Practical Bioinformatics

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Dictionaries

```
dictionary = {"A":"T","T":"A","G":"C","C":"G"}
dictionary["G"]
dictionary["N"] = "N"
dictionary.has_key("C")
```

Dictionaries

```
geneticCode = {"TTT":"F","TTC":"F","TTA":"L","TTG":"L",
               "CTT":"L","CTC":"L","CTA":"L","CTG":"L",
               "ATT":"I","ATC":"I","ATA":"I","ATG":"M",
               "GTT":"V","GTC":"V","GTA":"V","GTG":"V",

               "TCT":"S","TCC":"S","TCA":"S","TCG":"S",
               "CCT":"P","CCC":"P","CCA":"P","CCG":"P",
               "ACT":"T","ACC":"T","ACA":"T","ACG":"T",
               "GCT":"A","GCC":"A","GCA":"A","GCG":"A",

               "TAT":"Y","TAC":"Y","TAA":"*","TAG":"*",
               "CAT":"H","CAC":"H","CAA":"Q","CAG":"Q",
               "AAT":"N","AAC":"N","AAA":"K","AAG":"K",
               "GAT":"D","GAC":"D","GAA":"E","GAG":"E",

               "TGT":"C","TGC":"C","TGA":"*","TGG":"W",
               "CGT":"R","CGC":"R","CGA":"R","CGG":"R",
               "AGT":"S","AGC":"S","AGA":"R","AGG":"R",
               "GGT":"G","GGC":"G","GGA":"G","GGG":"G"}
```

Exercise: Transforming sequences

1. Write a function to return the antisense strand of a DNA sequence in 3'→5' orientation.
2. Write a function to return the complement of a DNA sequence in 5'→3' orientation.
3. Write a function to translate a DNA sequence

Why compare sequences?

Why compare sequences?

- To find genes with a common ancestor
- To infer conserved molecular mechanism and biological function
- To find short functional motifs
- To find repetitive elements within a sequence
- To predict cross-hybridizing sequences (*e.g.*, in RNAi or CRISPR design)
- To find genomic origin of imperfectly sequenced or spliced fragments (*e.g.*, in deep sequencing experiments)
- To predict nucleotide secondary structure

Nomenclature

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Orthologs	homologs arising from speciation.
Paralogs	homologs arising from duplication and divergence within a single genome.

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Homologs heritable elements with a common evolutionary origin.

Orthologs homologs arising from speciation.

Paralogs homologs arising from duplication and divergence within a single genome.

Xenologs homologs arising from horizontal transfer.

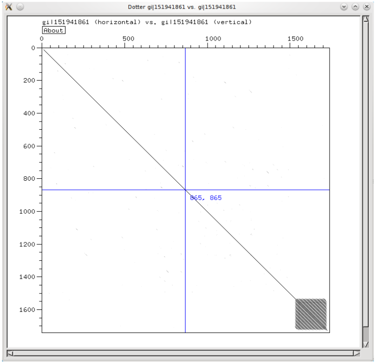
Onologs homologs arising from whole genome duplication.

Types of alignments

Global Alignment Each letter of each sequence is aligned to a letter or a gap (*e.g.*, Needleman-Wunsch)

Local Alignment An optimal pair of subsequences is taken from the two sequences and globally aligned (*e.g.*, Smith-Waterman)

Dotplots



Dotter gi|151941861 vs. gi|151941861

gi|151941861 (horizontal) vs. gi|151941861 (vertical)

1. Unbiased view of all ungapped alignments of two sequences
2. Noise can be filtered by applying a smoothing window to the diagonals.

Exercise: Scoring an ungapped alignment

```
s ={"A" :{"A" :  1.0 ,"T" :-1.0 ,"G" :-1.0 ,"C" :-1.0},
    "T" :{"A" :-1.0 ,"T" :  1.0 ,"G" :-1.0 ,"C" :-1.0},
    "G" :{"A" :-1.0 ,"T" :-1.0 ,"G" :  1.0 ,"C" :-1.0},
    "C" :{"A" :-1.0 ,"T" :-1.0 ,"G" :-1.0 ,"C" :  1.0}}
```

Exercise: Scoring an ungapped alignment

```
s ={"A":{"A": 1.0,"T":-1.0,"G":-1.0,"C":-1.0},
    "T":{"A":-1.0,"T": 1.0,"G":-1.0,"C":-1.0},
    "G":{"A":-1.0,"T":-1.0,"G": 1.0,"C":-1.0},
    "C":{"A":-1.0,"T":-1.0,"G":-1.0,"C": 1.0}}
```

$$S(x,y) = \sum_{i}^{N} s(x_i, y_i)$$

Exercise: Scoring an ungapped alignment

$$\begin{aligned}
s = \{ & "A" : \{"A" : \ 1.0, "T" : -1.0, "G" : -1.0, "C" : -1.0\}, \\
& "T" : \{"A" : -1.0, "T" : \ 1.0, "G" : -1.0, "C" : -1.0\}, \\
& "G" : \{"A" : -1.0, "T" : -1.0, "G" : \ 1.0, "C" : -1.0\}, \\
& "C" : \{"A" : -1.0, "T" : -1.0, "G" : -1.0, "C" : \ 1.0\}\}
\end{aligned}$$

$$S(x, y) = \sum_{i}^{N} s(x_i, y_i)$$

1. Given two equal length sequences and a scoring matrix, return the alignment score for a full length, ungapped alignment.

Exercise: Scoring an ungapped alignment

$$\begin{aligned} s = \{ & "A" : \{"A" : \ 1.0, "T" : -1.0, "G" : -1.0, "C" : -1.0\}, \\ & "T" : \{"A" : -1.0, "T" : \ 1.0, "G" : -1.0, "C" : -1.0\}, \\ & "G" : \{"A" : -1.0, "T" : -1.0, "G" : \ 1.0, "C" : -1.0\}, \\ & "C" : \{"A" : -1.0, "T" : -1.0, "G" : -1.0, "C" : \ 1.0\}\} \end{aligned}$$

$$S(x, y) = \sum_{i}^{N} s(x_i, y_i)$$

1. Given two equal length sequences and a scoring matrix, return the alignment score for a full length, ungapped alignment.

Exercise: Scoring a gapped alignment

1. Given two equal length gapped sequences (where "-" represents a gap) and a scoring matrix, calculate an alignment score with a -1 penalty for each base aligned to a gap.

Exercise: Scoring a gapped alignment

1. Given two equal length gapped sequences (where “-” represents a gap) and a scoring matrix, calculate an alignment score with a -1 penalty for each base aligned to a gap.
2. Write a new scoring function with separate penalties for opening a zero length gap (*e.g.*, G = -11) and extending an open gap by one base (*e.g.*, E = -1).

$$S_{gapped}(x,y) = S(x,y) + \sum_{i}^{gaps} (G + E * len(i))$$

Homework: Optimal ungapped alignment

$$S(x,y) = \sum_{i}^{N} s(x_i, y_i)$$

1. Given two sequences and a scoring matrix, find the offset that yields the best scoring ungapped alignment.