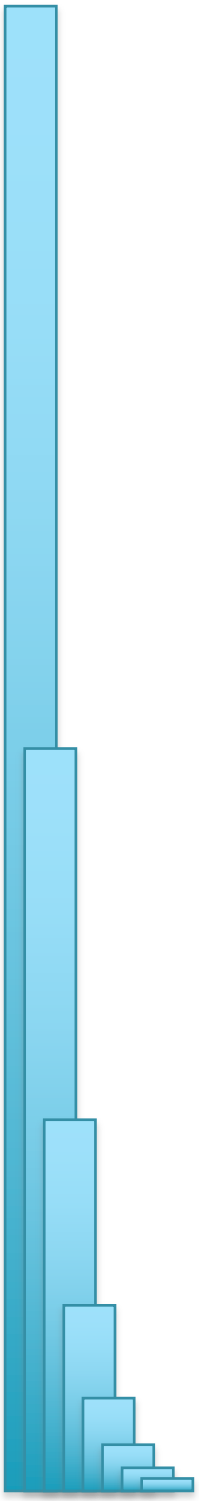
CS 600.226: Data Structures

Michael Schatz

Nov 16 2018

Lecture 33: BWT + Assembly



Assignment 8: Competitive Spelling Bee

Out on: November 9, 2018

Due by: November 16, 2018 before 10:00 pm

Collaboration: None

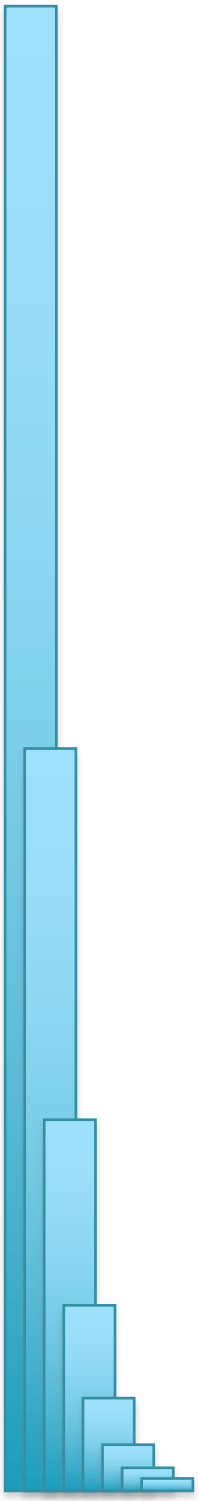
Grading:

- Packaging 10%,
- Style 10% (where applicable),
- Testing 10% (where applicable),
- Performance 30% (where applicable),
- Functionality 40% (where applicable)

Overview

Your "one" task for this assignment is to take the simple spell checker we give you and to turn it into the fastest, most memory-efficient spell checker in the course, subject to the constraints detailed below. You are expected to do this by (once again) implementing the Map interface, this time using one of several hash table techniques (your choice, see below).

Remember: javac –Xlint:all & checkstyle *.java & Junit & Jaybee BenchMarks



Assignment 9: StringOmics

Out on: November 16, 2018

Due by: November 30, 2018 before 10:00 pm

Collaboration: None

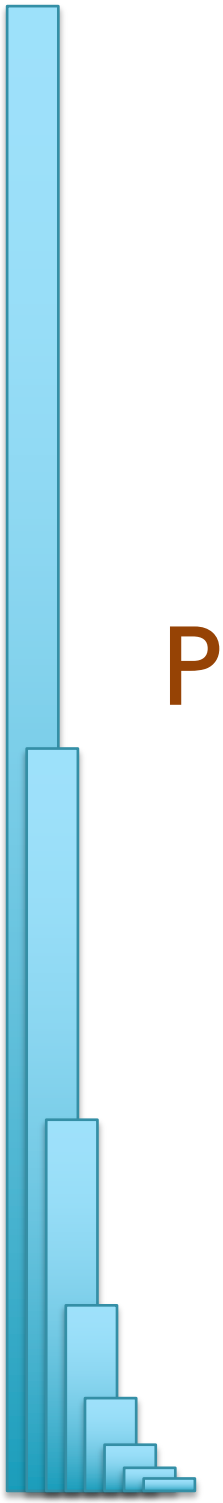
Grading:

- Packaging 10%,
- Style 10% (where applicable),
- Testing 10% (where applicable),
- Performance 10% (where applicable),
- Functionality 60% (where applicable)

Overview

The ninth assignment focuses on data structures and operations on strings. In this assignment you will implement encoding and decoding using the Burrows Wheeler Transform as well as encoding and decoding in a simple form of run length encoding. In the final problem you will be asked to measure the space savings using run length encoding with and without applying the Burrows Wheeler Transform first.

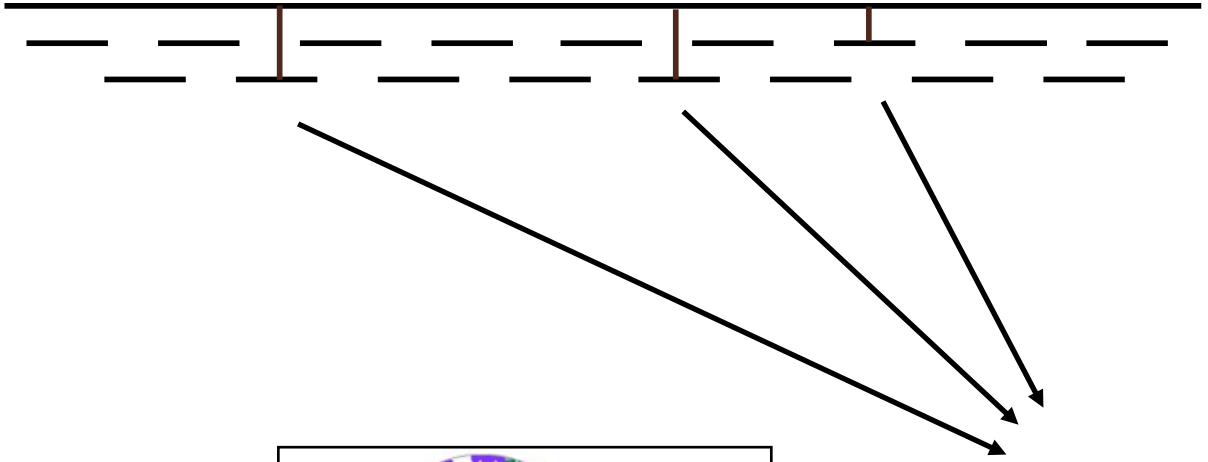
Remember: javac –Xlint:all & checkstyle *.java & Junit (No JayBee)

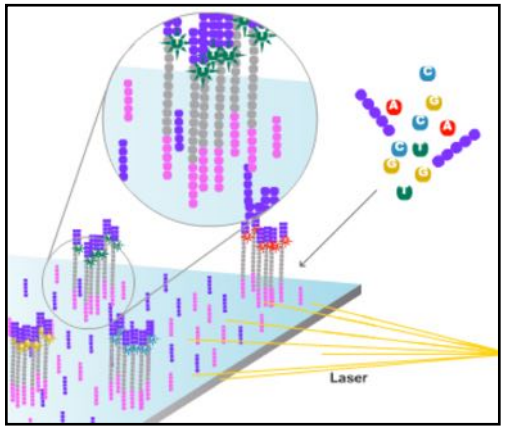


Part 1: Burrows Wheeler Transform

Personal Genomics

How does your genome compare to the reference?





Heart Disease

Cancer

Presidential smile

Exact Matching Review & Overview

Where is GATTACA in the human genome?

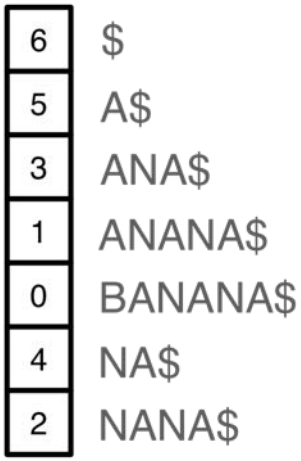
Brute Force (3 GB)

```
BANANA
BAN
  ANA
    NAN
      ANA
```

O(m * n)

Slow & Easy

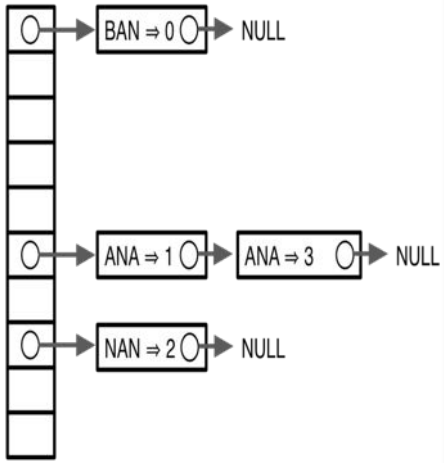
Suffix Array (>15 GB)



O(m + lg n)

Full-text index

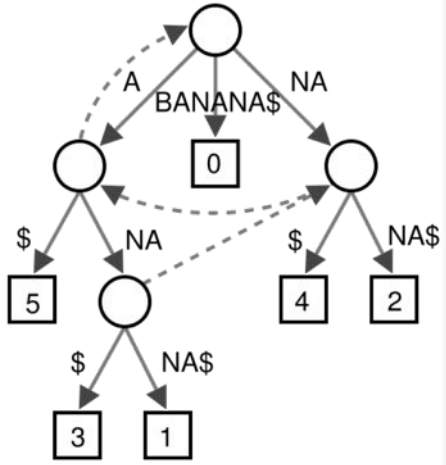
Hash Table (>15 GB)



O(1)

Fixed-length lookup

Suffix Tree (>51 GB)



O(m)

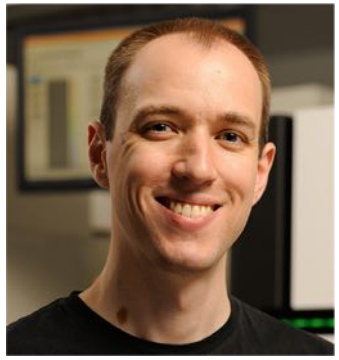
Full-text, but bulky

*** These are general techniques applicable to any text search problem ***

Algorithmic challenge

How can we combine the speed of a suffix array O(m + lg(n)) (or even O(m)) with the size of a brute force analysis (n bytes)?

What would such an index look like?

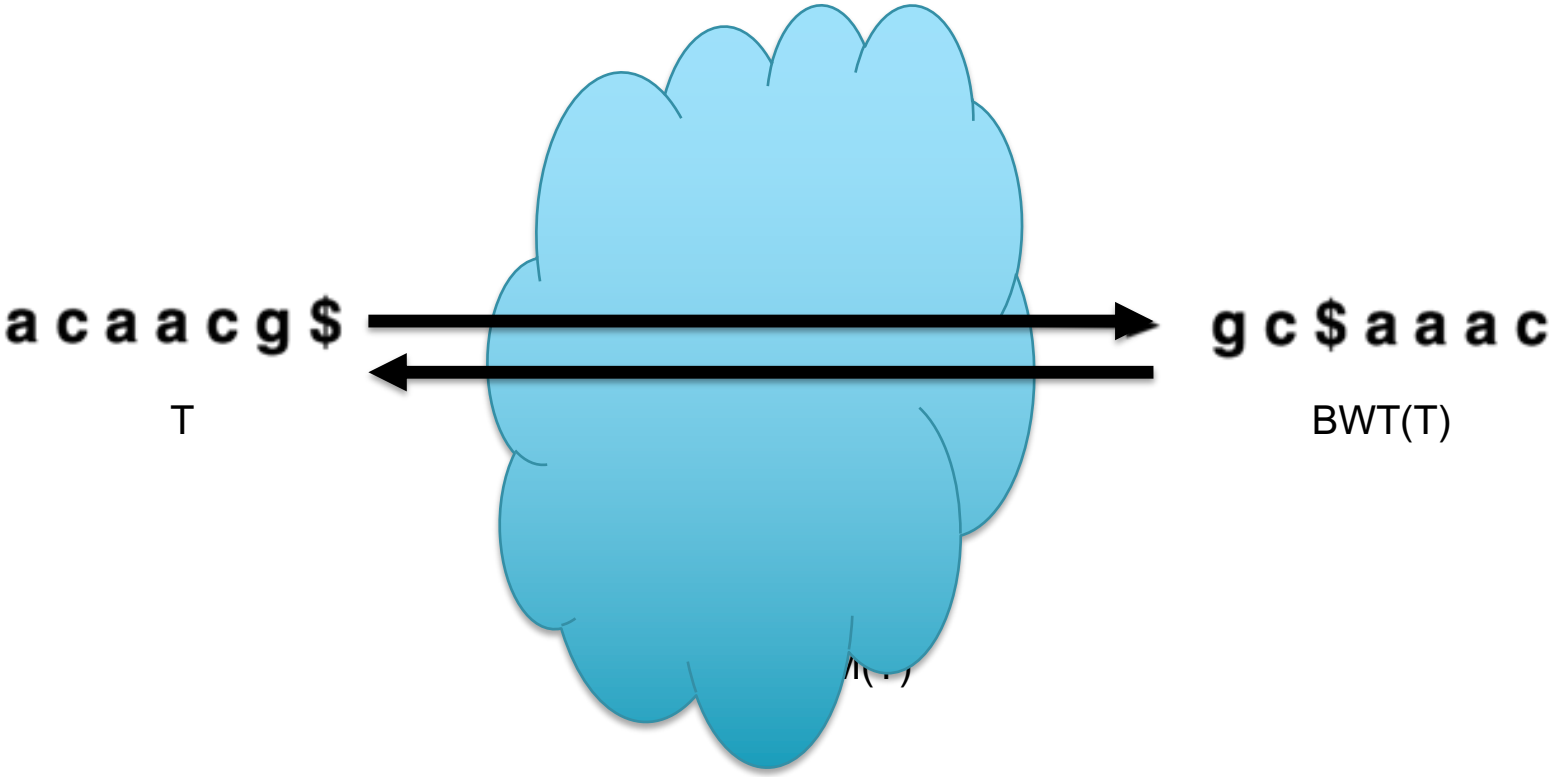


Bowtie: Ultrafast and memory efficient alignment of short DNA sequences to the human genome

Slides Courtesy of Ben Langmead

Burrows-Wheeler Transform

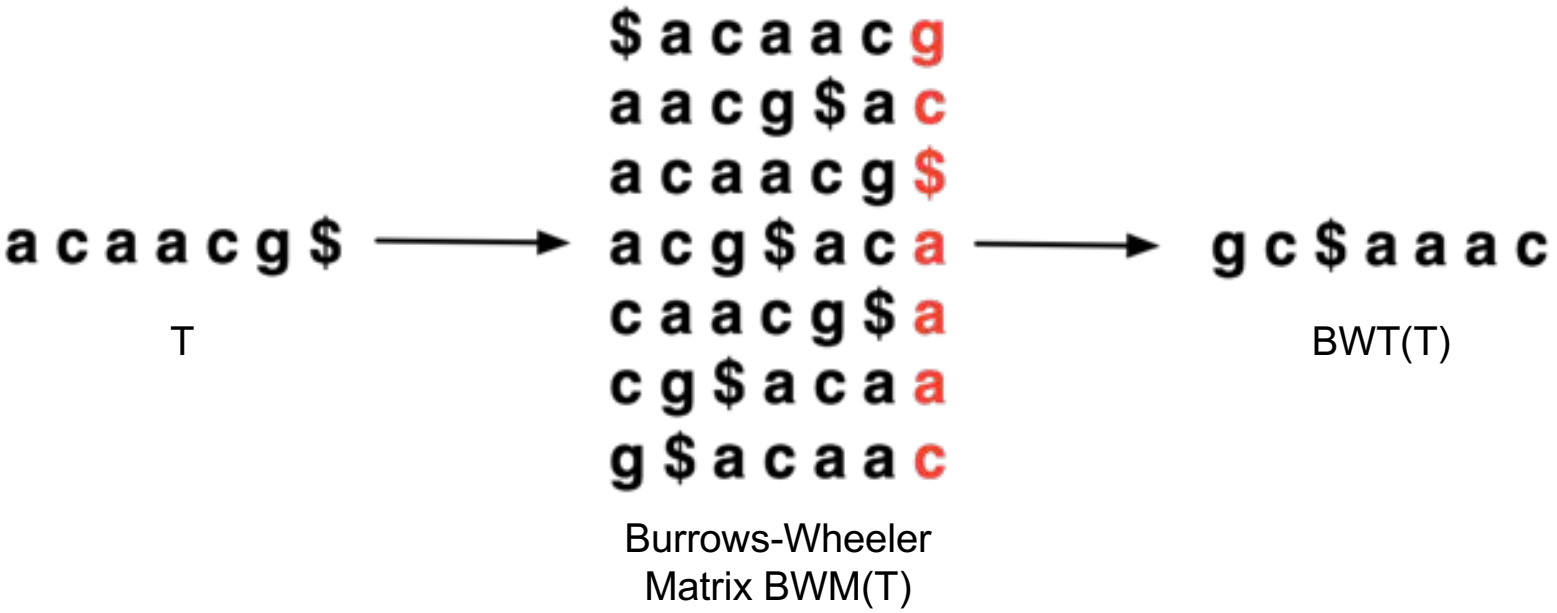
- Reversible permutation of the characters in a text



A block sorting lossless data compression algorithm.
Burrows M, Wheeler DJ (1994) *Digital Equipment Corporation.* Technical Report 124

Burrows-Wheeler Transform

- Permutation of the characters in a text

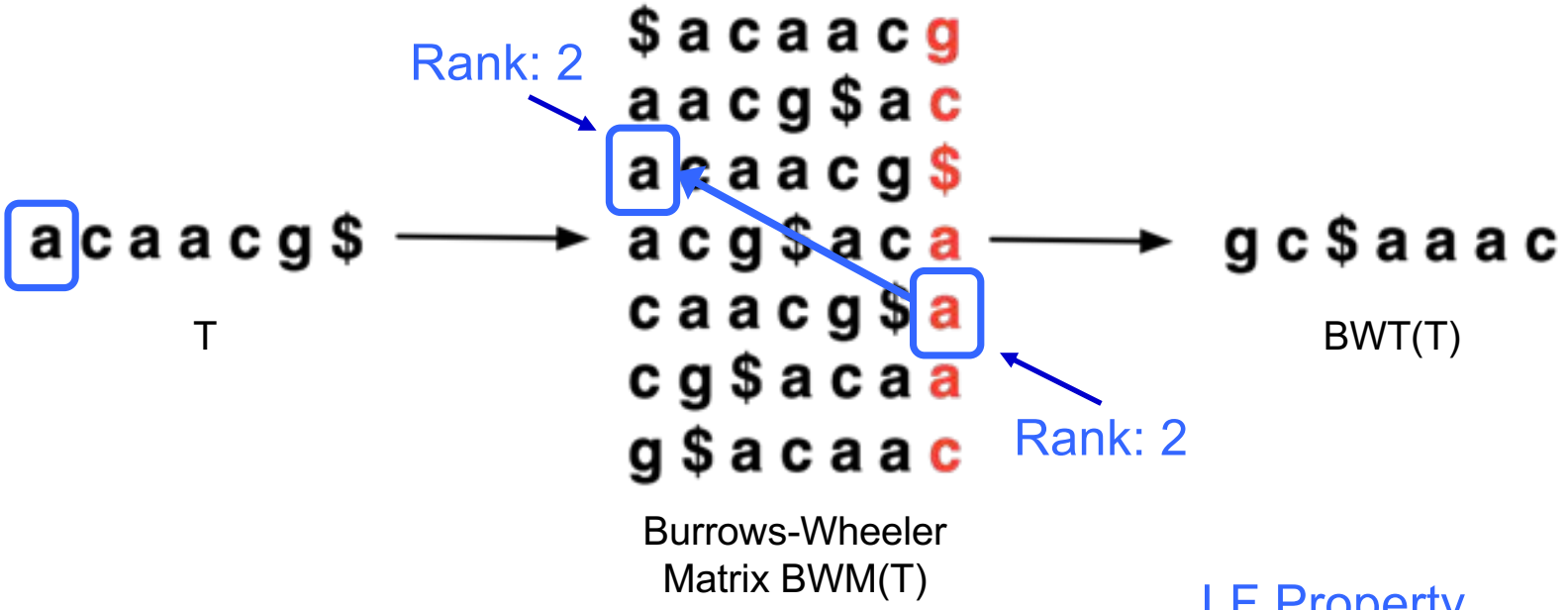


- BWT(T) is the index for T

A block sorting lossless data compression algorithm.
Burrows M, Wheeler DJ (1994) *Digital Equipment Corporation.* Technical Report 124

Burrows-Wheeler Transform

- Reversible permutation of the characters in a text



LF Property implicitly encodes Suffix Array

- BWT(T) is the index for T

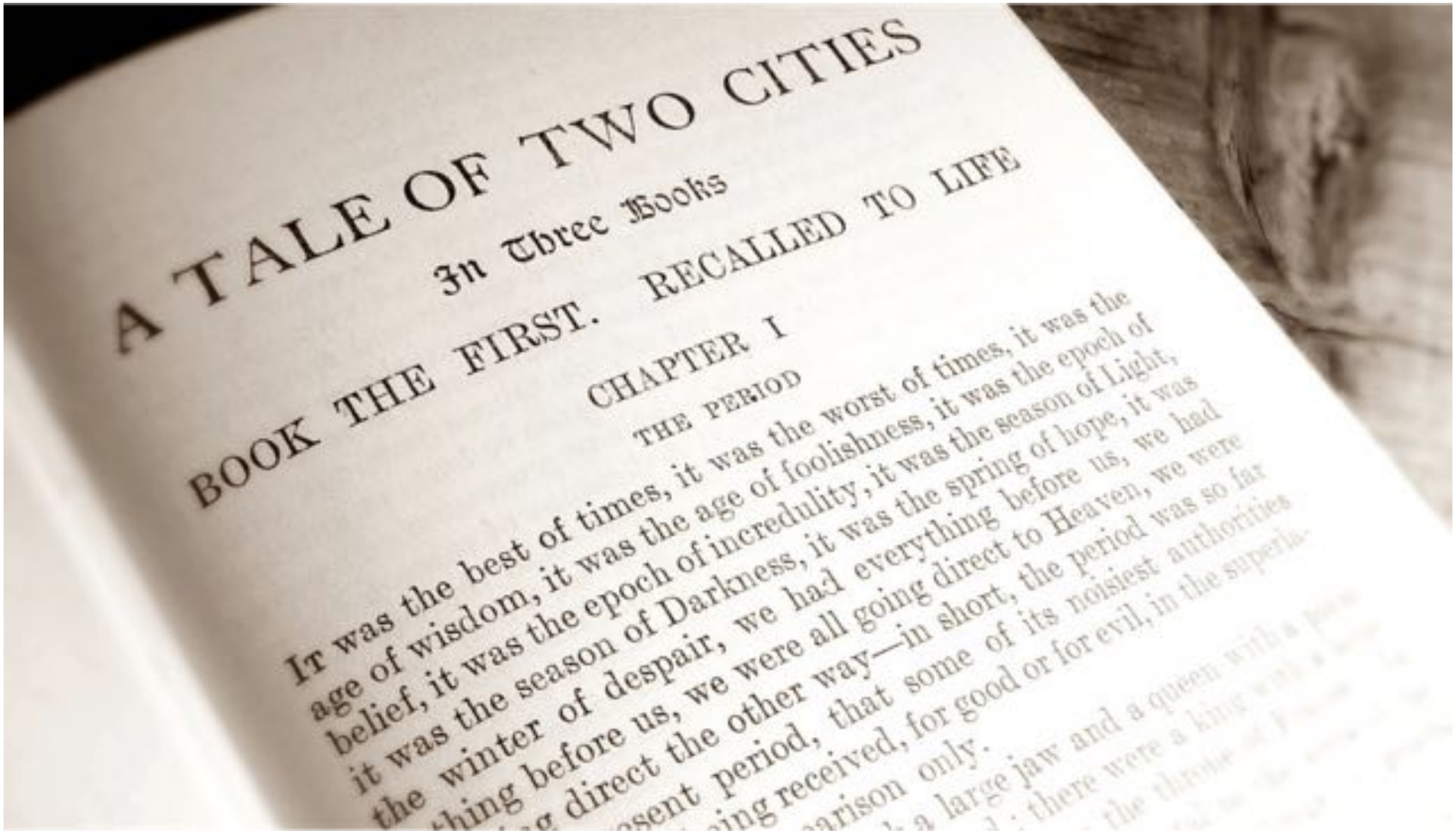
A block sorting lossless data compression algorithm.
Burrows M, Wheeler DJ (1994) *Digital Equipment Corporation.* Technical Report 124

Burrows-Wheeler Transform

- Recreating T from BWT(T)
  - Start in the first row and apply **LF** repeatedly, accumulating predecessors along the way

[Decode this BWT string: ACTGA$TTA]

Run Length Encoding



Run Length Encoding

ref[614]:

```
It_was_the_best_of_times,_it_was_the_worst_of_times,_it_was_the_age_
of_wisdom,_it_was_the_age_of_foolishness,_it_was_the_epoch_of_belief
,_it_was_the_epoch_of_incredulity,_it_was_the_season_of_Light,_it_wa
s_the_season_of_Darkness,_it_was_the_spring_of_hope,_it_was_the_wint
er_of_despair,_we_had_everything_before_us,_we_had_nothing_before_us
,_we_were_all_going_direct_to_Heaven,_we_were_all_going_direct_the_o
ther_way_-_in_short,_the_period_was_so_far_like_the_present_period,_
that_some_of_its_noisiest_authorities_insisted_on_its_being_received
,_for_good_or_for_evil,_in_the_superlative_degree_of_comparison_only.$
```

rle(ref)[614]:

```
It_was_the_best_of_times,_it_was_the_worst_of_times,_it_was_the_age_
of_wisdom,_it_was_the_age_of_fo2lishnes2,_it_was_the_epoch_of_belief
,_it_was_the_epoch_of_incredulity,_it_was_the_season_of_Light,_it_wa
s_the_season_of_Darknes2,_it_was_the_spring_of_hope,_it_was_the_wint
er_of_despair,_we_had_everything_before_us,_we_had_nothing_before_us
,_we_were_al2_going_direct_to_Heaven,_we_were_al2_going_direct_the_o
ther_way_-_in_short,_the_period_was_so_far_like_the_present_period,_
that_some_of_its_noisiest_authorities_insisted_on_its_being_received
,_for_go2d_or_for_evil,_in_the_superlative_degre2_of_comparison_only.$
```

Run Length Encoding

ref[614]:

```
It_was_the_best_of_times,_it_was_the_worst_of_times,_it_was_the_age_
of_wisdom,_it_was_the_age_of_foolishness,_it_was_the_epoch_of_belief
,_it_was_the_epoch_of_incredulity,_it_was_the_season_of_Light,_it_wa
s_the_season_of_Darkness,_it_was_the_spring_of_hope,_it_was_the_wint
er_of_despair,_we_had_everything_before_us,_we_had_nothing_before_us
,_we_were_all_going_direct_to_Heaven,_we_were_all_going_direct_the_o
ther_way_-_in_short,_the_period_was_so_far_like_the_present_period,_
that_some_of_its_noisiest_authorities_insisted_on_its_being_received
,_for_good_or_for_evil,_in_the_superlative_degree_of_comparison_only.$
```

bwt[614]:

```
.dlmssftysesdtrsns_y__$_yfofeeeetggsfefefggeedrofr,llreef-,fs,,,,,,,
,,nfrsdnnhereghettedndeteegeenstee,ssssst,esssnssffteedtttttttttr,,
,,eeefehh__p__fpDwwwwwwwwwweehl_ew_____eoo_neeeoaaeoo____sephhrrhvh
hwwegmghhhhhhhkrrwwhhssHrrrvtrribbdbcbvs__thwwpppvmmirdnnib__eooooo
oooooo____eennnnnnaai___ecc__ttttttttttttttttts_tsgltsLlvtt___hhoor
e_wrraddwlors_________r__lteirillre_ouaanooiioeoooooiiihkiiiiiio__iei
tsppioi_____________ggnodsc_sss_gfhf_fffhwh_nsmo__uee_siooooaeeeeoo_ii
cgppeeaoaeooeesseuutetaaaaaaaaaaai__ei_in__aaie_eeerei_hrsssnacciiIi
iiiiiiisn_____________oyoui__a_iiids__aiiaee_____________________tlar
```

Run Length Encoding

ref[614]:

```
It_was_the_best_of_times,_it_was_the_worst_of_times,_it_was_the_age_
of_wisdom,_it_was_the_age_of_foolishness,_it_was_the_epoch_of_belief
,_it_was_the_epoch_of_incredulity,_it_was_the_season_of_Light,_it_wa
s_the_season_of_Darkness,_it_was_the_spring_of_hope,_it_was_the_wint
er_of_despair,_we_had_everything_before_us,_we_had_nothing_before_us
,_we_were_all_going_direct_to_Heaven,_we_were_all_going_direct_the_o
ther_way_-_in_short,_the_period_was_so_far_like_the_present_period,_
that_some_of_its_noisiest_authorities_insisted_on_its_being_received
,_for_good_or_for_evil,_in_the_superlative_degree_of_comparison_only.$
```

bwt[614]:

```
.dlmssftysesdtrsns_y__$_yfofeeeetggsfefefggeedrofr,llreef-,fs,,,,,,,
,,nfrsdnnhereghettedndeteegeenstee,ssssst,esssnssffteedtttttttttr,,
,,eeefehh__p__fpDwwwwwwwwwweehl_ew_____eoo_neeeoaaeoo____sephhrrhvh
hwwegmghhhhhhhkrrwwhhssHrrrvtrribbdbcbvs__thwwpppvmmirdnnib__eooooo
oooooo____eennnnnnaai___ecc__ttttttttttttttttts_tsgltsLlvtt___hhoor
e_wrraddwlors_________r__lteirillre_ouaanooiioeoooooiiihkiiiiiio__iei
tsppioi_____________ggnodsc_sss_gfhf_fffhwh_nsmo__uee_siooooaeeeeoo_ii
cgppeeaoaeoo                                                sssnacciiIi
iiiiiiisn_____________oyoui__a_iiids__aiiaee_____________________tlar
```

Why does BWT(T) have long runs when T does not?

Run Length Encoding

bwt[614]:

```
.dlmssftysesdtrsns_y__$_yfofeeeetggsfefefggeedrofr,llreef-,fs,,,,,,,
,,nfrsdnnhereghettedndeteegeenstee,ssssst,esssnssffteedttttttttttr,,
,,eeefehh__p__fpDwwwwwwwwwwweehl_ew_____eoo_neeeoaaeoo____sephhrrhvh
hwwegmghhhhhhhkrrwwhhssHrrrvtrribbdbcbvs__thwwpppvmmirdnnib__eoooooo
oooooo____eennnnnnaai___ecc__ttttttttttttttttts_tsgltsLlvtt___hhoor
e_wrraddwlors_________r__lteirillre_ouaanooiioeoooiiihkiiiiiio__iei
tsppioi___________ggnodsc_sss_gfhf_fffhwh_nsmo__uee_siooaeeeeoo_ii
cgppeeaoaeooeesseuutetaaaaaaaaaaai__ei_in__aaie_eeerei_hrsssnacciiIi
iiiiiisn_____________oyoui__a_iiids__aiiaee_____________________tlar
```

rle(bwt)[464]:

```
.dlms2ftysesdtrsns_y_2$_yfofe4tg2sfefefg2e2drofr,l2re2f-,fs,9nfrsdn2
hereghet2edndete2ge2nste2,s5t,es3ns2f2te2dt10r,4e3feh2_2p_2fpDw11e2h
l_ew_5eo2_ne3oa2eo2_4seph2r2hvh2w2egmgh7kr2w2h2s2Hr3vtr2ib2dbcbvs_2t
hw2p3vm2irdn2ib_2eo12_4e2n6a2i_3ec2_2t18s_tsgltsLlvt2_3h2o2re_wr2ad2
wlors_9r_2lteiril2re_oua2no2i2oeo4i3hki6o_2ieitsp2ioi_12g2nodsc_s3_g
fhf_f3hwh_nsmo_2ue2_sio3ae4o2_i2cgp2e2aoaeo2e2s2eu2teta11i_2ei_in_2a
2ie_e3rei_hrs3nac2i2Ii7sn_15oyoui_2a_i3ds_2ai2ae2_21tlar
```

Run Length Encoding

ref[614]:

```
It_was_the_best_of_times,_it_was_the_worst_of_times,_it_was_the_age_
of_wisdom,_it_was_the_age_of_foolishness,_it_was_the_epoch_of_belief
,_it_was_the_epoch_of_incredulity,_it_was_the_season_of_Light,_it_wa
s_the_season_of_Darkness,_it_was_the_spring_of_hope,_it_was_the_wint
er_of_despair,_we_had_everything_before_us,_we_had_nothing_before_us
,_we_were_all_going_direct_to_Heaven,_we_were_all_going_direct_the_o
ther_way_-_in_short,_the_period_was_so_far_like_the_present_period,_
that_some_of_its_noisiest_authorities_insisted_on_its_being_received
,_for_good_or_for_evil,_in_the_superlative_degree_of_comparison_only.$
```

rle(bwt)[464]:

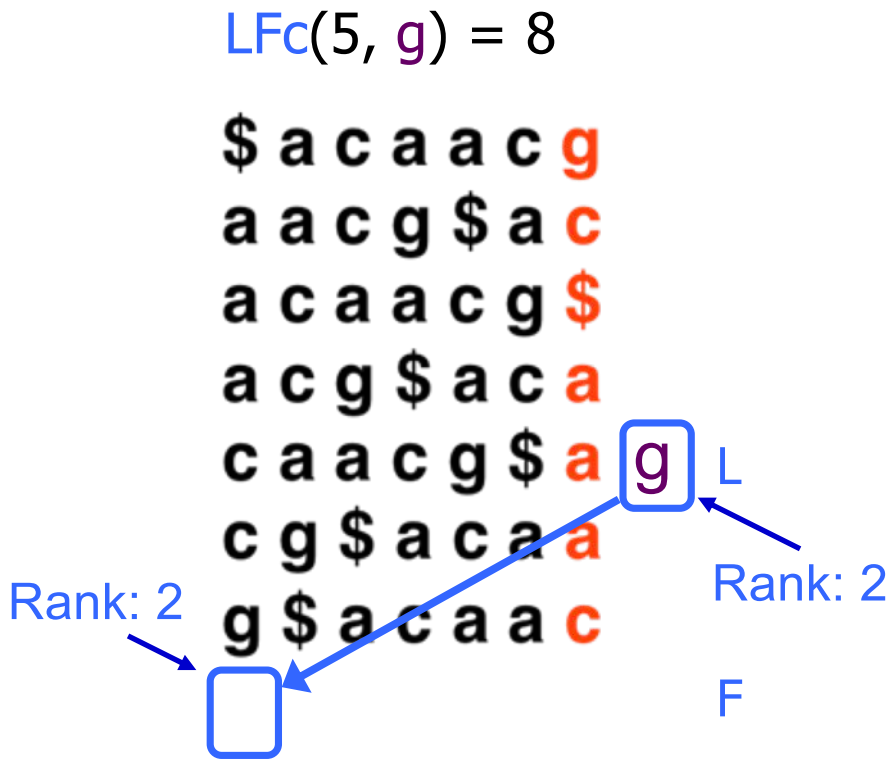
```
.dlms2ftysesdtrsns_y_2$_yfofe4tg2sfefefg2e2drofr,l2re2f-,fs,9nfrsdn2
hereghet2edndete2ge2nste2,s5t,es3ns2f2te2dt10r,4e3feh2_2p_2fpDw11e2h
l_ew_5eo2_ne3oa2eo2_4seph2r2hvh2w2egmgh7kr2w2h2s2Hr3vtr2ib2dbcbvs_2t
hw2p3vm2irdn2ib_2eo12_4e2n6a2i_3ec2_2t18s_tsgltsLlvt2_3h2o2re_wr2ad2
wlors_9r_2lteiril2re_oua2no2i2oeo4i3hki6o_2ieitsp2ioi_12g2nodsc_s3_g
fhf_f3hwh_nsmo_2ue2_sio3ae4o2_i2cgp2e2aoaeo2e2s2eu2teta11i_2ei_in_2a
2ie_e3rei_
```

Saved 614-464 = 150 bytes (24%) with zero loss of information!

Common to save 50% to 90% on real world files with bzip2

BWT Exact Matching

- **LFc**(r, c) does the same thing as **LF**(r) but it ignores r's actual final character and "pretends" it's c:



BWT Exact Matching

- Start with a range, (**top**, **bot**) encompassing all rows and repeatedly apply **LFc**:

  top = LFc(top, qc); bot = LFc(bot, qc)

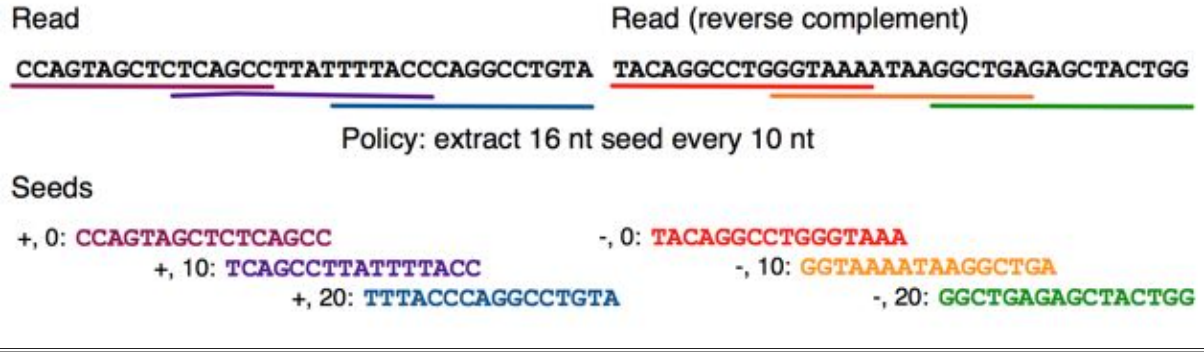
  qc = the next character to the left in the query

Ferragina P, Manzini G: Opportunistic data structures with applications. *FOCS. IEEE Computer Society; 2000.*

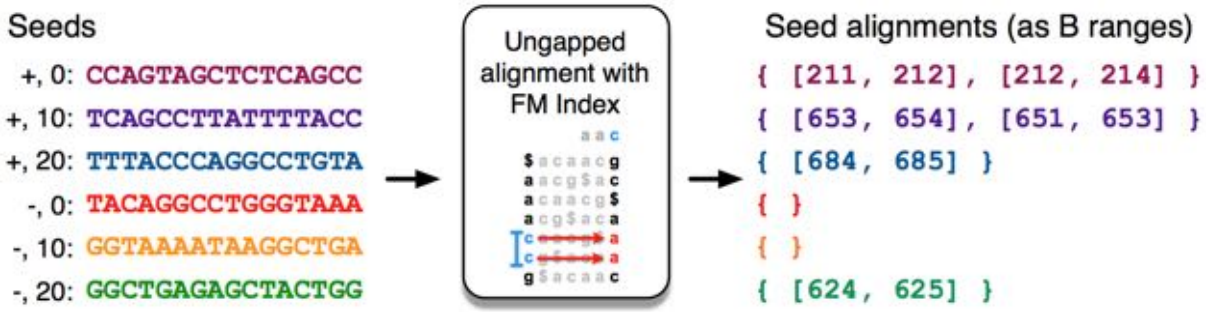
[Search for TTA this BWT string: ACTGA$TTA]

Algorithm Overview

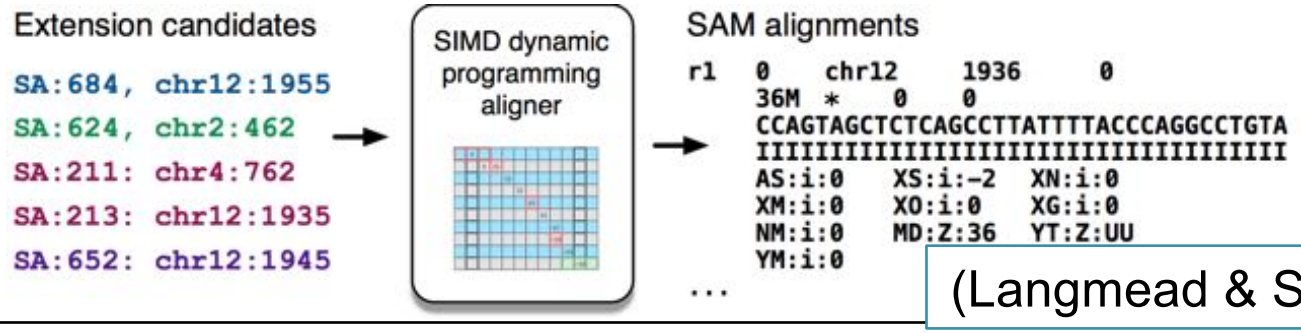
1. Split read into segments



2. Lookup each segment and prioritize

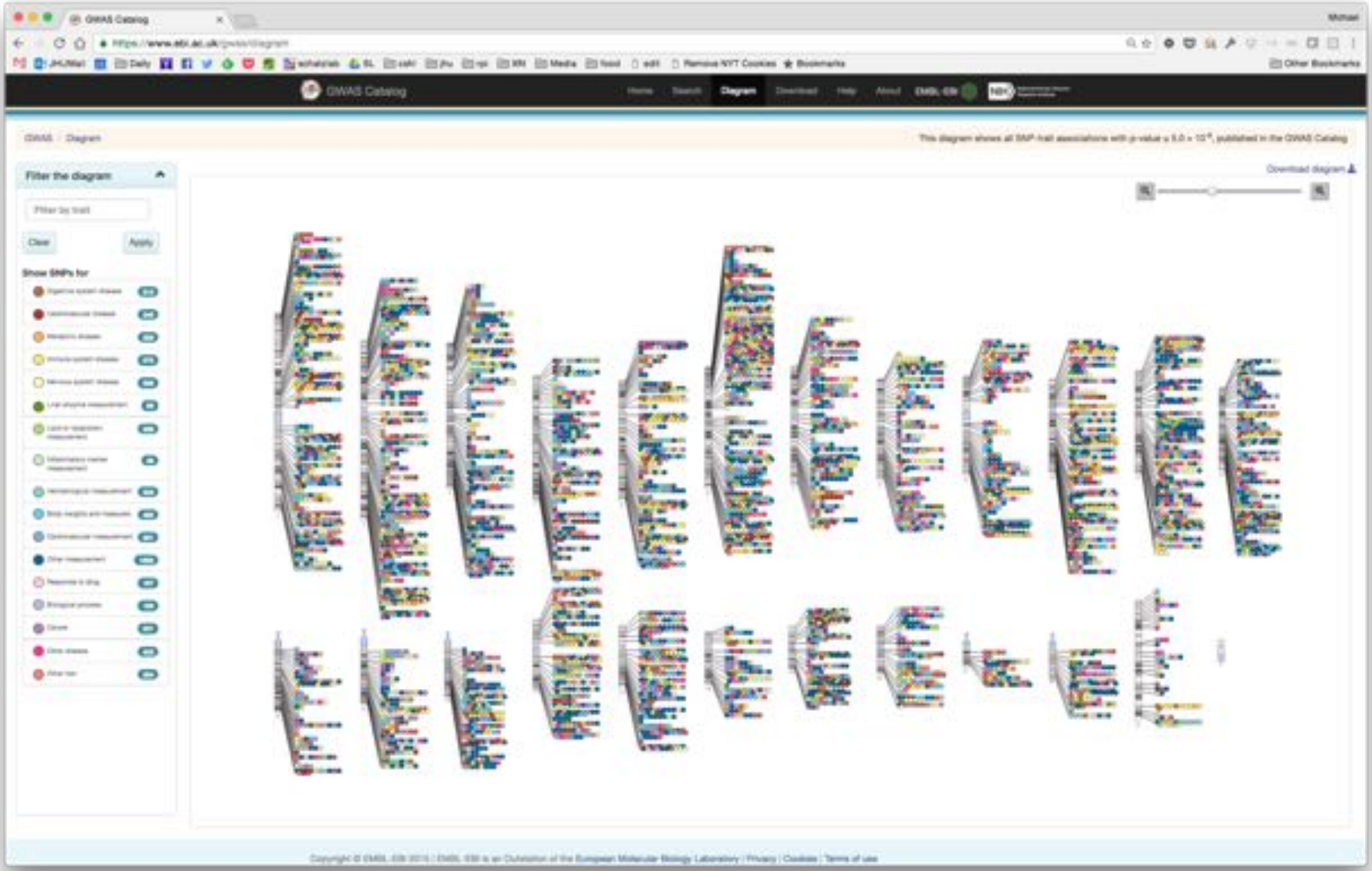


3. Evaluate end-to-end match

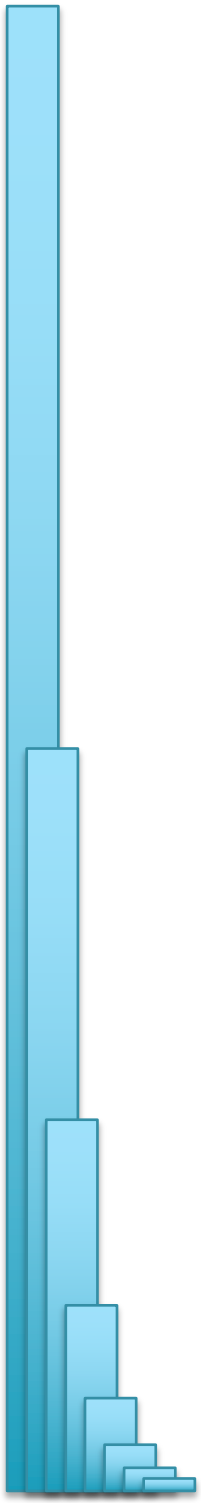


(Langmead & Salzberg, 2012)

Genetic Associations



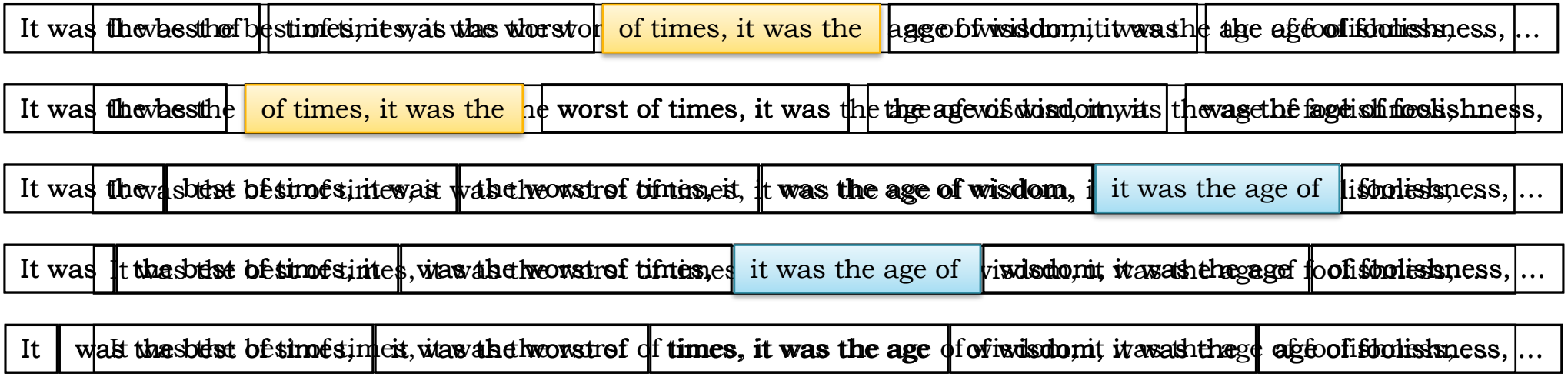
https://www.ebi.ac.uk/gwas/diagram



Part 3: Genome Assembly

Shredded Book Reconstruction

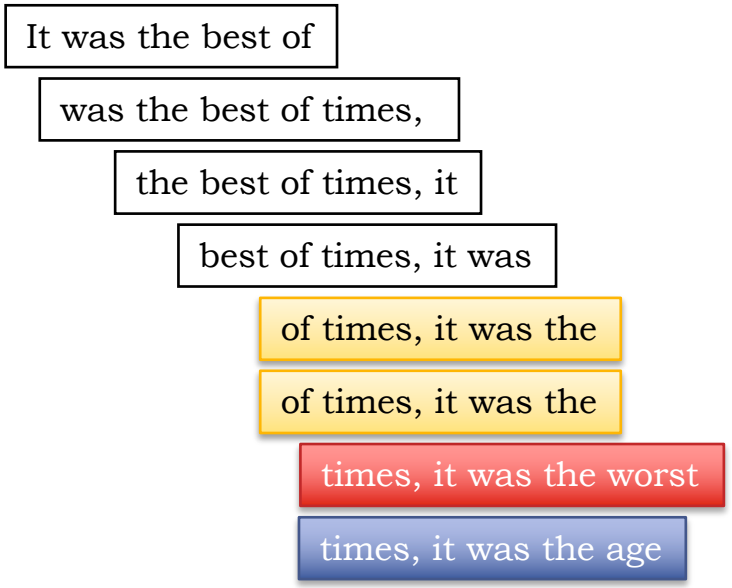
- Dickens accidentally shreds the first printing of A Tale of Two Cities
  - Text printed on 5 long spools



- How can he reconstruct the text?
  - 5 copies x 138, 656 words / 5 words per fragment = 138k fragments
  - The short fragments from every copy are mixed together
  - Some fragments are identical

Greedy Reconstruction

It was the best of
age of wisdom, it was
best of times, it was
it was the age of
it was the age of
it was the worst of
of times, it was the
of times, it was the
of wisdom, it was the
the age of wisdom, it
the best of times, it
the worst of times, it
times, it was the age
times, it was the worst
was the age of wisdom,
was the age of foolishness,
was the best of times,
was the worst of times,
wisdom, it was the age
worst of times, it was



The repeated sequence make the correct reconstruction ambiguous

- It was the best of times, it was the [worst/age]

Model the assembly problem as a graph problem

de Bruijn Graph Construction

- $D_k = (V,E)$
  - V = All length-k subfragments (k < l)
  - E = Directed edges between consecutive subfragments
    - Nodes overlap by k-1 words

Original Fragment

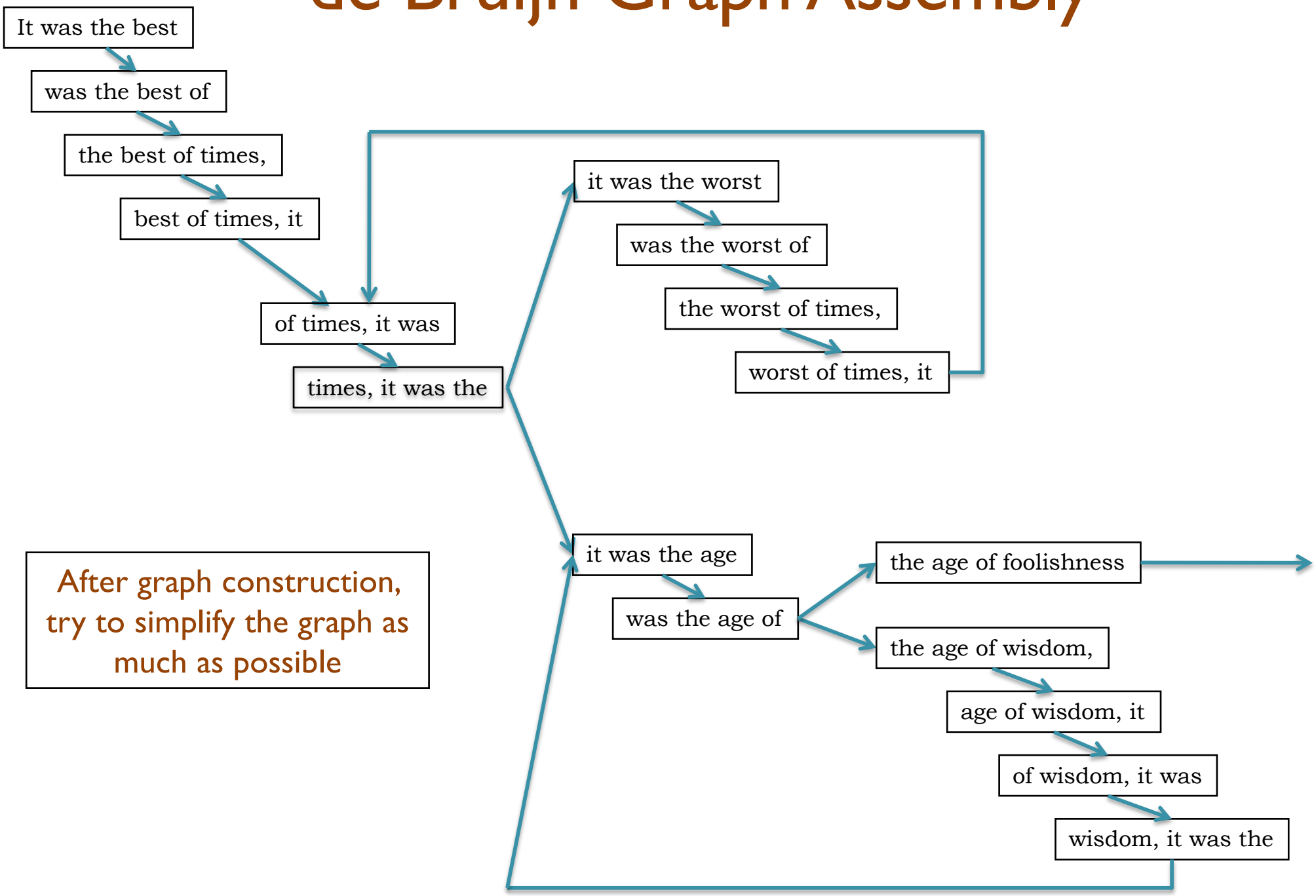
It was the best of

Directed Edge

- Locally constructed graph reveals the global sequence structure
  - Overlaps between sequences implicitly computed

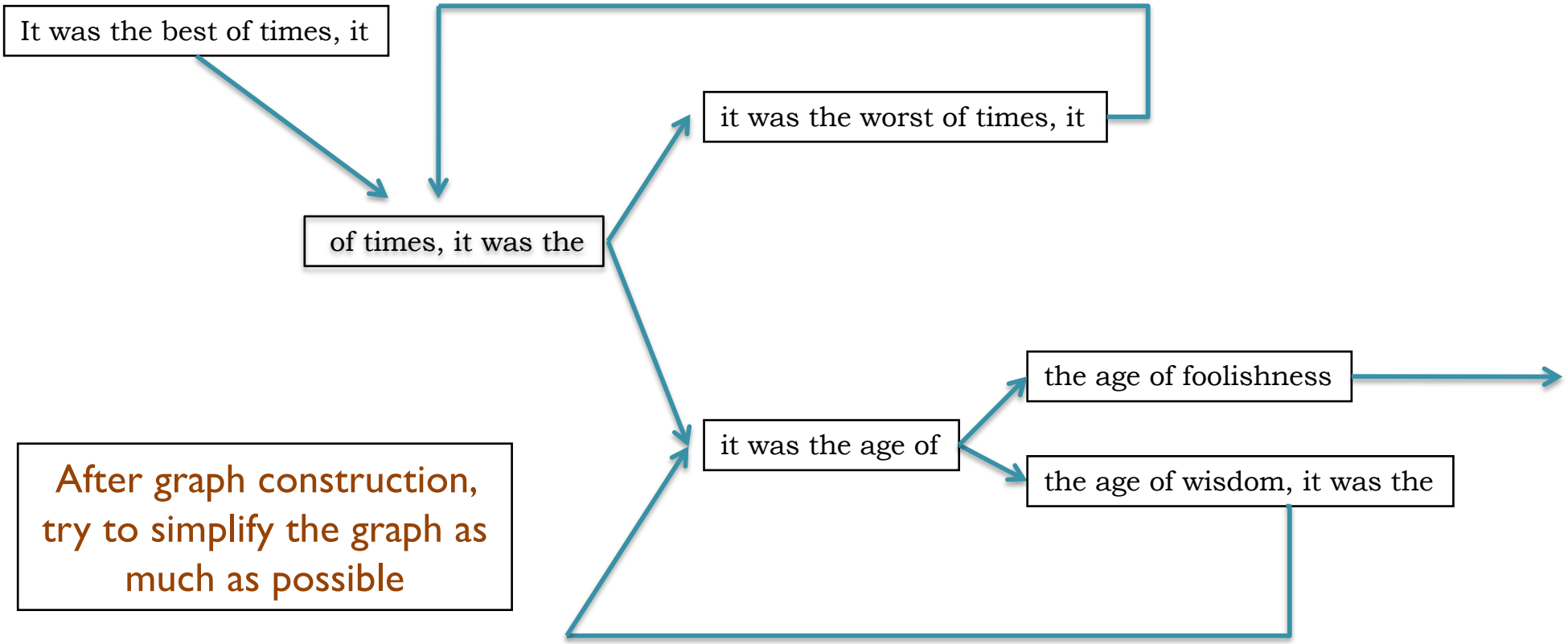
de Bruijn, 1946
Idury and Waterman, 1995
Pevzner, Tang, Waterman, 2001

de Bruijn Graph Assembly



After graph construction, try to simplify the graph as much as possible

de Bruijn Graph Assembly



After graph construction, try to simplify the graph as much as possible

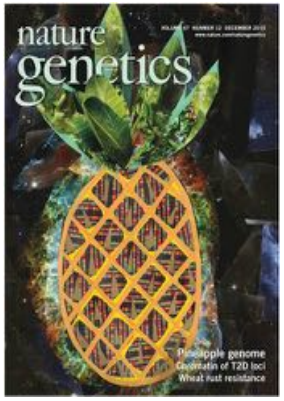
Genomics Across the Tree of Life



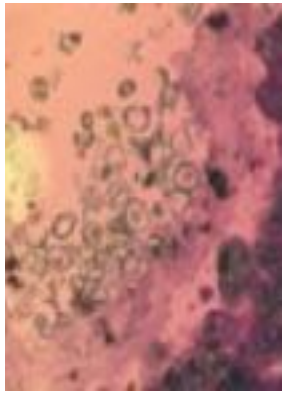
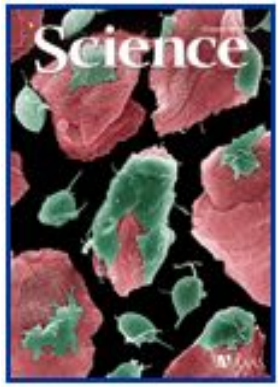


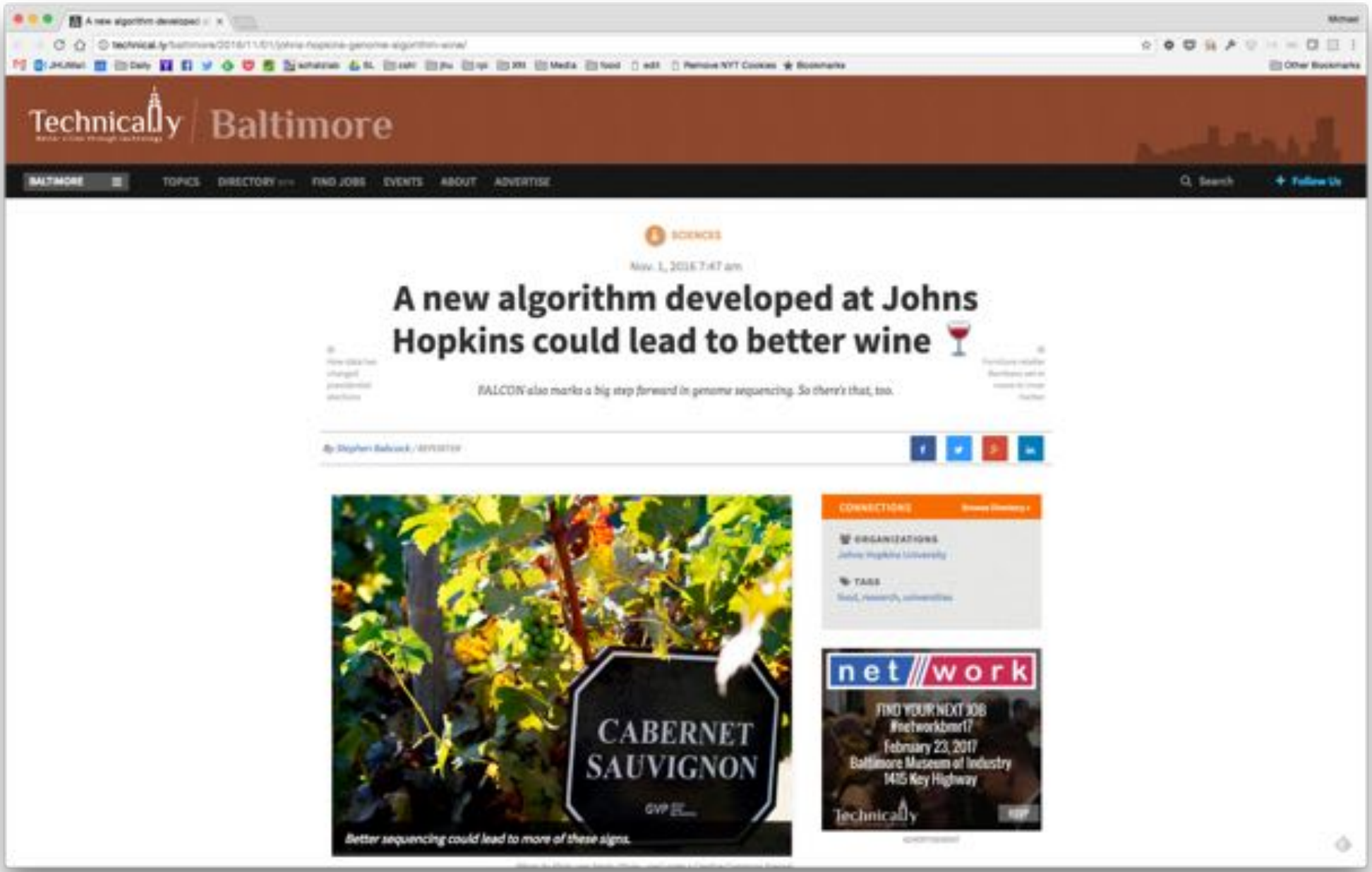










http://technical.ly/baltimore/2016/11/01/johns-hopkins-genome-algorithm-wine/

Next Steps

1. Reflect on the magic and power of Suffix Arrays and the BWT!

1. Assignment 9 due Friday November 30 @ 10pm