Junction 2014

Mathematical Insights in Computation

Molecular computation: RNA solutions to chess problems

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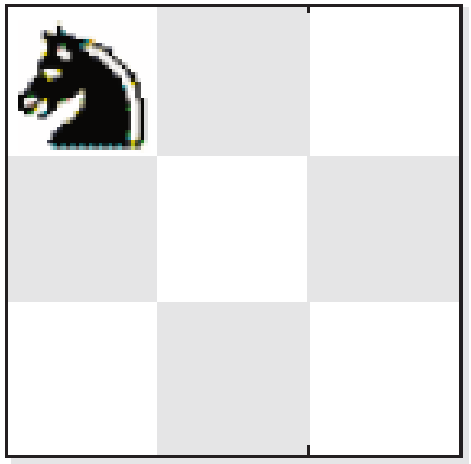
PNAS, February 15, 2000

The “Knight Problem”

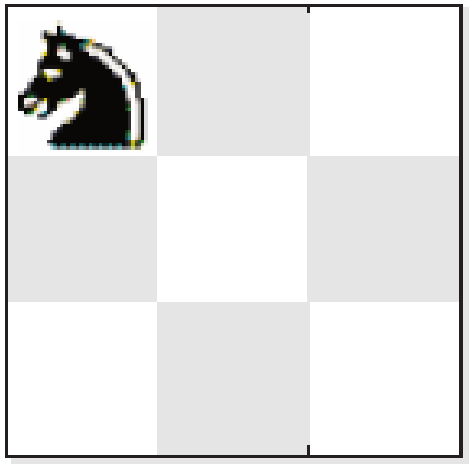
- Satisfiability problem
- How to arrange knights on $n \times n$ chessboard so that they cannot attack?



Overall Strategy

- Use bits to represent knight positions (a=1, b=0, c=0…)
- Use nucleic acid strands to mass-produce strings of bits
- Destroy all strings which don't satisfy the requirement:

((¬*h* & ¬*f*) or ¬*a*) & ((¬*g* & ¬*i*) or ¬*b*) & ((¬*d* & ¬*h*) or ¬*c*) & ((¬*c* & ¬*i*) or ¬*d*) & ((¬*a* & ¬*g*) or ¬*f*).



a	*b*	*c*
d	*e*	*f*
g	*h*	*i*

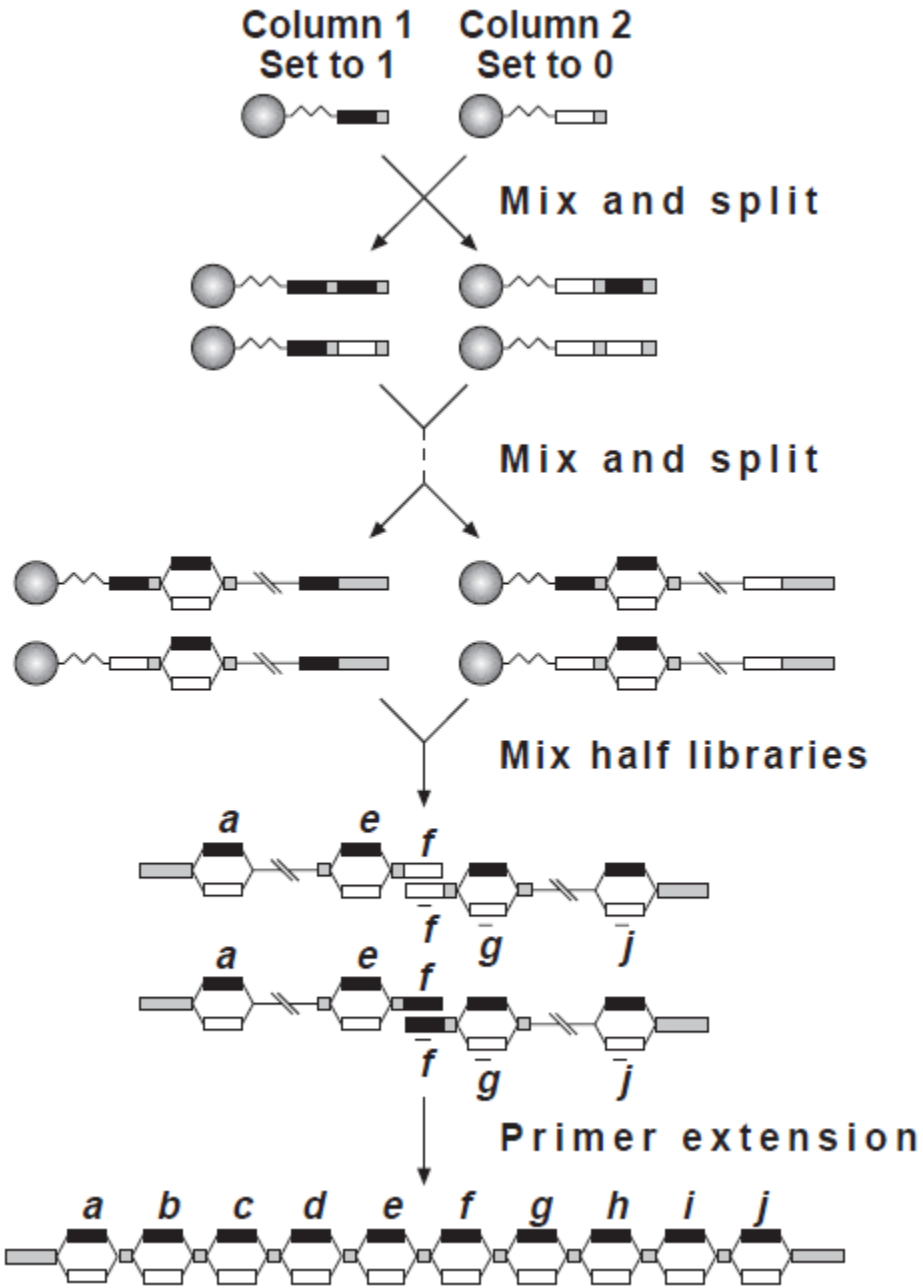
Setup

- Pick **DNA** sequences for all 10 bits (ignore j, the 10th)

Bit	Knight absent code, bit set to 0	Knight present code, bit set to 1
a	CTCTTACTCAATTCT	TCCTCACATTACTTA
b	CATATCAACATCTTA	ACTTCCTTTATATCC
c	ATCCTCCACTTCACA	TTATAACAAACATCC
d	TTAAAATCTTCCCTC	ACATAACCCTCTTCA
e	CTATTTATCCACACC	ACCTTACTTTCCATA
f	GCTTCAAACAATTCC	GTACATTCTCCCTAC
g	AACTCTCAAATTCAA	CATAATCTTATATTC
h	CTAACCTTTACTTCA	ATAATCACATACTTC
i	CATTCCTTATCCCAC	TCCACCAACTACCTA
j	CACCCTTTCTCCTCT	TTTTAAATTTCACAA

Setup

- Manufacture 10-bit **DNA** library
  - Synthesize, mix, split
  - 2^{10} strands
- Use in-vitro transcription to turn it into a **RNA** library



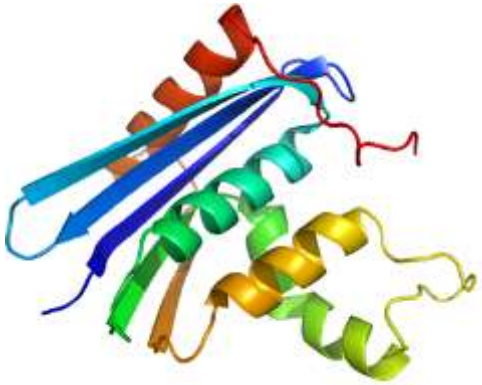
Setup

- Order short **DNA** which can selectively bind to to all possible bits: a_0, a_1, b_0, b_1, …

	Hybridizes to bit set to 0		Hybridizes to bit set to 1
a_0	AGAATTGAGTAAGAG	a_1	TAAGTAATGTGAGGA
b_0	gttatTAAGAGGTTGATATG	b_1	gttatGGATATAAAGGAAGT
c_0	TGTGAAGTGGAGGAT	c_1	GGATGTTTGTTATAA
d_0	gtaaaGAGGGAAGATTTTAA	d_1	gtaaaTGAAGAGGGTTATGT
e_0	GGTGTGGATAAATAG	e_1	TATGGAAAGTAAGGT
f_0	GGAATTGTTTGAAGC	f_1	GTAGGGAGAATGTAC
g_0	attgaTTGAATTTGAGAGTT	g_1	attgaGAATATAAGATTATG
h_0	TGAAGTAAAGGTTAG	h_1	GAAGTATGTGATTAT
i_0	GTGGGATAAGGAATG	i_1	TAGGTAGTTGGTGGA

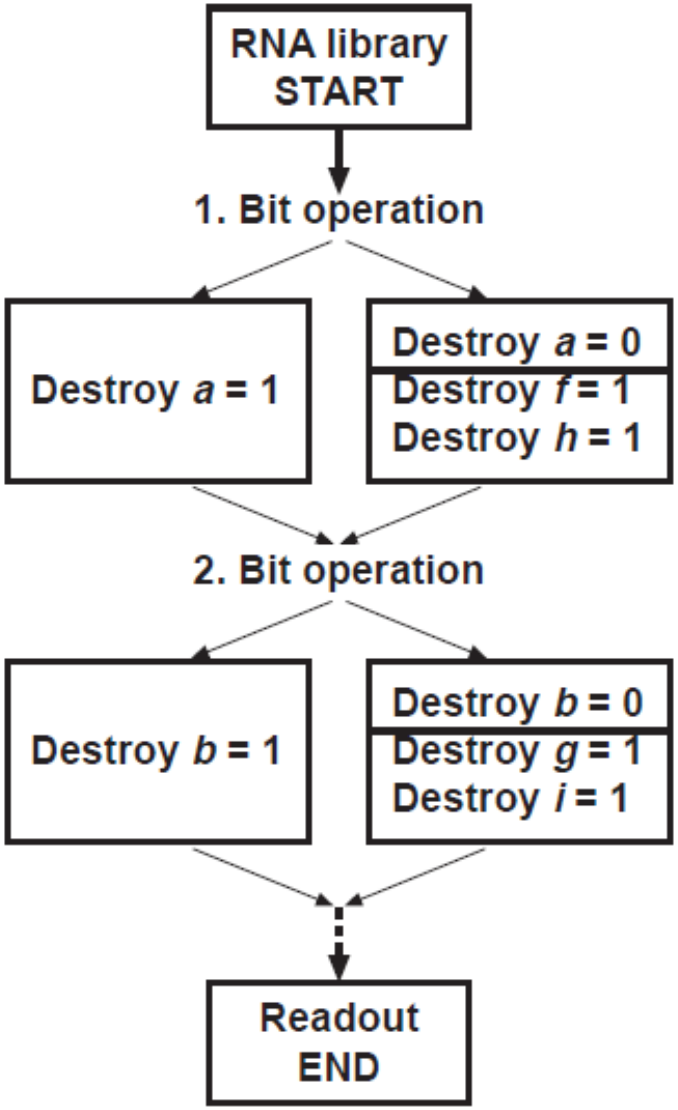
Boolean Operations

- Example: "$\neg a$"
  - Must destroy all RNA strands which contain sequence a_1 (5' UCCUCACAUUACUUA 3')
    - That is, *a* cannot be *true*
  - Add the short DNA strand which binds to a_1
    - (5' TAAGTAATGTGAGGA 3')
  - Add RNAse H
    - RNAse H destroys DNA/RNA complex (*must* be double-stranded)



Boolean Operations

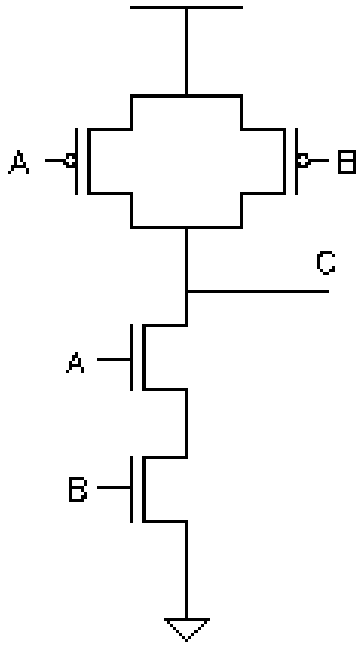
- Compute operations one by one
  - OR: split RNA library in two, perform each operation on half
  - AND: perform each operation in sequence



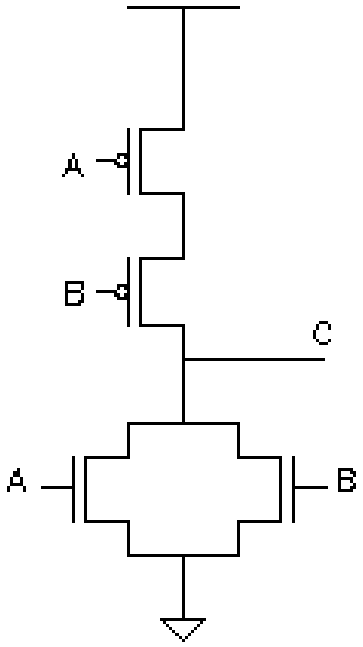
((¬*h* & ¬*f*) or ¬*a*) & ((¬*g* & ¬*i*) or ¬*b*) & ((¬*d* & ¬*h*) or ¬*c*) & ((¬*c* & ¬*i*) or ¬*d*) & ((¬*a* & ¬*g*) or ¬*f*).

Boolean Operations

- (Incidentally, there is a certain elegant symmetry between *sequential operations* and *parallel operations* that also shows up in electronic logic gates)



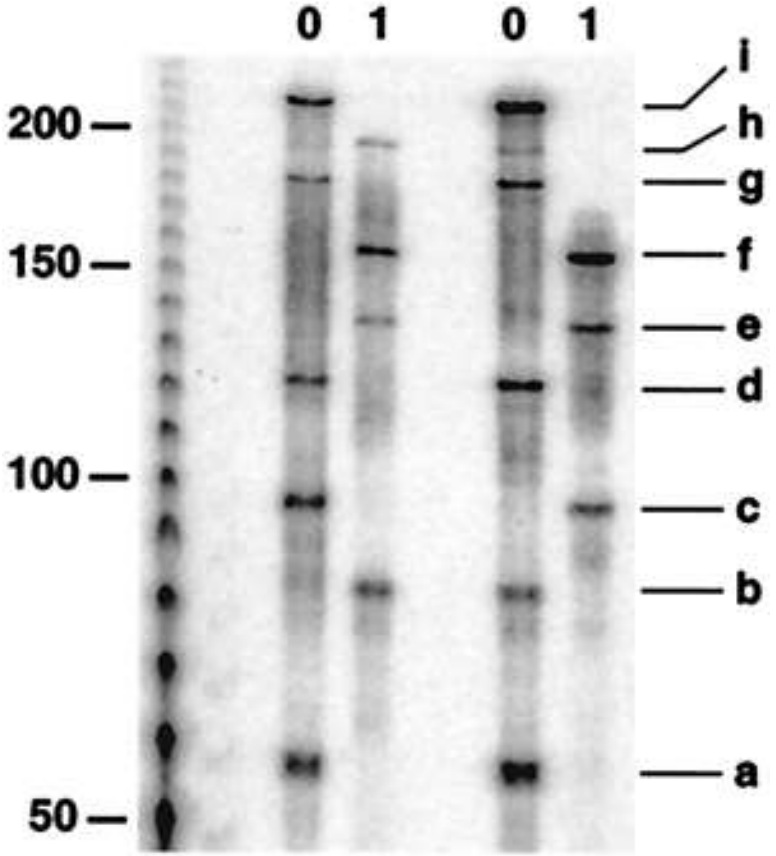
NAND



NOR

Results

- Read off results
  - Extra-clever PCR
    - Separate out only one type of strand
    - Separate out different bits
  - Gel electrophoresis
    - Bands present if bit present



Results

- 30 accurate, 1 inaccurate