Supporting Information: Improving the Performance of DNA Strand Displacement Circuits by Shadow Cancellation

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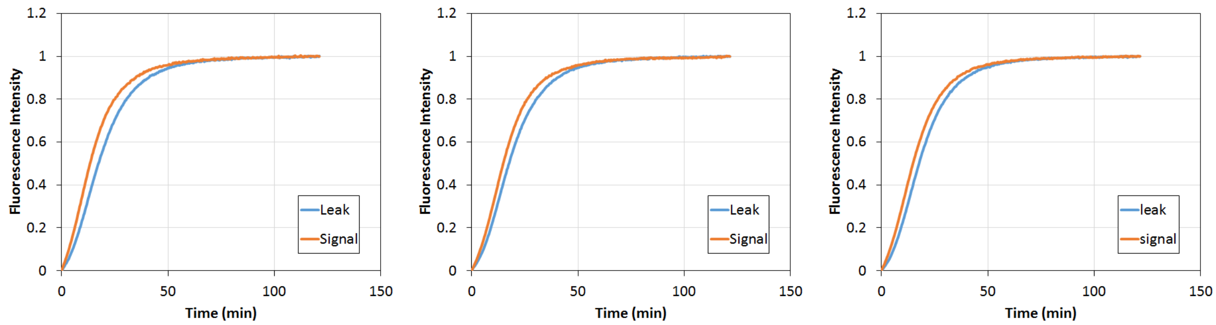
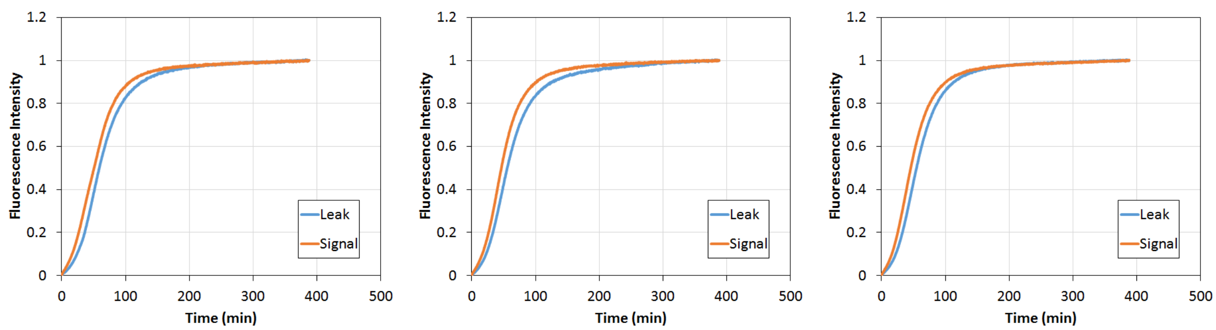
1 Three Repeats for Each Scenario

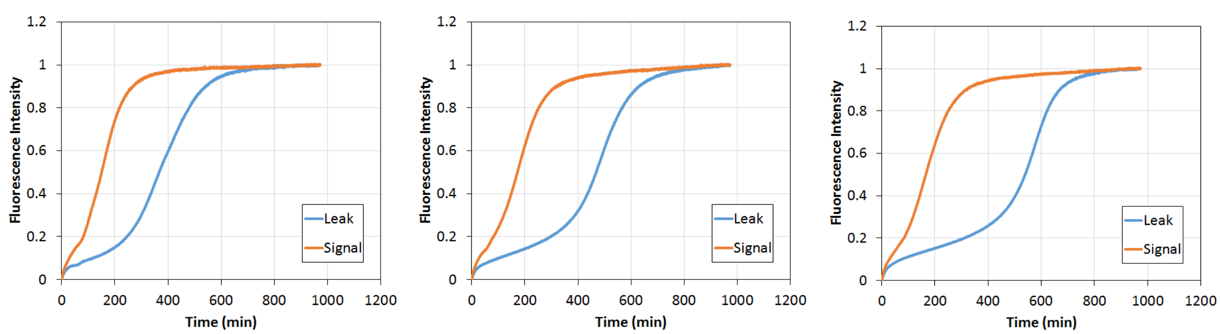
1.1 The amplifier



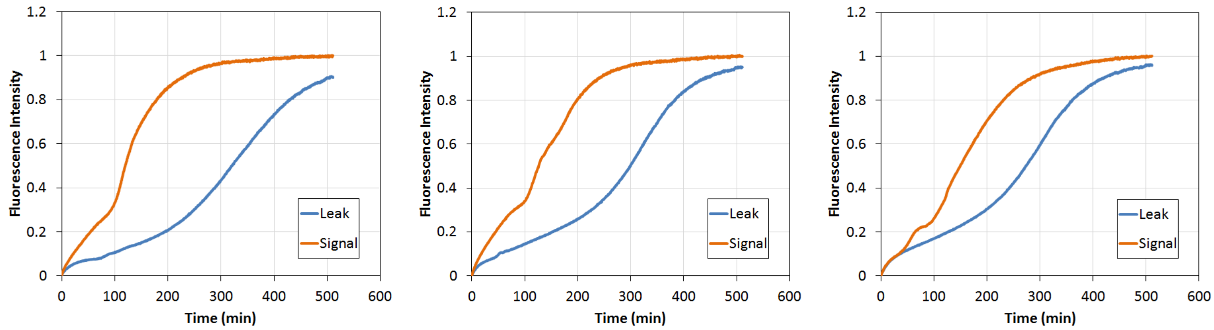
1.2 The amplifier with cancellation complexes



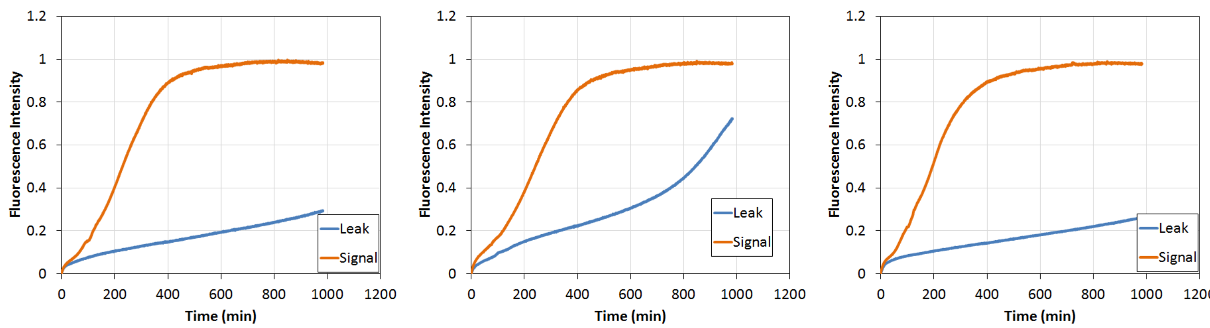
1.3 The amplifier with shadow cancellation (100% shadow, 75 nM of cancellation complexes)



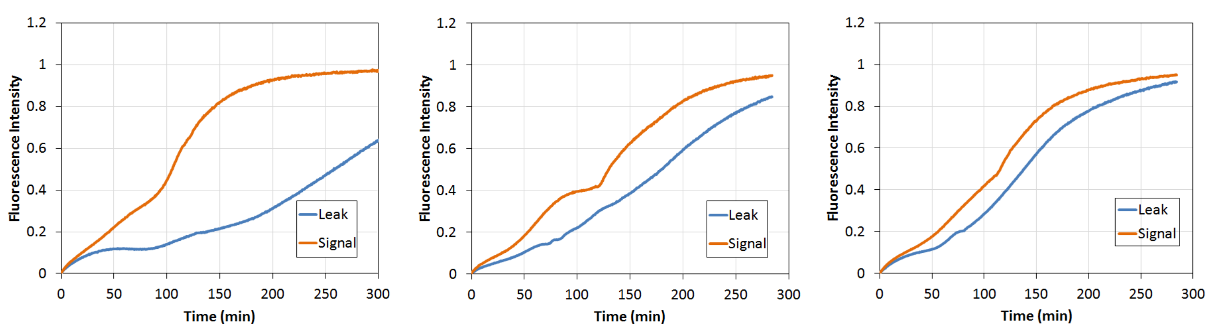
1.4 90% shadow



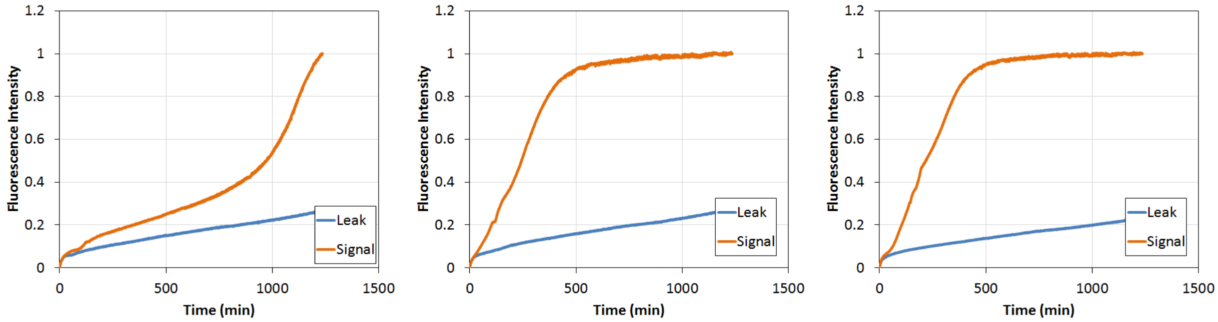
1.5 110% shadow



1.6 65 nM of cancellation complexes (C1 and C2)



1.7 85 nM of cancellation complexes (C1 and C2)



1.8 Statistical analysis on SBDs

Here we conduct a statistical analysis on SBDs in different scenarios to evaluate the performance of shadow cancellation. The method that we use is Welch's t-test. Except the scenario with 65 nM of C1 and C2, in all other scenarios, the difference is statistically significant (p-value < 0.05).

Table 1: SBDs from three repeats in different scenarios.

The amplifier	0.0953, 0.0713, 0.0609
100% shadow, 75 nM of C1 and C2	0.6330, 0.6300, 0.6293
90% shadow	0.6237, 0.5455, 0.4315
110% shadow	0.6659, 0.5882, 0.6738
65 nM of C1 and C2	0.5894, 0.2485, 0.1451
85 nM of C1 and C2	0.5554, 0.6653, 0.6832

Table 2: p-values from Welch's t-tests on SBDs.

	The amplifier
100% shadow, 75 nM of C1 and C2	0.0003
90% shadow	0.0124
110% shadow	0.0008
65 nM of C1 and C2	0.2008
85 nM of C1 and C2	0.0033

2 The Universality of Shadow Cancellation

Here, we study the effect of shadow cancellation on some abstract chemical reaction networks by simulation using LBS.[1,2]

2.1 Auto-catalytic amplifier

$$X_0 + G_{X0} \xrightarrow{k=0.0001} X_0 + X_0 + G_{X0-X0} \tag{1a}$$

$$G_{X0} \xrightarrow{10^{-6}*k} X_0 + G_{X0L} \tag{1b}$$

$$Y_0 + G_{Y0} \xrightarrow{k} Y_0 + Y_0 + G_{Y0-Y0} \tag{1c}$$

$$G_{Y0} \xrightarrow{10^{-6}*k} Y_0 + G_{Y0L} \tag{1d}$$

$$X_0 + Y_0 + C \xrightarrow{100*k} G_{X0-Y0-C} \tag{1e}$$

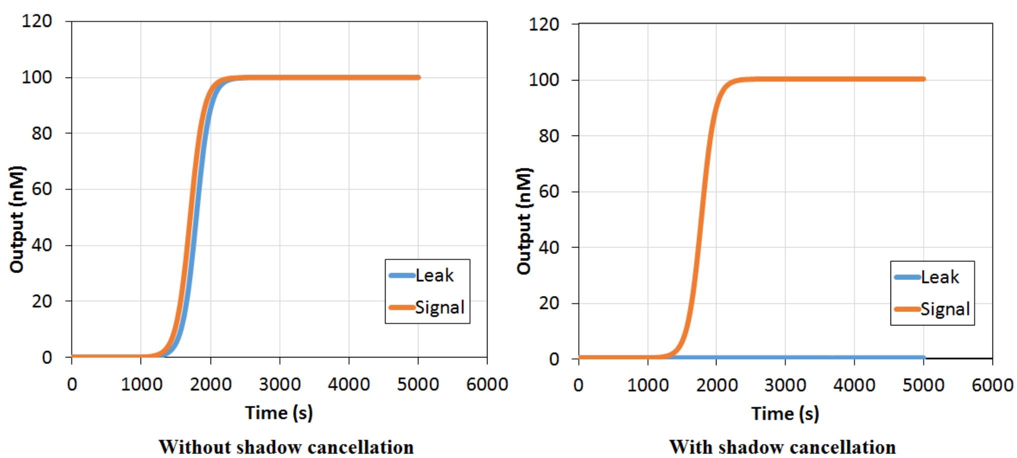


Figure 1: Simulation of shadow cancellation on an auto-catalytic amplifier. The initial state: $[G_{X0}]$ = $[G_{Y0}]$ = 100 nM. For the cases of "Leak", $[X_0]$ = 0 nM. For the cases of "Signal", $[X_0] = 10^{-6}$ nM. For the cases with shadow cancellation, [C] = 100 nM. X_0 is the output.

Reactions (1a) and (1b) describe the primary auto-catalytic amplifier, where (1a) is the designed amplification and (1b) is the leak (much slower than (1a)). Reactions (1c) and (1d) describe the shadow amplifier. Reaction (1e) describes the cancellation, which is faster than (1a) and (1c) such that it is preferred by X_0 and Y_0 when cancellation is needed. Shadow cancellation improves the performance of this auto-catalytic amplifier as shown in Figure 1.

2.2 Cross-catalytic amplifier

$$X_0 + G_{X0} \xrightarrow{k=0.0001} X_0 + X_1 + G_{X0-X0} \tag{2a}$$

$$X_1 + G_{X1} \xrightarrow{k} X_1 + X_0 + G_{X1-X1} \tag{2b}$$

$$G_{X0} \xrightarrow{10^{-6}*k} X_1 + G_{X0L} \tag{2c}$$

$$G_{X1} \xrightarrow{10^{-6}*k} X_0 + G_{X1L} \tag{2d}$$

$$Y_0 + G_{Y0} \xrightarrow{k} Y_0 + Y_1 + G_{Y0-Y0} \tag{2e}$$

$$Y_1 + G_{Y1} \xrightarrow{k} Y_1 + Y_0 + G_{Y1-Y1} \tag{2f}$$

$$G_{Y0} \xrightarrow{10^{-6}*k} Y_1 + G_{Y0L} \tag{2g}$$

$$G_{Y1} \xrightarrow{10^{-6}*k} Y_0 + G_{Y1L} \tag{2h}$$

$$X_0 + Y_0 + C_0 \xrightarrow{100*k} G_{X0-Y0-C0} \tag{2i}$$

$$X_1 + Y_1 + C_1 \xrightarrow{100*k} G_{X1-Y1-C1} \tag{2j}$$

Reactions (2a) to (2d) describe the primary cross-catalytic amplifier. (2a) and (2b) are the designed amplifications. (2c) and (2d) are the leak (much slower than (2a) and (2b)). Reactions (2e) to (2h) describe the shadow amplifier. Reactions (2i) and (2j) describe the cancellation. Shadow cancellation improves the performance of this cross-catalytic amplifier as shown in Figure 2.

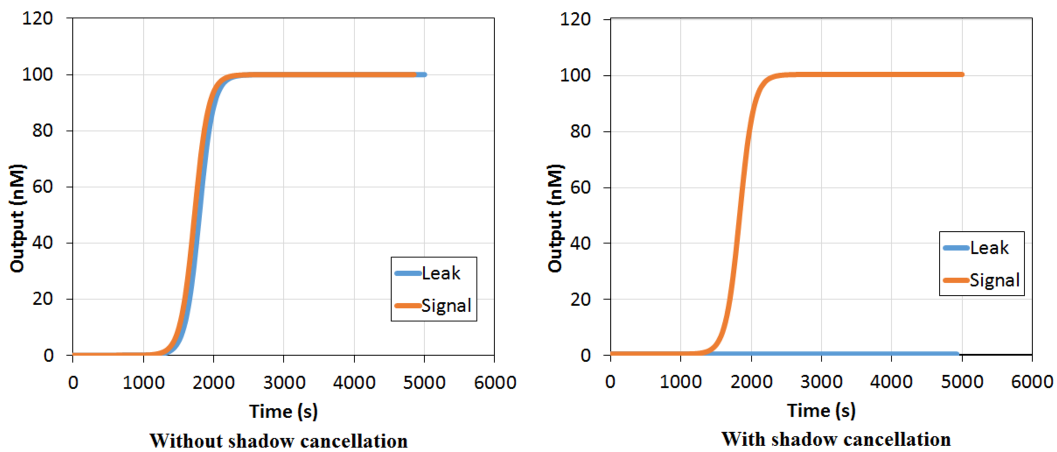


Figure 2: Simulation of shadow cancellation on a cross-catalytic amplifier. The initial state: $[G_{X0}] = [G_{X1}] = [G_{Y0}] = [G_{Y1}] = 100$ nM. For the cases of "Leak", $[X_0] = 0$ nM. For the cases of "Signal", $[X_0] = 10^{-6}$ nM. For the cases with shadow cancellation, $[C_1] = [C_2] = 100$ nM. X_0 is the output.

2.3 Quadratic amplifier

$$X_0 + G_{X0} \xrightarrow{k=0.0001} X_0 + X_1 + G_{X0-X0} \tag{3a}$$

$$X_1 + G_{X1} \xrightarrow{k} X_1 + X_2 + G_{X1-X1} \tag{3b}$$

$$G_{X0} \xrightarrow{10^{-6}*k} X_1 + G_{X0L} \tag{3c}$$

$$G_{X1} \xrightarrow{10^{-6}*k} X_2 + G_{X1L} \tag{3d}$$

$$Y_0 + G_{Y0} \xrightarrow{k} Y_0 + Y_1 + G_{Y0-Y0} \tag{3e}$$

$$Y_1 + G_{Y1} \xrightarrow{k} Y_1 + Y_2 + G_{Y1-Y1} \tag{3f}$$

$$G_{Y0} \xrightarrow{10^{-6}*k} Y_1 + G_{Y0L} \tag{3g}$$

$$G_{Y1} \xrightarrow{10^{-6}*k} Y_2 + G_{Y1L} \tag{3h}$$

$$X_0 + Y_0 + C_0 \xrightarrow{100*k} G_{X0-Y0-C0} \tag{3i}$$

$$X_1 + Y_1 + C_1 \xrightarrow{100*k} G_{X1-Y1-C1} \tag{3j}$$

Reactions (3a) to (3d) describe the primary quadratic amplifier. (3a) and (3b) are the designed amplifications. (3c) and (3d) are the leak (much slower than (3a) and (3b)). Reactions (3e) to (3h) describe the shadow amplifier. Reactions (3i) and (3j) describe the cancellation. Shadow cancellation improves the performance of this quadratic amplifier as shown in Figure 3.

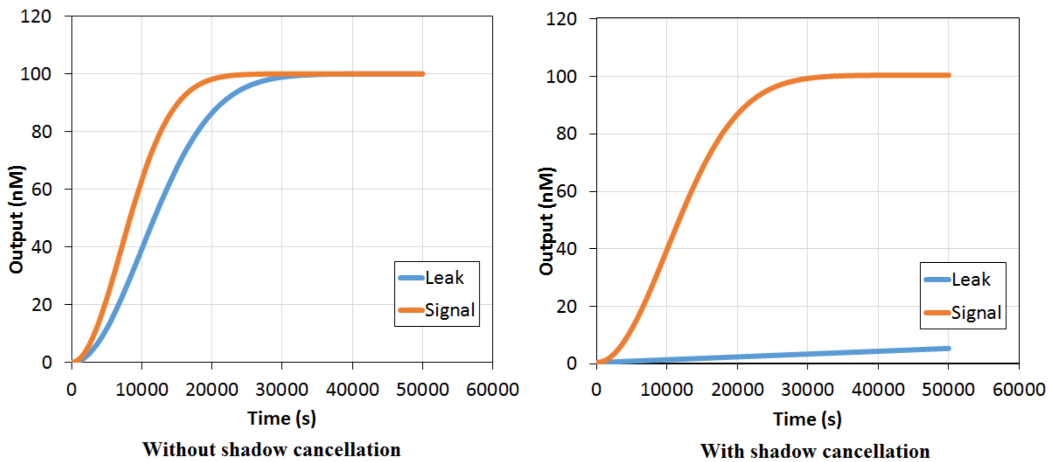


Figure 3: Simulation of shadow cancellation on a quadratic amplifier. The initial state: $[\mathrm{G}_{X0}] = [\mathrm{G}_{X1}] = [\mathrm{G}_{Y0}] = [\mathrm{G}_{Y1}] = 100$ nM. For the cases of "Leak", $[\mathrm{X}_0] = 0$ nM. For the cases of "Signal", $[\mathrm{X}_0] = 10^{-6}$ nM. For the cases with shadow cancellation, $[\mathrm{C}_1] = [\mathrm{C}_2] = 100$ nM. X_2 is the output.

References

(1) Pedersen, M.; Phillips, A. Towards Programming Languages for Genetic Engineering of Living Cells. *J. R. Soc. Interface* **2009**, *6*, S437–S450.

(2) Pedersen, M.; Plotkin, G. D. *Transactions on Computational Systems Biology XII*; Springer: Berlin, Heidelberg, 2010; pp 77–145.