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Photogenerated radicals in DNA - Hairpin

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ABSTRACT
Synthetic hairpin DNA is a promising organic material for biosensors and for preparation of physical qubits for quantum information science. This paper demonstrates the base principles of the hairpin DNA synthesis and its biradical forms generated by ultraviolet radiation. Such radical pairs form initially entangled 2-qubit singlet spin states.

Keywords: hairpin DNA, photogeneration , biradicals , molecular qubits

1. Introduction

Deoxyribonucleic acid (DNA) is a well-known biological macro molecule in which the genetic information of all living organisms from plants to viruses, bacteria to animals and humans, is encoded. DNA not only encodes the necessary information for all cells, but also plays an essential role in the formation of all proteins and enzymes for these cells. Synthetically obtained short DNA chains (from a few to several pairs of nucleotides) are called Hairpin DNA (h-DNA) because of the characteristic shape of such a double DNA chain. Synthetic DNA hairpins with embedded photosensitive elements provide an excellent material for electron or hole transfer studies along DNA strands involving radical forms of its base fragments. The short forms of DNA have already found wide application in high-sensitivity biosensors [1]. Such biosensors are used in biology, medicine, engineering.

Ionising radiation or other forms of radical generators is main cause of oxidative DNA damage which may leads to a cancer. Therefore, the study of radical forms of DNA was primary tusk in diagnostic of genetic diseases. In this paper we present radicals generated in h - DNA by ultraviolet radiation.

2. Structure and chemical preparation of h-DNA

DNA is biopolymer which is formed by double right handed spiral chain. The backbone of the single chain are molecules of phosphate and deoxyribose. To each of such monomer, the base: adenine (A), cytosine (C), guanine (G), thymine (T) are attached forming monomer called nucleotide (Fig. 1).

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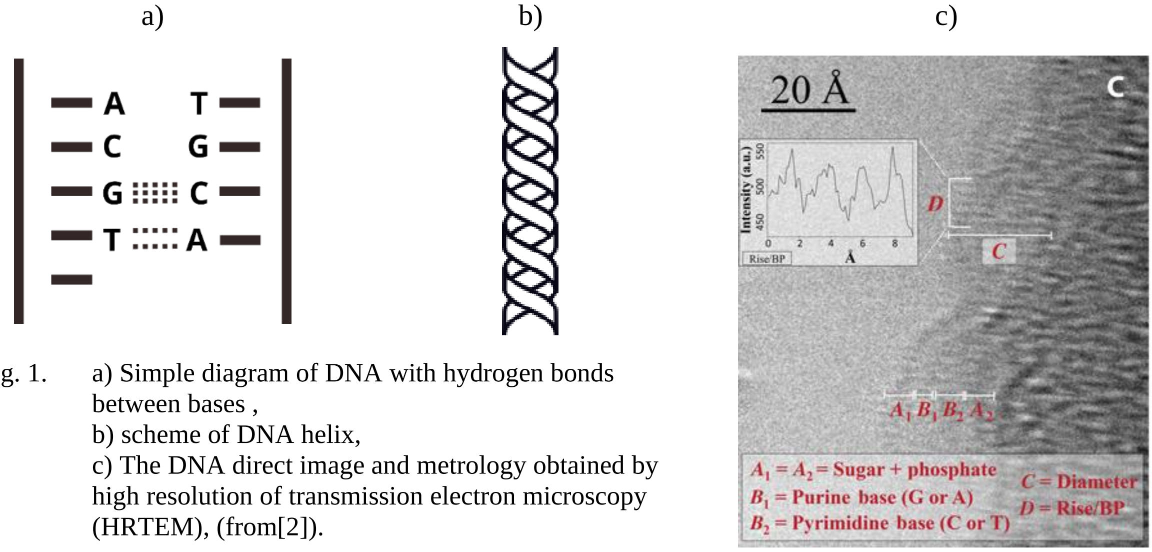

Fig. 1. a) Simple diagram of DNA with hydrogen bonds between bases ,
b) scheme of DNA helix,
c) The DNA direct image and metrology obtained by high resolution of transmission electron microscopy (HRTEM), (from[2]).

The bases are complementary connected between both chains (Fig.1b). Here complementary, means that an adenosine and a cytosine on one strand are connected with a thymine and a guanine on the second strand, respectively, forming a base pairs. The distance between neighbour nucleotides in the chain is 0.34 nm and the spiral lead is 3.4 nm.

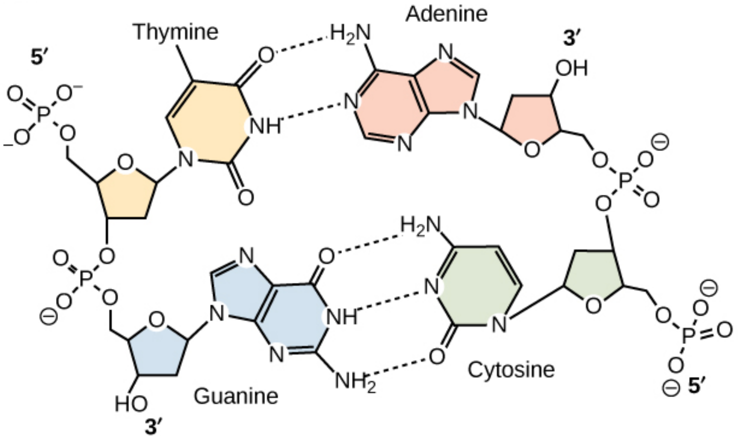

Fig. 2. Base nucleotides and electron bonds between complementary species. (from [3])

Many biochemical processes involving DNA produce short DNA fragments with a characteristic shape (Fig. 3a).

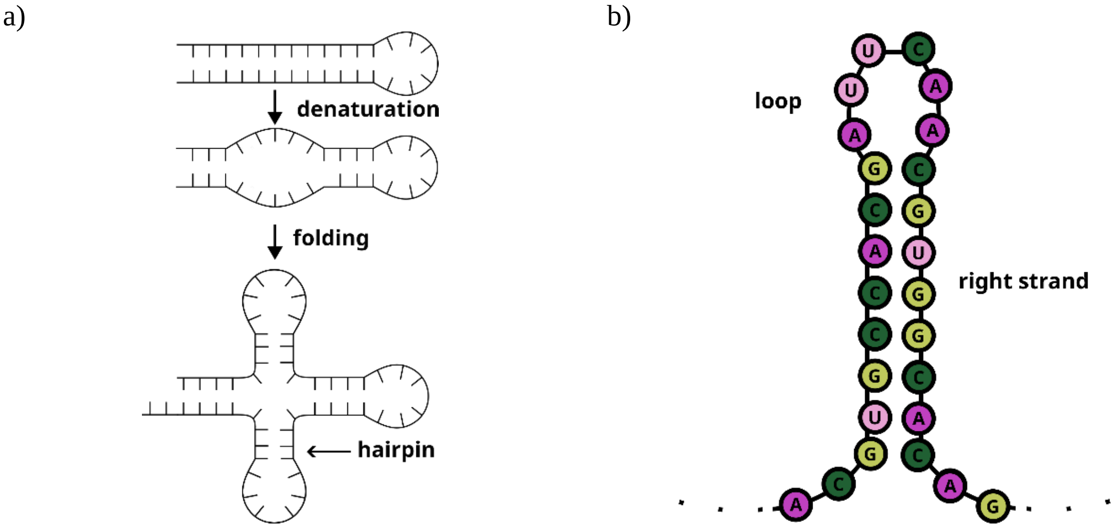

Fig. 3. a) Formation of cruciform DNA extrusions, b) scheme of hairpin DNA.

The explosive development of the artificial synthesis of nucleic acid-containing compounds was dictated by the application of these preparations in oligonucleotide – based therapeutics. The main strands of research into the synthesis of these compounds concern binding affinity, nuclease resistance, uptake, large scale synthesis, RNA folding, target accessibility, bioavailability, toxiticy, immune stimulation and many other [4,5].

The synthesis of h-DNA is binded with the long history of the synthesis of nucleic acids and chains of RNA and DNA initiated by Bob Letsinger between 1953 and 1965 (see Table 1). In fig. 4, the procedure used for preparation hairpin structures in which a loop is formed by chromofore molecule is presented [16].

Table 1. Historical development of chemical modifications and synthesis of oligonucleotides that contributed for approving of the oligonucleotide-based therapeutic.

Year	Method	Result	Application	Ref.
1953		Structure of DNA		Crick and Watson [6]
1955-1965		Initially synthesis of nucleotides and oligonucleotides		Tod et al. [7] Khorana et al. [8] Letsinger et al. [9]
1966	Phosphorothioates synthesis	Chemical modification of DNA (Phosphorothioates PS)		Eckstein [10]
1970	Phosphordiester approach	tRNA Synthesis	Alanine transfer ribonucleic acid from yeast	Agarwal et al [11]
1977	2' –O-TBDMS Chemistry			
1979		Synthesis and cloning of tyrosine tRNA gene		Brown et al. [12]
1984	Phosphoramidite approach	Automated DNA/RNA bioSynthesizer		Stec et al. [13]
1995	Second-generation antisense modifications 2'-o-(2-methoxyethyl)-RNA (MOE –RNA)			Martin [14]
1998-2018		Drugs: KYNAMRO, MACUGEN, ONPATRO, VITRAVENE, Etc. see Fig.3 and Table 1 in [15]	Oligonucleotic-base therapeutic See Table 1 in [15]	M. Egli and M. Manoharan [15]

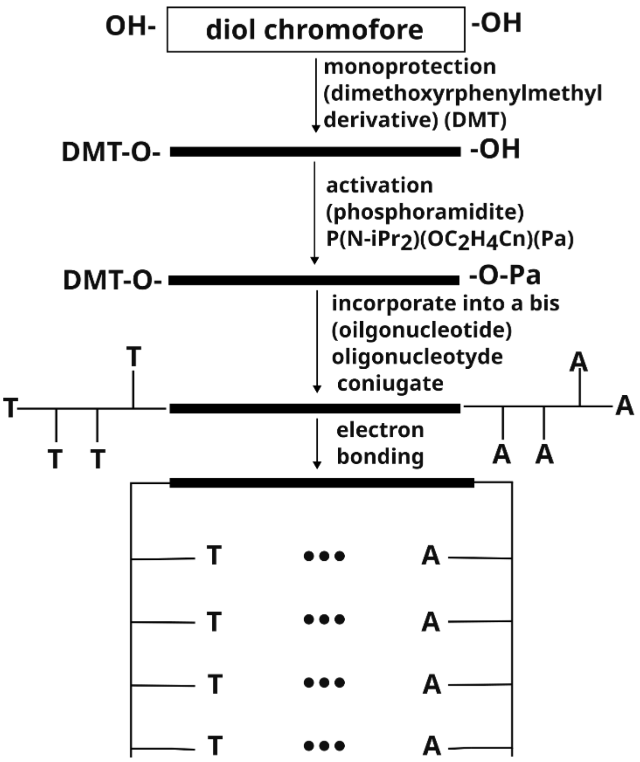

Fig. 4. Scheme of synthese of h-DNA molecule with a chromofore as a linker.

Olshansky et al.in papers [17, 18] have prepared a series of h-DNA with variuos number of pairs nucleotydes T-A and C-G in which naphtalenediimide (NDI) was the chromofore and a stilbenedieter (Sb) or tetratiofulvalene (TTF) were attached to the end of the chain as a termination (see Fig.5).

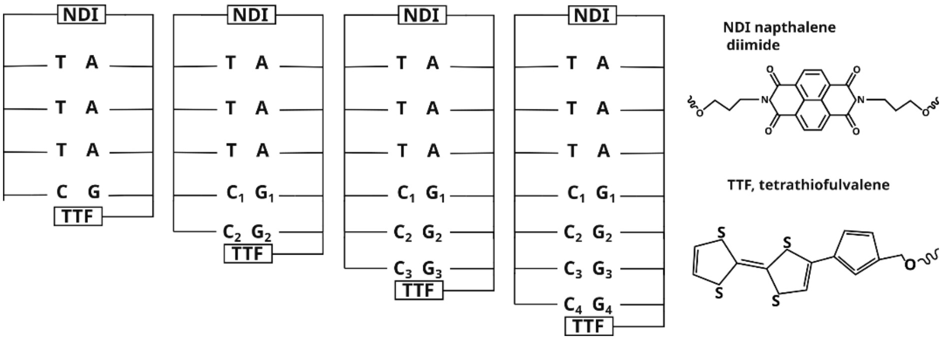

Fig. 5. Synthetic h-DNA with NDI (naphtalenediimide) linker and TTF (tetrarathiofulvalene) termination.

3. Photoexcitation in h-DNA

DNA photoexcitation processes have been thoroughly investigated on the basis of the rules of quantum mechanics (see e.g. [19]). The basic theoretical model of DNA chain photoexcitation is the Frenkel exciton model. In this model, the excitation of a DNA strand is a coherent jump of an electron from a base to a neighbouring base. The total excited state of the chain is a superposition of local photoexcitations. The basic parameter of the photoexcitation is the electronegativity difference between adjacent bases and can be regarded as an approximation of the dipole-dipole coupling represented by the donor-acceptor. Cohen and co-workers [20] experimentally showed that vertical base stacking, and not base pairing, determines the fate of excited singlet electronic states in single - and double - stranded oligonucleotides composed of adenine (A) and thymine (T) bases.

Energy diagram of the photogenerated radical pair in an donor-acceptor molecule is shown in Fig. 6. UV light absorption transfers molecules from the electronic ground state D-A, to the optically allowed Franck–Condon singlet state $^1A^*$. Thus the initialy state of the RP is singlet state. Photoexcitation produces singlet state. Singlet states undergos coherent evolution in time to the triplet and interconvert before decoherence. The coherence means that random phase is preserved [21].

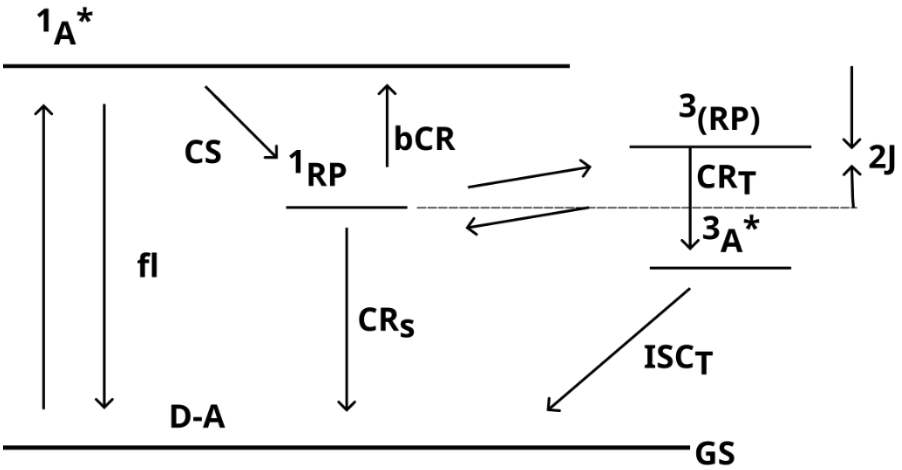

Fig. 6. Energy diagram of photogenerated singlet-born rdical pairs : fl - fluorescence, CS - charge separation; bCR -back charge recombination; CR_S-singlet charge recombination; CR_T- triplet charge recombination; ISC_T = intersystem crossing between local triplet excited and ground states, J – exchange interaction.

4. Evolution of the radical state of h-DNA. Biradicals

The excited state of the linker manifests itself by the absence of one electron.The transfer of an electron from the first base molecule to the linker causes this excited molecule to become an $D^{\bullet-}$ radical. At the same time, the base molecule has lost an electron and so is an kation $A_1^{\bullet+}$ radical. This creates the $D^{\bullet-}$ - $A_1^{\bullet+}$ radical pair (RP) (see CS transition in Figure 7). The jump of an electron from the second base to the first causes the radical state of the second base molecule $A_2^{\bullet+}$. The effect of this action is the movement of a hole along the chain. The distance **r** between radical spins increases with successive electron/hole jumps. The dipole energy of the interaction of such system of radicals decreases in proportion to $1/r^3$ and is lowest when the unpaired electron/hole is on the terminal donor end cap molecule. A scheme of the above process is shown in Fig. 7 a,b,c,d and the energy levels of the various stages of biradical formation are shown in Fig. 7e. Note the almost degenerate energies of the same base molecules.

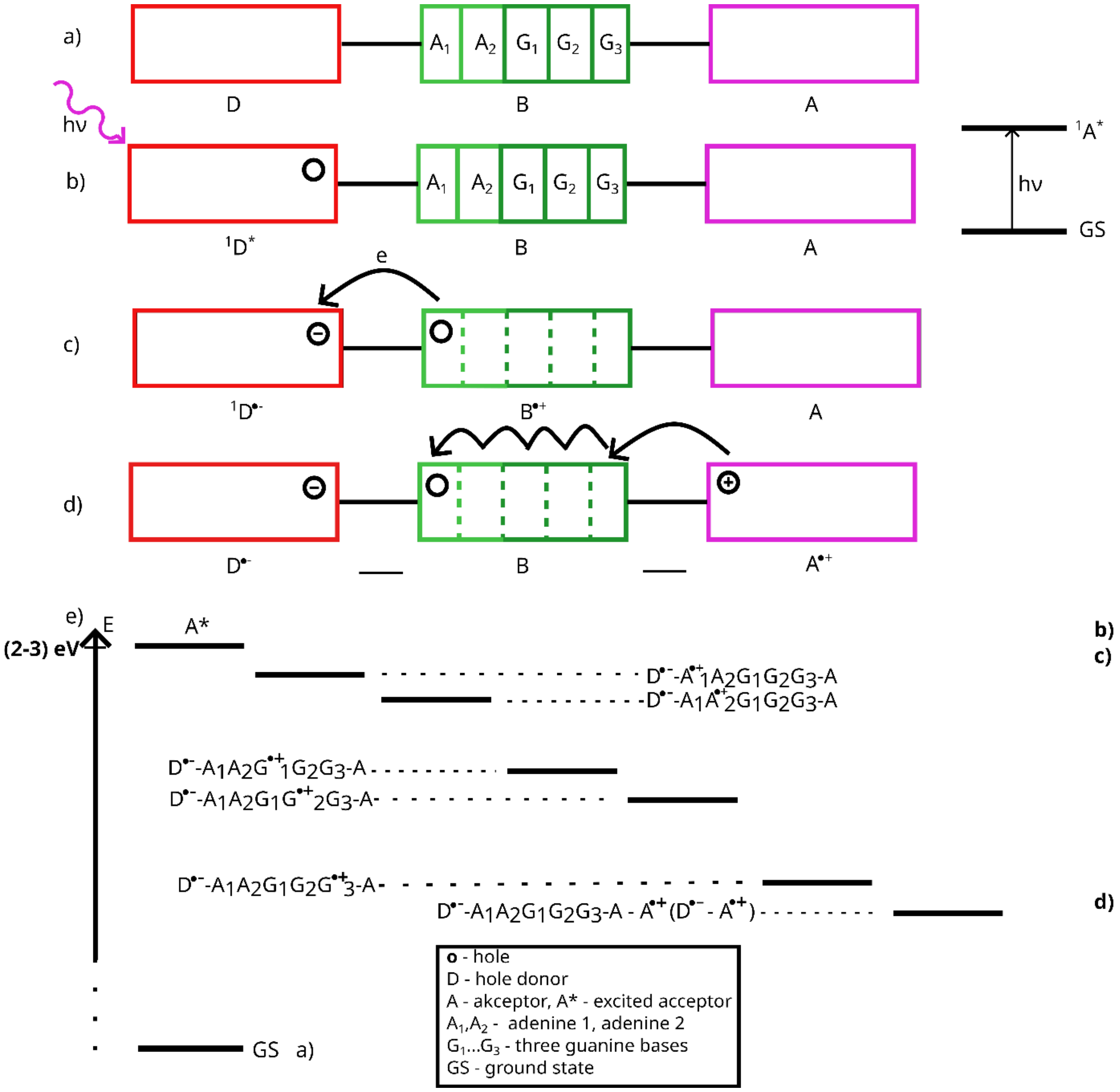

Fig. 7. Evolution of the radical states in the hairpin DNA: D - A_1A_2 G_1 G_2 G_3 - A, (D - hole donor, A_m G_n adenine and guanine bases respectivelly forming bridge B, A – hole akceptor). a) grand state of the hairpin DNA, b) excited state, (molecule D becomes the hole donor, c) transfer of the hole from D^+ to the first adenine base, d) consecutive transitions of the hole within bridge liding to the final biradical. (arrows represent electron transfer). e) evolution of the energy of the system after fotoexcitation.

5. Biradical model of the magnetoreception in migratory animals

Many species of animals, birds, fish, insects, insects, can travel many kilometres, or thousands of kilometres, with the ability to return exactly to the place from which they started their journey.

There are several theories describing this phenomenon [22] one of which is a mechanism based on biradicals suggesting that a coherent quantum mechanical interconversion mechanism between the singlet and triplet states of the biradical is responsible for the orientation of the molecule relative to the Earth's geomagnetic field. The Earth's magnetic field is weak: 25-65 μT. Such a weak field cannot change the rotational or oscillatory state of the molecule responsible for detecting this field because the thermal energy of the system is much higher and causes chaos in the state (e.g. orientation) of the molecule. However, a small magnetic field can change the state of the biradical formed on this molecule. But to form a biradical you need a quantum of energy of quite high energy e.g. UV radiation (2-3 eV). This is the process of photo-excitation of the molecule leading to the biradical.

P. J. Hore [23] gives an interesting mechanical analogy of the action of a weak factor, e.g. a magnetic field (in Fig.8, a bee illustrates this field) on the state of a molecule represented by a lump of stone (Fig. 8a). One bee will not change the arrangement of the lump in Fig.8a. However, an external agent of high energy can bring a solid into a state of unstable equilibrium (Fig. 8b). It can overturn either to the left or to the right. However, if a bee, whose mass is negligible in relation to the solid sits on the right face of the solid, the solid will roll to the right (Fig. 8c).

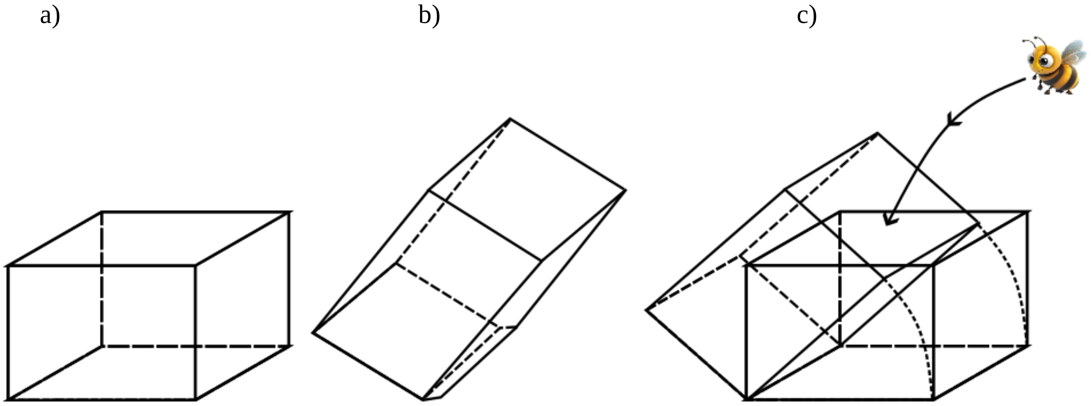

Fig. 8. Mechanical analogy of properties of radical pair in molecule.

6. Summary

DNA is one of the most important macromolecules in biology responsible for the life and development of all organisms. A small fragment of this macromolecule is the DNA hairpin. This is DNA containing a few or several nucleotides. The synthesis of such molecules with an assumed composition and architecture is already well established. Hairpin DNA containing, instead of a loop, a chromophore molecule (e.g. naphtalenediimide NDI) in which one end of the chain is terminated by an acceptor molecule (e.g. stilbene diether Sd) is sensitive to UV radiation. The effect of UV on h-DNA is the generation of an NDI$^{\bullet -}$ - Sd$^{\bullet +}$ biradical. Such biradicals on h-DNA have versatile applications in medicine and biology, e.g. new forms of photodynamic therapy, new biological sensors. Spectacular applications of h-DNA biradicals are proposals to create cubit arrays for quantum computing . The mysterious navigational properties of living organisms are attempted to be explained on the basis of the high sensitivity of h-DNA biradicals to the weak magnetic field of the Earth.

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