

**iScience, Volume 24**

**Supplemental information**

**Optimization-based Eukaryotic Genetic Circuit  
Design (EuGeneCiD) and modeling (EuGeneCiM)  
tools: Computational approach to synthetic biology**

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### A. Solution Quantity and Quality Results

### EuGeneCiD Results

NUMBER OF SOLUTIONS RETURNED				PERCENT OPTIMAL SOLUTIONS				CAUSE OF EUGENECID RUN ENDING			
	Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn
AND	1000	1000	1000	AND	75.50%	84.00%	82.20%	AND			
NIMPLY	1000	1000	1000	NIMPLY	55.10%	71.40%	60.60%	NIMPLY			
CNI	1000	1000	1000	CNI	70.50%	70.20%	57.80%	CNI			
HALF ADDER	328	595	335	HALF ADDER	8.23%	16.97%	12.54%	HALF ADDER			
NAND	1000	1000	1000	NAND	21.00%	31.70%	42.80%	NAND			
NOR	1000	1000	1000	NOR	80.40%	18.50%	13.00%	NOR			
OR	1000	1000	1000	OR	31.30%	39.30%	44.40%	OR			
XNOR	738	877	680	XNOR	25.47%	45.04%	53.38%	XNOR			
XOR	351	687	577	XOR	8.83%	6.11%	8.84%	XOR			

NUMBER OF SOLUTIONS RETURNED			
	Cd	Cu	Zn
BUFFER	1000	1000	1000

PERCENT OPTIMAL SOLUTIONS			
	Cd	Cu	Zn
BUFFER	73.50%	71.10%	78.40%

CAUSE OF EUGENECID RUN ENDING			
	Cd	Cu	Zn
BUFFER			

### B. Solution Size Results

■ Completed ■ Time Interrupted

SOLUTION MINIMUM SIZE				MODE SOLUTION SIZE				SOLUTION MAXIMUM SIZE			
	Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn
AND	2	2	2	AND	5	4	4	AND	5	5	5
NIMPLY	3	2	2	NIMPLY	5	4	4	NIMPLY	5	5	5
CNI	2	2	1	CNI	4	4	4	CNI	5	5	5
HALF ADDER	5	5	6	HALF ADDER	6	6	6	HALF ADDER	7	6	7
NAND	3	2	2	NAND	5	4	4	NAND	5	5	5
NOR	1	1	2	NOR	5	4	4	NOR	5	5	5
OR	1	1	2	OR	4	4	4	OR	5	5	5
XNOR	3	2	2	XNOR	6	5	5	XNOR	6	5	6
XOR	4	3	4	XOR	5	5	5	XOR	6	5	6

SOLUTION MINIMUM SIZE			
	Cd	Cu	Zn
BUFFER	1	1	1

MODE SOLUTION SIZE			
	Cd	Cu	Zn
BUFFER	5	5	5

SOLUTION MAXIMUM SIZE			
	Cd	Cu	Zn
BUFFER	5	6	6

### C. Solution Time Results

MINIMUM SOLUTION TIME (S)				MEAN SOLUTION TIME (S)				MAXIMUM SOLUTION TIME (S)			
	Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn
AND	1.22	1.14	1.02	AND	46.2	54.18	42.5	AND	193.33	314.11	210.08
NIMPLY	2.02	1.29	1.15	NIMPLY	74.08	61.1	96.61	NIMPLY	414.64	191.95	623.21
CNI	1.11	0.95	0.79	CNI	62.53	56.24	56.76	CNI	393.94	269.48	335.72
HALF ADDER	10.51	11.5	68.51	HALF ADDER	1836.87	1007.99	1776.34	HALF ADDER	10002.08	7069.24	10001.5
NAND	2.58	0.9	0.89	NAND	382.33	364.65	258.09	NAND	2803.98	5293.96	1950.73
NOR	0.78	0.82	0.82	NOR	37.53	20.25	55.3	NOR	263.66	81.39	231.61
OR	0.8	0.79	0.84	OR	283.26	248.57	244.04	OR	2651.75	1369.53	3180.24
XNOR	5.55	1.39	18.8	XNOR	809.54	681.9	877.64	XNOR	4667.97	3413.98	3210.01
XOR	24.73	3.4	16.8	XOR	1701.5	871.15	1030.31	XOR	10001.83	3249.65	7576.86

MINIMUM SOLUTION TIME (S)			
	Cd	Cu	Zn
BUFFER	0.547	0.578	0.581

MEAN SOLUTION TIME (S)			
	Cd	Cu	Zn
BUFFER	7.337	17.094	9.188

MAXIMUM SOLUTION TIME (S)			
	Cd	Cu	Zn
BUFFER	24.236	154.033	63.041

### D. Objective Results

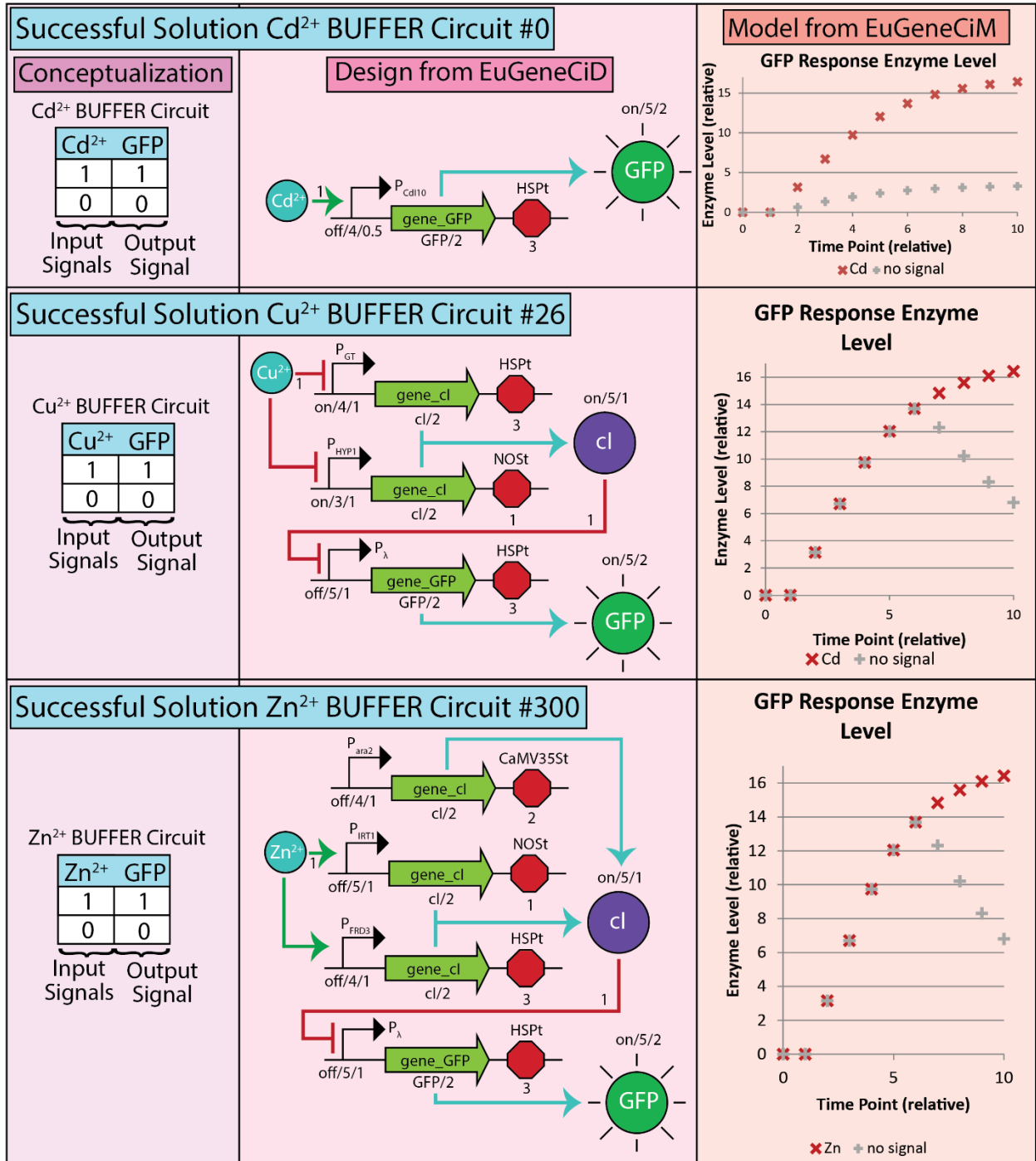
MIN. OBJECTIVE VALUE (SOLUTION NUMBER)				MAX. OBJECTIVE VALUE (SOLUTION NUMBER)			
	Cd/Cu	Cd/Zn	Cu/Zn		Cd/Cu	Cd/Zn	Cu/Zn
AND	-15.56 (366)	-19.09 (7)	-17.68 (699)	AND	5.61 (4)	5.61 (8)	5.61 (8)
NIMPLY	-4.95 (280)	-5.66 (691)	-5.66 (560)	NIMPLY	13.47 (22)	13.47 (6)	13.47 (9)
R-NIMPLY	-7.07 (611)	-7.07 (673)	-4.24 (589)	R-NIMPLY	13.47 (9)	13.47 (8)	13.47 (6)
HALF ADDER	15.91 (190)	7.91 (52)	20.78 (91)	HALF ADDER	40.41 (8)	40.41 (53)	43.78 (227)
NAND	37.04 (6)	37.04 (26)	37.04 (47)	NAND	51.63 (201)	57.81 (54)	60.61 (654)
NOR	-26.87 (412)	-26.87 (11)	-29.7 (640)	NOR	-2 (4)	8.49 (10)	-2 (4)
OR	39.85 (0)	43.78 (0)	43.78 (56)	OR	66.23 (41)	74.08 (76)	71.84 (77)
XNOR	-8.49 (147)	-7.84 (132)	-10.61 (511)	XNOR	13.47 (1)	13.47 (1)	13.47 (38)
XOR	27.44 (198)	26.67 (51)	24.75 (536)	XOR	38.15 (230)	37.04 (53)	40.41 (0)

MIN. OBJECTIVE VALUE (SOLUTION NUMBER)			
	Cd	Cu	Zn
BUFFER	4.49 (0)	4.49 (0)	4.49 (1)

MAX. OBJECTIVE VALUE (SOLUTION NUMBER)			
	Cd	Cu	Zn
BUFFER	6.37 (2)	6.37 (2)	5.61 (0)

**Figure S1: Results Tables.** Contains the data presented in Figure 5, but in a more compact and tabular form, allowing precise data points to be seen. Also contains new data tables which report on the minimum and maximum objective values of EuGeneCiD for each conceptualization as well as the solution number associated with that value. A. Shows data related to overall quality and quantity of the EuGeneCiD/EuGeneCiM runs, including number of solutions, percent of solutions which are optimal, and cause of the end of the run. B. Shows result tables related to solution size (in number of design triads) including minimum, mode, and maximum. C. Shows result tables related to solution time including minimum, mean, and maximum times. D. Shows result tables related to the minimum and maximum objective values of EuGeneCiD for a given design, as well as the design number associated with that value.

## Example Specific Results for BUFFER Conceptualizations



**Figure S2: Specific Example BUFFER Solution Results.** Shown in this image are three examples of successful BUFFER gate designs created by EuGeneCiD, presented in a similar manner to Figure 6. These successful examples include solutions for Cadmium, Copper, and Zinc signals using solutions of size one, three, and four respectively. This figure is included to show the applicability of the EuGeneCiD and EuGeneCiM workflow to circuits which have other than two inputs.