Introduction to Bioinformatics

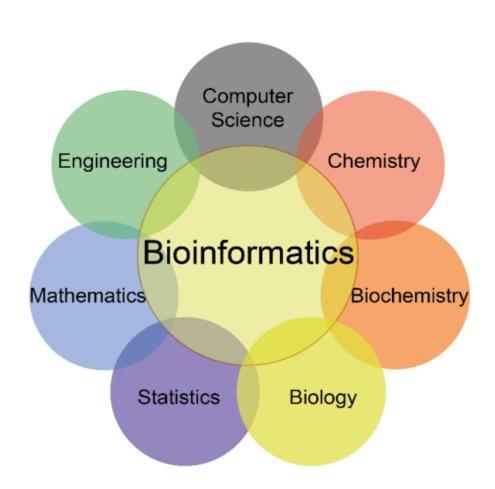
For Biochemistry Sem IV



Dr. Kusum Yadav
Assistant Professor
Department of Biochemistry
University of Lucknow, Lucknow
Mob-9452490044 Email-anukusum@gmail.com

Bioinformatics

- Bioinformatics is a branch of science that integrates computer science, mathematics and statistics, chemistry and engineering for analysis, exploration, integration and exploitation of biological sciences data, in Research and Development.
- Bioinformatics deals with storage, retrieval, analysis and interpretation of biological data using computer based software and tools.



History of Bioinformatics

- Bioinformatics emerged in mid 1990s.
- From 1965-78 Margaret O. Dayhoff established first database of protein sequences, published annually as series of volume entitled "Atlas of protein sequence and structure".
- During 1977 DNA sequences began to accumulate slowly in literature and it became more common to predict protein sequences by translating sequenced genes than by direct sequencing of proteins.
- Thus number of uncharacterised proteins began to increase.
- In 1980, there were enough DNA sequences to justify the establishment of the first nucleotide sequence database, GenBank at National Centre for Biotechnology Information (NCBI), USA. NCBI served as primary databank provider for information.

History of Bioinformatics (contd..)

- The European Molecular Biology Laboratory (EMBL) established at European Bioinformatics Institute (EBI) in 1980.
 The aim of this data library was to collect, organize and distribute nucleotide sequence data and related information.
- In 1986 DNA Data Bank was established by GemonNet, Japan.
- In 1984, the National Biomedical Research Foundation (NBRF) established the protein information Resource (PIR).
- All these data banks operate in close collaboration and regularly exchange data.
- Management and analysis of the rapidly accumulating sequence data required new computer software and statistical tools.
- This attracted scientists from computer science and mathematics to the fast emerging field of bioinformatics.

Objectives of Bioinformatics

- Development of new algorithms and statistics for assessing the relationships among large sets of biological data.
- Application of these tools for the analysis and interpretation of the various biological data.
- 3. Development of database for an efficient storage, access and management of the large body of various biological information.

Components of Bioinformatics

Data **Database Database Mining Tools**

Data

- Nucleic Acid Sequences
 - Raw DNA Sequences
 - Genomic sequence tags (GSTs)
 - cDNA sequences
 - Expressed sequence tags (ESTs)
 - Organellar DNA sequences
 - RNA Sequences
- Protein sequences
- > Protein structures
- Metabolic pathways
- **≻** Gel pictures
- > Literature

Databases

A database is a vast collection of data pertaining to a specific topic e.g. nucleotide sequence, protein sequence etc., in an electronic environment.

- They are heart of bioinformatics.
- Computerized storehouse of data (records).
- Allows extraction of specified records.
- Allows adding, changing, removing, and merging of records.
- Uses standardized formats.

Databases: Types

- Sequence Databases
- Structural Databases
- Enzyme Databases
- Micro-array Databases
- Clinical Database
- Pathway Databases
- Chemical Databases
- Integrated Databases
- Bibliographic Databases

Nucleotide Sequence Databases

- NCBI GenBank: (www.ncbi.nlm.nih.gov/GenBank)
- EMBL: (www.ebi.ac.uk/embl)
- DDBJ: (www.ddbj.nig.ac.jp)

The 3 databases are updated and exchanged on a daily basis and the accession numbers are consistent.

There are no legal restriction in the usage of these databases. However, there are some patented sequences in the database.

The International Nucleotide Sequence Database Collaboration (INSD)

National Center for Biotechnology Information (NCBI)



(일 **(2)** 🗎 4:17 pm





National Center for Biote... ncbi.nlm.nih.gov





Popular Resources

PubMed

Genome

SNP

Gene

Protein PubChem

Bookshelf PubMed Central



Sign in to NCBI

Search

S NCBI Resources	C How IO C			
National Center for Biotechnology Information	All Databa	ases 🕶		
NCBI Home		Welcome to NCBI	Ī.	
Resource List (A-Z)		The National Center for Biotechnology Information health by providing access to biomedical and geno		
All Resources				
Chemicals & Bioassays		About the NCBI Mission Organization NCBIN		
Data & Software				
DNA 8 RNA		Submit	Download	
Domains & Structures		Deposit data or manuscripts into NCBI databases	Transfer NCBI data	
Genes & Expression			to your computer	
Genetics & Medicine		NCBIdatabases	_	
Genomes & Maps				
Homology		100		
Literature				
Proteins				
Sequence Analysis		Develop	Analyze Identify an NCBI tool for your data	
Taxonomy		Use NCBI APIs and		
Training & Tutorials		code libraries to		
Variation		build applications	analysis task	
		_=	386	







now available on the NCBI FTP site. This release has 6.69 trillion bases and 1.68 Bulk track hub settings now in Genome Data Viewer You now have access to bulk settings ontions for track bulbs in the Genome

Research at NCBI

NCBI on Facebook

NCBI on YouTube

NCBI FTP Site

Privacy Policy

NCBI on Twitter

More...

30 Oct 2019

You are here: NCBI > National Center for Biotechnology Information

GETTING STARTED NCBI Help Manual Training & Tutorials Submit Data

RESOURCES Chemicals & Bioassays Data & Software DNA & RNA Domains & Structures Genes & Expression Genetics & Medicine Genomes & Maps Homology Literature Proteins Sequence Analysis Taxonomy Variation

POPULAR Bookshelf PubMed Central BLAST Nucleotide Genome SNP Gene Protein PubChem

FEATURED Genetic Testing Registry GenBank Reference Sequences Gene Expression Omnibus Genome Data Viewer Human Genome Mouse Genome Influenza Virus Primer-BLAST

Sequence Read Archive

Support Center NCBI INFORMATION

National Center for Biotechnology Information, U.S. National Library of Medicine 8600 Rockville Pike, Bethesda MD, 20894 USA Policies and Guidelines | Contact







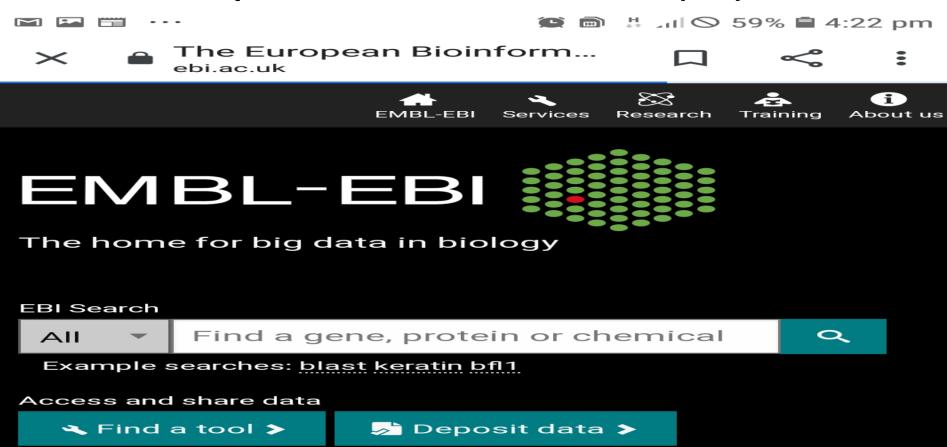


EMBL Database

European Molecular Biology Laboratory (EMBL):

- **❖** Maintained by *European Bioinformatics Institute* (EBI)
 - ✓ GSS (genome survey sequences)
 - **✓** HTC (high-throughput c-DNA sequences)
 - **✓** HTG (high-throughput genomic sequences)
 - ✓ EST (expressed sequence tag)
 - **✓** Patents

European Bioinformatics Institute (EBI)



We are EMBL-EBI

The European Bioinformatics Institute (EMBL-EBI) is part of EMBL, Europe's flagship laboratory for the life sciences. More about EMBL-EBI and our impact. >

Kusum Yadav, Department of Biochemistry



DDBJ (DNA Database of GenomNet, Japan)

- Developed in 1986 as a collaboration with EMBL and GenBank.
- Produced, maintained and distributed by the National Institute of Genetics, Japan.
- Sequences is submitted via Web based data submission tool.

GenomeNet, Japan





KEGG KEGG2 PATHWAY BRITE MEDICUS DBGET LinkDB



GenomeNet genome.jp



GenomeNet

Search All databases ▼ for

Go Clear

[English | Japanese]

GenomeNet
About GenomeNet
Release notes
Acknowledgments

DBGET
Overview
DB release info

KEGG

DB release info
KEGG
Community DBs
Bioinformatics tools
FTP
Feedback

GenomeNet Database Resources

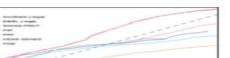
DBGET: Integrated Database Retrieval System DBGET search Link DB search SPARQL endpoint available KEGG: Kyoto Encyclopedia of Genes and Genomes KEGG2 - Table of contents KEGG PATHWAY - Systems information: pathways KEGG BRITE - Systems information: ontologies KEGG Organisms - Organism-specific entry points KEGG GENES - Genomic information KEGG LIGAND - Chemical information KEGG MEDICUS - Health information KEGG MGENES: Metagenome gene catalogs KEGG OC - KEGG ortholog clusters REST service is available SPARQL endpoint available Virus-Host DB: Hosts of sequenced viruses Taxonomy: Organism classification Reaction Ontology: Reaction classifications varDB: Antigenic variation database

GenomeNet Bioinformatics Tools

Sequence Analysis
BLAST / FASTA - Sequence similarity search
MOTIF - Sequence motif search
MAFT / CLUSTALW / PRRN - Multiple alignment
TREE - Phylogenetic analysis

Genome Analysis
ViPTree - The Viral Proteomic Tree Server
Kofam KOALA - Gene annotation and KEGG mapping
KAAS - KEGG automatic annotation server
EGassembler - EST consensus contigs
GENIES - Gene network prediction
DINIES - Drug-target network prediction
Chemical Analysis
SIMCOMP / SUBCOMP - Chemical structure search
REST service is available
KCAM - Glycan structure search
PathComp - Possible reaction path computation
PathSearch - Similar reaction path search
PathPred - Reaction pathway prediction
E-zyme - Enzymatic reaction prediction





DB growth curve

Kyoto University Bioinformatics Center

Other Databases

- ESTs Expressed Sequence Tags
 - dbEST (http://www.ncbi.nlm.nih.gov/dbEST)
 - GenBank subset with additional EST-specific data
 - Implemented in a Sybase relational database
- SNPs Single Nucleotide Polymorphisms
 - dbSNP (http://www.ncbi.nlm.nih.gov/SNP/)
 - Very similar to dbEST in philosophy and implementation
- Many commercial databases
 - Celera, Incyte, etc.

Protein Databases

Protein sequence database

- Functions as repository of raw data: two types
- Primary
- Secondary

Protein structure database

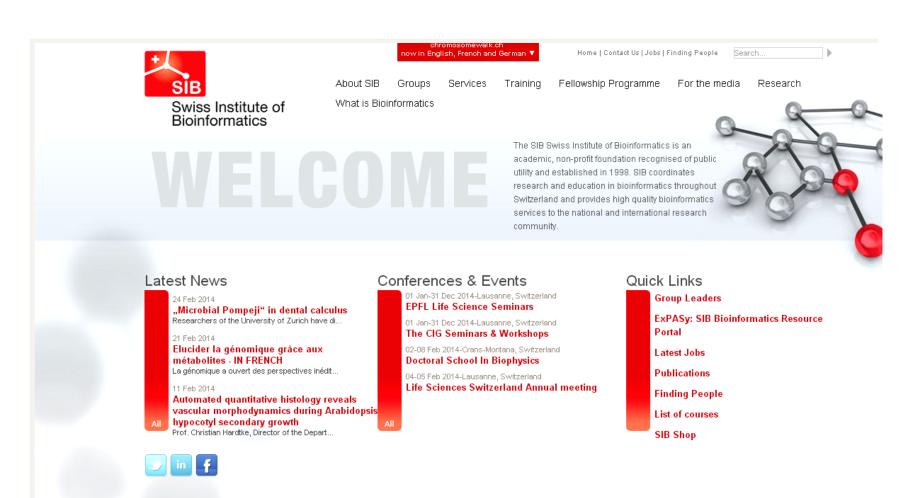
Primary databases

- 1. SWISS-PROT: Groups at Swiss Institute of Bioinformatics (SIB).
 - It annotate the sequences
 - Describe protein functions
 - Its domain structures
 - Its post translations modifications
 - Provides high level of annotation
 - Minimum level of redundancy
 - High level of integration with other databases

2. TrEMBL:

- Computer annotated supplements of SWISS-PROT that contains all the translations of EMBL nucleotide entries not yet integrated in SWISS-PROT.
- 2. PIR: Protein Information Resource, a division of NBRF in US.
 - Collaborated with Munich Information Centre for Protein Sequences (MIPS) and Japanese International Protein Sequence Database (JIPID).
 - One an search for entries
 - Do sequence similarity
 - PIR also produces MRL-3D (db of sequences extracted from 3D structures in PDB)

Swiss-Prot



Secondary databases

- Secondary db compile and filter sequence data from different primary db.
- These db contain information derived from protein sequences and help the user determine whether a new sequence belong to a known protein family.

1. PROSITE:

- db of short protein sequence patterns and profiles that characterise biologically significant sites in proteins
- It is based on regular expressions describing characteristic sequences of specific protein families and domains.
- It is part of SWISS-PROT, and maintained in the same way

2. PRINTS

- PRINTS provides a compendium of protein fingerprints (groups of conserved motifs that characterise a protein family)
- Now has a relational version, "PRINTS-S"

3. BLOCKS

- BLOCK patterns without gaps in aligned protein families defined by PROSITE, found by pattern searching and statistical sampling algorithms.
- Automatically determined un-gapped conserved segments

4. Pfam

- Db of protein families defined as domains
- For each domain, it contains a multiple alignment of a set of defining sequences and the other sequences in SWISS-PROT and TrEMBL that can be matched to the alignment.

Protein Structural Database

1. PDB (Protein Data Bank):

- Main db of 3D structures of biological macromolecules (determined by X-ray crystallography and NMR).
- PDB entrys contain the atomic coordinates, and some structural parameters connected with the atoms or computed from the structures (secondary structure).
- PDB provide primary archive of all 3D structures for macromolecules such as proteins,
 DNA, RNA and various complexes.

2. SCOP (Structural Classification of Proteins):

- Db was started to with objective to classify protein 3D structures in a hierarchical scheme of structural classes.
- It is based on data in a primary db, but adds information through analysis and organization (such as classification of 3D structures into hierarchical scheme of folds, super-families and families)

3. CATH (Class, architecture, topology, homologous super-family):

- CATH perform hierarchical classification of protein domain structures.
- Clusters proteins at four major structural levels Biochemistry

Enzyme Database

- **❖ BRENDA** [BRaunshchweig ENzyme DAtabase] (www.brenda.uni-koeln.de)
- **Enzyme**, a part of ExPaSy (Expert Protein Analysis System, the proteomic server of Swiss Institute of Bioinformatics)

Clinical Databases

Generally contain information from the Human

Human Gene Mutation Database, Cardiff, UK:

http://www.hgmd.org

Registers known mutations in the human genome and the diseases they cause.

OMIM database

Online Mendelian Inheritance in Man

http://www.ncbi.nlm.nih.gov/Omim

The OMIM database contains abstracts and texts describing genetic disorders to support genomics efforts and clinical genetics. It provides gene maps, and known disorder maps in tabular listing formats. Contains keyword search.

Kyoto Encyclopedia of Genes and Genomes (KEGG) www.genome.jp/kegg/

Database and associated software which integrates several databases such as,

- Pathway database
- Genes database
- Genome database
- Drug database
- Reaction database
- Compound database
- KO database etc.

Bibliographic Databases

Used for searching for reference articles

PubMed

- 1. It enables user to do keyword searches, provides links to a selection of full articles, and has text mining capabilities, e.g. provides links to related articles, and GenBank entries, among others.
- 2. It contains entries for more than 30 million abstracts of scientific publications.

Database Mining Tools (Analysis Tools)

Utilization of various databases requires the use of suitable search engines and analysis tools. These tools are called <u>Database mining tools</u> and the process of data utilization is known as database mining. Some Applysis Tools are as follows:

known as database mining. Some Analysis Tools are as follows:					
Analysis Tool	Function				
BLAST (NCBI, USA)	Used to analyse sequence information and detect homologous sequences				
ENTREZ (NCBI, USA)	Used to access literature (abstracts), sequence and structure db				
DNAPLOT (EBI, UK)	Sequence alignment tool				
LOCUS LINK (NCBI, USA)	Assessing information on homologous genes				
LIGAND (GenomNet, Japan)	A chemical db, allows search for a combination of enzymes and links to all publically accessible db.				
BRITE (GenomNet, Japan)	Biomolecular relations information transmission and expression db; links to all publically accessible db.				
TAXONOMY BROWSER (NCBI, USA)	Taxonomic classification of various species as well as genetic information				
STRUCTURE	It support Molecular Modelling Database (MMDB) and software				

tools for structure analysis Biochemistry

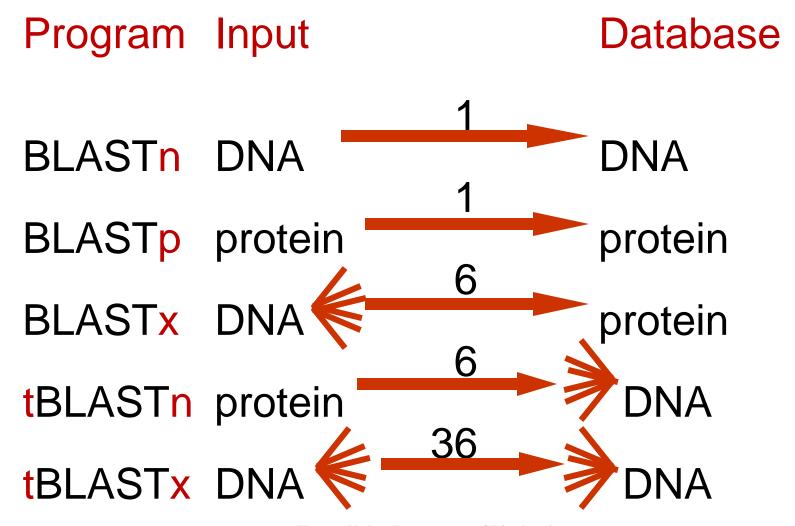
BLAST

(Basic Local Alignment Search Tool) for Homology Analyses

- BLASTn
 - Nucleotide query vs nucleotide database
- BLASTp
 - protein query vs protein database
- BLASTx
 - automatic 6-frame translation of nucleotide query vs protein database
 - If you have a DNA sequence and you want to now what protein (if any) it encodes, you can perform BLASTx search.
- tBLASTn
 - protein query vs automatic 6-frame translation of nucleotide database
 - You can use this program to ask whether a DNA or ESTs db contains a nucleotide sequence encoding a protein that matches your protein of interest.
- tBLASTx
 - automatic 6-frame translation of nucleotide query vs automatic 6-frame translation of nucleotide database ment of Biochemistry

BLAST

(Basic Local Alignment Search Tool) for Homology Analyses



SEQUENCE ALIGNMENT

What is Sequence Alignment?

A sequence alignment is a way of arranging the sequences of DNA or protein to identify regions of similarity that may be a consequence of functional, structural, or evolutionary relationships between the sequences.

Definitions

Similarity

The extent to which nucleotide or protein sequences are related. It is based upon identity plus conservation.

Identity

The extent to which two sequences are invariant.

Conservation

Changes at a specific position of an amino acid or (less commonly, DNA) sequence that preserve the physico-chemical properties of the original residue.

Types of alignment

- Pairwise alignment
- Multiple Alignment

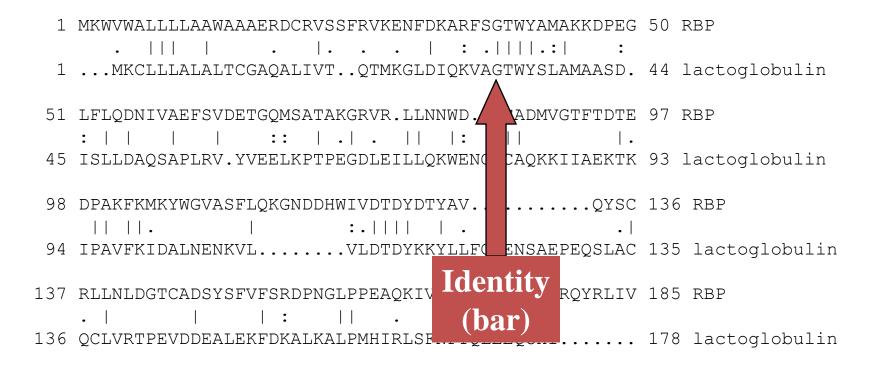
Pairwise alignment

- The process of lining up two sequences to achieve maximal levels of identity (and conservation, in the case of amino acid sequences) for the purpose of assessing the degree of similarity and the possibility of homology.
- Pairwise sequence alignment is the most fundamental operation of bioinformatics.

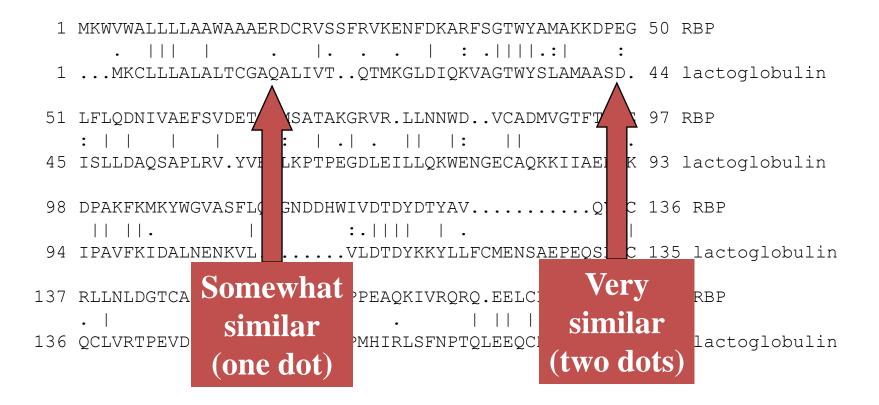
Pairwise alignment of retinol-binding protein 4 and b-lactoglobulin

1	MKWVWALLLLAAWAAAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEG	50	RBP
1	. . : . :: :MKCLLLALALTCGAQALIVTQTMKGLDIQKVAGTWYSLAMAASD.	44	lactoglobulin
51	LFLQDNIVAEFSVDETGQMSATAKGRVR.LLNNWDVCADMVGTFTDTE	97	RBP
45	: :: . . : 	93	lactoglobulin
98	DPAKFKMKYWGVASFLQKGNDDHWIVDTDYDTYAVQYSC	136	RBP
94	IPAVFKIDALNENKVLVLDTDYKKYLLFCMENSAEPEQSLAC	135	lactoglobulir
137	RLLNLDGTCADSYSFVFSRDPNGLPPEAQKIVRQRQ.EELCLARQYRLIV	185	RBP
136	. : . QCLVRTPEVDDEALEKFDKALKALPMHIRLSFNPTQLEEQCHI	178	lactoglobulir

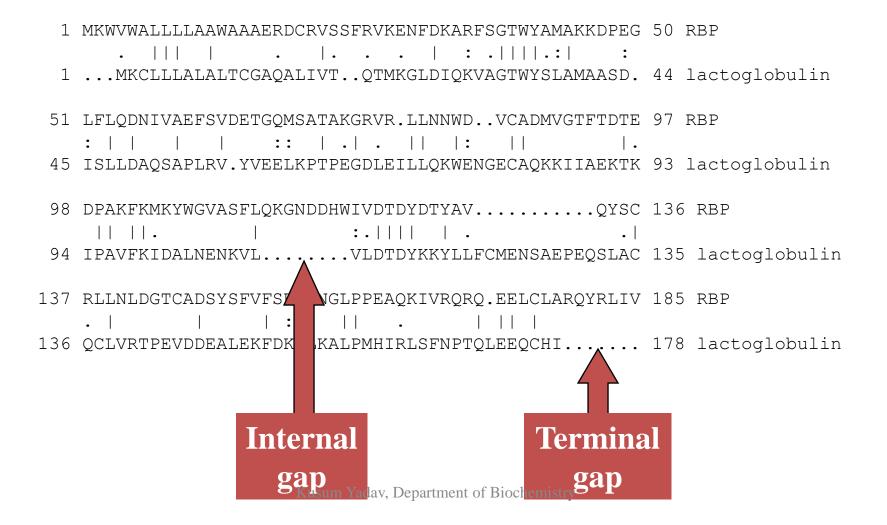
Pairwise alignment of retinol-binding protein and b-lactoglobulin

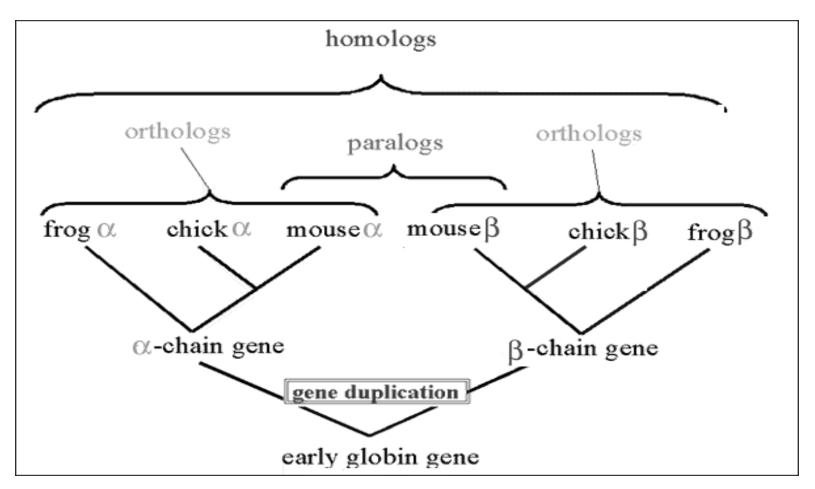


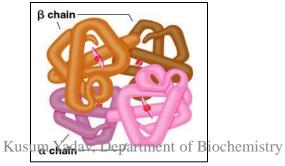
Pairwise alignment of retinol-binding protein and β -lactoglobulin



Pairwise alignment of retinol-binding protein and b-lactoglobulin





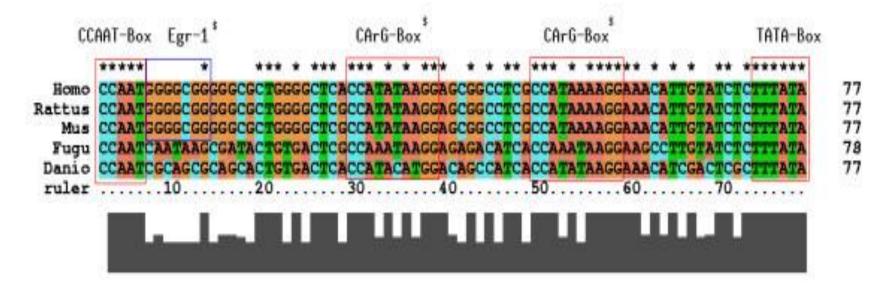


Sequence Analyses for relatedness

- Homologs: similar sequences in different organisms derived from a common ancestor sequence.
- Orthologs: homologous sequences in different related species
 that arose from a common ancestral gene during speciation.
 Orthologs are presumed to have similar biological function.
 e.g. Human and rats myoglobins both transport oxygen in
 muscle
- Paralogs: homologous genes within the same organism
 e.g. human α and β globins are paralogs. Paralogs are the result of gene duplication events
- Xenologs: similar sequences that have arisen out of horizontal transfer events (symbiosis, viruses, etc)

Multiple sequence Alignment

- Partial or complete alignment of three or more related proteins/ nucleotide sequences
- Conserved domain analysis
- Primer Designing



Tools of Multiple Alignment

- CLUSTALW
- T-Coffee
- MUSCLE
- KALIGN
- CLC & GCG WorkBench

Various categories of Analyses

1. Analysis of a single gene (protein) sequence

- Similarity with other known genes
- Phylogenetic trees; evolutionary relationships
- Identification of well-defined domains in the sequence
- Sequence features (physical properties, binding sites, modification sites)
- Prediction of sub-cellular localization
- Prediction of protein secondary and tertiary structures

2. Analysis of whole genomes

- Location of variuos genes on the chromosomes,
 correlation with function or evolution
- Expansion/duplication of gene families
- Which gene families are present, which missing?
- Presence or absence of biochemical pathways
- Identification of "missing" enzymes
- Large-scale events in the evolution of organisms

3. Analysis of genes and genomes with respect to function (Functional Annotation)

- Transcriptomics: Expression analysis; micro array data (mRNA/transcript analyses)
- Proteomics; protein qualitative and quantitative analyses, covalent modifications
- Comparison and analysis of biochemical pathways
- Deletion or mutant genotypes vs phenotypes
- Identification of essential genes, or genes involved in specific processes

4. Comparative genomics

• Identifying pathogen specific unique targets for designing novel drugs.

Phylogenetic Analysis

- The phylogenetic trees aim at reconstructing the history of successive divergence which took place during the evolution, between the considered sequences and their common ancestor.
- Nucleic acid and protein sequences are used to infer Phylogenetic relationships
- Molecular phylogeny methods allow the suggestion of phylogenetic trees, from a given set of aligned sequences.

Phylogenetic Analysis Tools

- **✓ MEGA**
- **✓PHYLIP**
- **✓ PAUP**
- **✓ Treeview**
- **✓ODEN**
- **✓ PHYLOWIN**
- **✓TREECON**
- **✓ DENDRON**



लखनऊ विश्वविद्यालय

University of Lucknow









