Final report:

Non-Equilibrium Plasma Interactions with Biomaterials, Biological Solutions and Tissues

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Outline

Summary:

Cold atmospheric pressure plasma discharges offer an abundant source of reactive oxygen and nitrogen species (RONS) at room temperature enabling unique interactions with biomaterials, biological solutions and tissues. These interactions particularly with living matter are presently an important intellectual frontier in plasma science with promising potential applications ranging from human health care to advanced biomaterial processing. Exciting case studies have been reported that illustrate the huge potential of cold atmospheric plasma technology in wound healing and cancer treatment.

The interaction of plasma with conducting and dielectric biomaterials such as tissue strongly influences the plasma properties. In turn this changes the impact of the plasma on the biomaterial. Particularly in the case of living matter, liquid based solutions are ubiquitous which complicates interfacial processes. The lack of insight into the underlying mechanisms of the interaction of plasma with wounds and tumors is currently a bottleneck for the further development of the technology and gives rise to many interesting scientific questions.

This project was focused on plasma properties and kinetics during plasma-biomaterial interactions. Both DC pulsed and RF driven atmospheric pressure plasma jets, extensively used by the plasma community were studied. The bio-interfaces included hydrogel as a tissue model, (saline) solutions, bacteria and virus. Plasma diagnostics used include Thomson scattering, Rayleigh scattering, Raman scattering, (two-photon absorption) laser induced fluorescence, optical emission spectroscopy, absorption spectroscopy, molecular beam mass spectrometry and fast imaging allowing to determine electron densities and temperatures, ionic species, reactive species including radicals, gas temperatures, gas composition, electric fields and solution components transferred to the gas phase.

Key outcomes of the project can be organized in three categories as follows:

- Gas phase reactive species production and transport
  - Measurements of radical generation, transport and recombination in plasma jets
  - Detailed comparison of reactive species production in Ar-H_2O with modeling results including reaction set validation
  - Ion kinetics in plasma jet including resulting memory effects
  - Impact of plasma on air admixing in jet effluents
- Plasma interaction with bio-interfaces including hydrogel and solutions
  - Measurement of transport of reactive species into hydrogels
  - Mechanism of plasma-induced pattern formation on hydrogels including role of surface charging

  - Measurements of the flux of radical species to a substrate in both H_2O and O_2 containing plasma jets by laser induced fluorescence and molecular beam mass spectrometry
  - E-field dynamics of a plasma jet impinging on a conductive substrate
  - Assessment of the impact of plasma-induced gas-liquid interface dynamics on plasma properties and plasma-induced liquid phase chemistry
  - Detailed measurements of plasma-instabilities during plasma-liquid interactions including the determination of stabilization mechanisms.
  - Dynamics and limitations of plasma penetration in high aspect ratio capillaries as a model of porous media
- Plasma-bio-interaction mechanisms
  - Mechanisms of inactivation of virus in air plasma and the role of transport limitations
  - Mechanisms of inactivation of bacteria by air and oxygen containing plasmas
  - Showing the capability of plasmas to inactive MRSA biofilms

1. <u>Key results from this project</u>

Dissertations and peer-reviewed publications are referred to with a capital letter and number, respectively, which corresponds to their number list reference in section 2 and 4 of the report.

In addition to the research described below, this project provided support to enable the PI to edit the 2017 Plasma roadmap [2] and to write a review and perspective paper. The roadmap gives guidance to future developments in the field of low temperature plasmas. The review paper introduces a framework for atmospheric pressure non-equilibrium plasmas which are intensively used for biomedical applications among other applications[1]. The perspective provides a detailed overview of remaining key science questions for plasma-liquid interactions [11].

a. <u>Gas phase reactive species production and transport</u>

Motivation:
Cold atmospheric pressure plasmas consist of a mixture of free electrons, ions, RONS, and energetic photons (UV). The reactive cocktail produced by plasmas can selectively inactivate bacteria without harming host (eukaryotic) cells. These properties make cold plasmas an attractive and novel wound healing technology. Clinical trials have shown significant reduction in bacteria load of the wound and improved healing. Furthermore, some case studies have shown the healing capability of plasmas for wounds where conventional treatments failed. While exciting studies have been reported that illustrate the huge potential of plasma technology, the lack of insight into the underlying mechanisms of the interaction of plasma with wounds and tumors is currently a bottleneck for the further development of the technology. The investigation of the processes underpinning plasma-bio-interactions requires a detailed understanding and description of the gas phase kinetics and resulting RONS produced by plasma jets typically used for such applications. This involves, reactive species generation but also species transport and the impact of the plasma on the fluid dynamics.

Results:
Impact of plasma on air admixing in jet effluents [3]
We investigated the flow effects induced by a nanosecond pulsed helium cold atmospheric pressure plasma jet impinging on a glass substrate which can have a significant impact on the production of RONS. The increase in gas temperature was less than 15 K. We have measured the air concentration distribution in the jet effluent by means of Rayleigh scattering exploiting the large difference in Rayleigh cross-section of air and helium. The obtained results show that the plasma causes a broadening of the helium channel suggesting an enhanced gas velocity and mixing with the ambient air. The impact of the plasma on the jet effluent is polarity dependent and is larger in the case of positive applied voltage pulses. Using an estimation of the

increased gas velocity required to obtain the observed air concentrations, we have shown that both gas heating and electrohydrodynamic (EHD) forces related to the propagation of an ionization front are not causing the observed phenomena. The surface charge which can exist for a much longer time than the duration of the applied voltage pulse is the primary cause of the EHD forces on the bulk charges which lead to significant different air concentration profiles in the jet effluent for plasma on and off cases.

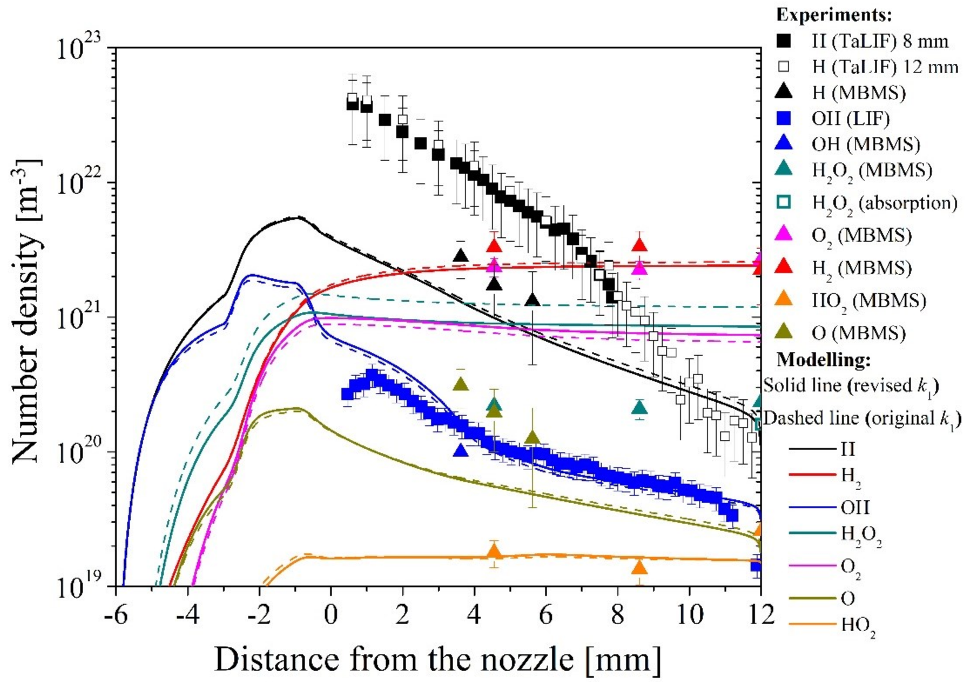

Figure 1: Detailed comparison of modelling and experimental study with as goal to elucidate the plasma chemistry in a humid Ar RF-driven APPJ. A [21].

Measurements of radical generation, transport and recombination in plasma jets [12, 19]
We measured the time-resolved axial density of hydroxyl (OH) and hydrogen radicals (H) in an atmospheric pressure plasma jet (APPJ) device and its effluent operating in a He–H_2O mixture using 1D laser induced fluorescence (LIF) and two-photon absorption LIF (TALIF). The results show that H and OH are mainly generated between the electrodes in the APPJ rather than by the guided streamer. The produced H and OH inside the jet are convectively transported to the jet effluent and determine the H and OH densities in jet effluent. The dominant production and destruction mechanisms of H and OH were obtained from a 0D model. The different production mechanisms of H and OH can explain the change in memory effect observed for OH (and not for H) for varying pulse repetition rates of the plasma generation. This was complemented with a study of the atomic hydrogen (H) generated by an atmospheric pressure radio frequency (RF) plasma jet in a He–H_2 mixture. The H density distribution for a continuous RF plasma jet is described in good approximation by a 1D plug flow model.

Detailed comparison of reactive species production in Ar-H_2O with modeling results including reaction set validation [21]
We performed a detailed comparison of a modelling and experimental study with as goal to elucidate the plasma chemistry in a humid Ar RF-driven APPJ (see figure 1). A large group of species including radicals (H, OH, O, HO_2) and long-lived species (H_2, O_2 and H_2O_2) in the jet effluent was experimentally quantified by molecular beam mass spectroscopy (MBMS). MBMS measurements of H_2O_2, OH and H were validated by direct comparison with a liquid phase colorimetric measurement, laser induced fluorescence (LIF) and Two-photon absorption LIF. While excellent agreement was found for OH and H_2O_2 by both techniques, a

significant difference was found for H and shown to be due to boundary layer effects at the MBMS sampling substrate. The measured O, OH, HO_2 and H_2, are in good agreement with the plug model while H and O_2 were underestimated and H_2O_2 overestimated by the model. The accuracy of both the used reaction set in the model and experiments and the discrepancies between them were critically assessed. The results presented in this work enable to assess the anticipated accuracy of available reaction sets and further data needs for describing H_2O vapor chemistry in low temperature plasmas which is crucial for plasma-biointeractions.

Ion kinetics in plasma jet including resulting memory effects [15,16]

We used MBMS to characterize ion fluxes produced by a modulated radiofrequency (RF)-driven atmospheric pressure plasma jet operating in a homogeneous gas environment (Ar + 1% O_2). The influence of the RF modulation frequency (100 Hz to 20 kHz) on the ion fluxes was investigated by time-resolved measurements. The absolute ion densities in the near afterglow region were found to be of the order of 10^{11} cm^{-3}. Significant differences in the dynamics of the positive and negative ions were found. These are explained by the presence of electrons at similar densities in the afterglow produced by electron detachment reactions from negative ions due to the large concentrations of atomic oxygen and singlet delta oxygen. Transitions in ion flux dynamics for different modulation frequencies and at the startup of the plasma were analyzed together with intensified charge coupled device images recording the plasma propagation in order to assess the dynamics of plasma plume propagation and how it is impacted by 'memory effects'. Quantitative measurements of the ion densities enabling these memory effects are reported. The results highlight the tremendous impact of memory effects on plasma propagation.

In addition, we measured the ion compositions in the effluent of an APPJ operating in ambient air for different feed gases including Ar + O_2, Ar + air and Ar + H_2O mixtures inspired by gas compositions used for biomedical applications. Changes in compositions of positive and negative ions as a function of nozzle-to-substrate distance along the plasma plume were analyzed and compared with a 1D plug flow model. Positive and negative ions were detected up to distances of 12 mm from the visible plasma plume tip. The measurements enable to follow the ion conversion pathways in the effluent of the APPJs as a function of distance from the nozzle. The trends in ion yield obtained from a 1D plug flow model showed generally a good agreement with the experimentally observed trends after addition of ionic reactions to the previously reported reaction set but also some distinctive differences were observed. The dominant positive ions in the far effluent are water ion clusters, the most stable ion for all gas mixtures investigated, while a large variety of negative ions was found for different gas mixtures.

b. Plasma interaction with bio-interfaces including hydrogel and solutions

Motivation:

Due to the strong interactions of plasma parameters with biomaterial interfaces, it is important that plasma properties need to be investigated during the plasma-biomaterial interface interaction. While plasma-surface interactions have been studied for decades for semiconductors in the microelectronics industry, biomaterials are intrinsically more complex and diverse. In view of the complexity of plasma-tissue interactions, many plasma-tissue interactions have been studied by replacing the tissue by soft hydrated hydrogels. Nonetheless, in spite of the many reported studies, limited quantitative information on species generation and transport in such systemsis available. In addition, cells and tissues are often kept in solution environments or contain a lot of water, adding additional complexity to the system through complex plasma-liquid interactions. There are many open questions on how reactive species are transferred from the plasma to the liquid phase and vice versa and how interfacial interactions influence the species transfer. Although not quantified in detail, there are strong indications of effects on the plasma induced by an increased amount of water vapor through modeling efforts.

The challenge of inhomogeneous interfaces and plasma penetration in micro-features is ubiquitous in many biomedical applications. This includes skin disinfection due to the presence of hair follicles, disinfection of catheters having narrow channels with extreme diameter-length aspect ratios and homogenous functionalization of porous biomaterials. While several modeling studies have been reported, detailed controlled studies on plasma penetration in micro-features with high aspect ratios remains limited.

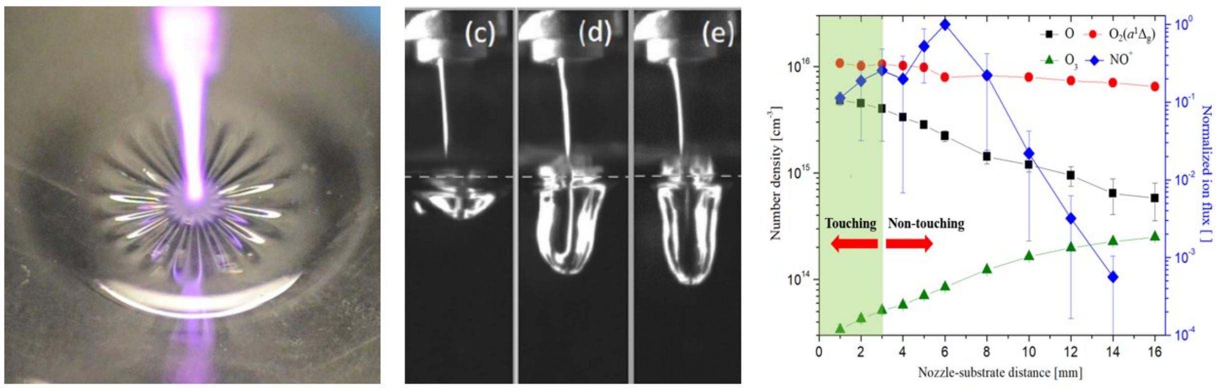

Figure 2: (left) Self-organized pattern formation during plasma-gel interaction [D]. (Middle) Dimple formation in solutions during plasma jet -liquid interaction [B,11]. (right) Dominant reactive species measured by molecular beam mass spectroscopy for RF-driven plasma jet both in touching and non-touching conditions [E,8].

Results:

Measurement of transport of reactive species into hydrogels [C,20]

We analyzed the diffusion of reactive oxygen species (in particular H_2O_2) and quantified the amount of plasma-produced H_2O_2 species that penetrates into a gelatin hydrogel, a model used to study plasma-tissue interactions. We show that the diffusion constant of H_2O_2 in 10% gelatin hydrogel is similar to its diffusion constant in water and that the production of H_2O_2 in the hydrogel is significantly less than the production of H_2O_2 in distilled water for the same plasma operation conditions suggesting that the scavenging of OH radicals at the plasma-gel interface significantly reduces the H_2O_2 production.

Mechanisms of plasma-induced pattern formation on hydrogels and the role of surface charging [D]

A gelatin-based model tissue has been commonly used by researchers to understand the plasma-tissue interaction. The distribution of reactive species was correlated with the star like pattern formed on the surface of the gel (see figure 2). We investigated the parameters influencing the formation of this star-like pattern using a pulsed dc helium-based plasma jet. The size of the plasma-induced pattern and the surrounding evaporation zone increased with increasing voltage and charge deposition on the gel surface. The charge deposition was larger for positive polarity compared to negative polarity discharges despite similar total energy. These results suggest that pattern formation correlates with charge deposition. There was no pattern observed in humidified helium plasma treatment although the charge deposition was found to be similar as in helium-oxygen plasma treatment which showed the formation of a pronounced pattern indicating the role of drying as a major factor for pattern formation in addition to the charging effect. The surface ionization waves, although very weak due to the finite conductivity of the gel were observed using time-resolved imaging and resembled a gear-like structure made of surface streamers which matched exactly with the number of filaments on the star-like pattern, indirectly linking the plasma morphology to the pattern structure. Electrical forces resulting from charging were estimated to be sufficient to cause gel deformation. The obtained results suggest some limitations on the use of hydrogels as a model for plasma-tissue interaction studies.

Measurements of the flux of radical species to a substrate in both H_2O and O_2 containing plasma jets to by laser induced fluorescence and molecular beam mass spectrometry

We determined the absolute flux of H, O, and OH radicals reaching a substrate by Comsol Multiphysics reacting fluid dynamics model incorporating detailed transport phenomena in the boundary layer near the substrate. The simulated results of H and OH densities in the jet effluent were experimentally verified by two-photon absorption laser induced fluorescence and laser induced fluorescence, respectively. We showed that the boundary layer effects in the interfacial region above the substrate can have a significant impact on the species fluxes to the substrate. This work was linked to previously obtained etching rates of polystyrene showing that OH and O were dominantly responsible for the observed etching. We complemented this work with spatially resolved measurements of reactive species including neutral and ionic species in an He+1% O_2 RF-driven APPJ by molecular beam mass spectrometry equipped with a dielectric sampling plate, enabling to detect species densities for APPJ operating remotely or in direct contact with a substrate while maintaining a diffuse substrate interaction. The spatially resolved distribution of the dominant reactive oxygen species (O, $O_2(a^1\Delta g)$ and O_3) is dominated by convection and, remarkably, shows minimum differences between touching and non-touching conditions (see figure 2).

E-field dynamics of a plasma jet impinging on a conductive substrate [10, 17]

Time and spatially resolved electric field measurements by Stark polarization spectroscopy in a nanosecond pulsed atmospheric pressure helium jet operating in ambient air and impinging on an indium tin oxide coated glass slide are reported as a first order approximation of a biomaterial. An automatic fitting procedure of the Stark shifted spectra taking into consideration constraints regarding Stark components' positions and intensities as well as molecular nitrogen emission subtraction was implemented. This allowed electric field vector component measurements both in the gas phase and at the interface when the jet impinges on the substrate and during the development of a surface ionization wave. The obtained results show an increase in the axial electric field in the jet effluent in the gas phase with a peak magnitude from 12 to 18 kV cm^{-1} before the ionization wave impinges on the substrate. A steep electric field enhancement to a peak value of about 24 kV cm^{-1} was observed when the ionization wave impinges on the surface. A peak radial electric field of about 27 kV cm^{-1} was measured off-axis in the surface ionization wave. These results are consistent with previously reported modelling predictions and are consistent with the possible important impact of electric fields on direct treatments of living matter. While Stark polarization spectroscopy is limited to electric field measurements from regions with emission, we illustrate that the capability to measure near surface electric fields in helium makes it a valuable complementary technique for the electric field-induced second harmonic (EFISH) technique. We have further used this technique to measure the formation of a sheath allowing us to analyze the transition from a Townsend to glow discharge.

Assessment of the impact of plasma-induced gas-liquid interface dynamics on plasma properties and plasma-induced liquid phase chemistry [B,11]

We performed detailed studies of the gas–liquid interfacial dynamics during the impingement of an argon radio frequency driven APPJ (see figure 2). The dynamics of the dimples generated during the impingement of the APPJ on the liquid depends on the plasma power, gas flow rate, size of the liquid container and the distance of the APPJ nozzle to the liquid surface. When the plasma is in contact with the liquid, the dimple oscillation frequency correlates with the dynamics of the plasma filament. At larger jet-liquid distances, the APPJ behaves similar to a gas jet although in most cases with an enhanced deformation of the liquid interface or change in dimple dynamics. The observed dimple oscillations can significantly enhance the decomposition efficiency of crystal violet by enhancing liquid phase convection. The conditions studied in this paper are similar to typical conditions for *in vitro* plasma-bio-interaction studies and the plasma-induced interfacial liquid dynamics, which is often not considered in many studies, might enhance plasma-induced liquid phase chemistry and reactivity.

Detailed measurements of plasma-instabilities during plasma-liquid interactions including the determination of stabilization mechanisms [19]

We investigated the impact of the applied voltage, pulse width and liquid conductivity on the plasma morphology and the OH generation for a positive pulsed DC atmospheric pressure plasma jet with He-0.1% H_2O mixture interacting with a liquid cathode. We adopted diagnostic techniques of fast imaging, 2D laser induced fluorescence (LIF) of OH and Thomson scattering spectroscopy. We show that plasma instabilities and enhanced evaporation occur and have a significant impact on the OH generation. At elevated plasma energies, it is found that the plasma contracts due to a thermal instability through Ohmic heating and the contraction coincides with a depletion in the OH density in the core due to electron impact dissociation. For lower plasma energies, the instability is suppressed/delayed by the equivalent series resistor of the liquid electrode. An estimation of the energy flux from the plasma to the liquid shows that the energy flux of the ions released into the liquid by positive ion hydration is dominant, and significantly larger than the energy needed to evaporate sufficient amount of water to account for the measured H_2O concentration increase near the plasma-liquid interface.

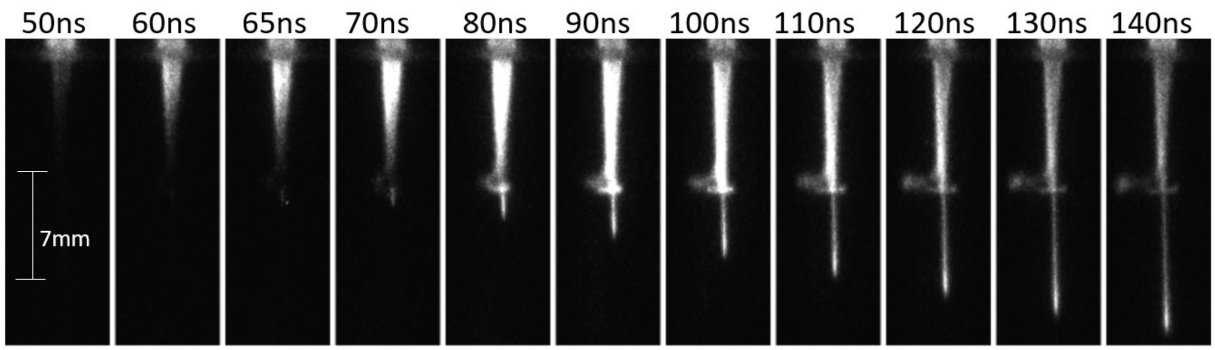

Figure 3: Dynamics of the ionization wave generated by a pulsed APPK and its penetration into a capillary with an inner diameter of 100 µm. (Jain and Bruggeman)

Dynamics and limitations of plasma penetration in high aspect ratio capillaries as a model of porous medium [A,5]

We studied, using a low voltage RF driven argon and helium plasma jet, the plasma penetration into a capillary tube with a large aspect ratio followed by its propagation inside the capillary. We determined the limitations on the penetration diameter, and the underpinning mechanisms of the plasma propagation and penetration process. Experimental results include time resolved imaging of plasma propagation and penetration in capillaries with different internal diameter and surface electric field measurements. We found that the time between the plasma jet in first contact with the capillary tube surface and the subsequent penetration into the capillary tube spans several RF cycles due to electric fields at the plasma-tube interface below 4 kV cm^{-1}. These low electric fields require Penning ionization and/or stepwise ionization and hence a buildup of the metastable and electron density is required to achieve a sufficiently large ionization rate near the capillary tube inlet to enable penetration and propagation. Furthermore, it is found that the propagation of the argon jet into the capillary occurs during the positive half cycle of the RF waveform and is very similar to the propagation of the jet in surrounding air. We have extended that work also an APPJ excited by nanosecond pulses as the example shown in figure 3.

c. Plasma-bio-interaction mechanisms

Motivation:

Fundamental plasma-bio interaction studies have shown that reactive species as H_2O_2, O_2^-, peroxynitrate and O_3 play an important role in the biological interaction of plasmas and cells. Despite the large amount of different RONS produced by plasma, the majority of the species that are suggested to be bactericidal are long-lived species and the role of many other bioactive plasma-produced species remains an open question. We have focused our study on the role of reactive nitrogen species and radicals such as atomic O produced in O_2 or air containing plasmas and how they impact virus and bacteria.

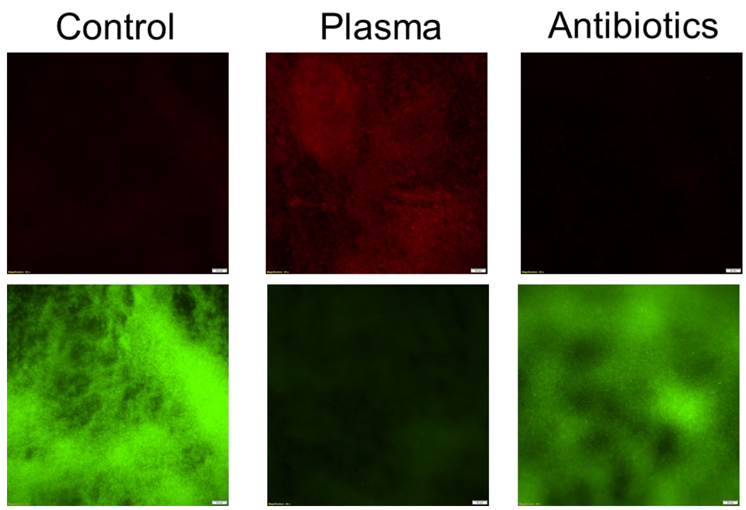

Figure 4: Comparison of plasma action (Ar+O_2 plasma jet for 6 min) and tetracycline (antibiotics, 10 µg/ml for 12 h) against methicillin resistant *Staphylococcus aureus* (MRSA) biofilm. The life-dead viability assay consisting of two fluorescent nucleic acid stains: SYTO 9 and propidium iodide. Propidium iodide penetrates only bacteria with damaged membranes, causing the emergence of red fluorescence only for the plasma treated biofilm. (Nandula, Kondeti, Granick, Bruggeman and Hunter)

Results:

Mechanisms of inactivation of virus in air plasma and the role of transport limitations [7, 14, 18]

We performed a comparative study of the effectiveness of surface decontamination against feline calicivirus (FCV) and *Salmonella spp* using four different plasma sources, a dielectric barrier discharge (DBD) in direct contact with the substrate and three remote plasma treatment sources: a 2D DBD, a volumetric DBD and a gliding arc discharge. The plasma sources were all operated in a jet-like mode in air at atmospheric pressure. The decontamination efficacy was enhanced by the presence of humidity on the sample surface and only direct contact between plasma and samples allowed the inactivation of pathogens on dry substrates. Across all sources, FCV was seen to be more susceptible to the plasma-generated species than *Salmonella spp*. The diminished effectiveness of the gliding arc discharge compared to the DBDs operating at the same power is most likely due to the low Henry's law constant of NO, the dominant reactive species generated by the gliding arc. Control experiments illustrate that the co-existence of O_3 and NO_2, as in the afterglow of the remote DBDs enhances the inactivation compared to the inactivation by O_3 or NO_2 only. A chemical kinetics model of the plasma effluent and the plasma treatments show a strong correlation between the gas-phase concentration of N_2O_5 and inactivation of the virus. We experimentally showed that the production of N_2O_5 coincides with the enhanced generation of reactive nitrogen species in the liquid phase. In addition, we have collaborated with colleagues at Drexel University and colleagues in Japan to review the state-of-the-art of plasma-virus inactivation and analyze key mechanisms enabling the inactivation.

Mechanisms of inactivation of bacteria by air and oxygen containing plasmas [B,4]

Different chemical pathways leading to the inactivation of *Pseudomonas aeruginosa* and *Staphylococcus aureus* by a cold APPJ in buffered and non-buffered solutions were investigated. As APPJs produce a complex mixture of reactive species in solution, a comprehensive set of diagnostics were used to assess the liquid phase chemistry. This includes absorption and electron paramagnetic resonance spectroscopy in addition to a scavenger study to assess the relative importance of the various plasma produced species involved in the inactivation of bacteria. Different modes of inactivation of bacteria were found for the same plasma source depending on the solution and the plasma feed gas. The inactivation of bacteria in saline is due to the production of short-lived species in the case of argon plasma when the plasma touches the liquid. Long-lived species (ClO^-) formed by the abundant amount of O radicals produced by the plasmas played a dominant role in the case of Ar +1% O_2 and Ar +1% air plasmas when the plasma is not in direct contact with the liquid. Inactivation of bacteria in distilled water was found to be due to the generation of short-lived species: $O^\cdot$ & O_2^- for Ar +1% O_2 plasma and O_2^- (and OH in absence of saline) for Ar plasma.

Showing the capability of plasmas to inactive MRSA biofilms [D]

This study demonstrates that cold atmospheric pressure plasmas can effectively inactivate MRSA bacteria within a biofilm (see figure 4). We investigated different biofilm treatment modalities and found that the effectiveness and distribution of bacteria inactivation can dependent on the treatment modality. Wet and indirect CAP treatment can inactivate bacteria in a large region of biofilm beyond the immediate vicinity of the plasma jet plume because the inactivation is enabled by long-lived plasma-produced species including OCl^- in the saline solution present. The dry CAP treatment can eliminate biofilm bacteria by etching the biofilm from the surface possibly enabled by the large flux of reactive oxygen atoms produced by the plasma jet.

2. Professional development

Five graduate students whose work was partially supported by this project completed their PhD or MS dissertations during the course of this project:

A. Amita Brahme, Penetration of Ar and He RF-driven plasma jets into micrometer sized capillary tubes (MS thesis – 07/01/2018)
B. Santosh Kondeti, Fundamental study of plasma interactions with polymers and liquids (PhD thesis – 01/31/2020)
C. Manikandan Suresh, Atmospheric pressure plasma-substrate interactions: H_2O_2 diffusion in hydrogels and plasma induced surface charging (MS thesis - 03/31/2020)
D. Sahil Mahajan, Star-Like Pattern Formation during Plasma-Hydrogel Interactions and Plasma-Enabled Biofilm Inactivation (MS thesis – 10/31/2021)
E. Jingkai Jiang, Molecular beam mass spectrometric investigation of plasma-material interactions motivated by plasma-catalysis (PhD thesis – 1/31/2022)

The following researchers have also been partially supported by this project and made contributions to research outcomes of this project:

- Harish Doddi
- Samyak Jain
- Mahsa Mirzaee
- Gaurav Nayak
- Marien Simeni Simeni
- Tanubhav Srivastava
- Eveline van Doremaele
- Yuanfu Yue

3. Infrastructure development

This project enabled the acquisition and development of new diagnostics in the High Temperature Plasma Laboratory at the University of Minnesota. We purchased and implemented an electric field probe that allowed us to measure time resolved surface electric fields to explain plasma penetration in micrometer sized high aspect ratio capillaries. In addition, within the framework of this project we also implemented Thomson scattering allowing for the first time to measure the evolution of the electron density and temperature during the development of a plasma instability in an atmospheric pressure glow discharge.

4. Products

In this section we list the peer-reviewed papers and presentations that reported results achieved in this project. The results of this project were reported in 20 peer-reviewed publications (+ 1 paper under review and 2 papers in preparation) and 36 conference presentations including 19 plenary and invited lectures. Many of these publications report collaborative studies and hence also acknowledge funding from collaborations. In addition a subsection of the publications significantly benefited from methods and techniques developed in the framework of other projects which have also been acknowledged.

a. Peer reviewed publications

1. P.J. Bruggeman, F. Iza and R. Brandenburg, Foundations of atmospheric pressure non-equilibrium plasmas, Plasma Sources Sci. Technol. 26 (2017) 123002 https://doi.org/10.1088/1361-6595/aa97af

2. I. Adamovich, S. Baalrud, A. Bogaerts, P. J. Bruggeman, M. Cappelli, V. Colombo, U. Czarnetzki, U. M. Ebert, J. G. Eden, P. Favia, D. B. Graves, S. Hamaguchi, G. Hieftje, M. Hori, I. D. Kaganovich, U. Kortshagen, M. J. Kushner, N. J. Mason, S. Mazouffre, S. Mededovic Thagard, H.-R. Metelmann, A. Mizuno, E. Moreau, A. B. Murphy, B. A. Niemira, G. S. Oehrlein, Z. Lj. Petrovic, L. C. Pitchford, Y.-K. Pu, S. Rauf, O. Sakai, S. Samukawa, S. Starikovskaia, J. L. Tennyson, K. Terashima, M. M. Turner, M. C. M. van de Sanden, A. Vardelle, The 2017 Plasma Roadmap: Low Temperature Plasma Science and Technology, J. Phys. D: Appl. Phys. 50 (2017) 323001 https://doi.org/10.1088/1361-6463/aa76f5

3. E.R.W. Van Doremaele, V.S.S.K Kondeti, P.J. Bruggeman, Effect of plasma on gas flow and air concentration in the effluent of a pulsed cold atmospheric pressure helium plasma jet, Plasma Sources Sci. Technol. 27 (9) (2018) 095006 https://doi.org/10.1088/1361-6595/aadbd3

4. V.S.S.K. Kondeti, C. Phan, K. Wende, H. Jablonowski, U. Gangal, J. Granick, R.C. Hunter and P.J. Bruggeman, Long-lived and short-lived reactive species produced by a cold atmospheric pressure plasma jet for the inactivation of Pseudomonas aeruginosa and Staphylococcus aureus, Free Radical Biology and Medicine 124 (2018) 275–287 https://doi.org/10.1016/j.freeradbiomed.2018.05.083

5. A. Brahme, Z.S. Chang, N. Zhao, V.S.S.K. Kondeti, P.J. Bruggeman, Penetration of Ar and He RF-driven plasma jets into micrometer-sized capillary tubes, J. Phys. D: Appl. Phys. 51 (41) (2018) 414002 https://doi.org/10.1088/1361-6463/aad883

6. V.S.S.K. Kondeti, Y.S. Zheng, P.S. Luan, G.S. Oehrlein and P.J. Bruggeman, O, H, and OH radical etching probability of polystyrene obtained for a radio frequency driven atmospheric pressure plasma jet. J. Vac. Sci. Technol. A, 38 (3) (2020) 033012 https://doi.org/10.1116/6.0000123

7. A. Moldgy, G. Nayak, H.A. Aboubakr, S.M. Goyal and P.J. Bruggeman, Inactivation of virus and bacteria using cold atmospheric pressure air plasmas and the role of reactive nitrogen species, J. Phys. D: Appl. Phys. 53 (43) (2020) 434004 https://doi.org/10.1088/1361-6463/aba066

8. J. Jiang and P.J. Bruggeman, Spatially resolved absolute densities of reactive species and positive ion flux in He-O_2 RF driven atmospheric pressure plasma jet: touching and non-touching with dielectric substrate, J. Phys. D: Appl. Phys., (2020) 53 (28) 28LT01 https://doi.org/10.1088/1361-6463/ab813d

9. Y. Yue, V.S.S.K. Kondeti and P.J. Bruggeman, Absolute atomic hydrogen density measurements in an atmospheric pressure plasma jet: generation, transport and recombination from the active discharge region to the effluent, Plasma Sources Sci. Technol. 29, 04LT01 (2020) https://doi.org/10.1088/1361-6595/ab7853

10. M. Mirzaee, M. Simeni Simeni and P. J. Bruggeman, Electric Field Dynamics in an Atmospheric Pressure Helium Plasma Jet Impinging on a Substrate, Phys. Plasmas 27 (2020) 123505 https://doi.org/10.1063/5.0021837

11. V.S.S.K. Kondeti and P.J. Bruggeman, The interaction of an atmospheric pressure plasma jet with liquid water: dimple dynamics and its impact on crystal violet decomposition, J. Phys. D: Appl. Phys. 54 (2021) 045204 (14pp) https://doi.org/10.1088/1361-6463/abbeb5.

12. Y. Yue, J. Jiang, VSSK Kondeti and P. Bruggeman, Spatially and temporally resolved H and OH densities in a nanosecond pulsed plasma jet: An analysis of the radical generation, transport, recombination and memory effects, J. Phys. D: Appl. Phys. 54 (2021) 115202 https://doi.org/10.1088/1361-6463/abce2a

13. P.J. Bruggeman, R.R. Frontiera, U.R. Kortshagen, M.J. Kushner, S. Linic, G.C. Schatz, H. Andaraarachchi, S. Exarhos, L.O. Jones, C.M. Mueller, C. Rich, C. Xu, Y. Yue and Y. Zhang, Plasma-Driven Solution Electrochemistry, J. Appl. Phys. 129 (2021) 200902 https://doi.org/10.1063/5.0044261

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15. J. Jiang and P. Bruggeman, Ion fluxes and memory effects in an Ar-O_2 modulated RF-driven atmospheric pressure plasma jet, Plasma Sources Sci. Technol. 30 (2021) 105007 https://doi.org/10.1088/1361-6595/ac2045

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18. S. Kumagai, C. Nishigori, T. Takeuchi, P. Bruggeman, K. Takashima, H. Takahashi, T. Kaneko, E. H. Choi, K. Nakazato, M. Kambara, and K. Ishikawa, Towards prevention and prediction of infectious diseases with virus sterilization using ultraviolet light and low-temperature plasma and bio-sensing devices for health and hygiene care, Jpn. J. Appl. Phys. 61 (2022) SA0808 https://doi.org/10.35848/1347-4065/ac1c3d

19. Y. Yue, V. S. S. K. Kondeti, N. Sadeghi, P. J. Bruggeman, Plasma dynamics, instabilities and OH generation in a pulsed atmospheric pressure plasma with liquid cathode: a diagnostic study, Plasma Sources Sci. Technol. (2022) https://doi.org/10.1088/1361-6595/ac4b64

20. M. Suresh, V. S. S. K. Kondeti and P. J. Bruggeman, Production and diffusion of H_2O_2 during the interaction of a direct current pulsed atmospheric pressure plasma jet on a hydrogel, J. Phys. D: Appl. Phys. (2022) https://doi.org/10.1088/1361-6463/ac4ec6

21. J. Jiang, V. S. S. K. Kondeti, G. Nayak and P. J. Bruggeman, Experimental and modeling studies of the plasma chemistry in a humid Ar radiofrequency atmospheric pressure plasma jet (under review)

b. Conference presentations

1. P. Bruggeman, Plasma-liquid interactions, 28th Summer school and International Symposium on the Physics (SPIG), August 29 - September 2nd, 2016, Belgrade, Serbia (plenary invited presentation)

2. P. Bruggeman, Key scientific questions on the path to saving the world with plasmas: a personal perspective, Gaseous Electronics Conference, October 10-14, 2016, Bochum, Germany (invited presentation)

3. V.S.S.K. Kondeti, C. Phan, K. Wende, U. Gangal, A. Schauer, J. Granick, R.C. Hunter and P.J. Bruggeman, Mechanisms of inactivation of bacteria in solution and biofilms by an atmospheric pressure plasma jet, MRS: Materials Research Society Fall Meeting, November 27- December 2, 2016 Boston, USA

4. P.J. Bruggeman, Plasma-liquid interactions: fundamentals and applications, ISPlasma2017/IC-PLANTS2017, March 1-5, 2017, Chubu University, Aichi, Japan (invited presentation)

5. P. Bruggeman, Plasma water vapor kinetics and plasma-liquid interactions, International Conference on Physics of Low Temperature Plasma, June 5-9, 2017, Kazan, Russia (plenary invited presentation)

6. P.J. Bruggeman, Plasma-liquid interactions, International Plasma Chemistry Society Summer School, July 28-29, 2017, Montreal, Canada (tutorial lecture)

7. V.S.S.K. Kondeti, C. Phan, K. Wende, H. Jablonowski, U. Gangal, J. Granick, R.C. Hunter and P.J. Bruggeman, The inactivation mechanism of planktonic bacteria in buffered and non-buffered solutions by an atmospheric pressure plasma jet 23rd International Symposium on Plasma Chemistry (ISPC), July 30-August 4, 2017, Montreal, Canada

8. P. J. Bruggeman, Plasma technologies II: developments at high pressure and in liquids, lecture on 21th European Summer School 'Low Temperature Plasma Physics: Basics and Applications', October 7-12, 2017, Bad Honnef, Germany (tutorial lecture)

9. P. Bruggeman, Plasma-liquid interactions: multiphase transport, 14^{th} International Conference on Flow Dynamics (ICFD2017), November 1-3, 2017, Sendai, Japan (invited presentation)

10. P. Bruggeman, Towards an understanding of plasma-liquid interactions in plasma medicine, 10^{th} EU-Japan Joint Symposium on Plasma Processing, December 4-7, 2017, Bankoku Shinryokan, Okinawa, Japan (invited presentation)

11. P. Bruggeman, Low temperature atmospheric pressure plasmas: an enabling technology for new applications, 10th Asia-Pacific International Symposium on the Basics and Applications of Plasma Technology, December 15-17, 2017, Taoyuan, Taiwan (invited plenary presentation)

12. M. Mirzaee and P.J. Bruggeman, Plasma-induced RONS in agarose gels by atmospheric pressure plasma jet, 7^{th} International Conference on Plasma Medicine, June 17-22, 2018, Philadelphia, USA

13. E. R. W. Van Doremaele, V.S.S.K. Kondeti and P.J. Bruggeman, Effect of plasma on helium gas flow in an atmospheric pressure plasma jet: absolute air concentration measurements by Rayleigh scattering, 7^{th} International Conference on Plasma Medicine, June 17-22, 2018, Philadelphia, USA

14. V.S.S.K. Kondeti, C.Q. Phan, K. Wende, H. Jablonowski, U. Gangal, J.L. Granick, R.C. Hunter and P.J. Bruggeman, The chemical mechanism of the inactivation of Pseudomonas aeruginosa and Staphylococcus aureus by an RF driven atmospheric pressure plasma jet, Gordon Research Conference on Plasma Processing Science, August 5-10, 2018, Smithfield, RI, USA

15. P. Bruggeman, Plasmas in liquids: What do we know and what can we still learn, 14eme Journees d`echanges du reseau des plasma froids, CNRS, October 15-18, 2018, La Rochelle, France (invited presentation)

16. P. Bruggeman. Peter Mark Memorial Award Lecture: Plasma-bio Interactions: Investigating Mechanisms to Enable New Applications, AVS 65^{th} International Symposium and Exhibition, October 21-26, 2018, Long Beach, CA, USA (invited presentation)

17. P. Bruggeman, Plasma-bio interactions: Linking plasma-induced liquid phase chemistry with the biological impact of plasma, MRS 2018 Material Research Society Fall Meeting and Exhibit, November 25-30, 2018, Boston, Massachusetts, USA (invited presentation)

18. V.S.S.K. Kondeti and P.J. Bruggeman, Absolute H density measurement in an RF driven Ar + 0.27% H_2O plasma, 13^{th} Frontiers in Low Temperature Plasma Diagnostics, May 13-16, 2019, Bad Honnef, Germany

19. V.S.S.K. Kondeti and P.J. Bruggeman, Absolute H density in an RF driven Ar + H_2O atmospheric pressure plasma jet by two photon absorption laser induced fluorescence, 24^{rd} International Symposium on Plasma Chemistry (ISPC), July 9- 14, 2019, Naples, Italy

20. P. J. Bruggeman, Overview of processing plasma generation, 24^{rd} International Plasma Chemistry Society Summer School, June 9-14, 2019, Naples, Italy (tutorial lecture)

21. M. Mirzaee, M. Simeni Simeni and P.J. Bruggeman, Electric Field measurement in a nanosecond pulsed atmospheric pressure plasma jet in helium, 46^{th} IEEE International Pulsed Power and Plasma Science meeting, Orlando, Florida, June 23-28, 2019

22. Y. Yue, V.S.S.K. Kondeti and P. Bruggeman, Atomic Hydrogen generation in the ionizing plasma region and effluent of a helium-water atmospheric pressure plasma jet by two-photon absorption laser induced fluorescence (TALIF), 46th IEEE International Pulsed Power and Plasma Science meeting, Orlando, Florida, June 23-28, 2019

23. A. Moldgy, G. Nayak, A.H. Aboubakr, S.M. Goyal and P.J. Bruggeman, The influence of surface humidity on disinfection using cold plasmas, IEEE Pulsed Power and Plasmas Conference, June 23-28, 2019, Orlando, Florida, USA (invited presentation)

24. P.J. Bruggeman, Low Temperature Plasmas; a Unique Non-Equilibrium State for Tackling Grand Societal Challenges, Biennial Conference of the Spanish Royal Society of Physics, July 15-19, 2019, Zaragoza, Spain (plenary invited presentation)

25. P.J. Bruggeman, Plasma-liquid interactions: fundamental studies elucidating biomedical and environmental applications, XL Annual Meeting of Brazilian Vacuum Society (CBrAVIC), October 7-10, 2019, State University of Sao Paulo, Guaratinguetá, Brazil (invited lecture)

26. P. J. Bruggeman, Plasma technologies II: developments at high pressure and in liquids, lecture on the 23rd European Summer School "Low Temperature Plasma Physics: Basics and Applications", October 5-10, 2019, Bad Honnef, Germany (tutorial lecture)

27. P. J. Bruggeman, Plasma technologies II: developments at high pressure and in liquids, lecture on the 24rd European Summer School "Low Temperature Plasma Physics: Basics and Applications", October 5-15, 2020, Bad Honnef, Germany (tutorial lecture, virtual)

28. P. Bruggeman Quantifying fluxes in atmospheric pressure plasmas to gain a quantitative understanding of plasma processes, International Conference on the Physics of Low Temperature Plasmas (PLTP 2020) November 9-13, 2020, Kazan, Republic of Tatarstan, Russia (plenary invited presentation, virtual)

29. P. Bruggeman Low Temperature Plasma: A Unique Non-Equilibrium Environment, 62nd Annual Meeting of the APS Division of Plasma Physics (DPP) Fall Meeting, November 9-13, 2020 (plenary invited review presentation, virtual)

30. P. Bruggeman, Plasma biology and chemistry for innovations in agriculture and the food cycle, 8th International Conference on Microelectronics and Plasma Technology and 9th International Symposium on Functional Materials, January 17-20, 2021, Jeju, Korea (plenary invited presentation, virtual)

31. G. Nayak, H. A. Aboubakr, A. Moldgy, J. Jiang, B. Olson, M. Torremorell, S. M. Goyal and P. J. Bruggeman, Plasmas for Decontamination of Airborne Viruses and Viruses on Surfaces, ISPlasma2021/ IC-PLANTS2021, March 7-11, 2021, Nagoya, Japan (invited presentation, virtual)

32. P. J. Bruggeman, Towards an Understanding of Plasma-bio Interactions: Tracking Reactive Species from the Plasma Source to the Biological Target, 8th International Conference on Plasma Medicine and 10th International Symposium on Plasma Bioscience, August 2-6, 2021, Incheon, Korea (invited presentation, virtual)

33. S. Dabhole, A. Moldgy, G. Nayak, H. Aboubakr, S. M. Goyal, P. J. Bruggeman, Virus Inactivation by Remote Plasma Treatment in a Batch Reactor 8th International Conference on Plasma Medicine

and 10th International Symposium on Plasma Bioscience, August 2-6, 2021, Incheon, Korea (virtual)

34. P.J. Bruggeman, Low temperature plasma: a perspective, CAMOST (Center for Atomic, Molecular, and Optical Science & Technology) online colloquium series organized by IIT-IISER Tirupati, India. August 16-20, 2021 (virtual)

35. P. Bruggeman, Pushing the boundaries of established plasma diagnostics, APS Gaseous Electronics Conference, 4-8 October 4-8, 2021 Huntsville, USA (invited presentation)

36. Y. Yue, K. Kondeti, N. Sadeghi and P.J. Bruggeman, On the OH density distribution in an atmospheric pressure plasma interacted with liquid cathode, APS Gaseous Electronics Conference, 4-8 October 4-8, 2021 Huntsville, USA