Outline: Feb 12

- Feedback from survey on Friday
- Python style and pair programming recap
- Continue: BWT and application to read mapping

Notes:
- Office hours today: 3-5pm
- Fill in partner form for Lab 4
Feedback from survey
Survey feedback: understand vs. confusing

- **Understand well:**
  - DBGs
  - overlap graphs
  - Eulerian walks
  - dynamic programming
  - global/local alignment
  - BWT process

- **Most confusing:**
  - BWT theory and read mapping
  - global vs. local alignment (many people)
  - dynamic programming
  - runtimes
  - Velvet & DBG failures/issues
  - graphing (?)
Survey feedback: in-class preferences

- Slides: less | more
- Board: less | more
- Group work: less | more
- Handouts: less | more
- Other: implementation discussion
Survey feedback: other

- **Office hours**: you can always make an appointment if you can’t make office hours (I am doing research off campus on Tuesdays)
- **Open door policy**: yes! You are welcome to come in if my door is open. If closed: on a deadline or skype research meeting
- **Labs**: command line input preferred over interactive
- **Piazza**: more student answers and discussion would be great
- **Lecture recording**:... maybe a future semester!
- **Slides before class**:... not usually!
Notes about pair programming
+
Python style
Pair programming

- Make font sizes A LOT larger (editor and terminal)

- Face machine toward both partners

- Work together on the assignment as much as possible

- Try to attend office hours together if possible (or make an appointment)

- Share lab feedback with your partner
Python style

- More comments
- More line breaks
- More function/method headers

- Avoid while True
- Avoid global variables
- Avoid long lines
- Avoid long main

```python
START_CODON = 'ATG'
STOP_CODONS = ['TAG', 'TGA', 'TAA']

def read_fasta(filename):
    """Read a fasta file to produce a single strand of DNA.
    Parameters: input filename (string)
    Return: DNA object
    """
    fasta_file = open(filename, 'r')
    fasta_file.readline() # header
    strand = ""
    for line in fasta_file:
        strand += line.strip()
    fasta_file.close()
    return DNA(strand)
```
Big picture – people asked:

- How do people come up with these algorithms?

- Where is this all going?
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  - Understand and re-implement existing algorithms from the literature
  - Apply to many different problems and edge cases
  - Find areas of improvement (runtime, accuracy, ease of use, etc)

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First part of the semester
(up through week 4):
*Algorithms for “getting the data”*

Beginning next week:
*Algorithms for “learning from the data”*
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First part of the semester (up through week 4):
Algorithms for “getting the data”

Beginning next week:
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- DNA sequencing
- Genome assembly
- Sequence alignment
- Read mapping
- Variant calling
Big picture – people asked:

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  - Understand and re-implement existing algorithms from the literature
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- **Where is this all going?**

  First part of the semester (up through week 4):
  *Algorithms for “getting the data”*
  - DNA sequencing
  - Genome assembly
  - Sequence alignment
  - Read mapping
  - Variant calling

  Beginning next week: *Algorithms for “learning from the data”*
  - Phylogenetic trees (speciation)
  - Ancestral genome reconstruction
  - Evolutionary history (natural selection, migration, admixture)
  - Genomic diversity visualization and interpretation
  - Cancer genetics
  - Disease-gene mapping
  - Pre-natal genetic testing
Global vs. Local Alignment
Example of local alignment picking up on small regions of high similarity
Example of local alignment picking up on small regions of high similarity
Example of local alignment picking up on small regions of high similarity

Max score: 57
Example of a poor global alignment

Global alignment forces the alignment to start at the lower right and end at the upper left (i.e. using each entire sequence)
Recap BWT
Goal: read mapping

- In read mapping, \( y = \text{entire genome} \) and \( x = \text{single read} \), and we want to know the position of the read.

- Dynamic programming approaches to alignment were designed for the case when \( \text{len}(x) \sim \text{len}(y) \) and \( x \) and \( y \) are potentially quite different.

- In read mapping, not only are the lengths extremely different, but we are aligning many \( x \)'s to the same \( y \), with high similarity between \( x \) and \( y \).

- Can we do better than \( O(GLn) \)? Where \( G = \text{len}(\text{genome}) \), \( L = \text{len}(\text{read}) \), \( n = \text{number of reads} \)
BWT

Reversible permutation of the characters of a string, used originally for compression

S

abaaba$

All cyclic permutations

Sort

Burrows-Wheeler Matrix

$ a b a a b a
a$ a b a a b
a a b a$ a b
ab a$ a b a
b a$ a b a
b a a b a$

Last column

abba$aa

BW(S)
<table>
<thead>
<tr>
<th>final char</th>
<th>sorted rotations</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>n to decompress. It achieves compression</td>
</tr>
<tr>
<td>o</td>
<td>n to perform only comparisons to a depth</td>
</tr>
<tr>
<td>o</td>
<td>n transformation} This section describes</td>
</tr>
<tr>
<td>o</td>
<td>n transformation} We use the example and</td>
</tr>
<tr>
<td>a</td>
<td>n treats the right-hand side as the most</td>
</tr>
<tr>
<td>a</td>
<td>n tree for each 16 kbyte input block, enc</td>
</tr>
<tr>
<td>a</td>
<td>n tree in the output stream, then encodes</td>
</tr>
<tr>
<td>i</td>
<td>n turn, set $L[i]$ to be the</td>
</tr>
<tr>
<td>i</td>
<td>n turn, set $R[i]$ to the</td>
</tr>
<tr>
<td>o</td>
<td>n unusual data. Like the algorithm of Man</td>
</tr>
<tr>
<td>a</td>
<td>n use a single set of probabilities table</td>
</tr>
<tr>
<td>e</td>
<td>n using the positions of the suffixes in</td>
</tr>
<tr>
<td>i</td>
<td>n value at a given point in the vector $R$</td>
</tr>
<tr>
<td>e</td>
<td>n we present modifications that improve t</td>
</tr>
<tr>
<td>e</td>
<td>n when the block size is quite large. Ho</td>
</tr>
<tr>
<td>i</td>
<td>n which codes that have not been seen in</td>
</tr>
<tr>
<td>i</td>
<td>n with $ch$ appear in the {\em same order</td>
</tr>
<tr>
<td>i</td>
<td>n with $ch$. In our exam</td>
</tr>
<tr>
<td>o</td>
<td>n with Huffman or arithmetic coding. Bri</td>
</tr>
<tr>
<td>o</td>
<td>n with figures given by Bell\cite{bell}.</td>
</tr>
</tbody>
</table>

Figure 1: Example of sorted rotations. Twenty consecutive rotations from the sorted list of rotations of a version of this paper are shown, together with the final character of each rotation.
<table>
<thead>
<tr>
<th>i</th>
<th>Sorted suffixes</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>a$</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>an$</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>ana$</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>banana$</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>na$</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>nana$</td>
<td>1</td>
</tr>
</tbody>
</table>

BWT: $ S = \text{banana}$

Suffix array:

1. 7
2. 6
3. 5
4. 4
5. 3
6. 2
FM-Index

Ferragina et al. (2000)

Example: \( S = \text{abaaba} \)$ (genome)

\( P = \text{aba} \) (read)

1. Start at end of pattern
2. Recurse!
Output
- indices of pattern in E column
- return: [4-5] inclusive

Want: return 1-4
- (Original string indices)

Problem: Scanning is slow

# of b's went from 0 to 2 → must be b1 + b2

Example:

<table>
<thead>
<tr>
<th>c</th>
<th>M(c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$</td>
<td>1</td>
</tr>
<tr>
<td>a</td>
<td>2</td>
</tr>
<tr>
<td>b</td>
<td>3</td>
</tr>
</tbody>
</table>

Store instead of E

Pattern: ...bc