm2. Reproduced with permission.[33.] 2017, Elsevier

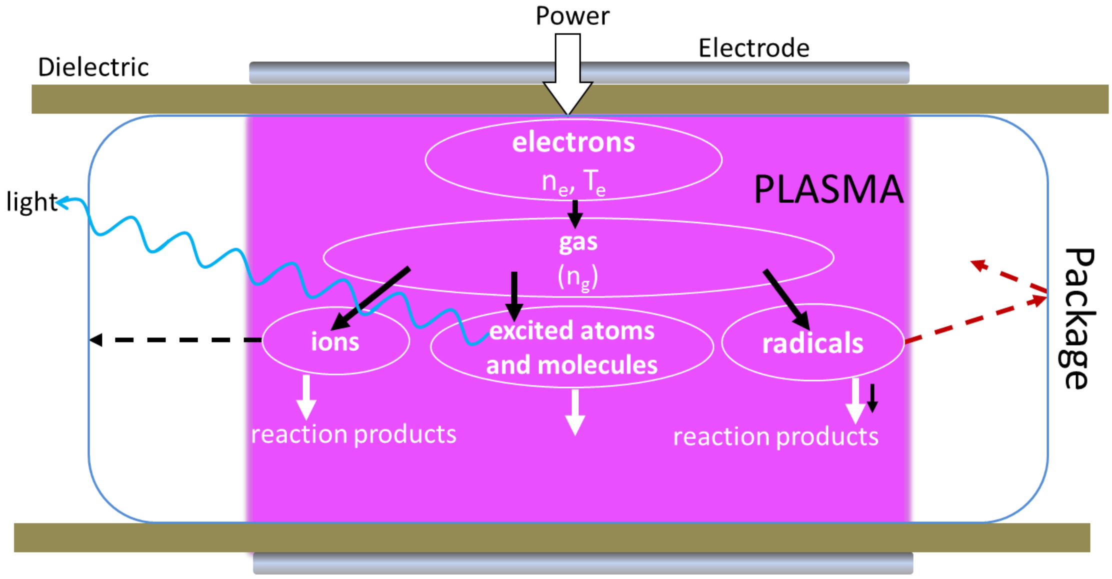

Figure 3. Schematic of plasma generation within the confines of a gas filled package