COMMENT

Reply to the "Comment on 'Theoretical Study of Polaron Formation in Poly(G)−Poly(C) Cations'"

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Adhikary and Sevilla[1] have commented on our theoretical study of polaron formation in poly(G)−poly(C) cations.[2] Adhikary and Sevilla's comment[1] clarified the interpretation of their experiments on the ESR spectrum of DNA oligomers, which reveal the localization of the hole in contiguous G sequences in B-DNA oligomers.[3] They also emphasized that their experimental results are supported by the theoretical calculations of Voityuk and Blancafort,[4,5] and Kumar and Sevilla.[6,7] According to our ONIOM calculations,[2] the hole in the poly(G)−poly(C) radical cation is delocalized over several guanine residues.

In the theoretical calculations of Blancafort and Voityuk,[5] the charge distributions in the π-stacked GAG and GTG single strand were investigated. Kumar and Sevilla's calculation[6] on the G−C radical cation with 11 water molecules was performed for only one G−C base pair, and the 11 water molecules were optimized to be nearly in the plane of G−C pair. These calculations do not accurately represent the real situation in B-DNA. For example, the GC + 11H$_2$O scheme[6] has an optimized geometry with two water molecules near the N$_1$(C) and N$_9$(G) atoms. This geometry is not feasible for B-DNA oligomers, because N$_1$(C) and N$_9$(G) are bonded with the sugar−phosphate backbone, and water molecules cannot be placed near them. Due to the presence of the sugar−phosphate backbone, these two water molecules must be neglected in the calculation of B-DNA. Furthermore, the neighboring water molecules must be neglected because they form a hydrogen-bonding network and do not form hydrogen bonds with the G−C base pair. Therefore, only seven water molecules can be added to a B-DNA oligomer according to Kumar and Sevilla's model.[6] We have optimized the B-DNA + 7H$_2$O system using ONIOM+PCM[8] method. The system is divided into two regions in our ONIOM calculation. The high layer is the π-stacked complementary base pairs and seven water molecules, which is treated at the B97D/6-31G(d) level. The low layer includes the sugar−phosphate backbone and sodium ions, which is treated with the Amber99SB force field including the parmbsc0 correction. The optimized cationic geometry of the 5′-GG-3′ duplex is shown in Figure 1. It is apparent that four water molecules do not remain in the plane of the first G−C pair. This makes intuitive sense, because these water molecules form hydrogen bonds not only with the first G−C pair but also with the second G−C pair.

Voityuk's model calculation[4] suggests that the hole in 5′-XGGY-3′ duplexes is localized. He also concluded that the contribution of the solvation parameter, which represents the environmental interactions, leads to the localization. It is well-known that DNA conformation, counterions, and solvation are very important in theoretical calculations of charge transfer in DNA.[4,9−13] Kumar and Sevilla[7] also have shown that the hole in G-stacks (GG and GGG) is localized on a single guanine using the M06-2X/6-31G* method. However, the sugar−phosphate backbone of DNA, counterions, and solvation were neglected in their calculation. Geometry optimization of these π stacks without the backbone would lose the B-DNA conformation. Hence, two dihedral angles (N$_{7a}$N$_{7b}$N$_{9b}$N$_{9a}$ and N$_{3a}$N$_{3b}$C$_{6b}$C$_{6a}$) and
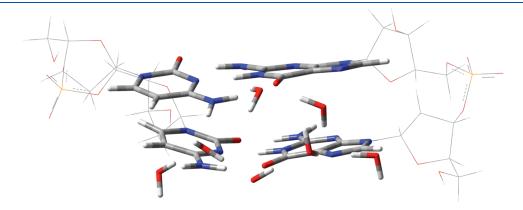

Figure 1. Optimized cationic geometry of the 5′-GG-3′ duplex with 7H$_2$O.

four angles ($N_{7a}N_{7b}N_{9b}$, $N_{7b}N_{9b}N_{9a}$, $N_{3a}N_{3b}C_{6b}$, and $N_{3b}C_{6b}C_{6a}$) between two adjacent bases, a and b, were constrained to keep the B-DNA conformation in their calculation. In fact, these arbitrary constraints can be easily described by a force field, such as Amber99SB.

In brief, ab initio calculations on DNA oligomers are necessary to obtain better results than those obtained with model calculations. In ab initio calculations, the DNA conformation, counterions, and solvent effects should be considered. Meanwhile, the CPU time requirements are also a key factor. The two-layer ONIOM method provides a reliable and feasible model to perform the required calculation. Our ONIOM calculation[2] is a good starting point for future studies. More elaborate ONIOM calculations are necessary to investigate the charge transfer in DNA.

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8950

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