# Strings and Exact Matching

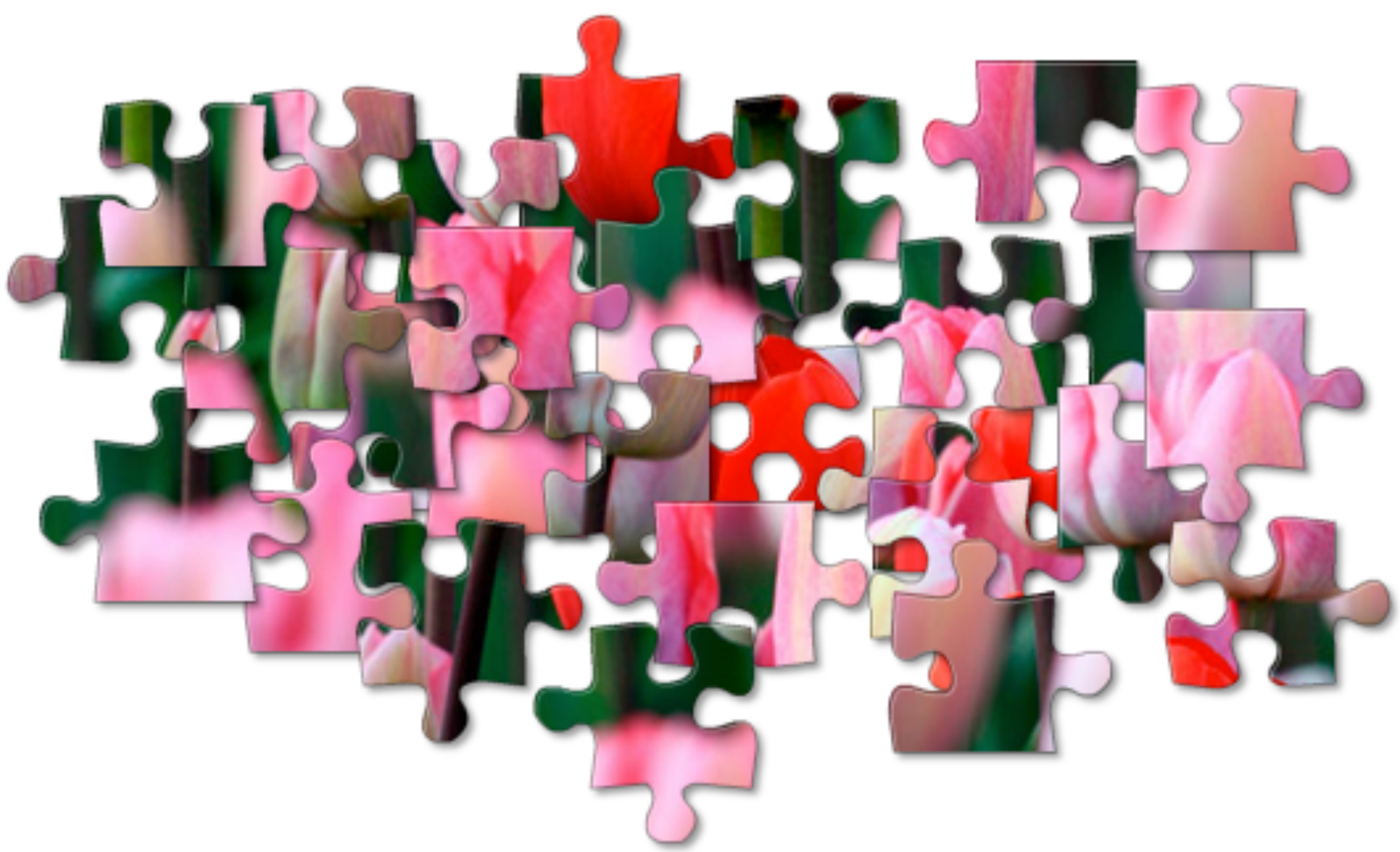
Ben Langmead

JOHNS HOPKINS
WHITING SCHOOL
*of* ENGINEERING

Department of Computer Science

# Reads are strings

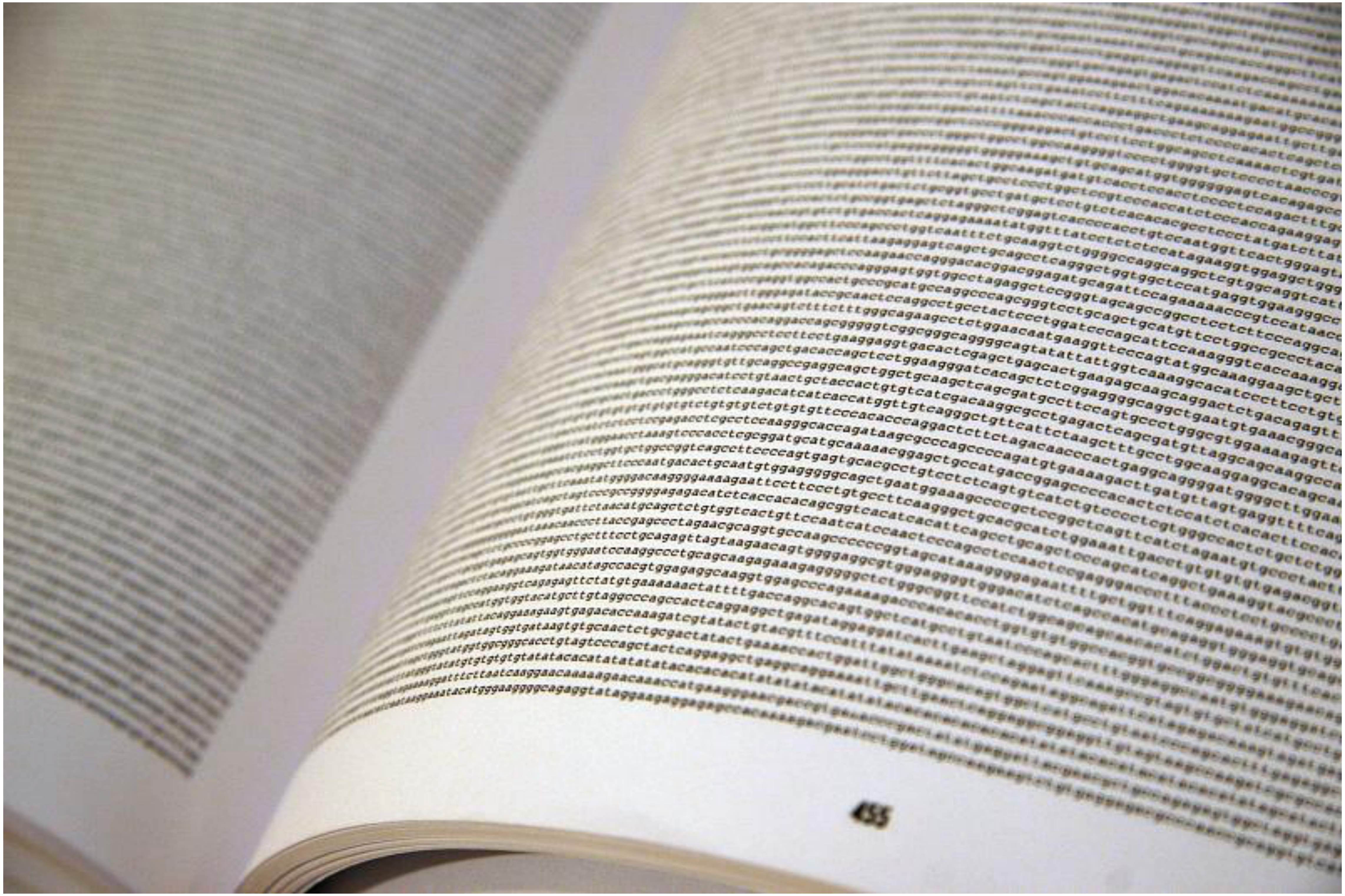
| | | |
|---|---|---|
| GTATGCACGCGATAG | TATGTCGCAGTATCT | CACCCTATGTCGCAG |
| TAGCATTGCGAGACG | GGTATGCACGCGATA | TGGAGCCGGAGCACC |
| TGTCTTTGATTCCTG | CGCGATAGCATTGCG | GCATTGCGAGACGCT |
| GACGCTGGAGCCGGA | GCACCCTATGTCGCA | GTATCTGTCTTTGAT |
| TATCGCACCTACGTT | CAATATTCGATCATG | GATCACAGGTCTATC |
| CACGGGAGCTCTCCA | TGCATTTGGTATTTT | CGTCTGGGGGGTATG |
| GTATGCACGCGATAG | ACCTACGTTCAATAT | TATTTATCGCACCTA |
| GCGAGACGCTGGAGC | CTATCACCCTATTAA | CTGTCTTTGATTCCT |
| CCTACGTTCAATATT | GCACCTACGTTCAAT | GTCTGGGGGGTATGC |
| GACGCTGGAGCCGGA | GCACCCTATGTCGCA | GTATCTGTCTTTGAT |
| TATCGCACCTACGTT | CAATATTCGATCATG | GATCACAGGTCTATC |
| CACGGGAGCTCTCCA | TGCATTTGGTATTTT | CGTCTGGGGGGTATG |



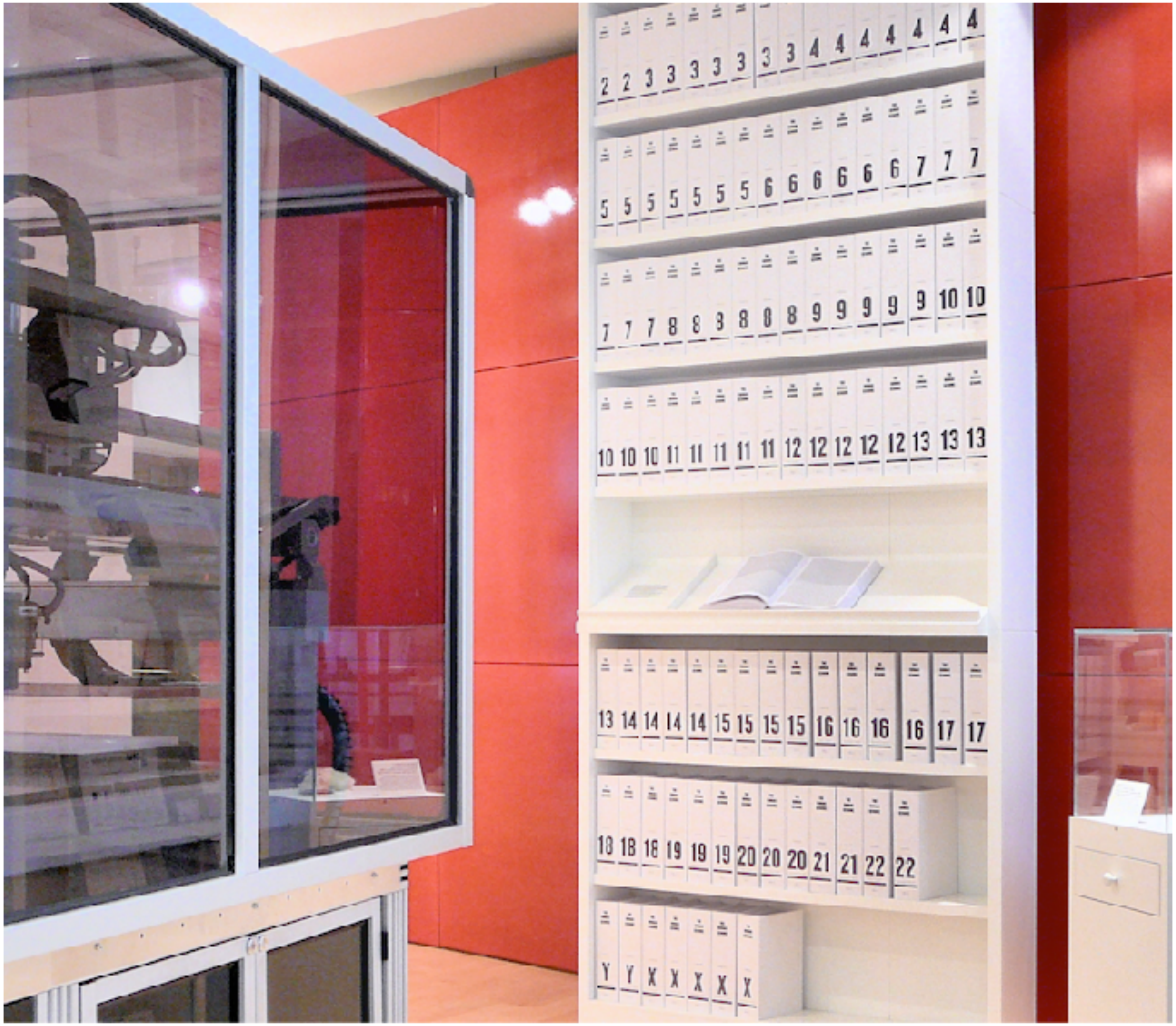
Sequencing reads are *strings;* sequences of characters

The strings are the only hints we get about *where the reads came from from* with respect to the longer DNA molecules...

... like pictures on puzzle pieces



What if I told you to find all the places where the string GATACCA occurs in here?



What if I told you to find all the places where the string GATACCA occurs in here?

# Strings

Read

**CTCAAACTCCTGACCTTTGGTGATCCACCCGCCTAGGCCTTC**

x billions

Reference


GATCACAGGTCTATCACCCTATTAACCACTCACGGGAGCTCTCCATGCATTTGGTATTTT
CGTCTGGGGGGTATGCACGCGATAGCATTGCGAGACGCTGGAGCCGGAGCACCCTATGTC
GCAGTATCTGTCTTTGATTCCTGCCTCATCCTATTATTTATCGCACCTACGTTCAATATT
ACAGGCGAACATACTTACTAAAGTGTGTTAATTAATTAATGCTTGTAGGACATAATAATA
ACAATTGAATGTCTGCACAGCCACTTTCCACACAGACATCATAACAAAAAATTTCCACCA
AACCCCCCCTCCCCCGCTTCTGGCCACAGCA AAAACA CTCTGCCAAACCCCAAAA
ACAAAGAACCCTAACACCAGCCTAACCA ATTTCAAATTTTATC TTTGGCGGTATGCAC
TTTTAACAGTCACCCCCCAACTAACA ATTATTTTCCCCTCCCACT CCATACTACTAAT
CTCATCAATACAACCCCCGCCCATC TACCCAGCACACACACACCGC CTAACCCCATA
CCCCGAACCAACCAAACCCCAAAG CACCCCCCACAGTTTATGTAGCT ACCTCCTCAAA
GCAATACACTGACCCGCTCAAACT CCTGGATTTTGGATCCACCCAGCGC TTGGCCTAAA
CTAGCCTTTCTATTAGCTCTTAG AAGATTACACATGCAAGCATCCCCG TCCAGTGAGT
TCACCCTCTAAATCACCACGATC AAAGGAACAAGCATCAAGCACGCAG AATGCAGCTC
AAAACGCTTAGCCTAGCCACACCC CCACGGGAAACAGCAGTGATTAACC TTAGCAATAA
ACGAAAGTTTAACTAAGCTATACT ACCCCAGGGTTGGTCAATTTCGT CCAGCCACCGC
GGTCACACGATTAACCCAAGTCAAT GAAGCCGGCGTAAAGAGTGTT TAGATCACCCCC
TCCCCAATAAAGCTAAAACTCACCTGA TTGTAAAAAACTCCAGTT ACACAAAATAGAC
TACGAAAGTGGCTTTAACATATCTGAACA ACAATAGCTAAGA GGGATTAGA
TACCCCACTATGCTTAGCCCTAAACCTCAACAG AACAA CGCCAGAA
CACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATA TAGAGG
AGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCT TATA
CCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACC AG
ACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTC
AAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAGTAA
AGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCT
AAGTATACTTCAAAGGACATTTAACTAAAACCCCTACGCATTTATATAGAGGAGACAA
CGTAACCTCAAACTCCTGCCTTTGGTGATCCACCCGCCTTGGCCTACCTGCATAATGAAG
AAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACCTA
GCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAATAA
AGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGATG
AAAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAATGAA
TTAACTAGAAATAACTTTGCAAGGAGAGCCAAAGCTAAGACCCCCGAAACCAGACGAGCT
ACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTATA
GGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTAG
TTCAACTTTAAATTTGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAGTC
CAAAGAGGAACAGCTCTTTGGACACTAGGAAAAAACCTTGTAGAGAGAGTAAAAAATTTA

We're going to *need* the right algorithms...

# Strings are well studied

Many kinds of data are string-like: books, web pages, files on your hard drive, medical records, chess games, ...

Algorithms for one kind of string are often applicable to others:

Regular expression matching can find files on your filesystem (grep), or bad network packets (snort)

Indexes for books and web pages (inverted indexing) can be used to index DNA sequences

Methods for understanding speech (HMMs) can be used to understand handwriting or identify genes in genomes

# Strings come from somewhere

Processes that give rise to real-world strings are complicated.  It helps to understand them.

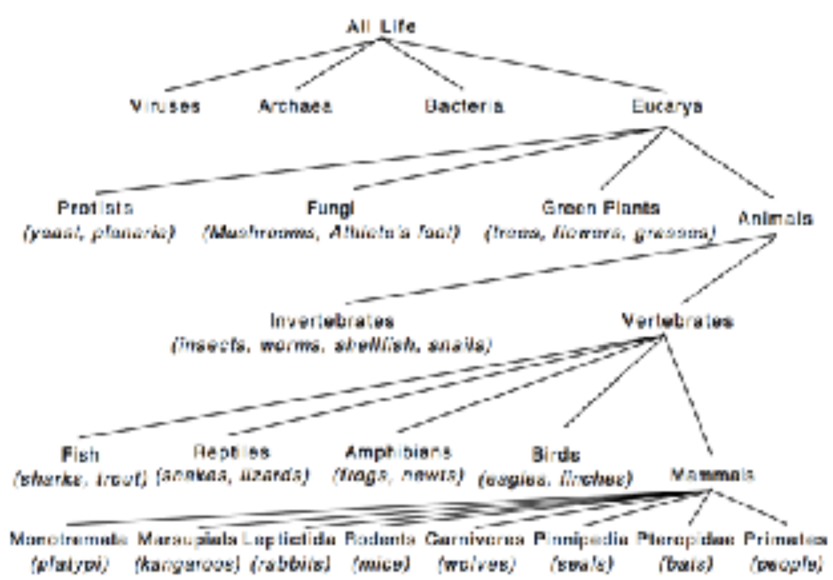
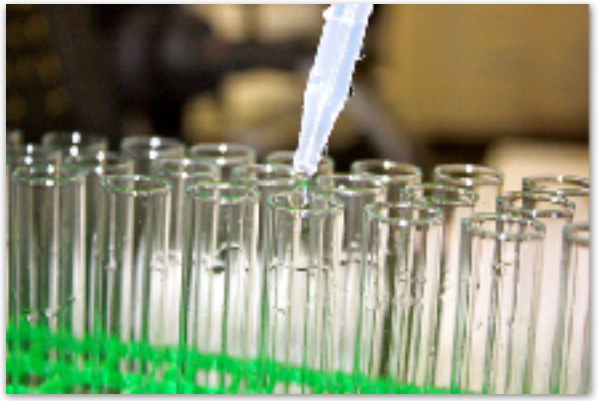
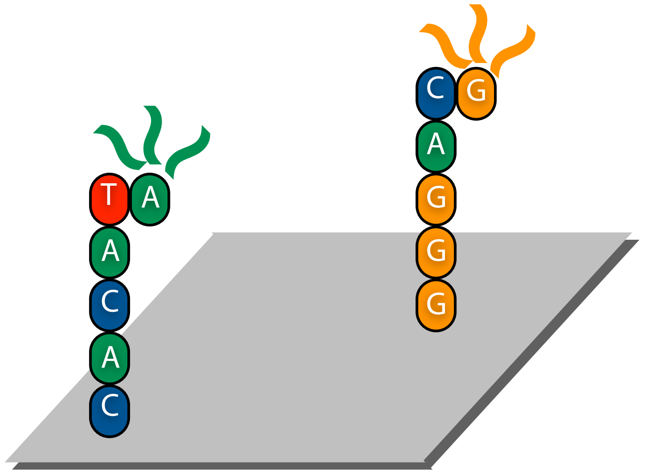



Figure from: Hunter, Lawrence. "Molecular biology for computer scientists." *Artificial intelligence and molecular biology* (1993): 1-46.

1. Evolution: Mutation
Recombination
(Retro)transposition



2. Lab procedures: PCR
Cell line passages




3. Sequencing: Fragmentation bias
Miscalled bases

# Strings have structure

One way to model a string-generating process is with coin flips:

{  = A,  = C,  = G,  = T }

But such strings lack internal patterns ("structure") exhibited by real strings

> 40% of the human genome is covered by *transposable elements*, which copy-and-paste themselves across the genome and mutate

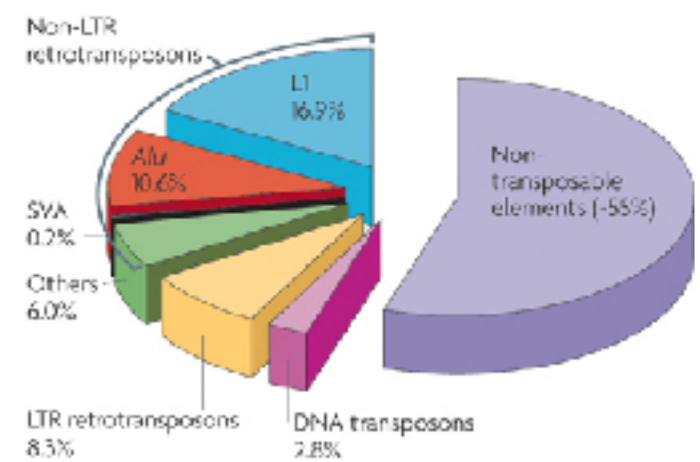



Image from: Cordaux R, Batzer MA. The impact of retrotransposons on human genome evolution. Nat Rev Genet. 2009 Oct;10(10):691-703

Slipped strand mis-pairing during DNA replication results in expansion or retraction of simple (*tandem*) repeats

••• ATATATATATATAT •••

••• ATATATATATATATATATAT •••

# String definitions

*String* $S$ is a finite sequence of characters

Characters are drawn from alphabet $\Sigma$

Usually, $\Sigma = \{ A, C, G, T \}$

$| S | =$ number of characters in $S$

```
>>> s = 'ACGT'
>>> len(s)
4
```

$\varepsilon$ is "empty string" $| \varepsilon | = 0$

```
>>> len('')
0
```

# String definitions

Positions within a string *S* are referred to with *offsets*

```
>>> s = 'ACGT'
>>> s[0]
'A'
>>> s[2]
'G'
```

Leftmost offset = 0 in Python and most other languages

# String definitions

*Concatenation* of $S$ and $T$, $ST$ = characters of $S$ followed by characters of $T$

```
>>> s = 'AACC'
>>> t = 'GGTT'
>>> s + t
'AACCGGTT'
```

# String definitions

*Substring* of *S* is a string occurring inside *S*

```
>>> s = 'AACCGGTT'
>>> s[2:6]
'CCGG' # substring of seq
```

*S* is a *substring* of *T* if there exist (possibly empty) strings *u* and *v* such that $T = uSv$

# String definitions

*Prefix* of *S* is a substring starting at the beginning of *S*

```
>>> s = 'AACCGGTT'
>>> s[0:6]
'AACCGG' # prefix
>>> s[:6] # same as above
'AACCGG'
```

*S* is a *prefix* of *T* if there exists a string *u* such that…

# String definitions

*Prefix* of *S* is a substring starting at the beginning of *S*

```
>>> s = 'AACCGGTT'
>>> s[0:6]
'AACCGG' # prefix
>>> s[:6] # same as above
'AACCGG'
```

*S* is a *prefix* of *T* if there exists a string *u* such that $T = Su$

# String definitions

*Suffix* is substring ending at end of *S*

```
>>> s = 'AACCGGTT'
>>> s[4:8]
'GGTT' # suffix
>>> s[4:] # like s[4:len(s)]
'GGTT'
>>> s[-4:] # like s[len(s)-4:len(s)]
'GGTT'
```

*S* is a *suffix* of *T* if there exists a string *u* such that…

# String definitions

*Suffix* is substring ending at end of $S$

```
>>> s = 'AACCGGTT'
>>> s[4:8]
'GGTT' # suffix
>>> s[4:] # like s[4:len(s)]
'GGTT'
>>> s[-4:] # like s[len(s)-4:len(s)]
'GGTT'
```

$S$ is a *suffix* of $T$ if there exists a string $u$ such that $T = uS$

# String definitions

Usually assume alphabet $\Sigma$ is finite, with $O(1)$ elements

Nucleic acid alphabet: { A, C, G, T }

Amino acid alphabet: { A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, V }

*Occasionally* we'll consider what happens as $|\Sigma|$ grows

# String definitions

http://j.mp/CG_StrBasics

# Exact matching

Find places where *pattern P* occurs as a substring of *text T*.
Each such place is an *occurrence* or *match*.

Let $n = |P|$, and let $m = |T|$ Assume $n \leq m$

*Alignment*: a way of putting *P's* characters opposite *T's*.
May or may not correspond to an match.

```
P: word
T: There would have been a time for such a word
   Alignment 1:     word       Alignment 2: word
```

# Exact matching

What's a simple algorithm for exact matching?

P: `word`

T:
```
There would have been a time for such a word
word word word word word word word word word
 word word word word word word word word
  word word word word word word word word
   word word word word word word word word
    word word word word word word word word
```

One occurrence

Try all possible alignments. For each, check if it matches.
This is the *naïve algorithm*.

# Exact matching: naïve algorithm

```
def naive(p, t):
    occurrences = []
    for i in range(len(t) - len(p) + 1):  # loop over alignments
        match = True
        for j in range(len(p)):           # loop over characters
            if t[i+j] != p[j]:            # compare characters
                match = False             # mismatch; reject alignment
                break
        if match:
          occurrences.append(i)           # all chars matched; record
    return occurrences
```

*P*: **word**

*T*: **There would have been a time for such a word**

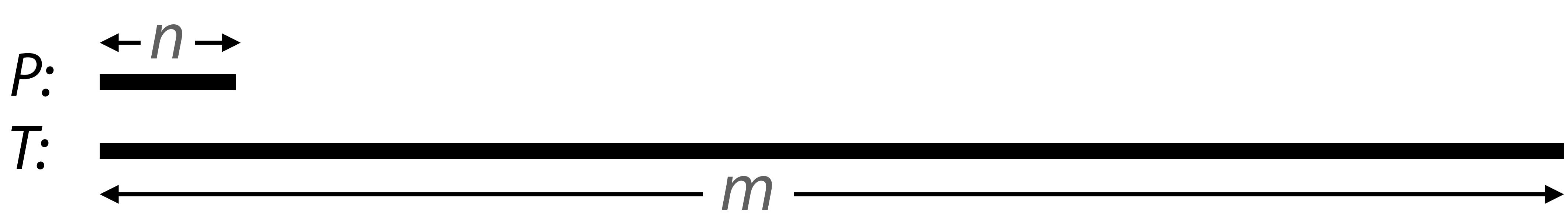
**word** **word** **word**

# Exact matching: naïve algorithm

$n = |P| \qquad m = |T|$

How many alignments are possible?

$m - n + 1$



# Exact matching: naïve algorithm

$n = |P| \qquad m = |T|$

Greatest # character comparisons possible?

$$n(m - n + 1)$$

*P:* **aaaa**

*T:* **aaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa**

**aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa**

**aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa**

**aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa**

**aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa**

**aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa**

# Exact matching: naïve algorithm

$n = |P| \qquad m = |T|$

**Least** # character comparisons possible?

$$m - \mathrm{n} + 1$$

*P:* **abbb**

*T:* **bbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbb**

```
abbb abbb abbb abbb abbb abbb abbb abbb abbb
 abbb abbb abbb abbb abbb abbb abbb abbb
  abbb abbb abbb abbb abbb abbb abbb abbb
   abbb abbb abbb abbb abbb abbb abbb abbb
    abbb abbb abbb abbb abbb abbb abbb abbb
```

# Exact matching: naïve algorithm

How many character comparisons in this example?

```
P: word
T: There would have been a time for such a word
   word word word word word word word word word
    word word word word word word word word
     word word word word word word word word
      word word word word word word word word
       word word word word word word word word
```

Hint: there are 41 possible alignments

# Exact matching: naïve algorithm

How many character comparisons in this example?

*P*: `word`

*T*: `There would have been a time for such a word`

```
word word word word word word word word word
 word word word word word word word word
  word word word word word word word word
   word word word word word word word word
    word word word word word word word word
```

40 mismatches + 6 matches = 46 character comparisons

Closer to the minimum (41) than the maximum (164)

# Exact matching: naïve algorithm

```
def naive(p, t):
    occurrences = []
    for i in range(len(t) - len(p) + 1):  # loop over alignments
        match = True
        for j in range(len(p)):           # loop over characters
            if t[i+j] != p[j]:            # compare characters
                match = False             # mismatch; reject alignment
                break
        if match:
          occurrences.append(i)           # all chars matched; record
    return occurrences
```

Even more naïve:
remove **break**

# Naïve algorithm implementation

http://bit.ly/CG_Naive

# Exact matching: better algorithms?

*P*: `word`

*T*: `There would have been a time for such a word`

`word`

*u* doesn't occur in *P*, so skip next two alignments

*P*: `word`

*T*: `There would have been a time for such a word`

`word`

`word` skip!

`word` skip!

`word`

We'll take such ideas further when we discuss Boyer-Moore