String Comparison

CMSC 423

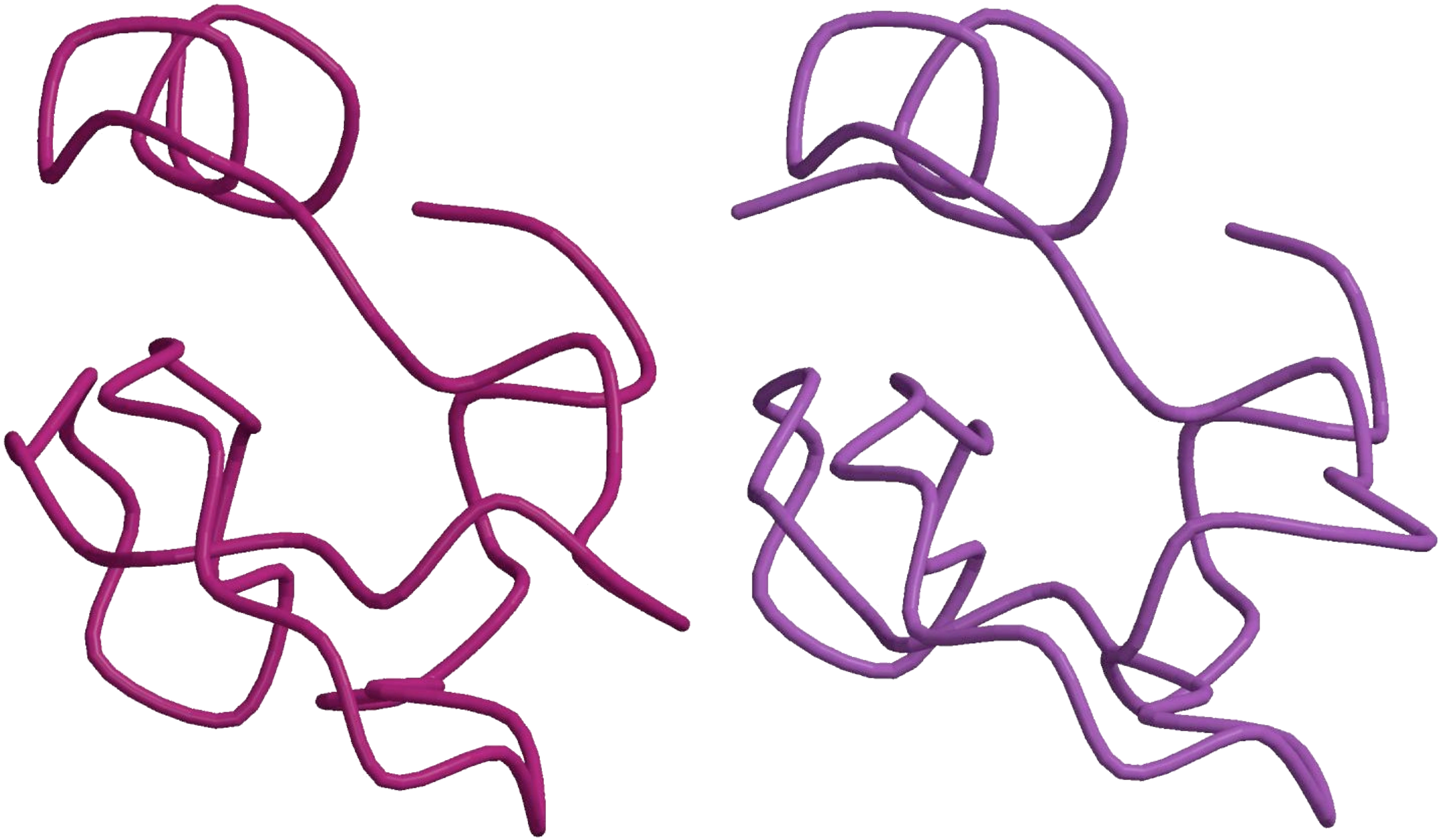
Why compare DNA or protein sequences?

Partial CTCF protein sequence in 8 organisms:

```
H. sapiens       -EDSSDS-ENAEPDLDDNEDEEEPAVEIEPEPE----------PQPVTPA
P. troglodytes   -EDSSDS-ENAEPDLDDNEDEEEPAVEIEPEPE----------PQPVTPA
C. lupus         -EDSSDS-ENAEPDLDDNEDEEEPAVEIEPEPE----------PQPVTPA
B. taurus        -EDSSDS-ENAEPDLDDNEDEEEPAVEIEPEPE----------PQPVTPA
M. musculus      -EDSSDSEENAEPDLDDNEEEEEPAVEIEPEPE--PQPQPPPPPQPVAPA
R. norvegicus    -EDSSDS-ENAEPDLDDNEEEEEPAVEIEPEPEPQPQPQPQPQPQPVAPA
G. gallus        -EDSSDSEENAEPDLDDNEDEEETAVEIEAEPE----------VSAEAPA
D. rerio         DDDDDDSDEHGEPDLDDIDEEDEDDL-LDEDQMGLLDQAPPSVPIP-APA
```

- Identify important sequences by finding conserved regions.
- Find genes similar to known genes.
- Understand evolutionary relationships and distances (D. rerio aka zebrafish is farther from humans than G. gallus aka chicken).
- Interface to databases of genetic sequences.
- As a step in genome assembly, and other sequence analysis tasks.
- Provide hints about protein structure and function (next slide).

Sequence can reveal structure



(a) 1dtk

(b) 5pti

1dtk   XAKY**C**KL**P**LRI**GPCK**RK**I**PSFY**Y**KW**KA**KQ**C**LP**F**D**Y**S**GC**GGNA**N**R**FK**TI**E**E**C**R**RTC**V**G**-
5pti   RPDF**C**LE**P**PYT**GPCK**AR**I**IRYF**Y**NA**KA**GL**C**QT**F**V**Y**G**GC**RAKR**N**N**FK**SA**E**D**C**M**RTC**G**G**A

Simple String Comparison Problems

Given: Two strings

$$a = a_1a_2a_3a_4 \ldots a_m$$
$$b = b_1b_2b_3b_4 \ldots b_n$$

where a_i, b_i are letters from some alphabet like {A,C,G,T}.

Compute how similar the two strings are.

What do we mean by “similar”?

Longest Common Subsequence: the longest subsequence with matching characters from the two strings.

```
A T - G T T A T A
A T C G T - C - C
```

Simple String Comparison Problems

Given: Two strings

$$a = a_1 a_2 a_3 a_4 \ldots a_m$$
$$b = b_1 b_2 b_3 b_4 \ldots b_n$$

where a_i, b_i are letters from some alphabet like {A,C,G,T}.

Compute how similar the two strings are.

What do we mean by "similar"?

Edit distance between strings *a* and *b* = the smallest number of the following operations that are needed to transform *a* into *b*:

- mutate (replace) a character
- delete a character
- insert a character

$$\text{riddle} \xrightarrow{\text{delete}} \text{ridle} \xrightarrow{\text{mutate}} \text{riple} \xrightarrow{\text{insert}} \text{triple}$$

Representing edits as alignments

```
prin-ciple
|||| |||xx
prinncipal
(1 gap, 2 mm)
```

```
misspell
||| ||||
mis-pell
(1 gap)
```

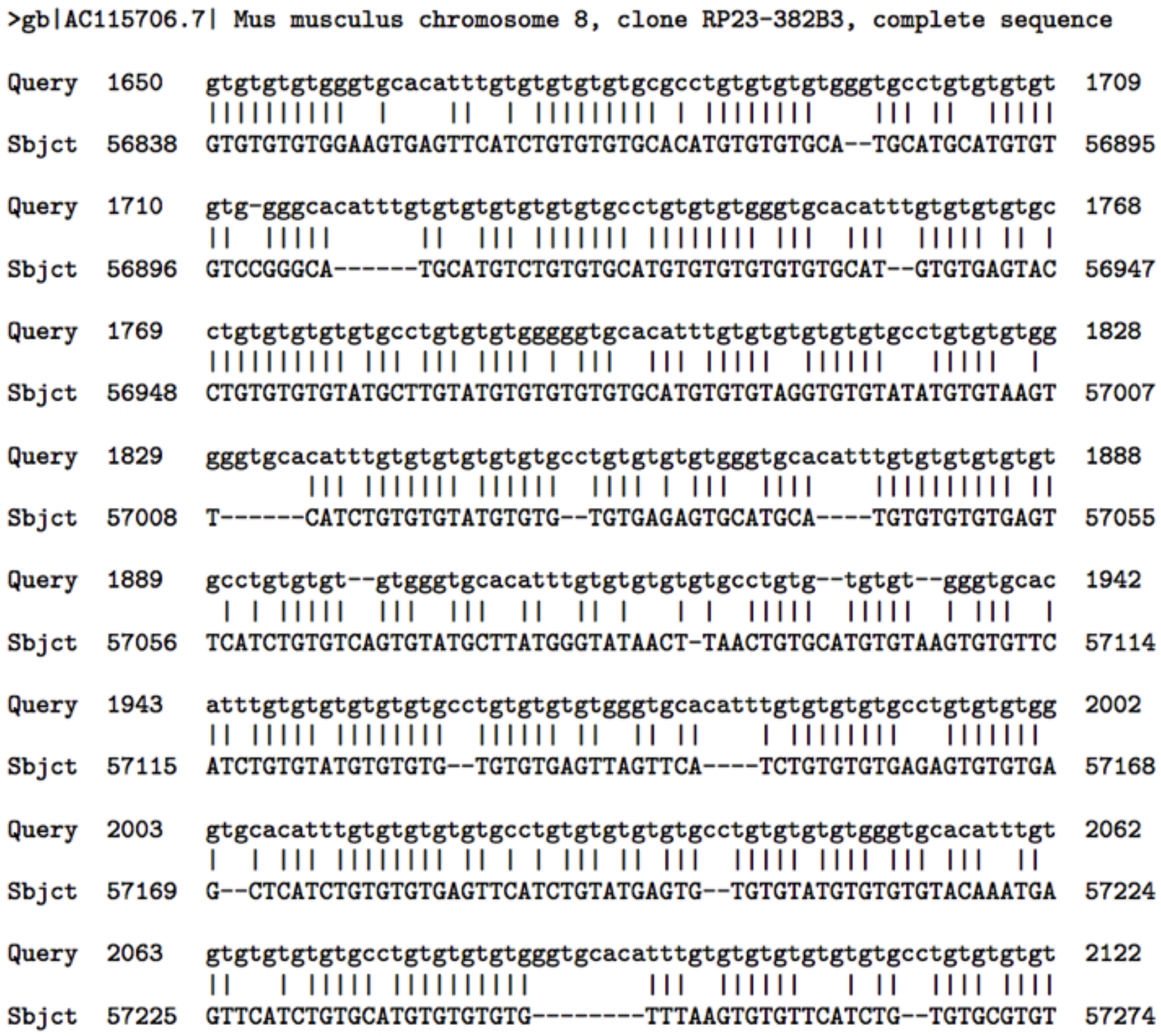
```
aa-bb-ccaabb
|x || | | |
ababbbc-a-b-
(5 gaps, 1 mm)
```

```
prin-cip-le
|||| ||| |
prinncipal-
(3 gaps, 0 mm)
```

```
prehistoric
   ||||||||
---historic
(3 gaps)
```

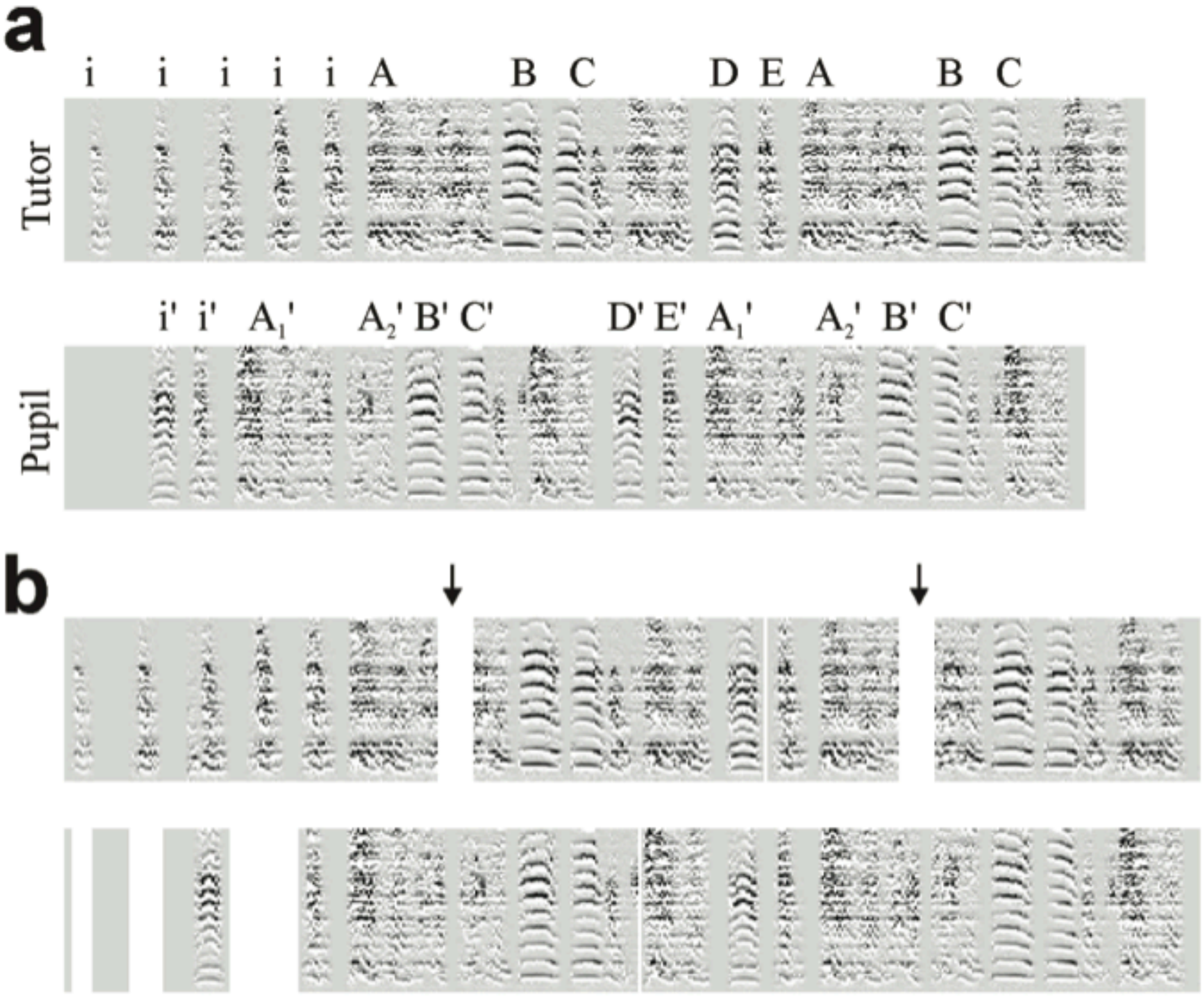
```
al-go-rithm-
|| xx ||x |
alKhwariz-mi
(4 gaps, 3 mm)
```

NCBI BLAST DNA Alignment



```
>gb|AC115706.7| Mus musculus chromosome 8, clone RP23-382B3, complete sequence

Query  1650   gtgtgtgtgggtgcacatttgtgtgtgtgtgcgcctgtgtgtgtgggtgcctgtgtgtgt  1709
              ||||||||||  |    ||  | ||||||||| | ||||||||    ||| ||  |||||
Sbjct  56838  GTGTGTGTGGAAGTGAGTTCATCTGTGTGTGCACATGTGTGTGCA--TGCATGCATGTGT  56895

Query  1710   gtg-gggcacatttgtgtgtgtgtgtgtgcctgtgtgtgggtgcacatttgtgtgtgtgc  1768
              ||  |||||      ||  ||| ||||||| |||||||| |||  |||  ||||| || |
Sbjct  56896  GTCCGGGCA------TGCATGTCTGTGTGCATGTGTGTGTGTGCAT--GTGTGAGTAC  56947

Query  1769   ctgtgtgtgtgtgcctgtgtgtgggggtgcacatttgtgtgtgtgtgtgcctgtgtgtgg  1828
              |||||||||| ||| ||| |||| | |||  ||| |||||  ||||||   |||||  |
Sbjct  56948  CTGTGTGTGTATGCTTGTATGTGTGTGTGTGCATGTGTGTAGGTGTGTATATGTGTAAGT  57007

Query  1829   gggtgcacatttgtgtgtgtgtgtgcctgtgtgtgtgggtgcacatttgtgtgtgtgtgt  1888
                     ||| ||||||| ||||||  |||| | |||  ||||    |||||||||| ||
Sbjct  57008  T------CATCTGTGTGTATGTGTG--TGTGAGAGTGCATGCA----TGTGTGTGTGAGT  57055

Query  1889   gcctgtgtgt--gtgggtgcacatttgtgtgtgtgtgcctgtg--tgtgt--gggtgcac  1942
               | | |||||  |||  |||  ||  || |   | |  |||||  |||||  | |||  |
Sbjct  57056  TCATCTGTGTCAGTGTATGCTTATGGGTATAACT-TAACTGTGCATGTGTAAGTGTGTTC  57114

Query  1943   atttgtgtgtgtgtgtgcctgtgtgtgtgggtgcacatttgtgtgtgtgcctgtgtgtgg  2002
              || ||||| ||||||||  |||||| ||  || ||    | ||||||||   |||||||
Sbjct  57115  ATCTGTGTATGTGTGTG--TGTGTGAGTTAGTTCA----TCTGTGTGTGAGAGTGTGTGA  57168

Query  2003   gtgcacatttgtgtgtgtgtgcctgtgtgtgtgtgcctgtgtgtgtgggtgcacatttgt  2062
              |  | ||| |||||||| || | | ||| || |||  ||||| |||| ||| |||  ||
Sbjct  57169  G--CTCATCTGTGTGTGAGTTCATCTGTATGAGTG--TGTGTATGTGTGTGTACAAATGA  57224

Query  2063   gtgtgtgtgtgcctgtgtgtgtgggtgcacatttgtgtgtgtgtgtgcctgtgtgtgt  2122
              ||   | ||||| ||||||||||        |||  ||||||   | ||  |||| ||||
Sbjct  57225  GTTCATCTGTGCATGTGTGTGTG--------TTTAAGTGTGTTCATCTG--TGTGCGTGT  57274
```

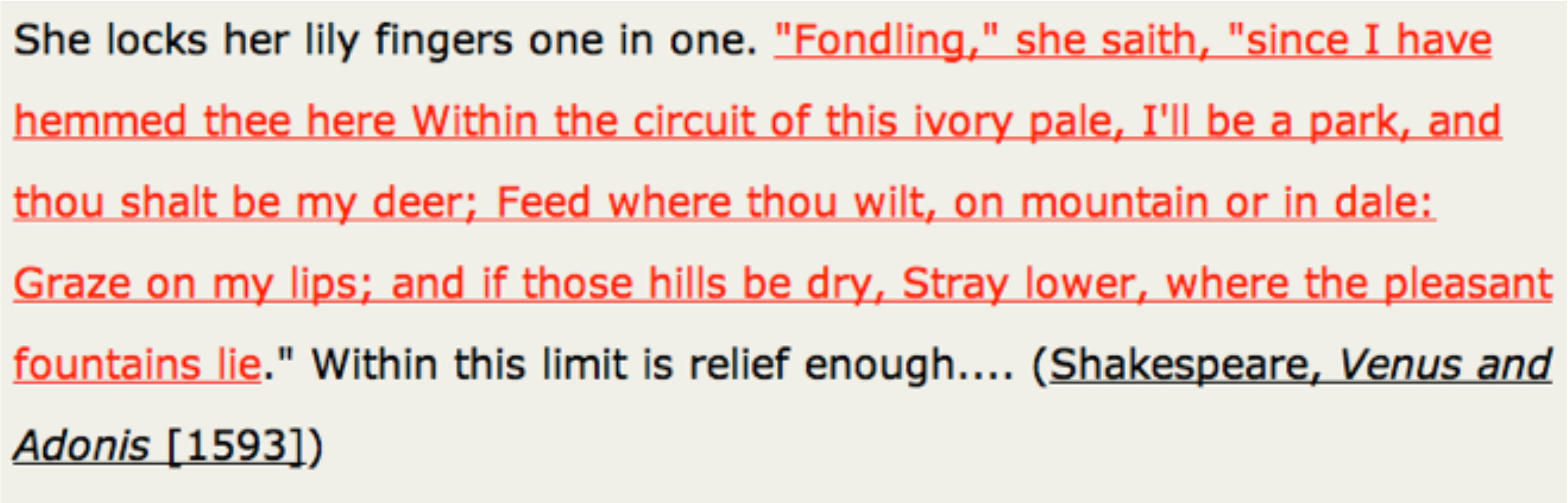
Comparing Bird Songs



Florian et al. Hidden Markov Models in the Neurosciences

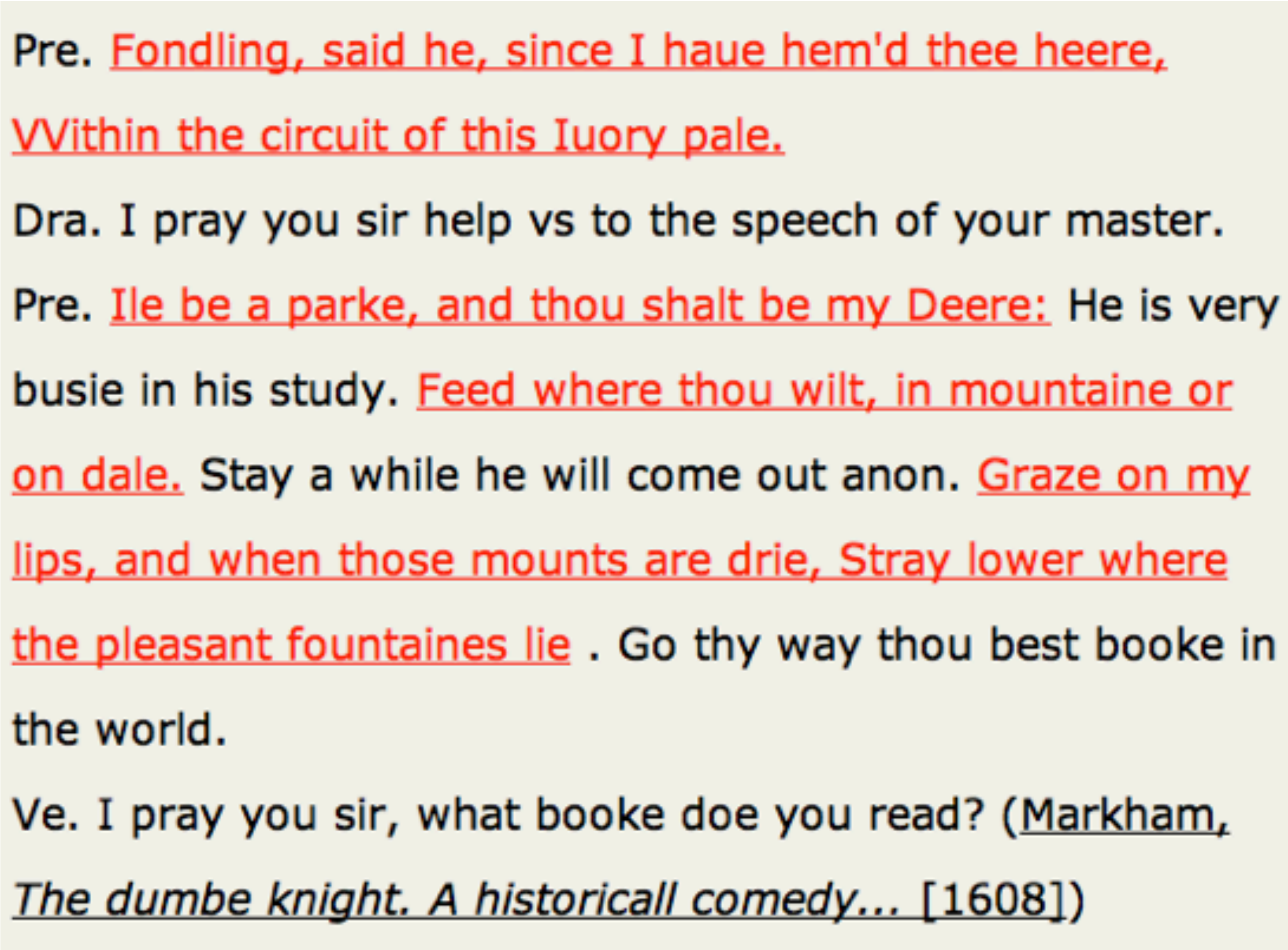
Tracing Textual Influences

Example from Horton, Olsen, Roe, Digital Studies / Le champ numérique, Vol 2, No 1 (2010)



She locks her lily fingers one in one. "Fondling," she saith, "since I have hemmed thee here Within the circuit of this ivory pale, I'll be a park, and thou shalt be my deer; Feed where thou wilt, on mountain or in dale: Graze on my lips; and if those hills be dry, Stray lower, where the pleasant fountains lie." Within this limit is relief enough.... (Shakespeare, *Venus and Adonis* [1593])

This later play by Markham references Shakespeare's poem.



Pre. Fondling, said he, since I haue hem'd thee heere, VVithin the circuit of this Iuory pale.

Dra. I pray you sir help vs to the speech of your master.

Pre. Ile be a parke, and thou shalt be my Deere: He is very busie in his study. Feed where thou wilt, in mountaine or on dale. Stay a while he will come out anon. Graze on my lips, and when those mounts are drie, Stray lower where the pleasant fountaines lie . Go thy way thou best booke in the world.

Ve. I pray you sir, what booke doe you read? (Markham, *The dumbe knight. A historicall comedy...* [1608])

Common passages identified by sequence alignment algorithms.

Algorithm for Computing Longest Common Subsequence

Consider the last characters of each string:

$$a = a_1 a_2 a_3 a_4 \ldots a_m$$
$$b = b_1 b_2 b_3 b_4 \ldots b_n$$

One of these possibilities must hold:

1. (a_m, b_n) are matched to each other

2. a_m is not matched at all

3. b_n is not matched at all

4. a_m is matched to some b_j $(j \neq n)$ and b_n is matched to some a_k $(k \neq m)$.

Algorithm for Computing Longest Common Subsequence

Consider the last characters of each string:

$$a = a_1a_2a_3a_4\ldots a_m$$
$$b = b_1b_2b_3b_4\ldots b_n$$

One of these possibilities must hold:

1. (a_m, b_n) are matched to each other

2. a_m is not matched at all

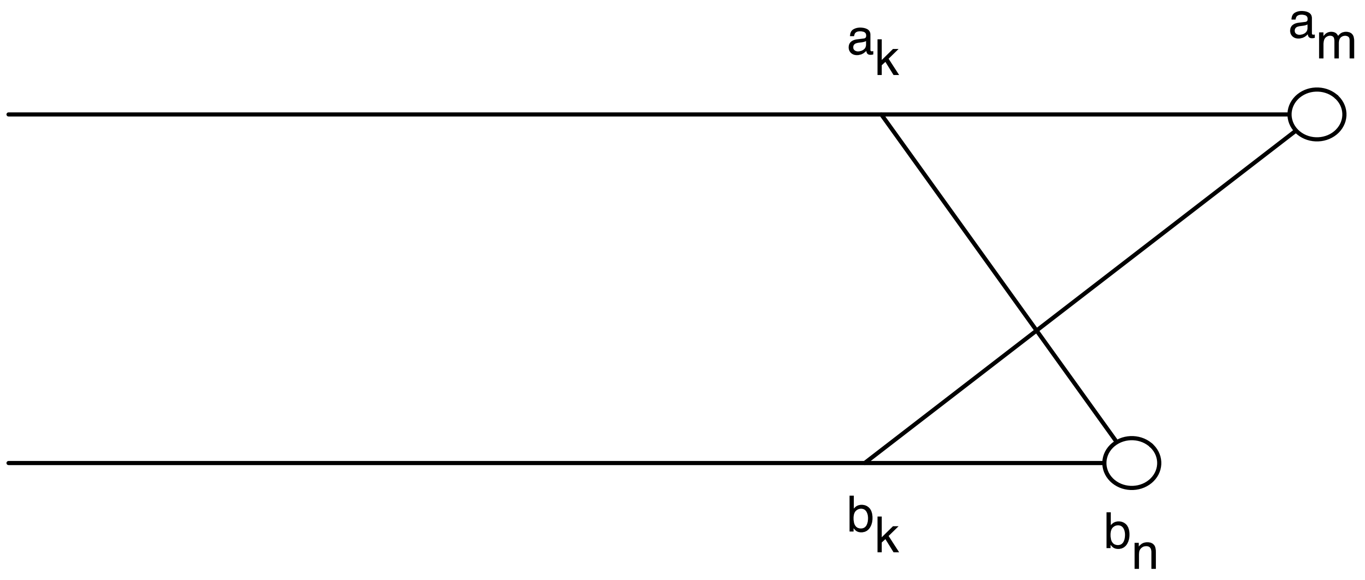
3. b_n is not matched at all

4. a_m is matched to some b_j $(j \neq n)$ and b_n is matched to some a_k $(k \neq m)$.

#4 can't happen! Why?

No Crossing Rule Forbids #4

4. a_m is matched to some b_j ($j \neq n$) and b_n is matched to some a_k ($k \neq m$).



So, the only possibilities for what happens to the last characters are:

1. (a_m, b_n) are matched to each other

2. a_m is not matched at all

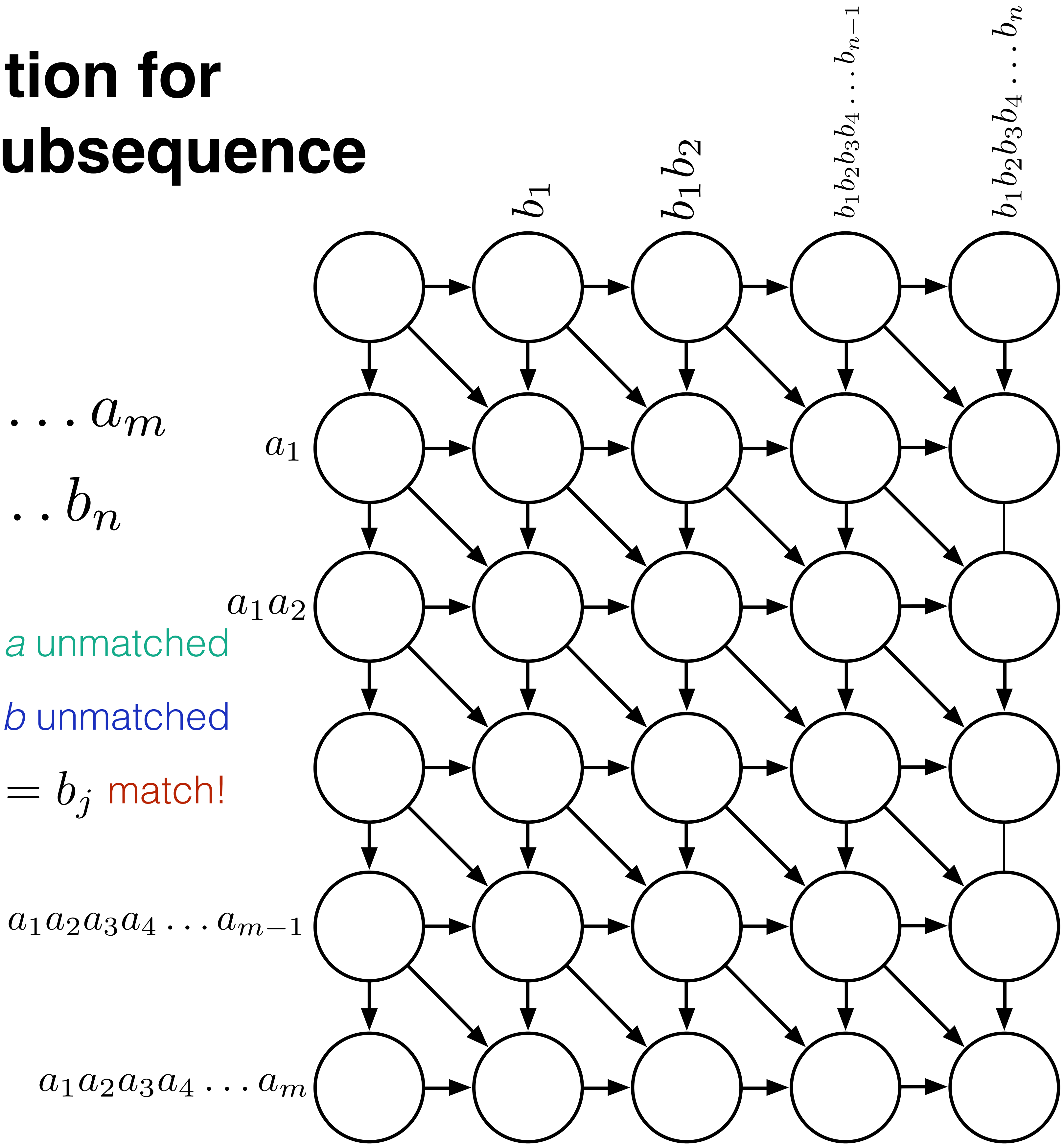
3. b_n is not matched at all

Recursive Solution for Longest Common Subsequence

$$a = a_1 a_2 a_3 a_4 \ldots a_m$$

$$b = b_1 b_2 b_3 b_4 \ldots b_n$$

$$s_{i,j} = \max \begin{cases} s_{i-1,j} & \text{char in } a \text{ unmatched} \\ s_{i,j-1} & \text{char in } b \text{ unmatched} \\ s_{i-1,j-1} + 1, \text{ if } a_i = b_j & \text{match!} \end{cases}$$


b_1
$b_1 b_2$
$b_1 b_2 b_3 b_4 \ldots b_{n-1}$
$b_1 b_2 b_3 b_4 \ldots b_n$
a_1
$a_1 a_2$
$a_1 a_2 a_3 a_4 \ldots a_{m-1}$
$a_1 a_2 a_3 a_4 \ldots a_m$

Dynamic Programming

The previous algorithm to solve LCS is an example of **dynamic programming**

Main idea of dynamic programming: solve the subproblems in an order so that when you need an answer, it's ready.

Requirements for DP to apply:

1. Optimal value of the original problem can be computed from some similar subproblems.

2. There are only a polynomial # of subproblems

3. There is a "natural" ordering of subproblems, so that you can solve a subproblem by only looking at **smaller** subproblems.

Serena Williams Winning Problem

p: the probability that Serena beats here opponent in a given single set

q=(1-p): the probability that the opponent beats Serena in a given single set

What is the probability that Serena wins a best-of-five match? vs.

What is the probability that Serena wins a best-of-three match?