Control of MarRAB Operon in *Escherichia coli* via Autoactivation and Autorepression

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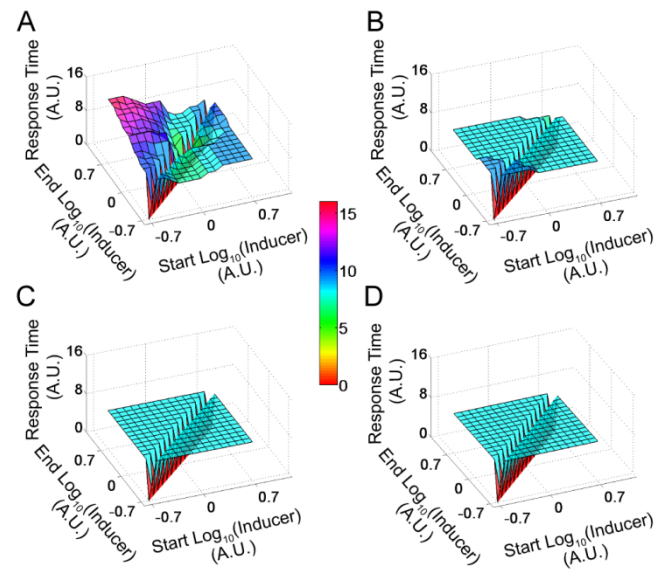
Figure S1. Response time calculated in varying inducer concentrations in (A) wild-type, and (B-D) evolved repressor-only designs. X-axis and Z-axis represent the "start" and "end" inducer concentration in logarithm where network moves from "start" to "end" during a switch. Y-axis captures the response time required to switch.
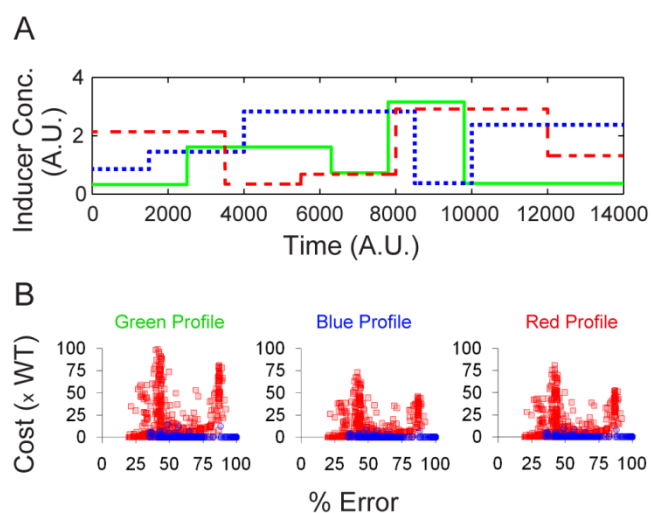
A

B

Figure S2. Comparison of control cost of response between wild-type, evolved activator-only, and evolved repressor-only designs. (A) Inducer concentration profiles generated where both the inducer levels and the time for which the level was sustained were randomly varied. **(B)** Control cost (across the three profiles) in the evolved activator-only (blue) and evolved repressor-only (red) designs was computed (in multiples of control cost of the wild-type design) and plotted against % error in mimicking response of WT design. For cost calculations, all regulators in a design in their free as well as bound to an inducer were taken into account.
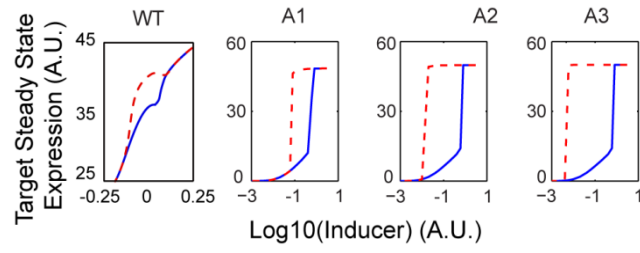
Figure S3. Hysteresis curve in wild-type and evolved activator-only designs. X-axis represents inducer. Blue curve represents transition from a lower to higher inducer concentration, and red dashed line represents a transition from maximum inducer concentration to a lower value. A1, A2, and A3 represent the three evolved activator-only designs.
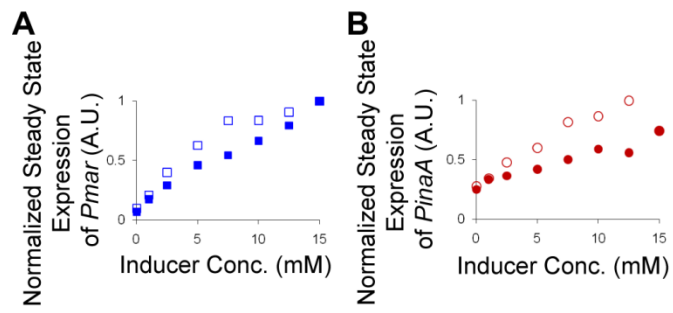
Figure S4. Comparison of memory storing capability in wild-type at higher concentration (15mM). X-axis represents the concentration of Sodium Salicylate (mM) and Y-axis represents the steady state expression of **(A)** P*mar* (Blue square) and **(B)** P*inaA* (Red circle) during both OFF to ON (Filled) and ON to OFF (Unfilled) condition.
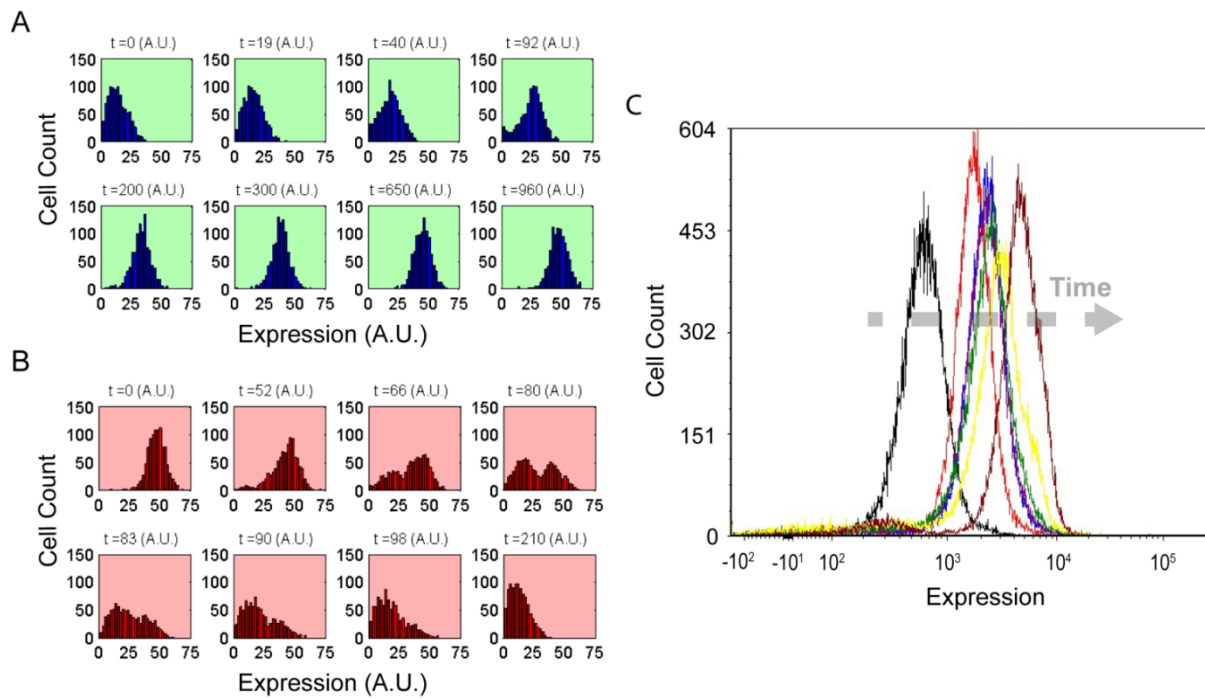
Figure S5. Target gene expression dynamics at a single-cell resolution. Wild-type design switches target gene expression like a rheostat with no cellular heterogeneity during **(A)** transition from OFF to ON state. However, two distinct populations are observed during **(B)** transition from ON to OFF state. **(C)** Single-cell resolution experimental data as cells transition from OFF (no Sodium Salicylate) to ON state (5 mM Sodium Salicylate) for *PinaA* promoter *at* time, t = 0 (black), 10 (red), 20 (blue), 30 (green), 60 (yellow), and 180 (maroon) minutes. Results in panels A and B are from stochastic simulations (and represent average of 200 independent simulations). Panel C is experimental results.