Supporting Information

Gated Transient Dissipative Dimerization of DNA Tetrahedra Nanostructures for Programmed DNAzymes Catalysis

Zhenzhen Li‡, Jianbang Wang‡, Zhixin Zhou‡, Michael P. O'Hagan & Itamar Willner*

The Institute of Chemistry, The Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Jerusalem 91904, Israel.

‡These authors contributed equally to this study.

*E-mail: Itamar.willner@mail.huji.ac.il
Materials

Nicking enzyme (Nt.BbvCI, 10,000 units mL⁻¹, 2.3 μM) and CutSmart®Buffer were purchased from New England BioLabs Inc.. Oligonucleotides were purchased from Integrated DNA Technologies. The Cy3-, Cy5-, FAM- and TAMRA-labeled oligonucleotides were purified by high-performance liquid chromatography. All the sequences of the oligonucleotides were listed below.

A13: 5'−ACACTACGTCAAGACAGCTTGCATCAGGTCACCATCAGGTA-3’
B13: 5'−ACGAGCGAGTTGTGAGATGCAAGCTGAAACTACCTCTCTGACAGTGAAGGTGTCACCTCGCAT-3’
C13: 5'−TCAACTCGTCTGAACTACCTTGCAATACTCCTCTGACAGTGAAGGTGTCACCTCGCAT-3’
D13: 5'−TCGACTGATGTGTAGCACTACGTGTAAGGACACCTCGCAT-3’
B7: 5'−TTAGGCGAGTGTCAGGGCAGGTGTCACCTCGCAT-3’
C7: 5'−CGCCCTAAAAAAGTGGAGAGAGACGACTGTG-3’
D7: 5'−AACGCTACACTTGCAACACCTC-3’
A13-CY3: 5'-CY3-CCATCACAAAAACAAAACACTACGTCAAGACAGCTTGCATCAGGTCACCATCAGGTA-3’
A13-CY5: 5'-ACACTACGTCAAGACAGCTTGCATCAGGTCACCATCAGGTA-3’
C13-FAM: 5'−TCAACTCGTCTGAACTACCTTGCAATACTCCTCTGACAGTGAAGGTGTCACCTCGCAT-3’
C13-FAM: 5'−TCAACTCGTCTGAACTACCTTGCAATACTCCTCTGACAGTGAAGGTGTCACCTCGCAT-3’
A7-TAMARA: 5'−TAMARA-GACACAACAAAAAACAAAACACTTGACAGCTCAGGTCACCATCAGGTA-3’
I1: 5'−GGTTTGTGATGGACGTTCTCTTGTC-3’
L1: 5'-GACAGAAAAGAGTGGAGGACGCTACACCCACACACACAGTC-3’
L1: 5'-GATGCGGCTAGCGTTCTCTTGTC-3’
I2: 5'−CGTTTGTGATGGACGTTCTCTTGTC-3’
L2: 5'-CAAGAAAAGAGTGGAGGACGCTACACCCACACACACACGC-3’
L2: 5'-GTGTACTCCAGGCTCAGTCAGGTCACCATCAGGTA-3’
B3: 5'-TTTTTTTTTTTTT-3’
B2: 5'-CCTTCTGTTCCTTTTTTTTTTT-3’
A13-E1: 5'−GTCCTACGCGATGGTTACCATCAGGACGCTACACAGTCAAGACAGCT
TGCATCACTGGTCACCAGAGTA-3’
A13-E2: 5’-ACACTACGTCAGAACAGCTTTGCATCATCTGGTCACCAGAGTAAACACAG
AAGAACTAACCACCCATGTTCAGT-3’
C13-E3: 5’-TCAACTCGCTCGTAACCTACACTGTGCAATACTCTGGTGACCAAAAAAAGAC
AAAGGATAACCACCCATGTTCTCTG-3’
A7-E4: 5’-CTGTTCAGCGATGTAGACACACAAACACAAAAAGAGCGTTAGCCACACACAC
AGTC-3’
S1: 5’-Cy5-ACTGAA TrAG GAGGAC-BHQ2-3’
S2: 5’-FAM-TCAGGA TrAG GAAACG-IBRQ-3’
T1: 5’-CTTGCTACACGATTCAGATTTAGGAATGTTCGACATGCGAGGGTGCTCAAATACGAC
GATTACAG-3’
T2: 5’-GGTGATAAAACGTGTAGCAAGCTTATCGACGGGAAGACATGGCCCATCCACT
ACTATGGCG-3’
T3: 5’-CCTCGCATGACTCAACTGCTGGATACGAGGGTGGCTCAAATACGAC
TATTGGAC-3’
T4.inner: 5’-GGTGATGGGCGGGTTGGG CCAGGCAGTTGAGACACATTTCTAAGTCTGA
AATTTATCAACCCGCAATAGATGACGTATCA-3’
T4.outer: 5’-GGTGATGGGCGGGTTGGG CAGTTGAGACGAAAACATTCTAAGTCTGAAATT
TATCACCACCGCATAGATGACCATTCAACCAGG-3’
G: 5’-GGTGATGGGCGGGTTGGG CAGCATGAAATCCAGG-3’
Cg: 5’-CCTGATTCTATGCTG-3’
The principles to design such transient system should include the following rules:
- The stability of the different duplexes involved in the reaction module are determined by the number and nature of base pairs. The energetic stabilization of the duplex is estimated using NUPACK software.
- The energetic stabilization of the rest reaction module is controlled by the energy level of the duplex L₁/I₁.
- The triggered transition of the rest module to the transient T₁/T₂ tetrahedra structure requires the intermediate products L₁/L₁' and I₁/T₁T₂ dimer that should be energetically more stable than L₁/I₁.
- The cleavage of the duplex L₁/L₁' separates the “waste” products of the fragmented pieces of L₁'. The released L₁ displaces I₁ from the dimer I₁/T₁T₂ guided by the enhanced energetic stability of L₁/I₁ as compared to I₁/T₁T₂.

The following scheme outlines the relative energy levels of the constituents associated with the transient operation of the network.

**Figure S1.** Scheme of the relative energy levels of the constituents associated with the transient operation of the network.
Figure S2. (A) Time-dependent fluorescence changes of Cy3 and Cy5 that follow the dynamic transient formation and depletion of the dimer structure T₁/T₂. (B) The ratio $F_{\text{Cy5}}/F_{\text{Cy3}}$ follows the formation and depletion of the dimer structure T₁/T₂.
Figure S3. (A) The fluorescence spectra of T₁ and T₂ upon the addition of different concentrations of I₁. (B) The derived calibration curve corresponding to the ratio of the intensities of Cy5 and Cy3, F₆₆₀/F₅₆₀, at different concentrations of I₁, yielding the supramolecular complex I₁/T₁T₂ (means ± standard deviation, n = 3).

It should be noted that the format of plotting the calibration curve yields a non-linear increase. This can be quantitatively rationalized as follows:

For this low concentration (1 μM) system, the fluorescence intensities of Cy3 (F₁) and Cy5 (F₂) are given by equation (i) and equation (ii):

(i) \( F₁ = α₁ * C_{cy3} \)
(ii) \( F₂ = α₂ * \frac{C_{cy5/cy3}}{C_{cy3}} \)

where Cy5/Cy3 corresponds to the concentration of Cy5 in the FRET luminescent complex composed of I₁/T₁T₂.

Since the start concentration of Cy3 is 1 μM, the transient concentration of Cy3 is given by equation (iii)

(iii) \( C_{cy3} = 1 - C_{cy5/cy3} \)

Thus, the ratio of \( \frac{F₂}{F₁} \) is given by equation (iv) that can be rewritten as follows:

(iv) \( \frac{F₂}{F₁} = \frac{a₂}{a₁} * \frac{C_{cy5/cy3}}{C_{cy3}} = \frac{a₂}{a₁} * \frac{C_{cy5/cy3}}{1-C_{cy5/cy3}} \)

That is, the ratio of \( \frac{F₂}{F₁} \) follows a classical parabolic function \( f = k * \frac{x}{1-x} \) as depicted in Figure S3(C) (k set as 0.117).
Kinetic equations of the dissipative Cy5/Cy3 FRET system shown in Figure 1:

\[ \begin{align*}
    L_1 + I_1 & \xrightarrow{k_1} L_1 I_1 \\
    L_1I_1 + L_1 & \xrightarrow{k_2} L_1I_1 + I_1 \\
    T_1 + T_2 + I_1 & \xrightarrow{k_3} T_1T_2I_1 \\
    L_1I_1' + E & \xrightarrow{k_4} L_1I_1^E \\
    L_1L_1^E & \xrightarrow{k_5} E + L_1L_1^+L_1^+ \\
    L_1L_1^+L_1^+ & \xrightarrow{k_6} L_1 + L_1^+ + L_1^+ 
\end{align*} \]

Derivatives:

\[ \begin{align*}
    \frac{dL_1}{dt} & = -k_1[L_1][I_1] + k_2[L_1I_1] + k_3[L_1L_1^+L_1^+] - k_4[L_1I_1][L_1^+] \\
    \frac{dI_1}{dt} & = -k_1[L_1][I_1] + k_2[L_1I_1] + k_3[L_1I_1][L_1^+] - k_4[L_1I_1][L_1^+] \\
    \frac{dL_1I_1'}{dt} & = k_3[L_1I_1][I_1^+] - k_4[L_1I_1][I_1^+] - k_5[L_1I_1][I_1^+] + k_6[L_1I_1][I_1^+] \\
    \frac{dL_1^1}{dt} & = -k_2[L_1I_1][I_1^+] + k_4[L_1I_1][I_1^+] \\
    \frac{dL_1I_1^+}{dt} & = k_3[L_1I_1][I_1^+] - k_4[L_1I_1][I_1^+] - k_5[L_1I_1][I_1^+] + k_6[L_1I_1][I_1^+] \\
    \frac{dT_1}{dt} & = -k_3[T_1][T_2][I_1] + k_4[T_1T_2I_1] \\
    \frac{dT_2}{dt} & = -k_3[T_1][T_2][I_1] + k_4[T_1T_2I_1] \\
    \frac{dT_1T_2}{dt} & = k_3[T_1T_2][I_1] - k_4[T_1T_2I_1] \\
    \frac{dE}{dt} & = -k_5[L_1L_1^E] + k_6[L_1L_1^E] + k_7[L_1L_1^E] \\
    \frac{dL_1E}{dt} & = k_3[L_1L_1^E][E] - k_4[L_1L_1^E][E] - k_5[L_1L_1^E][E] \\
    \frac{dL_1L_1^+E}{dt} & = k_3[L_1L_1^E][E] - k_4[L_1L_1^E][E] - k_5[L_1L_1^E][E] + k_6[L_1L_1^+][L_1^+] \\
    \frac{dL_1^1E}{dt} & = k_3[L_1L_1^E][E] - k_4[L_1L_1^E][E] - k_5[L_1L_1^E][E] + k_6[L_1L_1^+][L_1^+] \\
    \frac{dL_1^+E}{dt} & = k_3[L_1L_1^E][E] - k_4[L_1L_1^E][E] - k_5[L_1L_1^E][E] + k_6[L_1L_1^+][L_1^+] \\
    \frac{dL_1^+E}{dt} & = k_3[L_1L_1^E][E] - k_4[L_1L_1^E][E] - k_5[L_1L_1^E][E] + k_6[L_1L_1^+][L_1^+] \\
\end{align*} \]

Figure S4. Computational simulation of the dissipative Cy5/Cy3 FRET system shown in Figure 1. The kinetic scheme of the reactions associated with the time-dependent concentration changes during the dissipative transitions of FRET is summarized in above equations. Knowing the time-dependent concentration changes of the tetrahedron dimers associated with T_1/T_2, during the dissipative transitions of FRET, we computationally simulated the time-dependent concentration changes by using Matlab R2020a.
It is important to note that the computationally simulated rate constants have a meaning only if one or more of the rate-constants can be evaluated independently experiment and computationally, and the result should be compared to the analogy rate-constant being part of the overall kinetic model. According the values of $k_3$ and $k_{-3}$ in the presence of two concentrations of $I_1$ were evaluated as follows, Figure S5.

**Figure S5.** Time-dependent concentration changes of $T_1/T_2$ complex upon subjecting tetrahedra $T_1$ and $T_2$ to different concentrations of $I_1$: 0.4 μM and 0.8 μM. Dashed curves correspond to the computationally simulated kinetic profiles. Dotted curves represent the experimental data.

**Experimental (i)-dotted lines and computationally (ii)-dashed lines**

**Evaluation of the rate constants $k_3$ and $k_{-3}$ of the kinetic scheme in Figure S4.**

To evaluate the rate constants $k_3$ and $k_{-3}$ appearing in the kinetic scheme, equation (3) in Figure S4, the mixture of $T_1$ and $T_2$ (1 μM each) was subjected to two different concentrations of $I_1$ (0.4 μM and 0.8 μM), and the time-dependent concentration changes were evaluated by following the time-dependent fluorescence changes of the tetrahedron dimers associated with $T_1/T_2$, and translating them into concentrations by applying an appropriate calibration curve, Figure S3. From the kinetic profiles and using the Matlab R2020a program, the respective $k_3 = 5 \text{ μM}^{-2} \text{ min}^{-1}$ and $k_{-3} = 0.0236 \text{ min}^{-1}$ were derived. These values fit well with the computationally simulated rate constant following the overall kinetic model and Table S1.
Figure S6. Time-dependent gel electrophoretic characterization of the transient T₁, T₂ dimerization to T₁-T₂ according to Figure 1 upon the L₁'-triggered transient dimerization of the tetrahedra monomers. (A) Gel electrophoretic separated bands corresponding to the tetrahedra monomer (lower band) and T₁/T₂ tetrahedra dimer (upper bands). Bottom bands: lane 1 T₁, lane 2 T₂, lane 3 to lane 9 composition of the tetrahedra T₁ and T₂ triggered by L₁’ at different times of the transient process. Lane 3 at t = 0; lane 4 at t = 1 h; lane 5 at t = 3 h; lane 6 at t = 6 h; lane 7 at t = 12 h; lane 8 at t = 24 h; lane 9 at t = 48 h. The samples withdrawn from the reaction mixture were treated with trypsin to digest the nicking enzyme and retain the respective time-dependent composition of the transient dimerization process prior to the electrophoretic separation.

(B) Concentrations of the monomer mixture T₁, T₂ along the transient dimerization process. Due to the relatively low concentrations of the dimer T₁/T₂, the dissipative, transient, evaluation of the process was followed by quantitative analysis of the stained mixture of the T₁/T₂ monomer constituents along the transient process.

The quantitative evaluation of the transient electrophoretic separated monomers T₁/T₂ mixtures was performed by measuring the intensities of the stained bands using the ImageJ software and comparing the results the stained bands of T₁/T₂ at different known concentrations.
Figure S7. (A) The fluorescence spectra of T₃ and T₄ upon the addition of different concentrations of I₂. (B) The derived calibration curve corresponding to the ratio of the intensities of TAMRA and FAM, F₅₈₃/F₅₁₆, at different concentrations of I₂, yielding the supramolecular complex I₂/T₃T₄ (means ± standard deviation, n = 3).
Figure S8. (A) Transient concentration changes of the tetrahedra T₃/T₄ upon the fuel L₂’ triggered formation and depletion of the T₃/T₄ dimer in the presence of variable concentrations of the fuel strand L₂’: (a) = 2 μM, (b) = 4 μM, (c) = 6 μM, (d) = 8 μM. For all systems: L₂/I₂ = 1 μM; T₃ = 1 μM; T₄ = 1 μM and Nt.BbvCl 0.046 μM. (Dotted lines correspond to experimental results. Dashed curves a’, b’, c’, d’ correspond to the computational simulated transient, using the kinetic model presented in Figure S9). Curves c/c’ correspond to the experimental transient (dotted line) followed by the computational simulation (dashed line), using the kinetic model, leading to the derived rate constants tabulated in Table S2. Curves a/a’, b/b’ and d/d’ were first computationally simulated and subsequently experimentally validated. (B) Transient concentration changes of the tetrahedra T₃/T₄ upon the fuel L₂’ triggered formation and depletion of the T₃/T₄ dimer in the presence of variable concentrations of Nt.BbvCl: (a) = 0.0153 μM, (b) = 0.0306 μM, (c) = 0.046 μM, (d) = 0.0612 μM. For all systems: L₂/I₂ = 1 μM; T₃ = 1 μM; T₄ = 1 μM and fuel strand L₂’ = 4 μM. (Dotted lines correspond to experimental results. Dashed curves a’, b’, c’ and d’ correspond to the computational simulated transients, using the kinetic model presented in Figure S9). Curves a/a’, b/b’, c/c’ and d/d’ were first computationally simulated and subsequently experimentally validated.
Kinetic equations of the dissipative TAMRA/FAM FRET system shown in Figure 3:

\[
\begin{align*}
L_2 + I_2 & \xrightarrow{k_{-1}} L_2 I_2 \\
L_3 I_2 + L_2 & \xrightarrow{k_{+1}} L_3 I_2 + I_2 \\
T_3 + T_4 & \xrightarrow{k_{+3}} T_3 T_4 I_2 \\
L_2 L_2^* + E & \xrightarrow{k_{-4}} L_2 L_2^* E \\
L_2 L_2^* E & \xrightarrow{k_{-5}} E + L_2 L_2^* L_2 \\
L_3 L_2^* L_2^{'1} & \xrightarrow{k_{-6}} L_2 + L_2^* + L_2^{'1}
\end{align*}
\]

Derivatives:

\[
\begin{align*}
\frac{dL_2}{dt} &= -k_{1} [L_2] [I_2] + k_{-4} [L_2 I_2] + k_{+4} [L_2 L_2^*] - k \cdot [L_2] [L_2^*] \\
\frac{dI_2}{dt} &= -k_{1} [L_2] [I_2] + k \cdot [L_2 I_2] + k_{-4} [L_2 I_2] - k \cdot [L_2] [I_2] - k_{+4} [T_3 T_4 I_2] + k \cdot [T_3 T_4 I_2] \\
\frac{dL_3 I_2^*}{dt} &= k_{1} [I_2] [L_2^*] - k \cdot [L_3 I_2] - k_{-4} [L_2 I_2] + k \cdot [L_2 L_2^*] \\
\frac{dL_2^*}{dt} &= -k \cdot [L_2 I_2] [L_2^*] + k \cdot [L_2 I_2] \\
\frac{dL_2 L_2^*}{dt} &= k_{1} [L_2] [L_2^*] - k \cdot [L_2 L_2^*] [I_2] - k \cdot [L_2 L_2^*] [E] + k \cdot [L_2 L_2^*] \\
\frac{dT_3}{dt} &= -k_{-3} [T_3 I_2] [I_2] + k \cdot [T_3 T_4 I_2] \\
\frac{dT_3 I_2}{dt} &= -k_{-3} [T_3 I_2] [I_2] + k \cdot [T_3 T_4 I_2] \\
\frac{dT_3^*}{dt} &= k_{-3} [T_3 I_2] [I_2] - k \cdot [T_3 T_4 I_2] \\
\frac{dE}{dt} &= -k_{-1} [L_2] [E] + k \cdot [L_3 E] + k \cdot [L_2 L_2^*] \\
\frac{dT_3^* E}{dt} &= k_{1} [L_2] [E] - k \cdot [L_2 L_2^*] [E] - k \cdot [L_2 L_2^*] \\
\frac{dL_2 I_2^* L_2^{'1}}{dt} &= k_{1} [L_2] [L_2^*] - k_{-4} [L_2 I_2^*] [+ k \cdot [L_2] [I_2^*] [L_2^{'1}] \\
\frac{dL_2^* L_2^{'1}}{dt} &= k_{-4} [L_2 I_2^*] [L_2^{'1}] - k \cdot [L_2 I_2^*] [L_2^{'1}] \\
\frac{dL_2 L_2^*}{dt} &= k_{-4} [L_2 L_2^*] [L_2^{'1}] - k \cdot [L_2 I_2^*] [L_2^{'1}]
\end{align*}
\]

Figure S9. Computational simulation of the dissipative TAMRA/FAM FRET system shown in Figure 3. The kinetic scheme of the reactions associated with the time-dependent concentration changes during the dissipative transitions of FRET is summarized in above equations. Knowing the time-dependent concentration changes of the tetrahedron dimers associated with T_3/T_4, during the dissipative transitions of FRET, we computationally simulated the time-dependent concentration changes by using Matlab R2020a.
It is important to note that the computationally simulated rate constants have a meaning only if one or more of the rate-constants can be evaluated independently experiment and computationally, and the result should be compared to the analogy rate-constant being part of the overall kinetic model. According the values of $k_9$ and $k_{-9}$ in the presence of two concentrations of $I_2$ were evaluated as follows, Figure S10.

**Figure S10.** Time-dependent concentration changes of $T_3/T_4$ complex upon subjecting tetrahedra, $T_3$ and $T_4$, to different concentrations of $I_2$: 0.3 $\mu$M and 1.2 $\mu$M. Dashed curves correspond to the computationally simulated kinetic profiles. Dotted curves represent the experimental data.

**Experimental (i)-dotted lines and computationally (ii)-dashed lines**

**Evaluation of the rate constants $k_9$ and $k_{-9}$ of the kinetic scheme in Figure S9.**

To evaluate the rate constants $k_9$ and $k_{-9}$ appearing in the kinetic scheme, equation (9) in Figure S9, the mixture of $T_3$ and $T_4$ (1 $\mu$M each) was subjected to two different concentrations of $I_2$ (0.3 $\mu$M and 1.2 $\mu$M), and the time-dependent concentration changes were evaluated by following the time-dependent fluorescence changes of the tetrahedron dimers associated with $T_3/T_4$, and translating them into contents by applying an appropriate calibration curve, Figure S7. From the kinetic profiles and using the Matlab R2020a program, the respective $k_9 = 2.985$ $\mu$M$^{-2}$ min$^{-1}$ and $k_{-9} = 1.31$ min$^{-1}$ were derived.
Kinetic equations of the gated dissipative system (Figure 4, State A):

\[ L_1 + I_1 \xrightarrow{k_{14}} L_1 I_1 \]  
(1)
\[ L_1 I_1 + L_1 I_2 \xrightarrow{k_{62}} L_1 I_1 I_2 + I_1 \]  
(2)
\[ T_1 + T_2 + I_1 \xrightarrow{k_{52}} T_1 T_2 I_1 \]  
(3)
\[ L_1 L_1' + E \xrightarrow{k_{44}} L_1 L_1' E \]  
(4)
\[ L_1 L_2 \xrightarrow{k_5} E + L_1 L_2 \xrightarrow{k_6} L_1 + L_2 \]  
(5)
\[ L_1 L_2 \xrightarrow{k_{26}} L_1 + L_2 \xrightarrow{k_{22}} L_1 + L_2 \]  
(6)
\[ L_2 + I_2 \xrightarrow{k_{67}} L_2 I_2 \]  
(7)
\[ L_2 L_2 + L_2 \xrightarrow{k_{52}} L_2 L_2 + I_2 \]  
(8)
\[ T_3 + T_4 + I_2 \xrightarrow{k_{52}} T_3 T_4 I_2 \]  
(9)
\[ L_2 L_2' + E \xrightarrow{k_{44}} L_2 L_2' E \]  
(10)
\[ L_2 L_2' \xrightarrow{k_5} E + L_2 L_2' \xrightarrow{k_6} L_2 + L_2 \]  
(11)
\[ L_2 L_2' \xrightarrow{k_{26}} L_2 + L_2 \xrightarrow{k_{22}} L_2 + L_2 \]  
(12)

Derivatives:

\[ \frac{dL_1}{dt} = -k[L_1][I_1] + k \cdot [L_1 I_1] + k_6[L_1 I_1 I_2] - k \cdot [L_1][I_1] [L_2] \]  
\[ \frac{dL_2}{dt} = -k[L_1][I_1] + k \cdot [L_1 I_1] + k \cdot [L_1 I_1] - k \cdot [L_1 I_2] [I_1] + k \cdot [T_1][T_2][I_1] + k \cdot [T_1][T_2][I_1] \]  
\[ \frac{dL_1'}{dt} = k_5[L_1][I_1] - k \cdot [L_1 I_1] - k_6[L_1 I_1 I_2] + k \cdot [L_1 I_2][I_1] \]  
\[ \frac{dL_2'}{dt} = -k_5[L_1][I_1] + k \cdot [L_1 I_2][I_1] \]  
\[ \frac{dL_3'}{dt} = k_5[L_1][I_1] - k \cdot [L_1 I_2][I_1] - k \cdot [L_1 I_2][I_1] + k \cdot [L_1 I_2][I_1] \]  
\[ \frac{dT_1}{dt} = -k[T_1][T_2][I_1] + k \cdot [T_1][T_2][I_1] \]  
\[ \frac{dT_2}{dt} = -k[T_1][T_2][I_1] + k \cdot [T_1][T_2][I_1] \]  
\[ \frac{dT_1 T_2}{dt} = k[T_1][T_2][I_1] - k \cdot [T_1][T_2][I_1] \]  
\[ \frac{dE}{dt} = -k[L_1][I_1][E] + k \cdot [L_1 I_1][E] + k_6[L_1 I_1 I_2][E] - k_6[L_2 I_2][E] + k \cdot [L_2 I_2][E] + k \cdot [L_2 I_2][E] \]  
\[ \frac{dL_1 E}{dt} = k_5[L_1][I_1][E] - k \cdot [L_1 I_1][E] - k_6[L_1 I_1 I_2][E] \]  
\[ \frac{dL_2 E}{dt} = k_5[L_1][I_1][E] - k_6[L_1 I_1 I_2][E] - k_6[L_1 I_1 I_2][E] \]  
\[ \frac{dL_1 I_2'}{dt} = k_5[L_1][I_1][E] - k_6[L_1 I_1 I_2][E] + k \cdot [L_1][I_1 I_2][I_1] \]  
\[ \frac{dL_2 I_2'}{dt} = k_5[L_1][I_1][E] - k_6[L_1 I_1 I_2][E] \]  
\[ \frac{dL_1 I_2}{dt} = k_5[L_1][I_1][E] + k_6[L_1 I_1 I_2][E] - k \cdot [L_1 I_1][I_1 I_2][I_1] \]  
\[ \frac{dL_2 I_2}{dt} = k_5[L_1][I_1][E] - k_6[L_1 I_1 I_2][E] + k \cdot [L_1][I_1 I_2][I_1 I_2] \]
The kinetic scheme of the reactions associated with the time-dependent concentration changes during the dissipative transitions is summarized in above equations. Knowing the time-dependent concentration changes of the tetrahedron dimers $T_1/T_2$ and $T_3/T_4$ during the dissipative transitions, we computationally simulated the time-dependent concentration changes by using Matlab R2020a.
Kinetic equations of B1 gated dissipative system (Figure 4, State B):

\[ \begin{align*}
L_1 + I_1 & \xrightarrow{k_{11}} L_2 I_1 \\
L_1 I_1 + L_1 & \xrightarrow{k_{21}} L_1 L_1 I_1 + I_1 \\
T_1 + T_2 + I_1 & \xrightarrow{k_{31}} T_1 T_2 I_1 \\
L_1 L_1 E & \xrightarrow{k_{41}} E + L_1 L_1 E \cdot L_1 + L_1 E \\
L_1 L_1 L_1 E & \xrightarrow{k_{51}} L_1 L_1 E + L_1 L_1 E + L_1 L_1 E \\
T_1 + B_1 & \xrightarrow{k_{61}} T_1 B_1 \\
L_2 + I_2 & \xrightarrow{k_{71}} L_2 L_2 \\
L_2 + L_2 & \xrightarrow{k_{81}} L_2 L_2 + L_2 I_2 \\
T_3 + T_4 + I_2 & \xrightarrow{k_{91}} T_3 T_4 I_2 \\
L_2 L_2 E & \xrightarrow{k_{101}} L_2 L_2 E + L_2 L_2 E + L_2 L_2 E \\
L_2 L_2 L_2 E & \xrightarrow{k_{111}} E + L_2 L_2 L_2 E + L_2 L_2 E + L_2 L_2 E + L_2 L_2 E \\
L_2 L_2 L_2 L_2 E & \xrightarrow{k_{121}} L_2 L_2 L_2 E + L_2 L_2 L_2 E + L_2 L_2 L_2 E + L_2 L_2 L_2 E + L_2 L_2 L_2 E \\
\end{align*} \]

Derivatives:

\[ \begin{align*}
\frac{dl_1}{dt} & = -k \cdot [L_1] [I_1] + k \cdot [L_1 I_1] + k \cdot [L_1 L_1 I_1] - k \cdot [L_1 I] [L_1 I] \\
\frac{dl_2}{dt} & = -k \cdot [L_2] [I_2] + k \cdot [L_2 I_2] + k \cdot [L_2 L_2 I_2] - k \cdot [L_2 L_2 I_2] + k \cdot [L_2 I] [T_1 T_2] \\
\frac{dI_1}{dt} & = k \cdot [L_1] [I_1] - k \cdot [L_1 I_1] + k \cdot [L_1 L_1 I_1] + k \cdot [L_1 I_2 I_2] \\
\frac{dI_2}{dt} & = -k \cdot [L_2] [I_2] - k \cdot [L_2 I_2] + k \cdot [L_2 L_2 I_2] \\
\frac{dT_1}{dt} & = -k \cdot [T_1] [T_2] [I_1] + k \cdot [T_1 T_2 I_1] - k \cdot [T_1 I] [B_1] + k \cdot [T_1 T_2 B_1] \\
\frac{dT_2}{dt} & = -k \cdot [T_1] [T_2] [I_2] + k \cdot [T_1 T_2 I_2] \\
\frac{dT_1 T_2}{dt} & = k \cdot [T_1] [T_2] [I_1] - k \cdot [T_1 T_2 I_1] \\
\frac{dE}{dt} & = -k \cdot [L_1] [E] + k \cdot [L_1 L_1 E] + k \cdot [L_1 L_1 E] - k \cdot [L_2 L_2 E] + k \cdot [L_2 L_2 E] + k \cdot [L_2 L_2 E] \\
\frac{dL_1 I_1 E}{dt} & = k \cdot [L_1 L_1] [E] - k \cdot [L_1 L_1 E] - k \cdot [L_1 L_1 E] \\
\frac{dL_1 L_1 E}{dt} & = -k \cdot [L_1 L_1 E] - k \cdot [L_1 L_1 E] + k \cdot [L_1 L_1 E] [L_1] \\
\frac{dL_1 E}{dt} & = k \cdot [L_1 L_1] [E] - k \cdot [L_1 L_1 E] - k \cdot [L_1 L_1 E] \\
\frac{dL_1 L_1 E}{dt} & = k \cdot [L_1 L_1] [L_1] - k \cdot [L_1 L_1 E] [L_1] \\
\frac{dL_1 L_1 E}{dt} & = k \cdot [L_1 L_1] [L_1] - k \cdot [L_1 L_1 E] [L_1] \\
\end{align*} \]
Figure S12. Computational simulation of the Inhibitor B1-gated dissipative system (Figure 4, State B). The kinetic scheme of the reactions associated with the time-dependent concentration changes during the dissipative transitions is summarized in above equations. Knowing the time-dependent concentration changes of the tetrahedron dimers T1/T2 and T3/T4 during the dissipative transitions, we computationally simulated the time-dependent concentration changes by using Matlab R2020a.
Kinetic equations of B$_2$ gated dissipative system (Figure 4, State C):

\[ L_1 + I_1 \ \frac{k_1}{k_{-1}} \ L_2 I_1 \]  \hspace{1cm} (1)

\[ L_1 I_1 + I_1 \ \frac{k_2}{k_{-2}} \ L_1 L_2 I_1 + I_1 \]  \hspace{1cm} (2)

\[ T_1 + T_2 + I_1 \ \frac{k_{12}}{k_{-12}} \ T_2 T_4 T_2 I_1 \]  \hspace{1cm} (3)

\[ L_1 L_1 I_1 + E \ \frac{k_3}{k_{-3}} \ L_1 L_1 E \]  \hspace{1cm} (4)

\[ L_1 L_1 E \ \frac{k_1}{k_{-1}} \ E + L_1 L_2 L_2 I_2 \]  \hspace{1cm} (5)

\[ L_1 L_1, L_{1,2} \ \frac{k_0}{k_{-0}} \ L_1 L_{1,2} + L_{1,2,2} \]  \hspace{1cm} (6)

\[ L_2 + I_2 \ \frac{k_2}{k_{-2}} \ L_2 J_2 \]  \hspace{1cm} (7)

\[ L_2 J_2 + L_2 \ \frac{k_{12}}{k_{-12}} \ L_2 J_2 + I_2 \]  \hspace{1cm} (8)

\[ T_3 + T_4 + I_2 \ \frac{k_{12}}{k_{-12}} \ T_3 T_4 T_2 J_2 \]  \hspace{1cm} (9)

\[ L_2 J_2 \ \frac{k_4}{k_{-4}} \ L_2 J_2 E \]  \hspace{1cm} (10)

\[ L_2 J_2 \ \frac{k_1}{k_{-1}} \ E + L_2 J_2 \ \frac{k_{12}}{k_{-12}} \ L_{2,2} \]  \hspace{1cm} (11)

\[ L_2 J_2 \ \frac{k_0}{k_{-0}} \ L_2 L_{1,2} + L_{2,2,2} \]  \hspace{1cm} (12)

\[ T_3 + B_2 \ \frac{k_{12}}{k_{-12}} \ T_3 B_2 \]  \hspace{1cm} (14)

Derivatives:

\[ \frac{dL_1}{dt} = -k[L_1][I_1] + k \cdot [L_1][I_1] + k_o[L_1][L_{1,2}] - k \cdot [L_1][L_{1,2}] \]  

\[ \frac{dI_1}{dt} = -k[L_1][I_1] + k \cdot [L_1][I_1] + k \cdot [L_1][I_1] - k \cdot [L_1][I_1] + k \cdot [T_3][T_2][I_1] \]  

\[ \frac{dT_1}{dt} = k[L_1][I_1] - k \cdot [L_1][I_1] - k \cdot [L_1][I_1] + k \cdot [L_1][I_1] \]  

\[ \frac{dT_2}{dt} = -k \cdot [T_3][T_2][I_1] + k \cdot [T_3][T_2][I_1] \]  

\[ \frac{dT_3}{dt} = -k \cdot [T_3][T_2][I_1] + k \cdot [T_3][T_2][I_1] \]  

\[ \frac{dE}{dt} = -k[L_1][E] + k \cdot [L_1][E] + k \cdot [L_1][E] - k \cdot [L_2][E] + k \cdot [L_2][E] \]  

\[ \frac{dL_1,E}{dt} = k[L_1][E] - k \cdot [L_1][E] - k[L_1][E] \]  

\[ \frac{dL_1, L_{1,2}^2}{dt} = -k[L_1][E] - k[L_1][E] + k \cdot [L_1][L_{1,2}] \]  

\[ \frac{dL_1, L_{1,2}^2}{dt} = k[L_1][L_{1,2}] - k \cdot [L_1][L_{1,2}] \]  

\[ \frac{dL_2, L_{1,2}^2}{dt} = k[L_1][L_{1,2}] - k \cdot [L_1][L_{1,2}] \]
\[
\frac{d[L_3]}{dt} = -k_{11} [L_3][L_1] + k \cdot [L_3][L_2] + k_{13} [L_3][L_2][L_1] - k \cdot s[L_3][L_2][L_1]
\]

\[
\frac{d[L_1]}{dt} = -k_{11} [L_1][L_2] + k \cdot [L_1][L_2][L_3] - k_{13} [L_1][L_2][L_3] - k_{33} [T_3][T_4][L_2] + k \cdot s[T_3][T_4][L_2]
\]

\[
\frac{d[L_2]}{dt} = k_{12} [L_3][L_1] - k \cdot [L_2][L_3] - k_{13} [L_2][L_1][L_3] + k \cdot s[L_2][L_1][L_3]
\]

\[
\frac{d[L_3]}{dt} = -k_{11} [L_3][L_2] + k \cdot s[L_2][L_3][L_1]
\]

\[
\frac{d[L_4]}{dt} = k_{12} [L_3][L_2] - k \cdot s[L_2][L_3][L_1] - k_{13} [L_2][L_3][L_1] - k \cdot s[L_2][L_3][L_1]
\]

\[
\frac{d[T_3]}{dt} = -k_{33} [T_3][T_4][L_2] + k \cdot s[T_3][T_4][L_2] - k_{33} [T_3][T_4][L_2] + k \cdot s[T_3][T_4][L_2]
\]

\[
\frac{d[T_4]}{dt} = -k_{33} [T_3][T_4][L_2] + k \cdot s[T_3][T_4][L_2]
\]

\[
\frac{d[T_3][T_4]}{dt} = k_{12} [T_3][T_4][L_2] - k \cdot s[T_3][T_4][L_2]
\]

\[
\frac{d[L_3][E]}{dt} = k_{12} [L_3][E] - k \cdot s[L_3][L_2][E]
\]

\[
\frac{d[L_2][L_3][E]}{dt} = k_{12} [L_2][L_3][E] - k_{13} [L_2][L_3][E] + k \cdot s[L_2][L_3][E]
\]

\[
\frac{d[L_2][L_3][L_2][E]}{dt} = k_{12} [L_2][L_3][L_2][E] - k \cdot s[L_2][L_3][L_2][E]
\]

\[
\frac{d[L_2][L_3][L_2][L_3][E]}{dt} = k_{12} [L_2][L_3][L_2][L_3][E] - k \cdot s[L_2][L_3][L_2][L_3][E]
\]

\[
\frac{d[B_1]}{dt} = -k_{33} [T_3][B_2] + k \cdot s[T_3][B_2]
\]

\[
\frac{d[T_3][B_2]}{dt} = k_{33} [T_3][B_2] - k \cdot s[T_3][B_2]
\]

**Figure S13.** Computational simulation of the Inhibitor B2-gated dissipative system (Figure 4, State C). The kinetic scheme of the reactions associated with the time-dependent concentration changes during the dissipative transitions is summarized in above equations. Knowing the time-dependent concentration changes of the tetrahedron dimers T1/T2 and T3/T4 during the dissipative transitions, we computationally simulated the time-dependent concentration changes by using Matlab R2020a.
Figure S14. (A) Time-dependent Fluorescence intensity changes of the fragmented substrate of DNAzyme(1) and DNAzyme(2), in state 1: Panel I- the Cy5-labeled fragmented product of DNAzyme(1); Panel II- the FAM-labeled fragmented product of DNAzyme(2); (B) Time-dependent fluorescence intensity changes of fragmented fluorophore-generated substrate cleaved by the DNAzymes in state 2: Panel I-DNAzyme(1), in the presence of variable concentrations of B₁: (a) = 0.33 μM, (b) = 0.66 μM, (c) = 1 μM, (d) = 1.33 μM; Panel II-DNAzyme(2) in the presence of variable concentrations of B₁, (shown in Panel I), the DNAzyme(2) is unaffected by B₁. (C)
Time-dependent fluorescence intensity changes of the fragmented fluorophore-generated substrate cleaved by the DNAzymes in state 3: Panel I-DNAzyme(1), in the presence of variable concentrations of B$_2$ outlined in Panel II, the DNAzyme(1) is unaffected by B$_2$; Panel II-DNAzyme(2) in the presence of different concentrations of B$_2$, (a) = 0.33 μM, (b) = 0.66 μM, (c) = 1 μM, (d) = 1.33 μM.
Figure S15. (A) Fluorescence spectra of the fluorophore Cy5-modified fragmented strand at different concentrations. (B) Calibration curve corresponding to the fluorescence intensities of Cy5-modified fragmented strand at variable concentrations (means ± standard deviation, n = 3).
Figure S16. (A) Fluorescence spectra of the fluorophore FAM-modified fragmented strand at different concentrations. (B) Calibration curve corresponding to the fluorescence intensities of FAM-modified fragmented strand at variable concentrations (means ± standard deviation, n = 3).
Figure S17. (A) Schematic configuration of the hemin/Q-quadruplex modified tetrahedra structures, $T_A$/H-Q and $T_B$/H-Q, and the analog hemin/G-quadruplex structure, D/H-Q. The detailed sequences of the respective structures are provided in the list of sequences, page s3. The catalytic features of the hemin/G-quadruplex units, H/Q, were evaluated by following the $\text{H}_2\text{O}_2$ catalyzed oxidation of Amplex Red to Resorufin or the $\text{H}_2\text{O}_2$ catalyzed oxidation of dopamine to aminochrome. (B) Panel I- Time-dependent fluorescence changes generated upon the $\text{H}_2\text{O}_2$ oxidation of Amplex Red (80 μM) to Resorufin ($\lambda_{em} = 585$ nm) by: $T_A$/H-Q (0.1 μM), $T_B$/H-Q (0.1 μM), D/H-Q (0.1 μM) in the presence of $\text{H}_2\text{O}_2$ (5 mM). Panel II- Time-dependent absorbance changes generated upon the $\text{H}_2\text{O}_2$ oxidation of dopamine (1 mM) to aminochrome (absorbance at 480 nm) by: $T_A$/H-Q (0.2 μM), $T_B$/H-Q (0.2 μM), D/H-Q (0.2 μM) in
the presence of H$_2$O$_2$ (5 mM). (C) Panel I-Catalytic rates corresponding to the oxidation of Amplex Red to Resorufin by the different catalytic systems. Error bars derived from N = 3 experiments. Panel II- Catalytic rates corresponding to the oxidation of dopamine to aminochrome by the different catalytic systems. Error bars derived from N = 3 experiments.
**Table S1.** Rate constants derived from the computational simulation of the dissipative system shown in Figure 1.

| $k_1$ | 2.913 μM$^{-1}$ min$^{-1}$ | $k_3$ | 5 μM$^{-2}$ min$^{-1}$ | $k_5$ | 0.81 min$^{-1}$ |
| $k_{-1}$ | 0.00001 min$^{-1}$ | $k_{-3}$ | 0.0236 min$^{-1}$ | $k_6$ | 0.028 min$^{-1}$ |
| $k_2$ | 0.0845 μM$^{-1}$ min$^{-1}$ | $k_4$ | 5.00001 μM$^{-1}$ min$^{-1}$ | $k_{-6}$ | 0.00502 μM$^{-2}$ min$^{-1}$ |
| $k_{-2}$ | 50 μM$^{-1}$ min$^{-1}$ | $k_{-4}$ | 0.9988 min$^{-1}$ |
**Table S2.** Rate constants derived from the computational simulation of the dissipative system shown in Figure 3.*

| $k_7$  | 35 μM⁻¹ min⁻¹ | $k_9$  | 2.985 μM⁻² min⁻¹ | $k_5$  | 0.81 min⁻¹ |
|--------|----------------|--------|-------------------|--------|------------|
| $k_{-7}$ | 0.04 min⁻¹ | $k_{-9}$ | 1.31 min⁻¹ | $k_{-5}$ | 20.001 min⁻¹ |
| $k_8$  | 1.72 μM⁻¹ min⁻¹ | $k_4$  | 5.00001 μM⁻¹ min⁻¹ | $k_{-10}$ | 0.00001 μM⁻² min⁻¹ |
| $k_{-8}$ | 5.9 μM⁻¹ min⁻¹ | $k_{-4}$ | 0.9988 min⁻¹ |        |            |

*For independent evaluation of the rate constants $k_9$ and $k_{-9}$, see Figure S10. The independently evaluated values of $k_9$, $k_{-9}$ fit well with the simulated rate constants tabulated in Table S2, thus supporting the simulation process.*


**Table S3.** Rate constants derived from the computational simulation of the gated dissipative system (Figure 4, State A).

| $k_1$  | $2.913 \mu M^{-1} \text{ min}^{-1}$ | $k_4$  | $0.9988 \text{ min}^{-1}$ | $k_8$  | $5.9 \mu M^{-1} \text{ min}^{-1}$ |
|--------|----------------------------------|--------|--------------------------|--------|----------------------------------|
| $k_{-1}$ | $0.00001 \text{ min}^{-1}$ | $k_5$  | $0.81 \text{ min}^{-1}$ | $k_9$  | $2.985 \mu M^{-2} \text{ min}^{-1}$ |
| $k_2$  | $0.0845 \mu M^{-1} \text{ min}^{-1}$ | $k_6$  | $0.028 \text{ min}^{-1}$ | $k_{-9}$ | $1.31 \text{ min}^{-1}$ |
| $k_{-2}$ | $50 \mu M^{-1} \text{ min}^{-1}$ | $k_{-6}$ | $0.00502 \mu M^{-2} \text{ min}^{-1}$ | $k_{10}$ | $20.001 \text{ min}^{-1}$ |
| $k_3$  | $5 \mu M^{-2} \text{ min}^{-1}$ | $k_7$  | $35 \mu M^{-1} \text{ min}^{-1}$ | $k_{-10}$ | $0.00001 \mu M^{-2} \text{ min}^{-1}$ |
| $k_{-3}$ | $0.0236 \text{ min}^{-1}$ | $k_{-7}$ | $0.04 \text{ min}^{-1}$ | | |
| $k_4$  | $5.00001 \mu M^{-1} \text{ min}^{-1}$ | $k_8$  | $1.72 \mu M^{-1} \text{ min}^{-1}$ | | |

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Table S4. Rate constants derived from the computational simulation of the Blocker B₁-gated dissipative system (Figure 4, State B).

| $k_1$ | 2.913 $\mu$M$^{-1}$ min$^{-1}$ | $k_4$ | 0.9988 min$^{-1}$ | $k_8$ | 5.9 $\mu$M$^{-1}$ min$^{-1}$ |
|-------|-----------------|-------|-----------------|-------|-----------------|
| $k_{-1}$ | 0.00001 min$^{-1}$ | $k_5$ | 0.81 min$^{-1}$ | $k_9$ | 2.985 $\mu$M$^{2}$ min$^{-1}$ |
| $k_2$ | 0.0845 $\mu$M$^{-1}$ min$^{-1}$ | $k_6$ | 0.028 min$^{-1}$ | $k_{-9}$ | 1.31 min$^{-1}$ |
| $k_{-2}$ | 50 $\mu$M$^{-1}$ min$^{-1}$ | $k_{-6}$ | 0.00502 $\mu$M$^{2}$ min$^{-1}$ | $k_{10}$ | 20.001 min$^{-1}$ |
| $k_3$ | 5 $\mu$M$^{2}$ min$^{-1}$ | $k_7$ | 35 $\mu$M$^{-1}$ min$^{-1}$ | $k_{-10}$ | 0.00001 $\mu$M$^{2}$ min$^{-1}$ |
| $k_{-3}$ | 0.0236 min$^{-1}$ | $k_{-7}$ | 0.04 min$^{-1}$ | $k_{11}$ | 30 $\mu$M$^{-1}$ min$^{-1}$ |
| $k_4$ | 5.00001 $\mu$M$^{-1}$ min$^{-1}$ | $k_8$ | 1.72 $\mu$M$^{-1}$ min$^{-1}$ | $k_{-11}$ | 0.00001 min$^{-1}$ |
Table S5. Rate constants derived from the computational simulation of the Blocker $B_2$-gated dissipative system (Figure 4, State C).

| \(k_1\) | \(2.913 \mu M^{-1} \text{min}^{-1}\) | \(k_{-4}\) | \(0.9988 \text{min}^{-1}\) | \(k_{-8}\) | \(5.9 \mu M^{-1} \text{min}^{-1}\) |
| --- | --- | --- | --- | --- | --- |
| \(k_{-1}\) | \(0.00001 \text{min}^{-1}\) | \(k_5\) | \(0.81 \text{min}^{-1}\) | \(k_9\) | \(2.985 \mu M^{-2} \text{min}^{-1}\) |
| \(k_2\) | \(0.0845 \mu M^{-1} \text{min}^{-1}\) | \(k_6\) | \(0.028 \text{min}^{-1}\) | \(k_{-9}\) | \(1.31 \text{min}^{-1}\) |
| \(k_{-2}\) | \(50 \mu M^{-1} \text{min}^{-1}\) | \(k_{-6}\) | \(0.00502 \mu M^{-2} \text{min}^{-1}\) | \(k_{10}\) | \(20.001 \text{min}^{-1}\) |
| \(k_3\) | \(5 \mu M^{-2} \text{min}^{-1}\) | \(k_7\) | \(35 \mu M^{-1} \text{min}^{-1}\) | \(k_{10}\) | \(0.00001 \mu M^{-2} \text{min}^{-1}\) |
| \(k_{-3}\) | \(0.0236 \text{min}^{-1}\) | \(k_{-7}\) | \(0.04 \text{min}^{-1}\) | \(k_{12}\) | \(28.5268 \mu M^{-1} \text{min}^{-1}\) |
| \(k_4\) | \(5.00001 \mu M^{-1} \text{min}^{-1}\) | \(k_8\) | \(1.72 \mu M^{-1} \text{min}^{-1}\) | \(k_{-12}\) | \(0.00001 \text{min}^{-1}\) |