

Research and Reviews: Research Journal of Biology

Role of Bioinformatics in Various Aspects of Biological Research: A Mini Review

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Mini Review

Received: 20/03/2015

Revised : 26/03/2015

Accepted: 08/04/2015

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Keywords: Bioinformatics,
Biological research, Proteomics,
Agriculture

ABSTRACT

After completion of human genome sequencing in 2001, most of the researchers in biological science were involved in sequencing of other living organism to discover various uncovered facts of living system. And at the same time molecular biologist also were involved in proving of their basic central dogma concept and were doing extensive researches to show that how every complication and functionality was interrelated to human genome and DNA. With the help of system biology study and geneticist, complete world was generating enormous amount of data in field of biological research. To handle this huge data in files and experimental log books was getting difficult day by day, then bioinformatics came into picture to handle large data with help of computer and hence termed as computational biology also. Initially it was just a technique or tool to arrange data in particular fashion, but with its fast popularity and acceptance with major biological research areas, it is now a complete different field of study and expertise. It is now associated with most of the areas in biological researches being carried out in almost all over the world. It is widely accepted in field of molecular biology, proteomics, genomics, metabolomics, biotechnology, and agriculture by researchers and even in veterinary science researches also.

INTRODUCTION

Biological research is the most fundamental research to understand complete mechanism of living system. In recent decades, bioinformatics methods, with the use of knowledge accumulated in public databases such as NCBI, Pubmed and other databases, make it possible to systematically dissect large gene lists in an attempt to assemble a summary of the most enriched result in current biology [1,2], which is able to provide a huge contribution to biological research. In the same contrast, bioinformatics scanning approaches are emerging as alternative technologies that allow investigators to simultaneously measure the changes and regulation of genome-wide genes under certain biological conditions. These high-throughput technologies usually generate large gene of biological research interest lists as their final outputs [3,4]. If we see earlier traditional biological researches, we were able to study one gene or a few genes at a time [5-10].

But after introduction of bioinformatics and regularly generation of research database around world and keeping them publically available online to support biological researchers was a very unique idea and beneficial for new researcher as well as the scientists working in same research interest in different geographical location in this world [11-15]. Initially the complete aim of bioinformatics was just to handle data in biological research, but with increasing popularity and involvement of tool development to analyze data in a lesser time to complete research in fast and efficient manner [16-18], bioinformatics has acquire a bigger place than it was expected to. In later segment of review we can see how these tools and techniques have affected our biological research. It is a complete bridge which relates mathematics, computer and statistical science to biological research [19-23].

TOOLS AND TECHNIQUE

Bioinformatics is partly based on tools and technique used earlier to get complete analysis of biological experiments in a shorter period of time. The main aim of developing these tools was to perform those analysis tasks, which were very much time consuming and without which research cannot be taken further [24-31]. We can see a very small example of sequence alignment, where we have developed a tool for basic local alignment of sequence called "BLAST". BLAST was acronym for basic local alignment searching tool [32-39], which is now a day very popular among molecular biologist for their initial studies, and even for structural biologist who prefer to perform this before showing any structural and functional similarity between two genes. After that so many tools were also designed to perform multiple sequence alignment like "Clustal W" to get analysis report for more than two genes at a time [41-48]. Similarly for phylogenetic analysis also bioinformatics tools were developed and they were capable of generating various tree based on algorithms like UPGMA, and Neighbor joining methods etc [49-56]. These tools were designed with the help of computer algorithms and with root developing platform of computer languages [57]. Initially when biologists were not very much efficient with use of these programming language, they have started using perl and python to develop tools for biological research, but later on bioinformaticians who were equally efficient in other language platforms completely changed the scenario of biological research with involvement of C, C++ and Java to developed tools which were very efficient as well as user friendly interface [58-65].

Human Genome Sequencing

Human genome sequencing was the basic foundation for origin and evolution of this particular domain of biological research tool. This experiment was very big and time consuming and expected to reach its completion at some later point of time, but still it was completed 2 years early than it was expected to [66-72]. A detailed draft was reported in 2003 to show human genome project. This project was initially led by a student named Jim Kent. This project was world's largest collaborative biological project and showed big promises in field of molecular medicine and human evolution [74-81]. Although people were thinking about handling this huge data and keeping it safe, but this was just the beginning of research in molecular biology, after completion of this research project various related project were started to make new holes to understand biological machinery [81-87].

Molecular Biology Data

World has seen enormous amount of data generated by molecular biologists and the difficulties to handle them in previous decades during 20th century. After human genome project, there was a flood of biological research in field of molecular biology and biotechnology started, which was a great source of huge experimental data and to handle that bioinformatics came in existence [88-94]. Bioinformatics made all the data available online and very efficiently able to manage, modify and replace the complete data in a very shorter duration. Usually molecular biology experiments have lots of analysis and hence generate large data [95-104], that is why bioinformatics was first of all applied to molecular biology experimental data, but later on it was accepted by almost all fields of biological research.

Structural Bioinformatics

It is most emerging part of biological science. In this area mainly scientists focus on structure prediction by sequence similarity basis. They follow a common theory that if there is a sequence similarity, there must be some structural similarity and obviously there would be a functional similarity between those two genes [105-111]. Here people perform sequence analysis and based on the similarity they also generate 3D structure of molecules and check their stability also. With the help of creating maps from Ramchandran plot, scientists and researchers are able to perform stability checks of structures also [112-115].

Biotechnology

Research in biotechnology and awareness of research in this particular field by various countries involved in biological research are providing regular updates and contribution to make human life better and better. Bioinformatics has surely reduced the time consuming experimental procedure and it is bringing a huge difference in complete time taken in biotechnological research earlier [116-120]. It is also working in field of simulation of experiments online based on data models created with previous experimental lab data to predict the most probable result within a short span.

Software development

Mostly bioinformatics helps in keeping experimental data online to reach wide range of audience, and software or tool development work to make analysis of biological data very easy and less time consuming. There are a lot of tools developed by premier research institutes around world now available to use online for benefit of biological researchers [121-126].

Application of bioinformatics in current research

Currently almost every field of biological research has accepted this biological research weapon and following it, whether it is molecular biology or genetics, or even agriculture. There a complete new emerging field of genome informatics is there which is completely based on bioinformatics tools [127-133]. Apart from these there are so many areas where bioinformatics is readily being accepted with primary role in prediction of structure similarity and functional similarity in novel drug molecule research also. They perform initially tasks such as

- **SUBMITTING DNA SEQUENCES TO THE DATABASES**

- This is one of important thing in biological research, where scientists sequence DNA, and RNA, but until it is not getting deposited to any public sequence database, that cannot be beneficial for scientific community. It became very essential to submit all the sequenced data to public sequence repositories. Some of the important public repositories are DDBJ, EMBL, and Genbank.
- These sequence data can be submitted to repositories in two ways, either by email submission or by online submission through sequence submission tools. There are specific tools for every public sequence repository (Table 1) [134-154].
- After submission every database provides an unique accession number to submitted sequence after verification and duplication checks. If it is an unique sequence, then accession number is given as a single letter followed by 5 digit number, but recently due to huge number of submission two letters followed by 6 digit of number for accession number is now proposed.

Table 1: Public sequence depositories

SEQUENCE DATABASE	EMAIL SUBMISSION	TOOL	TOOL URL
DDBJ	ddbjsub@ddbj.nig.ac.jp	SAKURA	http://sakura.ddbj.nig.ac.jp/
EMBL	datasubs@ebi.ac.uk	WEBIN	http://www.ebi.ac.uk/submit/mission/webin.html
GENEBANK	gb-sub@ncbi.nlm.nih.gov	BANKIT	http://www3.ncbi.nlm.nih.gov/BankIt/

- **GENOMIC MAPPING AND MAPPING DATABASES**

- Gene mapping is one of the technique to estimate accurate position of gene and corresponding distance between related genes of similar type.
- After complete evaluation we can reach to a conclusion of genome map for complete genome for that particular organism.

Table 2: Human Genome Databases, Browsers and Variation Resources

Database	Description
dbVar	Database of Genomic Structural Variation
ENCODE Project	ENCyclopedia Of DNA Elements
Ensembl Human	Human genes generated automatically by the Ensembl gene builder
Entrez Gene	Searchable database of genes, defined by sequence and/or located in the NCBI Map Viewer
Genome Reference Consortium	Putting sequences into a chromosome context
GWAS	Central centralized compilation of summary level findings from genetic association studies
HapMap international HapMap Project	H-Invitational Database an integrated database of human genes and transcripts
Human Genome Segmental Duplication Database	A global analysis of human segmental duplications
Human Structural Variation Database	Genome browser
1000 Genomes	A Deep Catalog of Human Genetic Variation
UCSC Human Genome Browser Gateway	Genome browser
VEGA Human	Manual annotation of finished genome sequence

Some of other vertebrate databases are listed below in Table 2.

Table 2: Vertebrate databases and genome browsers

Database	Description
ZFIN	Zebrafish Information Network
Xenbase	A Xenopus web resource
VEGA	Vertebrate Genome Annotation containing manual annotation of vertebrate finished genome sequence
UCSC Genome Bioinformatics	Genome Browser
Tetraodon	Genome Browser
RGD	Rat Genome Database
Rabbit Genome Resources	Rabbit Genome Browser
Pig Genome Resources	Pig Genome Browser
lizardbase	A centralized and consolidated informatics resource for lizard research
MGI	Mouse Genome Informatics
Fugu	The Fugu genomics project
Ensembl	Genome databases for vertebrates and other eukaryotic species
Bovmap	mapping the Bovine genome

AgBase	A curated, open-source resource for functional analysis of agricultural plant and animal gene products
BirdBase	A Database of Avian Genes and Genomes
ARKdb	Species databases includes: Cat, Chicken, Cow, Deer, Horse, Pig, Salmon, Sheep, Tilapia, Turkey
AnolisGenome	A community resource site for Anolis genomics and genetic studies

These are List of some invertebrate databases and genome browsers available currently (Table 3) [154-169].

Table 3: List of some invertebrate databases and genome browsers

Database/ genome browser	Description
WormBase	The biology and genome of <i>C. elegans</i>
VectorBase	Invertebrate vectors of human pathogens
TAIR	The Arabidopsis Information Resource
StellaBase	Nematostella vectensis Genomics Database
SpBase	Strongylocentrotus purpuratus Sea Urchin Genome Database
SGD	Saccharomyces Genome Database
PomBase	A scientific resource for fission yeast
IGGI	International Glossina Genome Initiative
HGD	Hymenoptera Genome Database
Gramene	A resource for comparative grass genomics
GOBASE	The Organelle Genome Database
GenProtEC	E.Coli genome and proteome database
FlyBase	A database of the Drosophila genome
Ensembl Genomes	
EcoGene	The Database of Escherichia coli Sequence and Function
dictyBase	Central resource for Dictyostelid genomics
Dendrome	A Forest Tree Genome Database
Daphnia Genome Database	Genome browser
Chlamydb	The green alga Chlamydomonas reinhardtii and related species
ANISEED	Ascidian Network for InSitu Expression and Embryological Data
AspGDA	aspergillus Genome Database
BeetleBase	The model organism database for Tribolium castaneum
Caenorhabditis Genome Sequencing Projects	Genome browser
The Cotton Genome Database	Genome browser
Cacao Genome Database	Genome browser
Candida Genome Database	Genome browser

- **INFORMATION RETRIEVAL FROM BIOLOGICAL DATABASE**
 - Developing biological database and its availability online was one of the primary concerns at initial stage of biological research, but now as we have many biological database and

data is in form of text, table and pictures and many other formats. We should really know that how to retrieve exact data from a suitable database. Database may be of text retrieval, sequence retrieval or it may also include structural data retrieval importance [170-181].

- **SEQUENCE ALIGNMENT AND DATABASE SEARCHING**
 - Alignment of sequence with compare to other relevant and similar sequence is very much needed in biological research to understand relation between two sequences and also to predict structure and function based on sequence similarity.
 - For basic alignment of sequences use of BLAST is very common. Based on number of sequences involved in sequencing, we can classify these alignments into pairwise alignment or multiple sequence alignment.

- **PREDICTIVE METHODS USING DNA SEQUENCES**
 - **Gene-finding strategies can be Classified into three major categories.**
 - Content-based methods rely on the overall, bulk properties of a sequence in making determination. Characteristics considered here include how often particular codons are used, the periodicity of repeats, and the compositional complexity of the sequence. Because different organisms use synonymous codons with different frequency, such clues can provide insight into determining regions that are more likely to be exons.
 - In site-based methods, the focus turns to the presence or absence of a specific sequence, pattern, or consensus. These methods are used to detect features such as donor and acceptor splice sites, binding sites for transcription factors, polyA tracts, and start and stop codons.
 - comparative methods make determinations based on sequence homology. Here, translated sequences are subjected to database searches against protein sequences to determine whether a previously characterized coding region corresponds to a region in the query sequence. Although this is conceptually the most straightforward of the methods, it is restrictive because most newly discovered genes do not have gene products that match anything in the protein databases.
 - Tools associated with these are Grail, Genscan, Fgenes, procrustes and many others developed with bioinformatics [182-191].

- **PREDICTIVE METHODS USING PROTEIN SEQUENCES**
 - There are tools based on predictive methods using protein sequences, such as PSLPred, NRpred, PSEAPred. There are other methods also based on motif level, residue level, signal level, peptide level, domain level and profile based [192-196].

- **SEQUENCE ASSEMBLY AND FINISHING METHODS**
 - At present, the sequencing process is often talked of as consisting of two parts, namely, assembly and finishing, but in practice there is considerable overlap between the two. Assembly is the process of attempting to order and align the readings, and finishing is the task of checking and editing the assembled data. This includes performing new sequencing experiments to fill gaps or to cover segments where the data is poor and adjudicating between conflicting readings when editing [197-211].

- **PHYLOGENETIC ANALYSIS**
 - Phylogenetic analysis is also one of the important implementation of bioinformatics in biological research. Phylogenetic analysis is study of ancestral history of an organism. Here after sequence and structural similarities we try to relate organism's ancestral history to show how origin of organism was related to each other and "what was order of evolution". We actually do evolutionary history analysis by phylogenetic analysis.
 - There are many tools available online as well as commercial packages also like PHYLIP. It uses tree generation methods with algorithms based on methods such as UPGMA, and neighbor joining [211-219].

- **COMPARATIVE GENOME ANALYSIS**
 - Comparative genome analysis is also being performed in various researches at many levels such as academics and professional researches. By comparing the finished reference sequence of the human genome with genomes of other organisms, researchers can identify regions of similarity and difference. This information can help scientists better understand the structure and function of human genes and thereby develop new strategies to combat human disease. Comparative genomics also provides a powerful tool for studying evolutionary changes among organisms, helping to identify genes that are conserved among species, as well as genes that give each organism its unique characteristics [220-226].

- **LARGE-SCALE GENOME ANALYSIS**
 - Large scale genome analysis is complete genome sequencing, and this application has much advancement as next generation sequencing and bioinformatics tools like illumina have been developed to analyze them very quickly. These tools are generally termed as sequencer and playing a vital role in modern biological research [227-231].

There are so many other application in pharmaceutical research also have been seen these days as it also deals with systems biology and pathways of metabolites and their relation to biological functioning similarity [232-241].

Recent Advancement

However bioinformatics is still in its nascent stage, but continuous improvement is making it more efficient [240]. Mostly with inclusion of various computer language incorporation in this field and development of software packages for analysis of biological data is contributing to recent advancement in this field [241-243]. Drug designing software packages like "Sanjeevni" developed by IIT Delhi, India [244-247], maestro from Schrodinger also is contributing a lot to it. Indian agricultural statistical research institute (IASRI) also is making a huge contribution towards bioinformatics research by creating so many databases on agricultural and biological area. Most recent use of bioinformatics has been seen in novel drug molecule discovery and ligand analysis for protein targets in human physiological cycle to receive most possible cure for lethal diseases in short period [248-251]. There is plenty of docking software available, which are very efficient and proved their accuracy also [252-253].

Review and conclusion

With inclusion of large number of tools and implementation of bioinformatics in various biological research areas, it is now showing its existence and importance simultaneously. Now a day every experiment in biological research is getting associated with bioinformatics. It has made research very simple and fast, but still validation for various techniques are still in process for its accuracy. We are able to get a lot of results in a minute, which was not possible by using wet lab techniques in biotechnology.

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