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$He+O_2+H_2O$ plasmas as a source of reactive oxygen species

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The effect of water in the chemistry of atmospheric-pressure $He+O_2$ plasmas is studied by means of a comprehensive global model. Water enables the generation of reactive oxygen species (ROS) cocktails that are rich not only in O, O_2^*, and O_3 but also in OH and H_2O_2. Due to its polar nature, water also leads to cluster formation, possibly affecting the plasma dynamics. Since the lifetime of many of the ROS is short, the plasma chemistry plays two roles: (i) direct interaction with superficial cells and (ii) triggering of a secondary chemistry that propagates the plasma treatment to regions away from the plasma-surface interface. © *2011 American Institute of Physics*. [doi:10.1063/1.3592775]

Atmospheric-pressure plasmas have received growing attention in recent years for their potential use in many scientific disciplines. In particular, we focus here on the use of low temperature atmospheric-pressure plasmas in "plasma medicine," an emerging scientific discipline that exploits the interaction of gas plasmas with biological materials for therapeutical purposes.[1,2] In many plasma medicine applications, reactive oxygen species (ROS) are believed to be of critical importance and therefore $He+O_2$ admixtures have often been used.

In most plasma medicine applications, however, water is also present. Since these plasmas are typically operated in open air, they are in contact with an environment that contains water vapor at typical concentrations of thousands of parts per million (ppm). More importantly, living cells are mostly found in moist environments. So even if water is not deliberately fed into the gas plasma, it is almost impossible to prevent the presence of water in the discharge. This could change the chemistry at play and thereby alter (for better or for worse) the effectiveness of the plasma treatment.

Motivated by this ubiquitous presence of water in plasma medicine applications, this letter reports on the influence of H_2O in the chemistry of otherwise reasonably well-understood $He+O_2$ plasmas. Particular emphasis is placed on the generation of ROS that are relevant in plasma medicine applications.

Building on comprehensive plasma chemistry models of $He+O_2$ and $He+H_2O$ plasmas,[3–5] we created a global model for $He+O_2+H_2O$ discharges. The model incorporates 55 species (see Table I) and accounts for 855 chemical reactions. Details of the numerical scheme can be found in Ref. 4.

According to previous computational and experimental studies, $He+O_2$ and $He+H_2O$ plasmas produce a maximum amount of ROS when the precursor (O_2 or H_2O) concentration is between 0.1% and 1%.[3,4,6] Therefore, in this work the total amount of precursor ($[O_2]+[H_2O]$) is fixed at 0.5%. To study the changes in plasma chemistry as a function of the precursor composition, the ratio (r) of H_2O concentration to O_2 concentration, i.e., $r=[H_2O]/[O_2]$, is swept from 0.01 to 100. All other parameters of the discharge are kept constant and the discharge geometry and input power ($40\ W/cm^3$) reflect those used in previous studies.[4,7]

The influence of the $[H_2O]/[O_2]$ ratio on the ionic composition of the plasma is shown in Fig. 1. Due to the polar nature of water molecules, hydrated ions form even at low water concentrations ($[H_2O]=50$ ppm; $r=0.01$). As a result the dominant ions even at low water concentration are $O_2^+\cdot(H_2O)_2$ and $O_3^-\cdot(H_2O)_2$. This contrasts with the dominant role of O_4^+ and O_3^- in a water free $He+O_2$ discharge (see Ref. 4). Hydration changes the mass of the ions and their transport coefficients, thereby influencing the plasma dynamics in ways not possible to analyze with the global model used in this study. These results, however, indicate that clusters should be accounted for in fluid and kinetic models of water containing plasmas. At high water concentrations, the density of nonhydrated ions, e.g., O_2^+ and O^-, become negligible and the discharge chemistry evolves to that of $He+H_2O$ plasmas.[3] An ion that is of particular relevance for biological systems is O_2^-.[8] This is produced in the plasma in decreasing quantities when r increases above ~0.1, and even at low

TABLE I. Species included in the model.

Simple ions	Cluster ions	Metastables and excited states	Ground state neutrals
He^+	HeH^+	$O(^1D)$	He
He_2^+	H_3^+	$O(^1S)$	O_2
H^+	O_4^+	$O_2(b^1\Sigma_g^+)$	H_2O
H^-	O_6^+	$O_2(a^1\Delta_g)$	H
H_2^+	$H_2O_2^+$	OH(A)	O
O^+	$H_4O_2^+$	$He(2^3S)$	H_2
O^-	$H^+\cdot(H_2O)_{n=1-7}$	$He(2^1S)$	OH
O_2^+	$O_2^+\cdot(H_2O)_{n=1-2}$	$He_2(a^3\Sigma_u^+)$	HO_2
O_2^-	O_3^-		H_2O_2
OH^+	O_4^-		O_3
OH^-	$H_2O_2^-$		
H_2O^+	$OH^-\cdot(H_2O)_{n=1-2}$		
HO_2^+	$O_2^-\cdot(H_2O)_{n=1-2}$		
	$O_3^-\cdot(H_2O)_{n=1-2}$		

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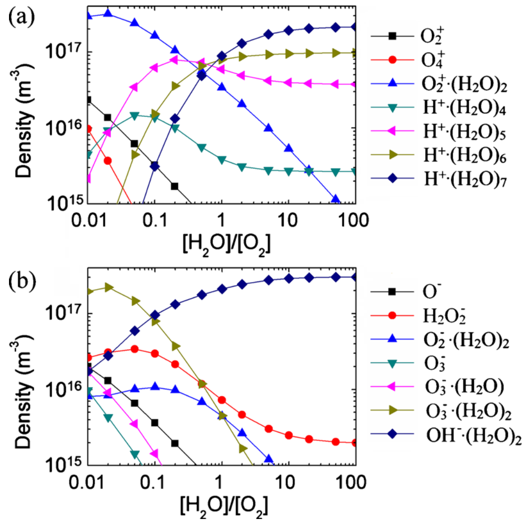

FIG. 1. (Color online) Density of (a) cations and (b) anions in a $He+O_2+H_2O$ plasma as a function of [H_2O]/[O_2]. [H_2O+O_2]=0.5%.

water concentration (r=0.01) O_2^- is found in hydrated form.

Only species crossing the plasma sheath will react with the biological target. The fluxes of key plasma species as a function of the [H_2O]/[O_2] ratio are shown in Fig. 2. The flux of neutral ROS is orders of magnitude larger than that of ions and helium metastables. Therefore, ROS are expected to dominate the chemical interaction. Ions could in a first approximation be neglected because their flux is small and at atmospheric pressure they are not very energetic.[9] However, charge accumulation from ions (and electrons) on the sample may create electric fields that could lead to important biological responses such as electroporation,[10] and these could interplay synergistically with the ROS chemistry. In continuous plasmas, the flux of anions (including superoxide) will be strongly limited by the confining effect of the plasma ambipolar field.

The actual composition of the thermal flux of neutral ROS from $He+O_2+H_2O$ plasmas is shown in Fig. 3. The main ROS are O, O_2^* [including $O_2(b^1\Sigma_g^+)$ and $O_2(a^1\Delta_g)$], O_3, OH, HO_2, and H_2O_2. As the ratio r increases from 0.01 to 100, the fluxes of O, O_2^*, and O_3 decrease monotonically while the ones of OH, HO_2, and H_2O_2 increase and reach a maximum at around $r=2$. The total flux of ROS remains within the same order of magnitude as the precursor composition changes over four orders of magnitude although it drops slightly when the ratio r increases above 1. This suggests that both O_2 and H_2O are good sources of ROS and that they can be used in conjunction to adjust the composition of the cocktail of ROS created in the plasma. At low water concentrations ($r \ll 1$) the main ROS are O, O_2^*, and O_3 whereas at high water concentrations ($r \gg 1$) OH and H_2O_2 dominate. A mixture containing reasonable amount of the five species can be obtained when $r \sim 1$. The slight higher production of ROS in O_2 rich admixtures can be attributed to the higher dissociative rate coefficient of oxygen molecules and the presence of reductive products, e.g., H, in H_2O rich plasmas.

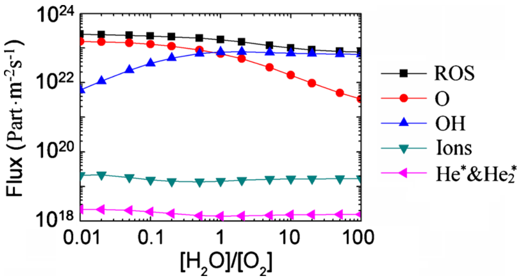

FIG. 2. (Color online) Electrode fluxes in a $He+O_2+H_2O$ plasma as a function of [H_2O]/[O_2] ratio. [H_2O+O_2]=0.5%.

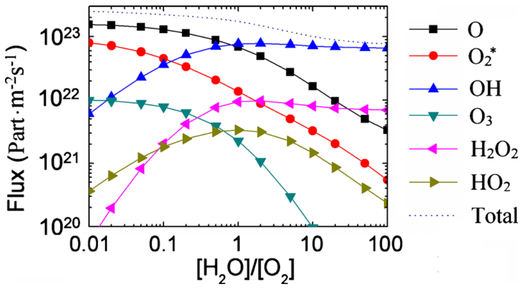

FIG. 3. (Color online) Flux of the main ROS in a $He+O_2+H_2O$ plasma as a function of the [H_2O]/[O_2] ratio. [H_2O+O_2]=0.5%.

The main reactions leading to the production of O and OH, i.e., the most abundant ROS (see Fig. 2), are electron impact dissociation (include dissociative excitation and dissociative attachment) of O_2 and H_2O, respectively. Since O can be produced from H_2O [$e+H_2O \rightarrow H_2+O(^3P,{}^1D,{}^1S)+e$], the decrease in O concentration as r increases is slower than the decrease in O_2^* and O_3. The decrease in O_3 is actually the fastest of the three as its main production reaction is $O+O_2+He \rightarrow O_3+He$ and both O and O_2 decrease when r increases. H_2O_2 and OH have a similar trend because H_2O_2 forms mainly by OH recombination.

Finally, it is noted that in many plasma medicine applications, the plasma treatment is required to reach beyond the surface of the biological sample, often through an aqueous environment with organic content. Regarding organic molecules, OH, O, and O_2^* have large rate coefficients (10^7-10^9 M^{-1} s^{-1}), orders of magnitude larger than those of O_3 and H_2O_2 ($<10^7$ M^{-1} s^{-1}).[11–14] As a result the latter are longer lived and can reach further away from the surface. Two extreme scenarios can be considered:

- Scenario 1—Target with very low concentration of organic compounds ([organic]$\ll$[ROS]): the inter- and self-reactions of ROS and potentially with water molecules dominate the destruction of ROS.
- Scenario 2—Target with high concentration of organic compounds ([organic]$\gg$[ROS]): in this case the inter- and self-reactions of ROS become negligible. This is the typical scenario one would encounter when treating human tissue.

As an example, we consider here the case of singlet delta oxygen $O_2(a^1\Delta_g)$. Its lifetime decreases from tens of minute in the gas plasma where its main loss is due to diffusion out of the discharge, to microsecond in a diluted aqueous solution (scenario 1) where it is quenched by water molecules, and to tens of nanosecond in a cell environment (scenario 2) where it reacts with organic compounds.[15,16] In the latter case, assuming a diffusion constant of $\sim 5 \times 10^{-5}$ cm^2/s, singlet oxygen diffuses $\sqrt{Dt} \sim 10$ nm, i.e., less than the size of a single cell. This simple calculation reflects the wellknown superficial nature of plasma treatments and supports, for example, the rapid decrease in the bactericidal properties of plasmas when bacteria are piled up or buried in biofilms.[17] Nevertheless, there is also evidence of long range effects of plasma treatments, for example, through liquid media.[2] This seems to suggest that stable compounds of biological relevance capable of reaching far beyond the size of a cell are generated at the plasma-medium interface.

In conclusion, $He+O_2+H_2O$ admixtures can be used to generate cocktails of ROS that contain all the main species typically encountered in $He+O_2$ and $He+H_2O$ plasmas. The overall amount of ROS generated in the plasma is relatively insensitive to the $[H_2O]/[O_2]$ ratio in the feed gas, although it decreases slightly with increasing water content due to the smaller dissociation rate of H_2O and the generation of reducing species such as H. The $[H_2O]/[O_2]$ ratio can be used to control the actual composition of the cocktail of ROS and maximum simultaneous production of O and OH is accomplished when $[H_2O]/[O_2]\sim 1$. ROS are expected to interact with biological samples by (i) reacting directly with superficial cells and (ii) triggering a secondary chemistry that will transport the effects of the plasma treatment beyond the gas/sample interface. Even at low water concentrations hydrated ions are found to be abundant, indicating that in most plasmas used for plasma medicine ionic clusters should be considered.

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