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Atmospheric pressure plasma jets onto a reactive water layer over tissue: pulse repetition rate as a control mechanism

Seth A Norberg¹, Guy M Parsey², Amanda M Lietz³, Eric Johnsen⁴ and Mark J Kushner^{2,5}

¹ Department of Civil and Mechanical Engineering, United States Military Academy, West Point, NY 10996, United States of America

² Department of Electrical Engineering and Computer Science, University of Michigan, 1301 Beal Ave., Ann Arbor, MI 48109-2122, United States of America

³ Department of Nuclear Engineering and Radiological Sciences, University of Michigan, 2355 Bonisteel Blvd., Ann Arbor, MI 48109-2104, United States of America

⁴ Department of Mechanical Engineering, University of Michigan, 2350 Hayward St., Ann Arbor, MI 48109-2125, United States of America

E-mail: seth.a.norberg.mil@mail.mil, parseygu@umich.edu, mjkush@umich.edu, lietz@umich.edu and ejohnsen@umich.edu

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Abstract

The use of plasma jets to treat tissue in the context of plasma medicine often involves a thin intervening liquid layer on top of the tissue. Plasma activated species first transport through and react in the liquid layer prior to reaching the tissue. Of the many parameters that can be used to control this process, pulse repetition frequency (PRF) stands out. Results from a computational investigation of multiple pulses at varying PRF from an atmospheric pressure plasma jet (APPJ) onto a reactive liquid layer are discussed, and three key trends are made clear. First, a high PRF (short time between pulses) enables the gaseous species produced during the previous pulse to remain in the vicinity of the plasma at the onset of the next pulse, thereby increasing the inventory of $(H)N_xO_y$ and O_3 in the gas phase. These species then solvate into the liquid, water in this case, and produce higher densities of aqueous ozone, nitrate, and peroxynitrite. With a lower PRF, reactants produced on a previous pulse are convected away prior to the next discharge pulse with more spatial separation of reactants both above and within the water. As a result, more of the hydroxyl anion (OH_{a0}) , ozone anion (OH_{3ag}^-) and nitric oxide (NO_{ag}) reach the tissue beneath the water. The second trend is that the production of H_2O_{2aq} and its fluence to the underlying tissue are relatively independent of the PRF. The precursors for H_2O_{2ac} are primarily produced by the surface ionization wave (SIW) on the top of the liquid, which then directly solvate into the liquid. Lastly, when the plasma plume touches the liquid, the SIW on the water layer increases the production of all aqueous species compared to configurations where the plasma plume does not touch the liquid. These trends are true for all PRF.

Keywords: atmospheric pressure plasma jet, plasma-liquid interactions, modeling, plasma medicine, control mechanisms

(Some figures may appear in colour only in the online journal)

⁵ Author to whom any correspondence should be addressed.

1. Introduction

Atmospheric pressure plasma jets (APPJs) are used for many facets of plasmas treating liquids and tissues in the context of plasma medicine [1-6]. The low-temperature plasmas produced in APPJs have many potentially beneficial outcomes when treating tissues, due to the electric fields, ultra-violet/ vacuum ultra-violet (UV/VUV) photons, and fluxes of charged and neutral reactants delivered to the tissue being treated [7, 8]. In many cases of treatment of, for example, wounds or cells in culture there is a thin layer of liquid covering the surface to be treated. The reactive species produced in the gas phase by the APPJ solvate into the liquid and continue reacting prior to reaching the tissue beneath the liquid. Whether the plasma effluent in an APPJ directly touches the liquid layer impacts the production of reactive species as well as the importance of electrical components of the plasma treatment [9-11]. In the non-touching case, the electric fields and UV/VUV radiation penetrating into the liquid layer are much reduced as are the incident fluxes of short lived species produced by the discharge. One extreme case of indirect treatment, at least in time, is plasma activated water (PAW) or plasma activated medium (PAM). PAW/M are produced by using a plasma source to activate the medium and introducing the PAW/M to the tissue at a later time—sometimes days later [12-14]. A recent review and roadmap of plasma-liquid interactions by Bruggeman et al provides a comprehensive overview of the research challenges in plasma-liquid interactions [15].

The deployment of plasma medical procedures will likely require control mechanisms for the plasma source so that the desired or required reactants can be reliably delivered to the tissue, particularly in the case of liquid covered tissue [16]. Depending on the desired method of treatment, there may be different requirements to tailor the reactive oxygen and nitrogen species (RONS) penetrating through the liquid layer to the surface below [17–19]. The intrinsic variability of APPJs when used in a clinical setting (e.g. location of ground planes, environmental humidity and temperature, different patient-to-patient characteristics) emphasize this need for control.

In prior studies, pulse repetition frequency (PRF) was identified as a controlling factor in the production of RONS by APPJs in the gas phase [20]. This dependence on PRF is based on the influence of gas residence time of reactive species in volumes in which the following plasma pulse will produce additional reactants. This residence time is determined by gas flow rate and the inter-pulse period. High PRF (or low flow rate) results in RONS produced during prior pulses reacting with newly produced RONS in the current discharge pulse, and so favors production of RONS that require several collisions with other RONS to produce. Low PRF (or high flow rate) results in RONS largely flowing out of the reaction zone prior to the next discharge pulse, and successive pulses being largely independent, favoring production of primary RONS (those produced directly by the discharge pulse or by collisions with the ambient gases.) The hypothesis investigated in this paper is that PRF may also be used as a control mechanism in activating thin liquid layers and delivering reactants to the underlying tissue.

In the last few years there has been a considerable amount of experimental work aimed at understanding the methods and selectivity of RONS production. Gorbanev et al used isotopic labelling and electron paramagnetic resonance spectroscopy to determine the origin of various species in an APPJ impinging on liquid [21]. Most of the ROS measured originated from admixtures in the plasma gas phase (rather than the liquid H₂O). Uchida et al demonstrated selectivity in the ratio of NO_{2aq}^{-} to H_2O_{2aq} as a function of whether plasma directly interacted with the liquid [22]. (The subscript 'aq' denotes an aqueous or in liquid-water species.) The ratio of NO_{2aq}^{-} to H_2O_{2aq} ranged from 0.02 to 1.2 by changing the nozzle height from 2 to 9 cm. Elg et al investigated admixtures in an APPJ directed at the liquid surface and found that oxygen atoms only reach the liquid if there is no O_2 admixture in the jet [23]. The distance between the jet outlet and the liquid surface was found to be a critical parameter in determining the flux of O to the surface. Kovačević et al showed a strong sensitivity of APPJ liquid target systems to non-electrical parameters such as gas flow rate and target distance [24]. These parameters resulted in changes to the discharge such as excited species distributions, electric field in the ionization wave (IW), and interaction time of the plasma being in contact with the liquid. Finally, a recent review by Reuter et al provides a synopsis of the experimental and computational research related to the kINPen APPJ, and indirectly other APPJs, in the context of diagnostics of underlying mechanisms [25].

In this paper, we discuss results from a computational investigation of APPJ activation of thin water layers over tissue as a function of PRF. Repetition rate is discussed as a control mechanism for treating tissue under liquid. The production of in-water reactive species and fluences through the liquid to the underlying tissue are discussed over 100 pulses as a function of PRF and plasma-liquid contact, or lack thereof. In practice, exposure of liquids to APPJs even for short periods results in the liquid receiving tens to thousands of pulses. This investigation of multiple APPJ pulses is intended to make closer connection to actual clinical use of APPJs to treat thin liquid layers. The example system consists of an APPJ sustained in a He/O₂ = 99.8/0.2 gas mixture flowing into humid air onto a 200 μ m water layer. The computational model is described in section 2, followed by a discussion of the results in section 3 for APPJs having PRFs from 1kHz to 1 MHz. Concluding remarks are in section 4.

2. Description of the model

With the goal of investigating the consequences of multiple pulses from APPJs activating a thin liquid layer covering tissue, this paper extends the prior studies of a single discharge pulse from a He/O₂ APPJ onto a liquid layer [26] and multiple pulses from a similar APPJ into ambient humid air [20]. As in these prior works, the numerical investigation was performed with *nonPDPSIM*, a plasma hydrodynamics model described in detail in [20]. Using an unstructured, triangular

mesh, the model used four modules in this investigation. The first addresses the flow dynamics using a modified version of the axisymmetric Navier–Stokes equations employing a second-order finite volume discretization scheme and implicit time steps on the order of μ s. The second module addresses plasma transport in which Poisson's equation for the electric potential and the continuity equations for charged species are solved. The third addresses neutral transport and reaction chemistry. The fourth addresses radiation transport. The liquid layer is included in the latter three modules, treated essentially as a dense plasma with material properties adjusted for density (e.g. dielectric constant) and using the same algorithms as in the gas phase, albeit with a separate reaction mechanism.

While ions and photons directly enter into the liquid, transport of neutral gas phase species into the liquid is limited by Henry's law equilibrium at the surface of the liquid [27]. Henry's law states that at constant temperature, the equilibrium density of a gas dissolved in a liquid is proportional to the partial pressure of that species in the gas phase. In *nonP*-*DPSIM* this equilibrium is enforced as a limiting value of the density of a gas phase species and its aqueous counterpart at the surface of the water. This limiting equilibrium is reached by using an effective diffusion coefficient for transport between a numerical node in the mesh on the surface of the water and the adjacent numerical node in the gas. For a given neutral species with densities of n_g and n_l on neighboring gas and liquid nodes respectively, the diffusion flux from the gas node to the liquid node is defined as

$$\phi_{g \to l} = \begin{cases} \frac{D_g}{\Delta r} \left(1 - \frac{n_l}{n_g h} \right) \left(n_g - n_l \right), & n_l \leqslant n_g h \\ 0, & n_l > n_g h \end{cases}$$
(1)

where Δr is the separation between nodes, D_g is the gas phase diffusion coefficient, and *h* is the Henry's constant for the species. Analogously, the flux from the liquid to the gas node is defined as

$$\phi_{l \to g} = \begin{cases} \frac{D_l}{\Delta r} \left(1 - \frac{n_g}{(n_l/h)} \right) \left(n_l - n_g \right), & n_g \leq (n_l/h) \\ 0, & n_g > (n_l/h) \end{cases}$$
(2)

where D_l is the species liquid diffusion coefficient. If the species density is zero at the surface of the liquid, the diffusion coefficient for transport into the liquid has its unconstrained gas phase value, while that for diffusion out of the liquid is zero. As the density in the liquid at the surface of the liquid approaches its equilibrium value, the effective diffusion coefficient approaches zero. When densities at the surface are in equilibrium, effective diffusion coefficients for both entering and leaving the liquid are zero. If the liquid is supersaturated (that is, the density at the surface is greater than its equilibrium value), diffusion occurs only out of the liquid. Transport of the liquid species from the surface into the gas proceed with their unconstrained diffusion coefficients.

The multiple discharge pulses in this investigation were addressed in the following manner, essentially the same as in [20]. After establishing the flow field, the plasma dynamics module in which Poisson's equation is solved is executed for the first discharge pulse until the resulting plasma IW dissipates and ion species in the gas phase decay to negligible densities. This typically occurs on times scales of tens of nanoseconds. Source functions for reactive species are recorded during this first pulse. Following the first pulse, Poisson's equation is not solved, charge neutrality is enforced and the afterglow period is computed until the next pulse. With the rationale that the production of reactive species occurs nearly instantaneously compared to the inter-pulse period, the second (and subsequent) discharge pulses are represented as instantaneous production of reactive species using the source functions from the first pulse. This technique enables a large number of discharge pulses and afterglow periods to be simulated, but does not capture the change in source functions that may result from changes in species densities on later pulses, nor the increasing conductivity of the water that may occur over many pulses.

The geometry of the APPJ was inspired by the kINPen device developed by the INP Plasmatis in Griefswald [25, 28, 29]. The cylindrically symmetric computational domain has 16800 nodes with several refinement zones that are finest at the electrode tip (37 μ m) and in the water layer (20 μ m) with gradual increase in cell size perpendicular to the water layer as shown in figure 1(a). The 0.5 mm pin electrode is at the center of a dielectric tube ($\varepsilon/\varepsilon_0 = 4$) that is 1.6 mm in diameter with walls 0.5 mm thick and that extends 5 mm beyond the tip of the electrode. The gap from the end of the tube to the water surface is 7.5 mm. Helium with 0.2% O₂ was first flowed at 4 slm through the tube to establish the flow field. Humid air $(N_2/O_2/H_2O = 79.5/20/0.5)$ flows at 4 slm coaxially to the APPJ to emulate flow entrainment and minimize the likelihood for turbulence or excessive vortices. Both streams (through the tube and coaxial to the tube) exit the gas outlet port on the outer radius of the computational domain. Evaporation from the 200 μ m water layer was included in the model by holding the density of H₂O at its saturated vapor pressure at the surface of the water. Although both turbulence and vortices can be important to the gas dynamics and propagation of IW in APPJs, we chose conditions that produce laminar flow fields to constrain the parameter space [29, 30].

The gas flow field showing densities of He, O_2 , N_2 and H_2O is in figure 1(b). The helium jet displaces the evaporating water vapor at small radii and rapidly convects water vapor radially outwards faster than rates of axial diffusion. The helium jet effectively blocks the ambient air from freely diffusing to the water layer.

The first discharge was a single -15 kV pulse with a 5 ns rise and a total duration of 52 ns. In order to limit the parameter space and to make connection to our previous studies on the consequences of PRF on gas phase chemistry [26], a fixed voltage of -15 kV was used in this investigation. This voltage enables simulation of direct (touching the liquid) and indirect (not-touching) plasma plumes by changing the duration of the voltage pulse instead of changing its amplitude. The discharge is initiated with a small spot of plasma (1 × 10¹¹ cm⁻³) 400 μ m in diameter at the tip of the electrode. After finishing the



Figure 1. Schematic and flow field of the 2D cylindrical geometry used in the model for an atmospheric pressure plasma jet incident on a thin water layer covering tissue. (a) The computational domain is 9 mm in radius and 2 cm high. The left section shows the triangular mesh and refinement zones near the pin electrode and the water layer. (b) The concentrations of O_2 , He, N_2 , and H_2O vapor as the He/O₂ flows into the humid air environment at 4 slm prior to discharge ignition. The densities of O_2 and H_2O are plotted over three and two decades.

series of pulses for each repetition rate, the flow of He/O_2 continued for 0.5 s to ensure that all reactive gaseous species flow out of the computational domain and that reactions in the liquid have nearly reached a terminal state. The gas phase reaction mechanism is the same as that used in [26], and tabulated in appendix 1 of [31].

The liquid layer was modeled as water initially containing 8 ppm dissolved O₂. The Henry's law constants for the species of interest differ by large factors. O₃ and most N_xO_y have constants ranging from 0.044 to 48.5 and are slow to transport into the liquid [32]. OH, N₂O₃ and HNO₂ transport into the water moderately quickly with Henry's law constants of 692



Figure 2. Plasma dynamics for the -15 kV plasma jet. (a) The formation and propagation of the IW are shown by the electron impact ionization source, S_e , using a log-scale over three decades at 13, 24, 34 and 47 ns during the discharge. At 47 ns, the restrike and surface IW are active. (b) Densities of cations at the end of the discharge pulse at 47 ns plotted over 3 decades. He⁺ and He₂⁺ are confined to the He column. N₂⁺, N₄⁺, H₂O⁺, and H₃O⁺ are formed through electron impact in the IW and SIW (N₂⁺, H₂O⁺) and subsequent charge exchange with the humid air (N₄⁺, H₃O⁺). The O₂⁺ in the tube results from the electron impact ionization of the seeded O₂. Maximum densities are shown in each frame.

to 1150 [32]. H_2O_2 , HNO₃ and ONOOH have large Henry's law constants, $1.92-4.8 \times 10^6$, and quickly solvate into the water. The water reaction mechanism is the same as discussed in [33]. Though species diffuse through the liquid, the bulk motion of the liquid is neglected.

3. Scaling of plasma activation of water with repetition rate

3.1. IW properties

During application of a -15 kV pulse (5 ns rise and fall times for a total duration of 52 ns), an IW is launched from the tip

of the electrode, as shown by the electron impact ionization source term, S_e , in figure 2(a). The IW quickly transitions to the inner wall of the tube and, by 16 ns, begins to exit the tube. Upon exiting the tube, the IW transitions onto the axis, and propagates through the helium gas channel toward the water layer having a maximum S_e of 5×10^{21} cm⁻³ s⁻¹. At 32 ns, the IW strikes the surface of the water and continues as a surface ionization wave (SIW) across the top of the water through the saturated water vapor. Shortly after the IW strikes the surface, a restrike, or positive IW, propagates back up the plasma column [34]. The electron density increases as the restrike propagates upwards and a conduction channel develops. The ionization source shown at the end of the high voltage portion of the pulse at 47 ns is at the greatest radial extent of the SIW, approximately 3 mm from the axis. This occurs as the ionization source in the plasma column due to the restrike is retreating into the tube.

The densities of cations (positive ions) at 47 ns for the sums of He⁺ and He₂⁺, N₂⁺ and N₄⁺, and H₂O⁺ and H₃O⁺ are shown in figure 2(b). He⁺ is dominantly produced by electron impact ionization with threshold energy of 24.6 eV and secondarily by Penning and stepwise ionization. The peak density of He⁺ at 47 ns is 2.4×10^{13} and that of He₂⁺ is 1×10^{13} cm⁻³. The latter is primarily produced through three-body associative charge exchange of He. The helium ions are depleted through charge exchange with O₂, ion–ion recombination, and electron–ion recombination which produces excited helium atoms.

The nitrogen cation, N_2^+ requires 15.5 eV for production by electron impact from the ground state, and through associative charge exchange, produces N₄⁺. These ions are dominantly found in the plume outside of the tube. The influx of air by diffusion into the He plume can reach the axis downstream of the tube but is not able to back-diffuse into the tube to produce a significant N2 density in the tube. The nitrogen ions are primarily produced through electron impact ionization with the N₂ that has diffused into the plume, but also through charge exchange from helium ions and Penning ionization with He excited states. N₂⁺ has a peak density of 3.1×10^{13} cm⁻³ at 47 ns and that of N₄⁺ is 1.1×10^{14} cm⁻³. O₂⁺ (peak of 1.1×10^{14} cm^{-3}) is produced both in the tube and in the effluent upon contact with air through electron impact reactions and Penning ionization with He excited states. As the SIW spreads along the surface of the water, it is nearly devoid of He ions. Sufficient air and water vapor has diffused into the He plume to quickly charge exchange with any He ions that might be produced. H_2O^+ is produced through electron impact ionization and charge exchange reactions, and H_3O^+ is formed by associative reactions with H_2O , $H_2O^+ + H_2O \rightarrow H_3O^+ + OH$. The H₂O⁺ is also quickly depleted by dissociative electron-ion recombination. The highest density of H_2O^+ , 5×10^{12} cm⁻³, is at the surface of the water layer coincident with the extent of the SIW where the H₂O density is the highest. These ions rapidly diffuse into and react with the water layer.

RONS are produced in the plasma effluent through a series of reactions which includes electron impact dissociation of O_2 in the tube, and electron impact dissociation of O_2 , N_2 and H_2O during the interaction of the IW with the ambient. The densities of RONS are shown in figure 3 at the end of the



Figure 3. Density of reactive oxygen species (ROS) and reactive nitrogen species (RNS) at the end of the discharge pulse (47 ns) over three decades on a log-scale. The maximum density is listed at the top of each frame. The locally high concentrations on the surface of the water layer result from the spread of the SIW.

discharge pulse. OH is produced outside of the tube, predominantly in the He plume and in the saturated water vapor at the surface of the water. In spite of the H₂O density being small in the He plume, this is where the IW propagates, and therefore where most electron impact processes occur. The density of O_3 is low $(1.2 \times 10^{10} \text{ cm}^{-3})$ at this early time in the pulsed cycle, as at least a few microseconds are required to convert O atoms to O_3 by collisions with O_2 . The density of O_3 will accumulate as O atoms produced by the IW react with the O2 in the feedgas and with the O₂ that has diffused into the plume from the ambient. Through electron impact excitation, N₂^{*} and N_2^{**} , representing $N_2(A^3\Sigma, B^3\Pi)$ and $N_2(C^3\Pi$ and higher), are produced dominantly in the plume, in the same manner as OH. The N₂ excited states are quenched by dissociative excitation transfer to O_2 producing O atoms. The N_2^{**} also reacts with O atoms to form nitrogen oxide (NO) in the effluent. NO then reacts with O and OH to produce higher order N_xO_y (comprised of NO, NO₂, NO₃, N₂O₃, N₂O₄, and N₂O₅) and nitric acids (HNO_x) comprised of HNO₂, HNO₃, and ONOOH. The N_2^{**} that reaches the vicinity of the water surface is a source of OH through production of VUV photons that photodissociate H₂O in the saturated vapor layer. These VUV photons passing into the liquid photodissociate and photoionize the water, producing OH_{aq} . and $H_2O^+_{aq}$.

3.2. Gas and liquid reactant densities versus PRF

Following the procedures described in section 2 for modeling multiple pulses, simulations were performed for 100 pulses at repetition rates of 1 kHz to 1 MHz. For example, the OH densities during the 100th pulse for a 100 kHz PRF (10 μ s inter-pulse period) are shown in figure 4(a). At 0.27 μ s after the discharge pulse, the density of OH is highest at the radial



Figure 4. Time evolution of the densities of selected RONS at a PRF of 100 kHz. (a) The density of OH shown at 0.1 μ s, 0.27 μ s 1.27 μ s and 9.8 μ s after the 100th pulse begins. (b) The density of O₃ following the 5th, 15th, 75th and 100th pulses. (c) The density of (H)N_xO_y as it accumulates in the effluent following the 5th, 15th, 75th and 100th pulses. The images are plotted on log-scales over 2 decades, with the maximum value indicated in each frame.

extent of the SIW on the surface of the water layer. Over a single 10 μ s cycle, convection does not significantly transport the OH, though gas phase reactions of OH do deplete its density, forming H₂O₂, H₂O, nitric acids and HO₂. The OH is also depleted by solvation into the water. By the 100th pulse at 100 kHz the interpulse dynamics of OH shown in figure 4(a) are in a quasi-steady state, repeating every pulse.

The densities of O_3 and $(H)N_xO_y$ are shown in figures 4(b) and (c) after the 5th, 15th, 75th and 100th pulses at 100 kHz. In contrast to OH, O_3 and the (H)N_xO_y are less reactive (slower to react in the gas phase) and so accumulate in the gas phase over the course of 100 pulses. The maximum densities of O₃ and $(H)N_xO_y$ move with the gas flow from the He plume after the 5th pulse, to along the surface of the water layer at the 15th pulse. A quasi-steady state distribution of densities is reached after the 75th pulse. Ozone production increases with the production of O atoms from each new pulse combining with the O_2 in the feedgas and in the ambient. (H)N_xO_y increases through the 100 pulses as the high pulse repetition rate (and short interpulse period) allows (H) N_xO_y to accumulate and react with other RONS. Over the course of many pulses, primary (H)N_xO_y such as NO further react to from higher N_xO_y such as N_2O_5 and eventually HNO_x. For example, at the end of the 5th pulse, the maximum NO density adjacent to the water layer is 5×10^{14} cm⁻³ while the peak of the density of HNO_x is 3×10^{13} cm⁻³. At the end of the 75th pulse, the density of NO has increased by a factor of 2 to 1×10^{15} cm⁻³ and the density of HNO_x has increased by a factor of 8 to 2.4×10^{14} cm^{-3} , both over a larger spatial domain above the liquid.

The densities of OH, O_3 and $(H)N_xO_y$ are shown in figure 5 during the 100th pulse for 1 kHz PRF. At this PRF, the next pulse would occur at 1 ms. Densities are shown for OH immediately after the pulse and at 25 μ s, 100 μ s and 1 ms after the pulse. OH is dominantly produced during the voltage pulse by electron impact dissociation of H₂O. Immediately after the pulse, insufficient time has passed for the density of OH to be depleted by either reactions or flow, and so it spatial distribution largely reflects where OH is formed. The concentrations of OH are then largely depleted by reactions and solvation into the liquid before the advective flow can significantly transport the OH towards the exit. The exception is on axis where the higher flow speed clears the He dominated plume of OH on similar time scales to depletion by reactions. The residual OH from the previous pulse moves out of the computational domain as the next pulse is introduced.

The density of O_3 is also shown immediately after the voltage pulse and at 25 μ s, 100 μ s and 1 ms after the pulse. Recall that O₃ is dominantly formed by a three-body assisted reaction of O with O2, which requires a few to tens of microseconds to occur. The density of O_3 immediately after the pulse, a time of about 50 ns, in large part reflects the O₃ density at the end of the prior pulse as O atoms produced by the IW have had insufficient time to react to form O_3 . At 25 μ s, O₃ then occurs in two distinct regions. The first region is in the He plume, and is due to the O formation in the IW of the previous pulse, now having sufficient time to react to form O₃. The second region is above the liquid water and at large radius, which is the residual density from the previous discharge pulses. By 100 μ s, O₃ is flowing out of the tube, while increasing its density on axis as O atoms produced in the IW contact the surrounding air. By 1 ms, the production of O₃ has ceased as all of the O atoms produced by the IW have been consumed. At this time, the *slug* of O₃ produced by the discharge pulse flows radially outward.



Figure 5. Time evolution of the densities of selected RONS at a PRF of 1 kHz. The densities of (a) OH, (b) O₃ and (c) (H)N_xO_y are shown at 1 μ s, 25 μ s, 100 μ s and 1 ms after the 100th pulse begins. The images are plotted on 3 decade log-scales with the maximum value indicated in each frame.

A similar sequence of events occurs for $(H)N_xO_y$, whose densities are shown immediately after the voltage pulse and at 25 μ s, 100 μ s and 1 ms. At 25 μ s, the $(H)N_xO_y$ is dominated by NO, produced during the discharge pulse, with a low density plume exiting towards the pump remaining from the previous discharge pulse. At 100 μ s, the dominant $(H)N_xO_y$ is still NO due largely to the lack of accumulation of reactants and depletion of the higher N_xO_y by advection. When operating at 100 kHz, there was sufficient buildup of reactants pulse to pulse to enable conversion of NO to higher N_xO_y . As the lower



Figure 6. The distribution of aqueous RONS in the water layer at 100 ms after the 100th pulse. (a) 100 kHz and (b) 1 kHz. The images are shown on a 3 decade log-scale with the maximum value shown in each frame. The *y*-axis has been expanded to show the detail at the interface.

 N_xO_y (NO, NO₂) react with the OH produced in the saturated layer above the water, HNO_x are formed (HNO₂, HNO₃). The large Henry's law constants for the HNO_x increase their rate of depletion by solvation into the water. By 1 ms, comparatively little (H)N_xO_y remains in the effluent. The densities of both O₃ and N_xO_y decrease by an order of magnitude when operating at 1 kHz compared to 100 kHz. This decrease is in large part a result of advection during the interpulse period that clears reactant species from the volume. Accumulation of reactants when operating at 100 kHz results from the IW propagating through the same volume of gas on successive pulses, enabling RONS to accumulate in that volume.

Aqueous species after 100 pulses of exposure to the plasma jet, followed by additional flow time for a total of 100 ms are shown in figure 6 for PRFs of 100 kHz and 1 kHz to a depth of 100 μ m. The dimensions of the nozzle and the 8 mm wide water layer are indicated at the bottom of the frame. Recall that neutral gas phase species solvate into the liquid at a rate limited by Henry's law equilibrium at the top surface of the liquid. Charged species in this model directly solvate into the water layer. The density of O_{3aq} in the liquid layer is at a maximum near the centerline beneath the nozzle for all PRFs in spite of the O₃ density being more widely distributed. In some cases, O_{3aq} is supersaturated on axis compared to its gas phase density. This supersaturation is a consequence of O atoms also solvating on axis and reacting with O_{2aq} in the water to form O_{3aq}. The near axis location of the maximum density of O_{3aq}

(as opposed to downstream) indicates that O atom solvation and reaction with the dissolved O_2 makes a major contribution to the production of O_{3aq} . At high PRF, O_3 production becomes limited by the finite amount of dissolved O_{2aq} . This production of O_{3aq} differs from plasmas sustained in air where few O atoms survive to reach the water, as most atoms will first produce O_3 in the gas. The broader distribution of O_{3aq} at 100 kHz reflects the higher density of O_3 in the gas due to accumulation pulse-to-pulse. In the absence of hydrocarbons in the water layer, O_{3aq} is a terminal species.

The width of the high density of H_2O_{2aq} corresponds to both the extent of the SIW and the effect of the jet displacing the water vapor from the region beneath the nozzle. H_2O_{2aq} is produced primarily by the self-reaction of OH_{aq} in the near surface layer of the water. OH in the gas phase is produced through dissociative electron impact excitation of H_2O , dissociative recombination of H_2O^+ and photodissociation of H_2O by VUV. The gaseous OH then solvates into the liquid. These processes are only one-step removed from electron impact processes in the SIW, and so solvation of OH will correlate with the spatial extent of the SIW. OH and H_2O_2 rapidly solvate due to their adjacency to the water layer where OH is produced by the SIW, so H_2O_{2aq} is not particularly sensitive to PRF.

The superoxide anion O_{2aq}^- is dominantly produced by solvated electrons attaching to dissolved O_2 . The highest concentration of O_{2aq}^- therefore corresponds to sites where electrons solvate, which are dominantly on or near the axis where the IW strikes the water. O_{3aq}^- is formed from reaction of $O_{aq}^$ and dissolved O_{2aq} . O_{aq}^- primarily results from the aqueous reaction of solvated electrons and O_{aq} , both of which are produced dominantly on or near the axis. As a result, O_{aq}^- is not terribly sensitive to PRF. The wider radial extent of O_3 enables a broader distribution of O_{3aq}^- . Both O_{2aq}^- and O_{3aq}^- are effectively terminal species.

The radial distribution of $NO_{2 aq}^{-}$ for 1 kHz compared to 100 kHz can largely be traced to the kinetics of NO_{aq}. A key distinction between the low PRF (1kHz) and high PRF (100kHz) plasma treatment of the water is that the higher PRF promotes the accumulation of gaseous RONS above the water layer, leading to higher peak concentrations of OH, O, O₃, and NO. These RONS then solvate and produce higher densities of aqueous species; including $NO_{2\,aq}^{-}$ by hydrolysis of HNO_{2aq}. The solvating ROS are dominantly on axis whereas the solvating RNS are more broadly distributed. NO_{aq} rapidly reacts with ROS. At high PRF, the solvated NO_{aq} from the previous pulse is not able to diffuse from the surface before a high density ROS solvates during the current pulse. The coincidence of the ROS and NO_{aq} depletes NO_{aq}, and all subsequent N_xO_{yaq} having NO_{aq} as a precursor. At lower PRFs such as 1kHz, NO_{aq} is able to diffuse from the surface between pulses, and so avoid reaction with the large density of ROS which solvates on the next pulse. NO_{aq} and NO⁻² aq react with O⁻² and H₂O_{2aq} respectively to form both $ONOO_{aq}^{-}$ and NO_{3aq}^{-} . Moving to larger radii, the densities of O_{2aq}^- and H_2O_{2aq} are depleted by these reactions to negligible values, which then allow the NO_{aq} and NO_{2aq}^{-} to accumulate at larger radius.

The time dependence of volume averaged densities of aqueous species for PRFs of 1kHz, 10kHz, 100 KHz and

1 MHz are shown in figure 7 for a total elapsed time of 0.5 s and densities exceeding 1×10^{10} cm⁻³. The elapsed time encompasses the 100 pulses at the specified PRF and the remaining time required to reach 0.5 s. The average species concentrations are within the entire 8 mm radius and 200 μ m deep water layer. A saw tooth pattern of a density indicates production and consumption of the species on each pulse. A stair-step pattern indicates accumulation of the species from pulse-to-pulse with little consumption.

As the PRF is increased, the dominant aqueous anions transition from O_{2aq}^{-} to $ONOO_{aq}^{-}$ and NO_{3aq}^{-} . The early dominance of O_{2aq}^{-} is in part a consequence of the O_{2} initially dissolved in the water. With this initial density of O_{2aq}, solvated electrons quickly attach to form O_{2ac}^{-} . With increasing repetition rate, the gas phase densities of $(H)N_xO_y$ species increase which, with large Henry's law constants, solvate and hydrolyze, resulting in an increase in $ONOO_{aq}^{-}$ and NO_{3aq}^{-} . The dominant cation which balances the negative ions is $H_3O_{aq}^+$ which is produced through both charge exchange of $H_2O_{aq}^+$ with water, to form $H_3O_{aq}^+$ and OH_{aq} , and by hydrolysis of aqueous(H)N_xO_y. The density of OH_{aq} follows a saw-tooth pattern, resulting from its generation by electron attachment to OH_{aq} and then being consumed through neutralization with the hydronium ion to form aqueous hydrogen atoms and OH_{aq} . The average OH_{aq}^{-} density increases with PRF due to the increasing rate of solvation of OH from the gas phase. In the afterglow, the solvation of OH from the gas phase ends, removing the source term for OH_{aa}^{-} , leading to a decrease in its density during the afterglow period.

The dominant neutrals are O_{3aq} and H_2O_{2aq} . The density of O_{3aq} varies on by a factor of two between 1 kHz and 1 MHz after 0.5 s. Since O_3 has a low Henry's law constant, the O_3 density at the surface quickly saturates, thereby limiting large increases in the O_{3aq} density. Since there is initially dissolved O_2 in the water, it is possible to supersaturate the water with O_{3aq} . (Supersaturation refers to producing a density of O_{3aq} larger than its local equilibrium value of $h[O_3]$.) The supersaturation results from solvation of O atoms which then react with O_{2aq} to form O_{3aq} . Once supersaturated, O_{3aq} leaves the water into the gas phase to return to equilibrium.

The density of H_2O_{2aq} is relatively unaffected by PRF with all final densities between $7-10 \times 10^{14}$ cm⁻³. The production of H_2O_{2aq} is dominated by bimolecular reactions of OH_{aq} . The gas phase OH which solvates to form OH_{aq} is largely produced by the SIW propagating through the saturated water vapor at the surface of the water, thereby enabling its rapid solvation. HO_{2aq} , is the third most dominant neutral with peak densities of $0.8-3.5 \times 10^{-14}$ cm⁻³ during pulsing, produced primarily through the reaction of aqueous hydrogen atoms and dissolved O_2 . H_{aq} is produced by solvation from the gas phase, photodissociation of the water and neutralization reactions of $H_3O_{aq}^+$. Consumption of H_{aq} is through reactions with HO_{2aq} to produce H_2O_{2aq} and with H_2O_{2aq} producing OH_{aq} .

The aqueous RNS tend to accumulate with increasing number of pulses, and are particularly sensitive to the accumulation of gas phase densities of $(H)N_xO_y$ facilitated by high PRF. For example, nitric acids are nearly absent at low PRF as their gas phase precursors are convected out of the domain before reacting with each other. With increasing PRF, gas



Figure 7. The time evolution of the liquid volume average densities of (left) charged and (right) neutral RONS for different PRF. The sawtooth pattern represents each pulse and subsequent destruction or growth of RONS. (a) 1 kHz, (b) 10 kHz, (c) 100 kHz and (d) 1 MHz.

phase HNO_x begins to form. However, despite their favorable Henry's law constants, the major source of HNO_{xaq} is not due to solvation of its gaseous counterparts. The favorable coincidence of OH_{aq} and NO_{aq} enable production of HNO_{2aq}

during the pulsing. HNO_{3aq} is primarily formed when NO_{2aq}^{-} and $H_{3}O_{aq}^{+}$ as well as NO_{aq} and HO_{2aq} are in direct proximity. These acids are consumed by hydrolysis reactions to form the hydronium ion and NO_{xaq}^{-} .



Figure 8. Fluences of aqueous (top) neutral and (bottom) charged RONS to the tissue beneath the water layer. The figure compares fluences normalized to a PRF of 10 kHz. Higher PRF favors fluences of $(H)N_xO_{yaq}$. One hundred pulses have occured for all PRF except for 100 Hz which has 50 pulses.

When pulsing terminates, the slowly reacting and terminal aqueous species (e.g. O_{3aq} , H_2O_{2aq}) diffuse to the tissue below the liquid where, in this mechanism, these species are consumed by reaction with the tissue. With their gaseous precursors are no longer being produced, the densities of more reactive aqueous species (e.g. OH_{aq} , HO_{2aq}) quickly decay.

3.3. Fluences to tissue

The time integrated fluxes of species reaching the underlying tissue (the fluences) are of critical importance to the treatment of the tissue. The fluences of selected species to the tissue beneath the water layer following 100 pulses with a total elapsed time of 0.5 s are shown in figure 8 for different PRF. (Values for a PRF of 100 Hz are included though only 50 pulses have occurred in this case.) These values are spatially integrated and have been normalized by fluences at the intermediate 10 kHz. Operating at higher PRF enables accumulation of reactants in proximity of the water layer and results in increased H₃O_{aq}⁺, HNO_{2aq}, NO_{3aq}⁻ and ONOO_{aq}⁻ densities, and subsequently larger fluences reaching the underlying tissue. Conversely, at lower PRF, the typically reactive OH_{aq}^{-} , O_{3aq}^{-} , and NO_{aq} are able to diffuse away from the immediate vicinity of the surface where reactants solvate on the next pulse. These

species are then less likely to react with just solvated reactants near the surface, and so they preferentially reach the tissue with low PRF.

The fluence of H₂O_{2aq} is generally a weak function of PRF since its precursors are directly produced by electron impact in the IW and SIW, with the latter being in immediate contact with the water in the nearly stagnant boundary layer. In this case, flow dynamics have a smaller effect. H₂O_{2aq} also has a high Henry's law constant and so typically does not saturate the surface of the liquid, thereby enabling nearly continuous solvation. The unusual spike in fluence of HO_{2aq} and O_{2aq}^{-} for the 1 MHz case is caused by the high levels of H_{aq} resulting from the reaction $e_{aq} + H_2O_{aq}^+$ dissociating to produce H_{aq} and OH_{aq} . The high PRF enables these two species to overlap whereas the longer interpulse period at lower PRF enables both species to dissipate between pulses. The dissociative recombination reaction is faster than the charge exchange of $H_2O_{aq}^+$ to produce of $H_3O_{aq}^+$, and so produces a larger density of H_{aq} . The H_{aq} then reacts with the dissolved O_{2aq} to produce HO_{2aq}. Subsequent reactions of HO_{2aq} and H_2O_{aq} yield O_{2aq}^- and $H_3O_{aq}^+$ leading to the increased spike in the fluences of those species.

3.4. Plasma plume touching versus not touching the liquid

APPJs where the IW does not touch the water layer were also investigated. The IW was prevented from striking the water by shortening the voltage pulse length to a total of 31 ns, also resulting in a smaller amount of energy deposition. Two cases of non-touching APPJs were considered-100 pulses at PRFs of 1 kHz and 100 kHz with a total elapsed time of 0.5 s. The resulting aqueous densities which exceed 1×10^{10} cm⁻³ are shown in figure 9. Comparing the non-touching results with the 1 kHz and 100 kHz cases where the IW does touch the water, there is an overall decrease in the densities of all aqueous species and the saw tooth variation in density, prominent in the touching cases, is minimal for the non-touching cases. A portion of this decrease in aqueous densities is simply that the shorter discharge pulse produces fewer reactive species. In the absence of contact with the water, a restrike does not develop, and less energy is deposited. However, the proximity of the IW to the water and there being a SIW for the touching case are important to the production short lived species such as OH_{aq} and e_{aq} , and all species whose trace their origin to OH_{aq} and e_{aq} . The production of O_{3aq} and H_2O_{2aq} are sensitive to the proximity of the IW to the surface of the water and its propagation through the saturated water vapor, whereas the precursor species to RNS are less sensitive to electron impact driven processes in contact with the water. NO_{aq} is more sensitive to the total density of other RONS, because it can react with O_{2aq}^{-} , HO_{2aq}, and OH_{aq} to from N_xO_{yaq} and HNO_{xaq}. So the decreased density of most RONS in the absence of touching results in a slower conversion of NO_{aq} to higher order RNS.

The lack of spiking or stair-stepping in the densities of nearly all species reflects their manner of transport from the gas to the liquid. In the touching case, precursors are formed in the immediate vicinity of the surface by the IW and SIW (or by photodissociation in the water), enabling those species



Figure 9. The time evolution of the liquid volume average densities of (left) charged and (right) neutral RONS for the non-touching cases for 100 pulses at PRFs of (a) 1 kHz and (b) 100 kHz.

to quickly solvate into the liquid before the next IW or SIW arrives. In the non-touching cases, the precursor species produced by electron impact must convect through the plume to reach the surface. If the convection time is commensurate or longer than the interpulse period, the densities arriving at the surface are, in a sense, an average over the interpulse period. The remote formation of reactants is partly responsible for the reduction in aqueous densities. The further from the liquid gas phase reactants are formed, the less likely the species will diffuse or convect to the surface of the liquid, as the free-flow streamlines direct these species away from the liquid.

 $H_3O_{aq}^+$ is the dominant positive ion in all cases, touching and non-touching, indicating acidification of the water. In touching cases, the densities of both NO_{3aq}^- and $ONOO_{aq}^$ are comparable in concentration to O_{2aq}^- , whereas in the non-touching cases, their densities are one to two orders of magnitude smaller than O_{2aq}^- . The production of O_{2aq}^- is generally enhanced when the IW strikes and propagates along the surface of the water layer, as this enables the direct solvation of electrons, which then attach to the dissolved oxygen. For this reason, one would expect large relative decreases in $O_{2aq}^$ for the non-touching cases. However, the production of NO in close proximity of the water surface is also a prerequisite for solvation of (H)NO_x species, precursors to NO_{3aq}^- and $ONOO_{aq}^{-}$. Since the advective speeds are low near the surface, formation of (H)NO_x species away from the surface, results in those species being preferentially convected out of the domain prior to diffusing to the surface to solvate.

Comparing the non-touching 1kHz and 100kHz cases shown in figure 9 highlights the loss of the stair-step behavior of touching cases, and disparity between convection and diffusion speeds. In the non-touching 1 kHz case, radical species are predominantly produced in a plume above the liquid layer near the exit of the nozzle. Over the course of one interpulse period, the plume convects to and across the liquid surface before exiting the computational domain. For short lived species having large Henry's law constants, such as OH, each successive pulse increases the liquid concentration before the plume of gas phase reactants convects away during the interpulse period. For species requiring several gas phase reactions to be formed and having small Henry's law constants, such as NO and NO₂, aqueous densities at the surface reach saturation with each pulse and are therefore limited by the low density of gas phase reactants at low PRF. Conversely in the 100kHz case, the reactive species in the plume accumulate over all 100 pulses resulting in higher densities than for each single 1 kHz pulse. This increase in density increases the saturation concentration for species with small Henry's law constants



Figure 10. Fluences of charged and neutral aqueous RONS to the tissue beneath the water layer for the touching and not-touching cases for PRFs of 1 kHz and 100 kHz. The fluences are normalized by the 1 kHz touching case. The label 'T' identifies the *touching* cases.

and also acts as a reservoir feeding highly-reactive short lived species into the liquid, thereby smoothing the volume averaged densities.

The trends in species densities as a function of PRF, touching versus non-touching, are then reflected in the fluences, f, to the tissue under the water layer as shown in figure 10. The fluences for 1 kHz and 100 kHz, normalized by the 1 kHz touching case, are shown. The touch versus no-touch dependencies, coupled with PRF, enable some amount of control of not only the magnitude but the ratio of fluences of difference species. For example, the fluence of H_2O_{2aq} , $f(H_2O_{2aq})$, decreases for no-touch compared to the touching cases. On the other hand for touching cases, $f(H_2O_{2ag})$ is relatively constant whereas $f(NO_{xaq}^{-})$ increases with PRF, and so the fluence ratio $f(NO_{xaq}^{-})/f(H_2O_{2aq}^{-})$ can be controlled with PRF. OH_{aq} and NO_{aq} are both intermediate species, which convert to terminal species on a timescale that decreases with increasing density of other RONS. This makes their densities (and fluences) less sensitive to touch versus no-touch. Without touching, the production of these species is lower, but their lifetime is longer due to a lower density of the other RONS with which they react. So the ratio of fluences of intermediate neutrals, OH_{aq} and NO_{aq}, to more stable neutrals, O_{3aq} , HO_{2aq} , and H_2O_{2aq} , can be controlled by touching versus non-touching.

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4. Concluding remarks

Control mechanisms will likely be required in the deployment of APPJs for plasma medical procedures. This is particularly true for treating liquid covered tissue. Environmental and patient-to-patient variability translate to variability in either the reactants delivered to the tissue or the requirements of the reactants for a given patient. In this paper, results from a computational investigation have been discussed in the context of using PRF of an APPJ as a control mechanism for the delivery of reactants to tissue under thin liquid layers.

Three trends have been identified from this computational investigation. The first is the effect of high PRF on production of NO and O₃ in the gas phase and the subsequent production of HNO_{xaq} and NO_{xaq}^{-} species such as nitrate and peroxynitrite. A lower PRF results in the gaseous species being cleared from the region above the water layer prior to the next discharge pulse. There is also sufficient time for solvating aqueous species to diffuse away from the surface of the water layer between pulses. This transport minimizes the overlap at the surface between species solvating during the previous pulse and with those introduced by the current pulse. At higher PRF, there is more overlap of reactants both in the gas phase and in the liquid from pulse-to-pulse. The end result is that the fluence of RNS to the tissue generally increases with PRF compared to fluences of ROS. The exception is the fluence of O3aq which also increases with PRF. Second, as long as the plasma plumes touch the liquid, the production of H₂O_{2aq} and its fluence to the tissue has little dependence on PRF since transport of its precursors to the water from remote locations is not a major source. In this model, hydrogen peroxide is a terminal species.

Lastly, if the plasma plume touches the water layer, the production of all aqueous species generally increases. However, on a relative basis, the production of aqueous RNS is less sensitive to touching versus not-touching than ROS at all PRF. Those species most sensitive to touching versus not-touching are those that trace their origin to solvation of electrons, O atoms or OH. Due to the different dependencies of fluences on PRF and touching, the ratios of fluences to the tissue can be controlled by judicious choice of PRF and distance to the sample.

PRF is a particularly attractive control mechanism for APPJ treatment of tissue as there are no physical changes required in the plasma source. In principle, PRF can be changed by purely electronic means, and will produce changes in gas phase reactants incident onto the tissue in the matter of ms (or the gas phase clearing time). The time required to change reactants to the tissue under the liquid will be on the order of the convective transport time, though even that timescale can be affected by PRF. For example, pulses of NO_{aq} in the liquid can be produced by varying PRF from high-to-low, and pulses of HNO_{xaq} by varying PRF from low-to-high, thereby creating mixes of reactants that could not be produced using a single PRF. This procedure opens the possibility of digital processing-the APPJ analogue of atomic layer processing in microelectronics [35]—whereby alternating pulses of reactants are used to leverage or overcome saturating or self-limiting processes in a manner not possible with steady state processing.

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ORCID iDs

Guy M Parsey https://orcid.org/0000-0002-9924-9732 Amanda M Lietz https://orcid.org/0000-0001-6423-5042 Eric Johnsen https://orcid.org/0000-0001-9530-408X Mark J Kushner https://orcid.org/0000-0001-7437-8573

References

- [1] Kong M G, Kroesen G, Morfill G, Nosenko T, Shimizu T, van Dijk J and Zimmerman J L 2009 Plasma medicine: an introductory review *New J. Phys.* 11 115012
- [2] Metelmann H-R et al 2015 Head and neck cancer treatment and physical plasma Clin. Plasma Med. 3 17
- [3] Chen Z, Lin L, Gjika E, Cheng X, Canady J and Keidar M 2018 Selective treatment of pancreatic cancer cells by plasma-activated saline solutions *Trans. Radiat. Plasma Med. Sci.* 2 116
- [4] Reuter S, Tresp H, Wende K, Hammer M, Winter J, Masur K, Schmidt-Bleker A and Weltmann K-D 2012 From RONS to ROS: tailoring plasma jet treatment of skin cells *Trans. Plasma Sci.* 40 2986
- [5] Mohades S, Laroussi M and Maruthamuthu V 2017 Moderate plasma active media suppresses proliferation and migration of MDCK epithelial cells J. Phys. D: Appl. Phys. 50 185205
- [6] Graves D B 2014 Reactive species from cold atmospheric plasma: implications for cancer therapy *Plasma Process*. *Polym.* 11 1120
- [7] Kaushik N, Uddin N, Sim G B, Hong Y J, Baik K Y, Kim C H, Lee S J, Kaushik N K and Choi E H 2015 Responses of solid tumor cells in DMEM to reactive oxygen [A] species generated by non-thermal plasma and chemically induced ROS systems *Nat. Sci. Rep.* 5 8587
- [8] Miller V, Lin A, Fridman G, Dobrynin D and Fridman A 2014 Plasma stimulation of migration of macrophages *Plasma Process. Polym.* **11** 1193
- [9] Van Ham B T J, Hoffman S, Brandenburg R and Bruggeman P J 2014 *In situ* absolute air, O₃ and NO densities in the effluent of a cold RF argon atmospheric pressure plasma jet obtained by molecular beam mass spectrometry *J. Phys. D: Appl. Phys.* 47 224013
- [10] Liu Z, Zhou C, Liu D, Xu D, Xia W, Cui Q, Wang B and Kong W G 2018 Production and correlation of reactive oxygen and nitrogen species in gas- and liquid-phase generated by helium plasma jets under different pulse widths *Phys. Plasmas* 25 013528
- [11] Szili E J et al 2018 Modelling the helium plasma jet delivery of reactive species into a 3D cancer tumour Plasma Sources Sci. Technol. 27 014001
- [12] Wende K et al 2015 Identification of the biologically active liquid chemistry induced by a non-thermal atmospheric pressure plasma jet *Biointerphases* 10 029518
- [13] Traylor M J, Pavlovich M J, Karim S, Hait P, Sakiyama Y, Clark D S and Graves D B 2011 Long-term antibacterial

efficacy of air plasma-activated water J. Phys. D: Appl. Phys. 44 472001

- [14] von Woedtke Th, Haertel B, Weltmann K-D and Lindequist U 2013 Plasma pharmacy—physical plasma in pharmaceutical applications *Pharmazie* 68 492
- [15] Bruggeman P J et al 2016 Plasma–liquid interactions: a review and roadmap Plasma Sources Sci. Technol. 25 053002
- [16] Gidon D, Curtis B, Paulson J A, Graves D B and Mesbah A 2018 Model-based feedback control of a kHz-excited atmospheric pressure plasma jet *IEEE. Trans. Radiat. Plasma Med. Sci.* 2 129
- [17] Xu D, Liu D, Wang B, Chen C, Chen Z, Li D, Yang Y, Chen H and Kong M G 2015 *In situ* OH generation from O₂⁻ and H₂O₂ plays a critical role in plasma-induced cell death *PLoS One* 10 e0128205
- [18] Park J, Lee H, Lee H J, Kim G C, Kim D Y, Han S and Song K 2016 Non-thermal atmospheric pressure plasma efficiently promotes the proliferation of adipose tissuederived stem cells by activating NO-response pathways *Sci. Rep.* 6 39298
- [19] Aboubakr H A, Gangal U, Youssef M M, Goyal S M and Bruggeman P J 2016 Inactivation of virus in solution by cold atmospheric pressure plasma: identification of chemical inactivation pathways J. Phys. D: Appl. Phys. 49 204001
- [20] Norberg S A, Johnsen E and Kushner M J 2015 Formation of reactive oxygen and nitrogen species by repetitive negatively pulsed helium atmospheric pressure plasma jets propagating into humid air *Plasma Sources Sci. Technol.* 24 035026
- [21] Gorbanev Y, O'Connell D and Chechik V 2016 Non-thermal plasma in contact with water: the origin of species *Chemistry* A 22 3496
- [22] Uchida G, Nakajima A, Ito T, Takenaka K, Kawasaki T, Koga K, Shiratani M and Setsuhara Y 2016 Effects of nonthermal plasma jet irradiation on the selective production of H₂O₂ and NO₂⁻ in liquid water J. Appl. Phys. 120 203302
- [23] Elg D T, Yang I W and Graves D B 2017 Production of TEMPO by O atoms in atmospheric pressure non-thermal plasma– liquid interactions J. Phys. D: Appl. Phys. 50 475201
- [24] Kovacevic V V, Sretenovic G B, Slikboer E, Guaitella O, Sobota A and Kuraica M M 2018 The effect of liquid target on a nonthermal plasma jet—imaging, electric fields, visualization of gas flow and optical emission spectroscopy J. Phys. D: Appl. Phys. 51 065202
- [25] Reuter S, von Woedtke T and Weltmann K D 2018 The kINPen—a review on physics and chemistry of the atmospheric pressure plasma jet and its applications *J. Phys. D: Appl. Phys.* **51** 233001
- [26] Norberg S A, Tian W, Johnsen E and Kushner M J 2014 Atmospheric pressure plasma jets interacting with liquid covered tissue: touching and not-touching the liquid J. Phys. D: Appl. Phys. 47 475203
- [27] Tian W, Lietz A M and Kushner M J 2016 The consequences of air flow on the distribution of aqueous species during dielectric barrier discharge treatment of thin water layers *Plasma Sources Sci. Technol.* 25 055020
- [28] Reuter S, Winter J, Schmidt-Bleker A, Tresp H, Hammer M and Weltmann K-D 2012 Controlling the ambient air affected reactive species composition in the effluent of an argon plasma jet *Trans. Plasma Sci.* **40** 2788
- [29] Iseni S, Schmmidt-Bleker A, Winter J, Weltmann K-D and Reuter S 2014 Atmospheric pressure streamer follows the turbulent argon air boundary in a MHz argon plasma jet

investigated by OH-tracer PLIF spectroscopy J. Phys. D: Appl. Phys. 47 152001

- [30] Robert E, Sarron V, Darny T, Ries D, Dozias S, Fontane J, Joly L and Pouvesle J-M 2014 Rare gas flux structuration in plasma jet experiments *Plasma Sources Sci. Technol.* 23 012003
- [31] Norberg S 2015 Modeling atmospheric pressure plasma jets: plasma dynamics, interaction with dielectric surfaces, liquid layers and cells *PhD Thesis* University of Michigan http:// hdl.handle.net/2027.42/113342
- [32] Sander R 2015 Compilation of Henry's law constants (version 4.0) for water as solvent *Atmos. Chem. Phys.* 15 4399
- [33] Tian W and Kushner M J 2014 Atmospheric pressure dielectric barrier discharges interacting with liquid covered tissue J. Phys. D: Appl. Phys. 47 165201
- [34] Darny T, Pouvesle J-M, Puech V, Douat C, Dozias S and Robert E 2017 Analysis of conductive target influence in plasma jet experiments through helium metastable and electric field measurements *Plasma Sources Sci. Technol.* 26 045008
- [35] Kanarik K J, Tan S and Gottoscho R A 2018 Atomic layer etching: rethinking the art of etch *J. Phys. Chem. Lett.* 9 4814