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BISC 478

HW3

In [1]:
```
from IPython.display import Image
from IPython.core.display import HTML

HTML("""
<style>
.output_png {
    display: table-cell;
    text-align: center;
    vertical-align: middle;
}
.output_jpeg {
    display: table-cell;
    text-align: center;
    vertical-align: middle;
}
</style>
""")
```
Out[1]:

In [2]:
```
import numpy as np
```

Question 1 [25 points]

Guide tree for MSA

Given below are five sequences:
S1: GATTCA; S2: GTCTGA; S3: GATATT, S4: GTCAGC, S5: GAGACA.
The pair-wise sequence alignments for S1-S4 are as follows:

In [3]:
```
Image('img1-1.jpg')
```
Out[3]:

```
S1: G A T - T C A        S1: G A T - T C A
S2: G - T C T G A        S3: G A T A T T -

S1: G A T T C A - -      S2: G - T C T G A
S4: G - T C - A G C      S3: G A T A T - T

S2: G T C T G A          S3: G A T - A T T
S4: G T C A G C          S4: G - T C A G C
```

A) [10 points] Find pairwise alignment of S5 with other sequences. Use match score = 1 and -1 for mismatch and gap.

In [4]:
```
def getMatch(x: 'char', y: 'char', match_score: int, penalty_mismatch: int):
    """
    compares x and y and returns correct score depending on match or mismatch
    """
    if x == y:
        return match_score
    else:
        return penalty_mismatch

def fillM(X: str, Y: str, match_score: int, penalty_mismatch: int, penalty_gap: int):
    # create empty memoization matrix of size |X|+1 x |Y|+1
    M = np.empty((len(Y)+1,len(X)+1), dtype='int64')
    # initialize matrix with necessary default values
    for i in range(len(X)+1):
        M[0,i] = i * penalty_gap
    for j in range(len(Y)+1):
        M[j,0] = j * penalty_gap
    # fill in array
    # j >> jth row, i >> ith column
    for j in range(1, len(Y)+1):
        for i in range(1, len(X)+1):
            match = M[j-1,i-1] + getMatch(X[i-1], Y[j-1], match_score, penalty_mismatch)
            y_gap = M[j-1,i] + penalty_gap
            x_gap = M[j,i-1] + penalty_gap
            M[j,i] = max(match, y_gap, x_gap)
    return M

def findAlign(X: str, Y: str, M: 'numpy.ndarray', match_score: int, penalty_mismatch: int, penalty_gap: int):
    xlen = M.shape[1]
    ylen = M.shape[0]

    X = '_' + X
    Y = '_' + Y
    X_align = ''
    Y_align = ''
    opt_row = ylen-1
    opt_col = xlen-1

    if xlen == 1:
        return X_align, Y[1:]
    if ylen == 1:
        return X[1:], Y_align

    for row in range(ylen-1, -1, -1):
        for col in range(xlen-1, -1, -1):
            if opt_row == 0 and opt_col == 0:
                break
            if opt_row != row or opt_col != col:
                continue
            if M[row, col] == M[row-1, col-1] + getMatch(X[col], Y[row], match_score, penalty_mismatch):
                X_align += X[col]
                Y_align += Y[row]
                opt_row -= 1
                opt_col -= 1
            elif M[row, col] == M[row-1, col] + penalty_gap:
                X_align += '_'
                Y_align += Y[row]
                opt_row -= 1
            elif M[row, col] == M[row, col-1] + penalty_gap:
                X_align += X[col]
                Y_align += '_'
                opt_col -= 1
    return X_align[::-1], Y_align[::-1]
```

In [5]:
```
sequences = ['GATTCA', 'GTCTGA', 'GATATT', 'GTCAGC', 'GAGACA']
match = 1
mismatch = -1
gap = -1

for i in range(len(sequences)-1):
    m = fillM(sequences[i], sequences[-1], match, mismatch, gap)
    print('sequences:', i+1, len(sequences))
    print(findAlign(sequences[i], sequences[-1], m, match, mismatch, gap))
```

```
sequences: 1 5
('GATTCA', 'GAGACA')
sequences: 2 5
('GTCTGA', 'GAGACA')
sequences: 3 5
('GATATT', 'GAGACA')
sequences: 4 5
('GTCAG_C_', 'G__AGACA')
```

B) [15 points] Construct a guide tree for MSA for these sequences.

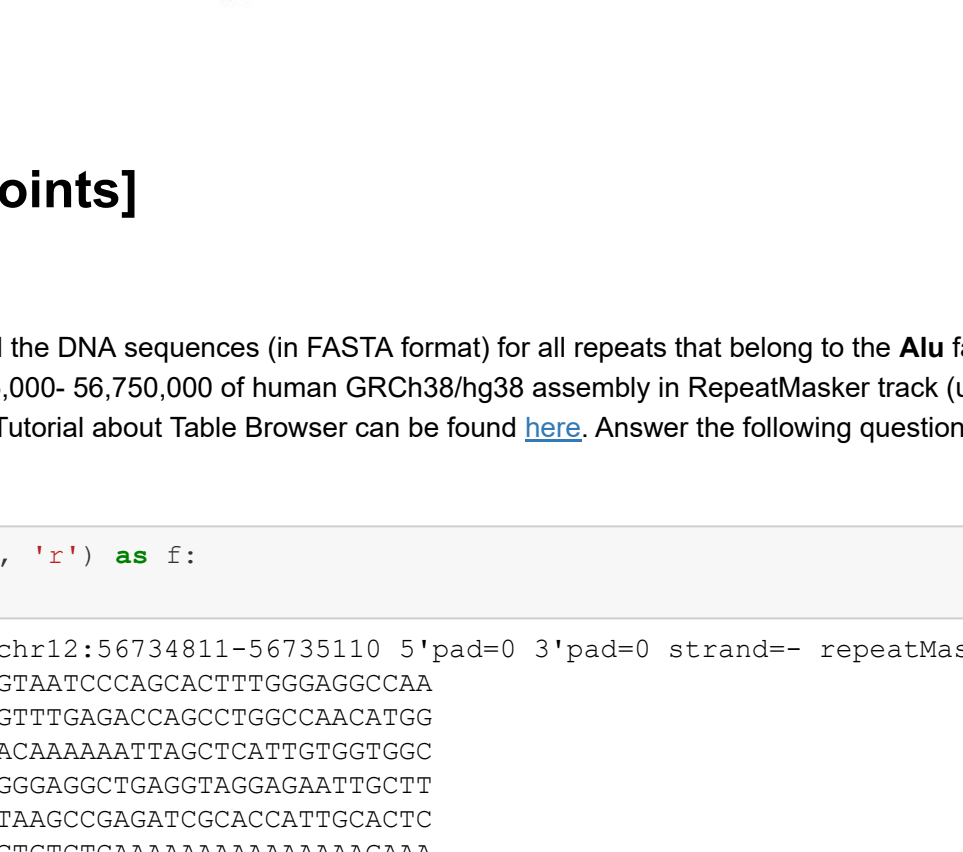
In [6]:
```
def getDistanceScore(x: 'char', y: 'char', match: int, mismatch: int, gap: int):
    d_mismatch = mismatch * -1 + match
    d_gap = gap * -1 + match
    d_match = match * -1 + match
    if x == y:
        return d_match
    elif x == '-' or y == '-':
        return d_gap
    else:
        return d_mismatch

def getDistance(X: str, Y: str, match: int, mismatch: int, gap: int):
    assert len(X) == len(Y)
    d = 0
    for i in range(len(X)):
        d += getDistanceScore(X[i], Y[i], match, mismatch, gap)
    return d

def fillDistanceM(sequences: list, match: int, mismatch: int, gap: int):
    M = np.empty((len(sequences), len(sequences)), dtype='int64')
    for i in range(len(sequences)):
        for j in range(len(sequences)):
            m = fillM(sequences[i], sequences[j], match, mismatch, gap)
            X, Y = findAlign(sequences[i], sequences[j], m, match, mismatch, gap)
            M[i, j] = getDistance(X, Y, match, mismatch, gap)
    return M

def convertToDict(D):
    distances = {}
    for i in range(D.shape[0]):
        for j in range(D.shape[1]):
            if i != j:
                distances[(str(i+1),str(j+1))] = D[i,j]
                distances[(str(j+1),str(i+1))] = D[i,j]
    return distances
```

In [7]:
```
class TreeNode:
    def __init__(self, key, distance, left, right):
        self.key = key
        self.distance = distance
        self.left = left
        self.right = right
        if left is None and right is None:
            self.leaves = 1
        elif left is None:
            self.leaves = self.right.leaves
        elif right is None:
            self.leaves = self.left.leaves
        else:
            self.leaves = self.left.leaves + self.right.leaves

    def print_helper(self):
        if self.left is None and self.right is None:
            return (self.key, self.distance, (), ())
        elif self.left is None:
            return (self.key, self.distance, (), self.right.print_helper())
        elif self.right is None:
            return (self.key, self.distance, self.left.print_helper(), ())
        else:
            return (self.key, self.distance, self.left.print_helper(), self.right.print_helper())

    def print(self):
        print(self.print_helper())

def findClosestPair(distances):
    """
    takes dictionary of distances and returns the key for the pair of nodes that are closest
    :param distance: dictionary of distances
    :return: key for the pair of nodes that are closest
    """
    key_min = list(distances.keys())[0]
    for key in distances:
        if distances[key] < distances[key_min]:
            key_min = key
    return key_min

def calcDist(new_node, node, distances):
    """
    calculates the distance between a newly made node and another node
    :param new_node: new TreeNode
    :param node: TreeNode
    :param distances: dictionary containing all the distances of parentless nodes (aside from children of new node)
    :return: distance between the new node and another node
    """
    key = (new_node.key, node.key)
    if key in distances:
        return distances[key]
    left = new_node.left
    right = new_node.right
    if node == left or node == right:
        return distances[(left.key, right.key)] / 2
    distance_left = distances[(left.key, node.key)] * left.leaves
    distance_right = distances[(right.key, node.key)] * right.leaves
    distance = (distance_left + distance_right) / new_node.leaves
    return distance

def updateDist(distances, new_node, nodes):
    """
    updates the dictionary by adding the distances between the new node and all the other nodes
    and removing old distances
    :param distances: dictionary of distances
    :param new_node: newly made TreeNode
    :param nodes: dictionary that maps keys to TreeNodes that do not have parent
    :return: updated dictionary
    """
    left = new_node.left.key
    right = new_node.right.key

    # add new distances
    for key in nodes:
        distance = calcDist(new_node, nodes[key], distances)
        distances[(key, new_node.key)] = distance
        distances[(new_node.key, key)] = distance
    # remove old distances
    keys = list(distances.keys())
    for key in keys:
        if new_node.key in key:
            continue
        if key[0] not in nodes or key[1] not in nodes:
            del distances[key]
    return distances

def upgma(distances, leafList):
    # dict for all the nodes that do not have a parent
    # maps key to node
    nodes = {}
    # create TreeNodes for all leaf nodes
    for leaf in leafList:
        node = TreeNode(leaf, 0, None, None)
        nodes[leaf] = node
    # remove all distances to self
    keys = list(distances.keys())
    for key in keys:
        if key[0] == key[1]:
            del distances[key]
    # add to tree using upgma until root reached
    while len(nodes) > 1:
        # instantiate new parent node
        key_min = findClosestPair(distances)
        key = '(' + key_min[0] + ',' + key_min[1] + ')'
        left = nodes[key_min[0]]
        right = nodes[key_min[1]]
        new_node = TreeNode(key, -1, left, right)
        # calculate distance to children
        dist_left = calcDist(new_node, new_node.left, distances)
        dist_right = calcDist(new_node, new_node.right, distances)
#       print(new_node.key, new_node.left.key, new_node.right.key, dist_left, dist_right)
        assert dist_left == dist_right
        new_node.distance = dist_left
        # remove children from nodes dict
        del nodes[key_min[0]]
        del nodes[key_min[1]]
        # get updated distances & remove distances of children
        distances = updateDist(distances, new_node, nodes)
        # add new node into nodes dict
        nodes[key] = new_node
#       print(nodes.keys())
#       print(distances)
    # return root
    key_root = list(nodes.keys())[0]
    return nodes[key_root]
```

In [8]:
```
D = fillDistanceM(sequences, match, mismatch, gap)
distances = convertToDict(D)
# print(distances)
leaves = []
for i in range(5):
    leaves.append(str(i+1))
root = upgma(distances, leaves)
root.print()
```

```
('((1,5),3)', 3.8333333333333335, ('(1,5)', 2.0, ('1', 0, (), ()), ('5', 0, (), ())), ('3', 0, (), ())), ('(2,4)', 2.0, ('2', 0, (), ()), ('4', 0, (), ())))
```

In [9]:
```
Image('img1-2.jpg')
```
Out[9]:



Question 2 [20 points]

MSA of Alu repeats

Go to UCSC Table Browser. Find the DNA sequences (in FASTA format) for all repeats that belong to the **Alu** family, and are located within the genomic region chr12:56,735,000- 56,750,000 of human GRCh38/hg38 assembly in RepeatMasker track (under repeats group). Select output format to be "sequence". Tutorial about Table Browser can be found here. Answer the following questions based on the output from the Table Browser.

In [10]:
```
with open('result.FASTA', 'r') as f:
    print(f.read())
```

```
>hg38_rmsk_AluSx3 range=chr12:56734811-56735110 5'pad=0 3'pad=0 strand=- repeatMasking=none
GACCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCAA
AGTGGGTGAATCATGAGGTCAGGAGTTTGAGACCAGCCTGGCCAACATGG
TGAAACCCTATCTCTACTAAAAATACAAAAAATTAGCTCATTGTGGTGGC
GGGCACCTATAATCCCAGCTAGTCGGGAGGCTGAGGTAGGAGAATTGCTT
GAACCTGGGAGGCGGAAGTTGCAGTAAGCCGAGATCGCACCATTGCACTC
CAGCCTGGGCAACAGAGTGACACTCTGTCTCAAAAAAAAAAAAAAAGAAA
>hg38_rmsk_AluSc range=chr12:56735126-56735397 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGACTGA
GGCAGGTGGATCACGAGGTCAAGAGATCAAAACCATCTTGGACAGCATGG
TGAAACCCCGTCTCTACTAAAAATACAAAAACTTAGCCGGGCATGGTGGC
ACACACCTATAGTCCCAGCTACTCAGGAGGCTGAGGCAGGAGAATCGCTT
GAACTCGGGAGGCGGAGGTTCCCGAGCCAAGATTGCACCACTGCATACCA
GCCTGGCAACAGAGCAAGACTC
>hg38_rmsk_AluJr range=chr12:56735408-56735621 5'pad=0 3'pad=0 strand=- repeatMasking=none
CCAAAAGGGCGTGACCAGAGCCTGAGCAACACAAGACCTTGTCTCTACTA
AAAATAAAAAAATTAGCCAGCTGTGGTGGCACTCCCTGTGATCCCAGCTAC
TTGGGAGGCTGAGGTGGGAGGATCATTTAAGCCAGGGAAGTCAAAGCTGC
AGTGAGCTGCAATTGCACCACTGCATTCTAGCCTGGGCAAAAAAGCAAGA
CAGTGTCTCAAAAA
>hg38_rmsk_AluSx1 range=chr12:56735650-56735950 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCCAGGCGTAGTGGCTGATGCCTGTAGGCCCAGCACTTTGGGAGGCCGA
GGCGGGTGGATCACCTGAGGTCAGGAGTTCAAGACCAGCCTGGCCAACAT
GGCGAAACCCCATCTTTACTAAAAATACAAAAATTATCTGGGCGTCGTGG
CGGGCGCCTATAATCCTAGCTACTCGGGAGGCTGAGGCAGAAGAATCGCT
TGAACCCAGGAGGTGGAGGTTGCAATAAGCCGAGATTGCCCCACTGCACT
CCAGCCTGGGAGACAGAGCAAGACTCCATCTCAAAAAAAAAAAAACAAGA
A
>hg38_rmsk_AluSx1 range=chr12:56736016-56736327 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCAGGGTGCGGTGGCTCATGCCTATAATCCCAGCACTTTGGGAGGCCGA
GGCAGGTGGATTACGTGAGGTCGTGAGTTCGAGACCAGCCTGACCAACAT
GGAGAAACCCTGTCTCTAGTAAAAATACAAAAATTAGCTGGACGTCGTGG
CGGGCACCTGTAACTCCAGCTACTCAGGAGGCTGAGGCAGGAGAATTGCT
TGAACCCAGGAGGCGGAGGTTGCAATGAGCTGAGATTGCACCATTGCACA
CCAGCCTGGGTGACAGAGTAAGACTCTTTCTCTAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAA
>hg38_rmsk_AluSx range=chr12:56736509-56736803 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCCGGGCGCAGTAGCTCACGCCTGTAATCCCAGCACTCTGGGAGGTCAA
GGTGGGTGGATCACCTGAGGTCAGGAGTTTGGGACCAGCCTGGCCAACAC
GGTTAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCAGGCATGGTGG
TGCACACCTGTAGTCCCAGCTATTCAGGAGGCTGAGGCACAAGAATCACT
TGAGCCCGGGAGGCAGAGGTTGCAGGGAGCTGAAGTTGCGCCACTGCACT
CCAGCCTGGGAAACAGAGTGAGACTTCGTCTCAAAAAAAAAAAAAA
>hg38_rmsk_AluJb range=chr12:56736810-56737062 5'pad=0 3'pad=0 strand=- repeatMasking=none
CTCACACCTGTAATCCCAGCACTTTGGGAGGCCGAGGCAAGAGGAGCCTA
GGAGTTTGAGACCACCCTGGGCAACACAGAGAGACCCTGTCTCTCCAAAA
AAAAAAATTTAGCTAGACATGCTGGCAGGCACCTGTGGTCTCAGCTACTC
AAGAGGCTGTTTGAGCCCAGGAGGTTAAGGCTGCAGTAAGCCTTGACCAC
ACCACTGTACTCCAGCCTGGGTGTCAGAGAGAGACCTTGTCTCAAAATGA
AAA
>hg38_rmsk_AluSp range=chr12:56737352-56737648 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCCAGGCGCGATGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCCA
GGTGGGTTGATCACCTGAGGTCCTGAGTTCGAGACCGGCCTGACCAACAT
GGAGAAACCCTGTCTATCCTAAAAATACAGAATTAGCCGGCTGTGGTGGC
ACATGCCTGTAATCCCAGCTGCTCGGAAGGCAGAGGCAGGAGAATCGCTT
GAACTCAGGAGGTGGAGGTTGCGGTGAGCCAAGATCACGCCATTGCACTC
CAGCCTGGGCAACAAGAGCAAAACTCCGTCTCAAAAAAAAAAAAAAA
>hg38_rmsk_AluSx1 range=chr12:56737721-56738024 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCTGGGCGCAGTGGCTCACGCCTGTAATCCCGGCTCTTTGGGAGGCCGA
GGCAGGCAAATCACTTGAGGTCAGGAGTTCAAGACCAGCCTGGCCAACAT
GGTGAAACCCCAACTCTGCTAAATATACAAAAATCAACCAGGCATGGTGG
AGGGCACCTGTAATCCCAGCTACTCGGGAAGCTGAGTCAGGAGAATCGCT
TGAACCCAGGAGGCAGGGGTTGCAGTGAGCCAAGATTGTGCCACTGCACT
CCAGCCTGGGCGGCAGAGGGAGACTGTCTCAAATAAACAAACAAAAAAAA
AGAA
>hg38_rmsk_AluSc range=chr12:56738549-56738844 5'pad=0 3'pad=0 strand=- repeatMasking=none
GGCGCGGTGGCTCATGCCTGTAATCCCAACACTTTGGGAGGGCAAAGCGC
GTGGATCACAAGGTCAAGAGATCGAGACCATCCTGGCCAACATGGTGAAA
CCCTGTCTCTACTAAAAATACAAAAATTAGCTGCGCTTGGTGGCATATGC
CTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGAAGAATCACTTGAACCT
GGGAGGCGGAGGTTGCAGTGAGCCAAGATCGCACCACCACACTCCGGCCT
GGCAACAGAGCAAGACTCCGTCTCAAAAACAAAAACAAAAACAAAA
>hg38_rmsk_AluJr range=chr12:56739539-56739829 5'pad=0 3'pad=0 strand=- repeatMasking=none
GCTGGACATGGTCATTCACACCTGTAATCCCAGCAACTCAGGAGGCTGAG
GCAAGAGGATTGTTTGAGGCCAGGAGTTCTGGGCAACATAGTGAGACCCC
AACTCAACAAAAATTGAAAAACTGGCCAGGCCAGGAGCAGTAGCTCACGT
CTATAATCCTAGCACTTTGGGAGACAACTGAGGTGGGAGGATCACTTGAG
CCCAGGACATCAAGCCTGCAGTGAGCTATGACCATGCTACTGTATGTACT
CTAGCATGGGTGACAAAGTGAGGCATTAACTCTAAAAAAGA
>hg38_rmsk_AluSg7 range=chr12:56739858-56740164 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GCCAGGTGCAGTGGCTCACGCCTGTAATCCCAGCACTCTGGGAGGCTGAG
GAGGGTGGATCACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGT
GAAACCCCGTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGCGG
GTACCTGTAATCCCAGCTACTTGGGAGGGTGAGGCAGAGAATTGCTTGAA
CCTGGAAGGCAGAGGCTGCAGTGAGCCAAGATCGCGCCACTGTACTCCAG
CCTGGGTGACAGAGTGGGACTCTGTCTCGAAAAAAAAGGAAAGAAAAAAA
ACAAAAA
>hg38_rmsk_AluJb range=chr12:56740498-56740764 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCTGGGCGCAGTGGCTCTTGTCTGTAATCCCAGCACTTTGGGAGACTGG
GGCAGGTGAATTGCTTGAGCTCAAGAGTTCAAGACCAACCTGGGCAACAT
GGCAAAACCCTGTCTACAAAATATTAGCTGGCTGTGGTAGCACATGCCTG
TAGTACCAGCTACTCAGGAGGGTGAGGCAGAAGGATCGCTTGAGCCGATC
GGTGAGCCGAGATTGCACCAGTGCACTCCAGCCTGGGTGACAGAGTGAGA
CTCTTTCTCGAAAAAAA
>hg38_rmsk_AluJb range=chr12:56740808-56741105 5'pad=0 3'pad=0 strand=- repeatMasking=none
GTGGTAGCTTGCTCCTGTAATCCCAGCACTTGAGGAGGGCAAGGTGGGCA
AATCACTTGAGCCCCAGAGTCTAACACCAGCCTAGGCCACATGTCTAAAC
ACCCTTTGTACAAAAAATACAAAAATTAGCTAGACGTGGTGGTGCATGCC
TGTAGTTCCAGCTACTCAAGAGGCTGAGGCAGGAGGATCACTTGAGCCTG
GGAAGTTGAGGCTGCAGTGAGCTGTGATGGTGCCACTGCACTCCAGCCTG
GGCAACAGAGTGAGACCCTGTCTCAAAAAAAAGAAAAAAAGAAAGAAA
>hg38_rmsk_AluSx range=chr12:56741971-56742262 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GACTGGGCGTGGTGGCTCATGCCTGTACTCCCAGCACTTTGGGAGGCAGA
GGTGGGTGGATCACGTGAGGTCAGGAGATCGAGACCAGCCTGGCCAACAT
GGTGAAACCCCATCTCTACTAAAAATAGAAAAATCAGCAGGGCATGGTGG
TGCACATCTGTAATCCTAGCTACTCTGGAGGCTGAGGCAGGAAAATTGCT
TAAATCTGCAAGGTGAAGGTTGCAGTGAGCTGAGATTGTGCCACTGTGCT
ACAGCCTGGGCAACAGAGTGAGACTCCATCTCAACAACAAAA
>hg38_rmsk_AluSg range=chr12:56742302-56742597 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCCGGGCACAGTGGCTCATGCCTGTATTCCCAATATTTTGGGAGGCTGA
GGTGGGTGGATCATTTGAGACCAGCTTGGCTGACATGGTGAGACCCCGTC
TCTATAAAAACACAAAAATTAGCTGGGCGTGGTGGCGTGTGCCTGCAGTC
CCAGCTATTTGGGAGGCTGAGGCAGGAGAATTGTTTGAACCCGGGAGGCG
GAGGTTGCAGTAAGCCAAGATCACACCACTGCACACTCCAGCCTGGGCAA
CACAGTATAAGACTCCGTCTTAAAAACAACAACAACAACAAAAAAA
>hg38_rmsk_AluSq2 range=chr12:56744227-56744509 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGGCACGGTGGCTCACACCTGTAATCCCAGCATTTTGGGAGGCTGAGGTG
GGTGGATCACCTGAGGTCAAGAGTTCAAGACCAGCCTGAATCCCATCTCT
ATTAAAAATACAAAAAATTAGCTGGGCATGGTGGCGCATGCCTGTAATCC
TAGCTACTCGGGAGGCTGAGGCAGGAGAGTCGCTTGAACTCGGGAGGCAG
AGGTTGCAGTGAGCCGAGATCGCATCATTGCACTCTAGCCAGGGTGACAA
GAGCGAGACTCCATCTCAAAAAAAAAAGAAAAA
>hg38_rmsk_AluSx1 range=chr12:56744810-56745123 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCTGGACGCAGTGGCTCACACTTGTAATCCCAGCACTTTGAGAGGCTGA
GGCGGGCGGATCACCTGAGGTCAGGAGTTCGAGACCAGCCTGACCAATAT
GATGAAACCCTGTTTCCACCTGCCAACACGCCTGGCTAAATACAAAAATT
AGCCGGGTGTGGTGGCAAGTGCCTGTAATCCCAGCTACTTGGGAGGCTGA
GACAGGAGAATTGCTTGAACCCGGGACGCGGAGGTTGTGGTGAGCCAAGA
TAGCGCCACTGCACTCCAGCCTGGGTAACAGAGCAAGACTCCGTCTCAAA
AAAAAAAAAAAAAA
>hg38_rmsk_AluJo range=chr12:56745130-56745438 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCTGGATGTAGTGGCTCACACCTGTAATCTCAGCATTTTGGGAGGCCTGA
AGTGGGAGGATAGTTTGAGTTTAGGAGTTCAAGAACACCCTGGGCAATAT
AGTGAGACCTTGTTTCTGCAAAAATTAAAAAATTGGCTGGGCGTGGTGGC
GCATGCCTTTAGTCCCAGCTACTCAGGAGGCTGAGGTAGAAGGGTCACTT
GAGACCAGGAGGTCAAGGCTGCAGTGAGCTGTGGTCACGTTACCGTACTC
CAGCCTGGGTGACAGGGTGAGACCGTGTCTCAAAACAAAACAAAACAAAA
CAAAAAAA
>hg38_rmsk_AluSx1 range=chr12:56745658-56745954 5'pad=0 3'pad=0 strand=+ repeatMasking=none
GGCCAGTGTGGTGGCTCATGTCTGTAATCCCAGCACTTTGGGAGGCTGAG
GTGGGTGAATCACCTGAGGCTAGGAGTTCTAGGCCAGCCTGGCCAACATG
GCGAAACCCAGTCTTTACTAAAAATACAAAATTTAGCTGGGCACAGTGGC
AGGAGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATTGCTT
```

A) [8 points] How many Alu repeats are there in the result?

In [11]:
```
with open('result.FASTA', 'r') as f:
    i = 0
    for line in f:
        if line[0] == '>':
            i += 1
    print(i)
```

```
25
```

25 repeats

B) [2 points] How many unique repeat names are there in the result?

In [12]:
```
with open('result.FASTA', 'r') as f:
    masks = set()
    for line in f:
        if line[0] == '>':
            info = line.split()
            mask = info[0].split('_')[-1]
            masks.add(mask)
    print(len(masks))
```

```
14
```

14 unique repeat names

C) [10 points] Take any one sequence for the following repeats: AluJb,AluJo,AluJr,AluSc,AluSg,AluSp,AluSx and AluSz. Use the EBI multiple sequence alignment tool Clustal Omega to align these sequences.

1) What is the percentage identity between AluJo and AluSp?

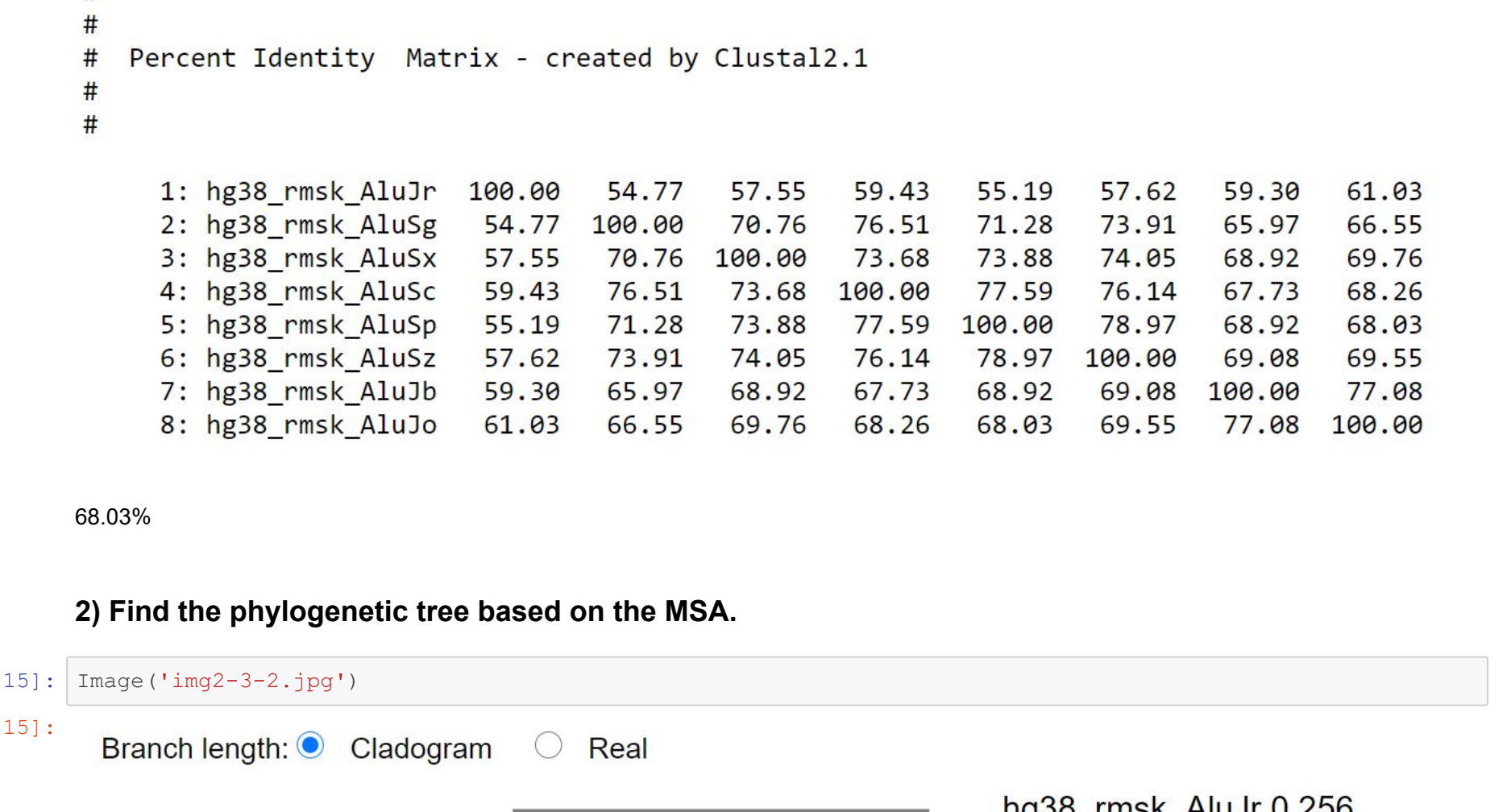
In [14]:
```
Image('img2-3-1.jpg')
```
Out[14]:

```
#
#
#  Percent Identity  Matrix - created by Clustal2.1
#
#

     1: hg38_rmsk_AluJr   100.00  54.77  57.55  59.43  55.19  57.62  59.30  61.03
     2: hg38_rmsk_AluJb    54.77 100.00  70.76  76.51  71.28  73.91  65.97  66.55
     3: hg38_rmsk_AluSc    57.55  70.76 100.00  73.68  73.88  74.05  68.92  69.76
     4: hg38_rmsk_AluSx    59.43  76.51  73.68 100.00  77.59  76.14  67.73  68.26
     5: hg38_rmsk_AluSp    55.19  71.28  73.88  77.59 100.00  78.97  68.92  68.03
     6: hg38_rmsk_AluSz    57.62  73.91  74.05  76.14  78.97 100.00  69.08  69.55
     7: hg38_rmsk_AluSg    59.30  65.97  68.92  67.73  68.92  69.08 100.00  77.08
     8: hg38_rmsk_AluJo    61.03  66.55  69.76  68.26  68.03  69.55  77.08 100.00
```

68.03%

2) Find the phylogenetic tree based on the MSA.

In [15]:
```
Image('img2-3-2.jpg')
```
Out[15]:



Question 3 [25 points]

De Bruijn graph

A) [5 points] Construct a De Bruijn graph for r1 = CGATTCTAAGT for k = 4?

In [16]:
```
def scanEdge(edge, sequences):
    indices = set()
    for i in range(len(sequences)):
        for j in range(len(sequences[i])-len(edge)+1):
            if edge == sequences[i][j:j+len(edge)]:
                indices.add((i, j))
    return indices

def enumerateEdges(sequences, k):
    edges = {}
    for i in range(len(sequences)):
        for j in range(len(sequences[i])-k+1):
            edge = sequences[i][j:j+k]
            if edge not in edges:
                indices = scanEdge(edge, sequences)
                edges[edge] = indices
    return edges

def scanNeighbors(node, edges):
    neighbors = set()
    for edge in edges:
        for j in range(len(edge)-len(node)+1):
            if node == edge[j:j+len(node)]:
                if j+len(node) < len(edge):
                    neighbors.add(edge[j+1:j+len(node)+1])
    return neighbors

def enumerateNodes(edges, k):
    nodes = {}
    for edge in edges:
        for j in range(len(edge)-(k-1)+1):
            node = edge[j:j+(k-1)]
            if node not in nodes:
                neighbors = scanNeighbors(node, edges)
                nodes[node] = neighbors
    return nodes
```

In [17]:
```
sequences1 = ['GTGCCG', 'GCGGCA', 'ATGTG', 'TGTGCC']
k1 = 3
```

In [18]:
```
sequence1 = ['CGATTCTAAGT']
k1 = 4
```

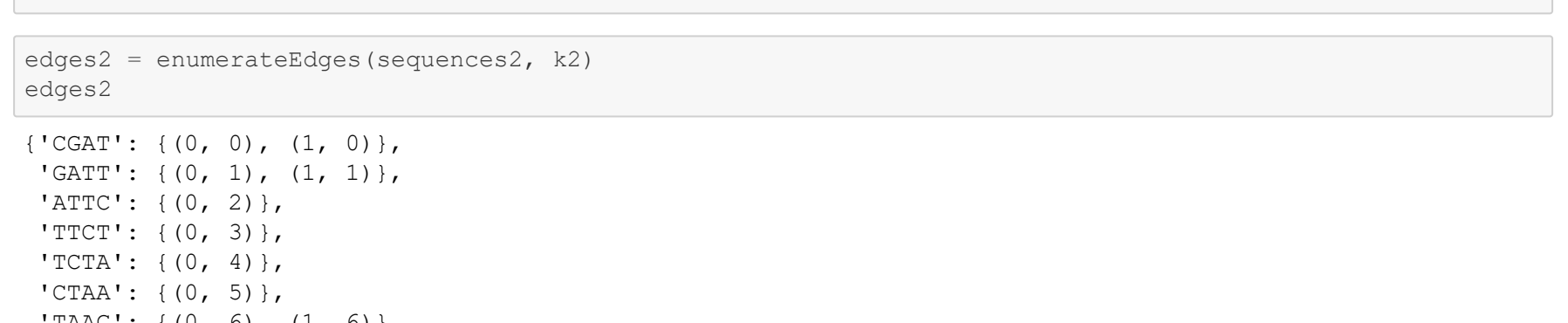
In [19]:
```
edges1 = enumerateEdges(sequence1, k1)
edges1
```
Out[19]:
```
{'CGAT': {(0, 0)},
 'GATT': {(0, 1)},
 'ATTC': {(0, 2)},
 'TTCT': {(0, 3)},
 'TCTA': {(0, 4)},
 'CTAA': {(0, 5)},
 'TAAG': {(0, 6)},
 'AAGT': {(0, 7)}}
```

```
In [20]: nodes1 = enumerateNodes(edges1, k1)
         nodes1
```

```
Out[20]: {'CGA': {'GAT'},
          'GAT': {'ATT'},
          'ATT': {'TTC'},
          'TTC': {'TCT'},
          'TCT': {'CTA'},
          'CTA': {'TAA'},
          'TAA': {'AAG'},
          'AAG': {'AGT'},
          'AGT': set()}
```

```
In [21]: Image('img3-1.jpg')
```

Out[21]:



B) [5 points] Now construct a De Bruijn graph for k = 4 given the information that there is a single-nucleotide variant (C/G) at position 6 of r1.

Hint: Now there are two possible sequences and you have to construct the graph for
r1 = CGATTCTAAGT r2 = CGATTGTAAGT

```
In [22]: sequences2 = ['CGATTCTAAGT', 'CGATTGTAAGT']
         k2 = 4
```

```
In [23]: edges2 = enumerateEdges(sequences2, k2)
         edges2
```

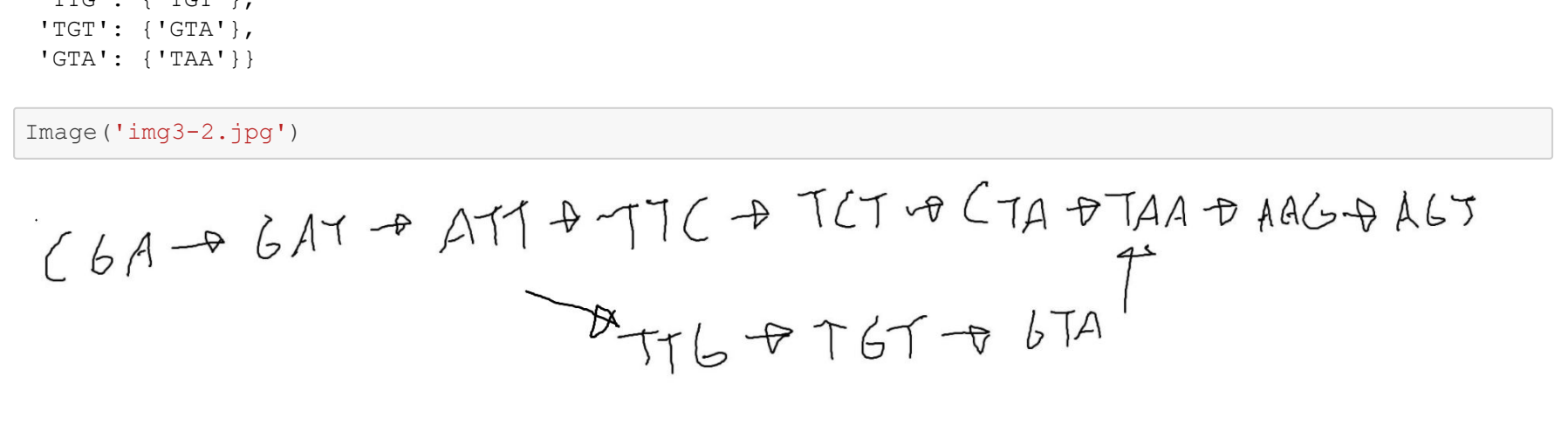
```
Out[23]: {'CGAT': {(0, 0), (1, 0)},
          'GATT': {(0, 1), (1, 1)},
          'ATTC': {(0, 2)},
          'TTCT': {(0, 3)},
          'TCTA': {(0, 4)},
          'CTAA': {(0, 5)},
          'TAAG': {(0, 6), (1, 6)},
          'AAGT': {(0, 7), (1, 7)},
          'ATTG': {(1, 2)},
          'TTGT': {(1, 3)},
          'TGTA': {(1, 4)},
          'GTAA': {(1, 5)}}
```

```
In [24]: nodes2 = enumerateNodes(edges2, k2)
         nodes2
```

```
Out[24]: {'CGA': {'GAT'},
          'GAT': {'ATT'},
          'ATT': {'TTC', 'TTG'},
          'TTC': {'TCT'},
          'TCT': {'CTA'},
          'CTA': {'TAA'},
          'TAA': {'AAG'},
          'AAG': {'AGT'},
          'AGT': set(),
          'TTG': {'TGT'},
          'TGT': {'GTA'},
          'GTA': {'TAA'}}
```

```
In [25]: Image('img3-2.jpg')
```

Out[25]:



C) [5 points] How many extra nodes are present in the graph (b) compared to the graph in part (a)?

```
In [26]: len(nodes2)-len(nodes1)
```

```
Out[26]: 3
```

D) [10 points] A 1Mb diploid genome is sequenced by a technology that produces perfect reads. There are no repeats in the genome longer than 25 bases, but there is a single-nucleotide variant every 1,000 bases. Assuming error-free sequencing by 100-base reads only from the forward strand and the spacing between two SNPs is greater than 50 bases, how many nodes are in the resulting De Bruijn graph built with k = 27

(100 - 27 + 1) * (1000000 / 100) + (1000000 / 1000) = 741000