Eur. Phys. J. D **35**, 429–435 (2005)
DOI: 10.1140/epjd/e2005-00218-2

THE EUROPEAN PHYSICAL JOURNAL D

DNA strand breaks induced by concerted interaction of H radicals and low-energy electrons

A computational study on the nucleotide of cytosine

I. Dąbkowska[1,2,3], J. Rak[2], and M. Gutowski[1,2,a]

[1] Chemical Sciences Division, Pacific Northwest National Laboratory, Richland, WA 99352, USA
[2] Department of Chemistry, University of Gdańsk, Sobieskiego 18, 80-952 Gdańsk, Poland
[3] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Flemingovo nam. 2 166 10, Prague 6, Czech Republic

Received 30 March 2005 / Received in final form 11 July 2005
Published online 9 August 2005 –

Abstract. We propose a mechanism of DNA single strand breaks induced by low-energy electrons. Density functional theory calculations have been performed on a neutral, hydrogenated, and/or negatively charged nucleotide of cytosine in the gas phase to identify barriers for the phosphate-sugar O–C bond cleavage. Attachment of the first excess electron induces intermolecular proton transfer to cytosine. The resulting neutral radical of hydrogenated cytosine binds another excess electron, and the excess charge is localized primarily on the C6 atom. A barrier encountered for proton transfer from the C2' atom of the adjacent sugar unit to the C6 atom of cytosine is 3.6 and 5.0 kcal/mol, based on the MPW1K and B3LYP electronic energies corrected for zero-point vibrations, respectively. The proton transfer is followed by a barrier-free sugar-phosphate C–O bond cleavage. The proton transfer is impossible for the neutral nucleotide, as there is no local minimum for the product. In the case of anionic and hydrogenated nucleotides the same barrier determined at the B3LYP level is as large as 29.3 and 22.4 kcal/mol respectively. This illustrates that the consecutive hydrogenation and electron attachment make the nucleotide of cytosine susceptible to a strand break. The rate of the C–O bond cleavage in the anion of hydrogenated nucleotide of cytosine is estimated to be ca. 10^{10} s^{-1}. The proposed mechanism proceeds through bound anionic states, not through metastable states with finite lifetimes and discrete energy positions with respect to the neutral target. The results suggest that at least for DNA without hydration even very low-energy electrons may cleave the DNA backbone.

PACS. 31.10.+z Theory of electronic structure, electronic transitions, and chemical binding – 34.10.+x General theories and models of atomic and molecular collisions and interactions (including statistical theories, transition state, stochastic and trajectory models etc.) – 36.40.-c Atomic and molecular clusters – 36.40.Wa Charged clusters

1 Introduction

Low energy electrons (LEE) are secondary particles, which are produced in large quantity ($\sim 4 \times 10^4$ per MeV of deposited energy) along all of the tracks of ionizing radiation. It has been suggested that these secondary species can be responsible for the mutagenic, genotoxic, and other potentially lethal DNA lesions [1,2].

The role of LEE as triggers of the DNA backbone cleavage was highlighted by the group of Sanche [3]. In their experiments, solid samples of clean DNA containing its structural water were irradiated with beams of low-energy (3.5–100 eV) electrons at constant current density and well defined kinetic energy. The irradiated DNA samples were tested for single- and double-strand breaks (SSB and DSB, respectively). The results proved that SSB and DSB occur for electrons with incident energies lower than the ionization threshold of DNA. The resonance structure of the damage quantum-yield versus incident electron energy suggested that the process proceeds via metastable, i.e., resonance, anionic states. Since then many experimental as well as theoretical studies addressed transformations of different building blocks of DNA induced by LEE [4–19].

Anionic shape resonances might play a decisive role in the recent gas phase experiments, in which electrons with subexcitation kinetic energies (0.6–2.5 eV) induce effective dehydrogenation of nucleic acid bases (NB) via dissociative electron attachment [4,7]

$$(\mathrm{NB}) + e^- \rightarrow (\mathrm{NB})^- \rightarrow (\mathrm{NB{-}H})^- + (\mathrm{H}^\bullet). \qquad (1)$$

A highly mobile radical $\mathrm{H}^\bullet$ is produced, which may induce further damage to DNA. An analogous decomposition

[a] e-mail: maciej.gutowski@pnl.gov

of a nucleoside of thymine (T) was reported with the C(sugar)–N(base) bond cleaved and the unpaired electron localized on either the $(T–H)^{\bullet}$ moiety or the sugar residue [8].

In addition to the dominant channel described by equation (1), more recent studies focused on [10]

$$(NB) + e^{-} \rightarrow (NB)^{-} \rightarrow (NB{-}H)^{\bullet} + H^{-}. \qquad (2)$$

It was found that site selectivity for H^{-}/D^{-} abstraction in thymine is dependent on the incident electron energy. The features due to H^{-}/D^{-} abstraction from the carbon positions resemble the energy dependence of single- and double-strand breaks observed in plasmid DNA.

Very recently the group of Sanche conducted an experiment on solid DNA fragments with even lower energy electrons 0–4 eV [13]. Their results revealed that collisions of these very slow electrons with DNA may lead to SSB's. Interestingly, the shape and the position of peaks of the damage quantum-yield versus incident electron energy closely resembles those obtained for NB's, where the main channel of alteration was shown to be the dissociation of a hydrogen atom, $H^{\bullet}$, see equation (1). The results of experimental studies [4–13] suggest that the dissociation of $H^{\bullet}$ and/or H^{-} may trigger cleavage of the DNA sugar-phosphate backbone.

The recent theoretical studies have been mainly focused on anionic resonance states localized on fragments of DNA and their role in formation of SSB's [14–17]. For the gas phase anionic nucleotide of cytosine, a barrier of 13 kcal/mol has to be surmounted to cleave the sugar-phosphate bond and the rate of bond cleavage was estimated as 10^{4} s^{-1} [14]. In a more recent study a broad range of kinetic energies of ballistic electrons and dielectric constants was considered and a magnitude of the barrier was in the 28.1–5.1 kcal/mol range [17]. Li et al. focused on the sugar-phosphate backbone rather than on NB's [15]. For the gas phase anionic sugar-phosphate-sugar system a barrier is lower than in the nucleotide of cytosine and amounts to 7–10 kcal/mol. The rate of the sugar-phosphate bond cleavage was estimated as 5×10^{6} s^{-1} [16]. Unfortunately, the rates of bond cleavage for these model systems are not competitive with electron autodetachment occurring approximately at ca. 10^{14} s^{-1}.

We have recently suggested that it might be premature to focus attention exclusively on anionic resonance states as critical intermediates leading to DNA strand breaks [20]. We consider that the primary role of resonance states is to allow for energy transfer between the impinging electron and the neutral target. In other words, we view anionic resonance states as doorways to bound valence anionic states. The latter may be involved in chemical transformations, such as DNA strand breaks, while the former are required to absorb excess electrons into the DNA environment [20]. This hypothesis is consistent with the observed resonance structure in the damage quantum-yield versus incident electron energy [3].

The existence of valence anionic states of NB's in the gas phase has been extensively studied both experimentally [21–23] and theoretically [24–29]. First, it was demonstrated in the elegant experiments from the Bowen's group that even a marginal solvation, such as a single water molecule, renders valence anions of some NB's adiabatically bound [23]. Moreover, solvation that results from the Watson-Crick pairing makes ground valence anionic state of pyrimidine bases adiabatically stable [19]. A bound valence anionic state localized on cytosine could not be identified in references [14,17] because the guanine moiety was missing in their model. In our opinion one should not preclude bound anionic states from consideration in the DNA environment even though an earlier experimental and computational results suggest that vertical electron attachment energies are negative for canonical tautomers of isolated NB's, i.e., the anions are electronically unbound at the optimal geometry of the neutral [21,24–29]. However, the valence anionic states become stabilized in the course of geometrical relaxations, tautomerizations, and interactions with their environment [18,19,24–29]. A clear advantage of dealing with bound anionic states is that the strand break formation does not have to compete with the very fast electron autodetachment process (ca. 10^{14} s^{-1}).

Another interesting property of valence anionic states of NB's is that they are susceptible to intermolecular proton transfer to the base, which yields highly reactive radicals, $(NB{+}H)^{\bullet}$. In a series of collaborative studies with the photoelectron spectroscopy group of Kit Bowen we demonstrated that excess electron attachment triggers a barrier-free intermolecular proton transfer (BFPT) from many weak acids (HA) to the NB with the new product moieties being a neutral hydrogenated base radical $(NB{+}H)^{\bullet}$ and the deprotonated acid, A^{-} [18,19]:

$$(NB)\ldots(HA) + e^{-} \rightarrow (NB + H)^{\bullet}\ldots(A^{-}). \qquad (3)$$

The driving force for proton transfer is the stabilization of the excess electron onto a π^{*} orbital of the base. A high electron affinity of $(NB{+}H)^{\bullet}$ and a high basicity of $(NB{+}H)^{-}$ are critical elements of the mechanism of SSB's presented in this report.

We have recently reported computational results for the anionic nucleotide of thymine and we identified a reaction pathway for the phosphate-sugar O–C bond cleavage with a very small barrier (<5 kcal/mol) [20]. An important question remains how sensitive is the barrier height to the nature of the nucleic acid base. Here we present the density functional theory results for a single nucleotide that contains cytosine (Cy) and we identify barriers for the phosphate-sugar O–C bond cleavage. We propose a process that advances through bound anionic states with respect to the neutral target. First, a neutral radical $(Cy{+}H)^{\bullet}$ is formed in the process of either intermolecular proton transfer to Cy induced by an excess electron or direct attack of $H^{\bullet}$. The resulting neutral radical $(Cy{+}H)^{\bullet}$ binds an excess electron, and the excess charge is localized primarily on the C6 atom. Only a small barrier (<5 kcal/mol) is encountered for proton transfer from the C2' atom of the adjacent sugar unit to the C6 atom of $(Cy{+}H)^{-}$. The rate of this proton transfer is estimated to be ca. 10^{10} s^{-1}. This proton transfer is followed by a barrier-free sugar phosphate C–O bond cleavage.

The proposed two step process requires that either $H^\bullet$ and a low-energy electron or two low-energy electrons interact with the same nucleotide. This scenario is plausible because high-energy (∼1 MeV) particles create in aqueous systems the so-called "spurs", which represent high concentrations of reactive species, such as radicals and low-energy electrons [30]. Thus these nucleotides which are in the neighborhood of a "spur" region can be exposed to many reactive species, including $H^\bullet$ radicals and low-energy electrons. It is a well-known feature that a single high-energy radiation event (track) produces clustered-type lesions in biomolecules [31].

2 Methods

The mechanism proposed by us applies first of all to gas phase transformations of nucleotides exposed to low-energy electrons. This environment is of interest in many experimental studies including the mass spectroscopy analysis of DNA. The possible effects of hydration will be discussed in Section 3. The advantage of gas phase studies is that experimental techniques like mass spectrometry and electron spectroscopy can easily be applied. These techniques allow detailed information on the properties of molecules and the dynamics of reactions to be explored [11].

Within the density functional theory (DFT) approach [32,33] we applied two different functionals: a Becke's three parameter hybrid functional (B3LYP) [34–36] and a modified Perdew-Wang 1-parameter method for kinetics (MPW1K) [37]; in both cases the 6-31++G**(6d) basis set was used [38]. The ability of the B3LYP method to predict excess electron binding energies has recently been reviewed and the results were found to be satisfactory for valence-type molecular anions [39]. However, B3LYP is known to underestimate kinetic barriers, so we decided to utilize the MPW1K functional, which was specifically designed to reproduce barrier heights of chemical reactions.

For initial geometries we excised a nucleotide of cytosine from B-DNA and neutralized it with hydrogen atoms. All the structures in our study were fully optimized and no geometry constraints were imposed. Gas-phase free energies were calculated by including zero-point vibration energies (ZPE), and temperature-dependent enthalpy terms and entropies determined in the rigid rotor — harmonic oscillator approximation. To identify the structures of transition states (TS) we initially used a semiempirical PM3 method [40], and then re-optimized the resulting structure at the DFT level of theory. All TS structures have only one imaginary frequency, which are related to normal modes responsible for the desired proton transfer. Additionally, to further confirm the correctness of our transition state structure, the intrinsic reaction coordinate (IRC) [38] was followed starting from the TS in both directions — towards the product and the substrate.

All the calculations were performed using the Gaussian03 [38] code on a cluster of 32 bit Xeon/SCI Dolphin processors.

3 Results

A scheme of the proposed strand break for the nucleotide of cytosine is shown in Figure 1; see the first structure for the labeling of atoms. In the first stage, the nucleic acid base is hydrogenated at the N3 position forming the $(Cy+H)^\bullet$. The $(Cy+H)^\bullet$ intermediate can be formed in at least two ways: (a) as an excess electron attachment to the base followed by an intermolecular proton transfer, or (b) as a direct attachment of the hydrogen atom. In the first case, an electron induced proton transfer may develop, without or with a very small barrier, whenever an anionic nucleic base interacts with proton donors, such as weak acids [18,19] or the complementary nucleic acid base; e.g., the intermolecular proton transfer occurs in the anionic Watson-Crick GC pair [41,42].

In the case of direct hydrogenation we anticipate two possible sources of hydrogen radicals: from surrounding water or from neighbouring NB's. The fact that radiolysis of water leads to formation of the $H^\bullet$ and $OH^\bullet$ radicals has been known for long [43]. Only recently, however, it was demonstrated that the highly mobile $H^\bullet$ radicals are produced in the course of interaction of low-energy electrons with NB's [6–11]. Our computational results indicate that the radical $H^\bullet$ binds to the N3 atom of Cy with a E+ZPE barrier of 1.99 kcal/mol (B3LYP/6-31++G** result).

In the second stage of the proposed mechanism, an electron is captured by the radical of a hydrogenated base and a closed-shell anion $(Cy+H)^-$ is formed. An electron vertical detachment energy for the anion is significant, ca. 32 kcal/mol, and the anion is adiabatically bound by 12 kcal/mol (B3LYP/6-31++G** result). The excess negative charge is formally localized on the C6 atom of Cy but it also spreads over the C4–C5 area.

We come to the third and critical stage of the proposed mechanism, in which a proton is transferred from the adjacent sugar to the negatively charged C6 atom of $(Cy+H)^-$. This is the C2' proton, which is the closest to C6 both in our DFT optimized geometry and in the B-DNA structure. The MPW1K barrier for proton transfer from the C2' atom of sugar to C6 of $(Cy+H)^-$ is 5.6, 3.4, and 4.2 kcal/mol in terms of electronic energy, electronic energy corrected for zero-point vibrations, and Gibbs free energy, respectively (Fig. 2). The corresponding B3LYP values are 6.9, 5.0, and 6.5 kcal/mol.

The proton transfer leads formally to a product, in which the negative charge is localized on the sugar unit. In our calculations, however, we could not identify the product of step (3) from Figure 1. Instead, as in the case of the nucleotide of thymine [20], we observe a spontaneous, barrier-free cleavage of the C–O sugar-phosphate bond (Fig. 2) with the negative charge localized on the phosphate unit. These finding were confirmed in the IRC calculations. One IRC path ended up with the exact structure of the substrate whereas a spontaneous sugar-phosphate bond break was observed along the second IRC path. In agreement with earlier computational studies, the strand break process is thermodynamically favorable [14–17,20].

The CH stretching frequency is at ca. 3000 cm^{-1}, which corresponds to a rate of vibration of 8.9×10^{13} s^{-1}.

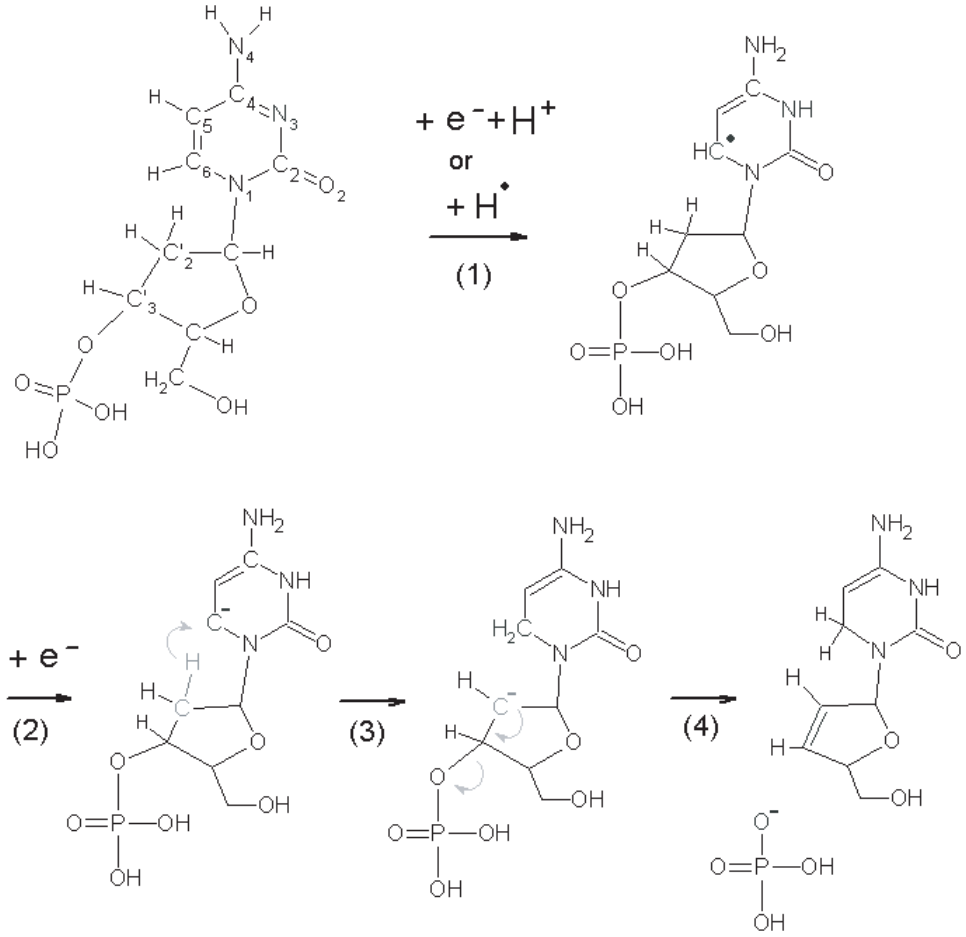

Fig. 1. Proposed mechanism of the DNA strand break induced by excess electrons.

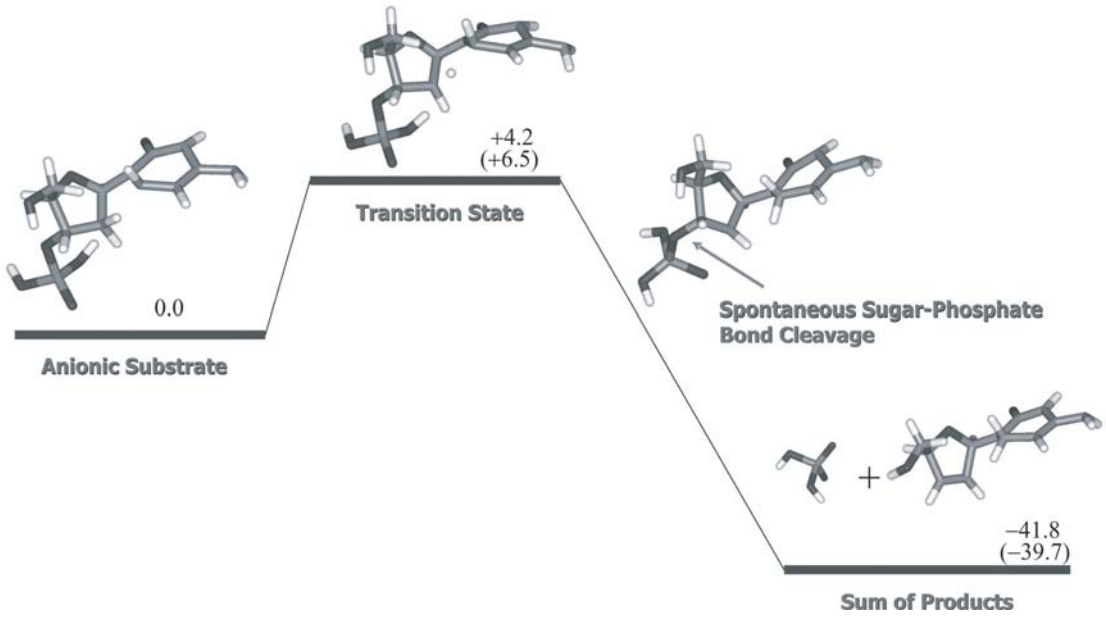

Fig. 2. MPW1K/6-31++G** and B3LYP/6-31++G** (in parentheses) free energies for a rupture of the sugar-phosphate bond in the nucleotide of cytosine upon interaction with $H^{\bullet}$ and an excess electron. All values in kcal/mol.

Table 1. The kinetic barrier for a proton transfer reaction from the C2' atom of sugar to C6 of the base (ΔG(TS)), and the free energy change for this reaction (ΔG). All quantities in kcal/mol.

System	ΔG(TS)	ΔG
cytidine	N/A[a]	N/A[a]
$(\text{cytidine})^-$	30.0	20.3[b]
(cytidine+H)	25.6	22.8[b]
$(\text{cytidine+H})^-$	6.5	–39.7[c]

[a]Product of the proton transfer step is geometrically unstable and collapses without a barrier to the reactant. [b]Product of the proton transfer step is geometrically stable. [c]Proton transfer step is followed be a barrier-free sugar-phosphate bond break.

The Boltzmann's probability for surmounting the 4.2 kcal/mol barrier at $T = 298$ K is 8.3×10^{-4} Thus the average rate of strand break formation from the anion of hydrogenated nucleotide is ca. 7.6×10^{10} s^{-1}. Other estimations of this rate from transition state theory are 5.0×10^9, 5.0×10^8 and 1.9×10^{10} s^{-1} when based on the difference of free enthalpies, electronic energies, and electronic energies corrected for zero-point vibration energies, respectively.

The unusual susceptibility to the sugar-phosphate bond break for cytidine with $(\text{Cy+H})^-$ rather than with Cy, Cy^-, or (Cy+H) is illustrated in Table 1. At the B3LYP level, the barrier for proton transfer from the C2' atom of sugar to C6 of the base is only 6.5 kcal/mol for $(\text{Cy+H})^-$. It increases to 25.6 kcal/mol for (Cy+H) and to 30.0 kcal/mol for Cy^-. For an unmodified cytidine, i.e., with Cy, the barrier could not be determined because the hypothetical product with the C2' proton transferred to C6 is geometrically unstable and collapses without a barrier to the reactant. The thermodynamics of the proton transfer reaction is also very sensitive to the form of Cy. ΔG for the reaction is +20.3 kcal/mol for Cy^-, +22.8 kcal/mol for (Cy+H), and –39.7 kcal/mol for $(\text{Cy+H})^-$. For the latter, the proton transfer step is followed be a barrier-free sugar-phosphate bond break. Clearly, the formation of $(\text{Cy+H})^-$, i.e., a reduction step followed by protonation and another reduction step, makes the modified nucleotide kinetically and thermodynamically susceptible to the sugar-phosphate bond break.

The results reported so far apply to the nucleotide of cytosine in the gas phase and may not apply to the water environment. Water represents a dissipative environment and in the case of reactions with charged particles involved, hydration can considerably alter the energy profile along the reaction coordinate [11]. Moreover, the C2' hydrogen of the sugar unit is expected to be much less protic than the hydrogens of water. With these reservations in mind we performed geometry optimizations for the Cy, (Cy+H), and $(\text{Cy+H})^-$ forms of cytidine with one water molecule placed initially between the base and the sugar unit. The calculations did not reveal any chemically relevant effect of water. First, even in the case of $(\text{Cy+H})^-$, we could not identify a water-assisted barrier-free proton transfer from C2' to C6. Second, we could not find any minimum energy structure with the water molecule in the region between the base and the sugar. Third, the water molecule was always repelled from the region between the base and the sugar and formed hydrogen bonds with the bridging oxygen of the sugar unit. These results are consistent with the crystallographic structure of B-DNA [44]. The closest water molecules are separated from the C6 atom of Cy by 4.9 and 5.1 Å (the oxygen-carbon distances), whereas the distance between C6 and C2' is only 3.1 Å. The results suggest that hydration might be not critical for the mechanism summarized in Figures 1 and 2. However, the problem should be carefully scrutinized in the future studies with an explicit treatment of water molecules, preferably at the level of ab initio molecular dynamics.

4 Discussion

The interaction of molecules with low-energy electrons can be described in terms of resonant and direct scattering [4]. The latter might involve excitations to dissociative electronic states. The direct scattering with dissociative states involved is believed to be responsible for a linearly increasing background in the damage quantum yield [5,13]. On the other hand, well defined peaks in the damage quantum yield versus incident electron energy were assigned to the resonant scattering and dissociative electron attachment (DEA) [3–13]. It is then a legitimate question to ask which electron-energy range the mechanism proposed by us applies to. The mechanism proposed by us applies to chemical transformations, which occur on potential energy surfaces of *bound* anionic states of nucleotides. These bound anionic states develop in the course of scattering of low-energy electrons on DNA. The resonance states play a particular role as they allow for efficient energy transfer from the impinging electron to various degrees of freedom of the neutral target. We view the resonance structure of the damage quantum yield as a manifestation of highly probable doorways the incident electrons go through. Whatever the history of an excess electron is, in a condense phase environment it will end up as a valence anion, solvated electron, or it will recombine with a positively charged species.

The focus on bound valence states rather than on unbound (resonance) states is the main difference between the previous theoretical studies [14–17] and the approach presented by us here and in reference [20]. In gas phase studies, in which the stability of valence anions is questionable, the DEA may indeed be the dominant mechanism of chemical transformations, such as the H^- and $\text{H}^\bullet$ abstractions [10,11]. The DEA mechanism was also proposed to interpret a decomposition of the nucleoside of thymine [8]. One might speculate that the excision of nucleobases from DNA might also occur in consequence of the DEA. So far, however, the kinetic barrier for DNA strand breaks determined theoretically for resonance anionic states were as large as 13 kcal/mol for cytidine [14] and 7–10 kcal/mol for the sugar-phosphate backbone [15,16]. The resulting rates of the sugar-phosphate bond cleavage were 10 to

8 orders of magnitude smaller than the rate of electron autodetachment from resonance anionic states. It is then not clear whether DEA is the only mechanism responsible for strand breaks in DNA exposed to low-energy electrons. It was our hypothesis that chemical transformations might also develop on potential energy surfaces of *bound* anionic states, which do not have to compete with electron autodetachment occurring approximately at ca. 10^{14} s^{-1} [20]. The anionic "bound-state" rather than "resonance" channel might be particularly important in condense phases, which stabilize valence anionic states [18,19,24–29,41,42].

A barrier of 4.2 kcal/mol (Fig. 2), based on free enthalpies determined here with the MPW1K functional for the nucleotide with $(Cy+H)^-$, is the smallest among the reported gas phase barriers for the cleavage of the C–O sugar-phosphate bond induced by excess electrons [14–17,20]. The estimated rate of the strand break formation in a nucleotide with $(Cy+H)^-$ is ca. 10^{10} s^{-1}. Thus the anionic "bound-state" channel might be important for strand breaks in DNA. The MPW1K barrier, determined in terms of electronic energies corrected for zero-point vibrations, increases from 3.4 kcal/mol for C2'H to 4.3 kcal/mol for C2'D. Thus, we predict that the substitution of hydrogen with deuterium at C2' should slow down the kinetics the sugar-phosphate bond cleavage in nucleotides with $(Cy+H)^-$.

A comparison of our past computational results for the nucleotide of thymine obtained with the B3LYP functional [20] with the current B3LYP value of the barrier height for the nucleotide of cytosine indicate that the latter might be less susceptible to strand breaks induced by excess electrons. On the other hand, the anionic GC pair is susceptible to intermolecular proton transfer, whereas the AT pair is not [19,41]. Thus the step (1) from Figure 1 of the proposed mechanism is facilitated for each nucleotide of cytosine but not for each nucleotide of thymine. An experimental characterization of the amount of single strand breaks induced by excess electrons in poly-AT and poly-GC DNA fragments would be very informative. So far, only neutral fragments desorbed from thin films of nonamers of deoxycytidine and thymidine, which were exposed to low-energy (1–30 eV) electrons, were analyzed [5]. The total effective cross-sections per base estimated for the CN, OCN, and CH_3CCO species production from fragmentation of the nonamers of deoxycytidine and thymidine are comparable and amount to 3.4×10^{-17} and 2.3×10^{-17} cm^2, respectively.

We expect that there might be pathways leading to DNA strand breaks that are even more favorable than the pathway identified by us so far, see Figures 1 and 2. In particular, we are considering proton transfer directly from the sugar moiety to the C6 carbon atoms of anionic pyrimidine bases. In addition, the role of metallic counteractions and explicit water molecules should be explored in ab initio molecular dynamics simulations. Thus a barrier reported by us should be viewed as an approximation to the barriers encountered along strand break pathways induced by excess electrons.

5 Summary

We explored a mechanism of the sugar-phosphate C–O bond rupture induced by low energy electrons in the gas phase nucleotide of cytosine. As in the case of the nucleotide of thymine [20], we analyzed a process that advances through bound anionic states, not through metastable states with finite lifetimes and discrete energy positions with respect to the neutral target. A clear advantage of dealing with bound anionic states is that the strand break formation does not have to compete with the very fast electron autodetachment process (ca. 10^{14} s^{-1}). The following steps have been identified:

1. the cytosine moiety is hydrogenated at the N3 position, producing $(Cy+H)^\bullet$. The hydrogenation develops as either an excess electron attachment followed by a barrier-free proton transfer from a proton donor, or in consequence of the attachment of $H^\bullet$ to the N3 atom of cytosine, which undergoes with a kinetic barrier smaller than 2 kcal/mol;
2. $(Cy+H)^\bullet$ binds an excess electron and forms a closed-shell moiety, $(Cy+H)^-$. $(Cy+H)^-$ is characterized by a significant electron vertical detachment energy of 32 kcal/mol and is adiabatically bound with respect to $(Cy+H)^\bullet$ by 12 kcal/mol. The excess charge is localized primarily on the C6 atom of $(Cy+H)^-$;
3. a proton is transferred from the C2' atom of the adjacent sugar unit to the C6 atom of $(Cy+H)^-$ with a barrier as small as 4.2 kcal/mol. The second proton transfer is followed by a barrier-free sugar-phosphate C–O bond cleavage.

The unusual susceptibility to the sugar-phosphate bond break for the nucleotide with $(Cy+H)^-$ was characterized. The rate of the C–O bond cleavage is estimated to be ca. 10^{10} s^{-1}, which makes the proposed mechanism very probable for gas phase or solid DNA without hydration. The relevance of this mechanism for hydrated DNA still needs to be explored. In the future study we intend to improve our model by replacing neutralizing protons with metallic counteractions, explicitly including hydration effects, and performing ab initio molecular dynamics simulations.

This work was supported by the: (i) Polish State Committee for Scientific Research (KBN) Grant 4T09A01224 (J.R. and I.D.) and (ii) US DOE Office of Biological and Environmental Research, Low Dose Radiation Research Program (M.G.). I.D. is a holder of the Polish Science Foundation Award. The calculations were performed in the computational center TASK in Gdañsk. PNNL is operated by Battelle for the U.S. DOE under Contract DE-AC06-76RLO 1830.

References

1. A.D. Lenherr, M.G. Omerod, Nature **225**, 546 (1970)
2. C. von Sonntag, *The Chemical Basis of Radiation Biology* (Taylor and Francis, Philadelphia, 1987)
3. B. Boudaïffa, P. Cloutier, D. Hunting, M.A. Huels, L. Sanche, Science **287**, 1658 (2000)

4. L. Sanche, Mass Spectrom. Rev. **21**, 349 (2002)
5. H. Abdoul-Carime, L. Sanche, Int. J. Radiat. Biol. **78**, 89 (2002)
6. G. Hanel, B. Gstir, S. Denifl, P. Scheier, M. Probst, B. Farizon, M. Farizon, E. Illenberger, T.D. Märk, Phys. Rev. Lett. **90**, 188104 (2003)
7. H. Abdoul-Carime, S. Golhke, E. Illenberger, Phys. Rev. Lett. **92**, 168103 (2004)
8. H. Abdoul-Carime, S. Golhke, E. Fischbach, J. Scheike, E. Illenberger, Chem. Phys. Lett. **387**, 267 (2002)
9. S. Ptasińska, S. Denifl, P. Scheier, T.D. Märk, J. Chem. Phys. **120**, 8505 (2004)
10. S. Ptasińska, S. Denifl, V. Grill, T.D. Märk, P. Scheier, S. Gohlke, M.A. Huels, E. Illenberger, Angew. Chem. Int. Ed. **44**, 1647 (2005)
11. S. Gohlke, E. Illenberger, Europhys. News, **33**, 207 (2002)
12. M.A. Huels, L. Parenteau, L. Sanche, J. Phys. Chem. B **108**, 16303 (2004)
13. F. Martin, P.D. Burrow, Z. Cai, P. Cloutier, D. Hunting, L. Sanche, Phys. Rev. Lett. **93**, 068101 (2004)
14. R. Barrios, P. Skurski, J. Simons, J. Phys. Chem. B **106**, 7991 (2002)
15. X. Li, M.D Sevilla, L. Sanche, J. Am. Chem. Soc. **125**, 13668 (2003)
16. J. Berdys, I. Anusiewicz, P. Skurski, J. Simons, J. Am. Chem. Soc. **126**, 6441 (2002)
17. J. Berdys, I. Anusiewicz, P. Skurski, J. Simons, J. Phys. Chem. A **108**, 2999 (2004)
18. M. Gutowski, I. Dąbkowska, J. Rak, S. Xu, J.M. Nilles, D. Radisic, K.H. Bowen Jr, Eur. Phys. J. D **20**, 431 (2002)
19. D. Radisic, K.H. Bowen Jr, I. Dąbkowska, P. Storoniak, J. Rak, M. Gutowski, J. Am. Chem. Soc. **127**, 6443 (2005), and references therein
20. I. Dąbkowska, J. Rak, M. Gutowski, J. Phys. Chem. B (2005, submitted)
21. K. Aflatooni, G.A. Gallup, P.D. Burrow, J. Phys. Chem. A **102**, 6205 (1998)
22. C. Defrançois, H. Abdoul-Carime, J.P. Schermann, J. Chem. Phys. **104**, 7792 (1996)
23. J.H. Hendricks, S.A. Lyapustina, H.L. de Clercq, K.H. Bowen Jr, J. Chem. Phys. **108**, 8 (1998)
24. X. Li, Z. Cai, M.D. Sevilla, J. Phys. Chem. A **106**, 1596 (2002), and references therein
25. M. Harańczyk, M. Gutowski, J. Am. Chem. Soc. **127**, 699 (2005)
26. M. Harańczyk, J. Rak, M. Gutowski, J. Phys. Chem. A (2005, accepted)
27. R.A. Bachorz, J. Rak, M. Gutowski, Phys. Chem. Chem. Phys. **7**, 2116 (2005)
28. M. Harańczyk, M. Gutowski, Angew. Chem. Int. Ed. (2005, accepted)
29. K. Mazurkiewicz, R.A. Bachorz, M. Gutowski, J. Rak, J. Phys. Chem. B (2005, submitted)
30. B.C. Garrett, D.A. Dixon, D.M. Camaioni, D.M. Chipman, M.A. Johnson, C.D. Jonah, G.A. Kimmel, J.H. Miller, T. Rescigno, P.J. Rossky, S.S. Xantheas, S.D. Colson, A.H. Laufer, D. Ray, P.F. Barbara, K.H. Bowen, S.E. Bradforth, I. Carmichael, R. Corrales, J.P. Cowin, M. Dupuis, J.A. Franz, M. Gutowski, K.D. Jordon, B.D. Kay, C.W. Mccurdy, D. Meisel, S. Mukamel, A.R. Nilsson, T.M. Orlando, N.G. Petrik, S.M. Pimblott, J.R. Rustad, G.K. Schenter, S.J. Singer, L. Wang, D.M. Bartels, K.H. Becker, J.V. Coe, K.B. Eisenthal, J.A. La Verne, S.V. Lymar, T.E. Madey, A. Tokmakoff, C. Wittig, T.S. Zwier, Chem. Rev. **105**, 355 (2005)
31. B. Sutherland, P.V. Bennett, O. Sidorkina, J. Laval, Biochem. **39**, 8026 (2000)
32. P. Hohenberg, W. Kohn, Phys. Rev. B **136**, 864 (1964)
33. W. Kohn, L. Sham, J. Phys. Rev. A **140**, 1133 (1965)
34. A.D. Becke, Phys. Rev. A, **38**, 3098 (1988)
35. A.D. Becke, J. Chem. Phys. **98**, 5648 (1993)
36. C. Lee, W. Yang, R.G. Paar, Phys. Rev. B **37**, 785 (1988)
37. B.J. Lynch, P.L. Fast, M. Harris, D.G. Truhlar, J. Phys. Chem. A **104**, 4811 (2000)
38. *Gaussian 03, Revision C.02*, M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery Jr, T. Vreven, K.N. Kudin, J.C. Burant, J. M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian, Inc., Wallingford CT, 2004
39. J.C. Rienstra-Kiracofe, G.S. Tschumper, H.F. Schaefer III, Chem. Rev. **102**, 231 (2002)
40. J.P. Stewart, J. Comput. Chem. **10**, 221 (1989)
41. A.O. Colson, M.D. Sevilla, Int. J. Radiat. Biol. **67**, 627 (1995)
42. X. Li, Z. Cai, M.D. Sevilla, J. Phys. Chem. A **106**, 9345 (2002)
43. C. Willis, A.W. Boyd, A.E. Rothwell, O.A. Miller, Int. J. Radiat. Phys. Chem. **1**, 373 (1969)
44. G.G. Prive, K. Yanagi, R.E. Dickerson, J. Mol. Biol. **217**, 177 (1991)