Supporting Information

Experiments:

Experimental procedure:

Purified oligonucleotides PS2.M were obtained from Sangon Biotechnology Co., Ltd. (Shanghai, China). The oligonucleotides were prepared in buffer (25 mM Tris-HAc free of any ions, pH 8.0) and quantified by measuring UV-visible absorption spectroscopy at 260 nm. Before using, the DNA solutions were heated at 88°C for 10 min and gradually cooled to room temperature. The initial system for the designed keypad lock was a mixture of 1μM PS2.M and 1μM ZnPPIX. Six copies of PS2.M solutions were prepared. The combinational inputs with various sequences were then respectively added into the solutions. The final concentration of cations were 200 mM for K⁺, 100 mM for Na⁺ and 20 uM for Pb²⁺. KAc and NaAc solutions were prepared with the Tris-HAc buffer directly. Pb(NO₃)₂ solution was prepared by first dissolve Pb(NO₃)₂ in 5% HNO₃ solution and then diluted into Tris-HAc solution. The final pH value of the solutions after adding the three metal ions was about 6.5 in the fluorescence and CD measurements.

The system could be reset by dialysis, centrifugal ultrafiltration and re-dispersing. Since G-quadruplexes were formed after adding the three inputs with various sequences. The systems were first heated at 75°C to release metal ions from the aptamer. Then the metal ions were removed with dialysis bag (3KD) at 75°C. After that the DNA solutions were concentrated through centrifugal ultrafiltration (Millipore centicon, 3KD) and then re-dispersed in the buffer solution and mixed with ZnPPIX. Thus, the system was reset and available for the next input signals.

Fluorescence measurements: The fluorescence spectra from 540 to 700 nm were recorded by using a Fluoromax-4 Spectrofluorometer (HORIBA Jobin Yvon, Inc., France) at room temperature.

Circular dichroism (CD) Measurements: The CD spectra of DNAs (concentration was 4 uM) in the Tris-HAc buffer were collected by a Jasco J-820 spectropolarimeter (Tokyo, Japan). During experiments the lamp was always kept under a stable stream of dry highly purified nitrogen. Three scans from 220 nm to 350 nm at 0.1 nm intervals were accumulated and averaged. The background of the buffer solution was subtracted from the CD data. The thermal melting experiments were performed at 263 nm, 295 nm and 311 nm for K-G4, Na-G4 and Pb-G4, respectively.
Results:

Figure s1. CD spectra of K-G4 (A), Pb-G4 (B) and Na-G4 (C) with different concentration of metal ions. The normalized CD intensity of K-G4 at around 263 nm (D), Pb-G4 at around 311 nm (E) and Na-G4 at around 295 nm (F) as a function of concentrations of the metal ions.

As shown in Fig. s1, the CD spectrum of metal ions stabilized G-quadruplex changed with increasing concentration of metal ions. For K-G4 (Fig. s1(A)) the positive peak around 263 nm gradually increases until the concentration of $K^+$ increases to 200 mM (Fig. s1(D)), indicating the saturated coordination between the DNA and metal ion. For Pb-G4 (Fig. s1(B)) and Na-G4 (Fig. s1(C)), the characteristic bands at around 311 nm and 295 nm gradually increase with increasing concentration of the metal ions. By plotting the normalized intensity of characteristic bands as a function of concentration of the metal ions, the concentration of 20 nM and 100 mM are selected for Pb$^{2+}$ (Fig. s1 (E)) and Na$^+$ (Fig. s1 (F)) respectively to make sure entire reaction of the DNA in the metal ion systems. The association constants were evaluated by fitting CD data according to the following equation: \[
\text{normalized CD intensity at characteristic peak} = \frac{K_a [M]^n}{1+ K_a [M]^n}.
\]

The association constants were evaluated as $1.68 \times 10^6 \text{M}^{-1}$, $1.05 \times 10^3 \text{M}^{-2}$ and $1.6 \times 10^3 \text{M}^{-1}$ for Pb-G4, K-G4 and Na-G4, respectively. The association constant of Pb-G4 is close to the reported value.\(^2\)
Figure s2. Fluorescence spectra (A) and normalized fluorescence intensity at 585 nm (B) of the system with respect to input sequences. The interval of each input was 10 mins.

Fig. s2 (A) shows fluorescent responses of the system according to different input sequences. Here, the interval of adding each input was ten minutes. Learned from Fig. s2 (B), it is obviously that keypad lock operation still could be realized in this case. The aptamer-based keypad lock can be opened with a strong fluorescent output only when input is adopted with the correct combination and sequence of “KNP”. Otherwise, the “lock” keeps “OFF” to deny the unauthorized access.

Figure s3. Fluorescence spectra (A) and normalized fluorescence intensity at 585 nm (B) with respect to input sequences after resetting the system.

The next input sequences were added into the mixture of PS2.M and ZnPPIX after resetting the system. Learned from Fig. s3 that the system still could implement keypad lock function.
References: