GBTK: A Toolkit for Grid Implementation of BLAST

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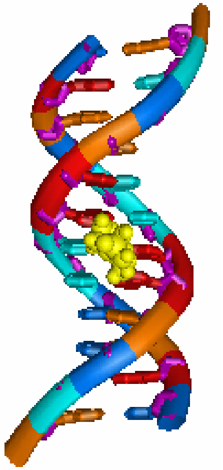
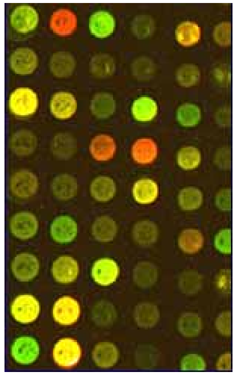
HIGH-THROUGHPUT TECHNIQUES ARE REVOLUTIONIZING LIFE SCIENCES

- DNA Sequencing
- Gene Expression Analysis With Microarrays
- Protein Profiling via High Throughput Mass Spectroscopy
- Protein-Protein Interactions
- Whole-Cell Response





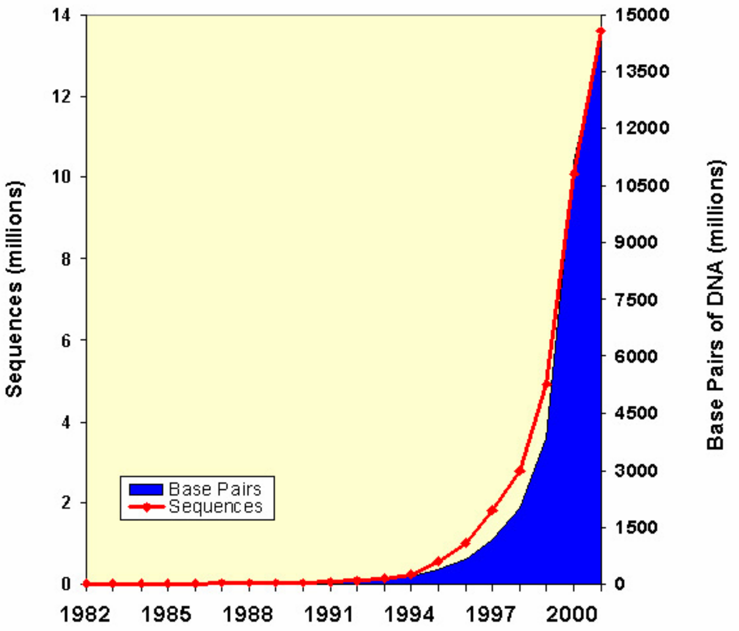
Need of High Performance Computing in Bioinformatics

- Complete Published Genome Projects: 200

  Archaeal:19

  Bacterial:153

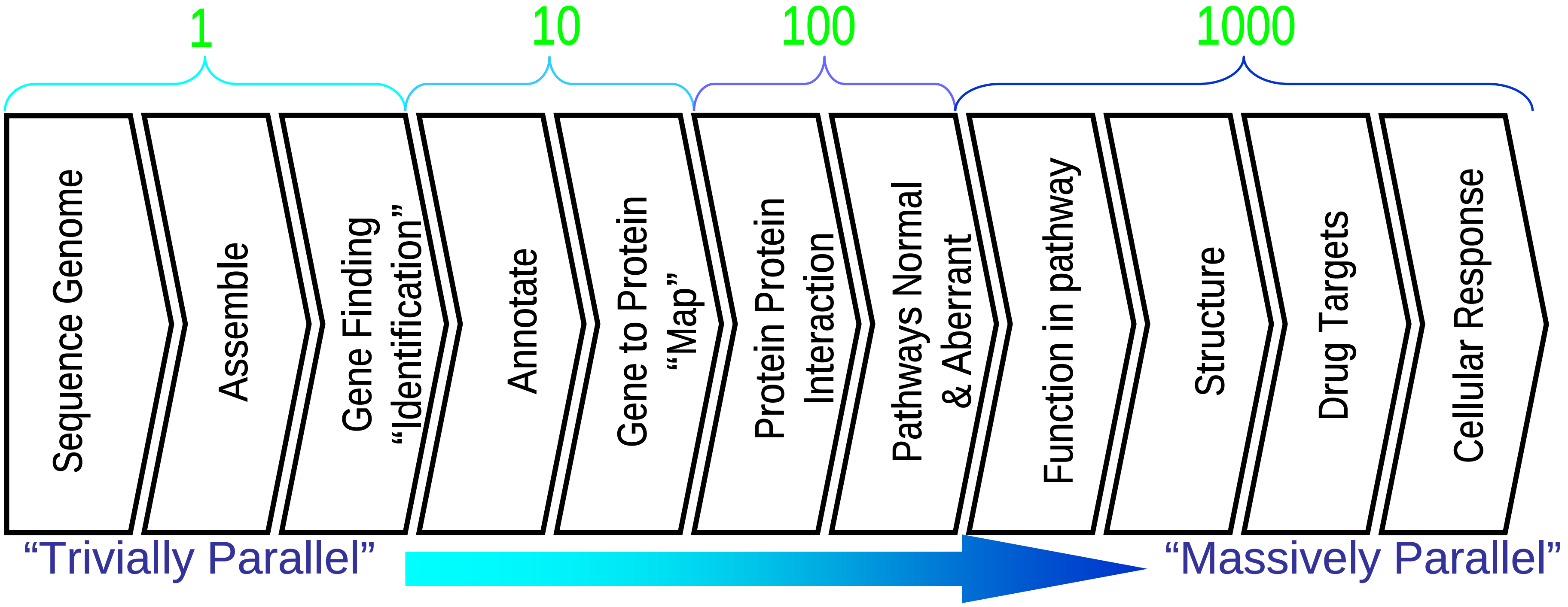
  Eukaryal:28
- Prokaryotic Ongoing Genome Projects: 508
- Eukaryotic Ongoing Genome Projects: 422
- http://www.genomesonline.org/



40.32 Gigabases from 35.53 million sequences

Release 142.0, June 2004

Computing For Life Sciences at the Terascale



1

10

100

1000

Sequence Genome

Assemble

Gene Finding "Identification"

Annotate

Gene to Protein "Map"

Protein Protein Interaction

Pathways Normal & Aberrant

Function in pathway

Structure

Drug Targets

Cellular Response

"Trivially Parallel"

"Massively Parallel"

Bioinformatics

Molecular Biophysics

Complex Systems

Grid Computing

- A type of parallel and distributed system that enables the sharing, selection and aggregation of geographically distributed autonomous resources dynamically at runtime depending on their availability, capability, performance, cost and users quality of service requirements.

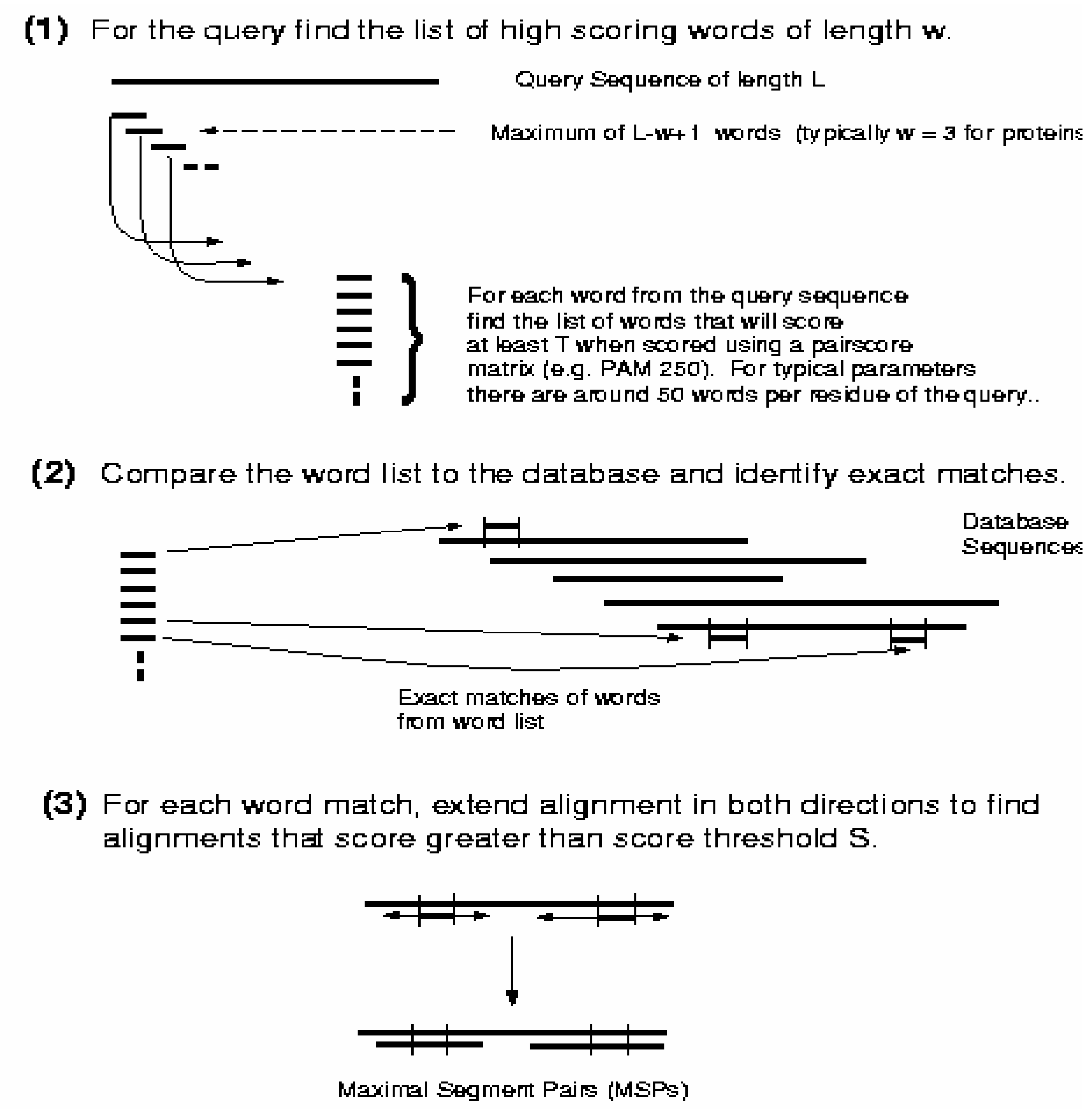
GRID Initiatives in Life Sciences

- BioGRID http://www.biogrid.jp
- NCBioGRID http://www.ncbiogrid.jp
- APBioGRID http://www.apbionet.org/apbiogrid/
- EuroGRID http://www.eurogrid.org
- Canadian BioGRID http://www.cbr.nrc.ca/
- MyGRID: http://www.mygrid.org.uk
- TeraGrid: http://www.teragrid.org

BLAST APPLICATION

- Basic Local Alignment Search Tool developed by Altschul *et. al.,* in 1990
- *Original Paper*: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. *J. Mol. Biol*. 215:403-10.
- Implements heuristic search method for finding maximal segment pairs (MSP) among a pair of sequences aligned
- http://www.ncbi.nlm.nih.gov/Class/ASHG/index.htm

BLAST ALGORITHM



(1) For the query find the list of high scoring words of length w.

Query Sequence of length L
Maximum of L-w+1 words (typically w = 3 for proteins

For each word from the query sequence find the list of words that will score at least T when scored using a pairscore matrix (e.g. PAM 250). For typical parameters there are around 50 words per residue of the query..

(2) Compare the word list to the database and identify exact matches.

Database
Sequences
Exact matches of words
from word list

(3) For each word match, extend alignment in both directions to find alignments that score greater than score threshold S.

BLAST ALGORITHM

- A list of words of size ‘W’ (e.g. W=4) are formed as an index of an array (an array of size 20^{W} for proteins)

- For the **Query** find the list of high scoring words of length ‘W’. Compare the word list to the database and identify exact matches

- For each word, extend alignment in both directions and find alignments that score greater than threshold score ‘S’

BLAST APPLICATIONS

- As BLAST algorithm is more selective and it can be best used for closely related sequences than for distantly related sequences

  E.g. Similar sequences like ORFs, Paralogs, repeat elements etc.
- BLAST programs are widely used for constructing Clusters of Orthologs (COGs) at NCBI (http://www.ncbi.nlm.nih.gov/COG)
- Reconstruct pathways by BLAST search of KEGG pathway diagrams (http://www.genome.ad.jp/kegg-bin/mk_homology_pathway_html)
- BLAST is used at EMBL for finding orthologues (http://dove.embl-heidelberg.de/Blast2e/)
- BLAST is also used in finding Alternate Splicing (AS) Sites

Motivation

- To build a web based system that can be able to spawn BLAST jobs on heterogeneous PARAM supercomputers scattered across Indian cities of Bangalore/Pune.

Requirements:

- Needed an application specific Grid framework that will help to utilize distributed computing resources.
- Framework should be “simple” and should be able to work on machines of various configurations.
- A light weight framework, to spawn BLAST jobs intelligently and retrieve outputs.

Web Services

- Basis of GRID computing
- Services offered via the web
- Applications communicate and exchange data using XML RPC or SOAP
- Independent of underlying platform, operating system or programming language

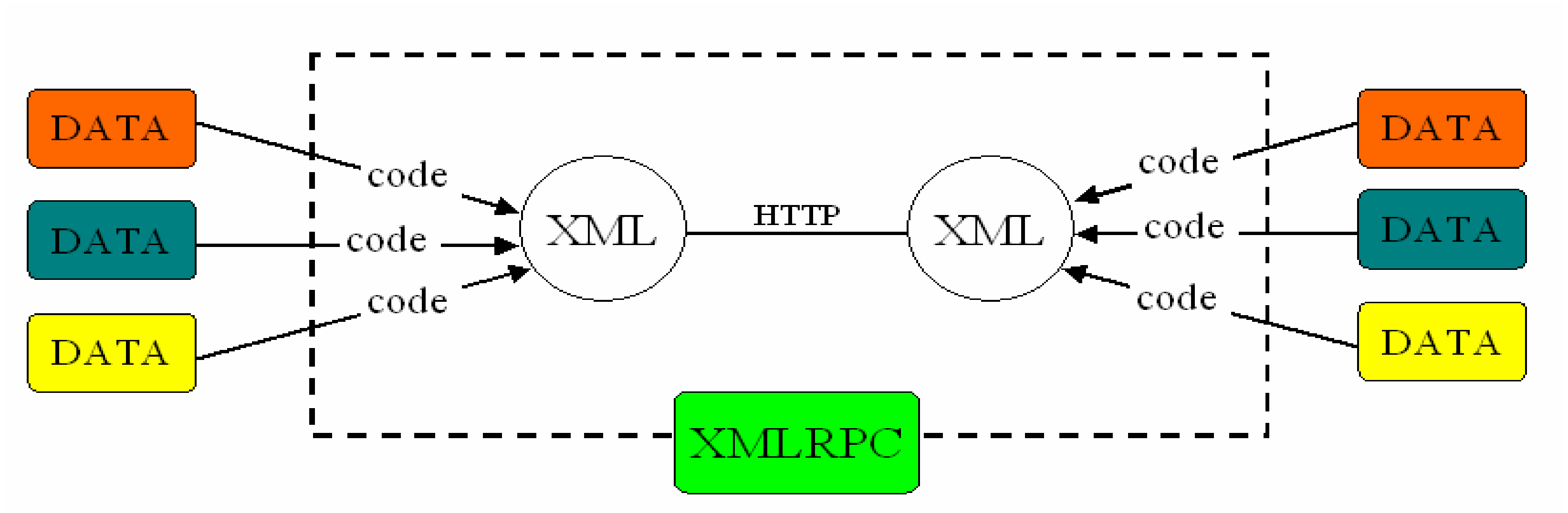
XML-RPC

- What is XML-RPC?

  Remote Procedure Calling protocol with XML format
- What can it do?

  - allows software running on disparate operating systems, running in different environments to make procedure calls over the Internet.
- XML-RPC is composed by an HTTP request and a HTTP response.
- The body of the request and the value returned from server is formatted by XML.

XML-RPC


DATA
DATA
DATA
code
code
code
XML
HTTP
XML
code
code
code
DATA
DATA
DATA
XMLRPC

GBTK: Concept

- Virtualization
- Enabling seamless access
- Distributed data
- Connect geographically spread heterogeneous computing resources
- Portal interface for running BLAST jobs

Hardware Environment

- PARAM Padma cluster (AIX, 1 Teraflop, 248cpu)
- PARAM 10000 cluster (Solaris, 100 Gigaflop, 140cpu)
- PARAM OpenFrame (Solaris, 6 cpu)
- SGI Octane2 (IRIX, 2 cpu)
- Intel PIII (Linux, 1cpu)
- Intel PIII (Windows, 1 cpu)

Hardware Resources: PARAM PADMA

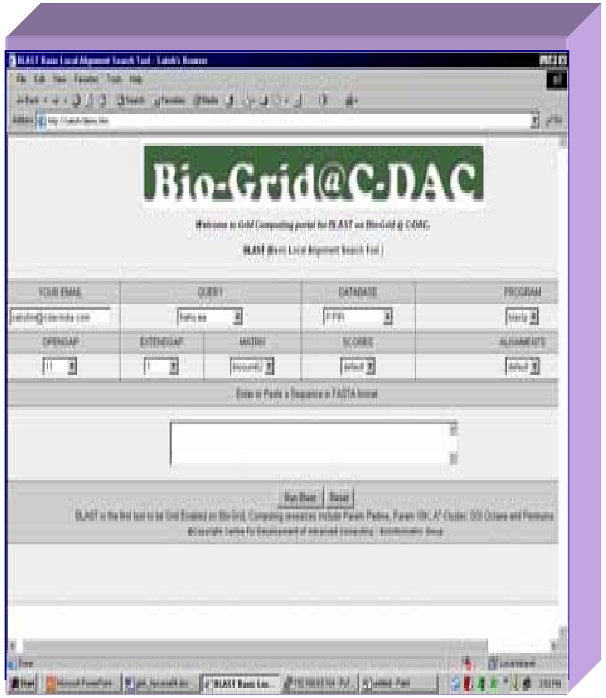
- Peak Computing Power - 1005 GF (~1 TF)
- Number of compute nodes - 54 Nos. of 4 Way SMP & 1 No. of 32 Way SMP
- No. of Processors - 248 (Power 4@1GHz)
- Aggregate Memory - 0.5 TeraBytes
- Internal Storage - 4.5 TeraBytes
- Operating System - AIX / LINUX
- Networks
  - PARAMNet-II @ 2.5 Gbps Full Duplex
  - Gigabit Ethernet @ 1 Gbps Full Duplex
- PARAMNet-II
  - in-house product
  - a high speed, low-latency switched network
  - Bandwidth – 2.5 Gbps

Hardware Resources: PARAM 10000

- Peak computing power of 100 Giga FLOPS
- Cluster of Sun Ultra e450 workstations 32 SMP compute nodes, each node with 4 processors (300 MHz)
- Physical memory: 1-2 GB
- Communication networks
  - Fast Ethernet
  - Myrinet
  - PARAMNet - in-house product

GRID BLAST

Domain Researchers



BLAST Basic Local Alignment Search Tool - Satish's Browser
File Edit View Favorites Tools Help

Bio-Grid@C-DAC

Welcome to Grid Computing portal for BLAST on BioGrid @ C-DAC

BLAST (Basic Local Alignment Search Tool)

YOUR EMAIL	QUERY		DATABASE	PROGRAM
[illegible]	[illegible]		[illegible]	[illegible]
OPENGAP	EXTENDGAP	MATRIX	SCORES	ALIGNMENTS
11	1	blosum62	default	default

Enter or Paste a Sequence in FASTA format

BLAST is the first tool to be Grid Enabled on Bio-Grid, Computing resources include Param Padma, Param 10K, A* Cluster, SGI Octane and Pentiums

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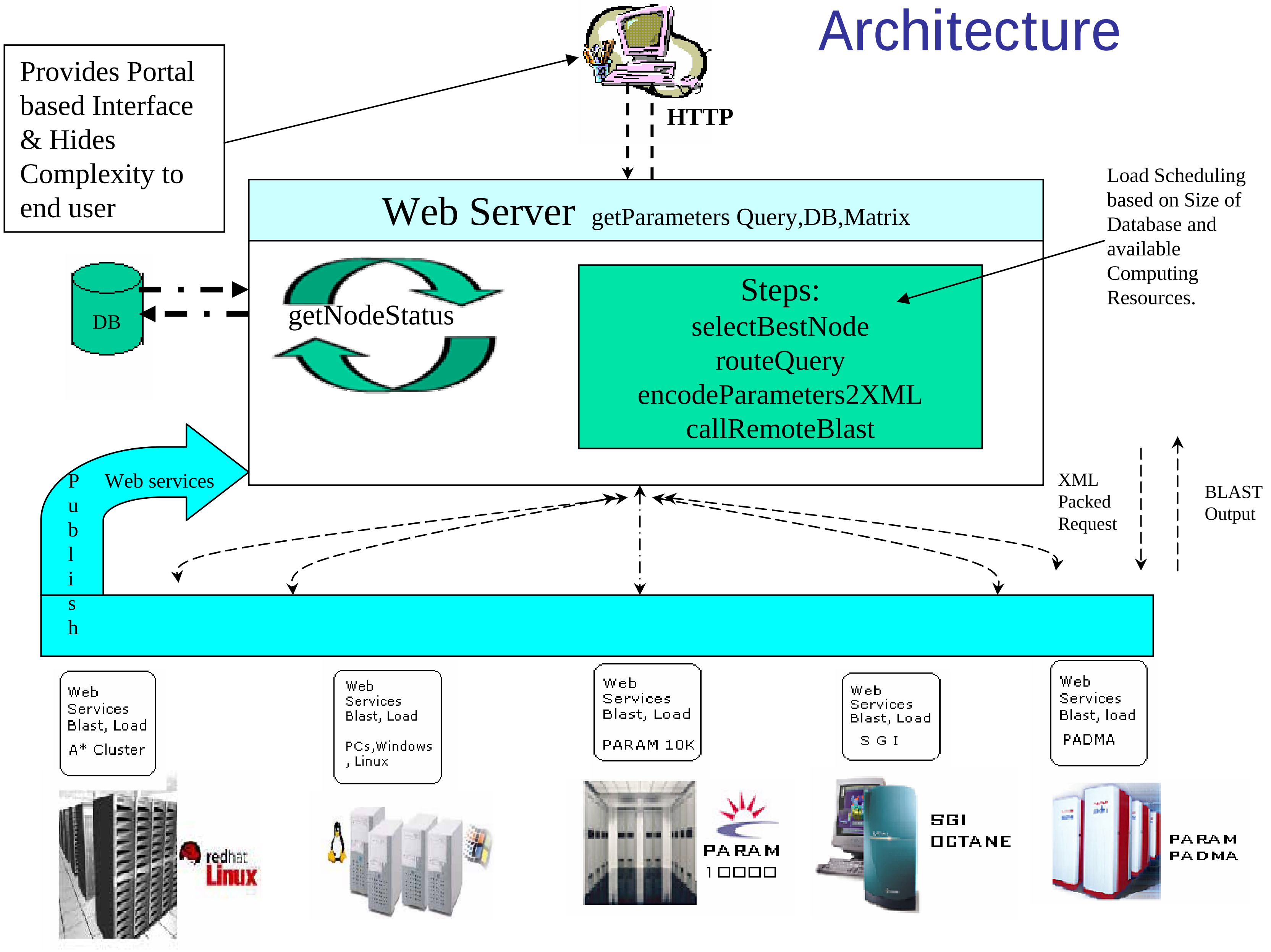
Web Browser

Computing Resources

GBTK: Features

- Application specific grid framework for BLAST
- Built on the concept of synchronized web services using RPC encoded as XML
- Light weight architecture
- Session tracking for distributed jobs
- Scheduling based on database availability and CPU load
- Capability of file transfer using remote copy protocol and secure copy protocol

Architecture



Provides Portal based Interface & Hides Complexity to end user

Load Scheduling based on Size of Database and available Computing Resources.

Implementation: Database Distribution

Databases distributed across the computing nodes without redundancy.

Node 1 PARAM Padma OS: AIX	Node 2 PARAM 10000 OS: Solaris	Node 3 PARAM OpenFrame OS: Solaris	Node 4 SGI Octane OS: IRIX	Node 5 Intel Box OS: Linux
EST_Human (2GB) EST_Mouse (1GB) Viral (105MB) Prokaryote (269MB)	Swissprot (43MB) Invertebrate (345MB) Trembl (170MB) NR (300MB)	PDB (3.82MB) Mitochondria (3.2MB) E.coli (4.7MB) Bacteriophage (4.9MB)	Prints (34MB) Mammalian (31MB) Yeast (3.3MB)	Vector (3.7MB) Syn P (0.9MB)

Implementation

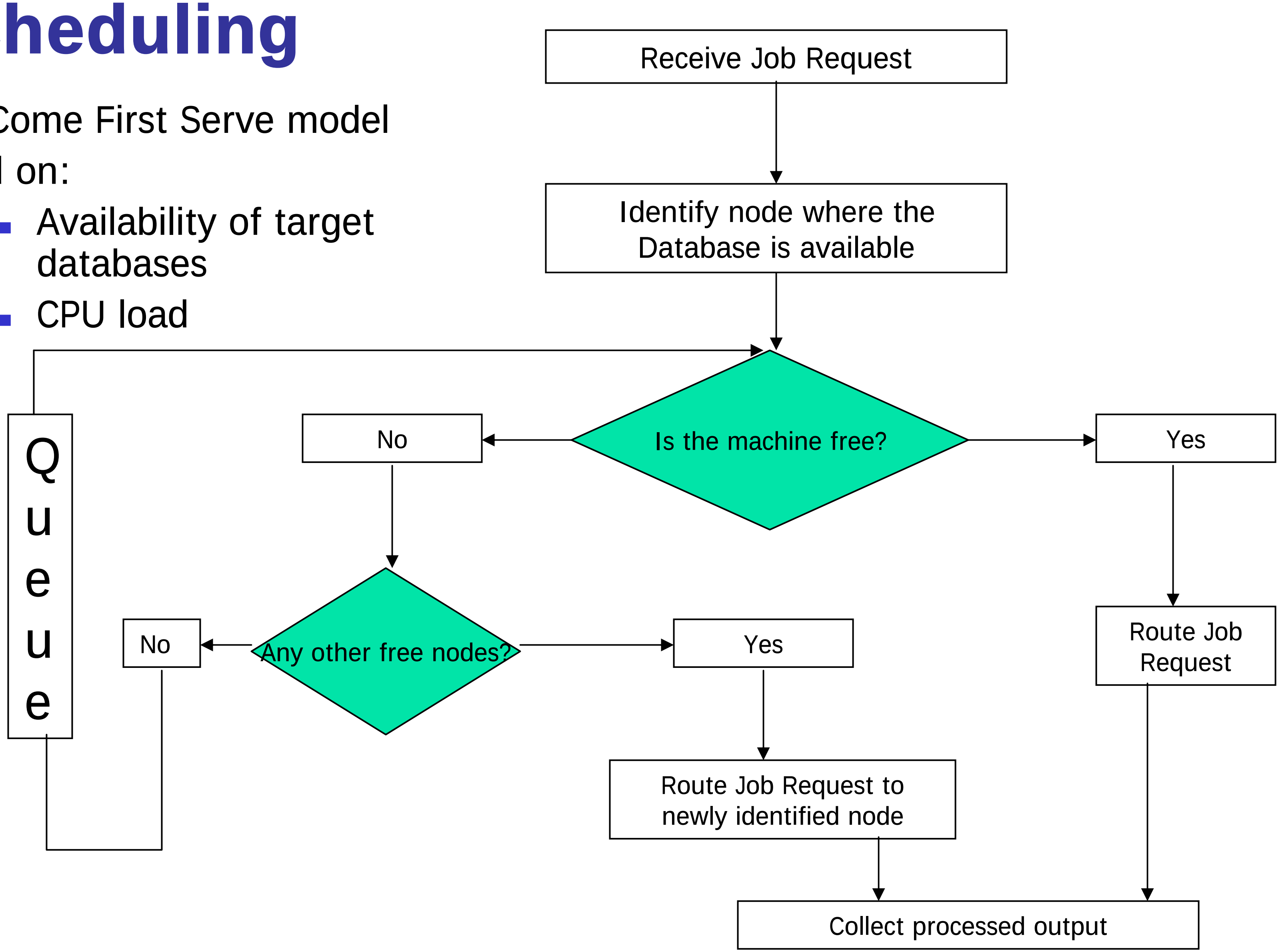
- Web Services model consists of three components
  - Producer of web services
  - Broker which maintains the registry of available services
  - Consumer who consumes web services via the Broker

Implementation

- All computing nodes provide web services namely
  - CPU load
  - Application web service (BLAST)
  - Heart Beat
  - Initiate File Transfer
  - Receive File Transfer
- The Broker also provides a web service called DB Registry which contains locations of the databases.
- When the Broker gets a BLAST job request, with the aid of the DB registry it identifies the node on which the job should be executed.

Scheduling

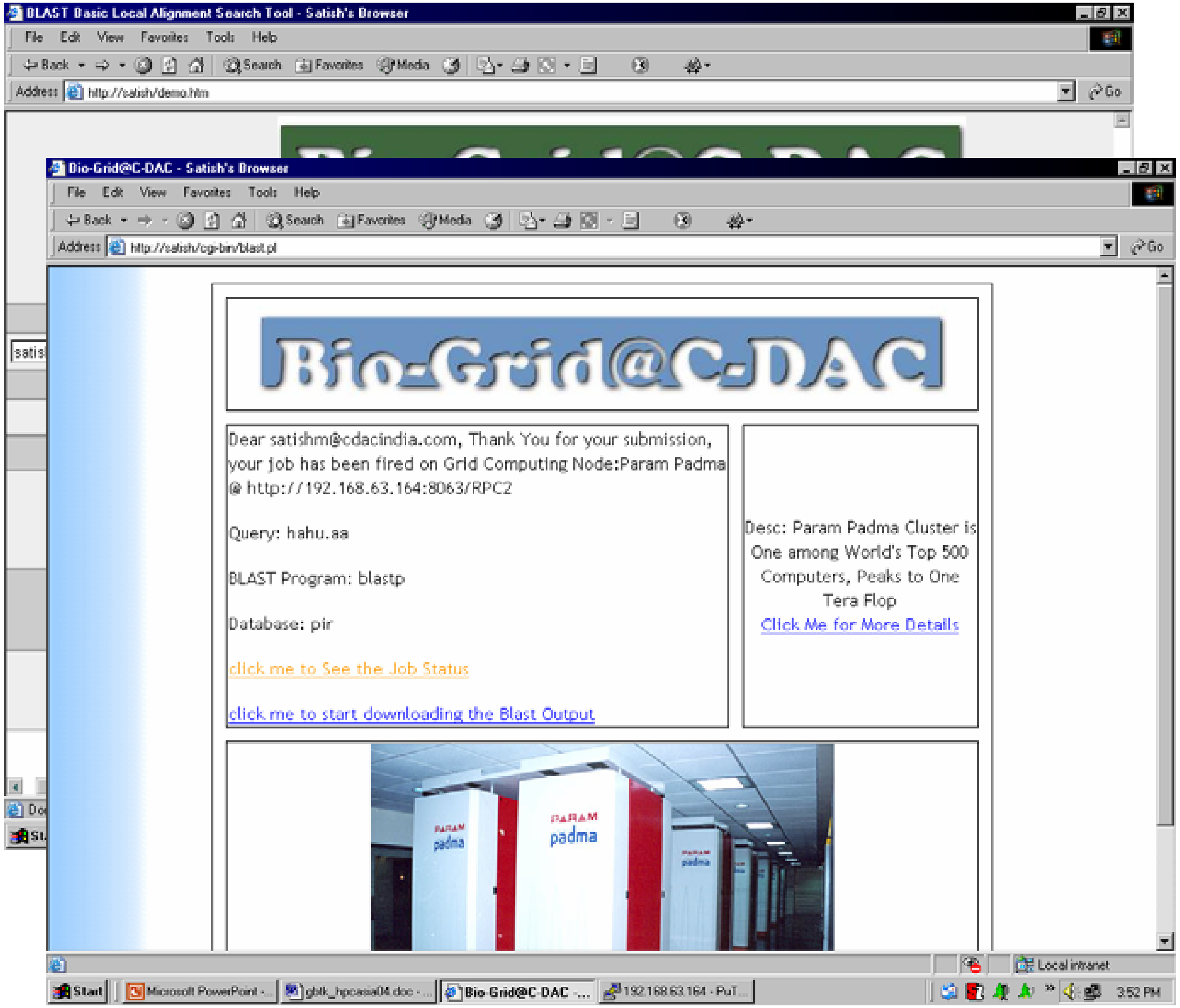
- First Come First Serve model
- Based on:
  - Availability of target databases
  - CPU load



User Interface

- GBTK provides a web based interface
- Uses CGI for receiving inputs from web pages
- Two categories
  - Master scripts: Retrieving inputs from the web and convert to XML & calling web services
  - Node scripts: Provide the web services functionality and wrappers for secured copy and remote copy data transfers
- Acknowledgment screen and status of job displayed

User Interface


BLAST Basic Local Alignment Search Tool - Satish's Browser
Bio-Grid@C-DAC - Satish's Browser
File Edit View Favorites Tools Help
Back Search Favorites Media
Address http://satish/demo.htm
Address http://satish/cgi-bin/blast.pl
Go
Bio-Grid@C-DAC
PARAM padma
Local intranet
Start
Microsoft PowerPoint -...
gblk_hpcasia04.doc -...
Bio Grid@C-DAC -...
192.168.63.164 - PuT...
3:52 PM

Dear satishm@cdacindia.com, Thank You for your submission, your job has been fired on Grid Computing Node:Param Padma @ http://192.168.63.164:8063/RPC2

Query: hahu.aa

BLAST Program: blastp

Database: pir

click me to See the Job Status

click me to start downloading the Blast Output

Desc: Param Padma Cluster is One among World's Top 500 Computers, Peaks to One Tera Flop

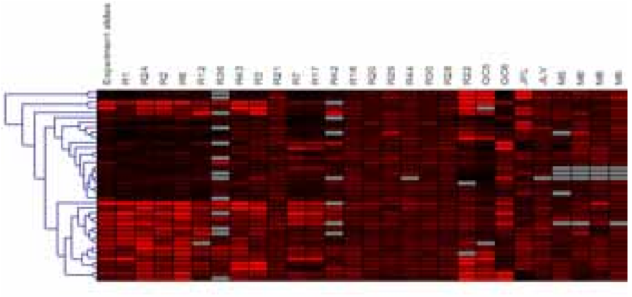
Click Me for More Details

- Web based Interface for the end user.
- Based on Apache Web server/ CGI.

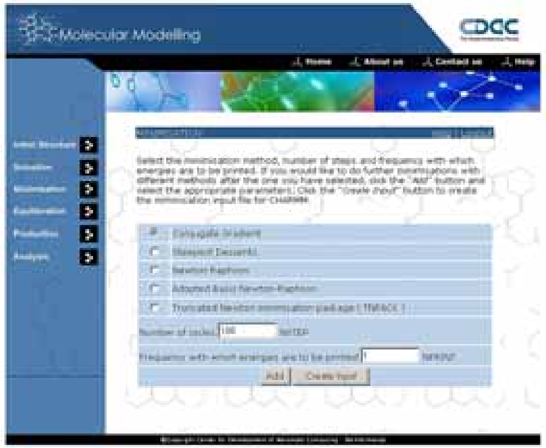
Conclusion

- GBTK is based on Service Oriented Architecture
- Use of commodity tools will help in rapid deployment of application specific grids
- GBTK provides location transparency
- GBTK is a generic framework and can be used for any other application

Microarray Analysis



Problem Solving Environments

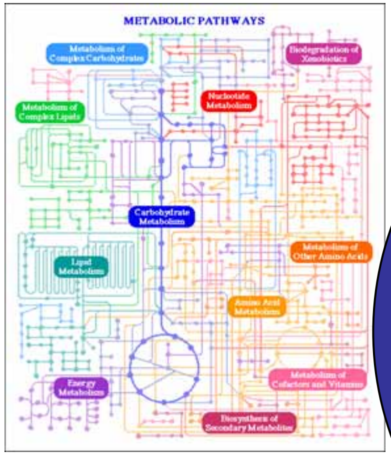


Select the minimization method, number of steps and frequency with which energies are to be printed. If you would like to do further minimizations with different methods after the one you have selected, click the "Add" button and select the appropriate parameters. Click the "Create Input" button to create the minimization input file for CHARMM.

● Conjugate Gradient
○ Steepest Descent
○ Newton Raphson
○ Adopted Basis Newton-Raphson
○ Truncated Newton minimization package (TNPACK)

Number of cycles: 100 NSTEP

Frequency with which energies are to be printed: 1 NPRINT

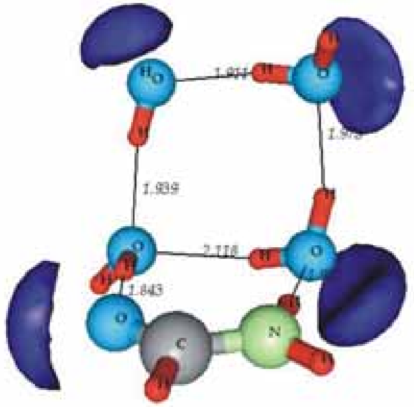

METABOLIC PATHWAYS
Metabolism of Complex Carbohydrates
Biodegradation of Xenobiotics
Metabolism of Complex Lipids
Nucleotide Metabolism
Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Other Amino Acids
Amino Acid Metabolism
Metabolism of Cofactors and Vitamins
Energy Metabolism
Biosynthesis of Secondary Metabolites

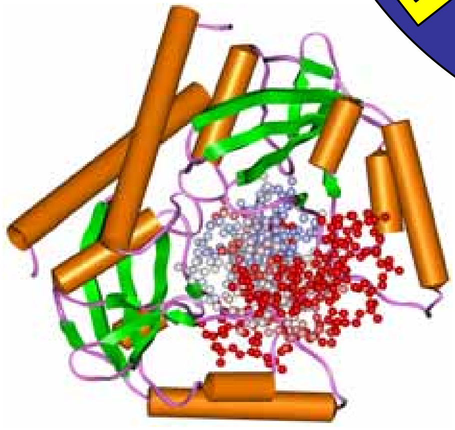
Metabolic Pathways

Bioinformatics

PARAM Padma

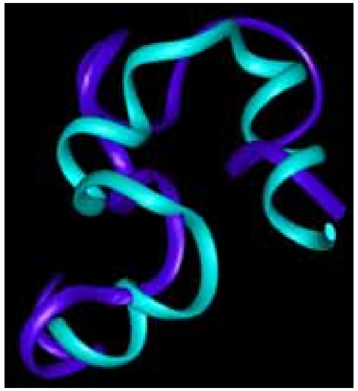
Ab-initio methods

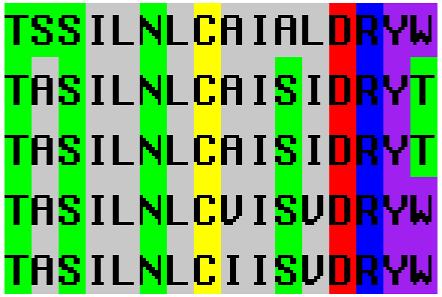




Molecular Modelling

Protein Structure Prediction





TSSILNLCAIALDRYW
TASILNLCAISIDRYT
TASILNLCAISIDRYT
TASILNLCVISVDRYW
TASILNLCIISVDRYW

Genome Sequence Analysis

THANK YOU

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