Supplementary information for

Sensing diclofenac with DNA aptamers : an atomistic picture from molecular modelling

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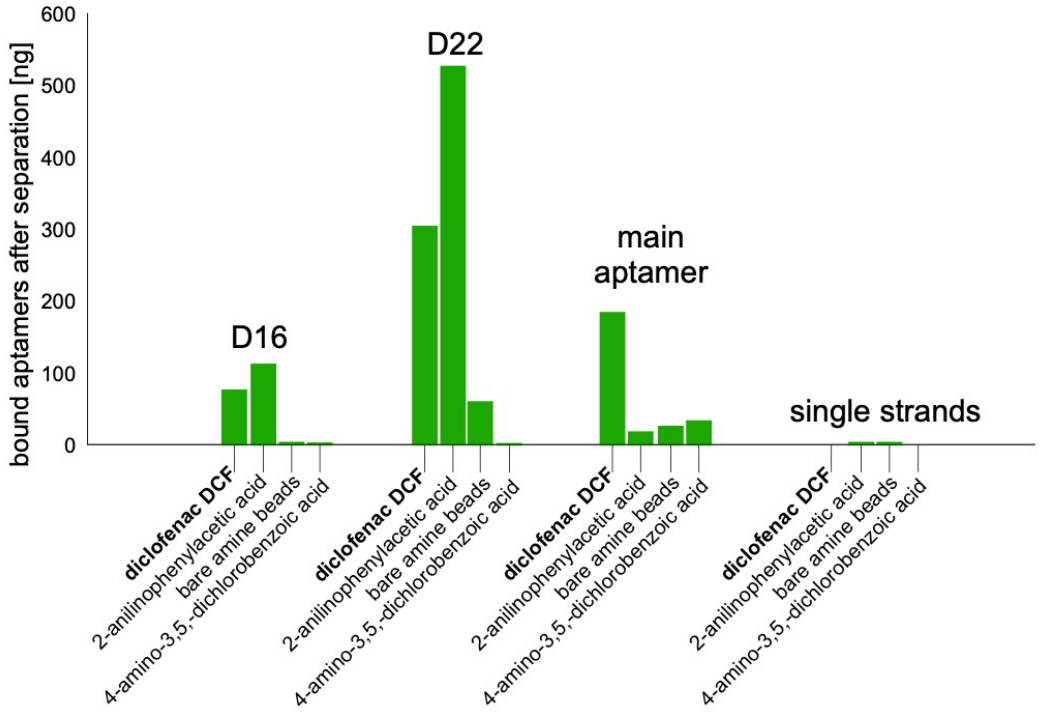

Figure S1. Adapted from ref. 25 (see main text bibliography) data. The plot shows the average quantity in ng that remains bound to DCF-coated amine beads after elution. The larger the value the higher the overall affinity of the aptamer receptor. A comparison with molecules that constitute different moieties of the full diclofenac structure shows that the main aptamer is the one with the best specificity to DCF. This likely comes from the presence of one or more binding sites for which the molecular poses combine a maximum of interactions of the full DCF structure.

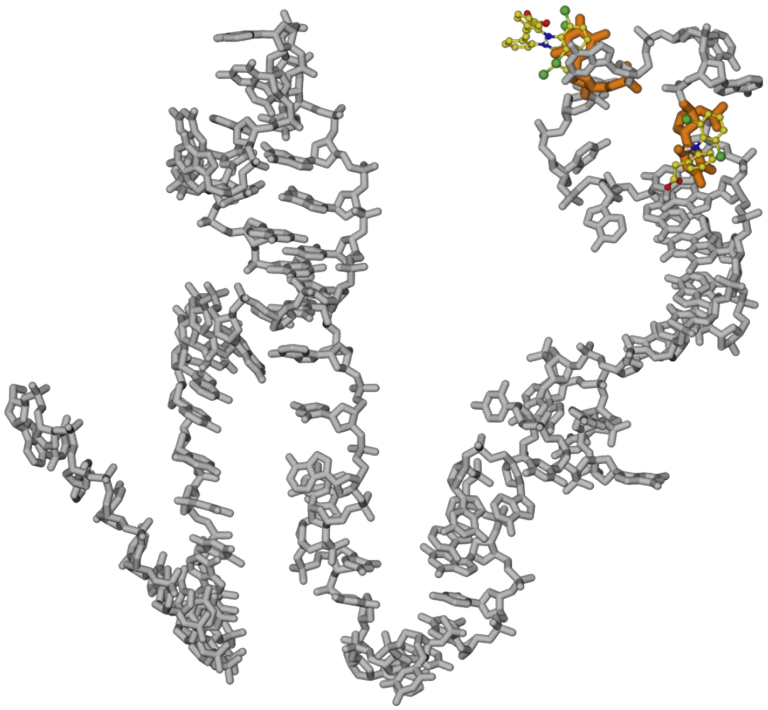

Figure S2. D16 best-scoring binding sites (-0.9 and -0.8 kcal/mol) localized on the loop formed in the region of the 3'-primer ending. The residues in orange are nucleotides T66 and T70, as discussed in the text.

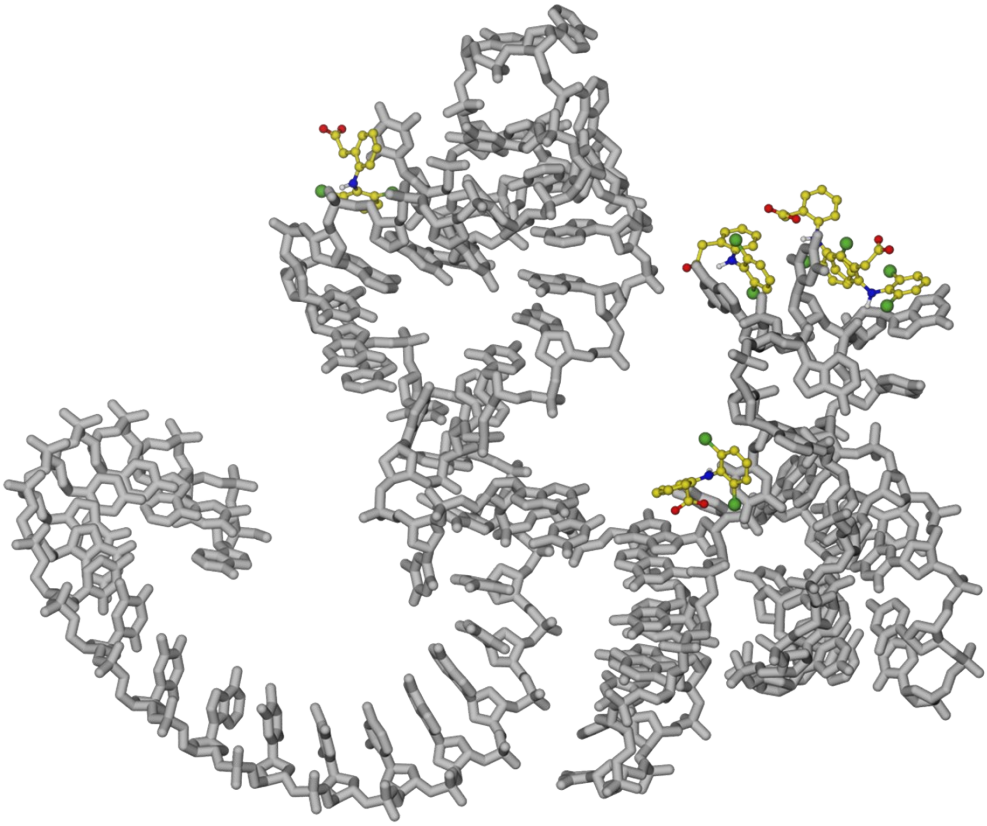

Figure S3. D22 binding sites with estimated docking score below -0.6 kcal/mol,

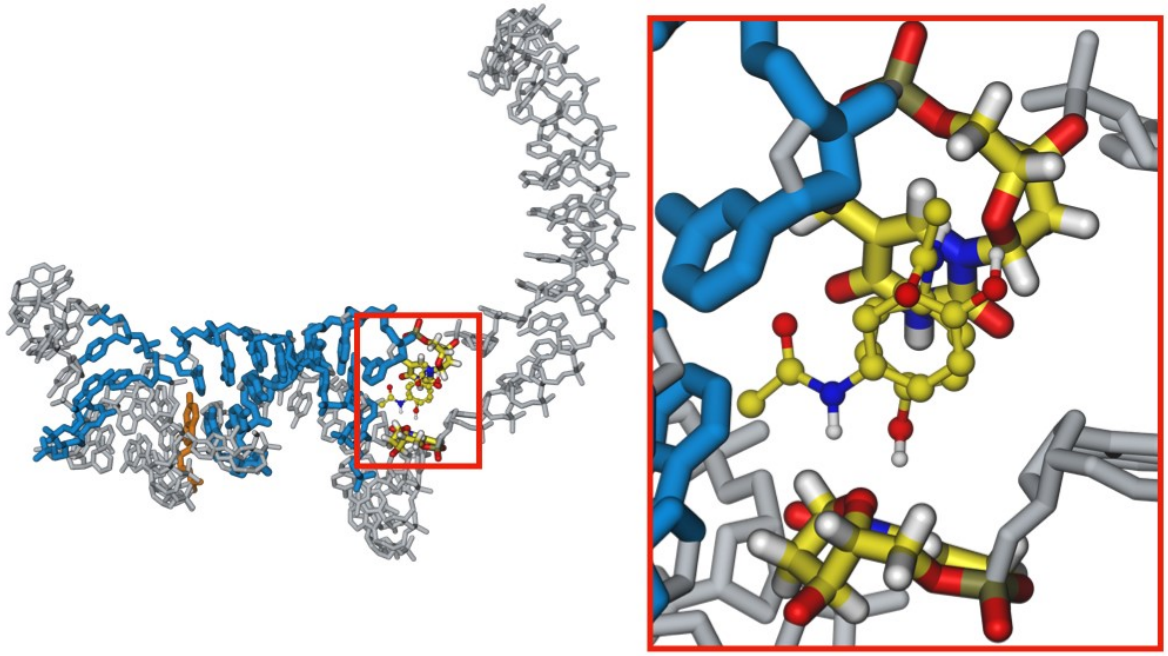

Figure S4. paracetamol binding site on the main aptamer. Two molecular poses with different orientations are shown in the inlet.

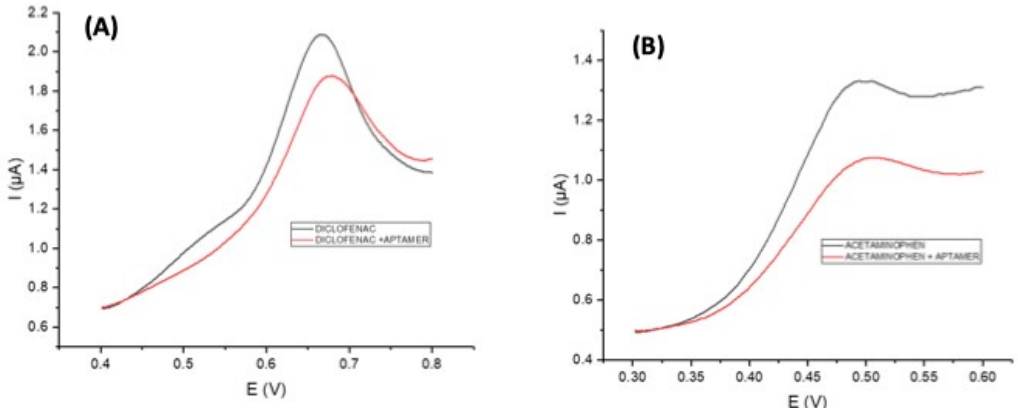

Figure S5 . Differential pulse voltammograms at platinum electrode in 0.1 mol/L KCl for (A) a 50 µM solution of diclofenac with (red) or without (black) 10 µM diclofenac-aptamer and (B) a 50 µM solution of paracetamol with (red) or without (black) 10 µM diclofenac-aptamer. Measurements were carried out with a CHI750E electrochemical analyzer (CHI, UK). The experiments were performed with a three-electrode system, bare Platinum electrode as working electrode, Ag/AgCl (3.0 M KCl) as reference electrode, and platinum wire as counter electrode. The lower height of the peaks plotted for the red lines with respect to the black ones for both species indicates a change in the concentration of the chemical species, proving that both diclofenac and paracetamol (acetaminophen) bind to the aptamer and are hence less available to participate in the reaction at the electrode.

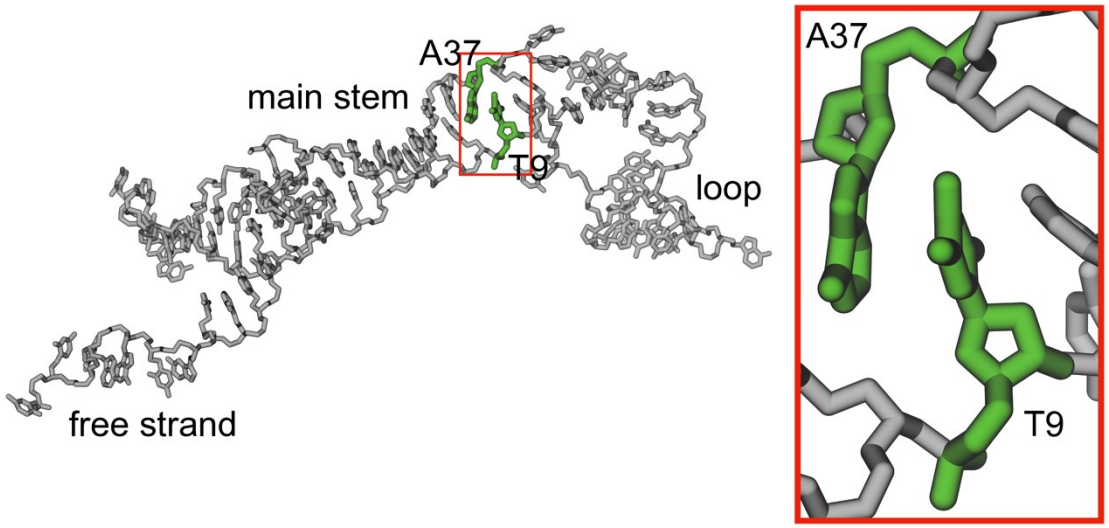

Figure S6. Stacking between residues A37 and T9 from the stem during the dynamics (@ 17.5 ns). The disruption of the Watson-Crick hydrogen bonding pattern due to the conformational disorder coming from the hairpin nucleotides sometime causes the pair to stack and lower the distance between their centers of mass. During the dynamics the pair is seen to undergo an oscillation between the stacked and the H-bound configuration.

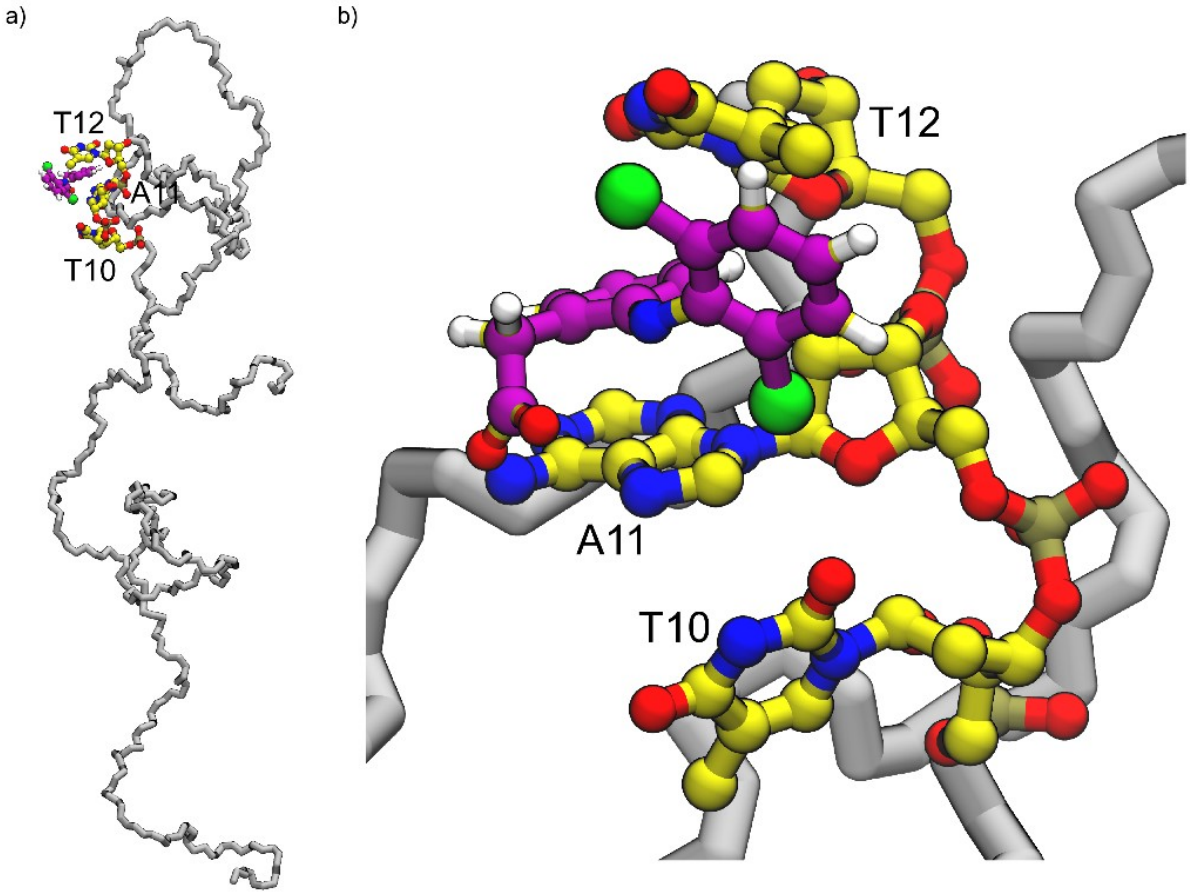

Figure S7. a) Snapshot of the full structure from the DCF-aptamer complex MD trajectory at 22.96 ns. b) highlight on DCF phenyl moiety that is shown to form the double stacking pattern with A11 and T12.

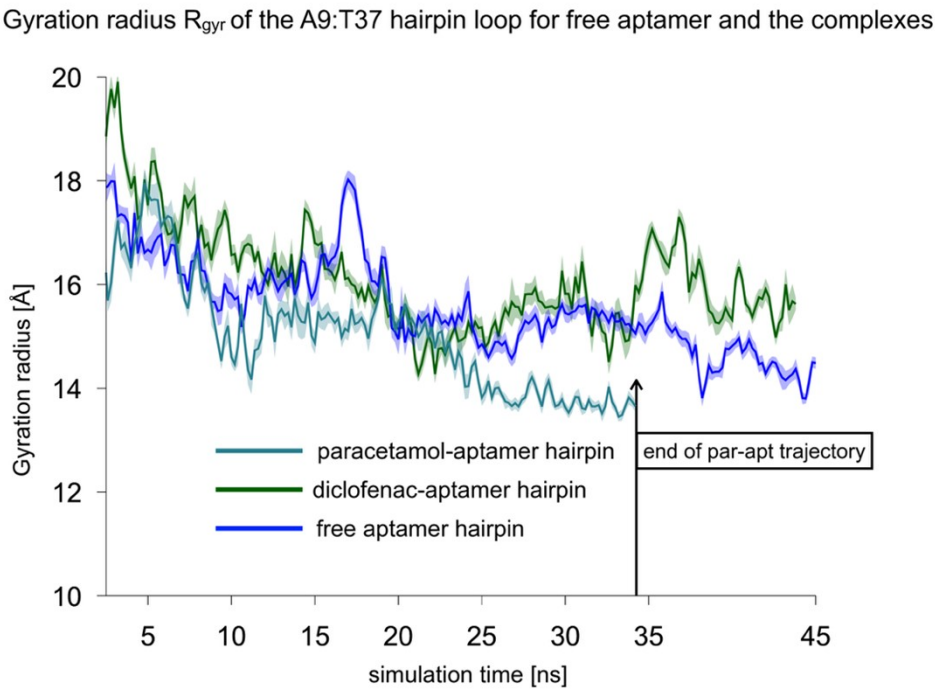

Figure S8. Gyration radius of the hairpin (A9 to T37) computed over the trajectories of the two complexes and the free aptamer. The plots indicate that the hairpin always proceeds towards a progressive compactification. The quantity is computed for each sampled frame (taken every 10 ps). The curves report the gyration radius' block-average for consecutive blocks of 20 frames and the bar is given by the standard deviation over the block, values range between 0.1 and 0.4 Å. The statistical significance of these results is limited given that only one trajectory has been considered for each system and ideally, multiple copies evolved independently should be considered when trying to elucidate conformational behaviours such as this.