DNA Microcomputing and the SAT Problem

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What Is DNA Microcomputing and Why Are We Interested In It?

- We are slowly approaching a point where computers will reach their maximum potential:
  - Moore's Law
Advantages of DNA Microcomputers

- **Supply of DNA**
- **DNA Size**
- **Higher Density**
- **More energy efficient**
  - DNA: $10^{19}$ operations / J
  - Supercomputer: $10^9$ ops / J
- **Calculations in parallel**
- **Greater potential speed**
  - DNA: $10^{14}$ operations per s
  - Supercomputer: $10^{12}$ ops per s
- **Possibility of computer in living cells**

The Mathematics Behind It

- **The Boolean satisfiability problem (SAT)**
  - Given an expression, is there some assignment of TRUE and FALSE values to the variables that will make the entire expression true?

- $p, p'$ (not $p$), $q, q', r, r'$ (3 variables)
- All possible combinations, $p\ q\ r'$, $p'\ q\ r$, etc.
- **Clauses:** $p$ OR $q$  
  Satisfies: $p\ q\ r$, $p\ q\ r'$, $p'\ q\ r$, $p\ q'\ r'$, $p'\ q'\ r'$, $p\ q'\ r$
- $p'$ OR $q$ OR $r'$  
  Satisfies: $p'\ q\ r$, $p'\ q\ r'$, $p\ q\ r$, $p\ q\ r'$
- $q'$ OR $r'$  
  Satisfies: $p'\ q\ r'$, $p\ q\ r'$
- $p'$ OR $r$  
  Satisfies: $p'\ q\ r'$
Basic Information To Keep In Mind

- DNA structure
- Restriction enzymes
- Methylases

How Methylation Works

<table>
<thead>
<tr>
<th>Restriction Enzyme</th>
<th>EcoRI Methylase</th>
<th>HindIII Methylase</th>
</tr>
</thead>
<tbody>
<tr>
<td>5'G A A T T H T C 3'</td>
<td>Cut</td>
<td>Cut</td>
</tr>
<tr>
<td>3' T T T C A G A A 5'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5' C T T C A G A A 3'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3' G A T T H T C 5'</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p (True) → p' (False)
Experimental Setup

- **Bluescript Plasmid DNA**

  - **Circular starting plasmid**
  - If restriction enzyme can cut
    - Then site is True
    - If can’t cut, then site is False

  ![Diagram of restriction enzymes and sites](image)

  - **HindIII**
  - **SmaI**
  - **BssHII**
  - **NotI**
  - **EcoRI**
  - **ClaI**

  **p** **p’** **q** **q’** **r** **r’**

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**Scheme for SAT Problem**

1. **First** perform pairs of methylation steps to create all logically consistent answers with lots of DNA.
2. **Second** Get rid of those DNAs that don’t satisfy the clauses by cutting.
3. **Third** detect whether there is an answer: Do we have any intact DNA?
4. **Fourth** Determine which variable assignments in the DNA by cutting DNA with various restriction enzymes.
Method

8 sites for REs \( p \ p' \ q \ q' \ r \ r' \ s \ s' \)

Methylase for site \( p \)  Methylase for site \( p' \)

\( m^p p' q q' r r' s s' \)

RE \( p \) can’t cut

\( n^p p' q q' r r' s s' \)

Logically consistent at \( p/p' \)

\( p^m p' q q' r r' s s' \)

RE \( p' \) can’t cut

\( n^p p' q q' r r' s s' \)

DNA Methylation partial success

Plasmid- detected at end by transformation of bacteria

So there is a solution!

What is nature of solution?

Cut DNA with each restriction enzyme

Only see product if enzyme did NOT cut

Product=enzyme is false

So \( p \) is False and
\( r \) is False, but
\( q \) is both True and False

We expected answer of FTF

Challenges- restriction enzymes not cut completely?

-also low level of final product
Challenges

- Efficiency
- Difficulty with amount of product obtained
- New methods of detection?

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