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Engineering DNA and Nucleobases for Present and Future Device Applications

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7.1 The Versatile World of Nucleic Acids

7.1.1 Introduction

Deoxyribose nucleic acid (DNA) is a marvelous molecule to behold in its biological world. Transcription, translation, and replication are self-perpetuated processes for genetic expression, which all depend upon the intricate structure, organization, and special affinities of the nucleobases in the long DNA double helix [1]. Beyond biological intent, these same self-assembling mechanisms have inspired seeds of research in unconventional uses of DNA for the past 10–20 years. For example, computer scientists are building DNA-based information storage [2–4] and biological computing [5, 6] inspired by its ability to organize incalculable amounts of biological data into well-defined libraries. Nanotechnology engineers and scientists leverage the Lego®-like molecules into building blocks for elaborate nanoscale structures [7]. The long polymeric chain and negatively charged backbone, which resemble the beginning of a molecular wire, have spurred electrical engineers and material scientists to investigate electronic charge transport properties and atomic-scale electronics. We are just beginning to learn what DNA can do outside of the cell in various practical applications, such as electronic devices, nanotechnology, biosensing, information storage, and molecular engineering. Increased collaboration between different DNA fields will yield exciting new devices that control electronic and nanostructure precision with dynamic or modular platforms.

This chapter highlights several burgeoning areas of DNA electronics, nanotechnology, and molecular engineering and focuses particularly on how these three areas have shared interest for future DNA-based applications. However, the breadth of these topics is very large for a single review chapter and readers will greatly benefit from additional material in existing reviews of DNA-related subtopics. DNA in electronic applications has been the subject of several reviews, including photonic/electronic devices [8, 9] and electron transport [10, 11]. The material science of DNA was reviewed in an article [12] and was the subject of a

Green Materials for Electronics, First Edition.
Edited by Mihai Irimia-Vladu, Eric D. Glowacki, Niyazi S. Sariciftci, and Siegfried Bauer.

collection of chapters [13] covering a wide range of topics from fundamental science to electronic devices. Other notable reviews on the accomplishments of DNA origami and self-assembled structures in DNA include nanotechnology [7, 14], molecular engineering [15], and sensors [16, 17]. Although it is difficult to list all of the important reviews and contributions, the most recent work is summarized in this chapter. Additional discussion is also included on the nucleic acid bases (nucleobases), which recently have become a focus as "green" material for electronics and are showing great promise [18].

Figure 7.1 shows the three major fronts that have propelled DNA as a material for electronic and nanostructure research (primarily from a device and application emphasis perspective). The first area of research is "DNA organic electronics." This particular field of research capitalizes on key electronic properties of DNA and/or of the nucleobases for thin-film organic devices, such as the organic field-effect transistors (OFETs) and organic light-emitting diodes (OLEDs), in order to optimize device charge transport properties and improve performance. The second research area is DNA nanotechnology, which uses DNA building blocks for nanostructures, ranging from simple 2D structures to complex nanomechanical devices. The field is often called DNA origami because of its ability to fold onto itself, forming complex structures made possible by the affinities of nucleobases for each other. The third field is "DNA molecular engineering,"

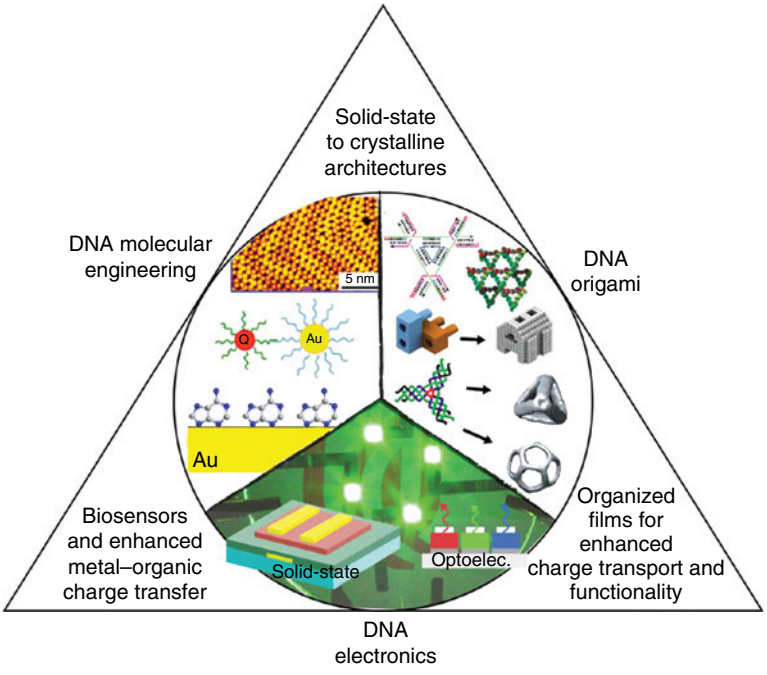


Figure 7.1 The circle encompasses the three major fields of DNA research in electronics and nanotechnology: (1) DNA origami – intermolecular bonding to form nanostructures [19–22]; (2) DNA molecular engineering – the interaction of DNA with non-DNA molecules [23–25]; and (3) DNA electronics – electronic properties in traditional solid-state devices [18]. The vertices of the triangle describe how the adjacent research fields relate to one another.

somewhat similar to DNA origami, but focusing on using DNA as a scaffold for bonds between nanoparticles. Molecular engineering also encompasses the interesting property of nucleic acid affinity for many metal electrodes, which has led to applications in biosensing and in improved metal/organic charge injection.

The vertices of the triangle in Figure 7.1 represent the fields of common interest between the three DNA-based research areas. DNA origami, for example, benefits the DNA electronics area by coupling known DNA electronic properties with self-assembled crystalline thin films to optimize device performance. DNA molecular engineering provides extensive knowledge in nucleic acid affinity to metal electrodes, which improves charge transfer between metal and organic materials and in turn creates improved biosensors. Finally, DNA molecular engineering, while very similar to DNA origami, incorporates additional functional materials, such as nanoparticles or quantum dots, into DNA scaffolds to expand material and application functionality. The triangle represents a rather simplistic view of DNA research, considering that there is an immeasurable amount of study done on the biopolymer, including research on chemical, material, genetic, and biological aspects. The discussion presented in this chapter is treated primarily from a device-oriented point of view that looks forward to applications of DNA science.

7.1.2 Natural and Artificial Synthesis Sources of Nucleic Acids

Natural DNA polymer is only 2–3 nm wide, but is composed of two conjoined nucleotide chains that can be billions of base pairs long. As illustrated in Figure 7.2, the two chains form a double-helix structure bound together by hydrogen bonds between nucleobases. Nucleotides are comprised of a phosphate group, a pentose, and a nitrogenous base (nucleobase). The DNA nucleobases are guanine (**G**), adenine (**A**), cytosine (**C**), and thymine (**T**). The ribonucleic acid (RNA) polymer, an important nucleotide chain for translating the DNA code into proteins, contains the bases **G**, **A**, **C**, and uracil (**U**). **G** has three hydrogen-bonding sites that pair with **C**, and **A** has two hydrogen-bonding sites that pair with either **T** or **U**.

Green electronics – the subject of this book – focuses on materials from environmentally responsible sources. Figure 7.3 lists a few of the natural and synthetic sources of DNA and nucleobases. DNA is found in the nucleus of every living cell, and can be extracted from plants and animals. Some sources have higher concentration of nucleic acids than others and it is easier to extract more DNA or nucleobases per volume. Salmon sperm, for example, is rich in DNA and has the added benefit of being a waste product of the fishing industry. The refining process begins by mechanically pulverizing the tissues, removing unwanted material by physical and chemical processes, combined with filtering and centrifugation to isolate pure DNA [26].

The nucleobases have historically been extracted from natural sources. Some non-mammalian sources such as wheat germ, bee pollen, and plants are known to be rich in certain bases [27–31]. The thymus, pancreas, and even bird feces are traditional sources from which bases are extracted by physical and chemical purification processes and then dried into a powder. Yeast naturally produces

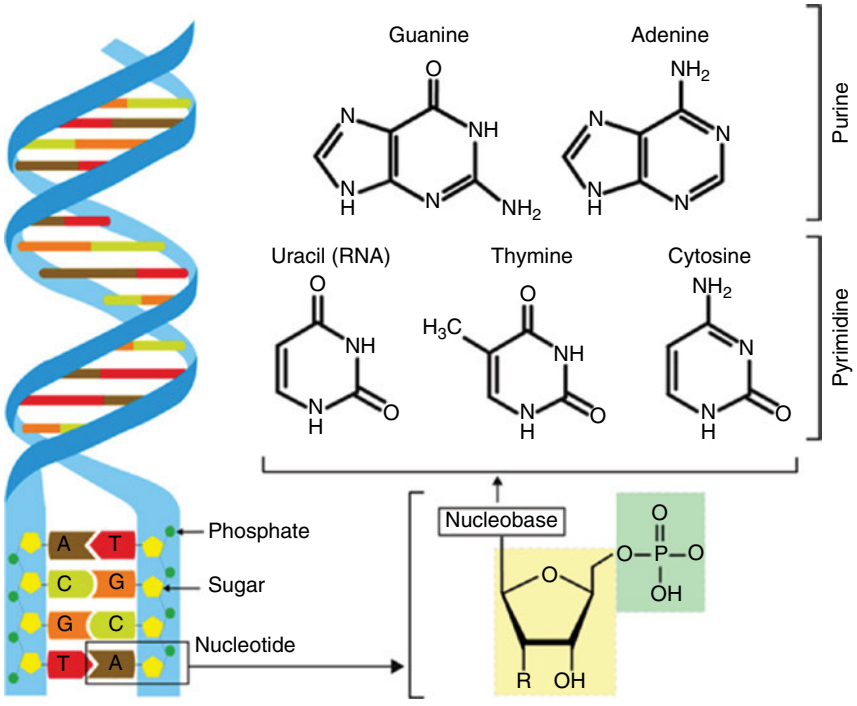


Figure 7.2 The DNA double helix consists of two interlocking and twisting chains of nucleotide units, each comprised of a sugar group, a phosphate group, and a nitrogen-containing nucleobase (either a pyrimidine or a purine). (Gomez *et al*. 2014 [18]. Reproduced with permission of John Wiley and Sons.)

	DNA	Nucleobase
Natural origin	Organ tissue Plant cells Salmon sperm	Biosynthesis (liver) Yeast Bee pollen Organ tissue Bird excrement Wheat germ
Synthetic	Solid phase synthesis Polymerase chain reaction (PCR) Molecular cloning	Abiotic reactions Fischer–Tropsch synthesis

Figure 7.3 Selected sources of natural and synthetic DNA and nucleobases.

phosphoribosyl pyrophosphate (PRPP), which is the precursor that catalyzes the synthesis of purines and pyrimidines [32, 33]. It is also known that the body metabolically produces the bases in the liver [27, 34].

Although natural sources are more desirable for green and sustainable electronics, nucleobases and DNA can also be created using synthetic processes.

Most of the bases can be derived from the Fischer–Tropsch synthesis by heating a gas mixture of CO, H_2, and CH_3 to 600 °C with a nickel–iron catalyst [35]. It also possible, although more hazardous, to create adenine from ammonia and hydrogen cyanide, as demonstrated from the work done on precursors to abiotic nucleic acids [36].

Naturally derived DNA is not always suitable for DNA nanotechnology, which requires sequence-specific strands. Oligonucleotide synthesis (a form of solid phase synthesis) has been a standard method for many years for constructing a particular DNA strand [37]. The polymerase chain reaction (PCR) is one of the most successful methods for replicating DNA strands from an existing template using an enzyme [38]. Another method, the so-called molecular cloning, can assemble DNA with cloning sites of plasmids or viral vectors in prokaryotic or eukaryotic sources [39]. While synthetic methods are available, extraction from natural sources offers the best pathway to produce large quantities of material that are relatively inexpensive and sustainable, and avoids hazardous precursors produced by artificial synthesis.

7.2 Nucleic Acids in Electronics

7.2.1 Introduction

The long DNA polymer has inspired early investigations of charge transport along its chain to adapt it as a nanowire [40]. Early studies also looked into DNA as a host for enhanced optical emission [41] of lumophores intercalated in the double-helix structure. The result was a wave of interest in using the material in organic electronics and intense investigation into DNA as an opto/electronic organic material [42]. Although attempts were made to deposit natural DNA salt (DNA^-–Na^+) into thin-film electronics, formation of uniform films from aqueous solutions was found to be difficult [43]. Therefore, the molecule was often complexed with cationic surfactants (e.g., CTAC cetyltrimethyl ammonium chloride) to its negatively charged backbone to form DNA–surfactant salts, such as DNA-–CTMA (cetyltrimethylammonium). The complexed chain could then be dissolved in alcohols and spin-coated [44].

There is a fundamental incompatibility between biomaterials and conventional organic molecules used in organic electronics, as pointed out by Solin and Inganäs [45]. Biomolecules have naturally evolved in a water-based environment and are hydrophilic, containing polar functional groups, whereas organic electronics generally use materials (polymers or small molecules) that have few polar groups and dissolve in organic solvents. A key question of both fundamental and practical importance is how the surfactant molecules alter the electronic as well as structural properties of the DNA, changing from being water soluble to organic solvent solubility, and then undergoing the critical "wet-to-dry" transition.

Interestingly, studies have indicated [46] that the DNA–surfactant complex in both wet (organic solvent solution) and dry (thin film) forms displayed chirality similar to that of DNA in aqueous form. This was explored by selecting combinations of surfactants and dye molecules that resulted in enhanced optical

characteristics. Both anionic (sulforhodamine SRh) and cationic (rhodamine perchlorate RhP) fluorescent dye molecules from the rhodamine family were found to be most likely embedded in the tails of the CTMA–surfactant molecules [47] radiating from the DNA chain rather than intercalated into the DNA double helix itself. A simplified model for this explanation is illustrated in Figure 7.4.

Early work with DNA–CTMA showed impressive versatility when incorporated as a dry film in many different types of devices, including OLEDs [42, 48], lasers [49], OFETs [50], and optical waveguides [42, 51]. However, the DNA–surfactant complex approach does present some complications in proceeding forward with next-generation devices: (i) the surfactant, a synthetic material, consists of a significant fraction of the overall complex, taking away from the goal

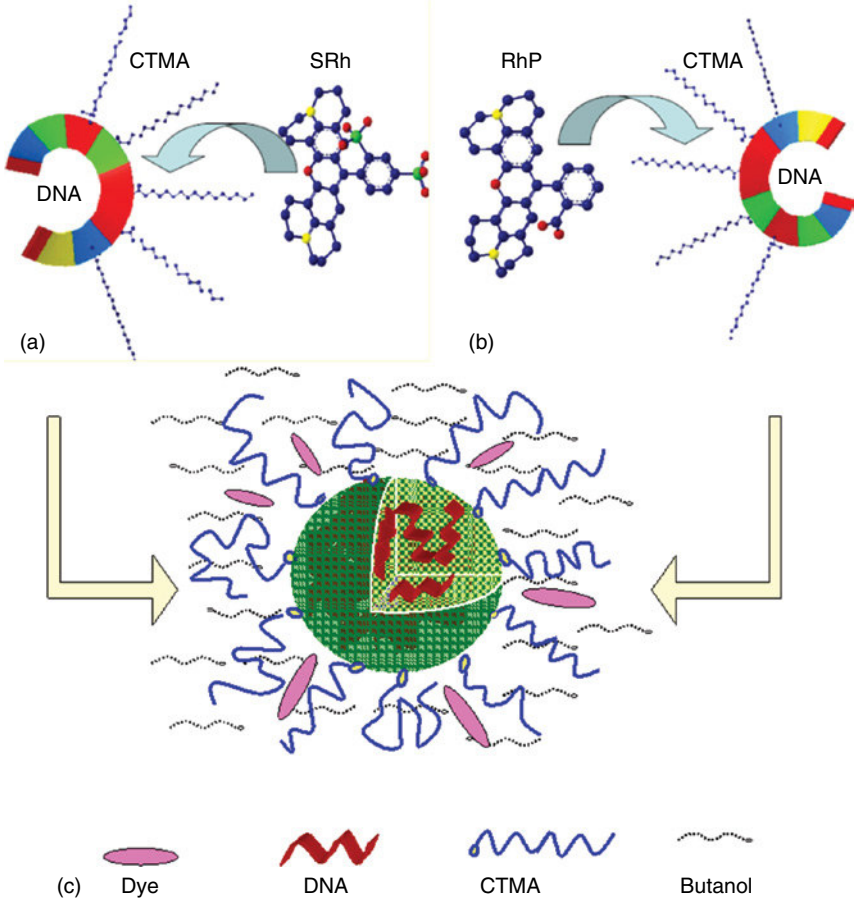


Figure 7.4 Proposed model for incorporation of (a) anionic (SRh) and (b) cationic (RhP) fluorescent dye molecules inside the DNA–surfactant (CTMA) polymer in organic solvent solution. (c) The final structure of the butanol in a micelle-like complex: DNA form together (green) and the dye (either SRh or RhP), intercalating between the CTMA strands on the outside. (You *et al*. 2009 [47]. Reproduced with permission of American Chemical Society.)

of all-natural devices; (ii) in terms of understanding and utilizing material characteristics for optimized device performance, the molecular complex makes it difficult to distinguish the electronic properties of the DNA polymer from those of the surfactant; (iii) thin-film fabrication is primarily limited to wet processing (e.g., spin-coating) in organic solvents; and (iv) the DNA complex fails to complement the working knowledge of the powerful techniques of DNA origami and molecular engineering that rely on affinity-based assembly rather than film formation of lipid films. This fourth point is especially pertinent to the future success of DNA electronics. DNA represents a unique class of organic materials that offers a potential of precise molecular control not typically offered by conventional organic electronics. Complexing the DNA with surfactants limits self-assembly properties. Retaining its ability to form well-ordered structures without the surfactant will be vital for DNA to flourish as an important material for nanotechnology and electronics.

Nucleobases, which are just beginning to emerge in organic electronics, may be able to provide more flexibility in material choice and properties. The nucleobases require no surfactant modification since they form high-quality thin films by thermal evaporation and readily integrate into typical organic electronic processes. In addition, nucleobases have a range of properties identified with its respective molecule, whereas in the case of DNA one has to resort to varying the polymer molecular weight and possibly the sequence of the polymer in order to modify charge transport and optical properties [52]. A discussion of the various known properties is presented in the next section.

7.2.2 Thin Film Properties

DNA–CTMA thin films have been well characterized, including their electrical, optical, and magnetic properties [8, 10, 12, 13]. DNA–CTMA is well known to be a good electron-blocking layer (EBL) and hole transporter in organic semiconductor devices owing to its energy levels. It has a high dielectric constant of $\kappa = 7.8$ at low frequencies (and up to $\kappa = 14$ in ceramic blends) [53] and a dielectric breakdown of 3–5 MV cm^{-1} (in sol–gel blends [54]), which has been used in capacitors and gate dielectrics. It has low optical loss in the visible range and near-IR communication wavelengths in waveguides [51].

The nucleobases have not been characterized as extensively as DNA but are rapidly proving to be a versatile set of materials for thin-film electronics. Table 7.1 summarizes many of their initial known properties. Dielectric constants range from 1.6 to 4.3 and breakdown values range from 0.9 to 3.5 MV cm^{-1}. Interestingly, **G** and **C** (with three hydrogen bonding sites) have higher dielectric constants, whereas **A** and **T** (with only two hydrogen bonding sites) have lower values [28]. The refractive index varies from 1.50 to 1.96 and temperature stability ranges from 260 to 465 °C. **G** has higher temperature stability (due to intermolecular hydrogen bonding) as well as refractive index, and **T** has both the lowest stability and refractive index [18]. Additional work needs to be done to determine conductivity of the nucleobases as thin films.

Atomic force microscopy (AFM) of thin films of the nucleobases reveals a diverse range of film quality. AFM images of 100 nm nucleobase films thermally

Table 7.1 Optoelectric properties of thin-film DNA and nucleobases for organic electronic devices.

Material	Orbitals (eV) [18, 48]		Energy gap (eV)	Dielectric constant[a]	Refractive index[b]	Thermal stability (°C)[c]	Hole mobility ($cm^2 V^{-1} s^{-1}$)	Dielectric breakdown field ($MV cm^{-1}$)
	HOMO	LUMO						
DNA–CTMA	5.6	0.9	4.7	7.8	1.54	250	0.001–0.01	3.0–3.5[d]
G	5.7	1.8	3.9	4.0	1.96	465	—	3.5
A	6.0	2.2	3.8	3.4	1.73	290	—	1.5
C	6.2	2.6	3.6	4.3	1.76	325	—	3.4
T	6.5	2.8	3.7	2.0	1.50	260	—	0.9
U	6.7	3.0	3.7	1.6	1.67	270	—	—
References	[17, 46]	[17, 46]		[18, 53]	[17, 24]	[18, 55]	[56]	[28, 54]

[a] At ~1 MHz.
[b] At 515 nm [18, 26].
[c] 95% remaining mass.
[d] Sol–gel.

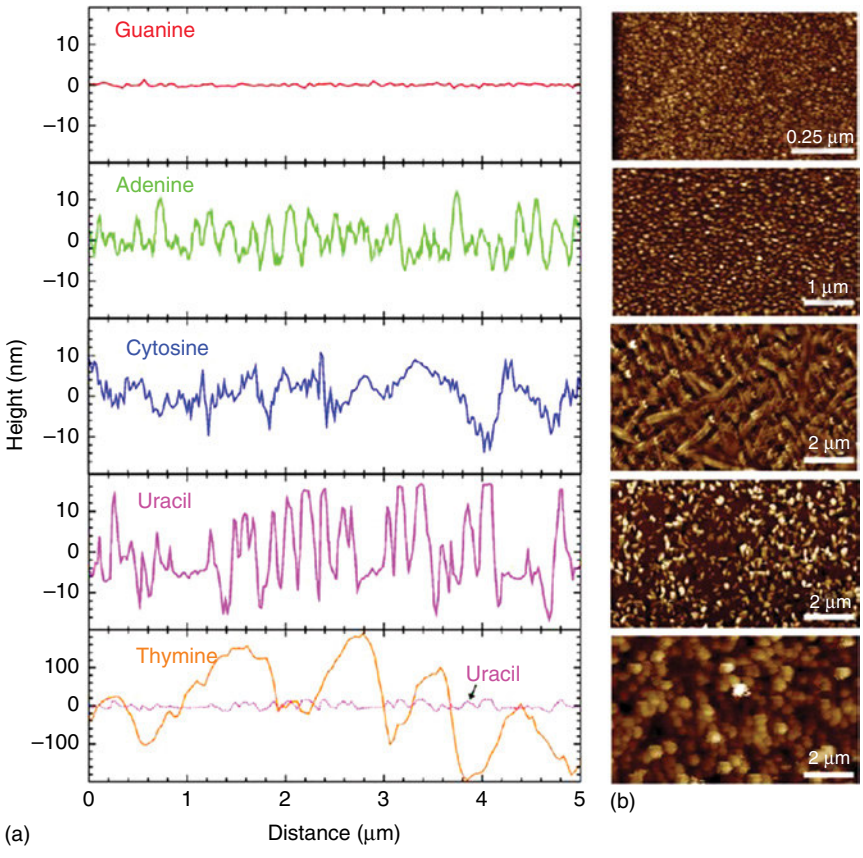


Figure 7.5 (a) Height distribution of nucleobase films sampled from corresponding AFM results and (b) AFM analysis of thin-film nucleobases (**G**, **A**, **C**, **U**, **T** from top to bottom, respectively) thermally evaporated to 100 nm on Si [57].

deposited on Si wafers are shown in Figure 7.5b. In order to compare the results, a cross-sectional view was created by sampling a 5 μm scan from each AFM image and the results plotted as vertical deflection versus horizontal distance in Figure 7.5a. The horizontal line scan was plotted on the same height scale, except for **T,** which is displayed in nearly 10 times larger in vertical range. The results show that the **G** film had the highest "quality" (i.e., lowest roughness) of the five bases with peak-to-peak range of under 1 nm, while the roughness of **T** was 100–1000 times greater than that of the other bases.

The energy levels of the nucleic acids cover a wide range of HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) values, enabling selection for optimized electron and hole transport in thin films. As shown in Figure 7.6, ITO, Au, and PEDOT have higher work functions (4.7–5.1 eV) and are often used as anodes for hole injection. Al electrodes coated with LiF have a lower work function (4.1–3.1 eV) and are typically used as cathodes for electron injection. In comparison, DNA–CTMA has low HOMO/LUMO levels of 5.6/0.9 eV, resulting in its successful electron-blocking/hole transport ability in OLEDs.

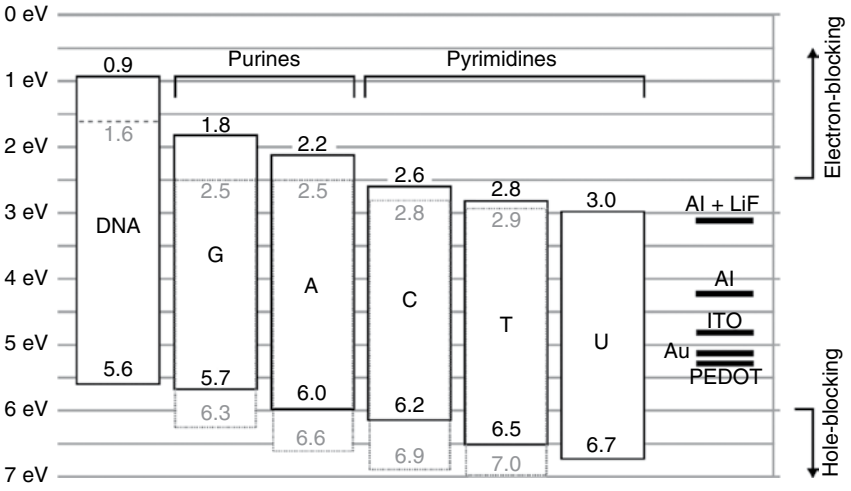


Figure 7.6 Energy levels of DNA and nucleobases showing that DNA and the purines are hole transporters while the pyrimidines have high energy levels and have electron transport abilities. Solid lines [18, 58] and dotted gray lines [59, 60] show two reported studies, as well as for DNA [48, 61].

The nucleobases have recently been explored for charge transport in thin film OLEDs demonstrating a large range of energy levels, and flexibility for charge transport control. The HOMO–LUMO energy gaps of the nucleobases are uniformly wide (3.6–3.9 eV), while the ionization potential (HOMO) increases monotonically, **G** < **A** < **C** < **T** < **U**, as seen in Figure 7.6. Consequently, **G** with the lowest ionization potential (HOMO) of 5.7 eV and an electron affinity (LUMO) of 1.8 eV is a strong hole acceptor while prohibiting electron transport. On the other hand, **U** has the highest ionization potential of 6.7 eV and the highest electron affinity of 3.0 eV, thus being a strong electron acceptor while prohibiting hole transport [18, 58]. Some variations in the reported studies exist [59, 62–66], most likely due to different measurement techniques and conditions, but the general trend among all studies is consistent. The introduction of the nucleobases has expanded the use of nucleic acids to both electron and hole transport (and blocking), offering a wide range of options for future device designs.

7.2.3 Nucleic Acids in Organic Electronic Devices

The impact of DNA-based materials in organic electronics has been surprisingly broad. This section will attempt to highlight several important devices, emphasizing some of the more recent devices and the use of nucleobases that would not have been included in past reviews.

Most of the studies and devices of DNA electronics originate from an enduring effort to verify DNA conductivity. The DNA molecule size and programmability leads it to be ideal for nanostructure electronics (see Section 7.3 for further discussion on DNA nanostructures). The first step in nanoelectronics is confirming long-range electronic conductivity along the DNA axis. It is beneficial to briefly discuss here the persevering efforts to elucidate the conduction mechanisms.

Early theoretical models [67] suggested that DNA is effectively a conducting wire and that there is sufficient delocalization to enable transport of charge over several nucleobase base pairs. It is generally believed that the conduction is via positive charge with short-range processes [68, 69]. The guanine molecule, having the highest energy HOMO, is widely accepted to be the primary carrier of the holes [69–71]. Theoretical simulation of a guanine-rich strand between two Au electrodes in Figure 7.7 shows the highest rate of hole hopping along strong localized orbitals from **G**. Despite this widely accepted model of charge transport along **G**, long-range electron transport has proved difficult to observe for a variety of reasons, resulting in a field saturated with contradictory or irreproducible results.

Many factors affect DNA–electron interactions, including electrochemical interactions with its environment and the substrates. One of the biggest difficulties lies in the intrinsic disorder and fragile nature of the native molecule with, apparently, even the slightest deformation skewing results thoroughly, as demonstrated by Heim *et al.* [72, 73]. Such changes are known to affect electronic properties from a conductor to insulator and certainly make it difficult to control any amount of current over any distance [74]. To further complicate matters, other studies [56, 75] suggested that the mechanisms of bulk material transport compared to single DNA strand are allegedly different.

In the reports, thin film layers of DNA–CTMA mobility values from ~0.001 to 0.01 $cm^2 V^{-1} s^{-1}$ were measured using time-of-flight techniques. The results suggested that the preferred routes of charge transport [75] was along the DNA backbone at low electric fields and laterally through the CTMA side-chains at high electric fields, instead of hole hopping along the nucleic acids as has typically been predicted.

A good overview of the complex nature of DNA charge transport chemistry has been summarized by Genereux and Barton [11]. A thorough review of the different reports since 2006 and comments on DNA conductivity is presented by

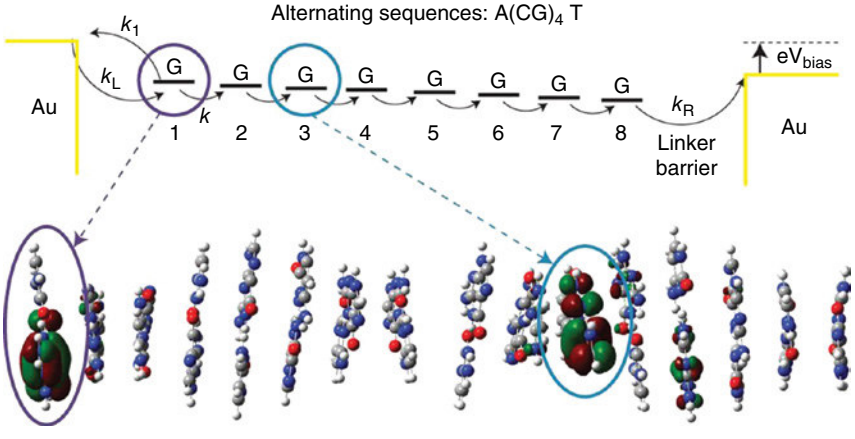


Figure 7.7 Hole hopping along HOMOs of the G bases in DNA contacted between Au electrodes in an electric field due to strong localized orbital levels in G. The hole transfer rates between G–G sites and G-electrodes are represented by constants *k*. (Xiang *et al*. 2015 [71]. Reprinted with permission of Macmillan Publishers Ltd.)

Taniguchi and Kawai [10]. The report concludes that conductivity results (ranging from insulating to semiconducting, and possibly metallic) depend on water content, base sequence, experimental environments, and doping of the DNA material being utilized. The large discrepancy and the difficulty in measuring conductivity have caused efforts to become stalemated over time.

A recent breakthrough by Livshits *et al.* [74] focuses on addressing many of the longstanding problems and may revive the field. They employ guanine-quadruplex DNA (G4-DNA), which is a guanine-only motif that forms a planar stacking. The guanine tetrad has greater rigidity than native DNA base pairs, and is thus able to withstand deformation. Gold electrodes with very sharp edge definition were evaporated using stencil lithography onto G4-DNA immobilized on an insulating (mica) surface. A conducting tip AFM simultaneously imaged and measured current along G4-DNA axis. An asymmetric current–voltage (*I–V*) characteristic was observed, with current decreasing (from ~100 to 10 pA) with increasing distance (from ~20 to 70 nm) between AFM tip and Au electrode.

The result showed an unequivocal demonstration of charge transport. Well-established *I–V* results in tandem with modeling indicate electronic transport by thermally activated hopping from one tetrad to the next, similar to mechanisms in conducting polymers. Although much work still remains in implementing more complex electrical circuits, the work offers a reliable indication of long range conductivity using nucleobases, which is a significant step forward in continuing the work on DNA-based molecular electronics.

In parallel with DNA conductivity over the years, nucleic acids have been studied in thin film devices with good success. The remaining section highlights DNA and nucleic acid thin films used in organic solid-state devices. DNA and nucleobases have been incorporated in many different components of OFETs, including the dielectric, charge injection, and semiconductor layers. Very early work used deoxyguanosine, a single-stranded DNA polymer with a **G**-only base sequence, deposited as a self-assembled p-channel for OFETs [76, 77]. This is significant because **G** is known to be a good hole transporter, and much work has been done investigating supramolecular architectures of guanosine derivatives (see review by Davis and Spada [78]). Unfortunately, no follow-up research with OFET channels using deoxyguanosine has been reported, but there may be new promise to explore this further, especially with the recent G4-DNA conduction reported by Livshits *et al.* [74].

DNA gate dielectrics has been common in OFETs since 2006. Some of the first devices contained DNA–CTMA as the gate dielectric to make memory elements, and OFETs with combined DNA–CTMA and Al_2O_3 gates that reduced hysteresis with relatively good turn-on [50]. An interesting approach [79] modified DNA with photoreactive side-chains that can result in cross-linked films upon UV irradiation, thereby changing the solubility and dielectric properties as seen in Figure 7.8. Cross-linking DNA–CTMA dielectric layers using a chemical agent is another approach [80] for improving the hysteresis of C_{60}-based OFETs. Another reported [53] modification is the formation of hybrid DNA films that incorporate high dielectric constant ceramics (such as $BaTiO_3$ and TiO_2) in order to improve the electrical properties of resultant devices. Another example of a photoactive layer incorporating the biopolymer is the DNA–CTMA:Ag nanocomposite displaying excellent memory switching effects,

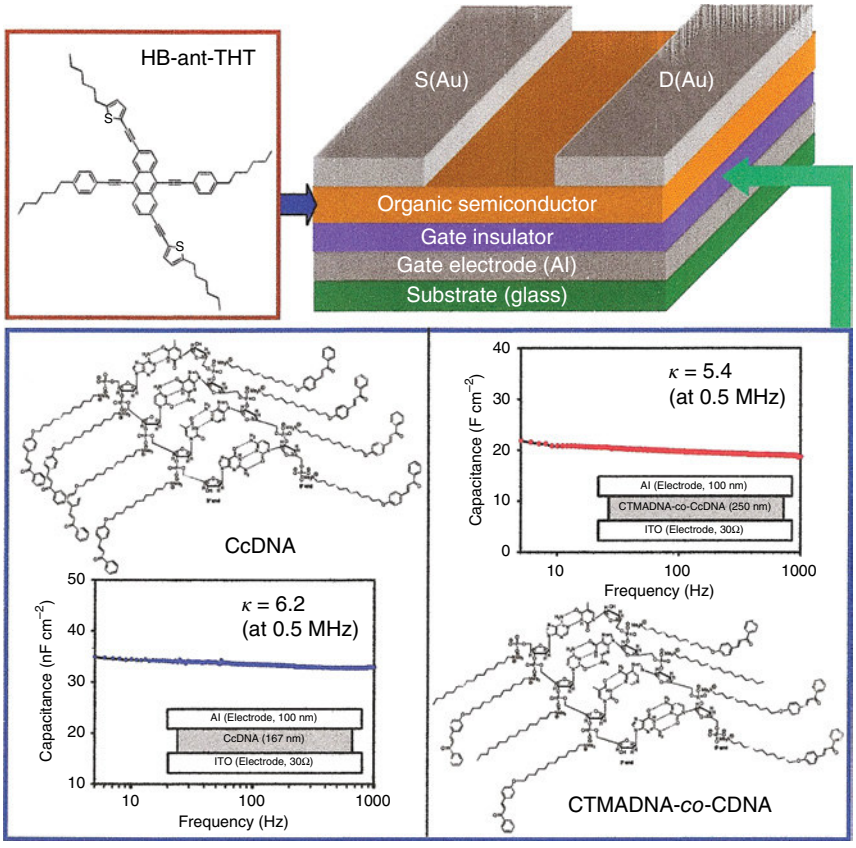


Figure 7.8 Two different DNA gate dielectrics in OTFTs using either CcDNA or CTMADNA-*co*-CcDNA (CTMA:chalcone = 3 : 7). The complexes were cross-linked under UV irradiation resulting in better gate insulations and higher field-effect mobilities. (Kim *et al*. 2010 [79]. Reproduced with permission of AIP Publishing.)

caused by the metallic affinity of DNA that induced nanoparticle synthesis upon light irradiation [81].

While DNA as a dielectric has been relatively useful, the incorporation of additional components and processes (such as surfactants, metallic or ceramic particles, cross-linking) adds complexity to the material processing and the fabrication of the eventual device. In addition, mobile ionic charges in DNA–surfactant molecules are thought [50, 80] to cause hysteresis in the electrical characteristics of OFETs. By comparison, nucleobases are small molecules that can be readily purified and produce consistent thin films by thermal evaporation. The use of nucleobases as dielectric layers in "all-natural" OFETs (see Figure 7.9a) was first demonstrated [28] by Irimia-Vladu *et al.* who reported breakdown fields of NB films ranging from ~1 to 4 MV cm^{-1}.

Lee *et al.* [59] used guanine to improve the hysteresis in inorganic semiconducting oxide (IGZO) thin-film FETs. In this case the guanine is embedded within an inorganic (Al_2O_3) dielectric layer deposited by atomic layer deposition

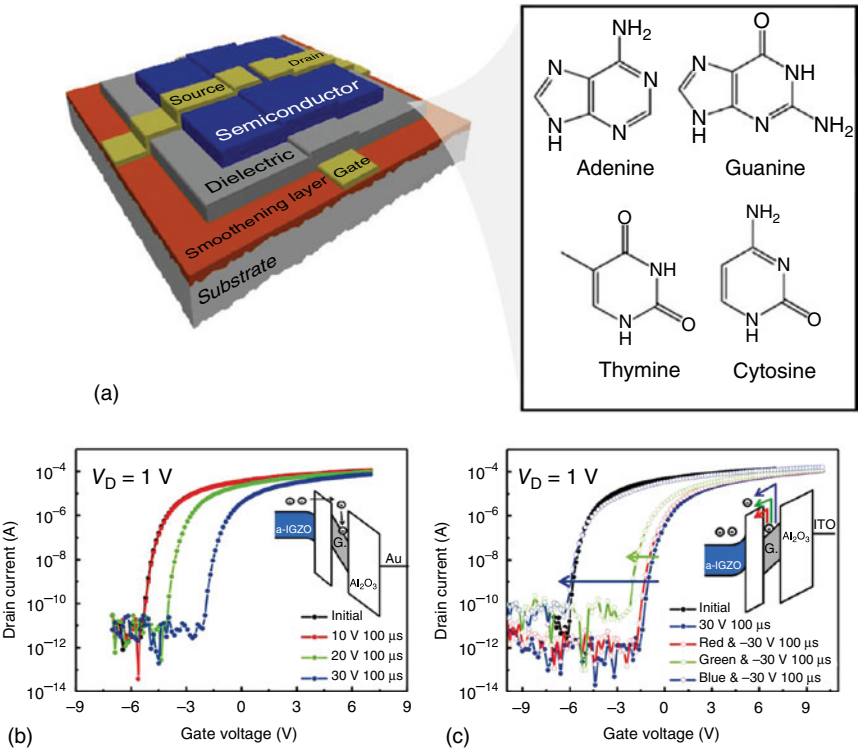


Figure 7.9 Use of nucleobases as dielectric layer in field-effect transistors: (a) dielectric layers in all-natural OFETs (Irimia-Vladu *et al*. 2010 [28]. Reproduced with permission of Elsevier.); (b) guanine in inorganic oxide semiconductor FET embedded as an interlayer within the inorganic dielectric (Al_2O_3) to improve turn-on voltage and hysteresis performance and trap charges at high electric fields (Lee *et al*. 2014 [59]. Reproduced with permission of American Chemical Society.); and (c) charges can be recovered upon exposure to high-energy (blue) photons. (Irimia-Vladu *et al*. 2010 [28]. Reproduced with permission of Elsevier.)

(ALD). The guanine is thought to getter H atoms produced during the ALD growth reaction, resulting in a more electrically stable FET operation. Interestingly, charge trapping (using voltage pulses) and de-trapping (using incident photons of sufficient energy) shown in Figure 7.9b,c, respectively, enable the use of these FETs in programmable applications. Subsequent work from the group also showed hybrid guanine/inorganic dielectric reported to improve charge injection performance [82] in nonvolatile memory inorganic (MoS_2 nanosheet) FETs offering excellent passivation and bias stress stabilization [83].

A major component of the research in DNA electronics has been related to its use in OLEDs. DNA–CTMA inserted into fluorescent OLEDs was initially reported by Hirata *et al.* [44] who investigated charge transport through several device structures and determined that the DNA layer preferentially transports holes. An OLED device with a DNA–CTMA layer was reported by Hagen *et al.* [48] to significantly improve both OLED efficiency and luminance. The performance increase was attributed [48] to the low electron affinity levels of the DNA

serving as an EBL to confine charge to the emitting layer. Nearly ideal performance was reported [42] by using DNA EBLs in phosphorescent OLEDs: maximum brightness of ~100 000 cd m^{-2} at 13 V (632 mA cm^{-2}); maximum current efficiency of ~90 cd A^{-1}; and luminous efficiency of 55 lm W^{-1} at 5 V (0.11 mA cm^{-2}). The same electron-blocking function for DNA layers was reported [84–86] in OLEDs utilizing polymer light-emitting layers as opposed to previously reported small molecule OLEDs.

All of these reports used similar methods of electron-blocking to increase emission efficiency and similar wet processing (spin-coating) to form DNA–CTMA films. DNA-CTMA deposited thin films by vacuum thermal evaporation have also been reported [55] in fluorescent OLEDs. Surprisingly, given the large molecular weight of the DNA-CTMA polymer, the method resulted in a 15 nm electron-blocking layer that also improved internal efficiency.

Maybe the most challenging and potentially most significant approach is to utilize the DNA film as the light-emitting layer, with DNA serving as the host material for lumophores. Photoluminescence from Eu complexes [55] incorporated into DNA films and electroluminescence from Ru complexes [87, 88] are among the few results that have been reported to date for this approach. Nakamura *et al.* have used [88] a DNA complex that aids in charge transfer from a phosphorescent emission to a fluorescent molecule, resulting in a voltage controlled color tunable OLED. In addition, Cho *et al.* have functionalized [89] DNA with a carbazolyl ammonium lipid as the triplet host material for a phosphorescent material system. The complexed host aids in energy transfer of triplet spin states in phosphorescent systems to emit light.

Interesting results have also been reported with organic dye molecules in DNA films and fibers. Yu *et al.* have reported [49] photoluminescence and distributed feedback lasing from sulforhodamine molecules incorporated in a DNA–CTMA layer formed on a SiO_2/Si grating. DNA–CTMA fibers formed by electrospinning and incorporating dye molecules have been reported [90] to produce stronger photoluminescence compared to equivalent thin films. Enhancement in the emission of various luminescent particles (such as quantum dots [91] and nanorods [92]) from the presence of DNA charge control layers has also been reported. Just recently, DNA was used to guide Alq3 rod crystallization in OLEDs, leveraging the DNA recognition sites to trigger photoluminescent enhancements by Alq3 [93]. These studies represent a new direction for DNA-based photonic materials, using DNA to self-assemble organic semiconductors or for new biosensor applications (see Section 7.3).

Finally, the most recent report in DNA-based luminescence comes from Reddy and Park [94], in which they complex curcumin, a natural phosphor, to CTMA in a biocrystalline form. The curcumin chromophore then readily binds to DNA. It is suggested that aligning with the DNA helix prevents aggregation-induced quenching effects. A quantum yield of 62% is achieved, making it a very promising green material for future OLEDs.

Use of DNA is emerging in other devices. Solar cells [95–97] are the most recent addition of devices benefiting from DNA. A perovskite solar cell [95] that employed DNA–CTMA reached a power conversion efficiency of 15.86%, with stable operation over 50 days in air. The mechanism relies on the electron-blocking

capability of the biopolymer, similar to its primary function in OLEDs. The results regarding biopolymers in solar cells require more attention, especially in light of the recent results with nucleobases in OLEDs (see below).

Other devices include an electrochemical supercapacitor, where the DNA is coated with a monomer of the cationic compound EDOT-N, which is a PEDOT derivative (3,4-ethylenedioxythiophene). EDOT-N binds to the negatively charged DNA backbone, intercalating into the helix structure, and self-polymerizing (using ammonium persulfate) *in situ.* The complex is formed into dry film electrodes with high porosity and large surface area. The electrode was used in an electrochemical supercapacitor by placing it in an electrolyte medium, resulting in a charge storage capacity of $32\,F\,g^{-1}$ [98].

While DNA has been investigated for OLEDs for approximately a decade, the DNA nucleobases have just recently made their appearance in OLEDs. Nucleobases have expanded the list of available materials for OLEDs with the advantage of diverse roles for each base layer. **A** and **T** have shown to have high performance as EBLs, resulting in higher efficiency and luminance performance (even exceeding previous DNA results), when used as very thin EBLs and hole transport layers (HTLs) [99]. Figure 7.10 shows results of replacing the N,N′-Di(1-naphthyl)-N,N′-diphenyl-(1,1′-biphenyl)-4,4′-diamine (NPB) and Bathocuproine (BCP) layers in the OLED structure, the EBL and hole-blocking layer (HBL) respectively, with nucleobases. The current photoemission and luminance characteristics of the resulting OLEDs follow the trend of the energy levels (see Section 7.2.2) of the nucleobases, namely **G** and **A** as EBL/HTLs and the pyrimidines **C**, **T**, and **U** as a HBL and electron transfer layer (ETL). These results greatly expand the utility of the nucleic acids and show that common organic semiconductors can be replaced with natural materials.

7.3 Nucleic Acids in Nanotechnology

7.3.1 Introduction

DNA nanotechnology leverages the self-assembling properties of DNA to build 2D and 3D nanostructures or nanomechanical devices. The discipline is often called DNA origami because of its intrinsic ability to fold onto itself with hairpin turns. Structural DNA nanotechnology has been most aptly described by Seeman, the pioneer of DNA origami for nearly 30 years, as meeting the challenge of putting "what you want where you want it in three dimensions (3D) when you want it there" [100]. Reif and LaBean groups at Duke university, responsible for many DNA assemblies, motors, and DNA computing since its early days, astutely describe DNA as a "smart glue" that can organize objects in 3D space and replicate a desired structure limitlessly for "massive parallelism" [101]. DNA nanotechnology forms complex structures by folding on itself with affinity-based nucleobases and creates structural rigidity with the phosphate-pentose backbone. The nanoscale structures have progressed beyond simple unit blocks and have emerged into applications for scaffolds and nanoscale tools [15, 101]. Figure 7.11 is based on a review [7] of the field that illustrates the two

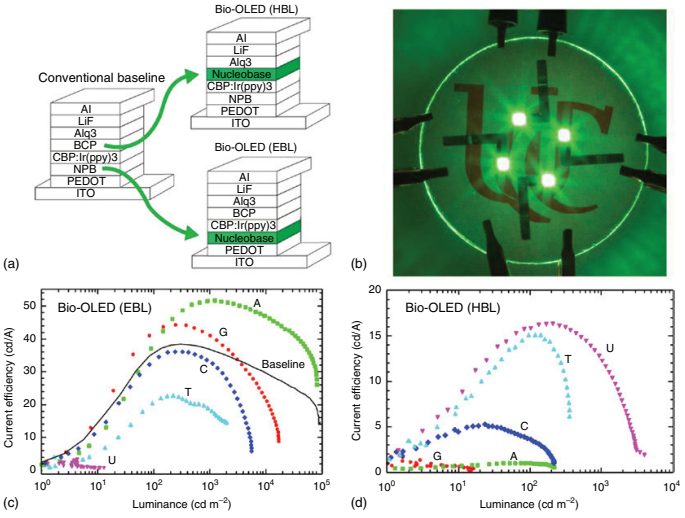


Figure 7.10 Use of nucleobases in OLED structures: (a) replacement of the HTL/EBL (NPB) and HBL (BCP) layer with nucleobases; (b) photograph of an operating OLED containing adenine EBL; (c) current emission efficiency versus luminance of the EBL-OLED showing **A** and **G** as good EBLs and of the HBL-OLED showing **T** and **U** as good HBLs (d). (Gomez *et al*. 2014 [18]. Reproduced with permission of John Wiley and Sons.)

primary approaches to DNA nanotechnology: (i) hybridization-based DNA that weaves DNA strands in pattern to create increasingly complex structures and (ii) nanoparticle-template DNA that covalently bonds nanoparticles to DNA and uses DNA as the linker to other nanoparticles.

As Figure 7.11 shows, the two major branches of DNA nanotechnology strive to increase the order and functionality of the material from simpler units. The units then repeat and join together to form 2D scaffolds and 3D lattices that eventually create functional materials. It is envisioned that the highly ordered and programmable DNA molecular arrangements will have broad applicability once fully matured. While a few applications in biosensors (Section 7.4.3) have emerged, the field has been met with great challenges. A recent review by Jones *et al*. [7] has summarized the current status of DNA nanotechnology and discussed motivation for future exploration. After many years of effort, the field has developed unfathomable precision in atomic control. However, the article acknowledges that "the hybridization-based and nanoparticle-templated subfields remain relatively isolated, with very few examples of overlap between disciplines" [7]. The authors discuss that the field has been primarily focused on controlling material at the smallest scale and synthesizing intricate nanostructures. Historically, however,

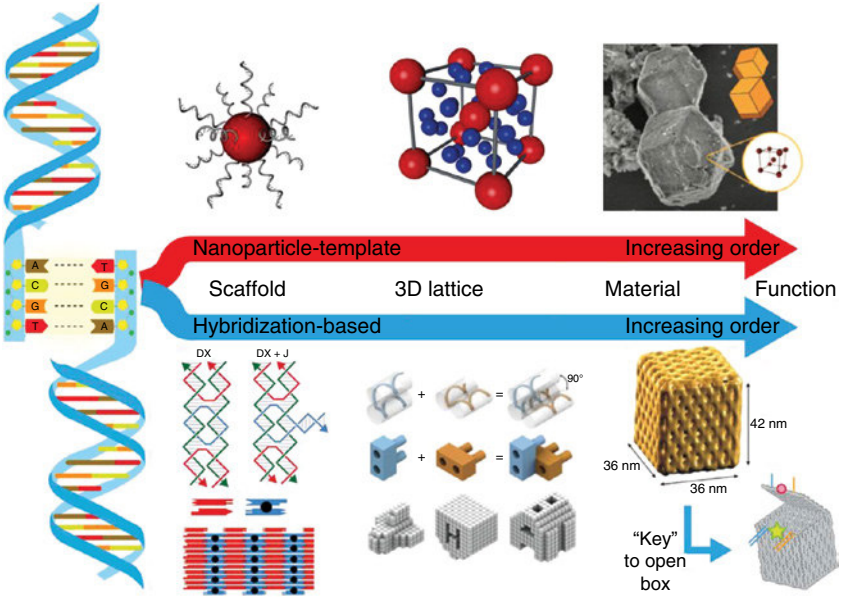


Figure 7.11 DNA nanotechnology based on sticky end DNA diverged into two fields: nanoparticle-template and hybridization-based lattice bonding. Nanoparticle-template uses DNA bound to nanoparticles to join to other nanoparticles. Hybridization-based DNA relies on sticky ends and crossovers (DNA weaving) to create rigid shapes and structures with other DNA polymers. In each respective subfield, the increasing order trend creates more functional superstructures. These two approaches have allowed a diverse set of programmable materials available for researchers in nanotechnology. (Figure adapted with permission from [7, 18, 20, 100, 102–105].)

the lasting success of nanostructures eventually depends on interaction with the macro-world.

Interfacing DNA nanotechnology with existing DNA electronics could utilize atomic manipulation to provide precise control over charge transport and device functionality. There have been a few examples of DNA origami in electronics, but the field is largely unexplored and has the potential to produce extraordinary and dynamic electronic manipulation based on highly ordered systems, a development similar to the history of inorganic semiconductors and devices.

7.3.2 DNA Nanotechnology

Both branches rely on DNA "sticky ends," which are short single-stranded protrusions from the end of the DNA polymer that bind to another sequence, either in the same strand or in a different single DNA strand, shown on the left side of Figure 7.11. This well-known technique, established from plasmid research, relies on exposing a portion of one strand of the end of a double DNA strand with the enzyme endonuclease, so that the nucleobases' affinity may result in binding to another exposed DNA strand containing the complementary sequences. Manipulating DNA is incredibly precise with well-established techniques of elongating, shortening, or otherwise modifying the strand [106]. The complementary exposed sequences stick together like Velcro® to form the glue for large superstructures.

Basic DNA origami requires the correct "sticky end" sequences and rigid structures formed by carefully placed crossovers. Crossovers are weavings of two single DNA strands that overlap and often bind together at a complimentary node. Once a basic unit is established, it is often easily repeated to create a much larger lattice. The DX (double crossover) lattice was one of the first DNA nanostructures that wove several complementary DNA strands together to provide structural integrity [104, 107]. It consists of two double helices that switch their connectivity from one helix to another to form a basic building block that can expand in both the *X* and *Y* directions. More complex variations have been made, such as the (TX) triple crossover [108]. The crossovers provide the rigidity, while the shape is created by the placement of the sticky ends. The tensegrity (word derived from "tension" and "integrity" [14]) triangle is an example of a 3D motif with extending sticky ends designed to link to itself [19, 22]. Unlike the DX motif, one of the arms is not coplanar and can create rhombohedral lattices.

To shift from a scaffold to a 3D lattice requires further rigidity. The three-point star is a complex structure created from four different crossover strands [21]. The unit binds to itself at all points and basic 3D shapes are readily formed and can be combined in several different arrangements to create polyhedral wireframes. A different approach uses "DNA bricks" that are single 32-nucleotide strands with four eight-base-pair interactions between bricks [20]. Each brick contains a 90° bend in the strand with a tail that connects with adjacent bricks in a hole and peg (Lego-like) model. Each brick can attach horizontally or vertically with its neighbors to continue construction in all dimensions. The DNA bricks form steps and cavities that have been shown to produce over 100 assortments of 3D structures, including the alphabet, symbols, and figurines with several

nanometer resolution. The DNA base sequence can be determined and synthesized resulting in a traceable and programmable system with precise control and predictable structures. The practice has become remarkably adroit at forming nanostructures, such as pillars, blocks, lattices, and even "smiley faces" with nanometer resolution [109].

Once 3D structure capability is established, more advanced materials and functions are possible. DNA origami has the advantage of motion through binding and releasing strands with enzymes to create nanomechanical motors [110] and structures that assemble and even "walk" [111–113]. Figure 7.11 shows an example of a DNA origami box that opens when a molecular "key" unlatches the structure [105], creating a possible drug delivery system. Placement, construction, and movement put the field in a position of developing interactive superstructures and dynamic systems. The long-term goals of the field are widespread, with many highlighted in the review article by Pinheiro *et al.* [15] including artificial cells, applications in cellular biophysics, and improved medical diagnostics and therapeutics.

The other main approach of DNA nanotechnology uses nanoparticle-templated DNA bonds. Instead of folding the DNA onto itself to form structures with the nucleotide chains, DNA oligonucleotides are bound to nanoparticles (such as Au nanoparticles) by strong interactions with the nucleobases and the gold surfaces or by functionalization. DNA polymers attached to these nanoparticles bind together with other template DNA and create ordered lattices of particles that otherwise would not be able to bind together. As the complexity increases, the material can be used in biosensors that bind to a variety of analytics [114–116] (see Section 7.4.3) and new materials that bind together with predictable DNA bonding instead of covalent interactions [102, 103, 117]. The hybridization and interaction of DNA with nanoparticles and metal to nucleic acid interactions, described in this chapter as DNA molecular engineering, is discussed in more detail in Section 7.4.

A very interesting application relevant to this chapter is the possible combination of DNA energy transfer and photonics. DNA origami could allow us to create complex circuitry with interconnected superstructures. Figure 7.12 shows a conceptual device [15] incorporating mechanisms of many components that have been independently considered, either theoretically or experimentally. A futuristic, but not unrealistic, "pick and place" system will require several different fields of collaboration. Functionalized DNA molecules provide tools for intended applications such as light harvesting with plasmonics; DNA origami assembles the structures in the precise locations while DNA organic electronics offers the knowledge of charge transfer.

7.3.3 Wet-to-Dry Transition

One challenging aspect of DNA origami is that it is formed in an aqueous solution under time-consuming annealing processes. In general, aqueous solutions are deleterious to most thin-film device processing and prevent direct application of conventional DNA constructs. As introduced in Section 7.2.1,

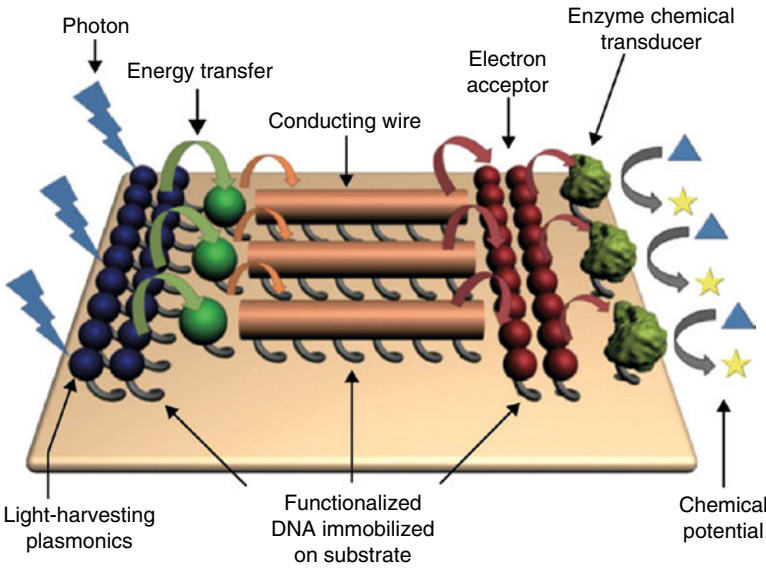


Figure 7.12 A conceptual design showing a cluster of DNA nanostructure units positioned by lattice networks and affinity bonding and functionalized by photonic molecular circuits or charge transfer/transducers. The modular design could be used as the basis for a variety of functions that could be quickly programmed and self-assembled, such as light harvesting, sensors, and chemical transducers. (Pinheiro *et al*. 2011 [15]. Reproduced with permission of Nature Publishing Group.)

DNA in aqueous solutions and thin films formed from DNA–surfactant organic solvent solutions have many similarities, thus providing a path for incorporation of crystalline DNA films. Scalability and practicality are also important aspects that need to be carefully considered, as design of even the smallest structure requires elaborate planning. There is ample opportunity to explore how such an ordered structure affects charge transport and functionality, but as yet there are few investigations to introduce DNA origami into solid-state electronics for green electronics.

Initial steps toward higher order systems in thin films could begin with DNA–CTMA. As shown in Figure 7.13a, Finch *et al.* have created [118] a wagon wheel structure of DNA bound with CTMA using DNA with sticky ends that binds to itself circularly. Upon drying, the wagon wheels retain their shape. Similarly, Figure 7.13b shows a DNA thin-film honeycomb structure created by Sun *et al.* [120] during the wet-to-dry transition. This is accomplished by DNA–surfactants and by slowly evaporating the solution to form honeycomb crystallites. Although the thin film electronic properties have not been studied, the fabrication process could be amenable to thin electronic films, while employing the relatively well-known DNA–CTMA molecules.

A polymer solar cell was reported [97] incorporating the two-dimensional DX-tile-based lattice as one of the layers. The polymer electrode, PEDOT:PSS, is dispersible in water and therefore a more involved method is required to get the

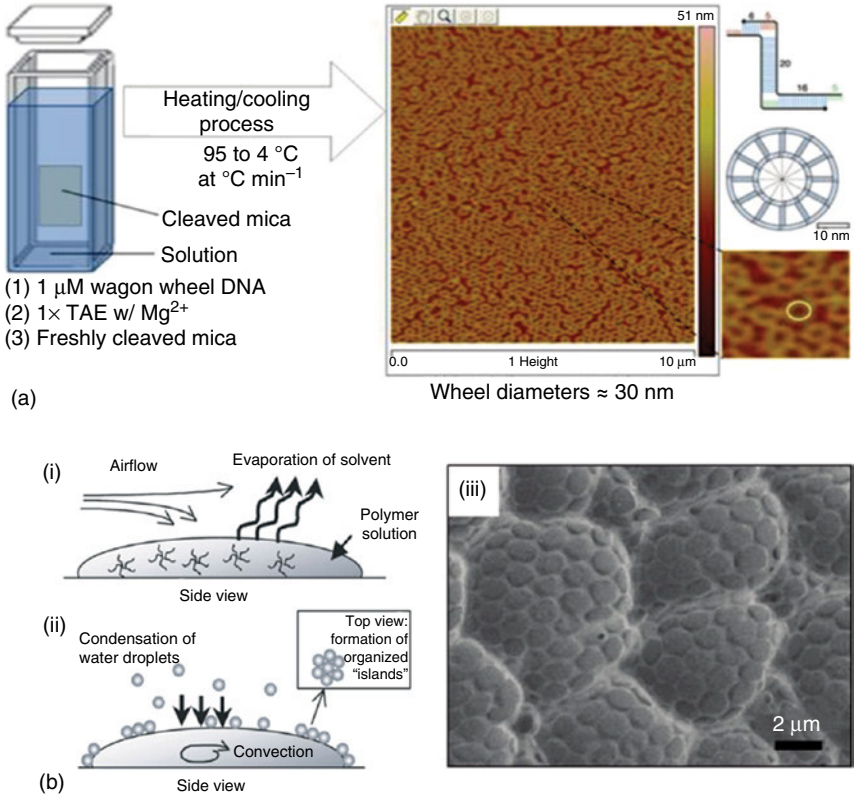


Figure 7.13 Self-arranged films that form without complex origami when transitioning from wet solutions to dry thin films [118, 119]. (a) Wagon wheel structure of DNA–CTMA circularly binding to its opposite sticky ends. (Gajria *et al*. 2011 [119]. Reproduced with permission of American Chemical Society.) (b) Gajria [119] reviews a DNA thin-film honeycomb structure created by Sun *et al*. where DNA–surfactant honeycomb crystallites are formed by controlled evaporation and condensation. (Sun *et al*. 2009 [120]. Reproduced with permission of John Wiley and Sons.)

nominally water-based DNA lattice to deposit on top. Lee *et al.* describe a dry–wet method in which the lattice was first formed in a DX configuration in a $1 \times \text{TAE/Mg}^{2+}$ buffer. The solution was centrifuged until the water evaporated and a dry DNA pellet was formed. The dry DNA DX pellet could be reformed in chlorobenzene, and the solution was dropped onto the PEDOT and annealed to leave behind a well-formed DX lattice as shown in Figure 7.14. The DNA lattice directs hole transport from the active region and blocks electrons to improve device efficiency by 10%, similar to many DNA OLED configurations. While no investigation was reported on the efficacy of the 2D lattice compared to non-latticed DNA, the work provides an effective method to exploring DNA lattices in traditional organic devices.

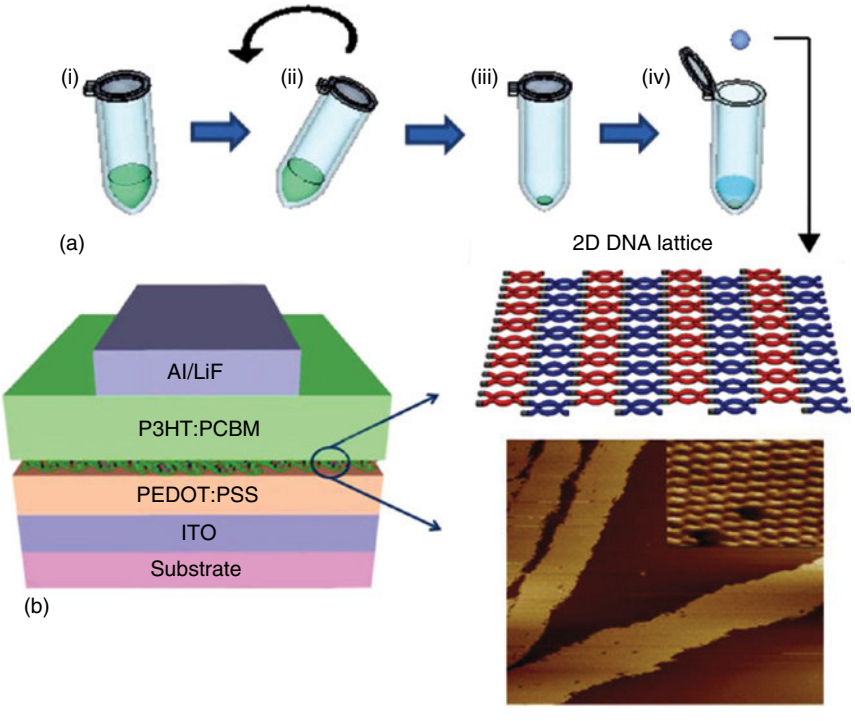


Figure 7.14 (a) Restoration of the DNA lattice into a thin film by dry–wet centrifugation processing. (b) Reconstructed DNA lattices deposited as a layer into thin-film solar cells as an electron-blocking layer. (Lee *et al*. 2011 [97]. Reproduced with permission of IOP Publishing.)

7.4 DNA Molecular Engineering

7.4.1 Introduction

The discussion on the final DNA research category for this chapter is the so-called DNA molecular engineering. DNA hybridization origami (blue section of the flow chart in Figure 7.11) is considered a separate category, primarily involving bonding of DNA strands to each other. The nanoparticle-templated DNA bonds (red section of the flow chart in Figure 7.11) are considered as part of the larger field of DNA molecular engineering, focusing on heterogeneous bonds and affinities between DNA and other materials. Within the field of DNA molecular engineering, DNA strands can be immobilized to different metallic or ionic particles and used as a template to "bond" different molecules together through a DNA linkage. Metal–nucleobase interaction (Section 7.4.2) directed by metal surfaces is also discussed.

DNA strands typically bind to nanoparticles such as quantum dots or gold nanoparticles by terminating one of the ends with either a thiol or a disulfide group causing the DNA to hybridize onto the surface with monolayer and orientation control [106]. Once the DNA strand is bound to the particle, the other end

of the DNA has a "sticky end" that is used to link to other DNA-bound particles. The DNA strands create a crystalline lattice that can control orientation, size, and frequency by substituting conventional atomic bonds with DNA links. Unlike DNA origami, intertwining strands are not necessary, since the inorganic core particles form the lattice and provide rigidity, but must follow several design rules described by Macfarlane *et al.* [103]. Since traditional molecular forces, such as electrostatic or covalent bonding, are replaced with DNA interconnection, the command over molecule placements can change the thermodynamic properties of the lattice. This could lead to new lattice arrangements that could have great potential in new material science and devices.

While much work is still necessary to bring DNA molecular engineering approach from its stable aqueous environment into traditional thin-film electronics, the vast amount of possible materials could have broad implications for electronics. Tan *et al.* [121] presents an excellent review of the field, particularly for plasmonic nanostructures templated with DNA. Gang and Tkachenko [122] also show some of the most significant achievements and challenges in the field. The field has been growing rapidly by demonstrating a growing array of structures from simple nanospheres to complex geometrical patterns such as snowflakes and hollow structures. The DNA molecular engineering field is closely tied to DNA origami, relying on a combination of different DNA motifs and plasmonic atoms, as shown in Figure 7.15, to create molecules, 2D crystals, 3D crystals, and polymers. Plasmonic nanostructures have been used for imaging in biological systems by linking quantum dots with gold nanoparticles. By using different DNA motifs and materials, there are many possibilities opening up with new organic molecules, polymers, and crystalline structures [121].

Tikhomirov *et al.* [123] provide a practical example (shown in Figure 7.16a) of how quantum dots can be linked together with short-strand DNA interconnects with precise distances, enabling effective energy transfer (in the example from green and orange to red quantum dot). A similar concept shown in Figure 7.16b by Maye *et al.* [23] shows a coupled quantum dot and an Au nanoparticle that are linked together in a heterodimer configuration to optically enhance the photoluminescence of the quantum dot by resonance with the Au nanoparticle plasmon. Samanta *et al.* [124] recently summarized several important developments of the field, and have also demonstrated a combination of DNA origami 2D lattice with DNA-templated plasmonics shown in Figure 7.16c.

7.4.2 Metal–Nucleobase Interaction and Self-assembly

Barth describes "molecular architectonics" [125] as highly ordered structures deposited onto metal substrates that self-assemble primarily by the influence of the atomic interactions and intrinsic adsorption of the substrate and surrounding molecules. DNA (and nucleobases) molecular engineering includes ongoing work in direct intrinsic adsorption affinities with metal layers that often self-assemble and bond through orbital interactions. DNA/nucleobase-to-metal affinities have been the basis of many biosensors, as well as improved electronic interaction between organic and metal interfaces. Nucleic acids have shown strong affinity for many different types of electrodes that often results in

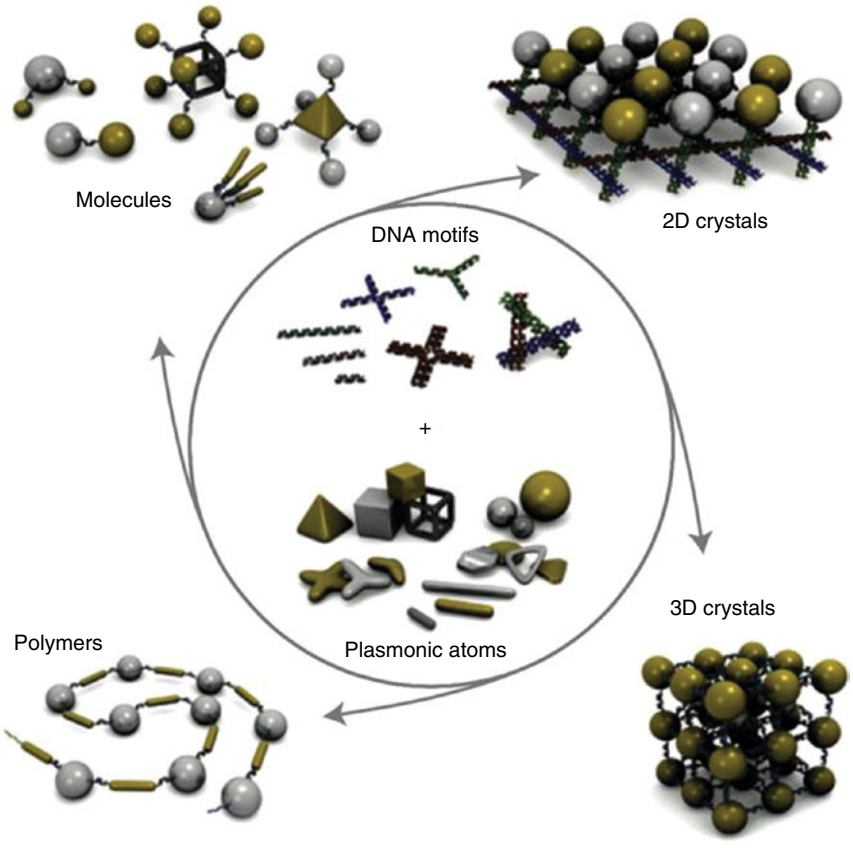


Figure 7.15 DNA nanostructure motifs functionalized with different plasmonic atoms result in molecules, 2D lattices, 3D crystals, or polymer chains that could potentially be designed with different properties. (Tan *et al*. 2011 [121]. Reproduced with permission of Nature Publishing Group.)

increased orbital overlap or order. While origami and nanotemplate bonding primarily focus on construction of nanostructures for mechanical purposes, the DNA-electrode assembly is the link between the powerful technique of DNA self-assembly and traditional solid-state electronics. This direction has initiated the introduction of ordered nucleic acids in sensors and improved metal/organic charge transfer interfaces.

The extensive knowledge of nucleobases/electrode interaction is rapidly growing, primarily for electrochemical analysis in biosensors. Sharma *et al.* [17] catalog many different electrodes and electrode modifications that have been used to detect or assemble nucleic acids. A large number of electrode materials have been investigated, including Au, Ag, Pt, Cu, ITO, TiO_2, graphene, diamond, carbon nanotubes, glassy carbon electrodes, and fullerene. While the motivation has been primarily to develop methods for DNA- or affinity-based sensing [126], the natural orbital interaction of the bases to electrodes has led to improvements in metal–organic interfaces.

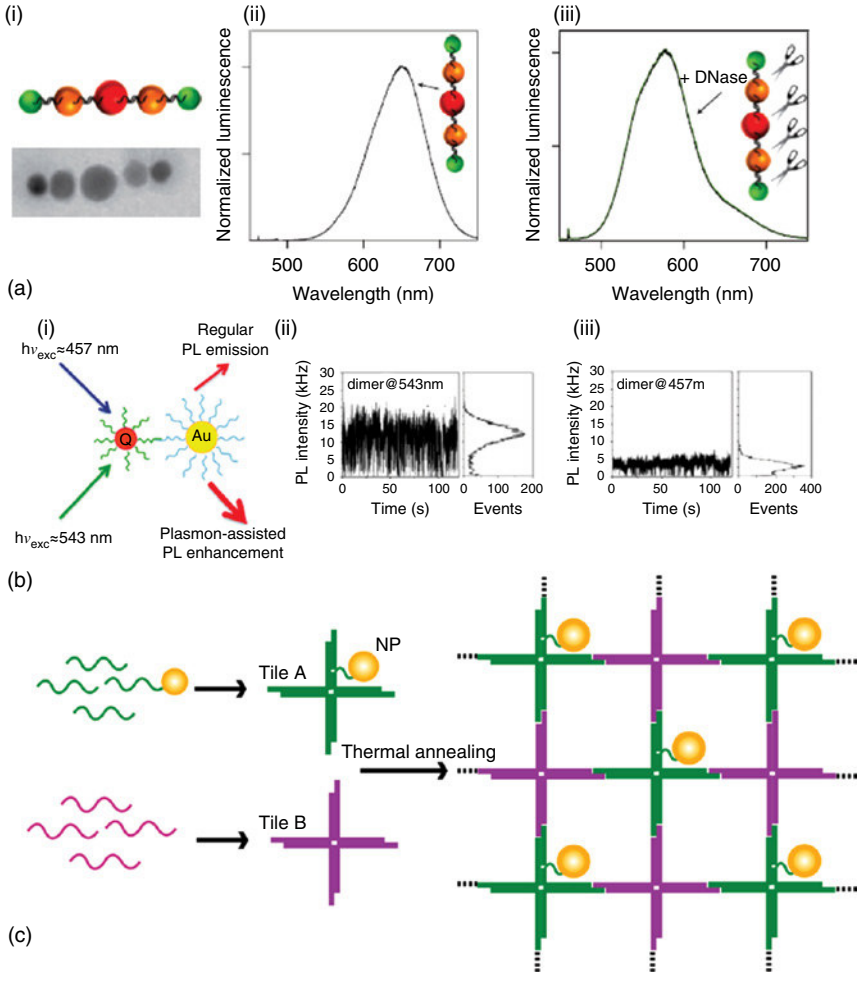


Figure 7.16 DNA molecular engineering can be used to create an array of particles. (a) (i) illustration and transmission electron microscopy (TEM) image of quantum dots linked together with DNA strands; (ii) original photoluminescence of the strand before cleaving and (iii) after cleaving. (b) (i) Quantum dot-Au nanoparticle heterodimer connected together by DNA; (ii) resonating at a precise wavelength (543 nm) inducing high fluorescence of the dye; (iii) compared to the same dimer when excited at 457 nm showing a lower fluorescent intensity. (Tikhomirov *et al.* 2011 [123]. Reproduced with permission of Nature Publishing Group.) (c) ssDNA functionalized with nanoparticles that incorporate into lattice tiles placed in designated locations [23, 123, 124]. (Samanta *et al.* 2015 [124]. Reproduced with permission of Royal Society of Chemistry.)

Nucleobases on gold electrodes have been extensively investigated [127–135] both theoretically (in density functional theory (DFT) calculations) [129, 131] and experimentally [25, 136, 137], showing an impressive capacity for self-organization, especially guanine and adenine on Au(111). Scanning tunneling microscopy (STM) images in Figure 7.17a with DFT overlays show large areas of self-assembly for adenine monolayer structures on the herringbone arrangement of Au(111) surfaces [127, 135]. X-ray diffraction revealed that adenine forms

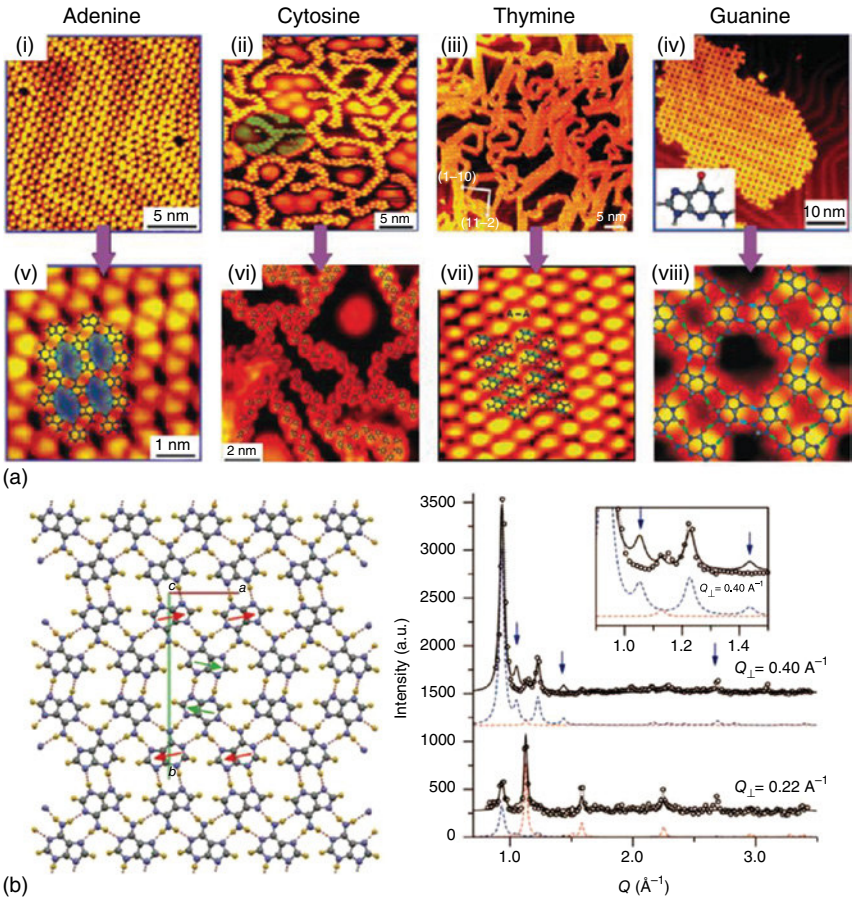


Figure 7.17 The potential of self-assembly of DNA bases on gold electrodes: (a) AFM showing the DNA bases on Au(111) [25]. (Liu *et al.* 2014, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3958828/. Used under CC-BY-3.0 http://creativecommons.org/licenses/by/3.0/.) (b) Computer simulations showing crystalline arrangement of adenine on Au(111) and confirmed with X-ray Diffraction results of adenine grown to 1000 Å [135].

"highly textured crystallite" structures that can be grown from monolayer thickness to several microns, as shown in Figure 7.17b [135]. The nucleobases show a promising advantage of self-organizing from thermal deposition onto metal surfaces without the need for designing specific DNA sequences.

The self-assembling properties coupled with orbital interactions with metal electrodes make the nucleobases a very intriguing candidate for DNA electronics. Several early papers on the topic observed the chemical and physical adsorption that supported the affinity of nucleobases to (nonoriented) gold. In 2002 Demers *et al.* [138] compared the rate of desorption between different oligonucleotide chains using thermal energy to indicate the strength of the NB-to-Au interaction. It was found that purines (guanine and adenine) have a very strong adsorption, while the pyrimidines have weaker adsorption strength purportedly "due to different types of surface binding moieties." In 2003 Kimura-Suda *et al.* [139]

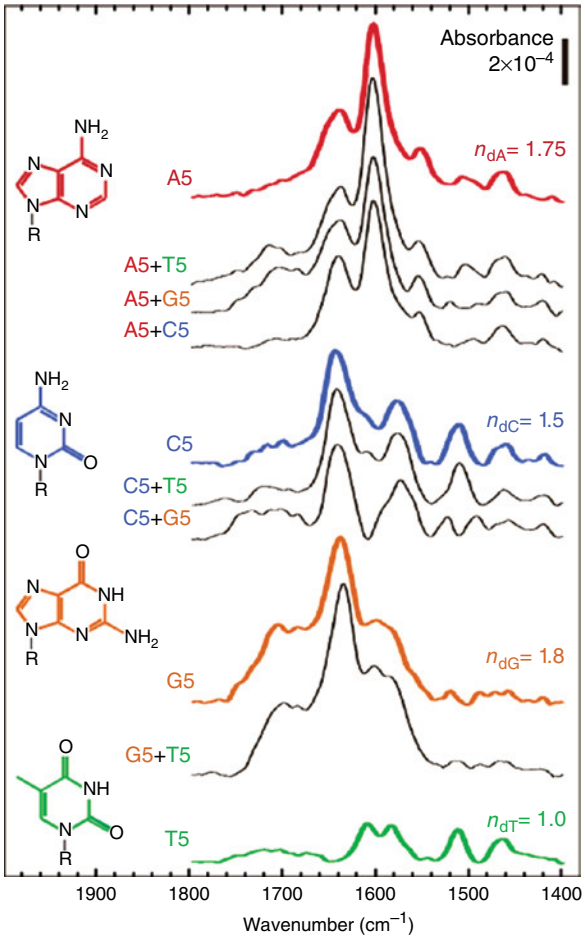


Figure 7.18 FTIR spectra of ssDNA (mixtures of different 5-mer homo-oligonucleotides) films adsorbed on Au from aqueous solutions compared to their reference spectra (bold lines). Non-bold lines show results of mixtures of two different 5-mer oligonucleotides and resultant FTIR spectra. Surface density, n ($\times 10^{14}$ nucleotides cm^{-2}), of each homo-oligonucleotide mixture was determined by XPS. (Kimura-Suda *et al*. 2003 [139]. Reproduced with permission of American Chemical Society.)

used Fourier transform infrared (FTIR) spectroscopy to determine the chemisorption of NB with equimolar mixtures of homo-oligonucleotides on Au. Figure 7.18 shows the FTIR signature of each of the oligonucleotides, as well FTIR results with mixed oligonucleotides in solution. The signature for 5-mer adenine was prominent in all oligonucleotide mixtures indicating the strong chemisorption of adenine on Au. The chemisorption was strong enough to denature the A–T bond in an oligonucleotide strand in order to preferentially bind to the bare gold electrode. The nature of chemical and physical adsorption suggests that the close proximity of the adenine to gold electrodes could influence charge injection from metal to organic layers [24].

7.4.3 DNA Biosensing

The extensive study of nucleic acid electrochemistry, well summarized by Paleček and Bartošík [140], has created a rich field of DNA biosensors. Early work showed that nucleobases could be individually discriminated on glassy carbon electrodes using cyclic voltammetry [126]. Very recently, nucleobase adsorption on graphene has pushed the efforts to develop a DNA base sensor for label-free DNA sequencing [141]. Graphene-based FETs have been fabricated with an exposed surface that allows the nucleobases to interact with the channel. Since the bases adsorb on graphene with different strengths, the change in charge carrier density due to dipole formation enables discrimination of specific bases. Although presumably no actual charge transfer occurs, the shift in work function (0.22, 0.15, 0.13, and 0.01 eV for **G**, **A**, **C**, and **T**, respectively) leads to impressively miniscule limits (1 nucleobase molecule per 10^4 nm^2 of graphene area) of detection.

In addition to traditional sequencing, properties of self-assembly on electrodes coupled with the selectivity of base pairs are ideal for biosensors for other molecules. Nucleic acids can be functionalized to receive a variety of small biomolecules [16]. The primary design uses tetrahedron nanostructures self-assembled by four oligonucleotide strands (see Figure 7.19a), as in DNA origami. The design of the tetrahedron nanostructure advantageously allows each vertex to be functionalized, for example, with fluorescent labels. In addition to ligands, the structure can fold upon itself by introducing a specific DNA sequence (Figure 7.19b,c). In another design, three of the vertices are functionalized with a thiol modification causing the structure to anchor to the gold substrate. The remaining vertex of the tetrahedron is functionalized with RNA or antibody/antigen sensors (Figure 7.19d). The tetrahedron shape has advantages over conventional hairpin sensors. Its shape and size make it exceptionally rigid and resistant to enzyme digestion. The functionalization of the three base vertices promotes proper spacing and correct orientation, and reduces overlapping to expose the sensor to the target.

Another similar application uses single-stranded DNA immobilized on Au gate electrodes of organic electrochemical transistors (OECTs) [146]. Complementary DNA strands in the analyte were detected with label-free methods by binding to the hybridized strands on the gate. The hybridization of the DNA on the gate results in gate voltage and consequently changes in the source–drain current. The device required no fluorescent label or additional antigen, relying solely on the change in work function induced by a "surface dipole formed by intrinsic charge of the DNA" [146]. The surface potential is further decreased after DNA hybridization owing to the negative charge of DNA backbone, resulting in an extremely sensitive OECT.

7.4.4 Electrode Self-assembly and Affinity in DNA Electronics

The high level organization and affinity of nucleobases and DNA on certain electrodes are also being investigated for new designs in organic electronic devices and charge injection layers. The motivation to switch to a biological hole injection layer over more established conventional charge injection layers (PEDOT, CuPC, C_{60}) has to do with the development of "green" or natural electronics and to eventually couple into the field of DNA origami. With the enormous body of

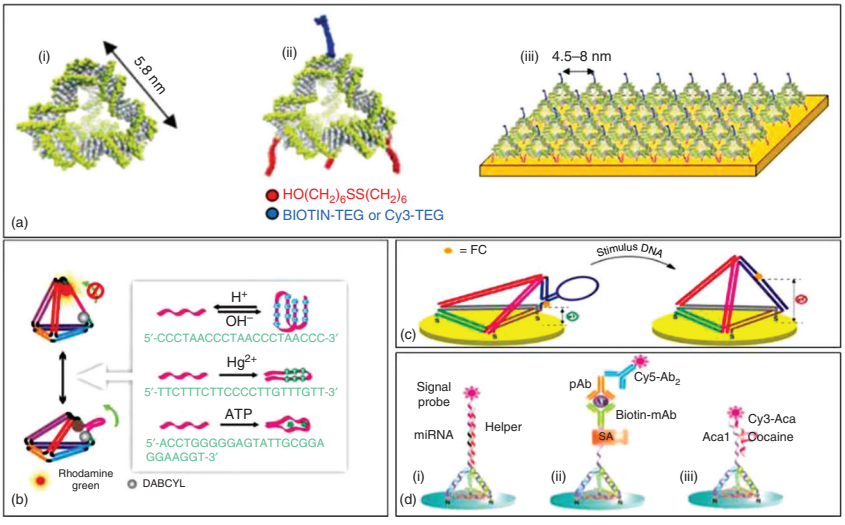


Figure 7.19 (a) Tetrahedral DNA nanostructures fixed to gold electrode and three points, with the fourth point containing a ligand. (b) The structure collapsing in chemical analyte causing either fluorescent emission or (c) electron transfer. (d) DNA tetrahedron functionalized with antibody/antigen in biosensor application [16, 142–145]. (Abi *et al*. 2014 [144]. Reprinted with permission of American Chemical Society; Li *et al*. 2014 [145]. Reprinted with permission of American Chemical Society.)

work on nucleic acid interaction with electrodes, it is somewhat surprising that more work has not been reported for charge injection layers. A few devices are highlighted here.

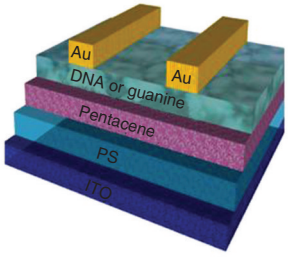
Several articles have recently reported on using DNA and nucleobases for charge injection layers in pentacene-based OFETs shown in Figure 7.20 [147–149]. The charge injection layer is placed between the Au source and drain electrodes and the pentacene semiconducting layer in order to facilitate charge transfer between the metal and the pentacene layers. The improvement is due to a reduced contact resistance between metal and organic layers, attributed to an interfacial dipole-induced energy shift. The effect is notable with guanine, but is even more pronounced with DNA. The DNA layer was deposited by spray-coating aqueous DNA solutions, resulting in a uniform film without the use of a surfactant [149]. Interestingly, an OFET device with "plain" DNA as an interlayer has three times greater mobility than devices using DNA–CTMA, indicating an adverse effect of the surfactant complex on charge mobility.

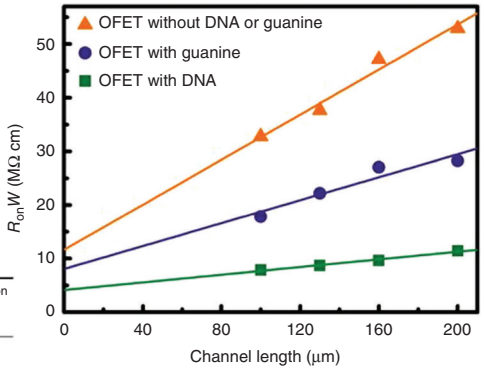
A similar approach by Gui *et al.* [148] fixed DNA as an injection layer by immobilizing the molecule to the electrode. This was accomplished by modifying an ssDNA with a mercapto group (SH) that binds the complex to the Au. Notable increases in both saturation current and carrier mobility were observed. The improvement is attributed to the high carrier density in the contact between the gold and the DNA complex.

The concept of a nucleic acid charge injection layer has also been extended to OLEDs by using adenine as a hole charge injection layer on Au. The results showed an improvement of OLED performance when a thin layer of adenine was deposited on Au compared to the device without the nucleobase. Luminance output for the adenine device was nearly 10 times greater than the reference device over the entire range. The current density (Figure 7.21a) of the adenine was only slightly higher, while the current efficiency exhibited an increase of three to seven times (peak values of $31.7\,\mathrm{cd\,A^{-1}}$ for adenine device vs $4.5\,\mathrm{cd\,A^{-1}}$ for conventional device) (Figure 7.21b). This provides significant evidence of enhanced hole injection from gold caused by adenine.

As was previously discussed, the adenine forms a strong chemical interaction with the Au layer [138, 139], which is attributed to the increase in the performance of the adenine OLED devices. Au surfaces are known [150] to have dipole orientations that impede hole injection, especially into organic semiconducting layers. A common hole injection layer, C_{60}, has been used to overcome this limitation. C_{60} is known to have a strong interaction with Au orbitals on the surface that causes a reversal in dipole moments due to its chemical adsorption with the metal [147, 149]. The reversed dipole favors increased charge injection from metal to organic layers. It is believed [24] that a similar mechanism of metal adsorption and dipole interaction also occurs with adenine and Au to favor increased charge injection.

This initial work has implications for the evolution of thin-film electronics toward green electronics. Furthermore, as the development of self-assembled nucleic acids on electrodes is better understood, the advantage of metal to organic interactions could play an important role in improving device performance. In addition to application in solid-state electronics, there is a wider possibility to develop the next generation of sequencing and biosensor devices.





	Contact resistanc (MΩ cm)	Field-effect mobility ($cm^2 V^{-1} s^{-1}$)	Threshold voltage (V)	Saturation current (μA)
Pentacene	11.620	0.020	31	0.178
Pentacene/guanine	8.041	0.036	25	0.506
Pentacene/DNA	4.134	0.104	23	1.656

Figure 7.20 DNA or guanine used as a charge injection layer in pentacene OFETs resulting in a decrease in contact resistance ($R_{on}W$) between gold and pentacene and leading to increased field-effect mobility (μ) and lower threshold voltages. (Wei *et al*. 2014 [147]. Reproduced with permission of IOP Publishing.)

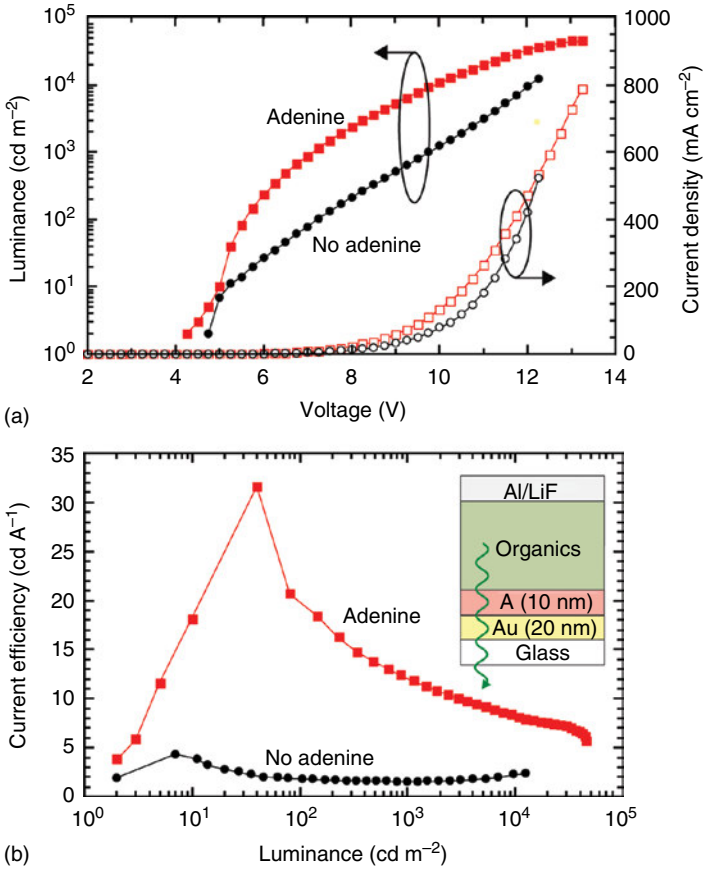


Figure 7.21 Effect of adenine on hole injection in OLEDs: (a) increased luminance versus voltage of OLED device with adenine compared to without adenine and (b) corresponding efficiency increase for adenine versus no adenine on Au (inset) OLED stack with adenine on Au [24, 57].

7.5 Summary and Future Outlook

In this chapter, we have reviewed the use of DNA and nucleobases in electronics, self-assembled origami, and molecular engineering. We have highlighted several notable reports that have been driving the trajectory of the fields for the last 20 years. The electronic properties of DNA and the nucleobases are diverse, and have been explored in a wide range of thin film solid-state devices and electronic conduction. DNA origami has been quite successful in developing tools to construct nanoscale structures with precise control. DNA molecular engineering has explored the intermolecular interactions of the bases with other materials and as a template to bind other materials together. Nucleic acids are a powerful and unparalleled set of tools for material manipulation and device design as represented in these three fields.

As we look toward the next 20 years for DNA and nucleobases, it is apparent that progress will be furthered by increased collaboration of knowledge among the fields. DNA has the opportunity to be a cornerstone in dynamic nanosystems that rely on both structural integrity and electronic manipulation made possible by self-assembled materials. DNA electronics should be intentionally designed with more ordered structures, and likewise, programming DNA origami and molecular engineering deliberately constructed with electronic application in mind. Not only will the nucleic acids be a green material, but they will also encompass a system of materials that have the unique ability for structural precision, enhanced electronic transfer, and modular systems.

Beyond the current uses of DNA, new directions of research into modified DNA materials could further expand its boundaries. For instance, peptide scaffolds, which have chemical and structural versatility, have been combined with nucleic acid base pairing interactions resulting in enhanced optical properties [151]. Other recent work has synthesized nucleobases with π-conjugated oligomers [152] resulting in tunable optoelectronic and electroactive molecules with potential use in new nucleobases, fluorescent OLEDs, or novel organic solar cell materials. Other work investigates the so-called size-expanded DNA [153], an artificial genetic system in which the nucleosides contain an additional benzene ring. The extension of the bases may offer improved opto/electronic properties [132, 154] and potential expansion for molecular engineering with gold nanoparticles [155]. New DNA derivatives such as these could provide more flexibility and functionality in material properties.

The next 20 years offer an opportunity for DNA and its nucleobases to meet progressively intricate and dynamic systems with a wide range of functionality. The nucleic acids have been shown to be highly programmable and self-assembling molecules that can conduct charge, move on command, and form the glue that link nanoparticles together. In its natural environment, the structure and affinity of DNA has been the foundation of complex biomachinery. Remarkably, this time-tested molecule continues to prove to be an indispensable architect for the modern nanoscale world.

Acknowledgments

The authors would like to acknowledge the contributions to DNA-based device research of previous graduate students in the Nanoelectronics Laboratory at the University of Cincinnati – J. Hagen, W. Li, and H. Spaeth. This research benefited greatly from a close collaboration with J. Grote and the support of the Air Force Research Laboratory over a number of years.

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