CompSci 590 HW2

Molecular Assembly and Computation

(Question one through Question seven)

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Problem 1: Enzyme-based DNA Computing

Design a set of enzyme-based DNA logic gates (AND gate and OR gate) with emphasis on:

• (a) leak reduction, explain how you aim to design your gates to be leakless

Answer:

OR gate: An OR is a gate with two inputs and one output. It sets the output to 1 when there is a binary 1 in at least one of its inputs. Its true table is as follows:

INPUT A	INPUT B	OUTPUT
0	0	0
0	1	1
1	0	1
1	1	1

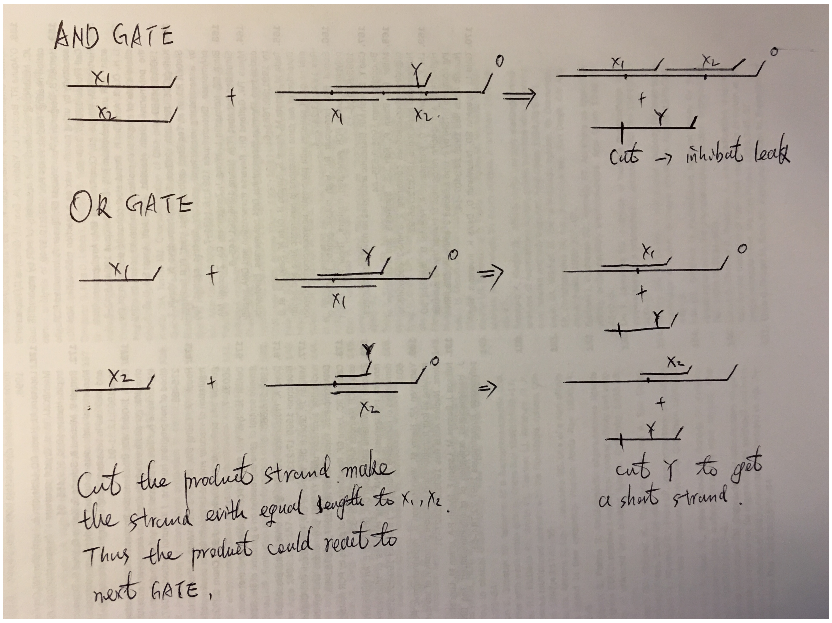
An example of OR gate

AND gate: An AND gate is a two input gate that only sets the output to 1 when both inputs are 1. The true table of this device is:

INPUT A	INPUT B	OUTPUT
0	0	0
0	1	0
1	0	0
1	1	1

An example of AND gate

LEAK: incorrect signal production.

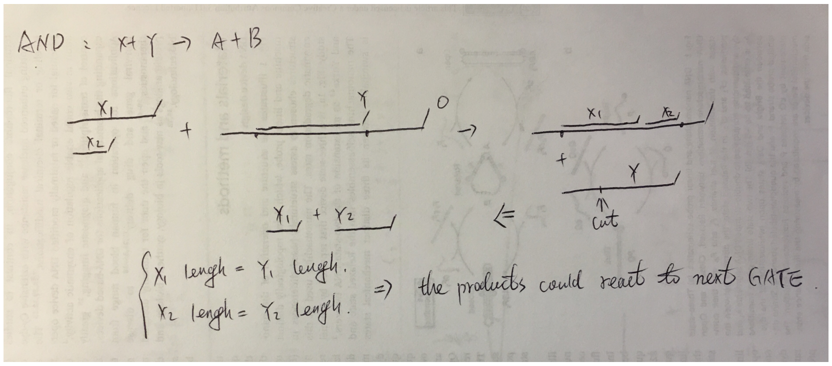


An implementation of X := AND(A, B) and X: =OR(A, B) with DNAzyme to cut the product strand

- (b) scalability which means that the gates should be able to work together as a circuit. You are allowed to use any enzyme.

Answer:
As shown in the previous figure, after cutting product stand Y into shorter strand, with the same length of input X1 and X2 strands, the product could react to next GATE. Also, since the reaction energy of Y strand to O stand is much less than the X1+X2 to O, so the reverse reaction could not happen, thus the leaking reaction is canceled.

When the output motifs from X;=AND(A, B) have equal length of the input A and B strands, then the reaction/computation could transfer to next step, which means the ourput X could be the reactant for next AND/OR gate, thus the logic gate could be able to work together as a circuit.
If we want $A + B -> X + Y$, we could revise the circulate in another way:



An example of $A + B- > X + Y$

As shown in this figure, the X1 and X2 are input strands, the Y is pre-product strand, cut it with DNAzyme, then we could get Y1 and Y2, with length of Y1 equal to X1, and length of Y2 equal to X2. in this way, the products could react with other GATE.

Cite:

1 Design of enzyme-interfaced DNA logic operations (AND, OR and INHIBIT) with an assaying application for single-base mismatch
2 Leakless DNA Strand Displacement Systems Fig 4 and Fig 5
3 Genetic Logic Gates and Flipping DNA, `http://www.nature.com/scitable/blog/bio2.0/genetic_logic_gates_and_flipping`
4 A simple DNA gate motif for synthesizing large-scale circuits

Problem 2: Enzyme-based DNA Computing

• (2a) Using class materials as well as literature search, find two different deoxyribozymes (DNAzymes) and describe in detail their properties. Using the DNAzymes you have chosen, construct a half-adder and a full-adder. Please cite all sources you have used to answer this question.

cite: `http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.87.1221&rep=rep1&type=pdf`

Answer:
Half-adder: A half adder gives an output consisting of two bits. One of them is the binary addition of the two inputs, in other words, the result of a XOR operation between the two bits. The other bit is the carry which can be implemented as the AND operation over the two inputs.

INPUT A	INPUT B	OUTPUT
0	0	0
0	1	1
1	0	1
1	1	0

An example of XOR gate

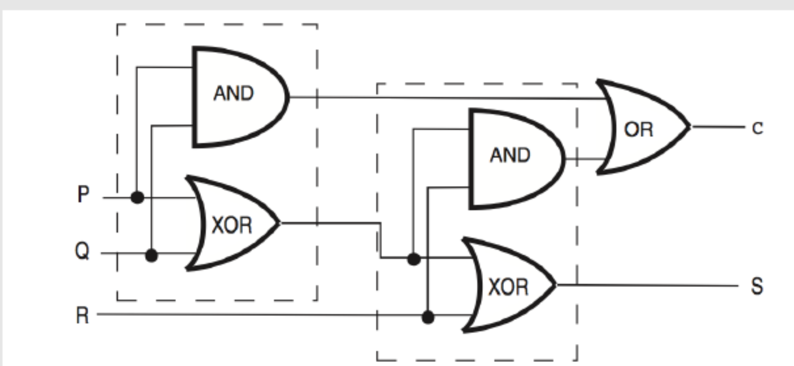
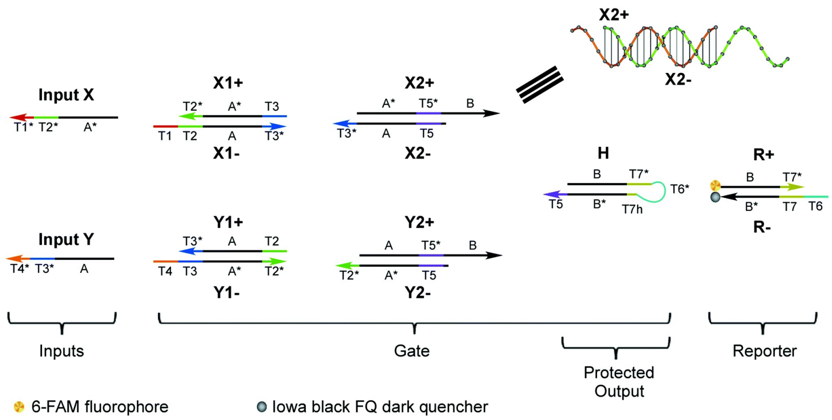


Figure 1. Full-Adder Digital Circuit implemented as two Half-Adders and joined by logical OR.

An example of two half adders sum to one full adder gate

Below is a DNA base half-adder:



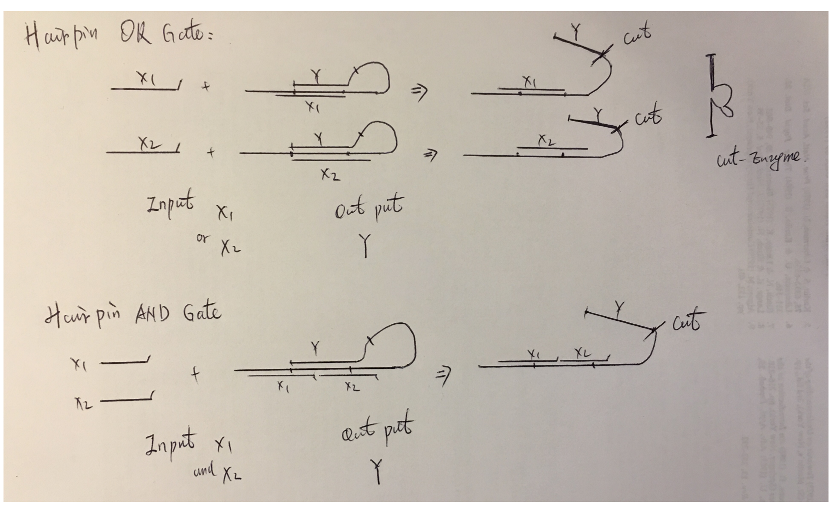
An example of half-adder gate)

Merge these two half adders together, we will get one full adder.

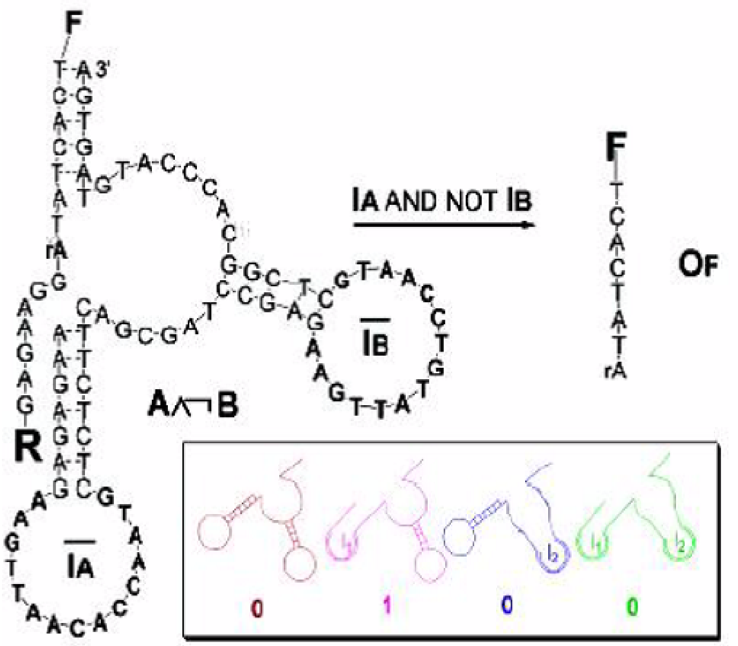
- (2b) Using class materials as well as literature search, construct hairpin-based OR, AND, and XOR gates. Describe an implementation of ripple-carry adder with the gates you have answered from the previous part. Please cite all sources you have used to answer this question.

Answer:

Ripple Carry Adder: A ripple carry adder is a digital circuit that produces the arithmetic sum of two binary numbers. It. can be constructed with full adders connected in cascaded (see section 2.1), with the carry output. from each full adder connected to the carry input of the next full adder in the chain.



An example of OR and AND gates with Hairpin structure



An example of XOR gates with Hairpin structure

Problem 3: Hybridization-based DNA Computing

- (3a) Read the article: `http://science.sciencemag.org/content/332/6034/1196` and write a paragraph of summary.

Answer:

Using a simple DNA reaction mechanism based on a reversible strand displacement process, we experimentally demonstrated several digital logic circuits, culminating in a four-bit square-root circuit that comprises 130 DNA strands. These multilayer circuits include thresholding and catalysis within every logical operation to perform digital signal restoration, which enables fast and reliable function in large circuits with roughly constant switching time and linear signal propagation delays. The design naturally incorporates other crucial elements for large-scale circuitry, such as general debugging tools, parallel circuit preparation, and an abstraction hierarchy supported by an automated circuit compiler.

- (3b) Design a DNA digital circuit to compute square roots for 2-bit numbers using seesaw gates.

- (3c) Simulate your circuit using LBS (Language for Biological Systems) in Visual GEC:

LBS (Language for Biological Systems): see `http://homepages.inf.ed.ac.uk/gdp/publications/Lang_Bio_Sys_Design_Spec.pdf`

Visual GEC: see `http://lepton.research.microsoft.com/webgec/`

Problem 4: (DNA-based Molecular Robotics)

- (4a) Every robotics system requires fuel to function. List the different types of fuel used currently in DNA robotic reactions and mention at least 3 examples (with references) for each.

- (4b) What role does concentration play in fueling robotic motion? Explain this for each of the different types of fuel.

- (4c) List 3 different ways of observing/reporting/confirming robotic motion (fluorescence, imaging, gel) and provide 3 examples (with references) on each.

- (4d) Summarize an example DNAzyne-based or hybridization based robotics demonstration from 2014 onwards, and argue why you consider it to be so.

Problem 5: Enzyme based DNA Robotics:

DNA Robotics is the study of designing DNA systems that can perform conformational changes/ display locomotion. In order to perform any change, energy is required. Let us take the example of a DNA walker - "A Unidirectional DNA Walker That Moves Autonomously along a Track" (See `https://users.cs.duke.edu/~reif/paper/harish/NanoRobotics/NanoRobotics.pdf` for an easier explanation of the article).

- (5a) What is the source of energy for this locomotion. Give the chemical reaction that is involved in this system that releases energy.

- (5b) Is this reaction reversible, i.e. can the walker move in the reverse direction?

- (5c) List all the enzymes involved in this particular walker, and the DNA recognition sequences that they cut.

- (5d) Currently this design is limited to 2 steps. Can this design be extended to 4 steps. If so, how? Will you need more enzymes?

Problem 6: DNAZyme based DNA Robotics:

- (6a) Read the article. Molecular robots guided by prescriptive landscapes.

- (6b) What is the difference between a DNAzyme and an enzyme. In one sentence.

- (6c) What is the source of energy for this locomotion. Give the chemical reaction that is involved in this system that releases energy.

- (6d) What type of molecule is cleaved by the DNAzyme?

Problem 7: DNA-based Molecular Robotics Design

- Design an arbitrary track, and a simple DNAzyme-based or hybridization-based DNA robotic system which can move along that track. You can use any sort of track. Submit the design to a simulation software (using NUPACK or canDo, for example, or both) with a simulation of two or more steps of locomotion, and provide the results of the simulation .