Fluigi: A CAD Framework for Combining Microfluidics and Synthetic Biology

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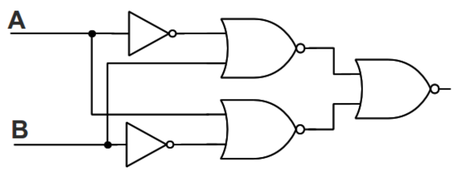
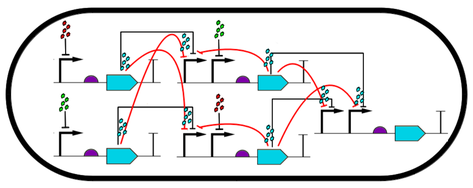
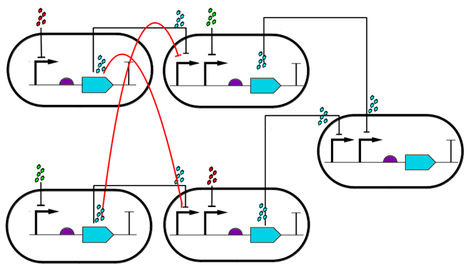
BACKGROUND AND MOTIVATION



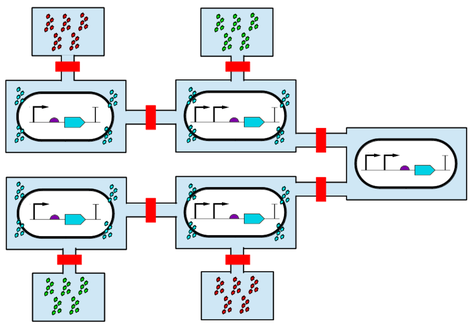
Logic circuit composed of inverters and NOR gates representing the function XOR



The same XOR gate implemented as genetic circuits in a single cell. Red arcs indicate the cross talk between proteins.

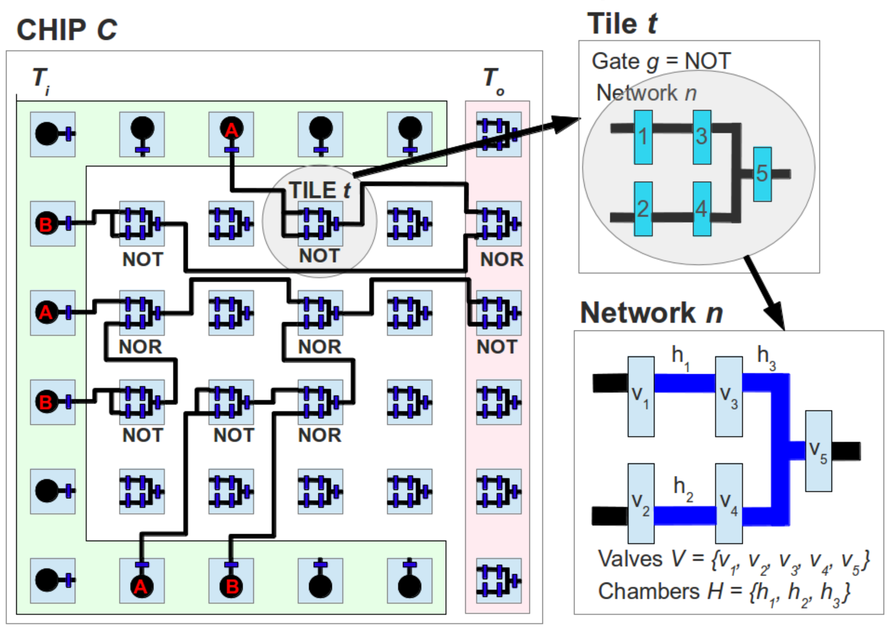


Separating the complex circuit into multiple cells will not eliminate issues caused by crosstalk.



Compartmentalization by microfluidic chambers will allow for precise application of input molecules to the circuit and potentially eliminated crosstalk.

MICROFLUIDIC ARCHITECTURE

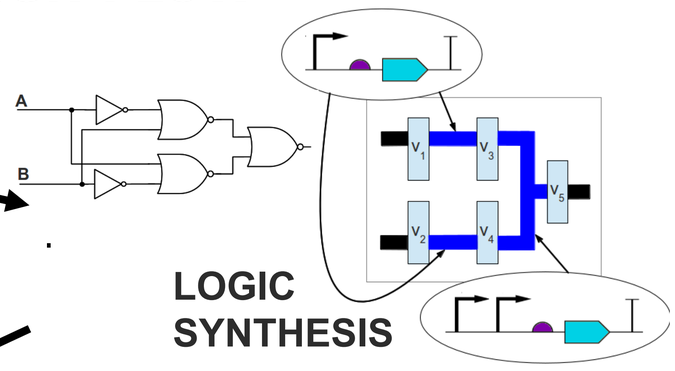


- Hypothetical chip structure used in Fluigi
- Chip C is composed of three types of tiles, logic, input, and output.
- Each tile is composed of a network of valves and chambers
- Input tiles highlighted in green. Output tiles highlighted in red.

DESIGN FLOW

```
module half_adder (a, b,
      sum, carry );
input  a;
input  b;
output sum;
output carry;
assign sum = a^b;
assign carry = a&b;
endmodule
```

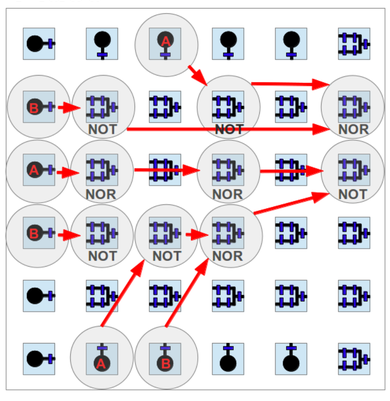
USER SPECIFICATION



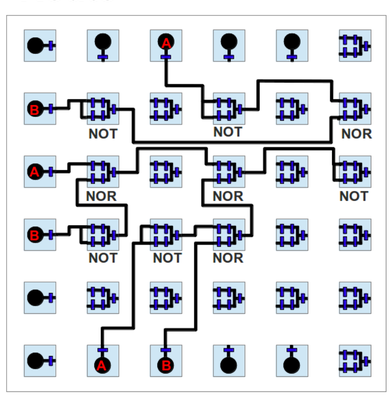
LOGIC SYNTHESIS

PHYSICAL DESIGN

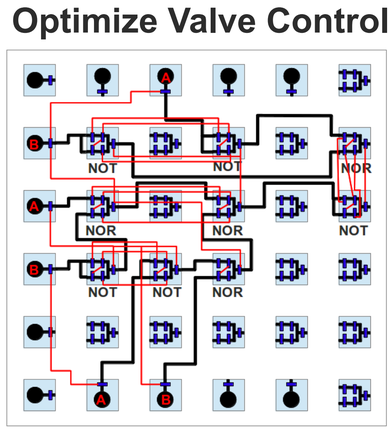
Place



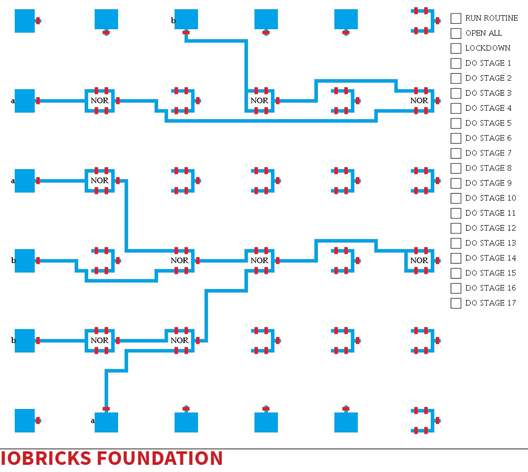
Route



Optimize Valve Control



SIMULATION



MANUFACTURING

Photo courtesy of Brandon Wong of the Khalil Lab

RESULTS

TABLE I. RESULTS OF FLUIGI FOR TWO INPUT BENCHMARK CIRCUITS

Chip Size (tiles x tiles)	Number of 2 Input Circuits	Average Tile Usage (%)	Average Unoptimized Control Lines	Average Optimized Lines	Average Line Reduction (%)
4x4	4	23.44	10.75	8	25.89
5x5	4	21.00	18.25	12	33.76
6x6	2	27.78	34	17	50.00

TABLE II. RESULTS OF FLUIGI FOR THREE INPUT BENCHMARK CIRCUITS

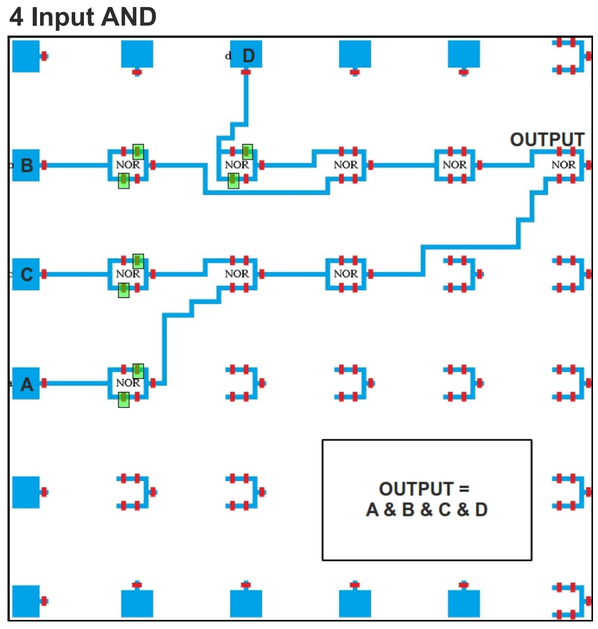
Chip Size (tiles x tiles)	Number of Three Input Circuits	Average Tile Usage (%)	Average Unoptimized Control Lines	Average Optimized Lines	Average Line Reduction (%)
4x4	12	23.44	10.75	8.00	25.89
5x5	49	27.59	23.24	15.02	35.03
6x6	125	34.53	43.18	20.81	51.09
7x7	57	41.28	72.05	28.86	59.45
8x8	5	42.50	100.00	29.80	70.22

TABLE III. RESULTS OF FLUIGI FOR EXAMPLE CIRCUITS

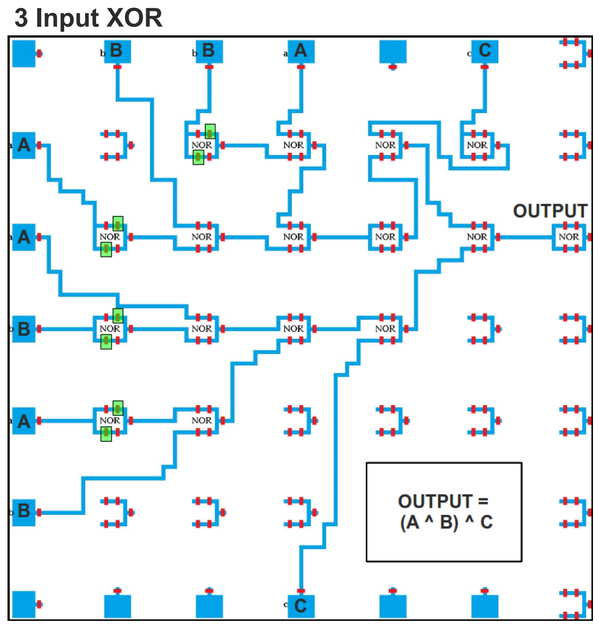
Circuit	Chip Size (tiles x tiles)	Gates Used	% Tile Usage	IO Locations Used	% IO Usage	Unoptimized Control Lines	Optimized Control Lines	% Control Line Reduction	Average Channel Length (px)	Channel Length Variation (px)
AND4	6x6	11	36.11	5	25.00	44	17	61.36	176	96
HALF ADDER	6x6	15	41.67	8	40.00	51	17	75	244	144
XOR3	7x7	26	53.06	11	45.83	90	29	67.78	219	120
8-3ENC	8x8	30	46.88	15	53.57	102	17	83.33	227	156

- Demonstrate Fluigi on all 2 input (Table 1) and 3 input (Table 2) boolean functions.
- Use of Fluigi reduces the number of control lines needed for both 2 input and 3 input benchmark circuits.
- Control line reduction most evident in larger chips, with chips size 6x6 or larger showing a minimum reduction of 50%.
- Demonstrate Fluigi on four sample circuits: half adder, 4 input AND gate, 3 input XOR gate, 8-3 encoder
- Output of Fluigi used both as a GUI for high level behavioral simulation and as a first approximation for photomask for chip fabrication

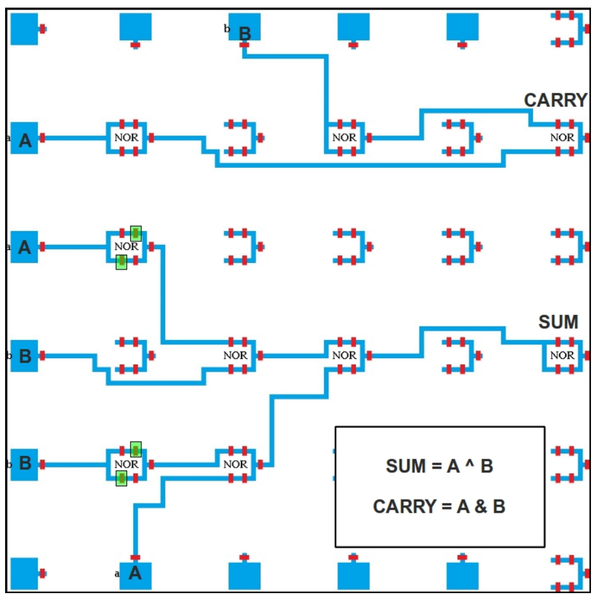
4 Input AND



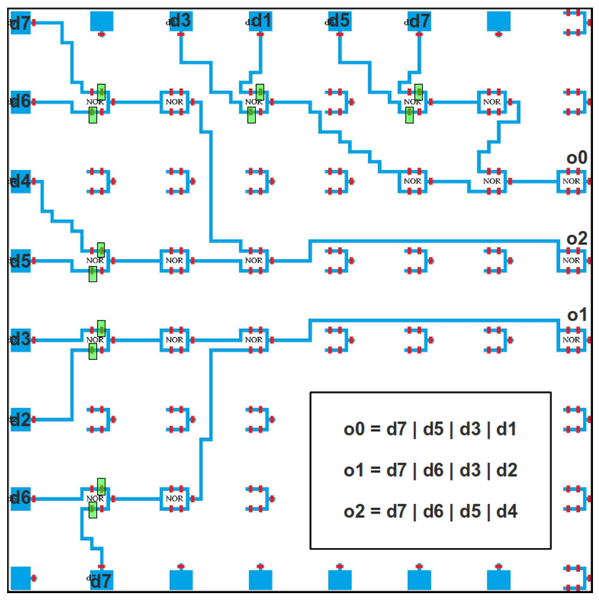
3 Input XOR



Half Adder



8-3 Encoder



DISCUSSION AND FUTURE WORK

- New paradigm for combining microfluidics, logic synthesis, physical design, and synthetic biology.
- New architecture for microfluidics based on the placement of genetic circuits in discrete chambers for computation
- Fluigi as a framework for a design flow going from a behavioral input file to a chip level behavioral simulation.
- Demonstrate Fluigi on all two and three input boolean functions as well as four specific example circuits.
- Next milestone is to fabricate a chip using the photomask generated by Fluigi and demonstrate control of the fluid flow through the generated control code.
- Future work includes optimization of the place and route algorithm to maximize chip utilization and further development of additional benchmark circuits for synthetic biology applications.
- The integration of microfluidics and synthetic biology has the capability to increase the scale of engineered biological systems for applications in cell-based therapeutics and biosensors, and produce new rapid prototyping platforms for the characterization of genetic devices.

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