CMSC423: Bioinformatic Algorithms, Databases and Tools
Lecture 9

inexact alignment

dynamic programming, gapped alignment

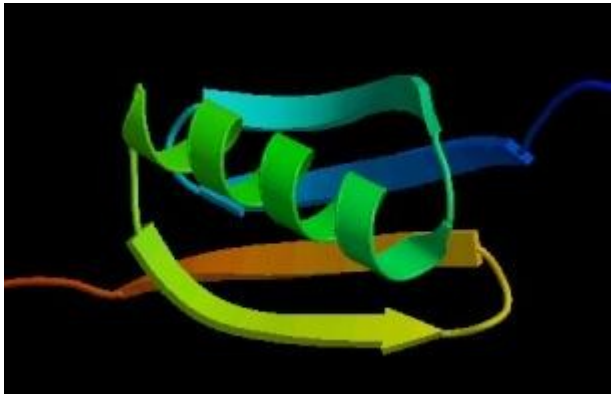
Inexact alignment

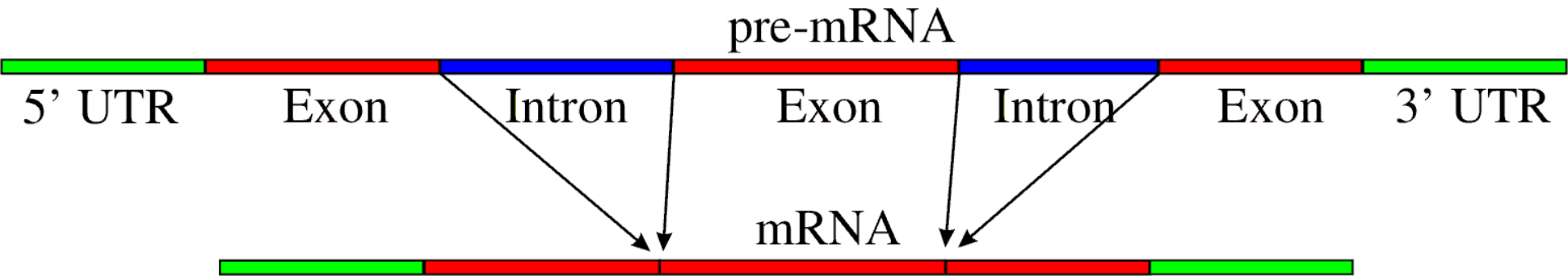
Inexact matching: why?

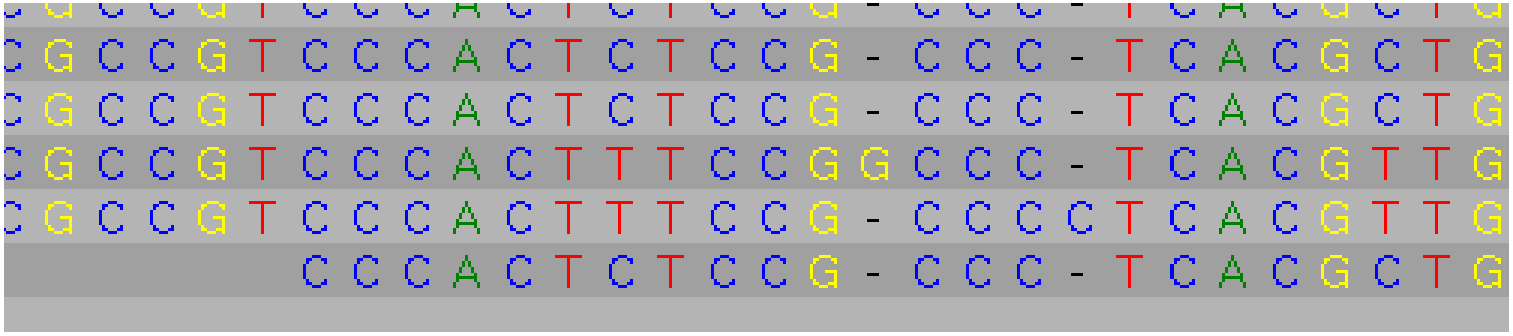
- Redundancy in genetic code: nucleotide sequence may differ, but proteins the same

```
S   Y   P   T   D
TCTTATCCTACTGAT
TCATACCCCACAGAC
```

- Different amino-acid sequences still fold the same way: function unchanged (generally changing an amino-acid with a similar one doesn't affect protein function)
- Aligning ESTs (RNA sequences) to DNA need to account for gaps corresponding to exons
- Need to account for sequencing errors
- Read chap 6.1!!! (define: ortholog, paralog, homolog)




pre-mRNA
5' UTR
Exon
Intron
Exon
Intron
Exon
3' UTR
mRNA


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

Several hemoglobins

```
HBB_HUMAN       FFESFGDLSTPDAVMGNPKVKAHGKKVL-----GAFSDGLAHLDNLKGTF
HBB_HORSE       FFDSFGDLSNPGAVMGNPKVKAHGKKVL-----HSFGEGVHHLDNLKGTF
HBA_HUMAN       YFPHF-DLS-----HGSAQVKGHGKKVA-----DALTNAVAHVDDMPNAL
HBA_HORSE       YFPHF-DLS-----HGSAQVKAHGKKVG-----DALTLAVGHLDDLPGAL
MYG_PHYCA       KFDRFKHLKTEAEMKASEDLKKHGVTVL-----TALGAILKKKGHHEAEL
GLB5_PETMA      FFPKFKGLTTADQLKKSADVRWHAERII-----NAVNDAVASMDDTEKMS
LGB2_LUPLU      LFSFLKGTSEVP--QNNPELQAHAGKVFKLVYEAAIQLQVTGVVVTDATL
                 *  :   .        . .:: *.  :        :.   :
```

From http://bioinfo.cnio.es/docus/courses/SEK2003Filogenias/seq_analysis/multiple.html

Warm-up – Longest Common Subsequence

- Given two strings of letters, identify longest string of letters that occurs, in the same order, in both strings

AG C GTAG

G C G A

GTCAG A

	A	G	C	G	T	A	G
G		1		1			1
T					1		
C			1				
A	1					1	
G		1		1			1
A	1					1	

- Find the longest chain of 1s, moving to the right and down

Dynamic programming

- Idea: re-use previously computed information
- LCS[i,j] – longest common subsequence of strings S1[1..i], S2[1..j]

i

		A	G	C	G	T	A	G
	G		1		1			1
	T					1		
	C			1				
j	A	1					1	
	G		1		1			1
	A	1					1	

LCS[i,j] is the maximum of:

1.if S1[i] = S2[j]
    LCS[i-1, j-1] + 1
  else
    LCS[i -1, j-1]
2. LCS[i – 1, j]
3. LCS[i, j – 1]

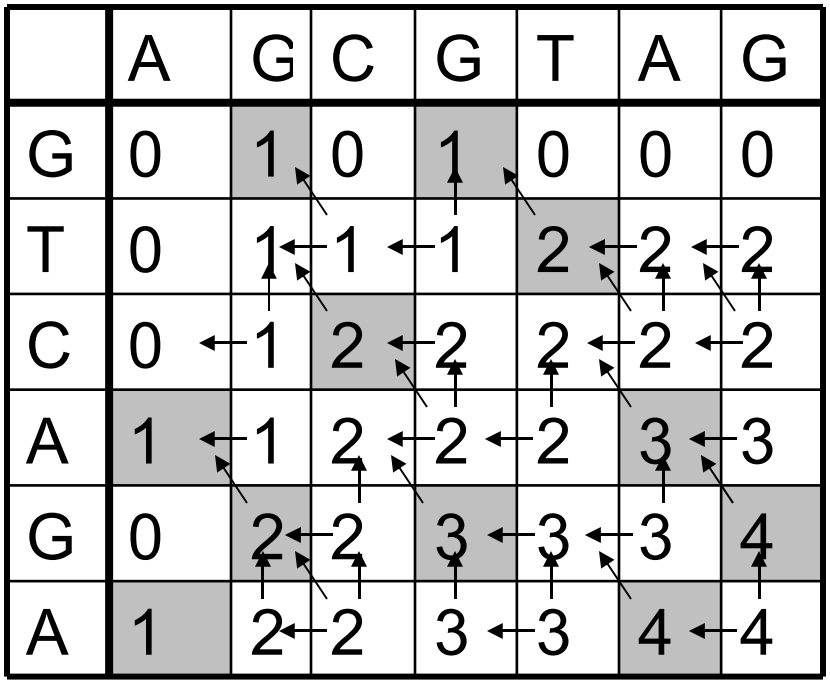
Goal: find LCS[m,n]

Computing the LCS table

Row 0 and column 0 easy to fill
Fill the rest column by column

Find the actual sequence:
trace-back pointers

	A	G	C	G	T	A	G
G	0	1	0	1	0	0	0
T	0	1					
C	0	1					
A	1	1					
G	0	2					
A	1	2					



Extending to sequence alignment

```
AG-C-GTAG
-GTCAG-A-
```

- **In LCS, mis-alignments were free**
- **What happens if we pay for our "mistakes"? (this also allows us to account for "similar" amino-acids)**
  - **Value[A, A] = 10**
  - **Value[A,G] = -5**
  - **Value[A,-] = -2**
  - **etc.**
- **The same dynamic programming algorithm works!**

The recurrences

AG-C-GTAG
-GTCAG-A-

Score[i,j] is the maximum of:

1. Score[i-1, j-1] + Value[S1[i],S2[j]]

```
AG-C-G        AG-C-G
-GTCAG        -GTCAT
```

2. Score[i – 1, j] + Value[S1[i], -] (S1[i] aligned to gap)

```
AG-C-GT
-GTCAG-
```

3. Score[i, j – 1] + Value[-, S2[j]] (S2[j] aligned to gap)

```
AG-C-
-GTCA
```

The dynamic programming table

Score[i,j] is the maximum of:

1. Score[i-1, j-1] + Value[S1[i-1],S2[j-1]] (S1[i-1], S2[j-1] aligned)
2. Score[i – 1, j] + Value[S1[i], -] (S1[i] aligned to gap)
3. Score[i, j – 1] + Value[-, S2[j]] (S2[j] aligned to gap)

	-	A	G	C	G	T	A	G
-	0	-2	-4	-6	-8	-10	-12	-14
G	-2	-4	8	6				
T	-4	-6	6	4				
C	-6	-8	4	16				
A	-8							
G	-10							
A	-14							

Value (A, A) = 10
Value (A, G) = -5
Value (A, -) = -2

Note: we only look at 3 adjacent boxes