PLNT4610 BIOINFORMATICS

MID-TERM EXAMINATION

08:30 - 9:45 Tuesday, October 23, 2012

Answer any combination of questions totalling to exactly 100 points. If you answer questions totalling more than 100 points, answers will be discarded at random until the total points equal 100. This exam is worth 20% of the course grade.

Hand in this question sheet along with your exam book. All questions must be answered in the exam book. The exam sheets will be shreded after the exam.

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1. (10 points) The Standard genetic code is shown below. If you think about comparing a DNA sequence verses a DNA database, or comparing a protein sequence vs. a protein database, how does the genetic code affect

a) the sensitivity of the search
b) the time required to do the search

```
TTT F Phe      TCT S Ser      TAT Y Tyr      TGT C Cys
TTC F Phe      TCC S Ser      TAC Y Tyr      TGC C Cys
TTA L Leu      TCA S Ser      TAA * Ter      TGA * Ter
TTG L Leu      TCG S Ser      TAG * Ter      TGG W Trp

CTT L Leu      CCT P Pro      CAT H His      CGT R Arg
CTC L Leu      CCC P Pro      CAC H His      CGC R Arg
CTA L Leu      CCA P Pro      CAA Q Gln      CGA R Arg
CTG L Leu      CCG P Pro      CAG Q Gln      CGG R Arg

ATT I Ile      ACT T Thr      AAT N Asn      AGT S Ser
ATC I Ile      ACC T Thr      AAC N Asn      AGC S Ser
ATA I Ile      ACA T Thr      AAA K Lys      AGA R Arg
ATG M Met      ACG T Thr      AAG K Lys      AGG R Arg

GTT V Val      GCT A Ala      GAT D Asp      GGT G Gly
GTC V Val      GCC A Ala      GAC D Asp      GGC G Gly
GTA V Val      GCA A Ala      GAA E Glu      GGA G Gly
GTG V Val      GCG A Ala      GAG E Glu      GGG G Gly
```

2. (10 points) What is the sequence complexity of the DNA molecules below?

a) 5'GCACTGTCGACACCA5'
   3'CGTGACAGCTGTGGT3'

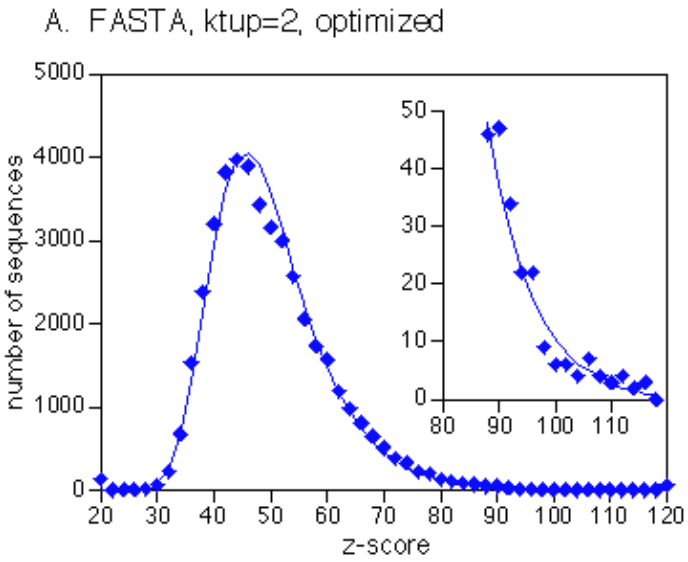
b) 5'GCACTGCACTGCACT3'
   3'CGTGACGTGACGTGA5'

3. (15 points) Create a table, similar to the one at right, that tells the time efficiency for each of the following tasks:

Choose from the following formulas for efficiency (one of them is NOT a correct answer):
$O(mn)$, $O(k^2 2^k n^k)$, $O(n^4)$, $O(n)$, $O(n^2)$

task	time efficiency
translate DNA to protein	
multiple sequence alignment	
sequence database search	
comparing a sequence with itself	
comparing two different sequences	

4. (15 points) The graph below illustrates scores from a FASTA search against a protein database. a) What is the distinction between the continuous curve and the diamonds?
b) This is not a normal, or Gaussian, Distribution, but rather, an Extreme Value Distribution (EVD). Based on the shape of the curve, what can you say about the difference between normally-distributed data, and data that falls on an EVD?
c) Draw a similar graph, showing what the curve would look like if many statistically significant "hits" were found in the database.



5. (5 points) It might seem trivial to generate the opposite strand of a sequence, so simple, in fact that you might be able to do it by a simple search and replace:

original sequence	AATCGTTTGCCCCCCTA
replace A with 1	11TCGTTTGCCCCCCT1
replace G with 2	11TC2TTT2CCCCCCT1
replace T with A	11AC2AAA2CCCCCCA1
replace C with G	11AG2AAA2GGGGGGA1
replace 1 with T	TTAG2AAA2GGGGGGAT
replace 2 with C	TTAGCAAACGGGGGGAT

What is the problem with this approach?

6. (10 points) Answer the following questions about the table below:

a) By random chance alone, what is the probability that an amino acid chosen from one protein will match a given amino acid from another protein?

b) By random chance alone, what is the probability that a nucleotide from one DNA sequence will match a nucleotide from another DNA sequence?

c) When comparing two amino acid sequences for similarity, if you use a k value of 3, how much would you expect to speed up the search?

d) Typically, proteins are only a few hundred amino acids long. How might that affect the actual speedup of the algorithm, given a k value of 3?

e) When comparing two DNA sequences, what is the probability a 20 base segment from one sequence will match a given 20 base segment from another sequence? Express the answer as an exponential number ie. scientific notation.

Table 2.	Avg. dist. between k-matches $\frac{1}{p^k}$			
Prob. of a match (**p**)	**k**= 2	3	4	5
0.050	400	8000		
0.075	178	2370		
0.100	100	1000		
0.150	44	296		
0.200	25	125		
0.250	16	64	256	1024
0.300	11	37	123	412
0.350	8	23	67	190
0.450	5	11	24	54
0.600	3	5	8	13
0.700	2	3	4	6
0.900	1	1	1	2

7. (20 points)

a) (10 points) Describe how scoring matrices are used in pairwise sequence comparisons. What do the numbers in the matrix correspond to. Give a general description of how they are derived. To help you answer this question, the commonly-used Blosum 45 matrix is given below.

b) (10 points) Also, draw a scoring matrix that could be used for comparing DNA sequences.

Blosum45 Amino Acid Similarity Matrix

	G	P	D	E	N	H	Q	K	R	S	T	A	M	V	I	L	F	Y	W	C
G	7																			
P	-2	9																		
D	-1	-1	7																	
E	-2	0	2	6																
N	0	-2	2	0	6															
H	-2	-2	0	0	1	10														
Q	-2	-1	0	2	0	1	6													
K	-2	-1	0	1	0	-1	1	5												
R	-2	-2	-1	0	0	0	1	3	7											
S	0	-1	0	0	1	-1	0	-1	-1	4										
T	-2	-1	-1	-1	0	-2	-1	-1	-1	2	5									
A	0	-1	-2	-1	-1	-2	-1	-1	-2	1	0	5								
M	-2	-2	-3	-2	-2	0	0	-1	-1	-2	-1	-1	6							
V	-3	-3	-3	-3	-3	-3	-3	-2	-2	-1	0	0	1	5						
I	-4	-2	-4	-3	-2	-3	-2	-3	-3	-2	-1	-1	2	3	5					
L	-3	-3	-3	-2	-3	-2	-2	-3	-2	-3	-1	-1	2	1	2	5				
F	-3	-3	-4	-3	-2	-2	-4	-3	-2	-2	-1	-2	0	0	0	1	8			
Y	-3	-3	-2	-2	-2	2	-1	-1	-1	-2	-1	-2	0	-1	0	0	3	8		
W	-2	-3	-4	-3	-4	-3	-2	-2	-2	-4	-3	-2	-2	-3	-2	-2	1	3	15	
C	-3	-4	-3	-3	-2	-3	-3	-3	-3	-1	-1	-1	-2	-1	-3	-2	-2	-3	-5	12

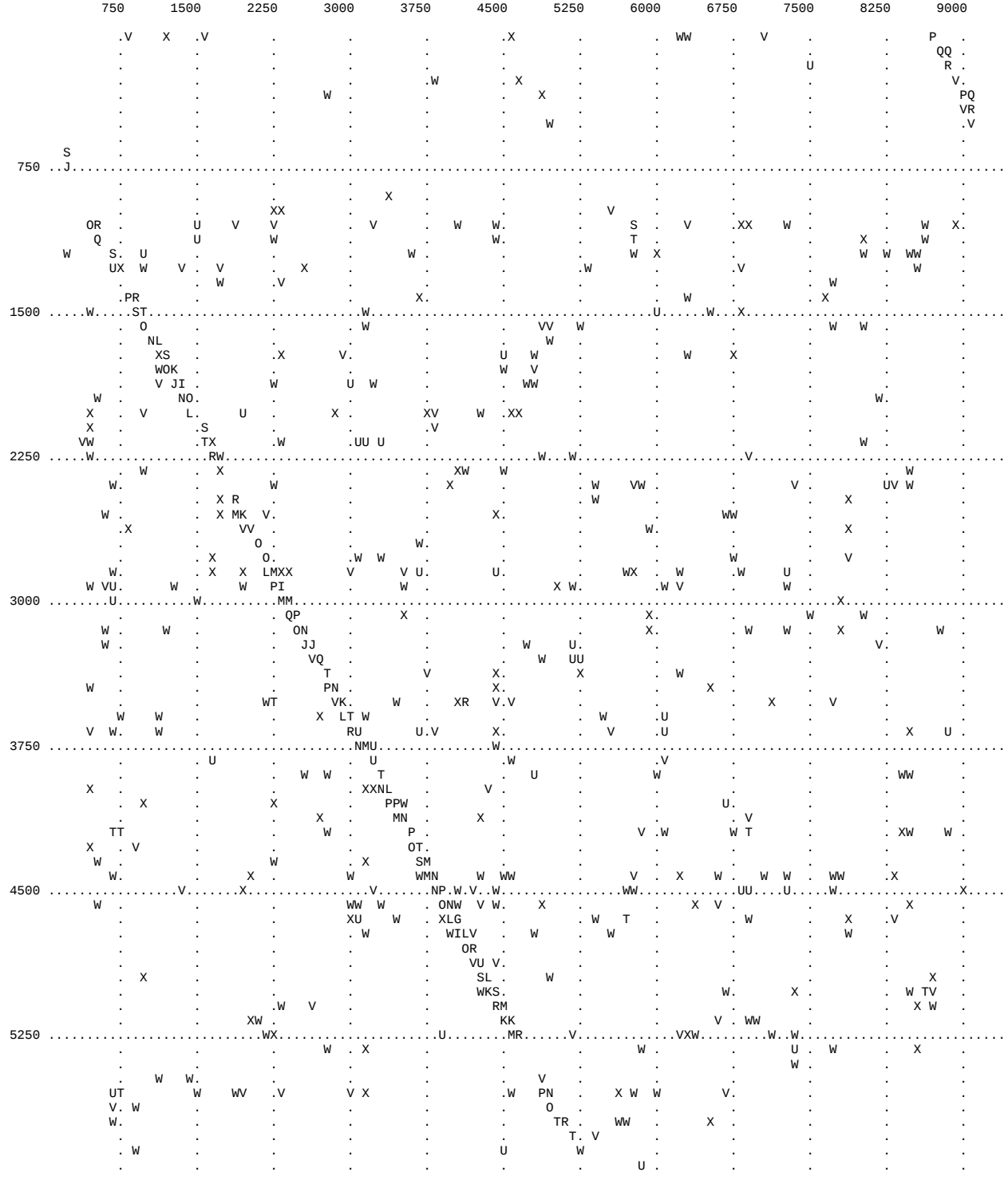
8. (15 points) Provide a word or phrase for a - e.

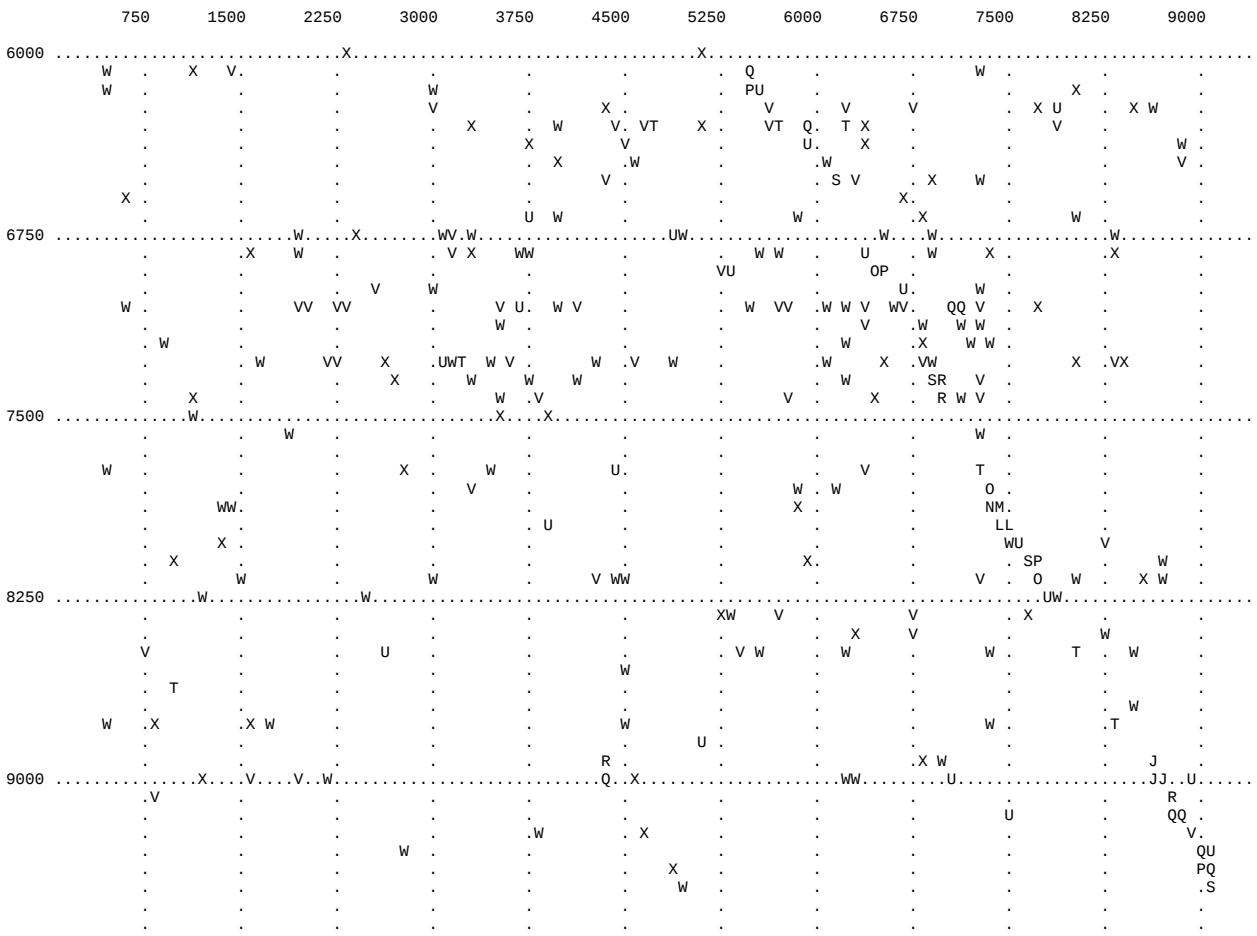
The programs CLUSTAL and TCOFFEE begin the process of creating a multiple alignment by creating a _____a_____ based on the _____b_____ between all sequences in the dataset. Next pairs of sequences that are most closely related to each other are _____c_____ by inserting gaps, if necessary. The resultant pairwise alignment is referred to as a profile. The algorithm repeats by aligning the most closely-related _____d_____ to each other. When all sequences have been included in the alignment, the alignment is complete. Since CLUSTAL/TCOFFEE use a heuristic alignment algorithm, the resultant alignment may not be the _____e_____ alignment.

9. (15 points) On the following pages, two RNA retroviruses, Human Immunodeficiency Virus (HIV) and Simian immunodeficiency virus (SIV) are compared in a dot-matrix similarity search. As well, an abbreviated annotation for the HIV sequence is also attached, showing the CDS (protein coding) features. For brevity, the corresponding features of SIV are not included.

a) Are all genes in HIV (ACCESSION NC_001802) also found in SIV (ACCESION NC_001549)?
b) What can you say about the intergenic regions of HIV, compared to SIV?
c) Are there any apparent major differences between the two genomes? What might be one possible explanation

```
D3HOM         Version  8/13/2001
X-axis: >NC_001802 (HIV)
Y-axis: >NC_001549 (SIV)
SIMILARITY RANGE:  25      MIN.PERCENT SIMILARITY:  55
SCALE FACTOR:    0.95      COMPRESSION:             75
```




750
1500
2250
3000
3750
4500
5250
6000
6750
7500
8250
9000
6000
6750
7500
8250
9000

```
GETOB          Version 1.3.2  13 Jun 2004
Please cite: Fristensky B. (1993) Feature expressions:
creating and manipulating sequence datasets.
Nucl. Acids Res. 21:5997-6003

NC_001802:CDS1
    join
        (
             336                 1637
             1637                 4642
        )


/gene="gag-pol"
/locus_tag="HIV1gp1"
/note="fusion protein consisting of the viral structural
proteins and enzymes; cleaved by the viral protease into
individual mature proteins; The processing products of the
Gag and Gag-Pol polyproteins were annotated with the help
of Pettit et al., 2003 and references therein; Pr160;
ribosomal slippage at slippery sequence tttttta
(1631..1637)"
/codon_start=1
/product="Gag-Pol"
//-----------------------------------------------
NC_001802:CDS2

     336         1838


/gene="gag"
/locus_tag="HIV1gp2"
/note="The processing products of the Gag and Gag-Pol
polyproteins were annotated with the help of Pettit et
al., 2003 and references therein"
/codon_start=1
/product="Pr55(Gag)"
//-----------------------------------------------
NC_001802:CDS3

     4587         5165


/gene="vif"
/locus_tag="HIV1gp3"
/note="p23; viral infectivity factor; viral accessory
protein important for virus replication in vivo"
/codon_start=1
/product="Vif"
//-----------------------------------------------
NC_001802:CDS4
    join
        (
             5105                5319
             5321                5396
        )

/gene="vpr"
/locus_tag="HIV1gp4"
/exception="artificial frameshift"
/note="p15; viral protein R; viral accessory protein
important for virus replication in vivo; involved in the
nuclear import of the HIV-1 preintegration complex;
induces G2 cell cycle arrest; influences mutation rates
during viral DNA synthesis; An artificial frameshift
eliminating the orf-disrupting nucleotide at position 5320
is introduced to obtain the typical HIV-1 Vpr protein
sequence. For this particular HIV-1 strain, HXB2, only a
short (78 amino acid long) variant of the Vpr sequence can
be obtained by translation of nucleotides 5105 through
5341 without the frameshift"
/codon_start=1
/product="Vpr"
//-----------------------------------------------
NC_001802:CDS5
    join
        (
             5377                5591
             7925                7970
        )

/gene="tat"
/locus_tag="HIV1gp5"
/note="p14; transcriptional activator; viral regulatory
protein required for virus replication; transactivates the
viral LTR promoter through interactions with cellular
transcription factors; associated with pathogenic effects
of the virus; the length of Tat varies depending on virus
strain or clade"
/codon_start=1
/product="Tat"
//-----------------------------------------------
NC_001802:CDS6
    join
        (
             5516                5591
             7925                8199
        )

/gene="rev"
/locus_tag="HIV1gp6"
/note="p19; regulator of expression of virion proteins;
prevents splicing of viral RNA; shuttles unspliced viral
RNA to the cytoplasm for expression of viral proteins and
incorporation of full length viral genomic RNA into
virions"
/codon_start=1
/product="Rev"
//-----------------------------------------------
NC_001802:CDS7
     5608         5856

/gene="vpu"
/locus_tag="HIV1gp7"
/note="p16; viral protein U; viral accessory protein
important for virus replication in vivo; promotes
degradation of CD4 and down-regulates cell surface
expression of MHC class I proteins; helps mediate
efficient virus particle release from infected cells;
reported to induce apoptosis by suppressing the nuclear
factor kappaB-dependent expression of antiapoptotic
factors; may attenuate the level of Env precursor(gp160)
biosynthesis; Vpu and gp160 are translated from different
reading frames of the same bicistronic mRNA"
/codon_start=1
/product="Vpu"
//-----------------------------------------------
NC_001802:CDS8
     5771         8341

/gene="env"
/locus_tag="HIV1gp8"
/note="gp160; envelope glycoprotein; envelope polyprotein;
cleaved by cellular proteases into mature proteins gp120
and gp41"
/codon_start=1
/product="Envelope surface glycoprotein gp160, precursor"
//-----------------------------------------------
NC_001802:CDS9
     8343         8963

/gene="nef"
/locus_tag="HIV1gp9"
/note="p27; negative factor; viral accessory protein;
important for virus replication in vivo; determinant of
HIV-1 pathogenesis; down-regulates cell surface CD4 and
MHC class I molecules; enhances virus infectivity through;
interactions with multiple cellular signaling proteins;
This particular nucleotide sequence has a premature stop
codon in place of a well-conserved tryptophan codon at
position 8712-8714 that truncates the HIV1 Nef protein
sequence to a 123 amino acids-long N-terminal portion (not
shown)"
/codon_start=1
/transl_except=(pos:8712..8714,aa:Trp)
/product="Nef"
```