

## Geometry and electronic structure of $M$ -DNA ( $M=\text{Zn}^{2+}$ , $\text{Co}^{2+}$ , and $\text{Fe}^{2+}$ )

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We have investigated, by means of first principles calculations, modified forms of DNA with divalent Zn, Co, Fe cations bonded to the two helix strands of poly(dC)-poly(dG). We propose a common stable structure that is consistent with the experimental reports for Zn-DNA. In all three cases, the band gap is much narrower, and the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) bands are considerably wider than those in dry DNA. In Zn-DNA, the HOMO LUMO bands are formed purely by guanine cytosine states, respectively, with no weight in the Zn atoms. Their large width arise from an increased overlap between  $\pi$  states of the bases, due to the helix deformation after the insertion of the Zn ion. Contrarily, the HOMO and LUMO bands of Co-DNA and Fe-DNA have a large weight on the metal atoms. These results offer promising perspectives for turning DNA into a conducting wire.

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The use of biomolecules as structural components may be the route for self-assembled systems able of storing information, replicating and functioning at the nanoscale. Structural DNA technology is an obvious way to face this challenge, since it is a stable polymer that can be easily handled and modified.<sup>1,2</sup> Therefore, the electrical properties of DNA and DNA-based molecules are of considerable interest for making nanodevices and biosensors. Unfortunately, the experimental results are still contradictory. Direct measurements show from no conduction at all,<sup>3-5</sup> to large dc,<sup>6</sup> or ac conductivity<sup>7</sup> or even superconductivity.<sup>8</sup> Several transport mechanisms have been proposed: Band-structure-like,<sup>9</sup> by tunneling,<sup>10</sup> solitonic,<sup>11</sup> and polaronic.<sup>12-14</sup> Theoretical efforts have been applied to clarify these discrepancies. First-principles studies in dry-DNA show an absence of conduction in one of the most favorable structures for band-structure conduction [poly(dC)-poly(dG)].<sup>4</sup> However, *ab initio* molecular dynamics in wet-DNA found that the presence of counterions could introduce new states into the gap,<sup>15</sup> and enhance conduction,<sup>16</sup> suggesting that DNA conductivity can be induced by doping. Although there is not a clear answer for the DNA conduction question, this debate is progressively leading towards a consensus that natural DNA is not a good electrical conductor.<sup>17</sup> Therefore, one of the central goals in this field is to transform DNA, or DNA-related molecules, into conducting wires. Great efforts have been made to modify the structure and to improve the conductivity of DNA, mainly by adding metallic atoms to it.<sup>18-23</sup> Aich *et al.* have reported the incorporation of divalent metal ions ( $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$  and  $\text{Ni}^{2+}$ ), replacing the imino proton into the helix.<sup>23</sup> Nevertheless, the exact position of these cations, their interaction with DNA, and their effects on its conductivity are still far from clear. In fact, direct measurements using atomic force microscopy (AFM) did not detect any increase of the conductivity of Zn-DNA.<sup>24</sup>

In this work we propose a common stable structure for metallated poly(dC)-poly(dG), with  $M=\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ , and  $\text{Fe}^{2+}$ , and we determine the electronic structure of periodic helices of these polymers. We will notate these compounds simply as  $M$ -DNA for brevity. The metal cations are located between the two DNA strands, replacing the imino protons, as suggested by Aich *et al.*<sup>23</sup> However, in contrast with that proposal, we have found that the metal cations are more stable in a tetrahedral geometry instead of square planar. We also show that different mechanisms can contribute to transform DNA into a semiconducting wire by the incorporation of metal atoms.

Our first principles density functional theory (DFT) simulations use the SIESTA code.<sup>25</sup> Despite the absence of formal van der Waals interactions, DFT provides a good description of the DNA structure.<sup>4,15</sup> We treat exchange and correlation within the generalized gradient approximation.<sup>26</sup> We use norm conserving pseudopotentials,<sup>27</sup> adding partial core corrections<sup>28</sup> for Zn, Fe and Co. The basis set is made of double- $\zeta$  numerical pseudo atomic orbitals,<sup>25,29</sup> with additional polarization functions in the metal ions, in phosphorous, and in the atoms involved in hydrogen bonds. We have checked that this basis yields structures for metal-nucleobase complexes in good agreement with the experimental ones.<sup>30</sup> We consider dry acidic DNA *in vacuo*, with protons as counterions in the phosphate groups, as in phosphoric acid. The geometries were optimized until the residual forces were less than 0.05 eV/Å. To simulate the periodic helical structures we use the A form of DNA, favored under dry conditions, with a unit cell of eleven C-M-G monomers and 737 atoms. Periodic boundary conditions were used in all directions, with enough empty space to discard the interaction between the repeated units. This methodology has been already applied successfully to investigate DNA properties.<sup>4,31</sup>

A definitive determination of the global energy minimum

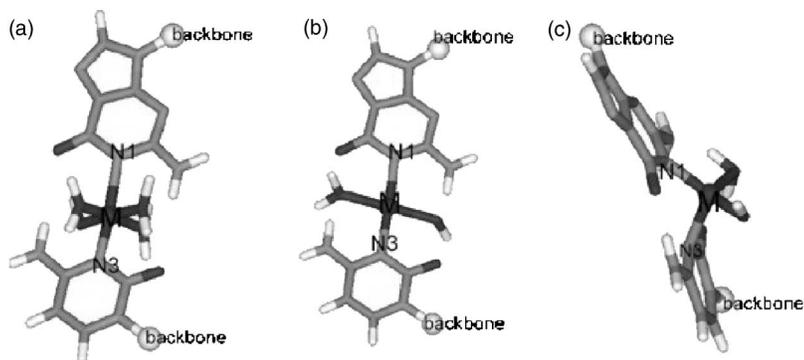


FIG. 1. Initial geometries of M-DNA monomers used in a limited structure search for periodic M-DNA. The metal ions are bonded to guanine and cytosine, and their remaining bonds are saturated by water molecules and a hydroxyl group. In (a)–(b) the metal ions are in octahedral, square-planar and tetrahedral environments, respectively.

would require a full conformational search, as well as to consider interactions with the solvent and/or supporting surface, what is beyond the present *ab initio* methods and computational capabilities. Still, one can obtain important clues and plausible structures from a limited search based on general chemical principles. Therefore, we have first relaxed a single C-Zn<sup>2+</sup>-G monomer, including the corresponding segments of the sugar-phosphate backbones, with fixed H atoms saturating the broken bonds at the extremes. We have used several trial initial geometries (see Fig. 1), with a Zn<sup>2+</sup> ion replacing the guanine imino proton and binding guanine and cytosine under different coordination geometries: Octahedral, square-planar, or tetrahedral. In order to get charge neutrality, the divalent Zn<sup>2+</sup> cation (that replaces a proton) was saturated with one hydroxyl group OH<sup>-</sup>, in addition to one or more neutral water molecules. The initial structures of octahedral and square-planar geometries converged to the same final geometry, with the Zn<sup>2+</sup> ion in a tetrahedral geometry and a single water molecule bound to it, in addition to the hydroxyl. Another initial structure, based on that proposed in Ref. 23 converged to a different, distorted tetrahedral geometry, which was unsuitable for periodical stacking. Figure 2 shows our final structure for a feasible M-DNA stacking, with the Zn<sup>2+</sup> ions stabilized in an energetically favorable tetrahedral geometry and the hydroxyl ligands bridging adja-

cent metal ions. We proceed in the same way for C-Co<sup>2+</sup>-G and C-Fe<sup>2+</sup>-G systems, achieving similar geometries.

The initial geometries of dimer and trimer fragments were generated from that of the isolated and relaxed monomer using  $x'_i = (x_i \cos \Delta\phi \mp y_i \sin \Delta\phi)$ ,  $y'_i = (x_i \sin \Delta\phi \pm y_i \cos \Delta\phi)$ , and  $z'_i = \pm \Delta z$ , where  $x$ ,  $y$ , and  $z$  are the coordinates of the central monomer and  $x'$ ,  $y'$ , and  $z'$  are those of the upper and lower ones. The initial values of  $\Delta\phi$  and  $\Delta z$  were taken from the A structure of pure DNA. These geometries, including the parameters  $\Delta\phi$  and  $\Delta z$ , were then relaxed by minimizing the energy of the central monomer, defined as  $E_3 - E_2$ , where  $E_2$  and  $E_3$  are the total energies of the dimer and trimer, respectively, with the same geometry. During the minimization, all the atoms were required to have the same positions as those in the central base pair of the trimer (except for helical translations-rotations). The final  $\Delta\phi$  was still close to the value  $360^\circ/11$  typical of A-form DNA. Therefore, using this value we generated a periodic 11-base pair helix by helical rotation-translation of the central base pair of the relaxed trimer. Its structure, which is similar for all the M-DNAs studied, is shown in Figs. 2 and 3 for Zn-DNA.

The insertion of the metal cations produces alterations in the helix twist, propeller twist, and tilt angles (Fig. 4). The geometry around the metal cations could be defined as a

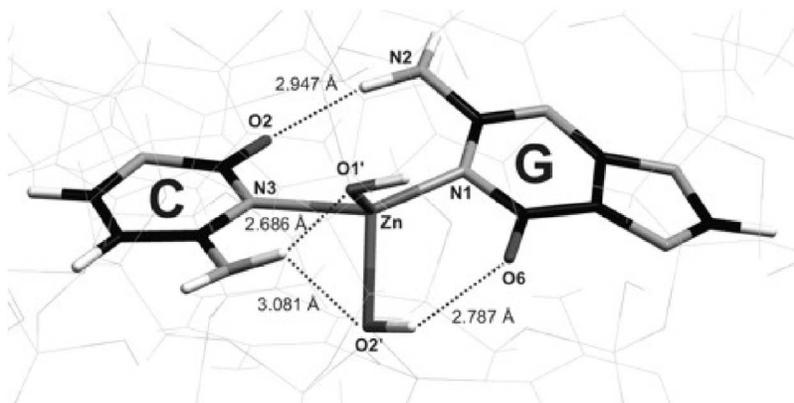


FIG. 2. Structure of a periodic unit of poly(dC)-Zn<sup>2+</sup>-poly(dG). The bivalent Zn cation substitutes the imino proton of the central guanine-cytosine (GC) hydrogen bond, replacing it by a coordination bond mediated by the metal ion, which remains close to the GC plane. Hydrogen bonds are shown as broken lines. The subsequent in-plane deformation of the base pair results also in the breaking of the hydrogen bond closer to the minor groove, leaving only that closer to the major groove. The coordination geometry of Zn<sup>2+</sup> is close to tetrahedral, with two in-plane bonds with nitrogen atoms of guanine and cytosine and two out-of-plane bonds with the oxygen atoms of two OH<sup>-</sup> ions. Each OH<sup>-</sup> ion binds to two consecutive metal ions, forming a zigzag chain along the minor groove of the deformed DNA helix.

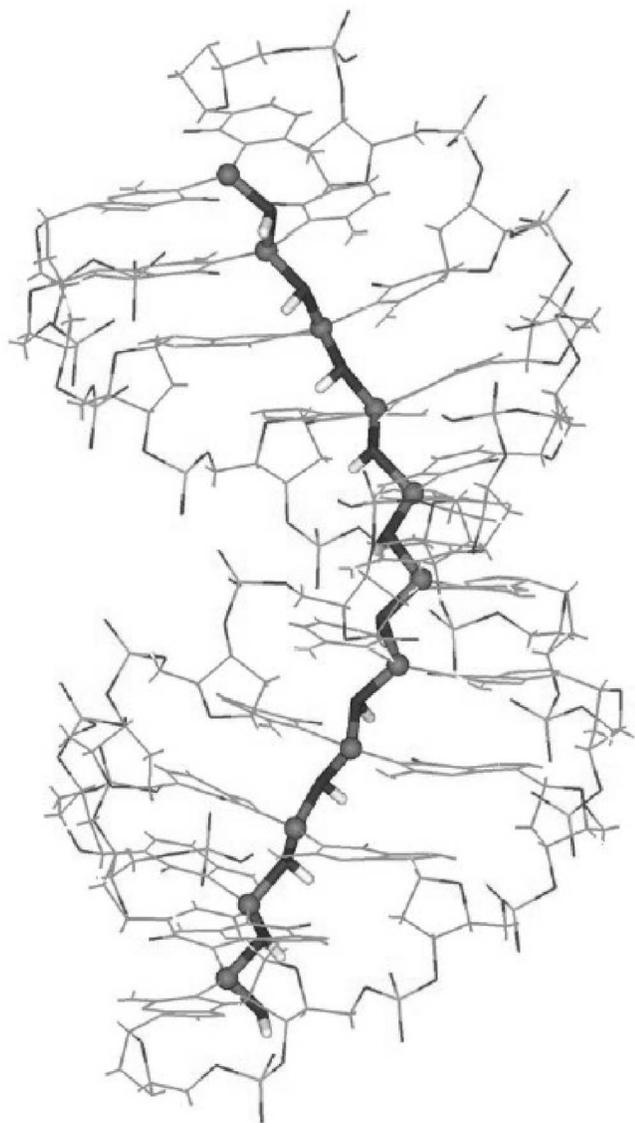


FIG. 3. Global view of the Zn-DNA helix.

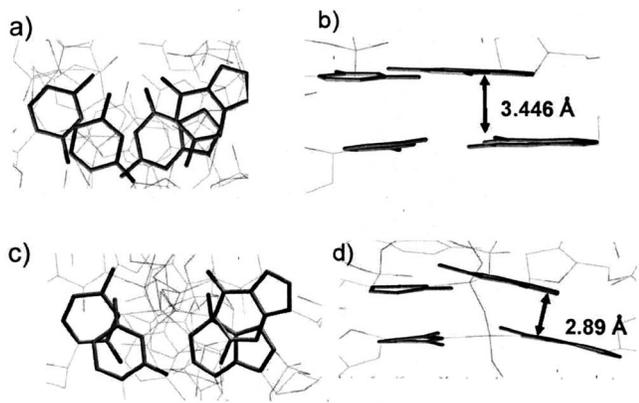


FIG. 4. Top and side views of the stacking between consecutive base-pairs in pure A-form DNA (upper panels) and in Zn-DNA (lower panels).

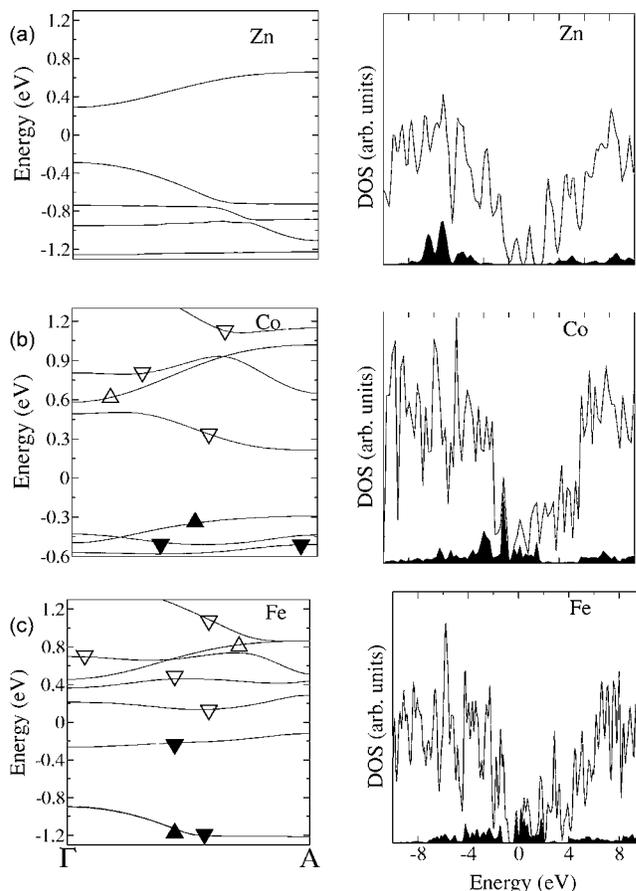


FIG. 5. Band structure (left) and density of states (DOS, right) of Zn-DNA, Co-DNA, and Fe-DNA. Upward- and downward-pointing triangles indicate up- and down-spin bands, with filled and empty signs indicating filled and empty states. The Fermi level is the zero of the energy scales. The magnetic moment per base pair is 0, 3, and 4 Bohr magnetons for Zn-DNA, Co-DNA, and Fe-DNA, respectively. Empty and filled curves are the total DOS and the projected DOS on the metal atoms.

distorted tetrahedron with distances and angles around the metal cations falling in the expected range found in similar metal-nucleobase complexes.<sup>32</sup> The most significant features found in the optimized structures relative to the guanine-cytosine interactions are: (i) The metal ion replaces the G-N(1)-H $\cdots$ N(3)-C H-bond while the G-N(2)-H $\cdots$ O(2)-C hydrogen-bond is conserved; (ii) the G-O(6) $\cdots$ H-N(4)-C bond is lost; (iii) three new H-bonds involving the oxygen of the OH-groups: O(1')-H $\cdots$ N(4)-C, O(2')-H $\cdots$ O(6)-G and O(2')-H $\cdots$ N(4)-C are formed, as shown in Fig 2.

We now turn to the electronic structure and its consequences for the conductivity of these chains, assuming the geometry obtained from our restricted structural search. Figure 5 shows the band structures and the density of states of Zn-DNA, Co-DNA, and Fe-DNA, close to the Fermi level.

In all cases, the incorporation of the metal ions results in a large reduction of the original DNA band gap<sup>4</sup> of 2.0 eV to much smaller values of 0.65 eV for Zn-DNA, 0.50 eV for Co-DNA, and 0.27 eV for Fe-DNA. This makes much more plausible the prospect of achieving wires with good conduction properties. Such a doping might be achieved naturally

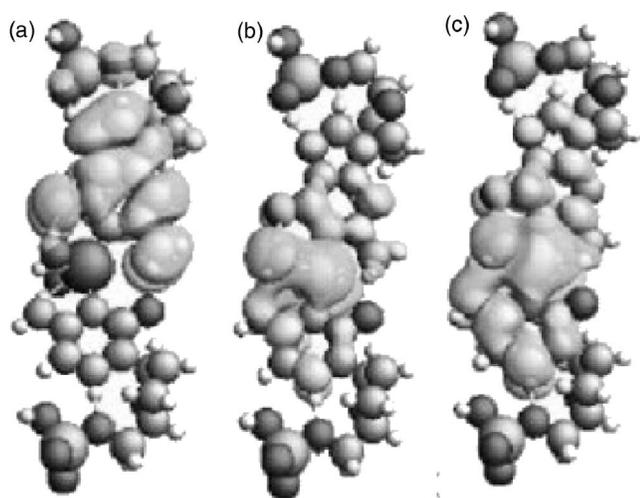


FIG. 6. Isosurface of constant electron density of the highest occupied molecular orbital in a monomer of (a) Zn-DNA; (b) Co-DNA; and (c) Fe-DNA.

by the presence of a variable concentration of counter ions attached to the phosphate groups after drying the wires. However, several effects must be taken into account. It is well known that DFT underestimates band gaps by as much as a factor of two. Also, real wires, even under nominally dry conditions, may have a number of water molecules attached to it. These polar molecules will tend to screen the electric field produced by the electrons in the occupied states, lowering their energies relative to the empty states<sup>33</sup> and thus increasing the band gaps. Finally, the conductivity of one-dimensional systems is very sensitive to the presence of disorder, which has not been considered in our calculations. Disorder will be introduced naturally by the potential created by water molecules and counter ions of the phosphate groups, as well as by the interaction with a supporting surface. Although it is unfeasible to simulate all these effects in a fully rigorous and realistic way, we need as many theoretical clues as possible to address the physical plausibility of achieving conducting wires, in order to orient the experimental efforts.

The sensitivity to disorder depends critically on the dispersion and spatial continuity of the band states responsible for conduction, i.e., on the width of the highest occupied (HOMO) and/or lowest unoccupied (LUMO) bands. Figure 5 shows the total density of states and the Mulliken partial density of states on the metal ion, for the three wires studied. We can see clearly that, in Zn-DNA, the states with a large weight in the metal ions are far from the Fermi level, what might suggest that Zn incorporation has a small effect on the conductivity. On the contrary, the states close to the Fermi level in Co-DNA and Fe-DNA have a large weight in the metal cations.

The same effect can be seen in Fig. 6, which shows an isosurface of constant density of HOMO states for the M-DNA monomers.

This state would be most involved in conductivity by holes, which would be the type of doping that might occur if some of the phosphate counter ions were missing after drying. In Co-DNA and Fe-DNA the HOMO states are localized around the metal ion, suggesting a large conductivity effect along the metal-hydroxyl chain. Contrarily, in Zn-DNA, the HOMO is strongly localized in guanine, as in pure DNA,<sup>4</sup> what raises the question of why the HOMO band of Zn-DNA is so much wider. The answer is in Fig. 4, which shows how the deformation produced by the Zn ion decreases the distance between consecutive guanine bases, and increases their  $\pi$ - $\pi$  hopping matrix elements, even though the stacking area of consecutive guanines is significantly reduced. A similar effect occurs for the LUMO states. As a result, the conductivity of all three Zn-DNA, Co-DNA, and Fe-DNA can increase drastically over that of pure DNA, although the mechanisms would be completely different. In addition the enhanced  $\pi$ - $\pi$  stacking effect in Zn-DNA suggests a new possible route to increase DNA conductivity, in which chemical modifications (not necessarily incorporation of metals) or externally induced strains, produce deformations that increase the stacking.

In conclusion, using *ab initio* calculations, we have found a stable structure for divalent metal-DNA complexes. Its main structural characteristic is a chain of *M*-OH, in which the metal cations are bonded to guanine and cytosine, replacing an imino proton. We have also determined the electronic structure of the metallated poly(dC)-poly(dG) complexes, with  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ , and  $\text{Fe}^{2+}$ . We find a large reduction of the energy gap in all three cases, which is more pronounced for the Co and Fe wires. Furthermore, in these two cases, the electronic states associated to the metal ions have a large weight around the Fermi energy, and specifically on the HOMO band. On the contrary, the HOMO and LUMO of Zn-DNA are localised on guanine and cytosine, as in pure DNA, and the states associated to the Zn ion are far from the Fermi level. This makes the binding in Zn-DNA resemble more that of a chain of cations in an insulating ionic compound. This is not surprising, given that the  $\text{Zn}^{2+}$  ion has a closed electron shell, while  $\text{Co}^{2+}$  and  $\text{Fe}^{2+}$  have open shell configurations. Despite this, the HOMO and LUMO bands of Zn-DNA are much wider than in pure DNA, and the energy gap is much narrower, due to the increased  $\pi$ - $\pi$  stacking produced by the strong deformations. All those evidence suggests that M-DNA chains are semiconductors with good conducting properties when suitably doped.

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