Supporting information for the paper:

"Ion-Induced DNAzyme Switches"

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Experimental Section

Materials: 4-(2-hydroxyethyl)piperazine-1 ethanesulfonic acid sodium salt (HEPES), sodium nitrate, magnesium acetate, 2,2'-azino-bis(3-ethylbenzothiazoline)-6-sulfonate ($ABTS^{2-}$) and all the different ions used were purchased from Sigma-Aldrich. DNA oligonucleotides (**3**) and (**7**) were purchased from Integrated DNA Technologies Inc. (Coralville, IA). All other oligonucleotide sequences were purchased from Sigma-Genosys. Amine functionalized magnetic particles were purchased from Fluka. Hemin was purchased from Porphyrin Products (Logan, UT), and it was used without further purification. A hemin stock solution (1.5mM) was prepared in DMSO and stored in the dark. Ultrapure water from NANOpure Diamond (Barnstead) source was used in all of the experiments.

The sequences are provide in table S1:

Table S1: Different DNA sequences used to construct the ion induced DNAzyme Switches.

Number	Sequence
(1)	5’ CCC CTT TTC CCC T TA ATG C CA CCC ATG T TA GAG A 3’
(2)	5’ C TGC TCA GCG ATG CAT TAT CCC CTT TTC CCC 3’
(3)	5’ Cy5-TGA CGA TrAG GAG CAG- Iowa Black RQ 3’
(5)	5’ ATA CGC TTA TCG GCA CAT GAG A TCT CTA TrA G GAG CAG GAG TGA ACT G 3’
(6)	5’ GTG ATG TTA CAAT TGC CAC CCA TGT TAG AGA 3’
(7)	5’ CTG CTC AGC GAT GCA CAT CCC TAA CCC TAA CCC TAA CCC 3’

Synthesis of modified magnetic particles: Amine functionalized magnetic particles (M.P) were incubated with N-(3-Dimethylaminopropyl)-N'-ethyl-carbodiimide (EDC) 2 mM, N-hydroxysulfosuccinimide (NHS 2 mM) and an excess of lipoic acid. The particles were then separated from the solution by means of an external magnet. The particles were resuspended in H_2O and dithiothreitol (DTT) was added in order to reduce the disulfide bond in the lipoic acid. Prior to use, the solution, consisting of the DTT, was extracted and the magnetic particles were resuspended in H_2O.

Instrumentation: Light emission measurements were performed using a Cary Eclipse Device (Varian Inc). The fluorophore Cy5.5 was excited at 680 nm. The absorption spectra of $ABTS^{\cdot-}$ were recorded at 414 nm with a Shimadzu UV-2401 spectrophotometer.

DNAzyme assays: The Hg^{2+}-induced Mg^{2+}-dependent DNAzyme system described in Scheme 1 consisted of **1** (4μM) ,**2** (4μM), **3** (3μM) and variable concentrations of Hg^{2+} in HEPES buffer (1 M $NaNO_3$, 20 mM MgAc) in a total volume of 50μL . The system was heated to 90 °C for 5 min, and gradually cooled down to 25 °C and incubated for 3 hours. Prior to measuring, 150μL of HEPES buffer 10 mM were added to each sample.

The Ag^{+}-induced DNAzyme cascade system described in Scheme 2 consisted of **5** (4μM) ,**6** (4μM), **7** (4μM) and variable concentrations of Ag^{+} in HEPES buffer (1 M $NaNO_3$, 20 mM MgAc) in a total volume of 50μL. The system was heated to 90 °C for 5 min, and gradually cooled down to 25°C and incubated for 3 hours. After incubation the solutions (50 μL) were diluted with HEPES buffer, 10 Mm, to a total volume of 200μL . Hemin (1.3×10^{-7} M), $ABTS^{2-}$ (2 mM) and H_2O_2 (2 mM) were added to allow the biocatalyzed oxidation of $ABTS^{2-}$ .The rate of this reaction was monitored at λ = 414 nm. Similarly, the Hg^{2+}- induced DNAzyme cascade was activated under the same condition with **1** (1μM), **2** (1μM), **7** (1μM) and variable concentrations of Hg^{2+}.

The ON-OFF DNAzyme systems were activated by the addition and removal of reduced lipoic acid-modified magnetic particle. Briefly, stock solutions consisting of **1** (4μM), **2**

(4μM), **3** (3μM) with 2μM of Hg^{2+} ions or **5** (4μM), **6** (4μM), **7** (4μM) with 2μM of Ag^{+} ions in HEPES buffer (1M $NaNO_3$, 20 mM MgAc) were prepared and incubated (90/60 minutes respectively) as described above. Then, 50μL were taken for measurement (On-state). The stock solution was then warmed to 70°C followed by the addition of reduced lipoic acid-modified magnetic particles and incubated at room temperature for 10 minutes. The magnetic particles were removed by an external magnet, and the solution was separated. As before, a sample of 50 μL was taken for the characterization of the OFF state. To reactivate the systems, Hg^{2+} / Ag^{+} ions (2 μM) were added to the stock solutions, respectively.