Genome 540 Discussion

January 11th, 2024

Clifford Rostomily

Genome Sciences
UNIVERSITY OF WASHINGTON

Logistical stuff

- Come talk to me after class for a slack invite if you are not registered but plan on registering
- When complete, email your homework to Phil and me

Agenda

- Assignment 1
- Burrows Wheeler
- Assignment 2
- C++ tips

Assignment #1

How do I look up the longest match?

- .gff file
  - General Feature Format
  - Each row is a feature, each column is info about the feature (e.g. position, name, ...)
  - Similar to a .bed file but specified for sequences
  - Either intersect it with the position of your sequence using bed tools, or scroll to the correct position
- Nucleotide BLAST
  - Link
  - Enter sequence, select organism, and hit BLAST

How do I define match length?

-
- Three pointers to suffixes
  - p14: AAAGGGGG (from seq2)
  - p10: ATAGGGGG (from seq1)
  - p11: ATCCCCC (from seq 2)
- What is the match length, and to what sequence (above or below)?

Small Example

Steps:

Seq. 1: TCAA

Seq. 2: ACTG

Seq. 2: CAGT (reverse complement)

Pointer array to suffixes

p1: TCAA
p2: CAA
p3: AA
p4: A
p5: ACTG
p6: CTG
p7: TG
p8: G
p9: CAGT
p10: AGT
p11: GT
p12: T

Sorted

A
AA
AGT
AATG
CAA
CAGT
CTG
G
GT
T
TCAA
TG

Iterate through sorted list

- find the longest match to seq1
- make a histogram of seq1 longest matches

Things to consider:

- Multiple seq1 suffixes in a row
- Need to look above and below to find longest match

Match Lengths:
1: 3
2: 1

The longest match length: 2
Number of match strings: 1

Other questions on Assignment 1?

- Read in two fasta files
  - Track # non-alpha characters
  - Also track base counts
- Combine the 3 sequences and store suffixes as an array/vector
  - Forward of seq1, forward and reverse complement of seq2 = 3
- Implement and run the suffix array algorithm
  - Returns a sorted list of pointers
- Iterate through results
  - Track longest match length of each seq1 suffix to either the forward or reverse strand of seq2
  - Track the longest overall match

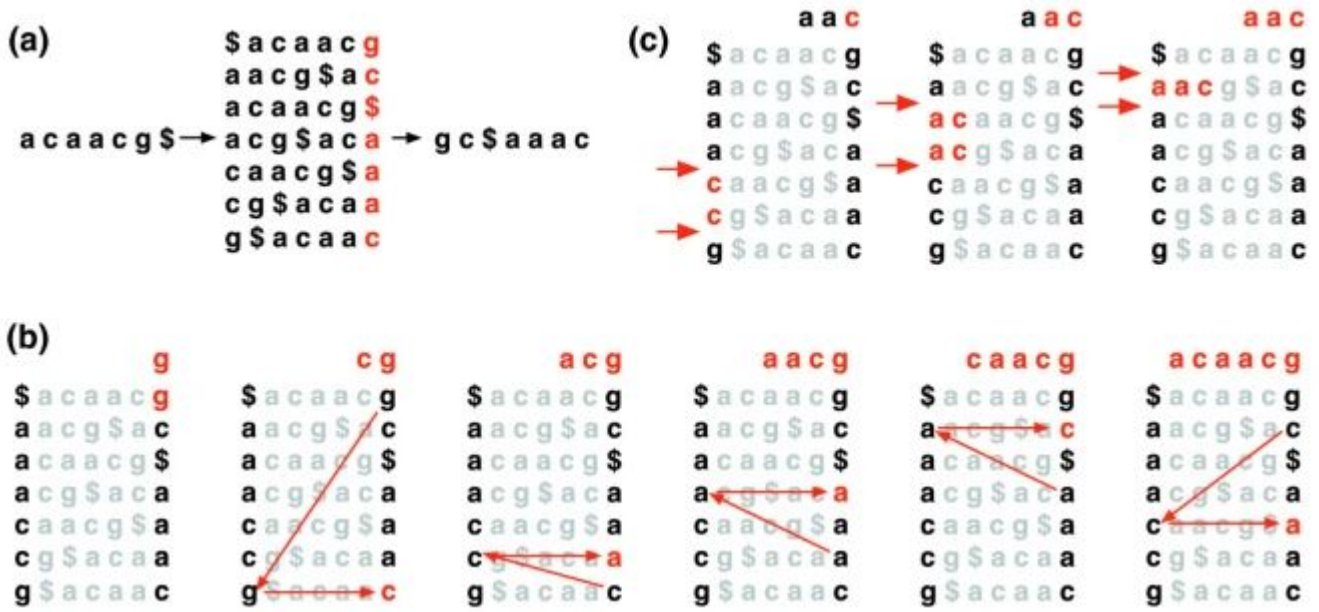
Burrows Wheeler

The Burrows Wheeler Transform

Transformation				
1. Input	2. All rotations	3. Sort into lexical order	4. Take the last column	5. Output
^BANANA$	^BANANA$ $^BANANA A$^BANAN NA$^BANA ANA$^BAN NANA$^BA ANANA$^B BANANA$^	ANANA$^B ANA$^BAN A$^BANAN BANANA$^ NANA$^BA NA$^BANA ^BANANA$ $^BANANA	ANANA$^B ANA$^BAN A$^BANAN BANANA$^ NANA$^BA NA$^BANA ^BANANA$ $^BANANA	BNN^AA$A

- Used originally for compression
- The Bowtie aligner uses it for compression and indexing

Bowtie



Langmead, **Trapnell**, Pop, Salzberg (2009) Genome Biology

Assignment #2

Part 1 - Write a program

- The program should:
  - Read in a fasta file
  - Determine the frequencies of the nucleotides and dinucleotides (based on the forward strand) and the length of the sequence
  - Generate 3 sequences of the same length as the input file using:
    - the length (equal frequency assumption)
    - nucleotide frequency (order 0-Markov)
    - dinucleotide frequency (order 1-Markov)
  - Save these sequences as fasta files

Part 2 - Simulate Sequences

- Using your program simulate 3 sequences from the mouse genomic region in HW1 using:
  - An equal frequency assumption
  - An order-0 Markov model
  - An order-1 Markov model
- Output sequences should be the same length as the input
- Store the sequences as fasta files

Part 3 - Run your HW1 on those seqs.

- Run your program from HW1 on each of those sequences
  - Sequence 1 should always be the 10Mb mouse region from HW1,
  - Sequence 2 should be your simulated sequence

C++ tips

Random numbers using rand()

- rand() is the base random number generator
- It generates numbers from 0 to RAND_MAX
- It can be bounded using the modulus operation (%)
- The standard <random> library was added in C++11 to offer other generators with better randomness
- A seed can be set with srand

```
// ------------------------------------------------------------
// generate random numbers using rand()
// rand() is the old C++ random number generator
// it works well if you aren't too picky about the distribution
// it generates numbers from 0 to RAND_MAX

// generate numbers from 0 to RAND_MAX
std::cout << "RAND_MAX = " << RAND_MAX << "\n";
std::cout << "using rand(): ";
for (int i = 0; i < 5; i++){
    std::cout << rand() << " ";
}
std::cout << "\n";

// To bound rand() to a specific range, use the modulus operator (%)
// This will give you a random number from 0 to 3
std::cout << "using rand() % 4: ";
for (int i = 0; i < 5; i++){
    std::cout << rand() % 4 << " ";
}
std::cout << "\n";
```

Random numbers using <random>

- If using random_device be sure to #include <random>
- <random> offers a number of random number generator functions with different speed/randomness tradeoffs

```
// ------------------------------------------------------------
// generate random numbers using random_device
// random_device is a C++11 random number generator
// it offers a number of different generators and distributions
// here we use the mt19937 generator and the uniform_int_distribution

// generate a random integer from 0-3
int seed = 1;
std::mt19937 gen(seed);
std::random_device rd;

int min = 0;
int max = 3;
std::uniform_int_distribution<> dist(min, max);

std::cout << "using uniform_int_distribution: ";
for (int i = 0; i < 5; i++){
    std::cout << dist(gen) << " ";
}
std::cout << "\n";
```

See you next week!

- HW1 due this Sunday, 11:59pm
- Please have your name in the filename of your homework assignment