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Review article

M-DNA: A novel metal ion complex of DNA studied by fluorescence techniques

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Abstract

M-DNA, a complex formed in solution between divalent metal ions (M) and duplex DNA, has been studied extensively using fluorescence quenching. This review examines the methods used to examine the formation of M-DNA, and its ability to serve as a pathway for electron transfer between donor and acceptor chromaphores. A mass action model for M-DNA formation is presented based upon the results of fluorescence quenching studies using fluorescein/QSY-7 labeled duplexes. From the mass action analysis, it was determined that ~1.4 protons are released per base pair, with k_{eq} on the order of 10^{-8}, indicative of a strong interaction. As resonance energy transfer is shown to be unlikely over the distances involved in this work, the observed quenching in M-DNA is discussed in terms of an electron hopping mechanism for electron transfer, with $k_{hop} = 2.5 \times 10^{11}\ s^{-1}$.

Keywords: M-DNA; Metal ion complex; Fluorescence quenching; Energy transfer; Electron transfer; Mass action

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1. Introduction

A recent report by the Royal Society states that “Nanoscience and nanotechnology are widely seen as having huge potential to bring benefits in areas as diverse as drug development, water decontamination, information and communications technologies, and the production of stronger, lighter materials” [1]. In the area of information technology, miniaturization is recognized to be the driving force with respect to future development in the industry; indeed, the International Technology Roadmap for Semiconductors has established a 90 nm length dimension as a manufacturing standard for memory cells in 2004, and anticipates a standard of 22 nm in 2016 [1]. It is recognized that advances in nanoscience have the potential to alter such a timeline, particularly if there are successes in the development of molecular wires. Research in the area of molecular wires is particularly focused on so-called “bottom-up” technologies, i.e., systems which are in part constructed atom by atom or molecule by molecule either through chemical synthesis, self-assembly, or positional assembly (using scanning probe microscopy and related techniques).

Of particular interest for the design of self-assembling molecular wires are biopolymers such as DNA [2]. In addition to being self-assembling, DNA has other advantageous features such as molecular recognition, that could serve as input/output mechanisms in the design of molecular electronics. A major drawback with the application of DNA to molecular wire development has been its capacity for electron transfer. Reports of electron transfer and/or conductivity for the common B-DNA structure have resulted in behaviors ranging

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from insulating [3,4] to semi-conducting [5–7] to conducting [8–10]; however it is generally agreed that the conductive properties must be improved if there is to be true potential for the application of DNA as a molecular wire. A recently reported complex of DNA, termed M-DNA (where M stands for divalent metal ions), provides an excellent opportunity for improving the electron transfer/conductive properties of DNA, without destroying the attractive molecular recognition properties. M-DNA is a complex of DNA and divalent metal ions, which forms spontaneously in aqueous solution under certain conditions of pH and metal ion concentration [11–14]. The proposed structure of M-DNA (based upon NMR, CD, and molecular modeling studies) consists of GC and AT base pairs, in which the imino proton of G and T have been replaced by a Zn^{2+} ion [12,14], resulting in an atomically thick "wire" of zinc ions sheathed by a DNA helix (Fig. 1).

The electron transfer/conductivity properties of M-DNA have been studied through direct measurement of the conductivity and by electrochemical methods [6,15–20]. Direct measurements of conductivity have shown M-DNA to exhibit metallic-like conduction [6]. Electrochemical studies of self-assembled M-DNA monolayers on gold surfaces have shown electron-transfer rates to be comparable to those for bare gold surfaces, with the rate for B-DNA being too slow to be measurable [15].

Fluorescence methods have been extensively employed to study electron transfer processes in duplex DNA in general; either through the spectroscopic study of donor/acceptor pairs separated by a DNA duplex, or through an examination of G–G cleavage events (as a function of increasing numbers of intervening base pairs) resulting from oxidative damage. Rates of DNA mediated electron transfer have shown both fast ($k \sim 10^6$–10^8 s^{-1}) and ultrafast ($k \sim 10^9$–10^{12} s^{-1}) kinetics for donor/acceptor pair systems [21], while oxidative cleavage events have been shown to occur over distances as large as 200 Å [22]. From the recent literature, it is apparent that the mechanism of charge transfer in DNA remains somewhat elusive [21–23]. Mechanisms have been proposed that include: (i) simple hopping [24–27], (ii) a combination of hopping and tunneling [28] and (iii) a more complex phonon-assisted polaron-like hopping mechanism [22]. Recent reports tend towards a weakly distance dependent hopping model [29,30]; however conformational distortions resulting from base motion may allow for the adoption of conformations active towards charge transfer which facilitates charge delocalization and thus electron transfer [31,32].

This work reviews the results of our fluorescence studies of M-DNA and their impact on the understanding of the electron transfer mechanism in M-DNA specifically, and in B-DNA in general. In addition, new results are presented for additional donor/acceptor pairs

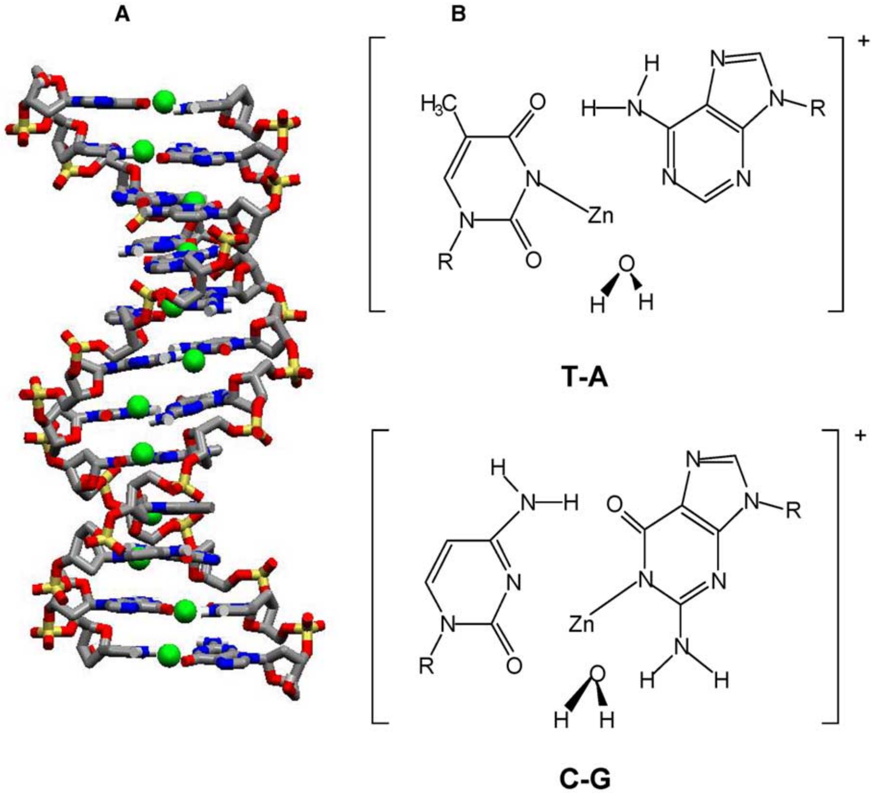

Fig. 1. Proposed structure (A, adapted from [12]) and base pairing (B) of M-DNA.