Nano-architectonics with porphyrin functionalized DNA

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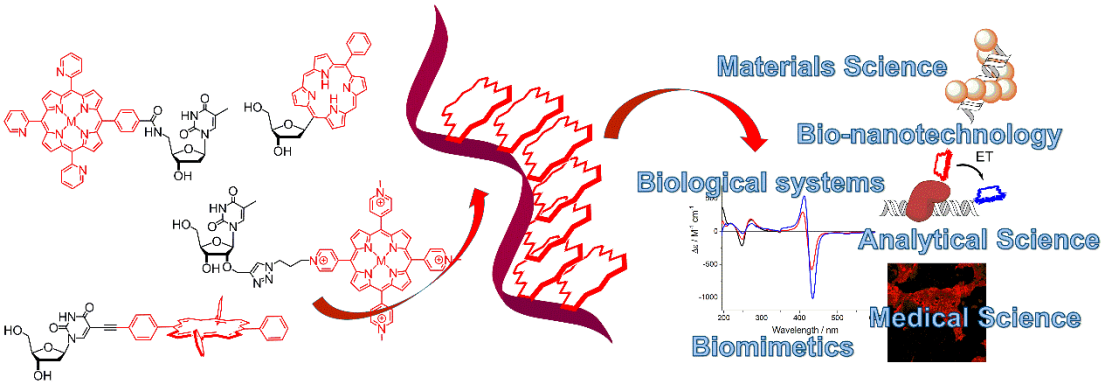
Conspectus: DNA is well-known as bearer of the genetic code. Since its structure elucidation nearly seven decades ago by Watson, Crick, Wilkins and Franklin, much has been learned about its detailed structure, function, and genetic coding. The development of automated solid-phase synthesis, and with it the availability of synthetic DNA with any desired sequence in lengths of up to hundreds of bases in the best case, has contributed much to the advancement of the field of DNA research. In addition, classic organic synthesis has allowed to introduce a very large number of modifications in the DNA in a sequence specific manner, which have initially been targeted at altering the biological function of DNA. However, in recent years DNA has become a very attractive scaffold in supramolecular chemistry, where DNA is taken out of its biological role and serves as both stick and glue molecule to assemble novel functional structures with nanometre precision. The attachment of functionalities to DNA has led to the creation of supramolecular systems with applications in light harvesting, energy and electron transfer, sensing, and catalysis. Functional DNA is clearly having a significant impact in the field of bio-inspired nano-systems.

Of particular interest is the use of porphyrins in supramolecular chemistry and bio-nanotechnology, because they are excellent functional groups due to their electronic properties which can be tailored through chemical modifications of the aromatic core, or through insertion of almost any metal of the periodic table into the central cavity. The porphyrins can either be attached to the nucleobase, to the phosphate group, or to the ribose moiety. Additionally, non-covalent templating through Watson-Crick base pairing forms an alternative and attractive approach. With this, the combination of two seemingly simple molecules gives rise to a highly complex system with unprecedented possibilities for modulation of function, and with it applications, particularly when combined with other functional groups. Here, an overview is given on the developments of using porphyrin modified DNA for the construction of functional assemblies. Strategies for the synthesis and characterisation are presented alongside selected applications where the porphyrin modification has proven to be particularly useful and superior to other modifiers, but also has revealed its limitations. We also discuss implications on property and behaviour of the porphyrin-DNA, where similar issues could arise when using other hydrophobic and bulky substituents on DNA. This includes particularly problems regarding synthesis of the building blocks, DNA synthesis, yields, solubility, and intermolecular interactions.


Materials Science
Bio-nanotechnology
Biological systems
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Analytical Science
Medical Science
Biomimetics
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1. Introduction

The construction of nano-sized functional molecules by means of a bottom-up approach is best addressed using the concepts of supramolecular chemistry, which is defined as chemistry beyond the molecule. Large chemical constructs are made up of a discrete number of self-assembled molecular subunits. Biological systems can be regarded as the ultimate supramolecular assemblies, as they combine tailored structure and function to form living organisms, where smaller subunits are organised through non-covalent interactions. Therefore, biology provides us with ideas and templates which are ideal to draw upon. In this respect, DNA has shown to be an exciting construction material, owing to its distinct properties such as the predictable three dimensional structure in form of the double helix, its programmable nature, and synthetic availability. The basic principle of working with DNA is relatively straight forward: the molecule forms a well-understood duplex through complementary base pairing of two antiparallel DNA strands, where the recognition is based on the Watson-Crick (WC) base pairs (bp) of A–T and G–C (Fig. 1).[1-3] Yet there is far more to DNA than just this concept. DNA can act both as rigid stick (double strand, dsDNA) with a persistence length of about 40–50 nm (120–150 bp), and flexible glue (single strand, ssDNA), giving access to a Lego-like building block system to create architectures with nanometre precision. By taking DNA out of its biological context, new systems have emerged which are starting to play a major role in materials science, electronics, diagnostics, medicinal chemistry and more.

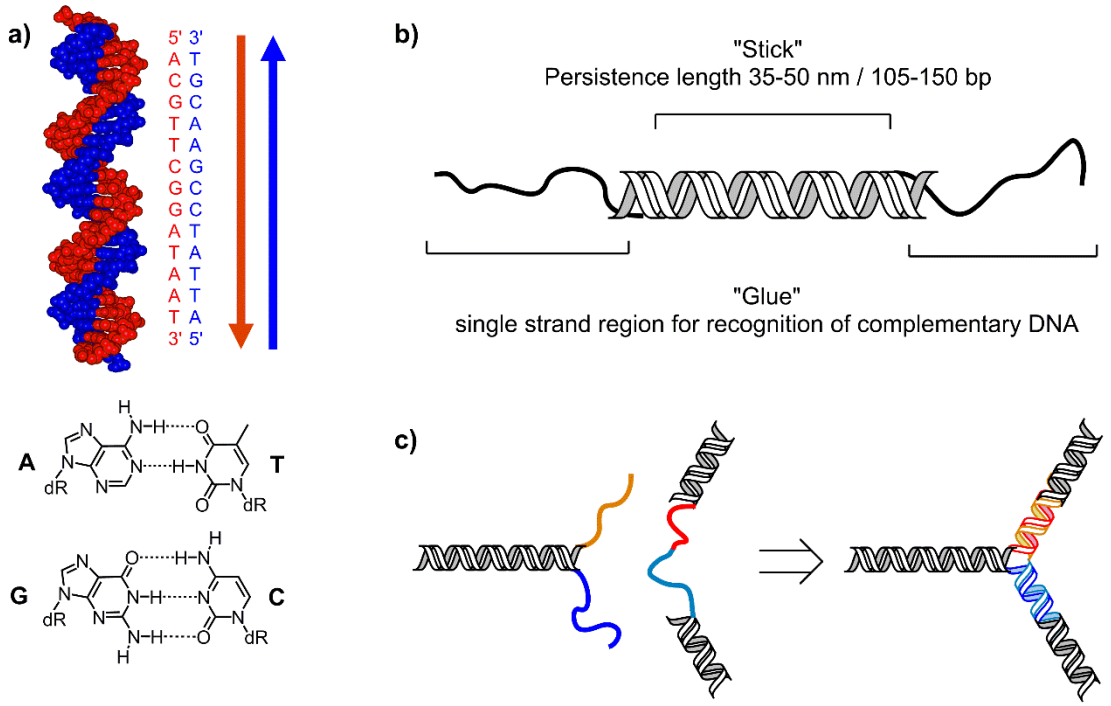

Fig. 1. a) Depiction of the DNA double helix (B-form) which is most commonly found in nature, with example of a complementary sequence for selective duplex formation *via* Watson-Crick base pairing of A=T and G≡C. b) DNA as rigid stick and flexible glue molecule for the construction of DNA nano-architectures. c) Concept of programmed self-assembly of DNA nano-structures: complementary ssDNA sequences (orange and red, light and dark blue) will hybridise to form pre-defined rigid constructs.

Whilst most of the DNA based nano-constructs are realised using unmodified DNA, it is intriguing to enhance the functionality of the nano-DNA systems by introducing functional groups not present in natural DNA. The various approaches showing the diversity of available functionalities have been reviewed independently,[4-6] in particular using organic chromophores,[7-10] and shall not be covered here in detail, but a focus is given on porphyrins as modifiers.[11] The formation of porphyrin assemblies is fascinating from the point of view of creating new functional materials, and applications in the fields of energy or electron transfer, light harvesting, optics, catalysis and many more have been reported numerously.[12-16] The optical and electrochemical properties of the porphyrins are very diverse and can be tuned by either chemically modifying the porphyrin core, or inserting metals in the central cavity, which is unique for porphyrins. Many different porphyrins and related compounds are available, though only few have been used for attachment to DNA. Out of the many templates that have been studied for creating porphyrin assemblies,[17-22] DNA is certainly among the most intriguing of scaffolds as it allows for easier control over sequence and structure, though peptides have not yet been fully explored in this respect and could provide a complementary template. The use of covalent chemistry in the formation of porphyrin assemblies has the advantage of taking control over sequence using the very same chemistries which are applied to the synthesis of the DNA, and starting from the same building blocks. Introduction of different porphyrins, potentially in combination with other functional entities, will give a well-defined array, where the porphyrins will be incorporated into a pre-determined spatial arrangement. Non-covalent approaches where modified porphyrin units self-assemble on a ssDNA template through hydrogen bonding provide an alternative route,[23,24] but this Account will focus on the formation, analysis and application of covalently modified DNA strands.

2. Covalent attachment of porphyrins to DNA

2.1. Single end-of-DNA porphyrin attachment

The first examples of porphyrins attached to DNA were reported by Meunier et al.[25] and Hélène et al.,[26] who created artificial nucleases with manganese porphyrins or chlorins, respectively (Fig. 2a). Around the same time, Czuchajowski et al. used the H-phosphonate approach to add pyridinium-porphyrin to form a photoreactive antisense oligo-deoxynucleotide (ODN).[27] This method was successful in adding one porphyrin modification to the DNA at its 5'-end. A similar approach was used by Berova and Balaz et al. to attach a porphyrin to the final phosphate group through mono-functional phosphoramidites, where it effectively acts as a cap on the blunt end of the DNA[28,29] and can even stabilise non-Watson-Crick G-A base pairs.[30] The groups showed that the porphyrins at the end of the DNA can act as a chiroptical marker for circular dichroism (CD) spectroscopy giving insight into structural aspects of the DNA and the environment of the porphyrin (Fig. 2b), which is strongly dependent on the solvent (salt concentration) and central metal of the porphyrin (which influences hydrophobicity and sterics through potential axial water ligands).[31-34] Since the porphyrin itself is achiral and produces no CD signal, its attachment to DNA invokes transfer of the chiral information of the DNA to the porphyrin. Porphyrins strongly absorb light around 420 nm (denoted Soret or B-band), thus the induced CD signal in this region provides an optimal handle to detect structural changes as it is well outside the window of the DNA absorbance. In this way, monitoring the structural change from B−DNA to Z−DNA with increasing salt concentration was successful.

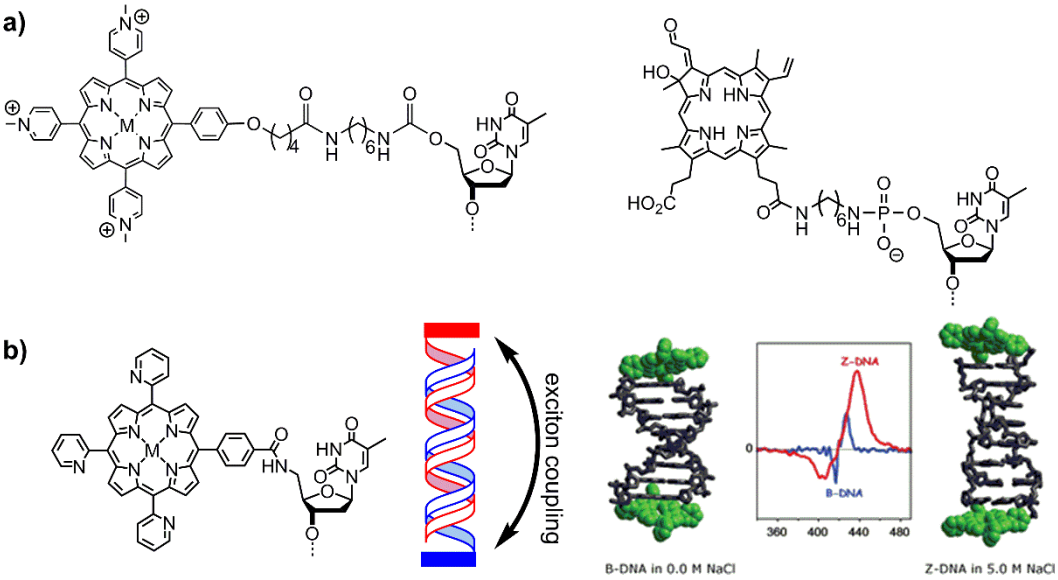

Fig. 2. a) First examples of end-of-DNA modification with porphyrinoids to create artificial sequence specific nucleases.[25,26] b) Structure (left) and schematic (middle) of porphyrins acting as caps (red and blue bars) for the blunt end of DNA; modelled DNA structure and induced Soret-band CD spectra of the porphyrins (right), showing DNA structure dependent exciton coupling. Reproduced from Ref.[28] with permission from the Royal Society of Chemistry.

Using the same methodology, Yamamura et al. developed a zinc porphyrin-DNA based on a *p*-tolylporphyrin.[35] The zinc porphyrin-DNA did not exhibit long range chromophore–chromophore exciton coupling at low salt concentration, but under high salt concentration strong interactions between porphyrins were observed. The system forms intermolecular stacks through interaction of the porphyrins, leading to the formation of insoluble aggregates. In fact, similar interstrand interactions were observed by Berova and Balaz,[34] though here the systems remained soluble in aqueous solvents. Again, the nature of the porphyrin plays an important factor in how the modified DNA behaves. Overall, those examples demonstrate the versatility of porphyrins attached to DNA with variable functionality, i.e. as enzyme mimic (artificial nuclease) or as chiroptical marker.

2.2. Porphyrins embedded within the DNA

Very different approaches to porphyrin-DNA were explored by Kool et al.,[36] Richert et al.,[37] and Murashima and Sugimoto,[38] where either the nucleobase or the entire nucleoside was replaced by a porphyrin (Fig. 3a). The porphyrin here is actually positioned within the interior base-stacking region of the DNA. Recently, Häner et al.[39] used this approach to create a four-porphyrin stack, where the complementary strands contain up to two porphyrins each; the interlocking nature of the array compensates the otherwise strongly destabilising effect of the porphyrin modification (Fig. 3b). Analysis of the constructs using CD, UV-Vis and fluorescence spectroscopy, showed that in all these cases the DNA still forms a B-type duplex, and that the porphyrins largely form a H-aggregate with concomitant exciton coupling; the porphyrin units also seem to stack very well with the neighbouring base pairs.

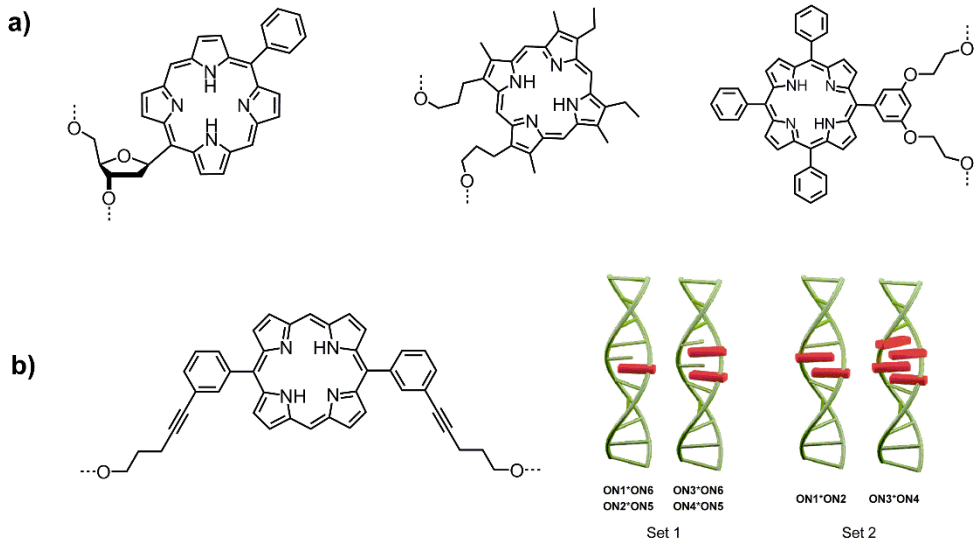

Fig. 3. a) Structures of base replacement[36] and nucleoside surrogates[37,38] for porphyrins embedded within the base stacking region of DNA. b) DNA interior porphyrin stack creating stable H-aggregates through interlocked formation of the assembly from complementary porphyrin modified DNA strands. Reprinted with permission from Ref. [39]; copyright 2014 American Chemical Society.

Weaker hybridization (i.e., lower melting temperature T_m) was seen in some of the systems, which depends on the nature of the modification, the nucleobase opposite to the porphyrin, and the number of adjacent porphyrins to create a stabilising stacking effect. As rule of thumb, an abasic site opposite to the porphyrin can reduce steric clashes, and stacking of multiple porphyrins within the DNA stabilises the duplex, though this has to be determined on a case by case basis.

2.3. Porphyrin located on the outside of the DNA

Several systems have been investigated to create porphyrin arrays with distinct composition, which are placed on the outside of the DNA, particularly within the minor or major groove. The attachment site of the porphyrin on the nucleoside will direct the porphyrin to the corresponding groove and is obviously crucial for the design of the array.

2.3.1 Porphyrin arrays in the minor groove

Strategies that have been explored to place the porphyrins into the minor groove of the DNA include the attachment of the porphyrins to the 2'-position of the ribose moiety, or to the phosphate group. Generally the porphyrins are attached *via* cross-linking, including amide formation with either long tethers, as explored by Meunier et al. (Fig. 4a),[40] direct amidation of 2'-amino ribose with carboxy-porphyrin as in the system by Sitaula and Reed,[41] or linking to a phosphoramidate through Michael addition as in the porphyrin-DNA of Majima et al. (Fig. 4b)[42] All provide alternative routes and represent a selection of the diversity of the chemistries that can be used. The study of Majima's system, which included both free-base and zinc metallated porphyrins attached to complementary strands, showed that a B-type DNA duplex was retained upon hybridisation, and the chromophores formed a face-to-face dimer near the minor groove of the ODN. The presence of the metal had a strong effect on the duplex formation and stability, where less stable dimers were obtained with two zinc-porphyrins. This confirms that the additional axial water ligands on the zinc make the zinc

porphyrins less hydrophobic and can prevent efficient π–π stacking, analogous to the intermolecular interactions described above. Therefore the choice of the central metal in the porphyrin not only influences the optical properties, but also has an impact on the overall structure and stability through modulating inter-porphyrin stacking.

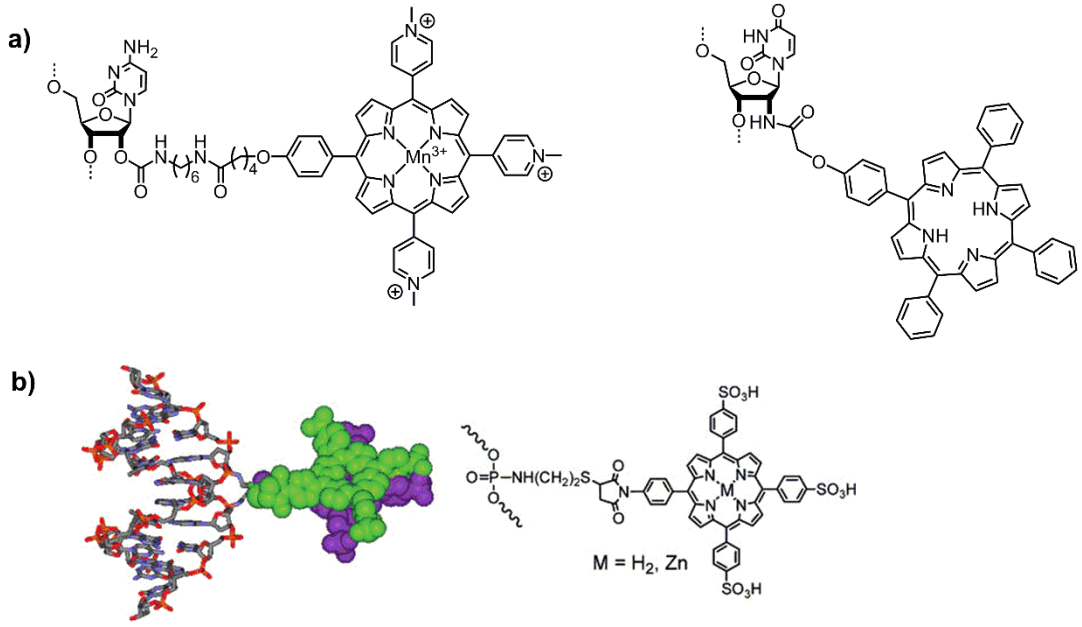

Fig. 4. a) Attachment of the porphyrin to the 2'-position of the ribose through tethers (left)[40] or direct amidation (right)[41] will position the substituents in the minor groove of the DNA. b) Conjugation to the phosphate backbone leads to external placement, and face-to-face stacked dimers can lead to a stabilising effect in the duplex, which is dependent on the central metal and its potential additional axial ligands. Reprinted with permission from Ref. [42]; copyright 2008 American Chemical Society.

Post-synthetic modification with a TMPyP-type porphyrin was achieved in a straight forward manner using cycloadditions, such as copper catalysed alkyne-azide click chemistry or Diels-Alder reaction, as shown by Wellner and Wagenknecht (Fig. 5a).[43] In this example, analysis of the T_m values and of the CD spectra revealed that the site of modification is not prevalent in the standard base-pairing, and that the porphyrins intercalate into the DNA. This, however, is strongly dependent on the coupling chemistry and with it the nature of the linker used, where sterically less demanding triazole linkers favour intercalation. Analogously, Filichev et al.[44] introduced the porphyrins *via* click chemistry but through the β-pyrrolic position, which provides a planar system between the porphyrin ring and substituent (Fig. 5b). A convenient microwave assisted method to synthesize multiporphyrin-DNA arrays consisting of one to four porphyrin units in various locations within the ODN strand was developed. Attachment of four porphyrins in adjacent DNA strands lead to a significant stabilization of the DNA duplex through the formation of H-aggregates of the porphyrins in the minor groove of the DNA. It should be noted that the minor groove arrays have in general been little explored and thus contribute a field of research with great potential to grow.

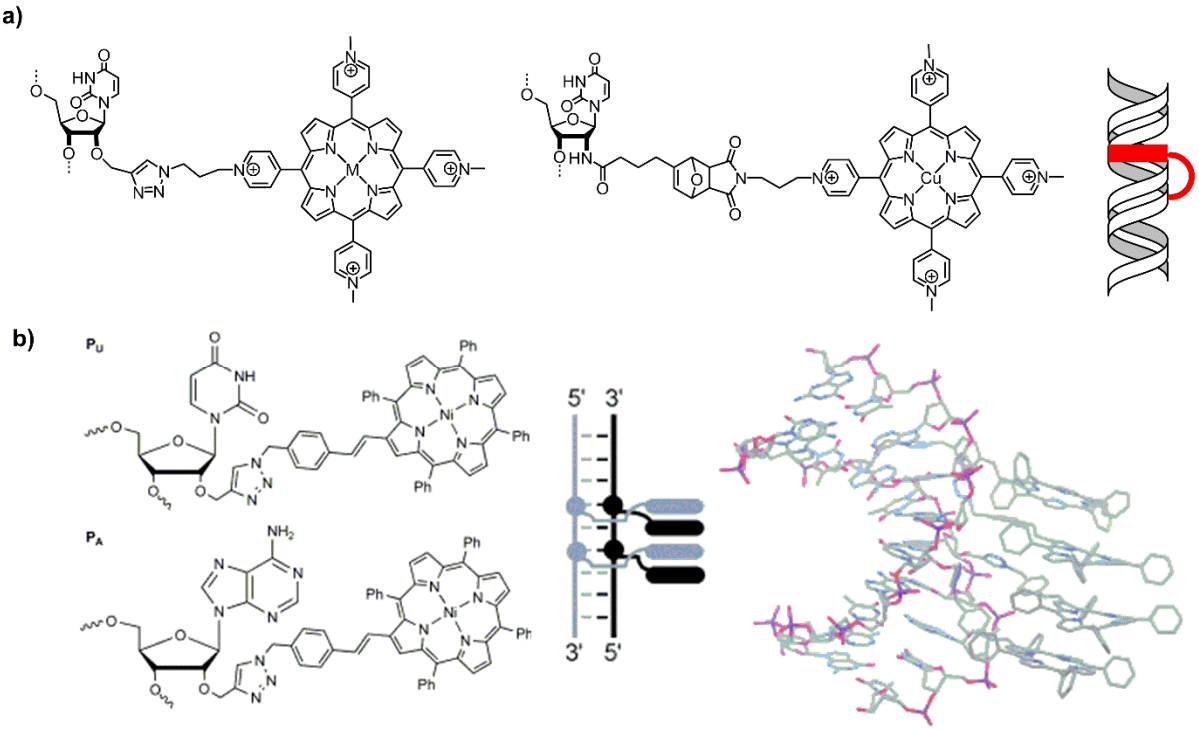

Fig. 5. a) Post-synthetic modification of DNA with porphyrins through click-chemistry or Diels-Alder reaction; the flexibility of the linker allows the porphyrin to intercalate into the DNA.[43] b) Attachment of the porphyrins through the β-pyrrolic position reduces steric hindrances, leading to stable H-aggregates of the porphyrins in the minor groove. Reprinted by permission of John Wiley & Sons, Inc. from Ref. [44]

2.3.2 Porphyrin arrays in the major groove

To create multiporphyrin arrays, where the porphyrins are held rigidly and in a predictable way on the DNA, new strategies had to be developed. We found that the use of *Sonogashira* coupling between 5-iodo-deoxyuridine (5-iodo-dU) and alkyne porphyrins is most versatile to synthesise building blocks for programmed insertion into DNA: the porphyrin is attached to the nucleobase and will protrude from the DNA into the major groove, leaving the Watson-Crick base recognition untouched.[45] The use of metallated porphyrins is crucial to avoid copper metallation during the coupling; most conveniently zinc is used, which is subsequently lost in the DNA synthesis, yielding the free-base porphyrin-DNA. As alternative methods, amide coupling,[46] click chemistry[47] or maleimide-thiol conjugation[48] can equally well be used. Structurally different modifiers such as diphenyl porphyrin (DPP-dU), tetraphenyl porphyrin (TPP-dU), or propargylamide-linked TPP (TPPA-dU) were thus synthesised (Fig. 6a) Phosphitylation is straight-forward, though the phosphoramidites are highly susceptible to oxidation due to the photosensitizing activity of the porphyrin. Silica gel column chromatography has thus to be performed under strict exclusion of light and oxygen, but precipitation from DCM-hexane is equally efficient for purification. The modifiers were successfully incorporated into DNA in variable numbers, ranging from one up to twelve porphyrins per DNA.[49-51] This demonstrates that there is virtually no limitation in the number of large modifications that can be attached to DNA, and the programmable nature of DNA synthesis allows for easy design of the modified strand. Purification and solubility of highly modified DNA can be an issue, which strongly depends on the nature of the porphyrin and the

overall length of the DNA. Purification is best performed by reverse phase HPLC using methanol and hexafluoro-isopropanol – triethylamine buffer.

The formation of DNA duplexes and the correct arrangement of the porphyrins in the major groove was confirmed by spectroscopy and molecular modelling, and the porphyrins form a nicely stacked helical chromophore array. While a single porphyrin shows the unperturbed absorption and emission properties, the multiporphyrin array display a significant broadening (TPP) or even splitting (DPP) of the porphyrin Soret band at 420 nm, and quenched fluorescence. The analysis of the dipoles of the porphyrins indicate that they are coupled as a combination of H- and J-aggregates.[51] We also observed that the porphyrins induce a stable helical arrangement in the ssDNA through stacking.[49] This means that the duplex is actually not required to form a helical stack of chromophores, which can potentially act as electronic wires due to efficient coupling. But this will have to be judged on a case-by-case basis.

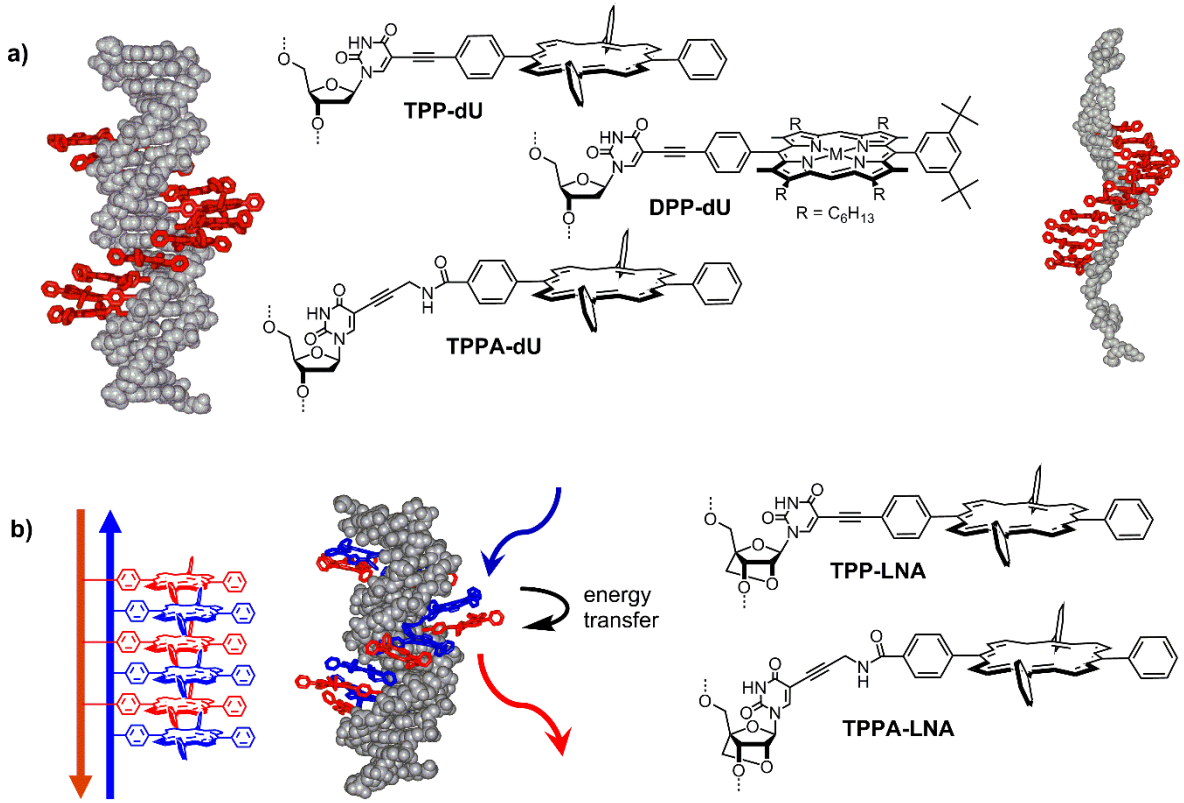

Fig. 6. a) First generation of porphyrin arrays with putative structure of the dsDNA array, and induced helical stack in the ssDNA.[49-51] Reprinted with permission from Ref. [49]; copyright 2007 American Chemical Society. b) Second generation zipper-porphyrin array, where the porphyrins are attached to both complementary DNA strands; different metallation leads to a photonic wire showing efficient energy transfer from ZnTPP to 2HTPP.[46,52,53] Reproduced from Ref. [46] with permission from the Royal Society of Chemistry.

Whilst this first generation of porphyrin-DNA was ideal for proof-of-concept, it also showed its limitations: the duplex stability is greatly reduced, which is strongly dependent on the nature of the porphyrin and the number of modifications. On average the thermodynamic destabilisation is greater for DPP (ΔT_m = −7 °C per porphyrin)[51] compared to TPP (ΔT_m = −3.5 °C per porphyrin),[49] and most likely arises from local structural perturbation of the DNA. A way around this issue is to create interlocked

arrays, called *zipper arrays*, where the porphyrins are attached to the complementary sequences in an alternate manner.[46,52] This has several consequences: firstly the DNA duplex is stabilised by >40 °C in a 12-porphyrin array (ΔT_m = +0.5 °C per porphyrin), and secondly the two porphyrin-DNA strands can be metallated separately with different metals. The duplex stability can further be increased by using the pre-organised "locked nucleic acid" (LNA, Fig. 6b) to give ΔT_m of up to +1.7 °C per porphyrin.[53] In terms of metallation, zinc, copper or cobalt were inserted post-synthetically. With a mixed zinc – free-base porphyrin the first reversible photonic wire based on a DNA scaffolding approach was created,[52] which shows efficient energy transfer in the annealed duplex state but not in the denatured single strand state.

The hydrophobic nature of the porphyrin has far reaching consequences on the structure and properties of the DNA. We found through spectroscopic studies (absorption and emission, CD, EPR, SAXS) that there are substantial intermolecular interactions through π-stacking of porphyrins, both in ssDNA and dsDNA,[46,53,54] similar to what has been reported by other groups.[34,35] Overall two to four DNA duplexes associate with an interstrand centre-to-centre distance of 6.5 – 8.9 Å of the porphyrins. Notably this does not lead to aggregation and precipitation, but to the formation of discrete bundles which remain soluble in water. These interactions are dominant at concentrations > 5μM DNA and >100 mM NaCl, but persist even in pure water. This so far prevents the analysis of pure intramolecular porphyrin interactions as there is always an intermolecular component present. On the other hand, this can lead to the stabilisation of non-canonical DNA structures, such as GA-duplexes,[30,55] i-motifs,[47] and G-quadruplexes,[56] in some cases leading to a change in the topology of those structures.[57] This feature could very well be advantageous in the design of photonic systems, as it could allow to organise the chromophores in different orientations with respect to each other than would be observed from a DNA duplex.[58] The intermolecular associations are also observed with small aromatic molecules, and might be a more general feature in modified DNA; this can be explored as molecular glue to add another level of interactions. [59,60]

3. Applications of porphyrin-DNA

The chemistries and design approaches are now well set, and it is timely to consider applications of the porphyrin-DNA. The potential creation of energy transfer systems has been mentioned above; here we would like to introduce two other applications that we are pursuing and where porphyrins show to be advantageous over other modifiers.

3.1 Porphyrins as electrochemical tags for DNA sensing

Porphyrins are not only optically active, but have a rich electrochemistry which again depends strongly on the structure, central metal and micro-environment. We used cobalt porpyrin-DNA to create highly sensitive geno-sensors (Fig. 7a).[61] The porphyrin is located close to the electrode surface, and we found that upon duplex formation the ionic current is greatly dimished. This is explained by placing the porphyrin into the hydrophobic major groove of the dsDNA and giving it limited access to the electrolyte, compared to the exposed single strand arrangement. The mechanism is distictively different to other distance based "signal on-off" systems. The selective detection of complementary strands including single-nucleotide polymorphism was demonstrated, and it was calculated that as few as 1000 DNA molecules can be measured. In this way, an Avian Influenza Virus (H5N1) based DNA sequence was detected at femtomolar levels from competing non-complementary sequences.

3.2 Porphyrin-DNA based lipid bilayer spanning nano-pores

Nanopores are currently under intense investigation; their facile insertion into membranes can be achieved on a single molecule level, and ionic current measurement through these nanopores gives raise to single molecule detectors. The research is focused on naturally occurring biological nanopores (e.g. α-hemolysin), solid-state nanopores and hybrids of the two, with a strong focus on single molecule DNA sequencing. We have thus explored the formation of DNA origami based nanopores to create simple and tunable systems, because proteins are inherently tricky to modify at precise positions. Our pores consist of a bundle of six hexagonally arranged DNA duplexes, stabilized through cross-over strands (Fig. 7b).[62] The DNA pore itself does not insert into the membrane due to the inherent energy mismatch to the hydrophobic environment of the membrane, therefore we initially added a hydrophobic belt consisting of ~70 ethyl groups. Insertion was demonstrated by a steady ionic current through the DNA origami pore. The alkyl belt can be replaced by only two porphyrins, located on opposite sides of the pore, which showed equally efficient insertion.[63] The porphyrin therefore clearly outweighs the alkyl groups by a large margin. The stable insertion of the DNA origami pores was confirmed by single molecule measurement of the ionic current, and by fluorescence spectroscopy. We have further minimalized the system by using a simple, six porphyrin-DNA duplex (Fig. 7c).[64] We could demonstrate that this DNA duplex inserts stably into lipid bilayers, creating the smallest possible DNA based nano-pore with maximum simplicity, which lacks a hollow central channel. By combining electrophysiology measurements with all-atom molecular dynamics simulations, we showed that ions flow at the DNA–lipid interface as the lipid head groups tilt toward the amphiphilic duplex, forming a toroidal pore filled with water and ions. The ionic current traces show well-defined insertion steps, closures, and gating, analogous to those observed for traditional protein channels or synthetic pores. In both larger and small pore, the porphyrin actually provides a very convenient handle with dual property, namely a hydrophobic anchor to efficiently embed the negatively charged DNA, which simultaneously acts as a chromophore to monitor the insertion and distribution of the DNA origami in the artificial membrane. It is interesting to note that the attachment site and number of porphyrins greatly influences the interaction with a lipid bilayer. While two porphyrins on opposite sides of DNA bundles direct larger constructs into the lipid bilayer, for simple dsDNA this may not be sufficient. In our case six porphyrins ensured complete trans-membrane insertion, while single porphyrin modification of DNA retains the DNA in the aqueous environment. This has been used by Börjesson and Albinsson[65-67] to arrange porphyrins within a lipid bilayer, and using the DNA as structural scaffold in the water phase where it shows normal duplex formation behaviour, thereby creating a range of photoactive systems (Fig. 7c). While this may sound counterintuitive, it can be explained by the overwhelming hydrophobic effect of the porphyrin, which compensates the energy barrier to insert the DNA only when in appropriate geometrical arrangement. Additionally, the linker length seems to be crucial as shorter linkers tend to embed the entire porphyrin-DNA, while longer linkers tend to only insert the porphyrin.

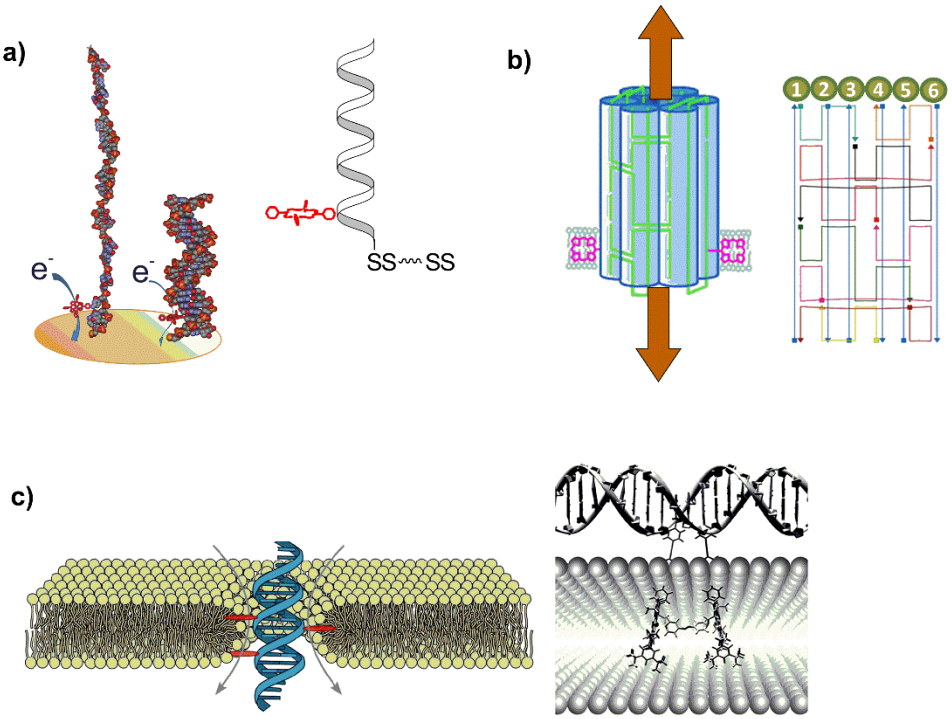

Fig. 7. a) Schematic of an electrochemical genosensor based on cobalt porphyrin with an efficient "signal-off" detection of the target sequence in the fM range.[61] b) DNA bundle consisting of six DNA helices with two porphyrins as lipophilic anchors to create artificial nano-pores with a 2 nm inner pore diameter, Reprinted by permission of John Wiley & Sons, Inc. from Ref. [63]. c) A minimal porphyrin-DNA pore where the current is induced through a flow of ions along the DNA backbone (left).[64] This is compared to a two-porphyrin-DNA with longer linkers and elongated distance between the porphyrin attachment sites (right), embedding the porphyrins in the membrane while keeping the underlying DNA scaffold in the aqueous environment. Reproduced from Ref. [66] with permission from the Royal Society of Chemistry.

4. Conclusions

DNA certainly is a most versatile supramolecular scaffold, not only for porphyrins, but for creating functional molecules in general, and for chromophore assemblies in particular. Porphyrins are ideal modifiers in many ways: their electronic properties can be fine-tuned, and their lipophilicity can be used for anchoring DNA in hydrophobic environments, though this may lead to formation of intermolecular interactions and solubility issues. So far porphyrin-DNA has mainly been used for basic studies in terms of structure and optical properties. However, as outlined above many applications are emerging and may well be far-reaching in the fields of artificial photosynthesis or medicine. Where is the field heading? Future efforts should be directed to include other functionalities for applications in opto-electronics which might be a major application;[7] a large number of DNA modifiers are available, also commercially, and the chemistries are well laid out to create functional DNA where we can (more or less) reliably predict their properties. The programmable nature of DNA allows positioning the functional groups in well-defined spatial arrangements, for example to alter the distance and avoid self-quenching through formation of H-aggregates. In addition, many other scaffolds for nano-arrays are compatible with DNA, such as MOFS, carbon nano–tubes and –sheets, oligopeptides / proteins, nanoparticles, dendrimers etc. Thus the future of DNA nano-architectonics will certainly see more advances through the combination of a diverse set of scaffolds (including DNA

origami) and modifiers, and it is timely to embed functional DNA into larger nano-systems to create truly tailored materials.

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Notes

The author declares no competing financial interest.

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Eugen Stulz studied chemistry in Bern (Switzerland), from where he obtained his PhD in 1998 in bioorganic chemistry, working on artificial nucleases. He received a SNF Fellowship to work as PDRA in Cambridge (UK), before starting his independent career in 2003 in Basel (Switzerland) as Treubel Fellow. In 2006 he was appointed lecturer in Southampton (UK), promoted senior lecturer in 2010 and associate professor in 2014. His current research interests focus on the use of DNA as construction material for functional nano-structures, with applications in molecular electronics and bio-medicinal chemistry.

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