Supporting Information

A biomimetic stress sensitive hydrogel controlled by DNA nanoswitches

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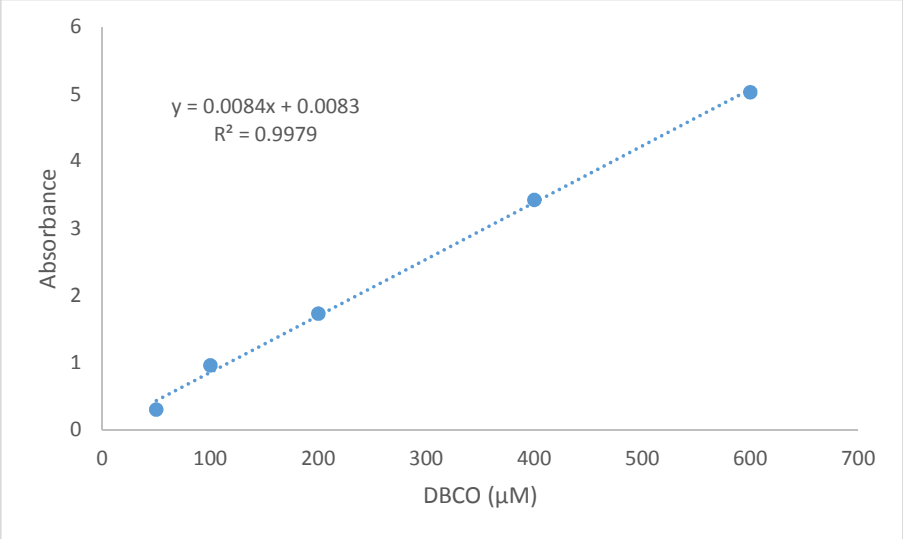

Samples	[DNA-DBCO] at 0 mins (Absorbance)	[DNA-DBCO] after 12 hours (Absorbance)
DNA A	~100 µM (0.958)	~ 4 µM (0.108)
DNA B	~100 µM (0.860)	~ 10 µM (0.112)
Control PIC, no DBCO	~ 5 µM (0.05)	~ 5 µM (0.06)

Figure S1. Yields of DBCO-DNA conjugation to N_3-functionalized PIC polymers. A standard curve was generated by measuring the absorbance of free concentrations of DBCO at 309 nm using a Nanodrop spectrophotometer (ND-1000, Thermo Scientific). The amount of DNA-DBCO clicked on DNA A and DNA B was determined by the absorbance of residual free DNA-DBCO after the click reaction. Comparing the amount of free DBCO before (0 min) and after incubation (12 hours) with the polymer reveals a high reaction efficiency of ~90 - 95 % for both DNA A and B oligonucleotides.

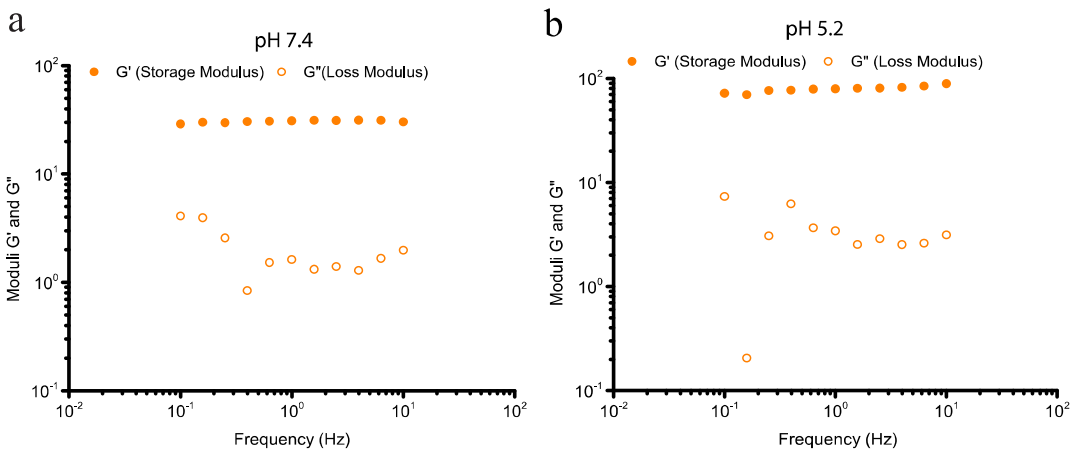

Figure S2. Frequency dependent rheology of PIC DNA hydrogels cross-linked with 0.9 equivalents DNA LC at pH 7.4 (a) or 5.2 (b). The hydrogels were stable and did not relax as demonstrated by measuring G' and G" over a range of frequencies (10^{-3} to 10 Hz). All measurements were performed at 30 °C in PBS, 10 mM $MgCl_2$, pH 7.4.

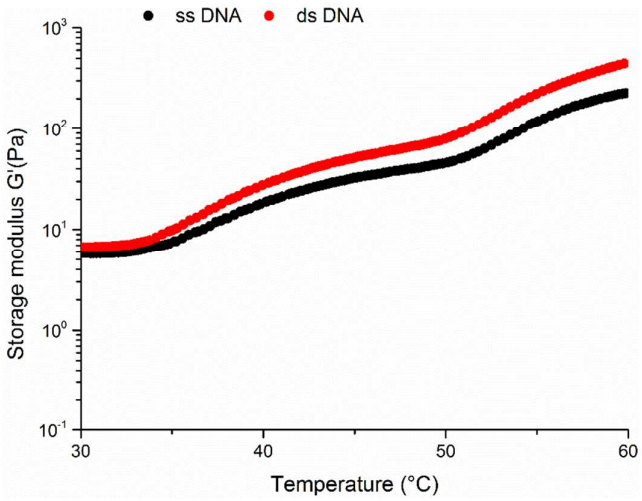

Figure S3. Temperature dependent rheological analysis of PIC-DNA hydrogel, covalently cross-linked with DNA AB (single-stranded) or DNA AB + C (double stranded). (1 ^{o}C min^{-1} at (1 Hz) and strain (2%) PBS, 10 mM $MgCl_2$.)

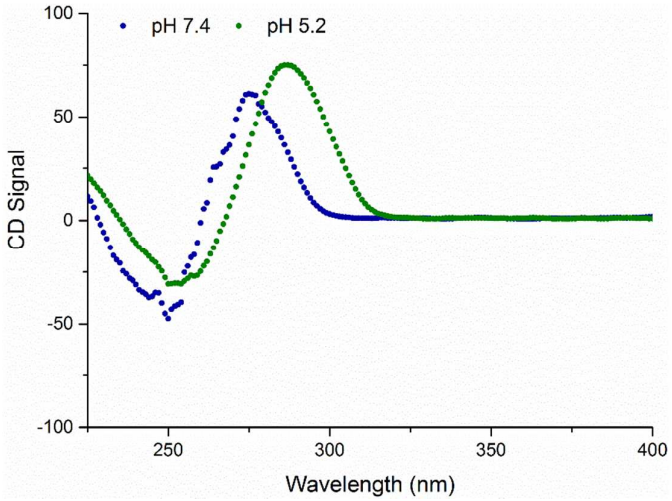

Figure S4. CD spectra to confirm formation of an i-motif in solution (25 ^{o}C, PBS.10 mM $MgCl_2$). The spectrum of DNA LC shows a large positive peak at ~ 260 nm at pH 7.4 and a larger positive peak, shifted to ~ 285 nm at pH 5.2. Simultaneously, the small negative peak becomes smaller and shifts to higher wavelength. Both are indicators of a switch to an i-motif structure at low pH.

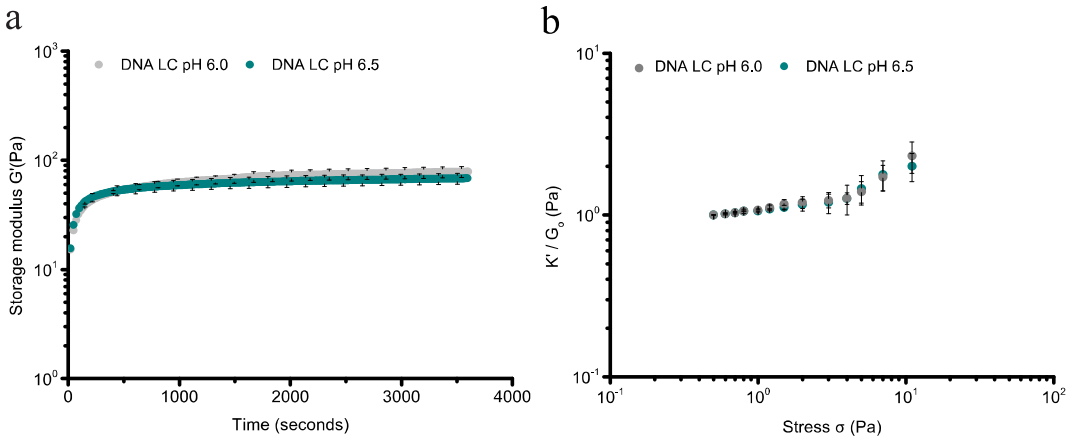

Figure S5. pH dependent rheological analysis of PIC-DNA cross-linked with 0.9 equivalents DNA LC to form the i-motif at 30 ^{o}C in PBS, 10 $\times$ 10^{-3} M $MgCl_2$. a) Time evolution of storage modulus G' after addition of DNA cross-linker LC at pH 6.0 (grey) and pH 6.5 (green). b) K'/G_0 as function of σ at pH 6.0 (grey) and pH 6.5 (green).

Table S1 Mechanical properties of hydrogel cross-linked with i-motif at pH 6.0 and 6.5

DNA construct		Rheological properties		
Cross-linker Sequence	**Contour Length (nm)**	**G_o (Pa)**	**σ_c (Pa)**	**σ_{max} (Pa)**
ss-DNA LC (pH 6.0)	~ 16 - 19	79 ± 9	4 ± 0.5	30
ss-DNA LC (pH 6.5)	~ 16 - 19	68.5 ± 8	4.5 ± 0.5	30

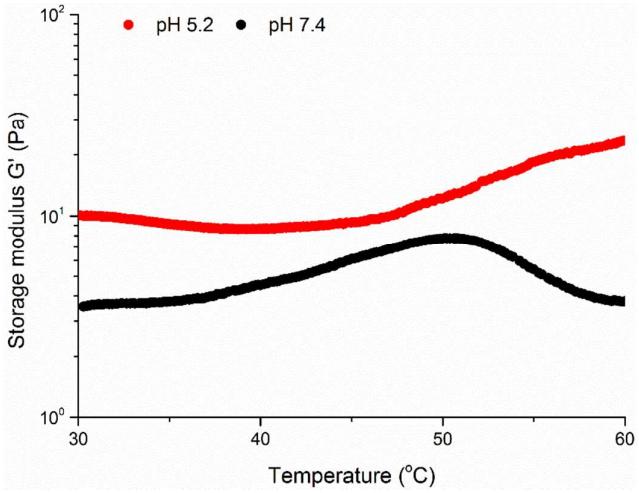

Figure S6. Rheological analysis of DNA triplex cross-linked PIC hydrogel at pH 7.4 and pH 5.2. Temperature dependent rheology was measured with ramping of 1 ^{o}C min^{-1} at (1 Hz) and strain (2%) PBS, 10 mM $MgCl_2$.

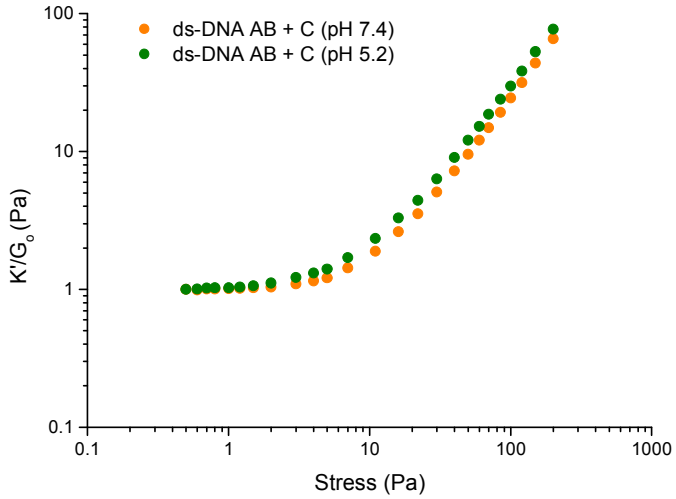

Figure S7. pH dependence of PIC DNA hydrogels covalently cross-linked with DNA AB + C at pH 7.4 (orange) and 5.2 (green).

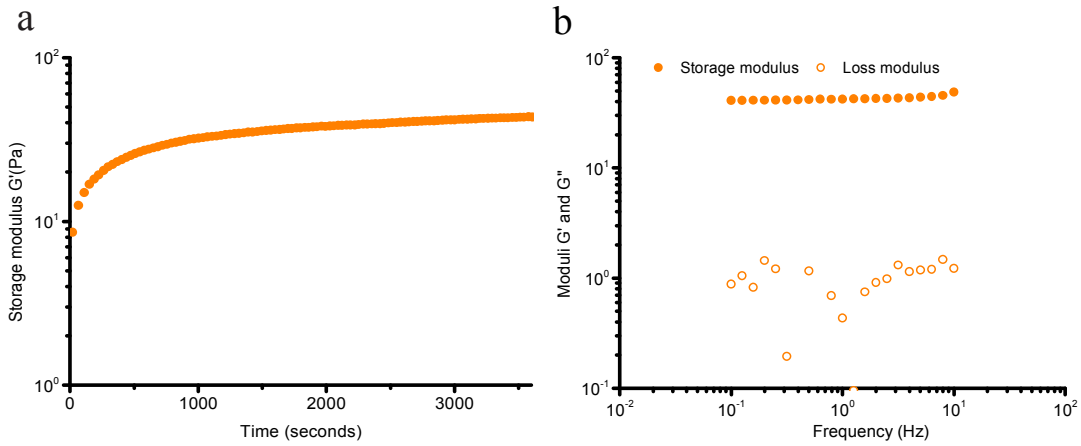

Figure S8 Rheology measurements of the PIC-DNA hydrogel cross-linked with DNA LC in the presence of 10 µg/ml BSA. a) Time evolution of the storage modulus (*G'*). b) G' and G" over a range of frequencies (10^{-3} to 10 Hz). Measurements were performed at 30 °C in PBS, 10 mM $MgCl_2$, pH 7.4.