Biological Data Formats

Biological Data: Characteristics

- ♦ Biological data is 'data' or 'measurements' collected from biological sources, which is stored or exchanged in a digital form.
- ♦ The amount and range of variability in data is high.
- Representations of the same data by different biologists can be different.

Types of Data

- Broad and diverse :
 - > Sequence
 - > annotated sequence feature
 - > gene expression data
 - > alignment data
 - > protein cluster data
 - > 3 –dimensional structure information
 - > Images
 - > Graphs
 - > semi-structured/unstructured text
- New bio-analytical procedures and progresses add new data types and so add more instability to the data types.

Data Organization

- Challenges to store and maintain the huge complex biological data:
 - Amounts of data increased almost exponentially in the last decade.
 - New types of data are coming into existence with evolving biological concepts.
 - Lack of standardization in nomenclature in biological data.
- Data Storage : Flat files and relational databases
 - Most of the biological data (estimated ~70%) are stored in text form.
 - Rest resides in different databases, ranging from indexed files to specialized relational databases.

Distribution of DATA

- ♦ Biological knowledge seems to be distributed among specialized databases/data sources.
- ♦ Each database has its own complex data structures reflecting the scientific concept they model.
- Many data sources have overlapping data elements with conflicting definition.
- ♦ Data sources are non-standard and often not well documented.
- ◆ Integration and conversion of data from heterogeneous data sources are very important for effective use of the biological information.
- ♦ Important to interpret the various data formats, downloading data from various data sources and conversion of the data to integrate information.

Disparate DATA sources

- Partial list of hundreds of databases exist today.
- Each database has its own complex data structures reflecting the scientific concept they model.
 - Genbank/EMBL
 - > Swissprot protein-curated, minimum redundancy
 - KEGG cellular pathways
 - > PDB protein structures
 - PIR protein database
 - > BIND protein-protein interaction

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Heterogeneous Data Formats

- ♦ Sequence
 - > Flat File
 - > FASTA (multi-FASTA)
 - > XML
- Annotation
 - > GFF
 - > XML
 - > Flat File
- ♦ Multi-Sequence Alignment
 - > ClustalW

Flat File Format

- GenBank, EMBL and DDBJ formed a collaboration in 1986.
- Sequence data moved to a defined flat file format with a shared feature table format and annotation standards.
- ♦ The flat file format from the sequence databases are still used today to access and display sequence and annotation.

LOCUS HUMPRPOA 2420 bp mRNA. linear PRI 13-JUL-1994 Human prion protein 27-30 mRNA, complete ods. DEFINITION ACCESSION M13667 VERSION M13667.1 GI:190469 KEYWORDS amyloid; prion protein; sialoglycoprotein. SOURCE Homo sapiens (human) ORGANISM Homo sapiens Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae: Homo. REFERENCE 1 (bases 1 to 2420) AUTHORS Liao, Y.C., Lebo, R.V., Clawson, G.A. and Smuckler, E.A. TITLE Human prion protein cDNA: molecular cloning, chromosomal mapping, and biological implications JOURNAL Science 233 (4761), 364-367 (1986) PUBMED 3014653 Original source text: Human, cDNA to mRNA, clones lambda [3,6,7]. COMMENT A single prion protein gene is found on chromosome 20 per haploid genome. FEATURES Location/Qualifiers source 1..2420 /organism="Homo sapiens" /mol_type="mRNA" /db xref="taxon:9606" 1..2420 gene /gene="PRNP" <1..2420 mRNA /gene="PRNP" /product="PrP mRNA" CDS 77..814 /gene="PRNP" /note="prion protein" /codon_start=1 /protein id="AAA19664.1" /db xref="GI:190470" translation="MLVLFVATWSDLGLCKKRPKPGGWNTGGSRYPGQGSPGGNRYPP/ QGGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQGGGTHSQWNKPSKPKTNM KHMAGAAAGAVVGGLGGYMLGSAMSRPIIHFGSDYEDRYYRENMHRYPNQVYYRPMDE YSNONNFVHDCVNITIKQHTVTTTTKGENFTETDVKMMERVVEQMCITQYERESQAYY QRGSSMVLFSSPPVILLISFLIFLIVG" ORIGIN 171 bp upstream of Smal site; chromosome 20. 1 cgagcagcca aggttogcca taatgactgc totoggtogt gaggagagga gaagctogog 61 gcgccgcggc tgctggatgc tggttctctt tgtggccaca tggagtgacc tgggcctctg 121 caagaagogc cogaagootg gaggatggaa cactgggggc agcogatacc cggggcaggg 181 cagccctgga ggcaaccgct acccacctca gggcggtggt ggctgggggc agcctcatgg 241 tggtggctgg gggcagcctc atggtggtgg ctgggggcag ccccatggtg gtggctgggg 301 acagcotcat ggtggtggct ggggtcaagg aggtggcacc cacagtcagt ggaacaagco 2161 tgaagtgtct aatgcattaa cttttgtaag gtactgaata cttaatatgt gggaaaccct 2221 tttgcgtggt ccttaggctt acaatgtgca ctgaatcgtt tcatgtaaga atccaaagtg 2281 gacaccatta acaggtottt gaaatatgca tgtactttat attttctata tttgtaactt 2341 tgcatgttct tgttttgtta tataaaaaaa ttgtaaatgt ttaatatctg actgaaatta

//

2401 aacgagccaa gatgagcacc

Header

Feature

Table

Sequence

GenBank: Header

```
LOCUS
            TVU35243
                                    1804 bp
                                               mRNA
                                                       linear
                                                                INV 30-JAN-2006
           Trichomonas vaginalis AP65-3 adhesin mRNA, complete cds.
DEFINITION
ACCESSION
            U35243
VERSION
           U35243.1 GI:1209523
KEYWORDS
SOURCE
            Trichomonas vaginalis
 ORGANISM Trichomonas vaginalis
            Eukaryota; Parabasalidea; Trichomonada; Trichomonadida;
            Trichomonadidae; Trichomonadinae; Trichomonas.
            1 (bases 1 to 1804)
REFERENCE
            O'Brien, J.L., Lauriano, C.M. and Alderete, J.F.
 AUTHORS
            Molecular characterization of a third malic enzyme-like AP65
 TITLE
            adhesin gene of Trichomonas vaginalis
           Microb. Pathog. 20 (6), 335-349 (1996)
 JOURNAL
  PUBMED
           8831829
            2 (bases 1 to 1804)
REFERENCE
           Alderete, J.F.
 AUTHORS
 TITLE
           Direct Submission
            Submitted (01-SEP-1995) John F. Alderete, University of Texas
 JOURNAL
            Health Science Center at San Antonio, Microbiology, 7703 Floyd Curl
            Drive, San Antonio, TX 78284-7758, USA
REFERENCE
            3 (bases 1 to 1804)
           Mundodi, V., Kucknoor, A.S., Klumpp, D.J., Chang, T.H. and
 AUTHORS
            Alderete, J.F.
            Silencing the ap65 gene reduces adherence to vaginal epithelial
 TITLE
            cells by Trichomonas vaginalis
  JOURNAL
           Mol. Microbiol. 53 (4), 1099-1108 (2004)
  PUBMED
           15306014
```

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GenBank: Features

Feature Identifiers

FEATURES

source

Features CDS

Location

Qualifiers

```
Location/Qualifiers
1..1580
/organism="Oryza sativa (japonica cultivar-group)"
/mol type="mRNA"
/db_xref="taxon:39947"
1..1580
/locus tag="OSJNBa0003019.7"
/note="similar to carnitine acylcarnitine translocase
GB:CAB55356 GI:5851675 (Homo sapiens); EST C26405,
AU093530, AU093531, AU108742 from this gene"
/db xref="GeneID:3054652"
79..969
/locus tag="OSJNBa0003019.7"
/codon start=1
/product="putative carnitine/acylcarnitine translocase"
/protein id="NP 922838.1"
/db xref="GI:37537072"
/db xref="GeneID:3054652"
/translation="MGDVVKDLVAGTVGGAANLIVGHPFDTIKVKLQSQPTPAPGQFP
KYAGAVDAVKQTIATEGPRGLYKGMGAPLATVAAFNALLFTVRGQMEALLRSEPGQPL
TVNQQVVAGAGAGVAVSFLACPTELIKCRLQAQSALAEAAAASGVALPKGPIDVAKHV
VREAGMKGLFKGLVPTMGREVPGNAVMFGVYEGTKQYLAGGQDTSNLGRGSLILSGGL
AGAVFWLSVYPTDVVKSVIOVDDYKKPRYSGSVDAFKKILAADGVKGLYKGFGPAMAR
SVPANAATFLAYEITRSALG"
```

GenBank: Sequence

```
Sequence Field
         Identifier
                                 1 ttttaqatta aaqatqctcq catcttcaqt cqctqctcca qtccqcaaca tctqcaqqqc
                                61 taageteeca geteteaaga caggaatgac ceteetteag gatggtgate tttecaaggg
                               121 etetgettte acaaaggaag aacgtgateg cettaacett egeggtetee teccatacaa
                               181 ggtcttcaca aaggatgaac aagctgctcg tatccgccgc cagttcgagt tgatgccaac
                               241 accaetecte aagtacatet teetegetaa egagegtgag aaaaaeteae agteettetg
                               301 gagatteete tteacacace caccaacaga gacaatgeca gttetetaca caccaacagt
                               361 tggtgaagec tgccagaagt gggctacaca ccgccagtca taccgtggca tctacatcac
                               421 accagaagac tetggcaaga teaaggacat ceteegcaac tacecaegec aggacateeg
                               481 etgeategte gttacagatg gtggeegtat eeteggtete ggtgateteg gtgetteegg
                               541 ccttggtatc ccagtcggca agettatgct ttacacactc atcggtcagg tccatccaga
                               601 teagacacte ceagteeagt tagatatggg tacagacege aaggaaatee tegeegacee
                               661 actotaccae ggetggegee atecaagaat aegtggeeca gaacacacaa agttegttge
                               721 cgagttcgtt gatgctgtca aggaagtctt tggcgagaca tgccttgtcc agttcgaaga
                               781 tttcgaaatg gaaactgctt tcaagcttct tgatcacttc cgctggcgct gcaactgctt
                               841 caacqatqat atcqaaqqca caqctqccqt cqctqctqct acactcqctt ccqctacaca
                               901 catggaagge gttecagate teaagaacca gaagateate tteateggeg etggetetge
                               961 tgctacaggc attgctaacc tcatcgttga tatggctgtt tcccgcggtg gcatctcacg
                              1021 caaqqatqct qaqaqaaaca tcatcatqtt cqatcacaaq qqtatqqtcc atqctqaccq
                              1081 taaqqatctc tacqacttca acaaqccata catqcacqac atqqaaqtct acqqctccqt
                              1141 ccttgagggt gtcaagaagt tcaaggctac atgcgtcatc ggcgtttctg gtgttccagg
                              1201 actcatcaca aaggaaatcg tccaggctac atgcgctaac tgcgagcgcc cagtcatcat
                              1261 gccactttcc aacccaacag tcaaggctga agctaagcca cacgatgtct accagtggtc
                              1321 caatggcaag geeetetgeg etacaggete tecatteeca gttgagacag teaacggaaa
                              1381 gaagacaate acageteagg etaacaacte etggatette eeagetgteg getaegeeet
                              1441 cgttacaaca cgcgctcgcc actgcccagg caaggtcttc gaagttgctg ctgaatccct
                              1501 tgetteeett gttaagaagg aagaceaega tatgggeaac etteteeeac eactegaeaa
                              1561 gatccgtgag tactcattcg gcatcgccct cgatgttgct aagtacctca tcaagaacga
                              1621 getegecaca geteteccae caaagggeac agageteaag gaetggetea aggeteaget
                              1681 ettegateca caggetgaat acgageaact etactaagea gtttttaaaa etettteaat
        Termination
                              1801 aaaa
            Line
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```

SWISSPROT/TrEMBL Format

- ♦ Swiss-Prot/ TrEMBL protein sequence database.
- ♦ Feature table is extended to capture structural features and biochemical information about the protein.

```
By similarity.
FΤ
    SIGNAL
                               Chloroplast ATP synthase a chain.
                      247
   CHAIN
                19
   TRANSMEM
                39 58
                                Potential.
               97 115
   TRANSMEM
                                Potential.
   TRANSMEM 134 153
                               Potential.
   TRANSMEM 221 240
                               Potential.
SQ SEQUENCE 247 AA; 27291 MW; 540649B34778E585 CRC64;
    MNIIPCSIKT LKGLYDISGV EVGQHFYWQI GGFQIHAQVL ITSWVVITIL LGSVIIAVRN
    PQTIPTDGQN FFEYVLEFIR DLSKTQIGEE YGPWVPFIGT MFLFIFVSNW SGALLPWKII
    OLPHGELAAP TNDINTTVAL ALLTSAAYFY AGLSNKGLSY FEKYIKPTPI LLPINILEDF
    TKPLSLSFRL FGNILADELV VVVLVSLVPL VVPIPVMFLG LFTSGIQALI FATLAAAYIG
    ESMEGHH
//
```

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FASTA Format : Significance

- The database flat file formats are unwieldy for sequence analysis.
 - > sometimes you need just the sequence for analysis.
 - other times you need to work with the annotations in the database or output generated by sequence analysis programs.
- Many formats have been created over the years for this purpose.
- ♦ FASTA format is the most common sequence format.

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FASTA Format – Example

A single FASTA sequence record from a sequence database:

Definition Line or Header begins with '>'

Width of sequence rows usually 60 letters.

Note: The MultiFASTA Format is composed of FASTA records concatenated together.

FASTA Format: Definition Line

- ♦ Definition line has the important identifier for the sequence.
- ♦ GenBank/EMBL/DDBJ
 - > gi|gi_number|gb|accession.version|locus
 - > gi|gi_number|embl|accession.version|locus
 - > gi|gi_number|dbj|accession.version|locus
- ♦ NCBI Reference Sequence
 - > ref|accession|locus
- ◆ PIR
 - > pir|entry
- ♦ SWISSPROT
 - > sp|accession|locus
- ♦ PDB
 - pdb|entry|chain

XML: Characteristics

- ♦ XML = eXtensible Markup Language
- ◆ Tag based like HTML
- Human readable
- ♦ Have inherent hierarchical data structures
- ♦ Easy to use for data exchange
- Many bioinformatics software tools are XMLcompliant
- ♦ The data to be contained is described using a Document type Definition (DTD) or an XML schema.

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XML: Example

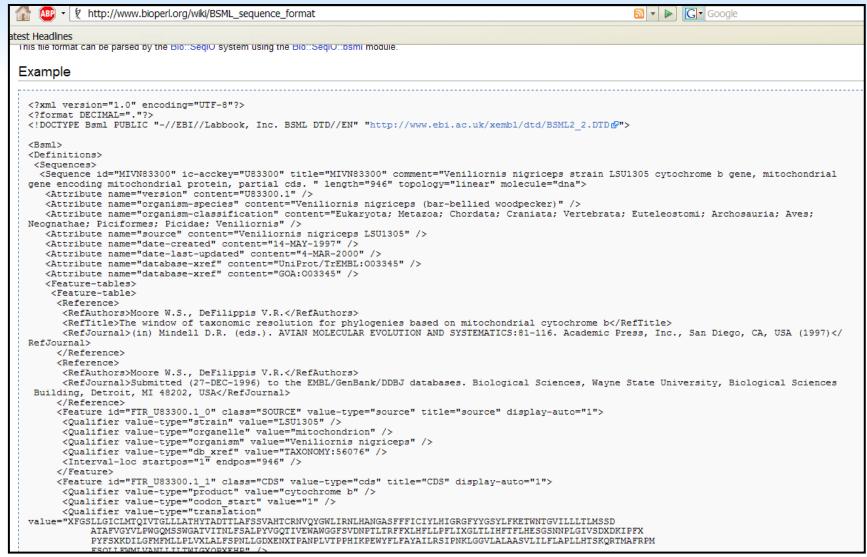
```
<?xml version="1.0" encoding="UTF-8"?>
     <?format DECIMAL="."?>
     <!DOCTYPE Bsml PUBLIC "-//EBI//Labbook, Inc. BSML DTD//EN"</pre>
                   "http://www.ebi.ac.uk/xembl/dtd/BSML2 2.DTD">
                   Root Tag
     <bsml>
     <definitions>

Start Tag
                                          Attributes
     <sequences>
     <sequence id="AB12345" title="AB12" molecule="dna"</pre>
     length="500" topology="linear"
     strand="ds"
     representation="raw">
     <seq-data>acgtacgtacgtacgtacgtcgcgaacgccg
     taact...</seq-data>
     </sequence>
                                            Character Data
     </sequences>
     </definitions> 	← End Tag
     </bsml> •
                     End Root Tag
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```

Bioinformatics Sequence Markup Language (BSML)

- ♦ XML Formats in Bioinformatics
 - Specially designed for a wide variety of information attached to biological sequences
- Allows modularization and improves portability.
- ♦ Flexible mean of describing any element of a sequence, sequence alignment, etc.
- ♦ BSML Objects can be downloaded from
 - http://bsml.sourceforge.net/

BSML



GFF: an Exchange Format for Feature Description

http://www.sanger.ac.uk/Software/formats/GFF/

GFF = General Feature Format

Tab delimited, easy for data parsing and processing.

Many annotation viewers accept this format in various 'dialects'.

Fields:

- 1. Reference Sequence: base seq to which the coordinates are anchored
- 2. Source: source of the annotation
- Type: Type of feature
- 4. Start
- 5. End (Start is always less than End)
- 6. Score: Used for holding numerical scores (similarity, etc)
- 7. Strand: "+',"-", or '." if unstranded
- 8. Frame: Signifies codon phase for coding sequence (CDS) features
- 9 Other attributes or/and comments

SEQ1	EMBL	atg	103	105		+	0
SEQ1	EMBL	exon	103	172		+	0
SEQ1	EMBL	splice5	172	173		+	
SEQ1	netgene	splice5	172	173	0.94	+	
SEQ1	genie	sp5-20	163	182	2.3	+	
SEQ1	genie	sp5-10	168	177	2.1	+	
SEQ2	grail	ATG	17	19	2.1	_	0

GFF3 Format

http://song.sourceforge.net/gff3.shtml

Extension of GFF by the Sequence Ontology (SO) and Generic Model Organism Database (GMOD) Projects

- -- Allows hierarchies more than one level deep
- -- Separated group membership and feature name/ID
- -- Attributes take the form of "Key=Value" pairs

7000

```
##qff-version
##sequence-region
                    ctq123 1 1497228
ctq123 . gene
                                               ID=qene00001; Name=EDEN
ctg123 . TF binding site 1000
                                1012
                                               Parent=gene 00001
                                               ID=nRNA00001; Parent=gene00001
ctq123 . nRNA
                         1050
                                9000
ctq123 . nRNA
                         1050
                                9000
                                               ID=nRNA00002; Parent=gene00001
ctq123 . nRNA
                         1300
                                               ID=nRNA00003; Parent=qene00001
                                1500
                                               Parent=nRNA00003
ctg123 . exon
                         1300
ctg123 . exon
                         1050
                                1500
                                               Parent=nRNA00001, nRNA00002
                         3000
                                3902
                                               Parent=nRNA00001, nRNA00003
ctg123 . exon
ctg123 . exon
                                               Parent=nRNA00001, nRNA00002, nRNA00003
                         5000
ctg123 . exon
                         7000
                                9000
                                               Parent=nRNA00001, nRNA00002, nRNA00003
ctg123 . CDS
                         1201
                                               ID=cds00001:Parent=nRNA00001
ctg123 . CDS
                         3000
                                3902
                                               ID=cds00001;Parent=nRNA00001
ctg123 . CDS
                         5000
                                               ID=cds00001:Parent=nRNA00001
ctg123 . CDS
                         7000
                                7600
                                               ID=cds00001:Parent=nRNA00001
ctg123 . CDS
                         1201
                                               ID=cds00002:Parent=nRNA00002
ctg123 . CDS
                         5000
                                5500
                                              ID=cds00002:Parent=nRNA00002
ctg123 . CDS
                         7000
                                7600
                                               ID=cds00002:Parent=nRNA00002
                                              ID=cds00003:Parent=nRNA00003
ctg123 . CDS
                                3902
                         3301
                                               ID=cds00003;Parent=nRNA00003
ctq123 . CDS
                         5000
                                5500
                                               ID=cds00003:Parent=nRNA00003
                         7000
                                7600
ctq123 . CDS
                                              ID=cds00004:Parent=nRNA00003
                         3391
                                3902
                                               ID=cds00004; Parent=nRNA00003
```

ID=cds00004:Parent=nRNA00003

ClustalW Alignment Format

A common multi-sequence alignment format is the alignments written by the ClustalW program. Most phylogenetic programs can take ClustalW alignments as input.

```
CLUSTAL W (1.74) multiple sequence alignment
```

```
ATP7B MOUSE
                   MDPRKNLASVGTMPEQERQVTAKE-ASRKILSKLALPGRPWEQSMKQSFAFDNVGYEGGL 59
ATP7B RAT
                    ----MPEQERKVTAKE-ASRKILSKLALPTRPWGQSMKQSFAFDNVGYEGGL 47
ATP7B HUMAN
                    ----MPEOEROITAREGASRKILSKLSLPTRAWEPAMKKSFAFDNVGYEGGL 48
ATP7B OVIS ARIES
                    -----MKPEEERPIIDREKASRRILSKLFQP-----AMKQSFAFDNNGYEDDL 43
                                **:** : :* ***:**** *
ATP7B MOUSE
                    DSTSSSPAATD-VVNILGMTCHSCVKSIEDRISSLKGIVNIKVSLEQGKHTVRYVPSVMN 118
ATP7B RAT
                    DSTCFILQLTTGVVSILGMTCHSCVKSIEDRISSLKGIVSIKVSLEQGSATVKYVPSVLN 107
ATP7B HUMAN
                    DGLGPSSQVATSTVRILGMTCQSCVKSIEDRISNLKGIISMKVSLEQDSATVKYVPSVVC 108
ATP7B OVIS ARIES
                    DGVCPS-QTAAGTISIVGMTCQSCVKSIEGRVSSLKGIVSIKVSLEQSSAEVRYVPSVVS 102
                            : : *:***:****** *: ****** . *: *****
ATP7B MOUSE
                    LQQICLQIEDMGFEASAAEGKAASWPSRSSPAQEAVVKLRVEGMTCQSCVSSIEGKIRKL 178
ATP7B RAT
                    LQQICLQIEDMGFEASAAEGKAASWPSRSSPAQEAVVKLRVEGMTCQSCVSSIEGKIRKL 167
ATP7B HUMAN
                    LQQVCHQIGDMGFEASIAEGKAASWPSRSLPAQEAVVKLRVEGMTCQSCVSSIEGKVRKL 168
ATP7B OVIS ARIES
                    LMQICHQIEDMGFQASVAEGKATSWASRVSPTSEAVVKLRVEGMTCQSCVSSIEGKIGKL 162
```

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What About Other Formats?

- ♦ Other Phylogenetics Analysis programs:
 - PAUP, Phylip, GCG/Pileup

- Pairwise alignment output BLAST, sim4, BLAT, GMAP
- Genefinding softwares variety of custom formats
- ◆ Tabulated/tab delimited summary formats

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Format Conversion

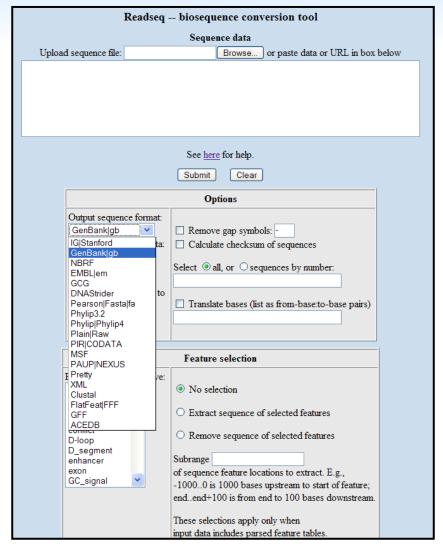
- ♦ There are several options:
 - > stand-alone tools
 - > web based tools
 - > the programming option

♦ Example: If you have to submit a sequence to genbank, you can convert the sequence to genbank format using the genbank conversion software.

Format Conversion Using "ReadSeq"

http://iubio.bio.indiana.edu/soft/molbio/readseq/java/

- ♦ Java based tool.
- ♦ Converts between many of the formats discussed in this lecture.
- Offered as command line interface or offered as a web based tool.



Summary

- ♦ It is important that you understand the complex and heterogeneous nature of the data.
- Familiarize yourself with commonly used data formats.
- ♦ Be aware of the Genbank, BSML and different flavors of GFF format.
- Keep in mind that there are many different custom data formats specifically for gene finding software.