Genetics and Bioinformatics

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Lecture 1: Setting the pace

1 Bioinformatics – what's in a name ?

Genetics

Molecular biology

Bioinformatics

2 Evolving trends in bioinformatics

Challenges

Topics in bioinformatics from a journal's perspective

3 Bioinformatics software

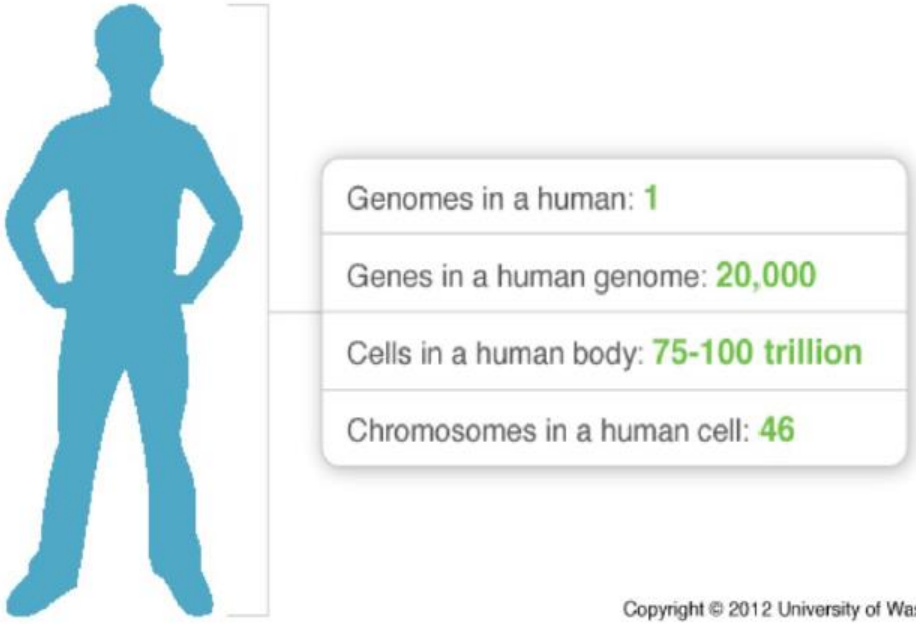
R and Bioconductor

1 Bioinformatics – what's in a name?

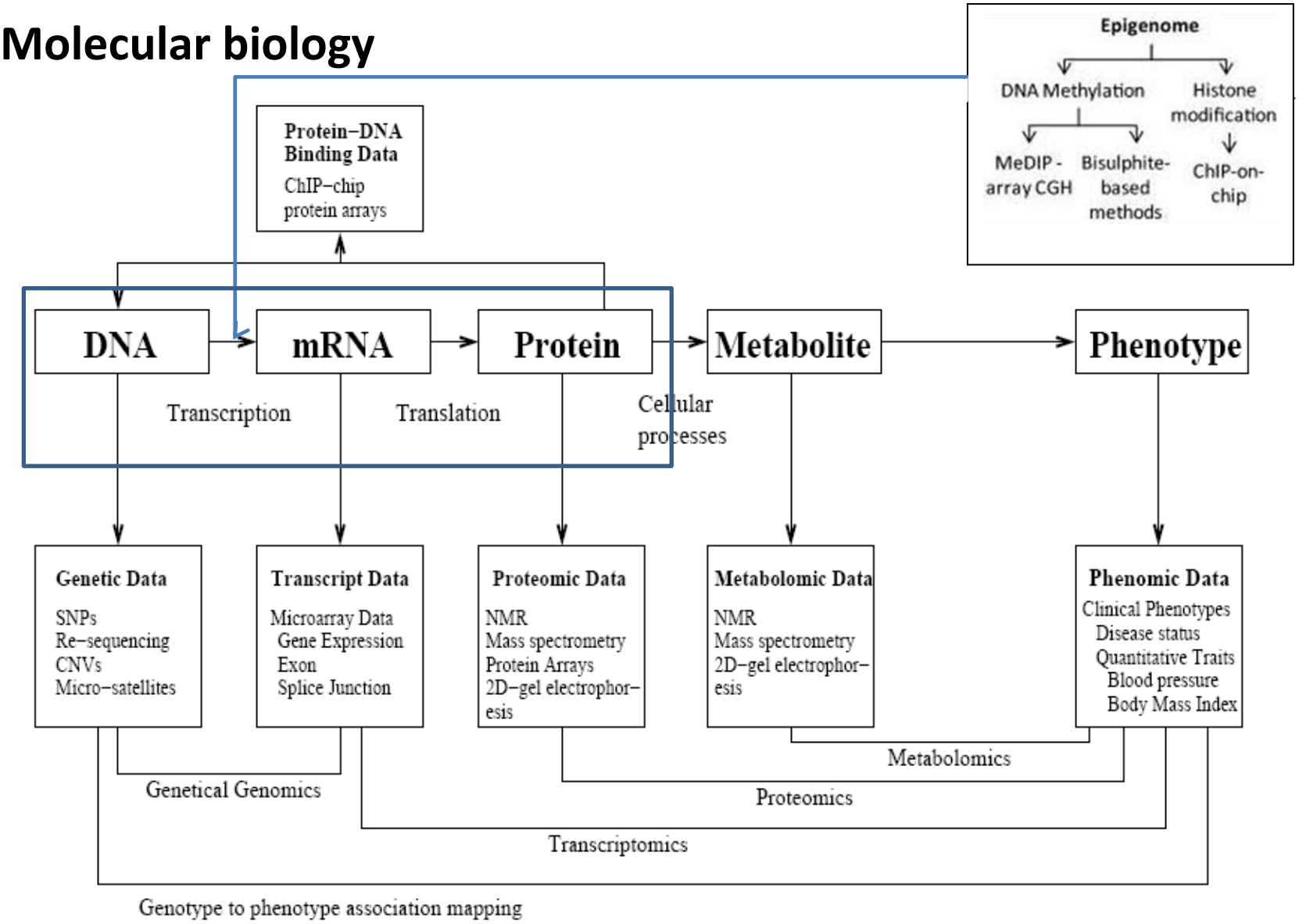
Genetics

- Genetics is the study of how traits such as hair color, eye color, and risk for disease are passed ("inherited") from parents to their children. Genetics influence how these inherited traits can be different from person to person.
- Your genetic information is called your genetic code or genome.

Your genome is made up of a chemical called deoxyribonucleic acid (DNA) and is stored in almost every cell in your body.



Molecular biology



(adapted from: Davies et al 2009, Integrative genomics and functional explanation)

Epigenetics – could the central dogma be in danger?

If parents are able to pass environmental information, in the form of epigenetic modifications, on to their offspring as well as their genetic code, epigenetic inheritance adds a whole new dimension to the modern picture of evolution. For over a hundred years we have accepted that the genetic code changes slowly, through the processes of random mutation and natural selection. Epigenetics creates the possibility for a much more rapid response to signals from the environment. It requires a completely different concept of information transfer – experiences had generations ago, such as a famine during your grandmothers time, could influence the way that your body develops, even in today's more plentiful western world.

(http://blogs.mcgill.ca/osscontributors/2014/01/07/)

Computational biology

- Biology = noun
- Computational = adjective

When I use my method (or those of others) to answer a biological question, I am doing science. I am learning new biology. The criteria for success has little to do with the computational tools that I use, and is all about whether the new biology is true and has been validated appropriately and to the standards of evidence expected among the biological community. The papers that result report new biological knowledge and are science papers. This is computational biology. (https://rbaltman.wordpress.com)

Computational biology = the study of biology using computational techniques. The goal is to learn new biology, knowledge about living sytems. It is about science.

Bioinformatics

- Bio(logy) + Informatics (2 nouns)

When I build a method (usually as software, and with my staff, students, post-docs–I never unfortunately do it myself anymore), I am engaging in an engineering activity: I design it to have certain performance characteristics, I build it using best engineering practices, I validate that it performs as I intended, and I create it to solve not just a single problem, but a class of similar problems that all should be solvable with the software. I then write papers about the method, and these are engineering papers. This is bioinformatics. (https://rbaltman.wordpress.com)

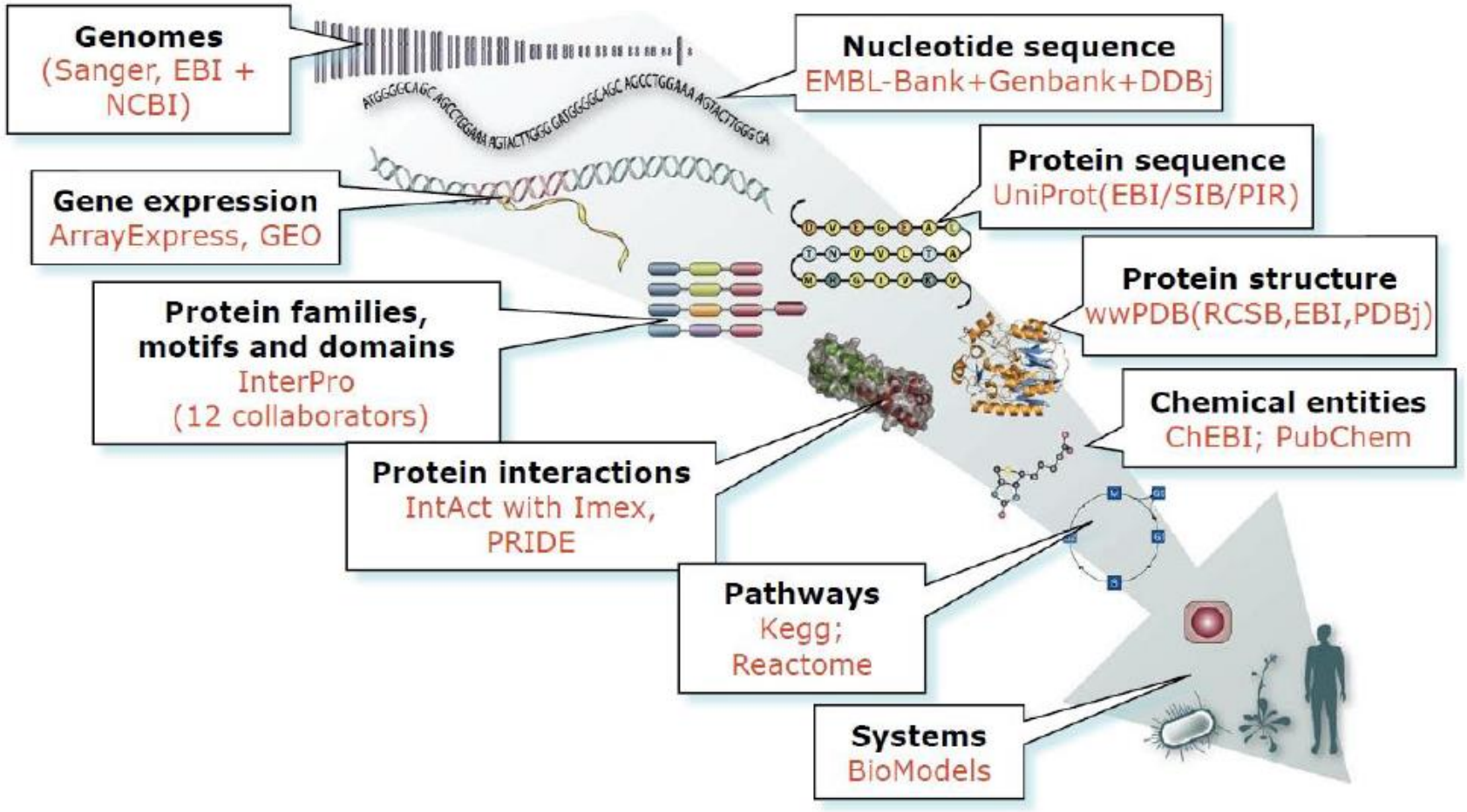
Bioinformatics = the creation of tools (algorithms, databases) that solve problems. The goal is to build useful tools that work on biological data. It is about engineering.

Genetic epidemiology

- Genetic epidemiology is a particular sub-discipline of epidemiology which considers genetic influences on human traits.
- As with any other epidemiologic studies, genetic epidemiology studies aim
  - to assess the public health importance of diseases,
  - to identify the populations at risk,
  - to identify the causes of the disease,
  - and to evaluate potential treatment or prevention strategies based on those findings
- Strategies of analysis include population studies and family studies.
  - Huge challenge is to combine big data repositories from population or family-studies (e.g., genomics, transcriptomics, metagenomics, metabolomics, epigenomics, ….) with clinical and demographic data:

BIOINFORMATICS

Integration with high-throughput omics (data-bases)



(Janet Thornton, EBI)

2 Evolving trends in bioinformatics

Challenges in bioinformatics

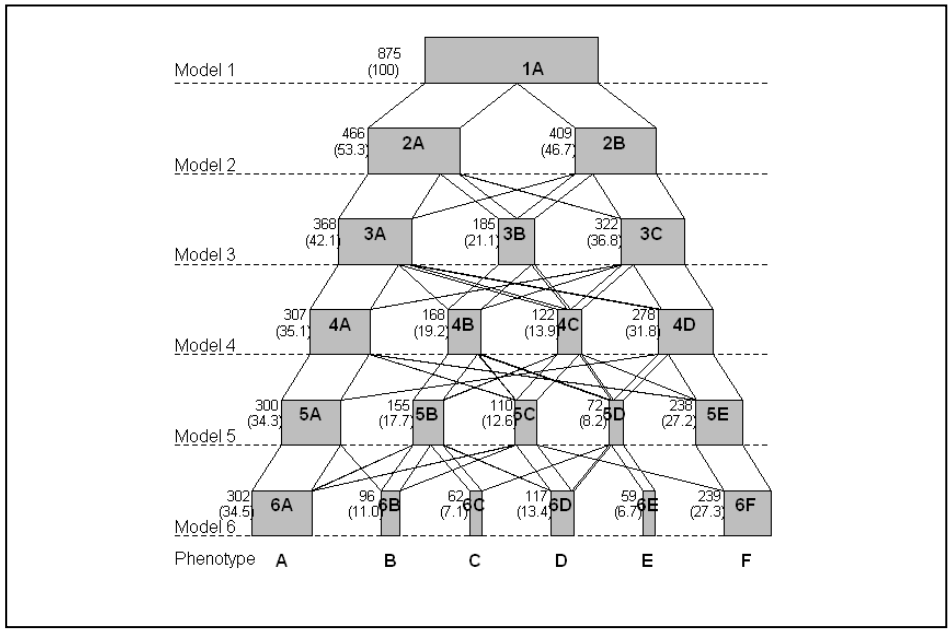
- Data deluge (availability, what to archive and what not?, …)
- Knowledge management (accessibility, usability, …)
- Predicting, not just explaining (what comes first: hypothesis generation, data collection? …)
- Precision medicine (alias: personalized medicine; holistic approach – correlating different causal associations – versus a reductionist approach – targeting very specific biomarkers, negative gold standards … negative controls)
- Speciation (loss in biodiversity, evolutionary units, “integrative taxonomy”: molecular, morphological, ecological and environmental information)
- Inferring the tree of life (unresolved orthology assignment, gene sampling pyramid

Topics in bioinformatics from a journal's perspective

(source: Scope of the journal "Bioinformatics")

Data and Text Mining

This category includes: New methods and tools for extracting biological information from text, databases and other sources of information. Description of tools to organize, distribute and represent this information. New methods for inferring and predicting biological features based on the extracted information. The submission of databases and repositories of annotated text, computational tools and general methodology for the work in this area are encouraged, provided that they have been previously tested.



The journal ….

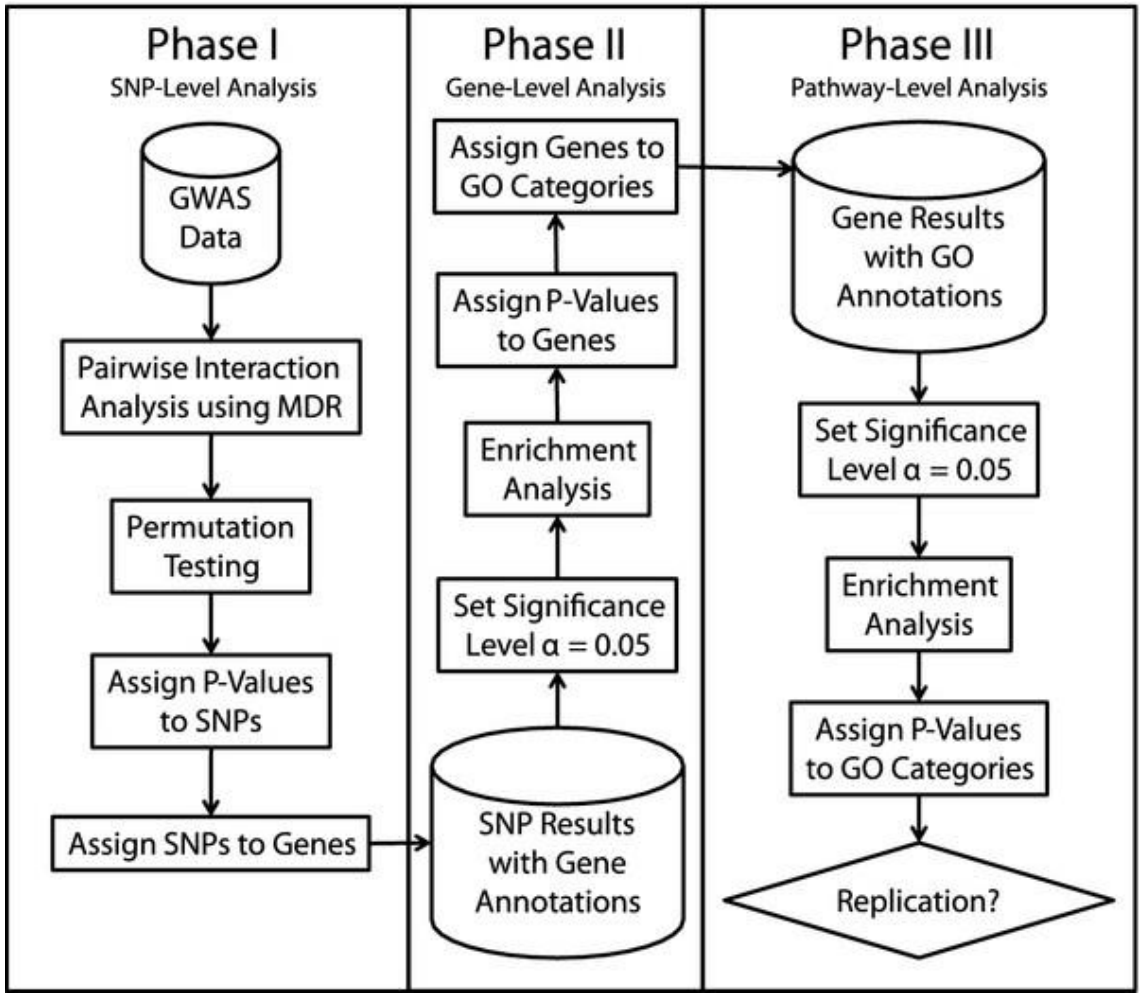
BioData Mining is an open access, peer reviewed, online journal encompassing research on all aspects of data mining applied to high-dimensional biological and biomedical data, focusing on computational aspects of knowledge discovery from large-scale genetic, transcriptomic, genomic, proteomic, and metabolomic data.

Topical areas include, but are not limited to:

- Development, evaluation, and application of novel data mining and machine learning algorithms.
- Adaptation, evaluation, and application of traditional data mining and machine learning algorithms.
- Open-source software for the application of data mining and machine learning algorithms.
- Design, development and integration of databases, software and web services for the storage, management, retrieval, and analysis of data from large scale studies.
- Pre-processing, post-processing, modeling, and interpretation of data mining and machine learning results for biological interpretation and knowledge discovery.

Databases and Ontologies

This category includes: Curated biological databases, data warehouses, eScience, web services, database integration, biologically-relevant ontologies.



(Kim et al. 2012)

Bioimage Informatics

This category includes novel methods for the acquisition, analysis and modeling of images produced by modern microscopy, with an emphasis on the application of innovative computational methods to solve challenging and significant biological problems at the molecular, sub-cellular, cellular, and tissue levels.

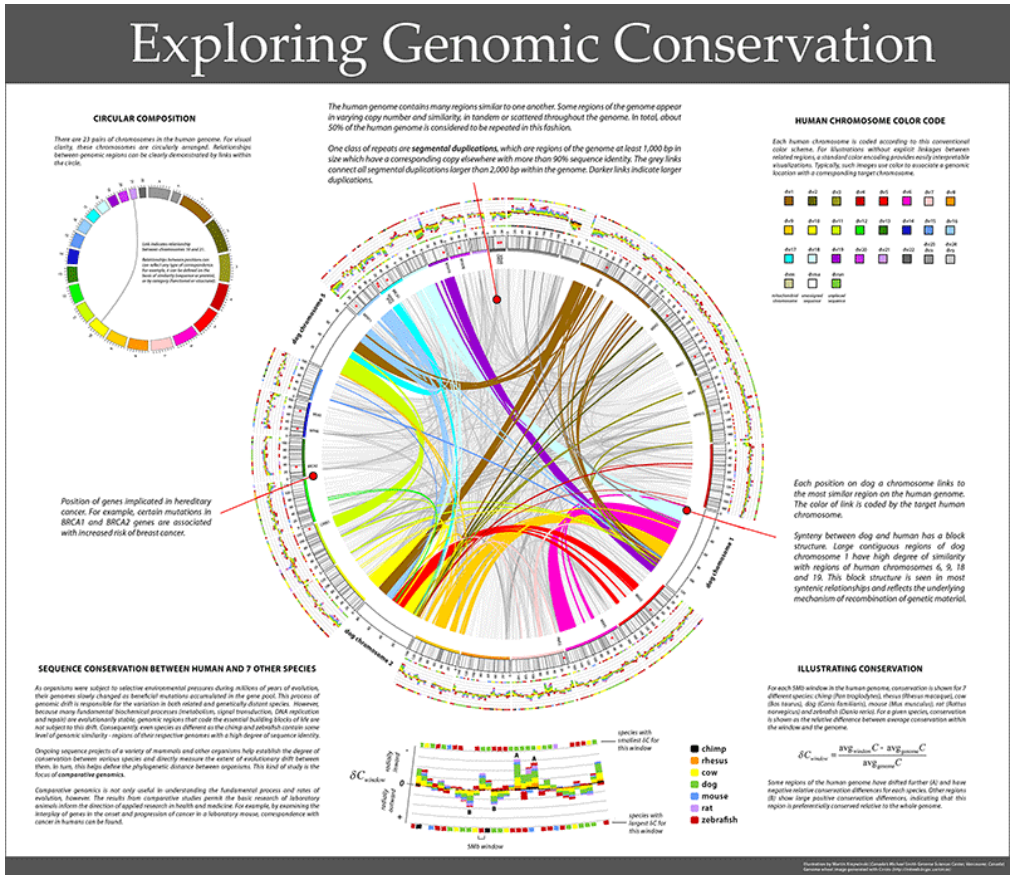
This category also encourages large-scale image informatics methods/applications/software, joint analysis of multiple heterogeneous datasets that include images as a component, and development of bioimage-related ontologies and image retrieval methods.

Genetics and Population Analysis

This category includes: Segregation analysis, linkage analysis, association analysis, map construction, population simulation, haplotyping, linkage disequilibrium, pedigree drawing, marker discovery, power calculation, genotype calling.

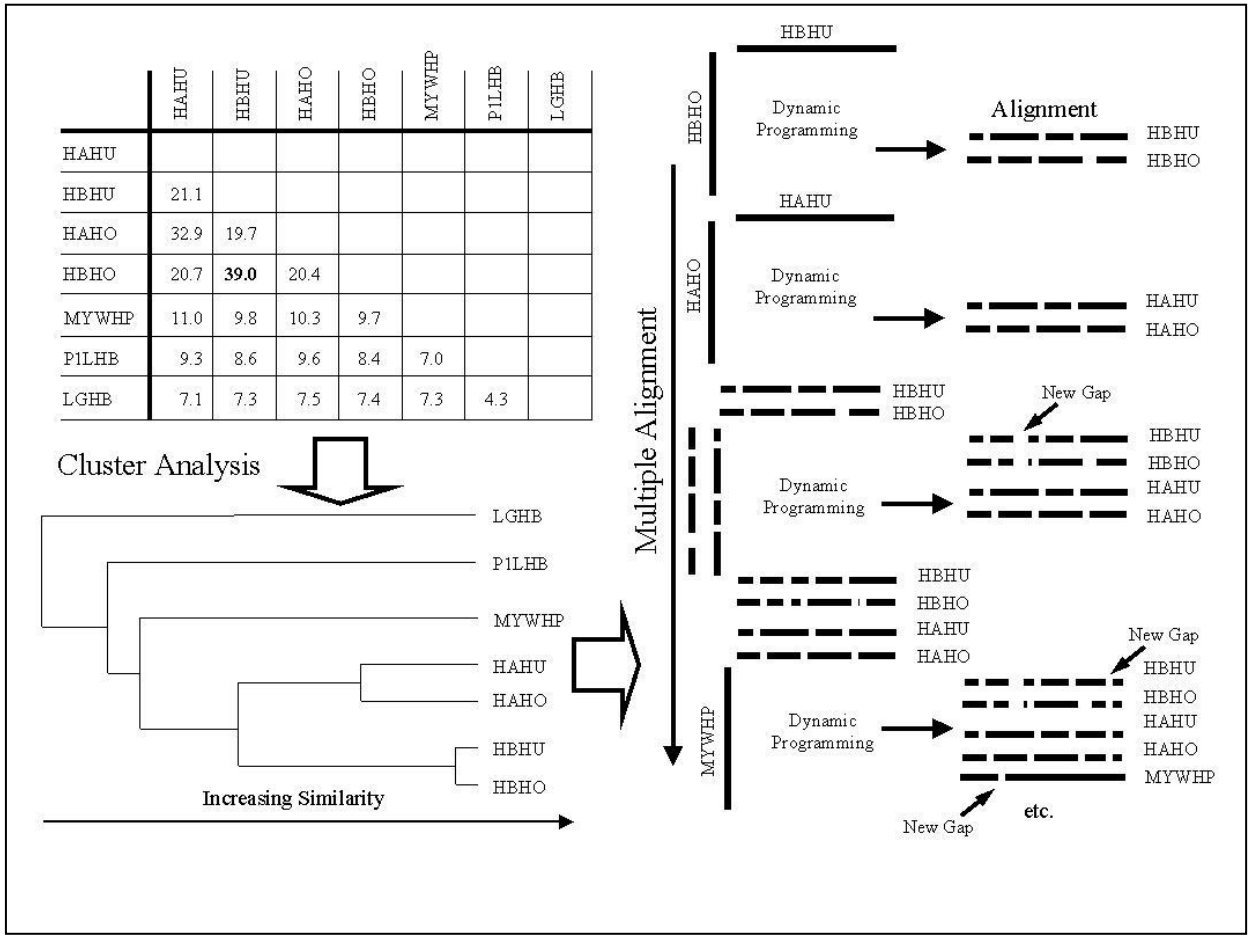
Genome analysis

This category includes: Comparative genomics, genome assembly, genome and chromosome annotation, identification of genomic features such as genes, splice sites and promoters.



Sequence analysis

This category includes: Multiple sequence alignment, sequence searches and clustering; prediction of function and localisation; novel domains and motifs; prediction of protein, RNA and DNA functional sites and other sequence features.

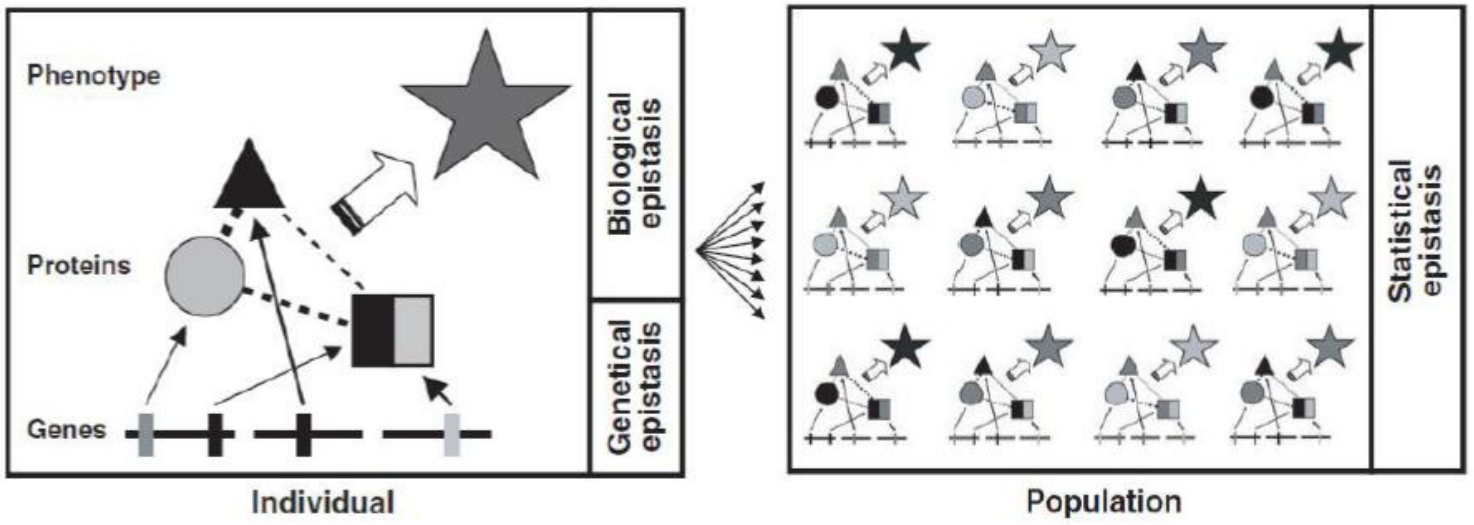


Phylogenetics

This category includes: novel phylogeny estimation procedures for molecular data including nucleotide sequence data, amino acid data, whole genomes, SNPs, etc., simultaneous multiple sequence alignment and phylogeny estimation, phylogenetic approaches for any aspect of molecular sequence analysis (see Sequence Analysis scope), models of molecular evolution, assessments of statistical support of resulting phylogenetic estimates, comparative methods, coalescent theory, approaches for comparing phylogenetic trees, methods for testing and/or mapping character change along a phylogeny.

Gene Expression

This category includes a wide range of applications relevant to the high-throughput analysis of expression of biological quantities, including microarrays (nucleic acid, protein, array CGH, genome tiling, and other arrays), RNA-seq, proteomics and mass spectrometry. Approaches to data analysis to be considered include statistical analysis of differential gene expression; expression-based classifiers; methods to determine or describe regulatory networks; pathway analysis; …



(Moore 2005)

Systems Biology

This category includes whole cell approaches to molecular biology. Any combination of experimentally collected whole cell systems, pathways or signaling cascades on RNA, proteins, genomes or metabolites that advances the understanding of molecular biology or molecular medicine will be considered. Interactions and binding within or between any of the categories will be considered including protein interaction networks, regulatory networks, metabolic and signaling pathways. Detailed analysis of the biological properties of the systems are of particular interest.

A sample of literature-based bioinformatics resources

BioData Mining

Bioinformatics

BMC Bioinformatics

Briefings in Bioinformatics

Genome Biology

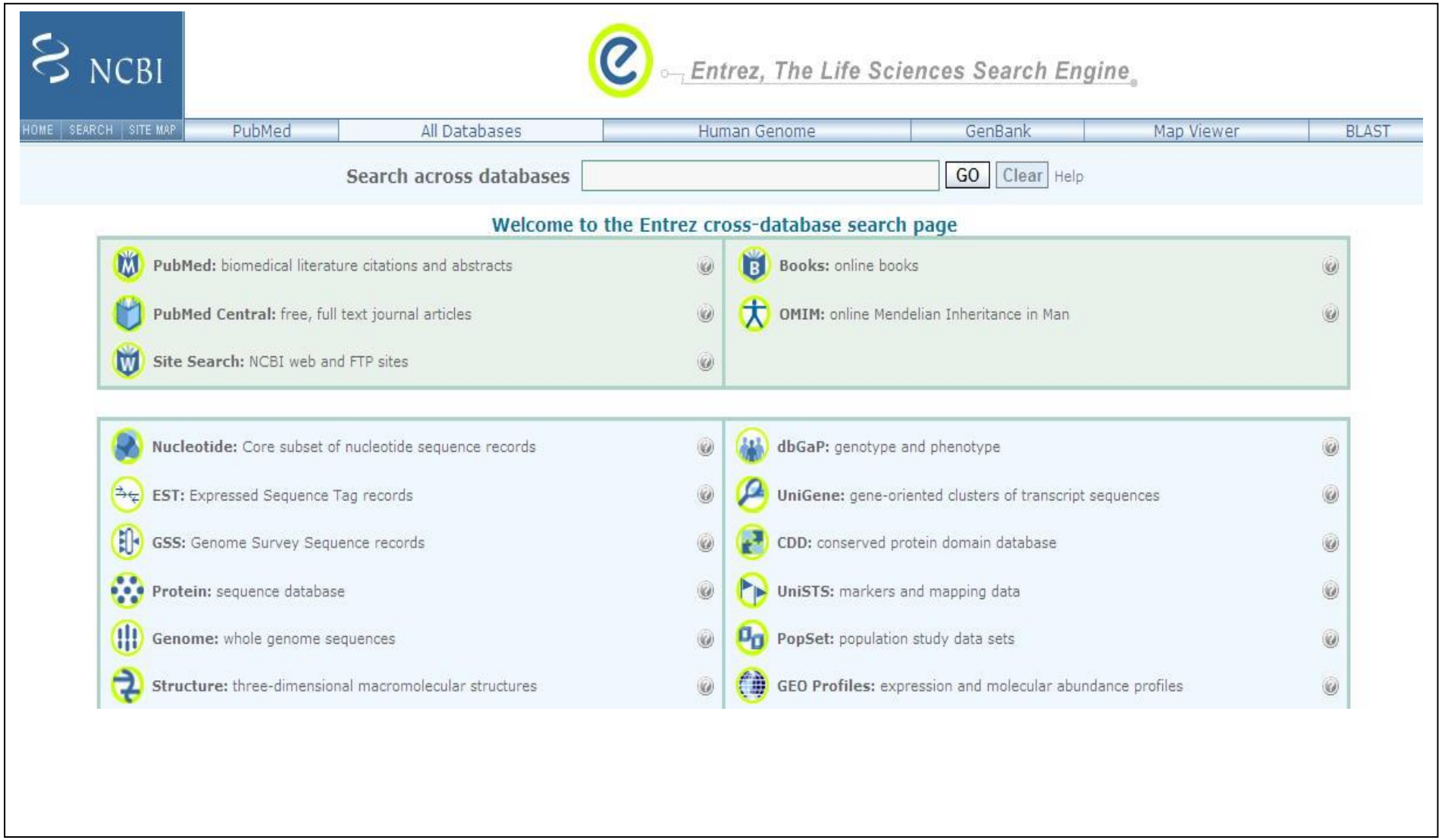
Genome Medicine

Journal of Integrative Bioinformatics

(http://www.bioinformatics.org/wiki/Journals)

3 Bioinformatics software

Data access and analysis – data mining



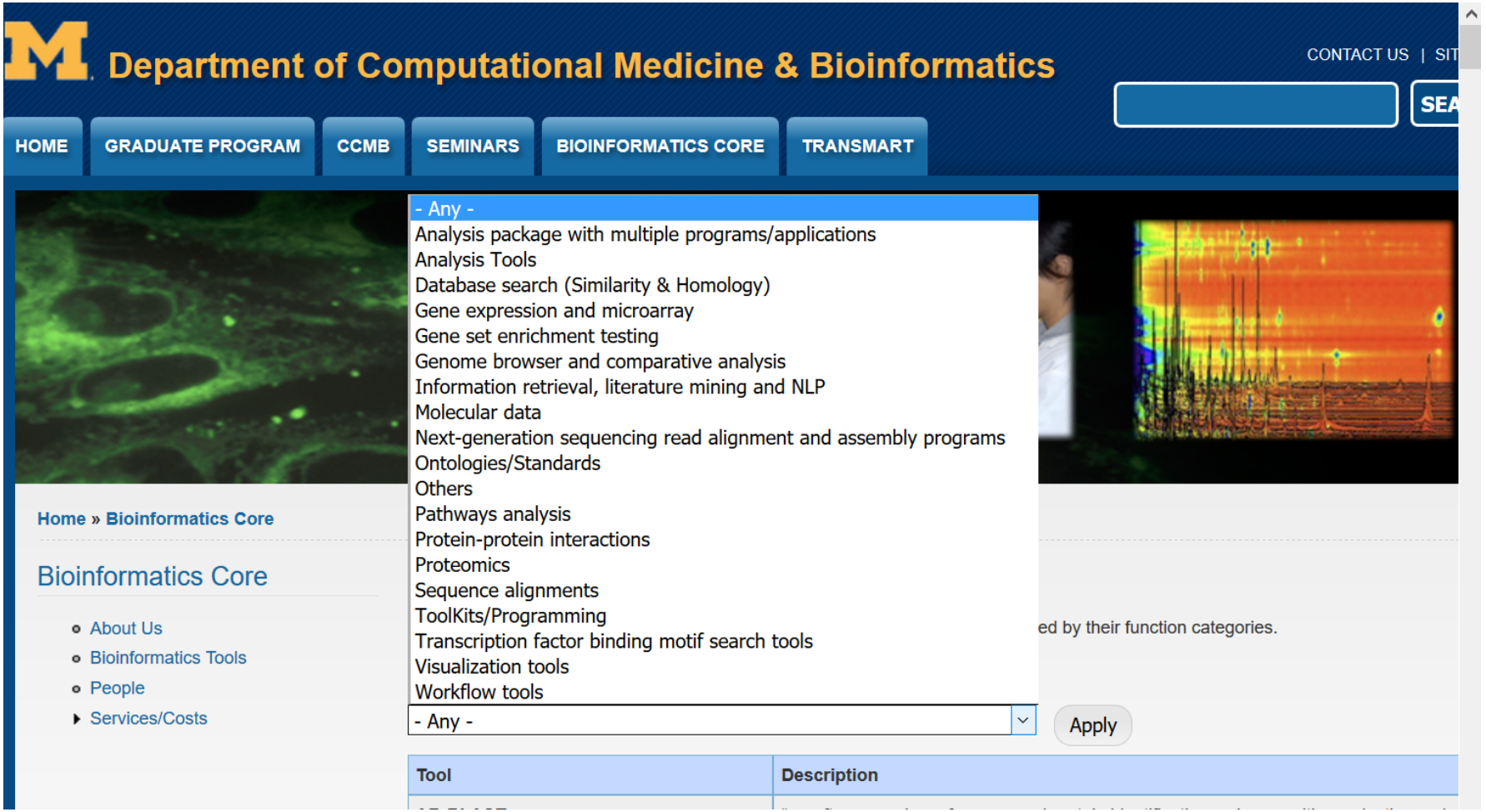
Principal internet resources for genome browsers and databases

Resource	Web address	Description	Sponsoring organizations
Open Helix	http://www.openhelix.com/tutorials.shtml	On-line tutorial material for all of the genome databases.	OpenHelix, LLC
UCSC Genome Browser	http://genome.ucsc.edu	Comprehensive, multi-species genome database providing genome browsing and batch querying.	Genome Bioinformatics Group, University of California, Santa Cruz
Ensembl Browser	http://www.ensembl.org	Comprehensive, multi-species genome database providing genome browsing and batch querying.	European Bioinformatics Institute (EBI) and the Sanger Center
NCBI MapViewer	http://www.ncbi.nlm.nih.gov/mapview	Multi-species genome browser focusing especially on genome mapping applications.	National Center for Biotechnology Information (NCBI)

Biomart	http://www.biomart.org/	Genome-database, batch-querying interface used by Ensembl and several single-genome databases.	Ontario Institute for Cancer Research and European Bioinformatics Institute
Galaxy	http://main.g2.bx.psu.edu	Integrated toolset for analyzing genome batch-querying data.	Center for Comparative Genomics and Bioinformatics. Penn State University
Taverna	http://taverna.sourceforge.net	Toolset for creating pipelines of bioinformatics analyses implemented via the Web services protocol.	Open Middleware Infrastructure Institute, University of Southampton (OMII-UK)
GMOD	http://www.gmod.org	Repository of software tools for developing generic genome databases.	A consortium of organizations operating as the Generic Model Organism Database project

(Schattner et al. 2009)

Bioinformatics tools



(http://www.ccmb.med.umich.edu/bioinf-core/tools)

Bioconductor (TA- sessions)

Method

Open Access

Bioconductor: open software development for computational biology and bioinformatics

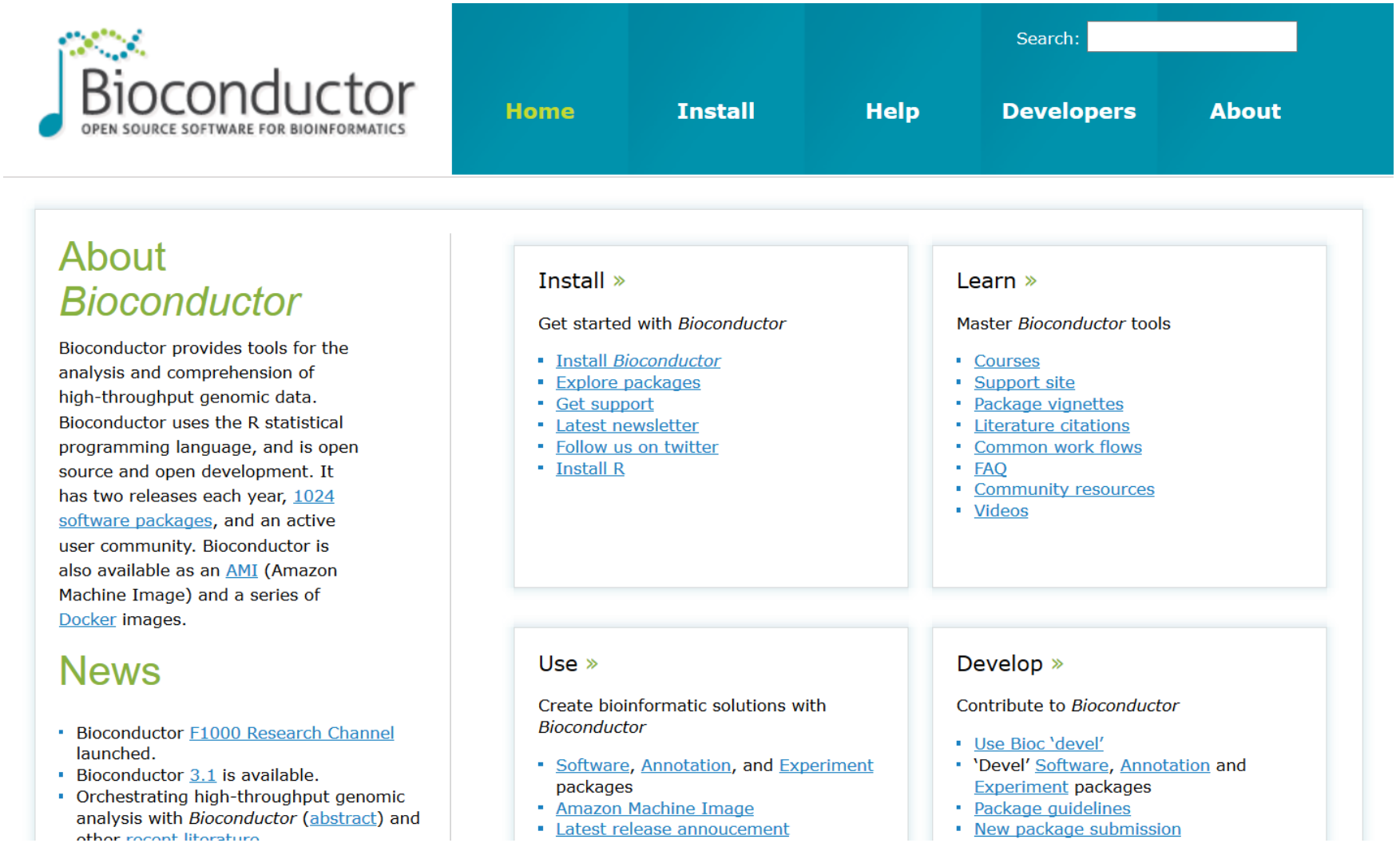
Robert C Gentleman[1], Vincent J Carey[2], Douglas M Bates[3], Ben Bolstad[4], Marcel Dettling[5], Sandrine Dudoit[4], Byron Ellis[6], Laurent Gautier[7], Yongchao Ge[8], Jeff Gentry[1], Kurt Hornik[9], Torsten Hothorn[10], Wolfgang Huber[11], Stefano Iacus[12], Rafael Irizarry[13], Friedrich Leisch[9], Cheng Li[1], Martin Maechler[5], Anthony J Rossini[14], Gunther Sawitzki[15], Colin Smith[16], Gordon Smyth[17], Luke Tierney[18], Jean YH Yang[19] and Jianhua Zhang[1]

Published: 15 September 2004

Genome ***Biology*** 2004, **5**:R80

The electronic version of this article is the complete one and can be found online at http://genomebiology.com/2004/5/10/R80

Received: 19 April 2004
Revised: 1 July 2004
Accepted: 3 August 2004



(http://www.bioconductor.org/)

R (TA- sessions)

- R is a freely available language and environment for statistical computing and graphics which provides a wide variety of statistical and graphical techniques: linear and nonlinear modelling, statistical tests, time series analysis, classification, clustering, etc.
  - Consult the R project homepage for further information.
  - The “R-community” is very responsive in addressing practical questions with the software (but consult the FAQ pages first!)
- CRAN is a network of ftp and web servers around the world that store identical, up-to-date, versions of code and documentation for R.

[Home]

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The R Project for Statistical Computing

Getting Started

R is a free software environment for statistical computing and graphics. It compiles and runs on a wide variety of UNIX platforms, Windows and MacOS. To **download R**, please choose your preferred CRAN mirror.

If you have questions about R like how to download and install the software, or what the license terms are, please read our answers to frequently asked questions before you send an email.

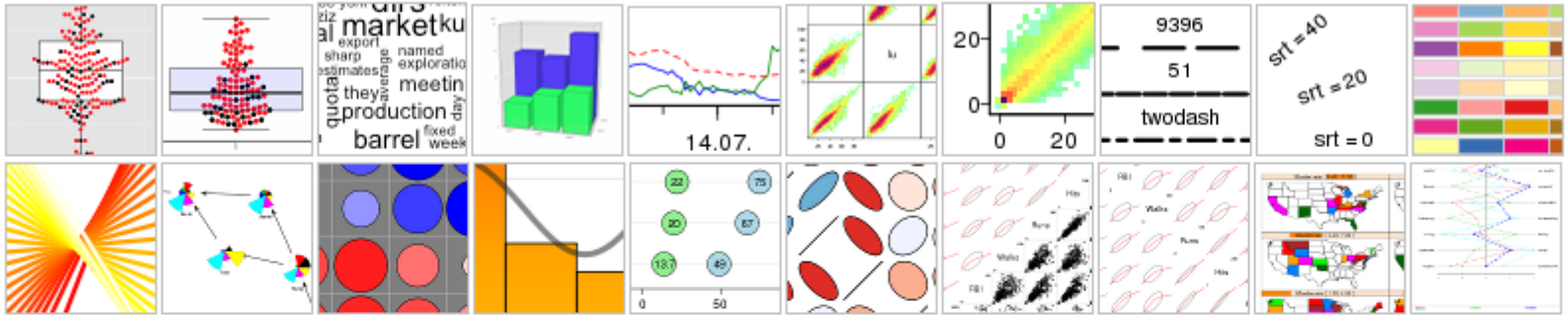
News

- **R version 3.2.2 (Fire Safety)** has been released on 2015-08-14.
- **The R Journal Volume 7/1** is available.
- **R version 3.1.3 (Smooth Sidewalk)** has been released on 2015-03-09.
- **useR! 2015**, will take place at the University of Aalborg, Denmark, June 30 - July 3, 2015.
- **useR! 2014**, took place at the University of California, Los Angeles, USA June 30 - July 3, 2014.

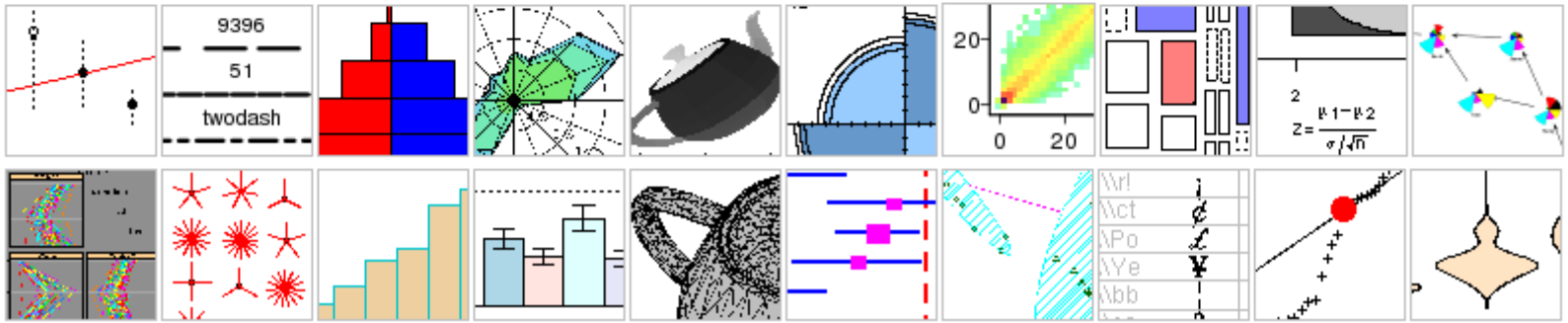
(https://www.r-project.org/)

The R graph gallery

» Last entries ...



» Random entries



- One of R's strengths is the ease with which well-designed publication-quality plots can be produced …