Two-faced behavior of water in the relaxation of inner-valence vacancies of biologically-relevant systems

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After ionization of an inner-valence electron of molecules, the resulting cation-radicals store substantial internal energy which allows for multiple relaxation scenarios in environment. The fastest and hence most efficient relaxation processes involve the ejection of an additional electron which carries away excess energy. This electron can be ejected from the molecule itself via the classical Auger decay if the single inner-valence ionization potential is higher than its lowest double ionization potential. Usually, this decay is followed by the fragmentation of the molecule. In environment, intermolecular Coulombic decay (ICD) is operative and the electron is kicked out from a neighbor thus preventing the fragmentation of the molecule. If the excess energy suffices, relaxation can also lead to electron transfer mediated decay (ETMD) resulting in two vacancies on neighboring molecules while the initially ionized molecule is reduced. These relaxation processes are thoroughly investigated for heterocycle-water complexes, specifically of the biologically relevant nitrogen containing heterocycles: imidazole, pyrrole, and pyridine. It is found that the hydrogen bonding site of the water molecule critically influences the nature and energetic availability of the electronic states involved in the various relaxation processes after single inner-valence ionization of the system. This site determines whether the attached water molecule is an electron-density acceptor or electron-density donor which in turn has an impact on closing or ensuring certain relaxation scenarios by stabilizing or destabilizing the involved vacancies. Our results indicate that the relaxation mechanisms of biological systems with inner-valence vacancies located on their carbon atoms are likely to strongly depend on the presence of electron-density donating or accepting neighbor, either water or other biomolecule. The ionization of the environment (here the water molecule) is discussed as well. It is shown that if the water molecule is initially ionized, this may result in the fragmentation of the heterocycle.

Introduction

Extreme (from 10 up to 124 eV) ultraviolet irradiation (XUV) of biological matter can cause inner-valence ionization, producing exited cation-radicals and deposing large amount of internal energy which can be released via a number of competing relaxation channels. In case the populated excited cationic state is higher in energy than the lowest double-ionization potential, the system can relax by emitting a secondary electron. A prominent example of such a pathway is the Auger decay in which the initial inner-valence vacancy is filled by an outer-valence electron and the excess energy is used to emit another outer-valence electron form the same molecule (Figure 1). The resulting two vacancies are thus located on initially ionized molecule and can often cause a bond braking or system fragmentation. Apart from some modifications in the energetics, the Auger process and its efficiency are very little affected by the chemical environment of the ionized molecule. The presence of weakly bound neighbors, as is the case of bio-matter and solutions, opens a whole plethora of very efficient, non-local electronic decay processes that involve electrons from the systems in the environment. These processes also terminate by creating two vacancies, which are however distributed on different molecules. This might substantially reduce the probability for fragmentation of the initially ionized molecule and thus might appear as a protective mechanism in bio-matter. The created radical cations in the environment, however, are usually highly reactive and can induce further structural changes and damages to the system purely chemically. The competition between these local and non-local decay mechanisms, as well as the follow-up complex dynamics, which are still far from being fully understood, determines the degree of damage induced by irradiating the system with XUV light. The detailed knowledge of these mechanisms are, therefore, the key to understand the radiation damage in bio-systems and to eventually develop protective strategies.

The presence of environment of the initially ionized molecule can open several decay channels even in cases when the local Auger decay is energetically forbidden. Typically, the most efficient of those is the interatomic or intermolecular...
Coulombic decay (ICD), in which the energy released from the relaxation of the initially ionized fragment is transferred to a neighboring atom or molecule that uses it to emit one of its electrons. As a result, two cation-radical monomers repelling each other and a low-energy electron are produced (Figure 1). The ICD was first predicted theoretically by Cederbaum and coworkers in 1997, and later confirmed experimentally for a large variety of atomic and molecular clusters. The process is proved to take place on an ultrashort timescale (usually in the femtosecond regime) and, contrary to the local decay mechanisms, its efficiency increases with the number of neighbors in the environment.

A somewhat slower, but in many cases the only possible decay mechanism, is the electron-transfer mediated decay (ETMD) process. In this process, an electron from a neighboring atom or molecule fills the initial vacancy causing the emission of another electron from the environment. As a result, two vacancies are formed on the neighboring fragment(s) while the initially ionized species becomes neutral (Figure 1).

Being non-local channels, ICD and ETMD are considered to cause ionization of biomolecules, when the environment is initially ionized and vice versa to distribute the internal energy to the environment when the biomolecule is ionized by the initial irradiation. It was shown both theoretically and experimentally that ICD is possible after inner-valence ionization of heteroatoms in simple molecules and also after ionization of C2s in larger systems, especially in conjugated ones. It was also shown that the entire inner-valence ionization energy region is open for ICD in comparatively large biologically relevant aromatic molecules. As the biological molecules are mostly solvated in water, the water molecule is considered as the universal partner in the ICD or ETMD after inner-valence ionization. It was shown that inner-valence ionization of the water molecule will be followed by ICD involving a neighboring organic molecule. The same was also recently demonstrated to be the case for liquid water and for the Tetrahydrofuran-H2O system (a model of solvated deoxyribose fragment in DNA). For the latter system, it was also theoretically predicted that the inner-valence ionization of water can undergo an ETMD with the Tetrahydrofuran, but this process could not be resolved experimentally as it occurs in the same energy region and produces the same final states as the Auger decay of oxygen 2s-1 states of Tetrahydrofuran.

Considering the case of bio-systems it is hard to overestimate the role of hydrogen bonding. It is known that in the event of ionization, intermolecular hydrogen bonding, being donor-acceptor by its nature, insure stabilization or destabilization of the vacancies which are formed. As shown for a number of systems, the Auger final states with two holes located on one molecule are significantly stabilized by the electron-density donating neighbor and destabilized by an electron-density acceptor. For systems of small molecules, which are usually object of both theoretical and experimental studies of electronic decay processes, the lowest Auger or ETMD final states are usually energetically higher than the lowest ICD states. However, for a number of molecular pairs with water it was shown that the corresponding energy gap is larger if the water molecule acts as electron-density acceptor, and smaller if water acts as the electron-density donor stabilizing the positive charges on the neighboring molecule. The aim of present work is to study the role of the donor-acceptor interactions with water in the case of inner-valence ionization for systems that mimic electron-density rich biomolecules. As such, we took nitrogen containing heterocycles: imidazole, pyrrole, and pyridine (see the scheme below).
Heterocycle-water complexes

Structures of heterocycle-water clusters were considered in numerous works\textsuperscript{31-36}. We thus used these results as a guide to choose the most thermodynamically stable complexes for the calculations of the ionization (IP) and double ionization (DIP) spectra needed for the further analyses. All geometries, normal modes, and basis-set superposition error (BSSE) corrections for the structures considered in this work were obtained using MP2/aug-cc-pVDZ level of theory, as implemented in the Gaussian16 program suit\textsuperscript{37}.

The preferable ways a water molecule binds to the heterocycles considered are shown in Figure 2\textsuperscript{35-36,38-41}. One can see that there are two principal types of water coordination: (i) by hydrogen to the lone pair of nitrogen; (ii) by oxygen to one of the hydrogens of the heterocycle. Therefore, with respect to the heterocycle, water acts as an electron-density acceptor (a-H\textsubscript{2}O) or electron-density donor (d-H\textsubscript{2}O), respectively (see Figure 2).

An important feature of imidazole molecule is the two nitrogen atoms differently incorporated in the aromatic system, one of which is of pyrrole type, the other one of pyridine type. According to Refs.\textsuperscript{38-41} O–H···N bonding in imidazole-a-H\textsubscript{2}O structure is more likely to form than O–H···N in imidazole-d-H\textsubscript{2}O (Figure 2). Our calculations show that the corresponding energy difference is 0.6 kcal/mol, which is consistent with the previous results\textsuperscript{38-41}. Nevertheless, both variants are experimentally observed\textsuperscript{41} and their relative abundance in some cases is found to be up to 1:1\textsuperscript{39}. We, therefore, considered both structures. This also allows us to directly compare the effect of the two types of hydrogen bonding on the local and non-local decay processes.

In most of the works on the Pyridine-water system\textsuperscript{35,36}, only O–H···N bonding type is considered. According to our results, Pyridine-a-H\textsubscript{2}O (Figure 2) is substantially lower in energy (up to 3.0 kcal/mol) compared to all alternative structures. We will, therefore, further consider only this structure.

The bonding nature of the nitrogen atom in pyrrole is different from pyridine, as the nitrogen provides two electrons to the pentahedral aromatic π-system and one electron to form a π-bond with the hydrogen atom. Thus, a hydrogen bond of O···H–N type is formed, providing Pyrrole-d-H\textsubscript{2}O structure (Figure 2)\textsuperscript{51,54} with water acting as an electron-density donor with respect to the pyrrole ring. The Pyrrole-d-H\textsubscript{2}O is more likely than the other possible structure with water hydrogen bonded to the pyrrole π-system (Pyrrole-a-H\textsubscript{2}O). According to our estimations, the energy difference is as large as 1.0 kcal/mol. To the best of our knowledge, only Pyrrole-d-H\textsubscript{2}O structure is obtained under experimental conditions and therefore only this structure was considered in this work.

Results and discussion

As was mentioned above, the system can relax from singly to doubly ionized state losing an additional electron if the energy of the dicaticionic state is lower than that of the initial cation. To determine the open channels, we can thus compare the single- and double-ionization spectra of the heterocycle-water complexes. To do so, we computed the IP and DIP spectra of Imidazole-a-H\textsubscript{2}O and Imidazole-d-H\textsubscript{2}O molecular pairs, as well as of Pyridine-a-H\textsubscript{2}O and Pyrrole-d-H\textsubscript{2}O (Figures 3 and 4). Those spectra were calculated using the third- (ADC(3)) and second- (ADC(2)) order algebraic diagrammatic construction scheme for obtaining the one- and two-particle propagators, respectively, in combination with cc-pVDZ bases sets (see methodology section for further details). The obtained spectra are depicted in Figures 3 and 4.

It can be seen that a large number of states in the inner-valence region lie in the cationic continuum, i.e. are above the lowest dicaticionic state, and thus can relax by emitting an electron, through one of the possible decay mechanisms, and form a dication. To distinguish the possible channels, the different types of dicaticionic states are marked by different colors in Figures 3 and 4 (middle panels). The states with two holes localized on different molecules are plotted in cyan and correspond to ICD final states, regardless of which molecule in the pair was initially ionized. Dications having both holes on the heterocycle (states plotted in orange) can be formed either through an Auger decay channel, if the initial vacancy is located on the heterocyclic molecule, or through an ETMD channel, if the initial vacancy is located on the water. As we will discuss later, the states with two vacancies located on the water molecule are not accessible in the energy range considered in this work.

The energy difference between singly and doubly ionized states corresponds to the energy of the emitted secondary electrons, which makes possible to model the secondary electron spectra, as described in \textsuperscript{22} and in the methodology section. If we assume

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure2.png}
\caption{Structures of the most stable complexes of imidazole, pyridine, and pyrrole with water. The indexes a and d indicate whether water acts as an electron-density acceptor or electron-density donor, respectively.}
\end{figure}
that all cationic states up to about 35 eV are initially populated, which covers all inner-valence ionizations, we obtain the electron spectra that are depicted in Figures 3 and 4, upper panels. The contributions of the different channels are also shown, indicating that ICD and ETMD electrons can be expected to contribute substantially to the secondary electron spectra. Despite the overall similarity of the IP spectra of Imidazole-$\alpha$-H$_2$O and Imidazole-$d$-H$_2$O, there are substantial differences that can be attributed to the acceptor or donor behavior of water towards imidazole. When water is bonded in an electron-density donating position, it stabilizes the vacancies on imidazole, resulting in lowering of the corresponding ionic states, and vice versa for the accepting position. Consequently, the first ionization potential of the two complexes corresponding in both cases to the removal of an electron from the imidazole, appears with an energy difference of 0.8 eV (Figure 3). Moreover, the states corresponding to the water ionization, depicted with green lines in the lower panels of Figure 3, are systematically and substantially lower in energy for the Imidazole-$\alpha$-H$_2$O compared to the Imidazole-$d$-H$_2$O, due to the ability (or respectively the disability of Imidazole) to screen the vacancies formed on water. The largest difference is 2.5 eV and appears for the lowest IP of water (1b$_1^-$), while the smallest energy shift is observed for the third IP of water (1b$_2^-$). However, due to the stronger correlation effects present in Imidazole-$d$-H$_2$O, the removal of a 1b$_2$ electron from the donor water leads to a much richer structure, with large number of satellite states spread over several electronvolts.

In the case of dicationic heterocycle in Imidazole-$d$-H$_2$O system, the water stabilizes the Imidazole$^{++}$ states with rather pronounced energy downshift of about 1 eV relative to the isolated Imidazole molecule. At the same time, the energy of the lowest ICD state is relatively high (compared to Imidazole-$\alpha$-H$_2$O), which together results in vanishing of the gap between the lowest ICD and Auger states (Figure 4). To the best of our...
knowledge, the possibility to close the energy gap between lowest ICD and Auger states, due to the donor-acceptor intermolecular interactions, was not reported previously. To support this result we made similar calculations for the Pyrrole-d-H2O system (Figure 4b), where water preferably coordinates to the nitrogen atom in a donating position, similar to Imidazole-d-H2O. Here the stabilization of doubly ionized states relative to isolated pyrrole molecule is 1.1 eV, resulting in the first Auger state to be 1 eV lower than the first ICD state. In contrast, in Imidazole-a-H2O molecular pair, the electron-density accepting behavior of water causes destabilization of the states of doubly charged imidazole and thus an upshift of the energies of the Auger final states. The latter, together with the lowering of the ICD final states, results in a 3 eV gap between the lowest ICD and Auger states (Fig. 3a). Similar behavior is obtained for the Pyridine-a-H2O system, where the water is preferably coordinated to the nitrogen atom and acts as an electron-density acceptor (Fig. 4a). Consequently, the Auger final states are slightly destabilized compared to the isolated pyridine and the first one appears 1.5 eV higher than the lowest state of ICD type. In the case of electron-density accepting behavior of water, the lowering of the final ICD states results in much more intense ICD electron spectrum, as can be seen by comparing Imidazole-a-H2O and Imidazole-d-H2O (Figure 3). Due to the different heterocycles involved, such direct comparison cannot be made for Pyridine-a-H2O and Pyrrole-d-H2O systems.

In isolated imidazole, pyrrole, and pyridine radical cations, the energetically deepest inner-valence ionized states correspond to ionization out of the N2s orbital. In all cases, the system can then undergo Auger decay, which will most likely cause molecule fragmentation. In the presence of water, regardless of its position, additional ICD channels open for such initial states, resulting in vacancy separation and thus providing routes for the heterocycle ring to avoid fragmentation. Slightly lower in the energy, in the region from about 22 to 26 eV, the deepest C2s−1 ionized states appear which cannot decay electronically in the case of isolated heterocycles. The electron-
density donating position of water in the vicinity of pyrrole results in lowering of the Pyrrole"+-H2O states, which opens the Auger decay of the lowest C2s⁻¹ vacancy in the pyrrole (Figure 4). Although our results show that the lowest ICD and Auger final states in Imidazole-d-H2O are lying at the center of the C2s⁻¹ band (Figure 3), we cannot claim that these channels are open. This is due to the tendency of the ADC(2) method to lower the DIP energies, sometimes by up to about 0.5-1.0 eV,⁴²,⁴³, and thus both the ICD and Auger decay are more likely to be energetically closed. In contrast, the impact of the electron-density accepting water molecule in both Imidazole-o-H2O (Figure 3a) and Pyrrole-o-H2O (Figure 4a) is such that the ICD channel is open for the C2s ionized radical-cations, while the Auger decay is closed.

Let us now turn to the processes that can be initiated by an inner-valence ionization of the water molecule, or by the population of the O2s⁻¹ states that in all complexes considered in this work lie between 31 and 34.5 eV. Here, an additional type of final states, which are not depicted in figures 3 and 4, should be mentioned. Namely, the states with two vacancies on the water molecule, corresponding to the final states of an Auger decay within the water. It is known that the lowest doubly ionized state of a single water molecule has energy above 38 eV, which is shifted down to about 36.5 in water dimer in the electron-density accepting molecule.⁴⁳ In the molecular pairs of heterocycles with water considered in this work, there are also energy shifts of the dicaticionic states of water due to the donor or acceptor behavior of the neighboring heterocycle. In case the water molecule acts as electron-density acceptor (Imidazole-o-H2O and Pyrrole-o-H2O), the lowest state corresponding to two vacancies on the water appears at 34.3 and 34.4 eV, respectively, which is more than 1 eV higher than the O2s⁻¹ band (Figs. 3a and 4a, lower panels). When water is in a donating position, the lowest H2O⁺⁺ state appears even higher in energy, reaching 39.7 and 39.5 eV in Imidazole-d-H2O and Pyrrole-d-H2O, respectively. The possibility for a local Auger decay after inner-valence ionization of water is therefore energetically closed in all studied molecular complexes. Instead, the O2s⁻¹ states can decay by ionizing the neighboring in an ICD or ETMD process to the large number of lower lying doubly ionized states (Figures 3 and 4). As a result, the ETMD-electron spectra, coming solely from the decay of the water O2s⁻¹ vacancy, are quite broad. Moreover, when water acts as an electron-density donor, the O2s⁻¹ band shifts to higher energies, while the lowest states with two vacancies on the heterocycle shift to lower energies, which together insures a larger energy gap between the possible initial and final states of ETMD. This results in a more pronounced and broad ETMD-electron spectrum for Imidazole-d-H2O compared to Imidazole-o-H2O (Figure 3), as well as for Pyrrole-d-H2O compared to Pyrrole-o-H2O (Figure 4).

Conclusions

The energetics of the electron decaying channels of inner-valence ionized molecular pairs of imidazole, pyrrole, and pyridine with water have been studied, considering the preferable sites for the water molecule to form a hydrogen bond with the heterocycle.

In the case of inner-valence ionization of the heterocycle, the system can undergo both Auger and ICD processes, while in the case of water inner-valence ionization, ICD and ETMD relaxations are possible.

Our results reveal that the location of water is critical for the nature of the lowest dicaticionic states. The presence of water in an electron-density accepting position destabilizes the heterocycle"+-water final states, while the lowest states of heterocycle'-water type appear to be quite low in energy, which together results in a 1.5 to 3 eV gap between the lowest Auger and ICD states, opening the ICD channel for the lowest C2s⁻¹ state of the heterocycle. In the case of water located in electron-density donating position, the screening of the positive charges leads to stabilization of the heterocycle"+-water final states. The downshift of the latter is so pronounced that in the presence of water, the Auger decay channel opens for the lowest C2s⁻¹ state of pyrrole. In addition, the energy gap between the lowest Auger and ICD states closes completely in both imidazole-d-H2O and pyrrole-d-H2O complexes.

According to the present results, the ICD and ETMD electrons can be expected to contribute substantially to the secondary electron spectra of the systems in the relatively wide energy interval. One can expect that this contribution will be even higher with more water molecules surrounding the heterocycle, due to the additional non-local relaxation channels that will open between water and the solvated molecule.

Our results indicate that the relaxation mechanisms of biological systems with inner-valence vacancies located on their carbon atoms are likely to strongly depend on the presence of electron-density donating or accepting neighbor, either water or other biomolecule. They also show that in the case of inner-valence ionization of water in a vicinity of a biomolecule, the single or even double ionization of the latter is likely to happened, due to the non-local relaxation processes such as ICD or ETMD.

Author Contributions

A.D.S., A.I.K., and L.S.C. designed the research. A.D.S. and E.K.G. performed the calculations. All authors discussed the results. A.D.S. and A.I.K. wrote the paper with contributions from all coauthors.

Conflicts of interest

There are no conflicts to declare.

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Computational details

Optimal geometries of all the structures considered in this work, as well as the normal modes, and basis-set superposition errors (BSSE) corrections were obtained using MP2/aug-cc-pVDZ level of theory, as implemented in the Gaussian16 program suite.\textsuperscript{44–47} The vertical single-ionization spectra of all the complexes considered were computed using the third-order algebraic diamagrammatic construction\textsuperscript{44–47} (ADC(3)) scheme (in its non-Dyson variant\textsuperscript{48}) for approximating the one-particle Green’s function. The ADC(3) method is applicable in situations where the breakdown of the molecular orbital picture of ionization\textsuperscript{49} takes place. The latter phenomenon manifests itself by a strong redistribution of spectral intensity from the 1h main spectrum into the 2h–1p satellites and is typical for the inner-valence vacancy region considered in this work. The ADC(3) method was previously used in various applications including computations of ionization spectra of valence,\textsuperscript{49,50} inner-valence,\textsuperscript{51–53} and K-shell\textsuperscript{54} orbitals, and is proved to be a valuable tool for spectroscopic studies. The ionization spectra reported in this work were computed using the in-house ADC(3) code linked to the GAMESS-UK program suite\textsuperscript{55,56} using cc-pVDZ basis sets. To account for the vibrational broadening and experimental resolution, the resulting spectra were convoluted with Gaussians with FWHM (full width at half maximum) of 0.4 eV. The double-ionization spectra of the complexes were obtained at the ADC(2) level of theory for obtaining the particle-particle propagator\textsuperscript{57,58} with cc-pVDZ basis sets, again using our in-house computer program. The character of the final doubly ionized states with respect to the location of the vacancies (holes) was determined by analyzing the leading wavefunction amplitudes for each state using the two-hole population analysis proposed in Ref.\textsuperscript{59}. The final ICD states are characterized by vacancies residing on different molecules, while in the final Auger and ETMD states both vacancies are located on the same molecule. The difference between the latter processes is the initial vacancy, which is localized on the same molecule, in the case of an Auger transition, or on the different one, in the case of an ETMD process. Based on the calculations described above, the electron kinetic energy distribution spectra can also be modeled, as described in\textsuperscript{27} by subtracting the energy of each individual line of the DIP-spectrum from each of the lines of the IP-spectrum which is energetically open for decay into this particular final dicatomic state. The probability of each transition is evaluated with respect to the populations of the initial and the final states, assuming that it is independent of the energy differences between the states. The resulting spectra were convoluted with a Gaussian having a FWHM of 0.5 eV. Such a simplified approach has proven to be quite effective when compared to experimental data.\textsuperscript{24}
