Electronic supporting information

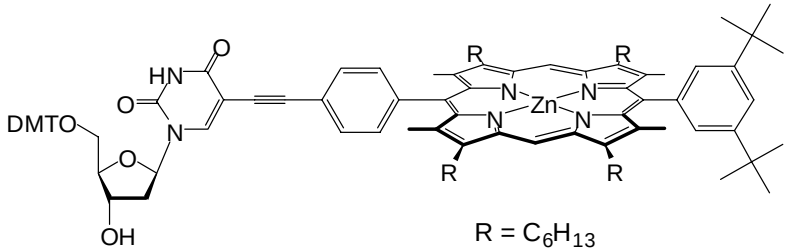
Supramolecular helical porphyrin arrays using DNA as scaffold

Imenne Bouamaied, ThaoNguyen Nguyen, Thomas Rühl and Eugen Stulz*

General:

All reagents and solvents were purchased from Fluka or Sigma-Aldrich and used as received, except 5-iodo deoxyuridine (Rasayan Inc., Encinitas, CA, USA) and DNA synthesis reagents (Glen Res., Cambio, Cambridge, UK or Link Technologies. Ltd., Bellshill, Scotland). NMR spectra were recorded on Varian Gemini VXR400; chemical shifts (δ) are indicated in ppm, relative to the solvent signals of the partially deuterated nuclei of chloroform-d1 (δ = 7.26 ppm). Absorbance and emission spectra were recorded on Perkin-Elmer Bio-Lambda II spectrometer and FluoroMax-2, respectively. Molar extinction coefficients (ε) are referred to a cell path of 1 cm at 260 nm for oligonucleotides. MALDI-ToF MS were measured on Perseptive Biosystems Voyager-DE PRO. CD spectra were recorded using a Chirascan Circular Dichroism Spectrometer. The data was given in mdeg and corrected to delta epsilon using the formula $\Delta\varepsilon = \theta / (10 \times \text{conc.} \times \text{pathlength} \times 3298)$; conc. is in mol/litre, pathlength is 1 cm.

5-Porphyrinyl-2'-deoxy-5'-DMT-dU

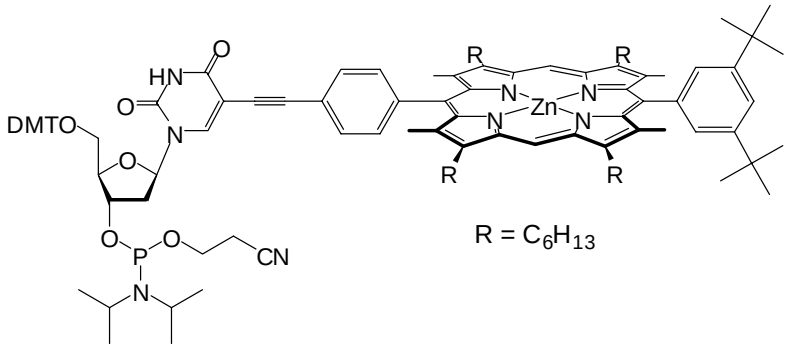


To a solution of 5'-O-DMT-iodouracil[1] (374 mg, 0.57 mmol, 3 eq) in DMF (4 ml) with molecular sieves (4 Å), CuI (29.2 mg, 0.45 mmol, 80 %) was added in the dark under Argon. TEA (0.16 ml, 0.76 mmol, 4 eq.) was added when all the CuI was dissolved. The acetylene porphyrin[2] (200 mg, 0.19 mmol, 1eq) was dissolved in DMF (4 ml) and added to the mixture. Finally, 88.5 mg (0.23 mmol, 40%) of $Pd(PPh_3)_4$ was added, and the reaction mixture was stirred under argon for 48 h. The solution was diluted with EA (80 ml), washed with a solution of H_2O/NaCl (1:1, 6×35 ml) and dried over Na_2SO_4. Evaporation of the solvent at reduced pressure, followed by a chromatography column on silica gel (gradient of DCM/MeOH from 100:0.5 to 100:1) afforded the 5'-O-DMT-dU^{ZnDPP} (294 mg, 0.18 mmol, 98%) as a purple solid.

$C_{100}H_{120}N_6O_7Zn$: 1580.85 g/mol. **MALDI-ToF-MS**: m/z: 1581.4 $[M]^{\bullet+}$. **TLC**: R_f = 0.44 (DCM/MeOH 100:3). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ (ppm) = 10.11 (s, 2H, H-meso), 8.16 (s, 1H, -NH), 7.94, (m, 2H, H-arom.), 7.85 (m, 3H, H-arom.), 7.77 (m, 4H, H-arom.), 7.59 (m, 2H, H-arom.), 7.49 (m, 4H, H-arom.), 7;40 (m, 3H, H-arom.), 6.92 (m, 4H, m-arom.), 6.39 (m, 1H,

H-1'), 4.59 (m, 2H, H-3' + H-4'), 4.15 (m, 1H, -OH(3')), 3.97 (m, 8H, -CH_2-C5H_{11}), 3.62 (m, 2H, H-5'), 2.58 (m, 2H, H-2'), 2.45 (s, 12H, -CH_3), 2.19 (m, 8H, -CH_2-CH_2-C_4H_9), 1.77 (m, 8H, -C_2H_4-CH_2-C_3H_7), 1.52 (m, 26H, -C_3H_6-CH_2-C_2H_5 + –C(CH_3)$_3$), 1.40 (m, 8H, -C_4H_8-CH_2-CH_3), 0.92 (m, 12H, -$C_{10}H_5$-CH_3).

5-Porphyrinyl-2'-deoxy-5'-DMT-dU-CE 1



The protected 5'-O-DMT-dU^{ZnDPP} (146 mg, 92 µmol, 1 eq) was co-evaporated three times with dry pyridine, and dried on the vacuum line overnight. The product was dissolved in dry DCM (2 ml) with molecular sieves (4Å, powder) and stirred for an hour in dark. Then, DIPEA (70 µl, 368 µmol, 4 eq) and 2-CEP-Cl (62 µl, 276 µmol, 3 eq) were added and the reaction mixture was stirred 2.5 hours under argon and in the dark. The mixture was evaporated and put directly on a chromatography column (DCM/EA, 1:1) under argon. The 5'-O-DMT-dU^{ZnDPP} phosphoramidite **1** (131 mg, 73 µmol, 80%) was obtained as a purple solid which was kept under argon and in the dark.

$C_{109}H_{137}N_8O_8PZn$: 1780.96 g/mol. **MALDI-ToF-MS**: m/z: 1781.2 $[M]^{\bullet+}$. **TLC**: Rf = 0.85 (DCM/AcOEt 1:1). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ (ppm) = 10.09 (2H, s, H-meso), 8.05 (s, 1H, -NH), 8.05-7.98 (m, 5H, H-aro,), 7.77 (m, 4H, H-arom.), 7.59 (m, 2H, H-arom.), 7.49 (m, 4H, H-arom.), 7;40 (m, 3H, H-arom.), 6.92 (m, 4H, m-arom.), 6.22-6.20 (m, 1H, H-1'), 4.59 (m, 2H, H-3' + H-4'), 4.15 (m, 1H, -OH(3')), 3.97 (m, 8H, -CH_2-C5H_{11}), 3.90-3.93 (2H, m, -CH_2CH_2CN), 3.62 (m, 2H, H-5'), 2.97-2.92 (2H, m, NCH(CH_3)$_2$), 2.60-2.63 (2H, m, -CH_2CN), 2.58 (m, 2H, H-2'), 2.47 (s, 12H, -CH_3), 2.19 (m, 8H, -CH_2-CH_2-C_4H_9), 1.77 (m, 8H, -C_2H_4-CH_2-C_3H_7), 1.52 (m, 26H, -C_3H_6-CH_2-C_2H_5 + –C(CH_3)$_3$), 1.40 (m, 8H, -C_4H_8-CH_2-CH_3), 1.07 (12H, s, NCH(CH_3)$_2$), 0.92 (m, 12H, -$C_{10}H_5$-CH_3). **^{31}P NMR** (162 MHz, $CDCl_3$): δ_P 146.2, 145.6.

DNA Synthesis and purification

The oligonucleotides were synthesized on an Applied Biosystems Expedite synthesizer on solid support (Glen Research, CPG, pore size 500 Å) on a 1.0 µmol scale. The synthesis was carried out in the standard mode using 2-cyanoethyl-*N*,*N*-diisopropylphosphoramidites. The coupling time for incorporation of the modified nucleotide was increased from 40 s to 600 s using a 25 mM solution of **1** in DCM-MeCN 1:1. The synthesis was carried out in trityl-ON mode using F-DMT-dC/dT-CE (Glen Res.) as last nucleotide for the fluorous affinity purification.[3] After the synthesis, the solid phases were dried and incubated overnight with 2 ml concentrated ammonium hydroxide - dioxane 1:1 at 40° C. Without removing the ammonia and dioxane, the mixture was diluted with an equal amount of loading buffer, and the samples

were purified using fluorous affinity chromatography as described in the manual (Glen Research). All measurements were done in 100 mM NaCl, 50 mM KH_2PO_4, pH 7.0, c(ODN) = 10^{-6}. For the hybridisation of the porphyrin strands **2-4** onto beads, the following sequence was synthesised on oligo-affinity support (OAS, Glen Res.):

(OAS)-3'-ATTGGCATCGATCAAAGCTTAGCAT

2 5'-CCGTAGCTAGT**P**TCGAATCGTA-3' *m/z*: calcd. 7755.6, found 7855
3 5'-CCGTAGCTAG**P**T**P**CGAATCGTA-3' *m/z*: calcd. 8731.2, found 8789
4 5'-CCGTAGCTAG**PPP**CGAATCGTA-3' *m/z*: calcd. 9706.0, found 9786
5 5'-CATCGTAGTA**P**A**P**A**P**A**P**ATCCGTACTC-3' *m/z*: calcd. 12190.7, found 12213
6 5'-TTTTT**PPPPP**TTTTTT-3' *m/z*: calcd. 10043.3, found 10075

Extinction coefficients and melting temperatures

ODN	log(ε_{260})	Tm [°C] by CD	Tm [°C] by UV
21-mer DNA	5.316	n.d.	63.5
27-mer DNA	5.428	n.d.	65.0
2	5.310	42.4	42.3
3	5.304	37.1	36.6
4	5.298	41.6	42.8
5	5.400	n.d.	37.0
6	5.087	n.d.	n.d.

The extinction coefficient was calculated using standard ε-values for DNA taking the different value for **1** into account (ε_{260} = 5866).

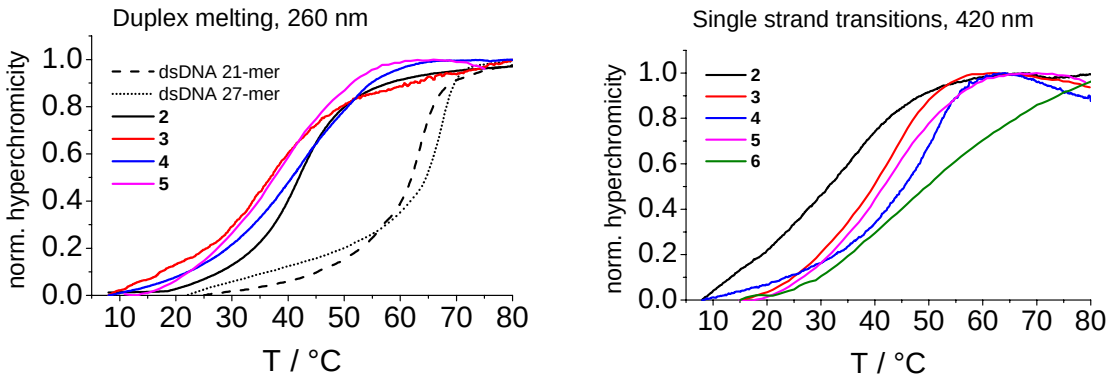
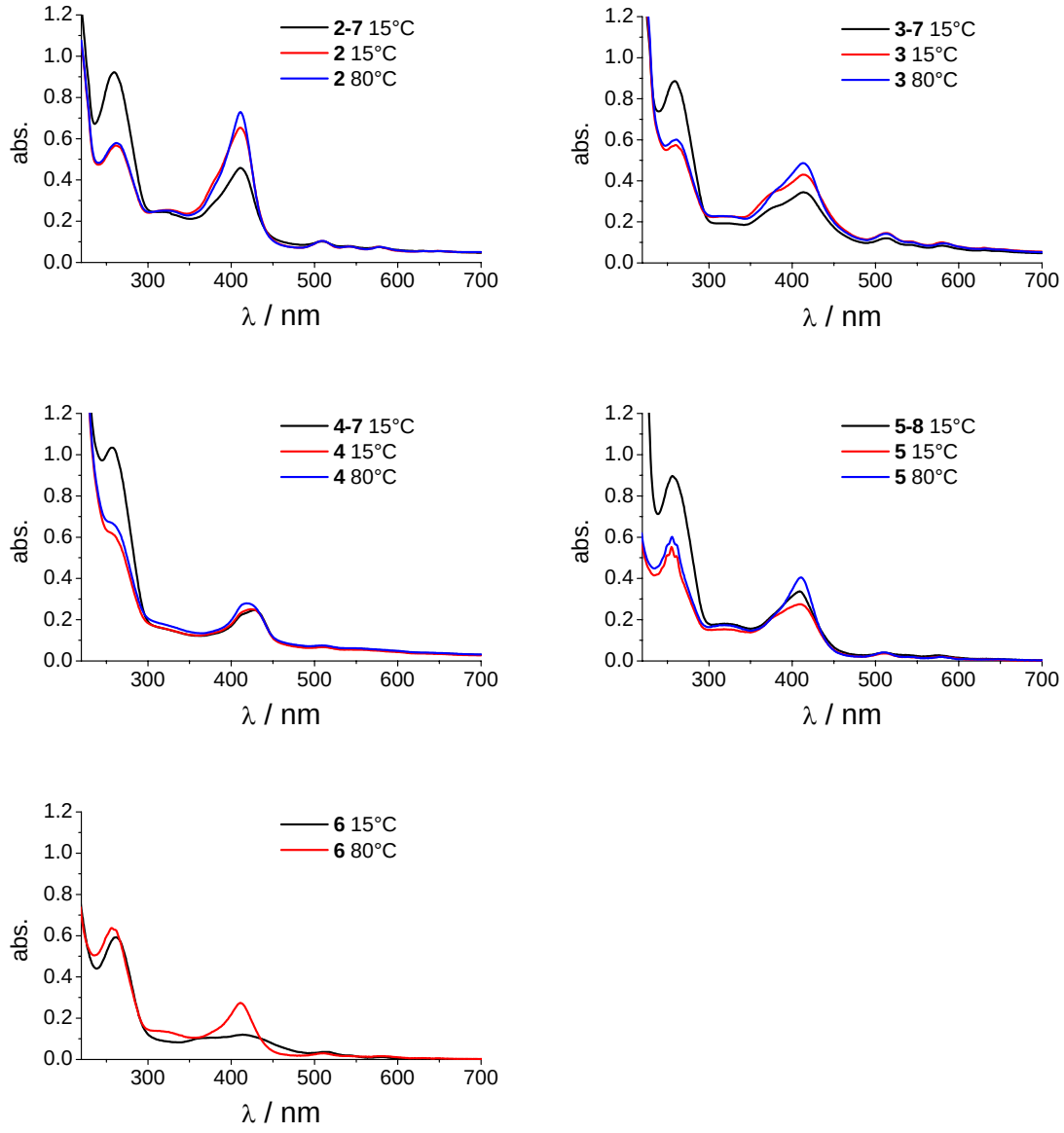


Fig. S1: Melting curves of the DNA duplexes (left) measured at 260 nm, and single strand transitions recorded at 415 nm (right).



FigS2: UV-vis spectra of the porphyrin-DNA strands as single strands at 15°C and 80°C, and as double strands at 15°C (exc. **6**: single strand only).

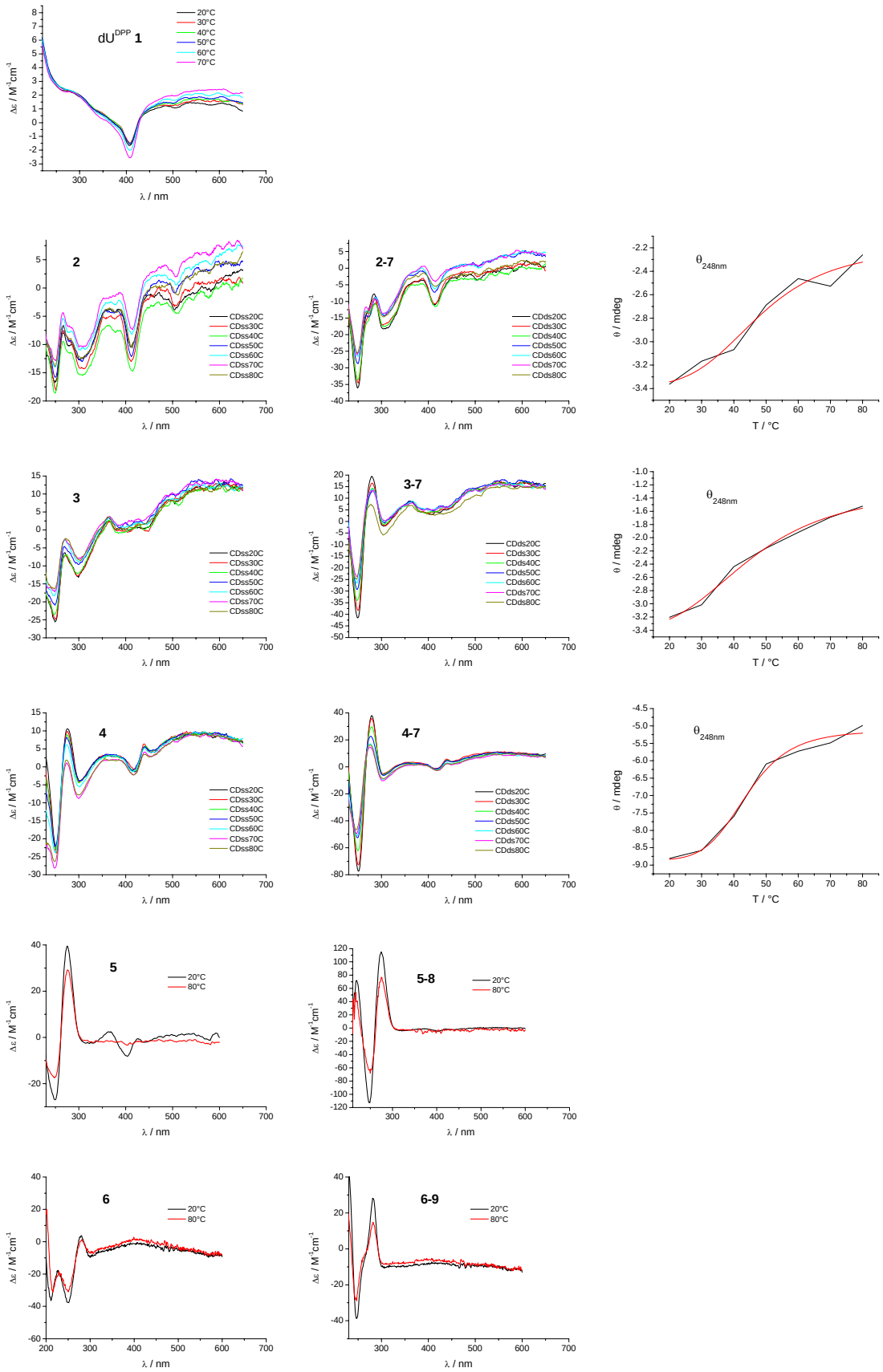


Fig. S3: CD spectra of the porphyrin single and double strands at different temperatures.

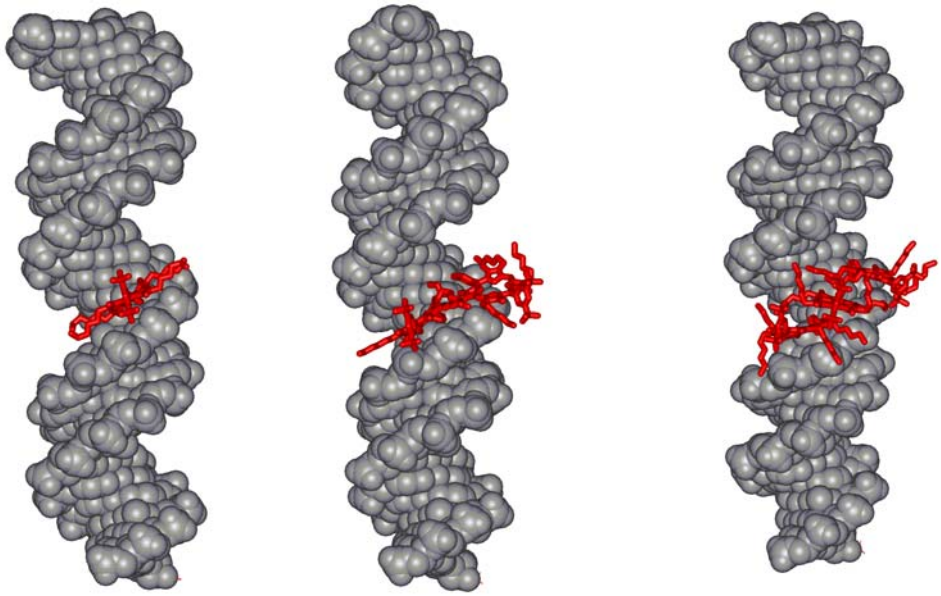


Fig. S4: Energy minimised structures of the porphyrin-DNA strands **2-4** using MacroModel (Amber*).[4]

5 5'-CATCGTAGTA**P**A**P**A**P**A**P**ATCCGTACTC-3'
8 3'-GTAGCATCATATATATATAGGCATGAG-5'
8x 3'-GTAGCATCATCTCTCTCTAGGCATGAG-5'

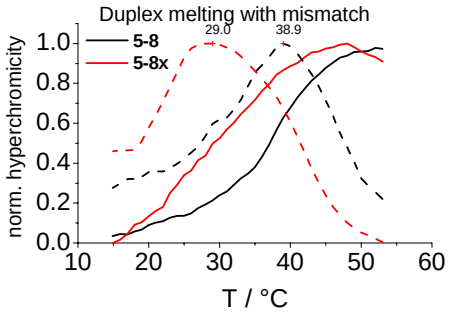


Fig. S5: Melting curves of the matching strands **5•8** and with C-T mismatches at the porphyrin modification sites (**5•8x**). The dashed lines are the first derivatives to determine T_m.

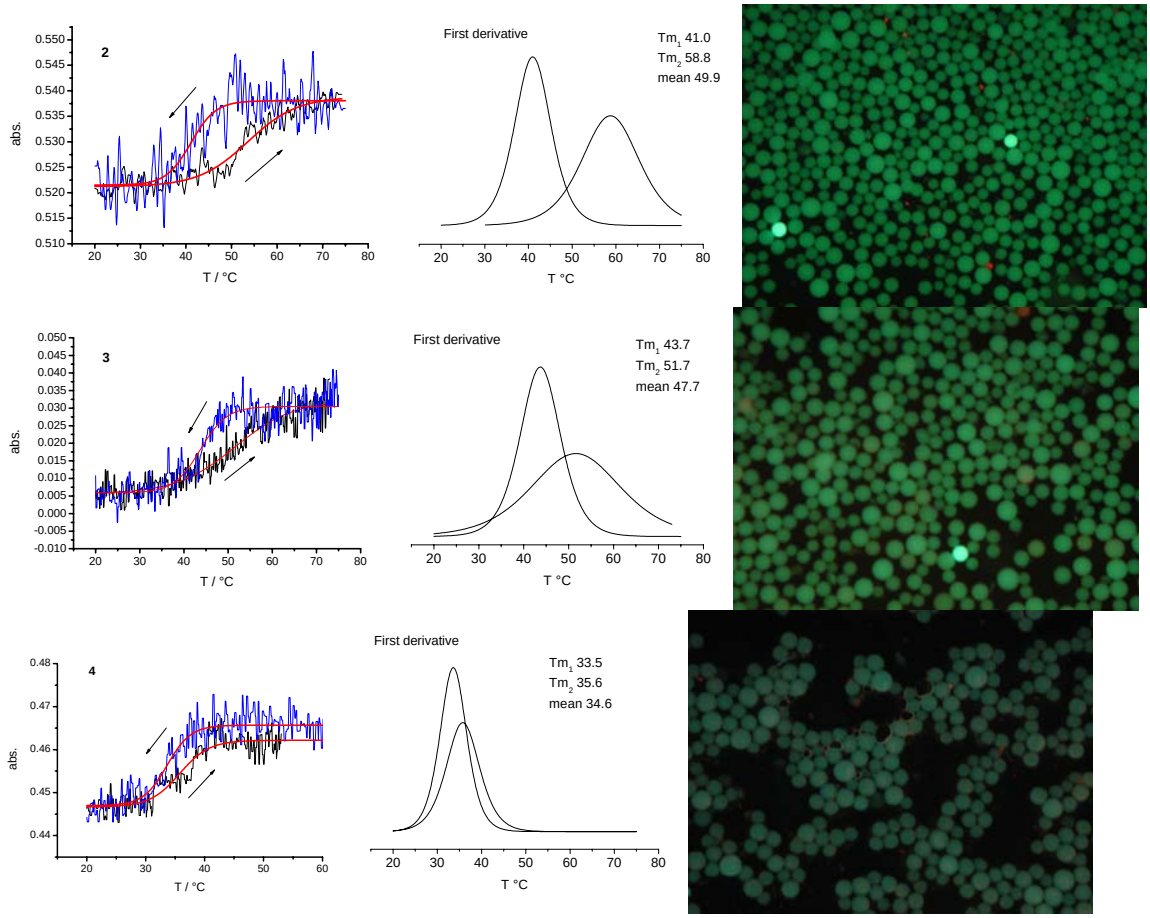


Fig. S5: Melting measurements of porphyrin-DNA strands on beads (black curve: melting, blue curve: annealing), first derivatives of the sigmoidal curve fitting, and fluorescence microscopy pictures of the beads (excitation 330-385, emission 420 nm).

1. D. A. Berry, K.-Y. Jung, D. S. Wise, A. D. Sercel, W. H. Pearson, H. Mackie, J. B. Randolph and R. L. Somers, *Tetrahedron Lett.*, 2004, **45**, 2457-2461.
2. E. Stulz, S. M. Scott, Y. F. Ng, A. D. Bond, S. J. Teat, S. L. Darling, N. Feeder and J. K. M. Sanders, *Inorg. Chem.*, 2003, **42**, 6564-6574.
3. C. Beller and W. Bannwarth, *Helv. Chim. Acta*, 2005, **88**, 171-179.
4. F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W. C. Still, *J. Comput. Chem.*, 1990, **11**, 440-467.